# Severe Hepatitis C Virus Recurrence Is Nearly Universal After Donation After Cardiac Death Liver Transplant

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## Abstract

***Objectives:*** **The rate of hepatitis C virus recurrence after donation after cardiac death liver transplant is not clearly defined.**

***Materials and Methods:*** **This is a retrospective review of 39 donations after cardiac death-liver transplant recipients. Biopsies were performed at 6, 12, 24, and 36 months for all hepatitis C virus positive donation after cardiac death recipients.**

***Results:*** **The 6-, 12-, 24-, and 36-month severe hepatitis C virus recurrence rates were 60%, 73%, 87%, and 94%. A histologic comparison group of 26 long-surviving hepatitis C virus positive donation after neurologic death recipients had severe hepatitis C virus recurrence 27%, 31%, 42%, and 52% of the time. Six of the 19 hepatitis C virus donation after cardiac death patients developed cirrhosis at a median of 56 months (range, 14-119 months). There was no significant 3-year allograft and patient survival difference between hepatitis C virus and nonhepatitis C virus donation after cardiac death recipients. The factors most associated with decreased survival in the entire cohort included biliary and vascular complications. Organs procured by our institution's attending surgeons were associated with a better 3-year allograft survival.**

***Conclusions:*** **Severe hepatitis C virus recurrence was nearly universal but did not lead to increased graft loss when compared with nonhepatitis C virus donation after cardiac death at 3 years. These data may justify early interferon treatment in these at-risk patients.**

**Key words:** *Donation after cardiac death, Liver transplant, Biliary complications, Severe hepatitis C virus recurrence*

Approximately 30% to 50% of transplants are performed for hepatitis C virus cirrhosis.[1, 2] Recurrence occurs at reperfusion.[3] Most patients demonstrate histologic evidence of chronic hepatitis within the first year.[4] Cirrhosis develops in 25% to 30% of patients by 5 years.[5] The combination of older donors and recipients, prolonged cold ischemic time, *cytomegalovirus* infection, rejection, abrupt changes in immunosuppression, nonwhite recipients, female recipients, and posttransplant diabetes are established risk factors.[2, 6-10]

The burden of hepatitis C virus infection has contributed to the increased use of donors after cardiac death.[11] From 2000, donation after cardiac death (DCD) liver transplants have increased 10 fold.[a, 12] Forty-two percent of these DCD transplants were for hepatitis C virus.[b] Initial publications reported acceptable short-term patient and graft survival.[13] However, later reviews demonstrated diminished long-term outcomes and higher rates of biliary[14,15] and hepatic artery complications.[16]

Prolonged rewarming predisposes the liver to severe recurrent hepatitis C virus disease.[17] Donation after cardiac death organs are subject to significant ischemia reperfusion injury by nature of the warm ischemia at the time of donation as well as implant.

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***Acknowledgements:*** *[a]Based on organ procurement and transplant network data as of September 1, 2009. This work was supported in part by Health Resources and Services Administration contract 234-2005-370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.*

*[b]Based on organ procurement and transplant network data as of October 2, 2009. This work was supported in part by Health Resources and Services Administration contract 234-2005-370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.*

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***Experimental and Clinical Transplantation (2011) 2: 105-112***

Nevertheless, the incidence of severe hepatitis C virus recurrence after DCD from liver transplant is unknown. It is also unclear whether severe hepatitis C virus recurrence affects
long-term allograft and patient survival.

We sought to review our donations after cardiac death, and to determine the rate of severe hepatitis C virus recurrence after DCD in liver transplant. As a comparison group, we analyzed 26 hepatitis C virus donors after neurologic death recipients in terms of severe hepatitis C virus recurrence and the development of cirrhosis. We also compared the outcomes of hepatitis C virus and nonhepatitis C virus DCD in liver transplant.

## Materials and Methods

After institutional review board approval, a retrospective review of all donations after cardiac death in liver transplant recipients from 1995 to 2008 was done. Thirty-nine patients were identified (21 hepatitis C virus and 18 nonhepatitis C virus). All 21 hepatitis C virus patients were antibody and polymerase chain reaction positive. We also identified 26 long-surviving donors after neurologic death hepatitis C virus recipients who were transplanted within 1 month (ie, liver transplant date matched) of the DCD recipients to serve as a "histology control arm" for severe hepatitis C virus recurrence.

We collected the following variables for the DCD recipients:

*Donor:* Age, height, weight, sex, race, donor risk index, ischemic times, and pretransplant biopsy.

*Recipient:* Cause of liver disease, age, height, weight, sex, race, model for end-stage liver disease (MELD), length of hospital stay, cytomegalovirus serology, insulin use, recipient aspartate amino - transferase, alanine aminotransferase, and total bilirubin levels at 1, 6, and 12 months after liver transplant, patient and graft survival, causes of deaths, and retransplants.

*Complications:* Hepatic artery thrombosis/ stenosis, portal vein thrombosis, primary non - function, rejections, and biliary complications (ie, bile leak, biliary stenosis, biliary obstruction, and ischemic cholangiopathy), and development of cirrhosis.

For the hepatitis C virus donors after neurologic death recipients, we collected the following variables:

*Donor:* Age, height, weight, sex, race, ischemic times, and pretransplant biopsy.

*Recipient:* Age, height, weight, sex, race, MELD, and development of cirrhosis.

Table 1 shows the definitions of terms used in this study.

Thirty-six donors were classified as Maastricht type 3.[18] The dissection was performed per established techniques.[19] University of Wisconsin solution was always used. A liver biopsy was obtained when necessary.

Recipient operative technique usually included venovenous bypass, with portal reperfusion after either conventional or piggyback hepatectomy. Post - operative immunosuppression usually consisted of prednisone and calcineurin inhibitors. Occasional patients received interleukin-2 blockade (basiliximab and daclizumab), mycophenolate mofetil, or sirolimus. Almost all patients received induction with cortico- steroids that were tapered over 4 to 6 months. Biopsy- proven rejection episodes were treated with corticosteroid boluses, or increased calcineurin inhibitors dosages, or both. Recalcitrant rejection was treated with a monoclonal or polyclonal antibody preparation.

**Table 1.** Definitions of terms used in the current study.

| Term | Definitions |
|---|---|
| HCV recipients | Patients with positive HCV antibody |
| Severe HCV recurrence | HCV recurrence was assessed by protocol liver biopsies. It was defined as grade 2 and/or stage 2 or higher by Batts and Ludwig score |
| Rapid severe HCV recurrence | Grade 2 and/or stage 2 within 12 months |
| Cirrhosis | Stage 4 or any radiologic evidence of cirrhosis |
| Ischemic cholangiopathy | Nonanastomotic biliary strictures in the presence of a patent hepatic artery |
| Primary nonfunction | Allograft loss without hepatic artery thrombosis or PVT |
| New onset posttransplant diabetes | The requirement of insulin or oral hypoglycemic agents after transplant |
| Donor overall warm ischemic time | The time from withdrawal of mechanical ventilation/life support to perfusion with preservation solution* |
| Donor true warm ischemic time | Always a fraction of DOWIT. That time from true loss of perfusion (ie, mean arterial pressure < 50 mm Hg) or oxygenation ($O_2$ saturation < 70%) until infusion of preservation solution* |
| Cold ischemic time | The time from cannulation of the aorta and flushing of the organs until reperfusion in the recipient |
| Recipient warm ischemic time | The time from when the organ was removed from cold storage until reperfusion in the recipient |

***Abbreviations:*** DOWIT, donor overall warm ischemic time; HCV, Hepatitis C virus; PVT, portal vein thrombosis

*Manzarbeitia CY, Ortiz JA, Jeon H, et al. Long-term outcome of controlled, non-heart-beating donor liver transplantation. Transplantation. 2004;78(2):211-215.

Posttransplant biopsies were performed in all hepatitis C virus recipients at 6 months, 12 months, and then yearly, or when clinically indicated. They were classified according to Batts and Ludwig criteria. Patients with grade/stage 2 hepatitis C virus recurrence were considered for interferon and ribavirin based therapy.

**Statistical Analyses**

Categoric variables were compared using the Fisher exact test, and continuous variables were analyzed using the Mann-Whitney *U* test. Statistical analysis of survival and other outcome data were performed using the Kaplan-Meier method, and survival was compared using the log-rank test. A $P$ value of $< .05$ was considered significant. Statistical analyses were performed with SPSS software for Windows (Statistical Product and Service Solutions, version 10.0, SSPS Inc, Chicago, IL, USA).

## Results

Thirty-nine patients underwent a liver transplant using DCD grafts. There were 21 hepatitis C virus and 18 nonhepatitis C virus donations after cardiac death in liver transplant recipients (Table 2). The median follow-up was 43 months (Kaplan-Meier follow-up ranged from 5 to 147 months) for the nonhepatitis C virus group and 53 months (range, 0 to 113 months) for the hepatitis C virus group. There was 1 intraoperative death (hence, zero months follow-up). There were no significant differences for any of the demographics, variables, or outcomes studied between the 2 groups (Table 2). Of the donor after neurologic death hepatitis C virus recipients (the histologic comparison group), the median age was 53 years (range, 24-72 years) with mean body mass index of 28.4 kg/m$^2$. There were 18 males, 22 were white. The mean MELD score was 21 (± 8.8). There were no significant differences in the donor and recipient demographics between the donor after neurologic death and DCD in the hepatitis C virus groups.

The cause of end-stage liver disease in the entire DCD cohort was hepatitis C virus (21/39, 54%), alcoholic cirrhosis (8/39, 20.5%), cryptogenic cirrhosis (5/39, 13%), autoimmune and fulminant hepatic failure (2/39, 5% each), and primary biliary cirrhosis (1/39, 2.5%).

Of the 39 donor grafts, 19 were procured locally (12 hepatitis C virus vs 7 nonhepatitis C virus) and 20 were procured from outside the local area (9 hepatitis C virus vs 11 nonhepatitis C virus). Twenty-eight of the 39 organs were retrieved by our institution's attending surgeons. All donor biopsies showed less than 10% macrosteatosis

Of the 26 donors in the after neurologic death in the hepatitis C virus group, the median donor age was 43 (range, 11-79), with a mean body mass index of 24 kg/m$^2$ (range, ± 4.83 kg/m$^2$). Eleven donors were male and 20 were white. The median warm ischemic time was 56 minutes (range, 21-86 minutes) and the median cold ischemic time was 539 minutes (range, 401-721 minutes).

Immunosuppression regimens varied and are summarized in Table 2. These variables were too small to compare statistically. There were no significant differences in the 1- and 3-year patient and allograft survival between the 2 DCD groups ($P > .05$) (Table 2; Figure 1). In the hepatitis C virus group, 2 patients died within 3 months, and 1 was retransplanted with a donor after neurologic death graft on postoperative day 4. Two nonhepatitis C virus patients were retransplanted at 2 and 8 months. Organs procured by our institution's attending surgeons were associated with a more than 3-year allograft survival ($P = .023$).

Post-liver transplant complications are summarized in Table 3. The rate of complications was comparable between the 2 donations after the cardiac death groups.

There was an association between hepatic artery thrombosis and diminished 1-year allograft and patient survival ($P = .009$; $P = .022$). There were 4 long-term survivors with perioperative hepatic artery thrombosis.

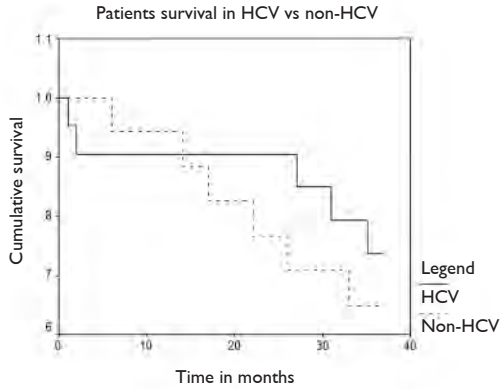


**Figure 1.** Kaplan-Meier plot showing patient survival in hepatitis C virus vs nonhepatitis C virus patients.

**Table 2.** Recipient and donor baseline demographic and clinical information.

| Variables | | | HCV group (n=21) | Non-HCV group (n=18) | *P* value |
|---|---|---|---|---|---|
| **Recipient characteristics** | | | | | |
| Sex, n (%) | | | | | .512 |
| | Male | | 13 (62) | 7 (39) | |
| | Female | | 8 (38) | 11 (61) | |
| Race, n (%) | | | | | .212 |
| | White | | 16 (76) | 17 (94.5) | |
| | Nonwhite | | 5 (24) | 1 (5.5) | |
| | | Black | 4 (19) | 0 | |
| | | Asian | 1 (5) | 1 (5.5) | |
| Age at transplant (y), median (range) | | | 48 (30-64) | 54 (18-63) | .717 |
| BMI (kg/m$^2$), mean (SD) | | | 26.98 (± 4.05) | 26.6 (± 4.46) | .757 |
| MELD, mean (SD) | | | 15.2 (± 6.35) | 18.4 (± 8.35) | .192 |
| Average length of hospital stay (d) | | | 11.43 | 11.83 | .889 |
| Median follow-up (mo) | | | 53 | 43 | |
| RWIT (min), median (range) | | | 60 (39-83) | 65 (39-150) | .486 |
| Pre-LT-CMV + serology, n (%) | | | 12 (57) | 9 (50) | .276 |
| Post-LT day 4 labs, median (range) | | | | | |
| | ALT | | 463 (85-1000) | 328 (78-2840) | |
| | AST | | 138 (40-309) | 73.5 (19-1090) | |
| | Total bilirubin | | 3.6 (.57-7.3) | 3 (0.7-13.9) | |
| **Donor characteristics** | | | | | |
| Sex, n (%) | | | | | .688 |
| | Male | | 13 (62) | 10 (55.5) | |
| Race, n (%) | | | | | .611 |
| | White | | 14 (67) | 13 (72) | |
| | Nonwhite | | 7 (33) | 5 (28) | |
| | | Black | 5 (24) | 5 (28) | |
| | | Asian | 0 | 0 | |
| | | Hispanic | 1 | 0 | |
| | | Other | 1 | 0 | |
| Age (y), median (range) | | | 37 (16-66) | 27.5 (11-62) | .284 |
| BMI (kg/m$^2$), mean (SD) | | | 25.93 (± 4.32) | 25 (± 3.30) | .450 |
| Donor risk index, mean (SD) | | | 1.99 (± .47) | 2.01 (± 0.46) | .893 |
| Ischemic times, median (range) | | | | | |
| | DOWIT (min) | | 19 (9-33) | 23 (9-35) | .448 |
| | DTWIT (min) | | 15 (4-20) | 15 (5-26) | .320 |
| | CIT (min) | | 601(443-805) | 555 (402-774) | .689 |
| **Survival** | | | | | |
| Patient cumulative survival, (%) | | | | | |
| | 1 y | | 90 | 94 | .643 |
| | 3 y | | 74 | 65 | .559 |
| Graft cumulative survival, (%) | | | | | |
| | 1 y | | 86 | 89 | .768 |
| | 3 y | | 69 | 65 | .813 |
| **Immunosuppressive agent, n** | | | | | |
| Tacrolimus immunotherapy | | | 10 | 4 | |
| Received cyclosporine | | | 1 | 5 | |
| MMF | | | 9 | 12 | |
| Sirolimus | | | 2 | 3 | |
| Basiliximab | | | 1 | 1 | |
| Daclizumab and OKT3 | | | 0 | 1 | |
| OKT3 only 0 2 | | | | | |
| **Post-LT complications, n (%)** | | | | | |
| HAT/HAS | | | 4 (19) | 3 (17) | .847 |
| PVT | | | 0 | 0 | |
| PNF | | | 2 (9.5) a | 0 | .746 |
| Rejections | | | 9 (43) | 9 (50) | .656 |
| New onset post-LT diabetes | | | 6 (28.5) b | 4 (22) | .907 |
| Biliary complications | | | 5 (24) | 6 (33) | .510 |
| Concomitant hepatic artery and biliary complications | | | 1 (4.76) | 2 (11.11) | |
| Retransplantations | | | 1 (5) | 2 (11) | |
| Death | | | 8 (38) | 8 (44) | |
| Graft failure/sepsis | | | 6 | 6 | |
| Metastatic HCC | | | 1 | 0 | |
| PNF | | | 1 | 0 | |
| Cardiovascular disease | | | 0 | 2 | |

***Abbreviations:*** BMI, body mass index; CIT, cold ischemia time; DOWIT, donor overall warm ischemia time; DTWIT, donor true warm ischemia time; HAT/HAS, hepatic artery thrombosis/hepatic artery stenosis; HCC, hepatocellular carcinoma; HCV, Hepatitis C virus; LT, liver transplant; MMF, mycophenolate mofetil; PNF, primary nonfunction; PVT, portal vein thrombosis; RWIT, recipient warm ischemia time; SD, standard deviation

[a] Two patients in the HCV group developed PNF. Among those 2, one patient was retransplanted with a DND graft and is still alive. The other patient died the same day due to PNF.

[b] Among the HCV group, 23.8% (5) were started on daily insulin and 1 patient was started on an oral hypoglycemic agent.

**Table 3.** DCD and DND demographic information.

| Variables | DCD HCV+ group (n=21) | DND HCV+ group (n=26) |
|---|---|---|
| **Recipient characteristics** | | |
| Sex, n (%) | | |
| Male | 13 (62) | 18 (69.23) |
| Female | 8 (38) | 8 (30.76) |
| Race, n (%) | | |
| White | 16 (76) | 22 (84.61) |
| Nonwhite | 5 (24) | 4 (15.38) |
| Black | 4 (19) | 3 (11.53) |
| Asian | 1 (5) | 0 |
| Hispanic | 0 | 1 (3.84) |
| Age at transplant, (y) | | |
| median (range) | 48 (30-64) | 52.82 (24.37-72.12) |
| BMI (kg/m$^2$), mean (SD) | 26.98 (± 4.05) | 27.62 (4.64) |
| MELD, mean (SD) | 15.2 (± 6.35) | 21.04 (± 8.83) |
| RWIT (min), median (range) | 60 (39-83) | 56 (21-86) |
| CIT (min), median (range) | 601(443-805) | 539 (401-721) |
| **Donor characteristics** | | |
| Sex, n (%) | | |
| Male | 13 (62) | 11 (42.30) |
| Race, n (%) | | |
| White | 14 (67) | 20 (76.92) |
| Nonwhite | 7 (33) | 6 (23.07) |
| Black | 5 (24) | 6 (23.07) |
| Asian | 0 | 0 |
| Hispanic | 1 | 0 |
| Other | 1 | 0 |
| Age (y), median (range) | 37 (16-66) | 43 (11-68) |
| BMI (kg/m$^2$), mean (SD) | 25.93 (± 4.32) | 23.41 (± 4.83) |
| **Post-LT complications, n (%)** | | |
| HAT/HAS | 4 (19) | 3 (11.53) |
| PVT | 0 | 0 |
| Biliary complications | 5 (24) | 5 (19.23) |
| Concomitant hepatic artery and biliary complications | 1 (4.76) | 0 |
| Retransplantations | 1 (5) | 2 (7.69) |
| Death | 8 (38) | 14 (53.84) |

***Abbreviations:*** BMI, body mass index; CIT, cold ischemia time; HAT/HAS,hepatic artery thrombosis/hepatic artery stenosis; HCV, Hepatitis C virus; LT, liver transplant; MELD, model for end-stage liver disease; PVT, portal vein thrombosis; RWIT, recipient warm ischemia time; SD, standard deviation

There were no significant differences in the severity of biliary complications between the hepatitis C virus and nonhepatitis C virus groups ($P > .05$). Patients with biliary complications had mean allograft and patient survival of 24 months (± 20.3 months) and 30 months (± 19 months). Those patients who did not have biliary complications had allograft and patient survival of 64.6 months (± 43 months) vs 68 (± 42 months) ($P < .05$) (Figure 2). Higher donor body mass index was associated with biliary complications (mean body mass index 28 [± 4.4] vs 24 [± 3.2]; $P = .010$). Organs procured regionally had more biliary complications than those procured locally (45% vs 10.5%; $P = .017$). There was an association between ischemic cholangiopathy and diminished 3-year patient survival ($P = .046$).

Eight patients died in both the DCD groups (38% vs 44%). In the hepatitis C virus group, 6 patients

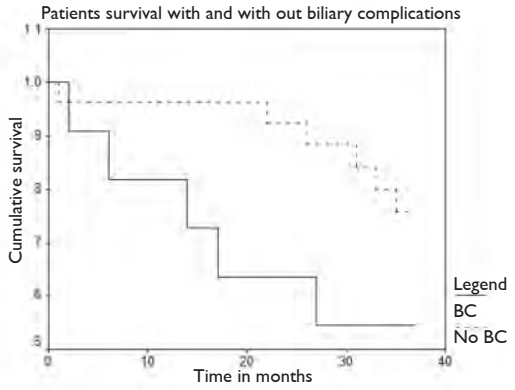


**Figure 2.** Kaplan-Meier plot showing patient survival in patients with and without biliary complications.

died of graft failure/sepsis, 1 died because of metastatic hepatocellular carcinoma, and 1 died of primary nonfunction. In the nonhepatitis C virus group, 6 patients died of graft failure/sepsis. Of these, 1 patient also had ischemic cholangiopathy. Two patients died of cardiac disease. Among the DCD hepatitis C virus recipients, 44 liver biopsy specimens were evaluated from 18 allografts (excluding 2 patients who died within 3 months and 1 who never underwent a biopsy). Overall, the 6-, 12-, 24-, and 36-month hepatitis C virus recurrence rates were 60% (9/15), 73% (11/15), 87% (14/16), and 94% (15/16). One patient did not have hepatitis C virus recurrence after 48 months.

Among the donor after neurologic death hepatitis C virus histologic comparison group (all long-term survivors), the 6-, 12-, 24-, and 36-month hepatitis C virus recurrence rates were 27% (7/26), 31% (8/26), 42% (11/26), and 52% (14/26). A higher rate of early 6- and 12-month hepatitis C virus recurrence rates was noted in the DCD group compared with the donor after the neurologic death group.

Six of the 19 hepatitis C virus patients (31.6%) (excluding 2 primary nonfunction) developed cirrhosis at a median of 56 months (range, 14-119 months). Four of the 6 patients with cirrhosis died at a median of 10.5 months (range, 2-41 months) after diagnosis. In the donor after neurologic death histologic comparison group, 15% of the patients (4/26) developed cirrhosis at a median of 51 months (range, 12-142 months).

Nine patients in each DCD group had at least 1 bout of acute cellular rejection. Acute cellular rejection was not associated with diminished patient, allograft survival, or rapid and severe hepatitis C virus recurrence. On univariate analysis, neither

acute cellular rejection nor rapid and severe hepatitis C virus recurrence demonstrated any associations with any of the studied variables. In the donor after neurologic death cohort, 1 patient had acute cellular rejection. Because of the low number, an analysis was not performed.

Of 21 donations after cardiac death hepatitis C virus patients, 7 (33.3%) were treated with interferon alpha 2a and ribavirin. Seventy-one percent (5/7) achieved a sustained virologic response. In the donor after neurologic death cohort, 1 patient was treated with interferon alone, and 2 patients were treated with interferon and ribavirin. Of these 3 patients, the first developed cirrhosis 86 months after the liver transplant but did have a sustained virologic response. The second patient had severe hepatitis C virus recurrence at 6 months but could not tolerate treatment. He died secondary to sepsis 16 months after his liver transplant. The third patient developed severe hepatitis C virus recurrence at 6 months and cirrhosis at 12 months. He received treatment for 1 month and died 1 year after his liver transplant secondary to decompensated liver disease

## Discussion

The demand for donor organs continues to outpace supply.[16] Statistical analyses suggest that DCD in liver transplant is beneficial for patients whose MELD score is higher than 24.[20] In properly selected donors and recipients, 1- and 3-year patient and graft survivals between DCD and donor after neurologic death are similar.[21] The results of our study also indicate a survival rate comparable to established norms.

Recent reviews indicate that ischemic cholangiopathy, which does not always lead to graft loss, may be an underappreciated source of major morbidity.[14, 15] Older donor age, cold ischemic time, perfusion solutions, and location of organs procured are some of the established risk factors.[22, 23] In our study, a total of 10% of the donations (4/39) after cardiac death recipients developed ischemic cholangiopathy. There were no variables associated with higher incidence of ischemic cholangiopathy, per se, but higher donor body mass index and donor location were associated with biliary complications (including ischemic cholangiopathy). Higher donor body mass index may be associated with larger livers and impaired infusion of preservation fluid. In our cohort, the rate of biliary complications was 28%. When present, they were multiple, severe, and associated with a higher rate of allograft loss and patient death. Ischemic times were not a factor. Procurements performed by the attending staff from our transplant center were associated with a lower rate of graft loss.

Despite the fact that severe hepatitis C virus recurrence was nearly universal at 3 years, it did not negatively affect patient survival when compared with the nonhepatitis C virus group. This may be a reflection of our relatively short follow-up. Graft losses were due to primary nonfunction, ischemic cholangiopathy, hepatic artery thrombosis, and patient death. The most important variables associated with allograft loss were biliary complications.

Forty-two percent of the donations after cardiac death transplants performed since 2000 were for hepatitis C virus.[2] Preservation and reperfusion injury of the liver is associated with hepatocyte death followed by rapid proliferation and an inflammatory response. In the setting of DCD and 2 bouts of ischemia, hepatitis C virus infiltration may be facilitated.[24, 25]

According to organ procurement and transplant network data,[b] hepatitis C virus positive DCD recipients demonstrated 1- and 3-year patient survival of 84 and 75%. Hepatitis C virus negative DCD recipients showed 1- and 3-year patient survival rates of 84 and 76%. One and 3-year allograft survival rates for hepatitis C virus positive DCD recipients were 74 and 63%, while 1- and 3-year graft survival rates for hepatitis C virus negative DCD recipients were 75 and 64%. Others have found similar results.[16, 26-30]

The incidence of severe hepatitis C virus recurrence, without graft loss, has not been extensively evaluated. In our study, almost 75% of the patients had severe hepatitis C virus recurrence by 12 months. However, this did not lead to a high rate of graft loss. There were no identifiable variables associated with severe hepatitis C virus recurrence. The hepatitis C virus recurrence rates in our DCD cohort were higher than in our donor after neurologic death histologic comparison group. Our donor after neurologic death histologic group was composed of long-term survivors with evaluable biopsy data. Therefore, complications, patient death, and graft loss in this group are not germane.

The Gainesville group[31] reported that for all hepatitis C virus positive donors after neurologic death in liver transplant recipients, the risk of

developing cirrhosis was 18% at 3.7 years. The probability of decompensation within 1 year of diagnosis was 30%. The 1-year survival of these decompensated posttransplant cirrhotics was 46%. European groups[32] have stated that cirrhosis occurs in 25% of recipients within a median of 5 years with a 42% cumulative probability of decompensation at 1 year. In our study, 31% of the DCD hepatitis C virus patients developed cirrhosis at 4.6 years. Sixty-six percent of these patients died at a median of 10.5 months. In our donor after neurologic death, long-term survivor comparison group, the rate of cirrhosis was 15%. The median time until cirrhosis development was 51 months. When we compared the rate of cirrhosis between the DCD and donor after neurologic death groups, the former exhibited a higher rate, but this did not reach statistical significance.

We present one of the largest single-center experiences with DCD liver transplant. This is also the only report that specifically addresses severe hepatitis C virus recurrence. Hepatitis C virus recurrence leading to death is captured in the UNOS database; histologic recurrence, in and of itself, is not. Although these patients were transplanted over a long period, their immunosuppressive regimens were relatively uniform. There is no indication in the literature that tacrolimus (our immunosuppressant of choice) is associated with a higher rate of hepatitis C virus recurrence. Similarly, our average duration of steroids (range, 4-6 months) reflects the knowledge that rapid or abrupt cessation of steroids may precipitate severe recurrence.[33] We maintained a relatively strict biopsy protocol. Patients were only treated when stage and or grade 2 recurrence was identified. Therefore, pre-emptive treatment did not affect the identification of severe recurrence. If there are era effects, they may have played a role in the rate of death, but the natural course of disease (up to stage or grade 2) was not manipulated.

Limitations of this study include its retrospective nature and small patient numbers and the possibility of selection bias. Generally, DCD organs were reserved for recipients who were deemed stable enough to withstand significant reperfusion injuries as reflected in their relatively low MELD scores. Many of these transplants were performed before the MELD era. Our donors after neurologic death with severe hepatitis C virus recurrence was only evaluated for severe hepatitis C virus recurrence, cirrhosis, and demographic variables. We could not capture the use of antifibrotic agents in any group.[34] We could not examine the effects of antiviral therapy. Successful treatment with interferon may be associated with histologic improvement, including stabilization of, or even a decrease, in fibrosis.[35] The numbers are too small with the various immunosuppression regimens to show any statistical relevance. Our database was not equipped to capture hepatitis C viral polymerase chain reaction calculations and exact rejection treatments. The lack of long-term follow-up may not have allowed recurrent hepatitis C virus to manifest as a cause of death. This may also hold true for malignancy.[36, 37]

In conclusion, severe hepatitis C virus recurrence was nearly universal but did not lead to increased graft loss at 3 years. Rapid severe recurrence does not predict early graft loss or patient death. When compared to date-matched donors after neurologic death hepatitis C virus recipients, the rate of severe hepatitis C virus recurrence was significantly higher in the DCD group. Studies are needed to define the effect of these complications on long-term survival, quality of life, and cost of care.

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