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Increasing Trends in Transplantation of Hepatitis C Virus–Positive Livers Into Uninfected Recipients

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The introduction of direct-acting antiviral (DAA) agents and the opioid epidemic have resulted in an increased interest in liver transplantation (LT) of organs from donors with hepatitis C virus (HCV)-related viremia.[1] In March of 2015, the Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) implemented a policy to perform HCV nucleic acid testing (NAT) in all HCV-seropositive donors. An open-label, single-center experience with 10 patients using a multistep informed consent reported successful transplantation of HCV-seropositive viremic (HCV-V) kidneys into HCV-seronegative recipients.[2] Subsequently, a case was reported in which an HCV-V liver was transplanted into a HCV-seronegative recipient.[3] In collaboration with OPTN/UNOS, we identified cases in which HCV-V deceased donor livers were transplanted into HCV-seronegative recipients.

Methods

By using the OPTN/UNOS database, we analyzed utilization trends in HCV-V and HCV-seropositive nonviremic (HCV-NV) liver donors from March 1, 2015, the earliest date that HCV NAT was implemented by OPTN/UNOS, to September 30, 2017. Donor HCV NAT was performed at the time of organ procurement. Kaplan–Meir survival analyses were performed to compare 1-year post-transplant patient and graft survival rates in HCV-

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Conflicts of interest

The authors disclose no conflicts.

seropositive (with and without viremia) and HCV-seronegative donor livers used for LT from March 1, 2015, to September 30, 2017. Demographics and clinical characteristics were compared among HCV-V and HCV-NV donor livers. Chi-square and Mann–Whitney *U* tests were used for comparisons between cohorts. Statistical significance was reached with a *P* value less than .05.

Results

From March 1, 2015, to September 30, 2017, HCV-seropositive donor livers constituted 7.0% (n = 1115) of all liver transplant surgeries in the United States. Among these HCV-seropositive livers, nearly two-thirds (n = 719; 65.1%) were HCV-V at the time of organ procurement with a positive NAT. A large proportion of HCV-V donors were used in UNOS regions 2 and 5 (n = 221; 30.74%), UNOS regions associated with the longest wait time to LT. Overall, there were 30 HCV-V livers that were transplanted into HCV-seronegative recipients (Table 1), with the majority occurring in 2017 (n = 22; 73.3%).

Drug overdose deaths accounted for more than half of all HCV-V deceased donor livers, a significantly higher proportion compared with all other deceased donor livers. Although HCV-V livers had a higher risk for disease transmission than HCV-seropositive NV and HCV-seronegative livers, the donors of HCV-V livers were younger in age with a lower liver donor risk index or risk for graft failure (Table 1). Furthermore, limited 1-year post-transplant recipient survival was comparable (HCV-V liver transplanted into HCV-seronegative recipient, 92.2%; HCV-NV liver transplanted into HCV-seronegative recipient, 91.9%; $P = .83$).

Compared with HCV-seronegative livers, HCV-seropositive livers suffered a significantly higher discard rate (HCV seropositive, 30.7%; HCV seronegative, 13.8%; $P < .001$). Among HCV-NV livers there was a sharp annual decrease in the discard rate from 31.2% in 2016 to 24.8% in 2017. In contrast, annual discard rates for HCV-V livers with NAT positivity continued to remain higher than 30% without any discernible decrease.

Discussion

In recent years, there has been increasing interest in using HCV-V deceased donor livers.[4] We observed an increase in the use of HCV-V livers in the United States in 2017, with an upward trend in transplantation of HCV-V livers into HCV-seronegative recipients. Because of the availability of efficacious and tolerable DAA agents in the post-transplant setting accompanied by the increase in drug overdose–related deaths resulting in an unprecedented surge in the number of young, otherwise healthy deceased donors with HCV-V livers and a favorable liver donor risk index, the utilization rate of HCV-V livers in HCV-seronegative recipients is steadily increasing.[5] Although HCV-NV livers now are being discarded at lower rates, discard rates have not changed appreciably for HCV-V livers.

The limitations of our report include the inability to determine details of DAA use, characteristics of discarded donors, viremia in recipients, and the possibility of post-transplant HCV transmission observed with used HCV-NV donors, particularly among donors who died as a result of drug overdose.[6] With the option to use DAA-based therapy

immediately after LT, HCV infection can be treated pre-emptively without significant hepatic dysfunction.[7] In addition, donor liver biopsies at the time of organ procurement can help evaluate for underlying liver fibrosis and steatosis, which can aid in the decision to use these procured donor livers. The timing and cost of DAA therapy, insurance authorization process, and donor and recipient selection remain undefined. Therefore, it is recommended that informed consent be obtained, and DAA therapy approval authorized by insurance or to conduct treatment in the context of a clinical trial.

Abbreviations used in this paper:

DAA	direct-acting antiviral
HCV	hepatitis C virus
HCV-NV	hepatitis C virus–seropositive nonviremic
HCV-V	hepatitis C virus–seropositive viremic
LT	liver transplantation
NAT	nucleic acid test
OPTN/UNOS	Organ Procurement and Transplantation Network/United Network for Organ Sharing

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Table 1.

Comparison of Characteristics and Outcomes in HCV-Infected, Seropositive, Nonviremic and Seronegative Donors Used for Liver Transplantation

	HCV infected (NAT positive) N = 719	HCV Nonviremic (NAT negative) N = 386	HCV Seronegative N = 14,661	*P* value
Median donor age, *y* (interquartile range)	33 (28–44)	39 (30–52)	41 (27–55)	<.001
Donor sex, n (%)				
Male	469 (65.23)	194 (50.26)	8827 (60.2)	<.001
Donor ethnicity, n (%)				
White	581 (80.81)	315 (81.60)	9309 (63.49)	<.001
Black	76 (10.57)	36 (9.32)	2706 (18.46)	
Hispanic	45 (6.26)	31 (8.03)	1925 (13.13)	
Median LDRI (interquartile range)[a]	1.21 (1.07–1.46)	1.32 (1.13–1.62)	1.38 (1.14–1.68)	<.001
PHS/CDC increased risk, n (%)[b]	589 (81.92)	279 (72.28)	3273 (22.32)	<.001
Median CIT, *h* (interquartile range)	5.83 (4.57–7.22)	5.75 (4.50–7.36)	5.80 (4.55–7.24)	.76
Donor cause of death, n (%)				
Drug intoxication	377 (52.43)	181 (46.89)	1521 (10.37)	<.001
Cardiovascular	76 (10.57)	67 (17.36)	2504 (17.08)	
Other	266 (37.00)	138 (35.75)	10,616 (72.41)	
Median recipient age, y (interquartile range)	60 (55–64)	60 (55–63)	58 (50–64)	<.001
Recipient sex, n (%)				
Male	565 (78.6)	278 (72)	9613 (65.7)	<.001
Recipient ethnicity, n (%)				
White	522 (72.60)	270 (69.95)	10,501 (71.63)	<.001
Black	92 (12.80)	59 (15.29)	1196 (8.16)	
Hispanic	85 (11.82)	41 (10.62)	2076 (14.16)	
Median MELD score at transplant (interquartile range)	17 [11–22]	17 [12–23]	22 [14–32]	<.001
HCV-seronegative recipient, n (%)	30 (4.17)	39 (10.99)	-	<.001
One-year patient survival rates, % (95% Cl)	92.15 (90.09–93.80)		91.73 (91.22–92.22)	.36
One-year graft survival rates, % (95% Cl)	91.73 (89.63–93.42)		89.67 (89.11–90.20)	.011
One-year patient survival rates, *%* (95% Cl)	92.18 (89.55–94.16)	91.88 (88.00–94.55)	-	.83
One-year graft survival rates, % (95% Cl)	92.04 (89.41–94.040)	90.86 (86.82–93.71)	-	.54

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CIT, cold ischemia time; MELD, model for end-stage liver disease; PHS/CDC Public Health Service/Centers for Disease Control and Prevention.

[a] Liver donor risk index (LDRI) score is a quantitative assessment of the risk of donor liver graft failure based on donor age, ethnicity, height, cause of death split or partial graft, cold ischemia time, and location of Organ.organs based on donor service area. The LDRI score was provided by the United Network for Organ Sharing.

[b] Public Health Service/Center for Disease Control high-risk donor for HCV, human immunodeficiency virus, and hepatitis B virus infection.