Trends in the use of hepatitis C viremic donor hearts

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ABSTRACT

Objective: To examine trends in utilization of hearts from hepatitis C virus (HCV) viremic donors for transplantation, a strategy to expand organ availability.

Methods: The United Network for Organ Sharing (UNOS) registry was queried for adult patients undergoing heart transplantation between 2015 and 2019. We excluded multiorgan transplants, incomplete data, and loss to follow-up. Nucleic acid testing (NAT) defined HCV status.

Results: Between 2015 and 2019, a total of 11,393 adults underwent heart transplantation: 326 from HCV NAT⁺ donors and 11,067 from NAT⁻ donors. The use of NAT⁺ hearts increased from 1 in 2015 to 137 in 2018 against a static number of NAT⁻ organs. The use of NAT⁺ hearts varied significantly across regions and individual centers. More than 75% of NAT⁺ hearts were transplanted in the Northeast region, leading to further travel (mean, 299 miles vs 173 miles for NAT⁻ transplantations; $P < .001$), with longer ischemic times (mean: 3.52 hours vs 3.10 hours; $P < .001$). More than one-half of NAT⁺ transplantations were performed by 5 individual centers, and a single institution accounted for >20% of all transplantations from viremic donors. Survival in the 2 groups did not differ by Kaplan-Meier analysis ($P = .240$), and multivariable regression showed no differences in acute rejection ($P = .455$) or 30-day mortality ($P = .490$). Of the 326 recipients of NAT⁺ hearts, 38 seroconverted and 14 became viremic within 1 year. Survival was 100% in the viremic patients and 97.4% in seroconverted patients at 1 year.

Conclusions: Heart transplantation from HCV viremic donors continues to increase but varies significantly across UNOS regions and individual centers. Short-term outcomes are comparable, but effects of seroconversion and long-term outcomes remain unclear. (J Thorac Cardiovasc Surg 2022;163:1873-85)

Regional variation in acceptance of hearts from HCV viremic donors.

CENTRAL MESSAGE

Hepatitis C virus viremic hearts are an underutilized resource in heart transplantation, with significant variation across regions and individual centers.

PERSPECTIVE

Donor availability is the principal limiting factor in heart transplantation. The use of hepatitis C virus (HCV) viremic hearts has expanded the donor pool by more than 100 additional transplantations per year. Although few regions currently use HCV nucleic acid testing-positive organs, the number will continue to increase as more institutions begin to accept them. Overall outcomes have been comparable thus far, but long-term results are pending.

See Commentaries on pages 1886, 1887, and 1889.

The primary limiting factor of heart transplantation is donor availability. In the past decade, the number of new listings for heart transplantation has increased by 49%, and the

number of active candidates listed has increased by 119%,¹ indicating that demand continues to rise.

The use of organs from hepatitis C virus (HCV)-positive donors to expand the donor pool has been debated since the 1990s. In 2001, the American Heart Association consensus guidelines approved the use of HCV⁺ hearts in selected higher-risk patients.² Early reports demonstrated high rates of HCV transmission (~80%) in these patients, and in the era of interferon-based treatment, this led to acute

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Scanning this QR code will take you to the table of contents to access supplementary information.

Abbreviations and Acronyms

DAA	= direct-acting antiviral
HCV	= hepatitis C virus
HR	= hazard ratio
MELD-XI	= Model for End-stage Liver Disease excluding international normalized ratio
NAT	= nucleic acid testing
SMD	= standardized mean difference
UNOS	= United Network for Organ Sharing

transaminitis, chronic liver disease, and increased mortality.²⁻⁴ In 2006, a multicenter study showed 1-, 5-, and 10-year mortality rates that doubled after HCV-positive heart transplantation.³ Analysis of the United Network for Organ Sharing (UNOS) registry from 1991 to 2014 similarly demonstrated worse overall survival (hazard ratio [HR], 1.41) and increased mortality as early as 30 days after transplantation with HCV-positive hearts (6.0% vs 4.4%; $P = .02$),⁴ leading to the abandonment of the use of HCV-positive donor organs.

This practice began to shift with the advent of direct-acting antivirals (DAAs) in 2014, which demonstrated cure rates >95%.⁵ HCV viremic donor organs began to be reconsidered for solid organ transplantations, and since then, multiple single-center studies have shown comparable 6-month and 1-year survival rates (~90%) with HCV-

positive heart donations.⁶⁻⁹ Although HCV transmission rates remained high, patients were treated with DAA therapy with >90% completion rates.⁶⁻⁸ All patients who completed therapy were cured, defined as a sustained virologic response 12 weeks after therapy, with no reports of relapse. Given these promising results, the use of HCV-positive hearts is rapidly increasing, changing the field of heart transplantation. In this study, we examined current trends in heart transplantation from HCV viremic donors and short-term outcomes after transplantation.

METHODS**Study Design**

The UNOS thoracic organ database was queried for adult patients undergoing heart transplantation between January 2015 and September 2019. Patients undergoing multiorgan transplantation, who had incomplete HCV data, and/or who were lost to follow-up were excluded (Figure 1). Independent variables with >10% unrecorded or missing values were excluded, and the majority of factors had <3% missing data. Complete case analysis excluded the rare cases with missing values from the multivariable regression analyses and propensity-matched model. Analysis was performed on data updated on September 31 2019, ensuring a minimum follow-up of 30 days. The median duration of follow-up was 580 days.

Donor HCV status was determined by nucleic acid testing (NAT) for viremia. Recipient NAT data were not routinely available, and recipient HCV status was classified by serology. UNOS data were analyzed for demographic, clinical, and transplantation characteristics of both donors and recipients. Acceptance of HCV NAT⁺ hearts was defined as recovered and transplanted hearts. In 2018, UNOS and the Organ Procurement and Transplantation Network revised the heart allocation system.¹⁰ To accommodate both heart allocation systems, we classified waitlist status according to

FIGURE 1. CONSORT diagram demonstrating the selection criteria used to identify final comparison groups of hepatitis C virus (HCV) nucleic acid testing (NAT)⁺ recipients vs HCV NAT⁻ patients in the United Network for Organ Sharing (UNOS) thoracic dataset. Data were obtained from the UNOS registry for the study period (January 2015 to September 2019). Donor HCV status was classified by NAT.

urgency as high priority (old status 1A or new status 1-2), intermediate priority (old status 1b or new status 3-4), or low priority (old status 2 or new status 5-6). Preoperative risk for liver dysfunction was characterized by MELD-XI, a modified Model for End-stage Liver Disease (MELD) score that excludes the international normalized ratio and has been validated in several heart transplantation studies.^{11,12} MELD-XI was calculated with the following equation based on laboratory values obtained at time of transplantation: $\text{MELD-XI} = 5.11 \times \ln(\text{serum bilirubin}) + 11.76 \times \ln(\text{serum creatinine}) + 9.44$.

Regional trends were observed across the 11 UNOS regions, and temporal trends by year of transplantation were reported. Institutional differences were observed with encrypted center codes and localized to 1 of the 11 UNOS regions. The proportion of transplantation centers performing HCV NAT⁺ heart transplants per region were compared, and variation among single centers was also noted.

Post-transplantation outcomes focused on acute rejection before discharge and 30-day mortality. Seroconversion was determined by positive HCV serology at the time of follow-up with previously negative antibodies before transplantation. Given significant missing data, we focus on summarizing available values, including serologic status at subsequent visits, coronary artery disease, renal dysfunction requiring dialysis, and hospitalizations for rejection or infection.

Statistical Analysis

All statistical analyses were performed in R. Categorical variables were compared using Fisher's exact test. The Mann-Whitney *U* test and Kruskal-Wallis test were used for comparison of continuous variables. Unadjusted Kaplan-Meier survival curves were generated for overall survival. Univariable and multivariable logistic regressions were performed to determine predictors of 30-day mortality and acute rejection. Multivariable factors were selected based on clinical reasoning or statistical significance in univariable analyses. In all tests, statistical significance was determined by a *P* value <.05.

Propensity score matching was conducted with a 3:1 ratio and nearest-neighbor matching as described previously, originally by Rosenbaum and colleagues¹³ and adapted by Deb and colleagues¹⁴ for cardiovascular research. The standardized mean difference (SMD) was calculated for each variable and means were compared in matched and unmatched groups. Propensity score was calculated using a logistic regression model with covariate selection based on significant differences (SMD >0.1) in the unmatched data and factors deemed clinically relevant based on experience and previous literature. Success of matching and similar distribution of covariates was confirmed by comparison of means between the HCV NAT⁺ and NAT⁻ cohorts using the SMD. Matched data were then analyzed for primary outcomes, including Kaplan-Meier survival and graft failure.

RESULTS

Study Population

A total of 11,393 adult patients underwent heart transplantation between January 2015 and September 2019. The patients received hearts from HCV viremic donors in 326 cases and from HCV-negative donors in 11,067 cases. Recipients of HCV NAT⁺ hearts were older (mean age, 53.4 vs 55.2; *P* = .010), and more likely to have positive HCV serology before transplantation (5.5% vs 2.1%; *P* < .001). Waitlist status differed significantly between the 2 cohorts. At the time of transplantation, 46.0% of HCV NAT⁺ heart recipients were in a high-priority status (1A or 1-2), compared with 64.8% of HCV NAT⁻ heart recipients (*P* < .001).

HCV NAT⁺ donors were more likely to be white (82.8% vs 64.1%; *P* < .001), with no significant between-group difference in age or sex. A higher percentage of HCV NAT⁺ donors had a history of smoking (50.6% vs 44.9%; *P* = .049), cocaine use (57.4% vs 23.8%; *P* < .001) or drug use (88.9% vs 55.7%; *P* < .001), and heavy alcohol intake (67.7% vs 30.5%; *P* < .001). They were less likely to be on inotropic support at the time of organ procurement (30.1% vs 38.7%; *P* = .001). Additional recipient and transplantation characteristics are summarized in Table 1.

Trends Over Time

Since the first HCV viremic heart transplantation in 2015, the number of HCV NAT⁺ transplantations has rapidly increased. A total of 137 HCV NAT⁺ transplants were performed in 2018, and 127 additional transplantations were performed by September 2019. In contrast, the number of HCV NAT⁻ transplants has remained stagnant since 2016, at approximately 2500 transplantations per year (Figure 2, A). After the initial HCV NAT⁺ transplantation performed in region 11, the number of regions adopting this practice as well as the number of HCV NAT⁺ transplantations within each region has increased (Figure 2, B). There was no significant change in patient selection over time for receipt of HCV viremic hearts (Tables 2, E1, and E2). However, in both cohorts, patient waitlist status at the time of transplantation changed significantly. Overall, the recipients of HCV NAT⁺ hearts were more likely to be in a low-priority status (class 2 or 5-6 by the new allocation system), which increased over time. The proportion of patients in a high-priority status (1A or 1-2) was decreased in both cohorts (Table 3). Of note, the new allocation system was initiated in October 2018, significantly influencing any trends from 2018 to 2019.

Regional and Institutional Variation

The utilization of HCV NAT⁺ hearts varied significantly across the different UNOS regions (Figure 3, A). More than 75% of HCV NAT⁺ hearts were transplanted in the Northeast or East Coast (Regions 1, 2, 9, 10, and 11). Region 11 performed 27.0% of the HCV NAT⁺ transplants, almost twice as many as the next highest region (Figure 3, B). Region 7 accepted the fewest (3 patients; 0.9%), with their first in April 2019. This distribution is not mirrored in the use of HCV NAT⁻ hearts and thus is not a reflection of skewed demand. Region 5 performed the most HCV NAT⁻ transplants (16.1%), followed by Region 11 (12.4%), and Region 3 (11.9%). Overall, HCV NAT⁻ transplantations were more evenly distributed (Figure 3, B).

On an institutional level, the use of HCV NAT⁺ hearts varied even more widely (Table E3). A total of 129 centers performed heart transplantations during the study period, and only 39 of these centers (30.2%) performed transplantations with hearts from HCV viremic donors. Almost one-

TABLE 1. Donor and recipient characteristics

Characteristic	HCV NAT ⁻ (N = 11,067)	HCV NAT ⁺ (N = 326)	P value
Recipient			
Age, y, mean (SD)	53.39 (12.83)	55.23 (11.93)	.010
Male sex, n (%)	8070 (72.9)	250 (76.7)	.148
Ethnicity, n (%)			.515
White	7129 (64.4)	223 (68.4)	
Asian	406 (3.7)	9 (2.8)	
Black	2407 (21.7)	65 (19.9)	
Hispanic	995 (9.0)	24 (7.4)	
Other	130 (1.2)	5 (1.5)	
Education, n (%)			.283
None	15 (0.1)	2 (0.6)	
Grade school (0-8)	348 (3.1)	6 (1.8)	
High school (9-12)	4128 (37.3)	124 (38.0)	
College/technical school	3085 (27.9)	86 (26.4)	
Associate/bachelor degree	2256 (20.4)	69 (21.2)	
Post-college degree	1005 (9.1)	33 (10.1)	
Unknown	229 (2.1)	6 (1.8)	
Primary payment method, n (%)			.696
Private insurance	55 (0.5)	2 (0.6)	
Public insurance	5176 (46.8)	145 (44.5)	
Other (self, donation, foreign government)	5836 (52.7)	179 (54.9)	
At time of transplantation			
Creatinine, mg/dL, mean (SD)	1.24 (0.65)	1.26 (0.40)	.734
Total bilirubin, mg/dL, mean (SD)	0.94 (1.57)	0.92 (0.78)	.846
MELD-XI score, mean (SD)	9.39 (5.48)	9.92 (5.30)	.087
ECMO, n (%)	192 (1.7)	9 (2.8)	.241
IABP, n (%)	1259 (11.4)	44 (13.5)	.272
VAD, n (%)	5251 (47.4)	147 (45.1)	.434
Requiring inotropic support, n (%)	3952 (35.7)	102 (31.3)	.113
HCV seropositive, n (%)	235 (2.1)	18 (5.5)	<.001
Diabetes, n (%)	3062 (27.7)	92 (28.3)	.853
Previous heart transplantation, n (%)	265 (2.4)	10 (3.1)	.550
Status at transplantation, n (%)			<.001
High (1A or 1-2*)	7173 (64.8)	150 (46.0)	
Intermediate (1B or 3-4*)	313 (2.8)	21 (6.4)	
Low (2 or 5-6*)	3581 (32.4)	155 (47.5)	
Donor			
Age, y, mean (SD)	32.18 (11.11)	33.35 (7.67)	.061
Male sex, n (%)	7702 (69.6)	240 (73.6)	.134
Ethnicity, n (%)			<.001
White	7093 (64.1)	270 (82.8)	
Asian	181 (1.6)	2 (0.6)	
Black	1798 (16.2)	24 (7.4)	
Hispanic	1807 (16.3)	24 (7.4)	
Other	188 (1.7)	6 (1.8)	
History of smoking, n (%)	4974 (44.9)	165 (50.6)	.049
History of cocaine use, n (%)	2593 (23.8)	182 (57.4)	<.001
History of other drug use, n (%)	6110 (55.7)	287 (88.9)	<.001
Current alcohol abuse, n (%)	1876 (30.5)	63 (67.7)	<.001
Requiring inotropic support, n (%)	4281 (38.8)	98 (30.2)	.002
LVEF <45%, n (%)	58 (0.5)	3 (0.9)	.562
Donor-recipient sex mismatch (F > M), n (%)	1459 (13.2)	36 (11.0)	.296
ABO identical, n (%)	9516 (86.0)	278 (85.3)	.778

(Continued)

TABLE 1. Continued

Characteristic	HCV NAT ⁻ (N = 11,067)	HCV NAT ⁺ (N = 326)	P value
ABO compatible, n (%)	1551 (14.0)	48 (14.7)	.778
HLA mismatch (number of mismatched alleles), n (%)			.639
0	11 (0.1)	0 (0.0)	
1	44 (0.4)	1 (0.4)	
2	271 (2.7)	8 (2.9)	
3	1096 (10.8)	39 (14.1)	
4	2571 (25.3)	66 (23.8)	
5	3828 (37.7)	107 (38.6)	
6	2337 (23.0)	56 (20.2)	
BMI discrepancy >20%, n (%)	4352 (39.4)	140 (42.9)	.212
Distance, mi, mean (SD)	172.70 (207.40)	299.03 (235.51)	<.001
Ischemic time, h, mean (SD)	3.10 (1.04)	3.52 (0.97)	<.001
Year of transplantation, n (%)			<.001
2015	1824 (16.5)	1 (0.3)	
2016	2535 (22.9)	12 (3.7)	
2017	2503 (22.6)	49 (15.0)	
2018	2498 (22.6)	137 (42.0)	
2019	1707 (15.4)	127 (39.0)	

Bold indicates *P* values less than .05. HCV, Hepatitis C virus; NAT, nucleic acid testing; SD, standard deviation; MELD-XI, Model for End-stage Liver Disease excluding INR; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; VAD, ventricular assist device; LVEF, left ventricular ejection fraction; *F* > *M*, female to male; HLA, human leukocyte antigen; BMI, body mass index. *Under the new allocation system (status 1-6).

half of the HCV NAT⁺ heart transplants were attributed to 5 institutions. A single institution performed 20.9% of the total HCV NAT⁺ transplants. Furthermore, the discrepancy in the proportion of centers performing in HCV NAT⁺ transplantations varied within each region as well (Figure 3, C). Although Region 11 performed the most HCV NAT⁺ transplants, only 33.3% of transplantation centers in this region participated in these procedures. The majority of Region 9 centers have adopted this practice, with 5 out of 7 transplantation centers (71.8%) performing HCV NAT⁺ heart transplantations. In contrast, out of 12 transplantation centers in Region 7, only 1 (8.3%) used hearts from HCV viremic donors (Figure 3, C).

The regional and institutional discrepancy in the utilization of HCV NAT⁺ heart transplantations is reflected in the distance traveled and organ ischemic times (Table 1). HCV NAT⁺ hearts traveled significantly farther (mean, 299 vs 173 miles; *P* < .001), leading to longer ischemic times (mean, 3.52 hours vs 3.10 hours; *P* < .001).

Outcomes

Overall survival was comparable between the 2 cohorts based on Kaplan–Meier analysis (*P* = .24; Figure 4, A). Propensity score matching was completed with recipients of HCV NAT⁻ hearts (n = 783) matched 3:1 with recipients of NAT⁺ donor hearts (n = 261). The propensity score was calculated using covariables deemed clinically relevant based on past experience and previous literature

or found to be significantly different between the cohorts (Table E4). After 3:1 propensity score matching, 783 recipients of NAT⁻ hearts and 261 recipients of NAT⁺ hearts were compared and continued to demonstrate no significant difference in overall survival (*P* = .24; Figure 4, B).

In the unmatched cohort, recipients of HCV NAT⁺ hearts had a 2.5% 30-day mortality rate, which did not differ significantly from the 3.3% mortality in the HCV NAT⁻ cohort (*P* = .527). With propensity matching, mortality rates were similar: 2.5% in the NAT⁺ cohort and 3.7% in the NAT⁻ cohort (*P* = .296). During the hospitalization for transplantation, 22.4% of HCV NAT⁺ recipients and 21.4% of HCV NAT⁻ recipients developed an acute rejection episode (*P* = .933), which remained similar after propensity score matching: 22.4% of the NAT⁺ group and 22.7% of the NAT⁻ cohort (*P* = .934). On multivariable analysis, donor HCV NAT status had no effect on 30-day mortality (HR, 0.76; 95% confidence interval, 0.32-1.55; *P* = .490) or the risk for acute rejection (HR, 0.89; 95% confidence interval, 0.65-1.20; *P* = .455). Significant positive and negative predictors of 30-day mortality and acute rejection episodes before discharge are summarized in Table 3.

Of the 326 recipients of HCV NAT⁺ hearts, serology data were available for 226 patients. A total of 185 patients were seronegative at all follow-up visits. At a median follow-up of 210 days, 41 patients (12.6%) had positive HCV

FIGURE 2. Frequency of heart transplants performed using hepatitis C virus (HCV) viremic donors over time. A, Total number of yearly heart transplantations from HCV nucleic acid testing (NAT)⁺ and HCV NAT⁻ donors was recorded over time. The graph displays values from 2015 to 2018, given that 2019 data are incomplete. B, Regional trends in the number of yearly heart transplantations from HCV NAT⁺ donors show an increasing number of United Network for Organ Sharing (UNOS) regions performing HCV NAT⁺ transplantations over time, as well as the number of yearly HCV NAT⁺ transplantations.

serology, 38 (11.7%) of whom had been HCV seronegative before transplantation. Four patients initially tested negative at the initial 6-month follow-up, with later seroconversion at 1 year post-transplantation. The remaining 34 patients demonstrated seropositivity at the initial visit, with 15 patients (39.5%) clearing the antibodies after 1 year. Fourteen patients tested positive for HCV viremia at a median follow-up of 362 days after transplantation (interquartile range, 191.5-401.5), 10 of whom were seronegative and 4 seropositive. Within the seroconverted cohort, 4 out of 28 patients (14.3%) who were evaluated demonstrated coronary artery disease, and 1 patient (3.6%) required dialysis. In comparison, 106 seronegative patients were evaluated for coronary artery

disease, and 11 (10.3%) were found to have coronary vasculopathy. Three seronegative patients developed renal dysfunction necessitating dialysis. Three seroconverted patients (7.9%) were hospitalized for infection compared with 23 seronegative patients (13.1%), and 4 seroconverted patients (10.9%) were admitted for rejection within 1 year compared with 18 seronegative patients (10.3%). All patients demonstrated adequate graft function, with the lowest recorded ejection fraction at 49%. At a median follow-up of 365 days, survival rates were 100% in patients with HCV viremia, 97.4% in patients who seroconverted, and 93.7% in seronegative patients. No data were available on receipt of DAA therapy or management of seroconversion.

TABLE 2. Trends in transplantation characteristics over time

Characteristic	HCV NAT ⁻				P value
	2015-6 (N = 4359)	2017 (N = 2503)	2018 (N = 2498)	2019 (N = 1707)	
Recipient					
Age, y, mean (SD)	53.42 (12.61)	53.41 (12.91)	53.77 (12.84)	52.71 (13.24)	.073
HCV seropositive, n (%)	83 (1.9)	49 (2.0)	71 (2.8)	32 (1.9)	.045
MELD-XI score, mean (SD)	9.57 (5.47)	9.30 (5.42)	9.27 (5.39)	9.23 (5.73)	.041
ECMO, n (%)	42 (1.0)	19 (0.8)	42 (1.7)	89 (5.2)	<.001
IABP, n (%)	327 (7.5)	207 (8.3)	227 (9.1)	498 (29.2)	<.001
VAD, n (%)	2206 (50.6)	1268 (50.7)	1169 (46.8)	608 (35.6)	<.001
Status at transplantation, n (%)					
High (1A or 1-2*)	2926 (67.1)	1674 (66.9)	1608 (64.4)	965 (56.5)	<.001
Intermediate (1B or 3-4*)	1329 (30.5)	772 (30.8)	799 (32.0)	681 (39.9)	
Low (2 or 5-6*)	104 (2.4)	57 (2.3)	91 (3.6)	61 (3.6)	
Donor					
History of cigarette use, n (%)	2035 (46.7)	1111 (44.4)	1120 (44.8)	708 (41.5)	.003
History of cocaine use, n (%)	918 (21.3)	580 (23.4)	639 (26.1)	456 (27.0)	<.001
History of other drug use, n (%)	2308 (53.4)	1369 (55.0)	1444 (58.5)	989 (58.3)	<.001
Distance, mi, mean (SD)	149.81 (195.86)	152.50 (194.03)	169.97 (202.41)	264.75 (235.39)	<.001
Ischemic time, h, mean (SD)	3.06 (1.03)	3.04 (1.07)	3.05 (1.03)	3.39 (1.01)	<.001
Characteristic	HCV NAT ⁺				P value
	2015-6 (N = 13)	2017 (N = 49)	2018 (N = 137)	2019 (N = 127)	
Recipient					
Age, y, mean (SD)	57.92 (5.71)	53.71 (10.85)	56.16 (12.18)	54.54 (12.50)	.439
HCV seropositive, n (%)	3 (23.1)	2 (4.1)	8 (5.8)	5 (3.9)	.037
MELD-XI score, mean (SD)	10.65 (5.88)	10.50 (5.48)	10.11 (4.79)	9.41 (5.68)	.541
ECMO, n (%)	0 (0.0)	0 (0.0)	3 (2.2)	6 (4.7)	.29
IABP, n (%)	0 (0.0)	5 (10.2)	14 (10.2)	25 (19.7)	.048
VAD, n (%)	10 (76.9)	19 (38.8)	60 (43.8)	58 (45.7)	.101
Status at transplantation, n (%)					
High (1A or 1-2*)	8 (61.5)	24 (49.0)	74 (54.0)	44 (34.6)	.002
Intermediate (1B or 3-4*)	1 (7.7)	6 (12.2)	10 (7.3)	4 (3.1)	
Low (2 or 5-6*)	4 (30.8)	19 (38.8)	53 (38.7)	79 (62.2)	
Donor					
History of cigarette use, n (%)	7 (53.8)	27 (55.1)	68 (49.6)	63 (49.6)	.907
History of cocaine use, n (%)	8 (61.5)	31 (64.6)	80 (59.3)	63 (52.1)	.44
History of other drug use, n (%)	13 (100.0)	40 (83.3)	119 (87.5)	115 (91.3)	.251
Distance, mi, mean (SD)	353.23 (285.14)	303.04 (247.20)	280.85 (216.28)	311.54 (246.43)	.6
Ischemic time, h, mean (SD)	3.63 (0.70)	3.47 (0.88)	3.51 (1.05)	3.53 (0.95)	.958

Bold indicates *P* values less than .05. HCV, Hepatitis C virus; NAT, nucleic acid testing; SD, standard deviation; MELD-XI, Model for End-stage Liver Disease excluding INR; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; VAD, ventricular assist device. *Under the new allocation system (status 1-6).

DISCUSSION

In this study, we examined the effects of HCV viremic heart donation on the field of transplantation in the era of DAA therapy. Recent multicenter studies demonstrate acceptable 1-year post-transplantation survival rates compared with HCV⁻ donors in HCV-seropositive cohorts (including both viremic and nonviremic donors)¹⁵ and a small HCV viremic cohort.¹⁶ We focus on HCV NAT⁺ donors, because seropositive nonviremic donors are unlikely to cause HCV transmission.¹⁷ Recipients of HCV viremic hearts were more likely to be HCV seropositive; however,

this represented only a small percentage of the cohort (5.5%), and our results reflect a primarily HCV-naïve population.

The observed differences in donor characteristics are linked to the two primary populations of HCV⁺ patients: baby boomers with chronic HCV and persons with a history of IV drug use. HCV⁺ donors were on average older, and more likely to have a history of polysubstance use. With the opioid epidemic in the United States, there has been a 200% increase in opioid-related deaths since 2000, leading to an increase in organ donation overall and particularly in

TABLE 3. Multivariable analysis of factors affecting perioperative outcomes

Factor	30-d mortality		Acute rejection before discharge	
	HR (95% CI)	P value	HR (95% CI)	P value
Donor-recipient sex mismatch (F > M)	1.54 (1.15-2.04)	.003	0.94 (0.81-1.09)	.396
ABO match				
Identical	Ref (Ref)	Ref	Ref (Ref)	Ref
Compatible	0.98 (0.69-1.35)	.899	1.01 (0.88-1.16)	.880
HLA allele mismatch	1.07 (0.97-1.20)	.185	1.12 (1.07-1.18)	<.001
BMI discrepancy >20%	1.08 (0.86-1.35)	.529	1.00 (0.91-1.11)	.969
Donor				
Age	1.01 (1.00-1.02)	.058	1.00 (0.99-1.00)	.508
Ethnicity				
White	Ref (Ref)	Ref	Ref (Ref)	Ref
Asian	1.40 (0.62-2.77)	.367	1.01 (0.66-1.52)	.950
Black	0.62 (0.43-0.88)	.009	0.81 (0.71-0.93)	.002
Hispanic	0.84 (0.60-1.16)	.303	1.02 (0.88-1.18)	.775
Other	0.81 (0.33-1.67)	.597	0.71 (0.45-1.08)	.120
LVEF <45%	0.00 (0.00-1.66)	.968	1.46 (0.77-2.67)	.228
HCV serostatus				
HCV NAT ⁻	Ref (Ref)	Ref	Ref (Ref)	Ref
HCV NAT ⁺	0.76 (0.32-1.55)	.490	0.89 (0.65-1.20)	.455
Recipient				
Age	1.01 (1.00-1.02)	.140	0.99 (0.98-0.99)	<.001
Ethnicity				
White	Ref (Ref)	Ref	Ref (Ref)	Ref
Asian	0.86 (0.43-1.54)	.629	0.87 (0.64-1.17)	.382
Black	0.55 (0.39-0.75)	<.001	1.03 (0.92-1.16)	.596
Hispanic	1.46 (1.01-2.06)	.039	1.10 (0.91-1.32)	.318
Other	0.88 (0.27-2.16)	.811	0.78 (0.43-1.31)	.368
At time of transplantation				
MELD-XI score	1.09 (1.07-1.10)	<.001	0.98 (0.97-0.99)	<.001
ECMO	2.95 (1.61-5.09)	<.001	0.69 (0.44-1.03)	.076
VAD	1.59 (1.25-2.01)	<.001	0.95 (0.86-1.06)	.368
HCV Ab ⁺	0.92 (0.41-1.81)	.831	1.01 (0.72-1.39)	.958
Status at transplantation				
High (1A or 1-2*)	Ref (Ref)	Ref	Ref (Ref)	Ref
Intermediate (1B or 3-4*)	1.00 (0.78-1.28)	1.000	0.98 (0.88-1.09)	.685
Low (2 or 5-6*)	1.51 (0.79-2.67)	.185	1.08 (1.03-1.13)	.002
Ischemic time	1.27 (1.15-1.39)	<.001	1.06 (1.00-1.12)	.065
Year of transplantation				
2015	Ref (Ref)	Ref	Ref (Ref)	Ref
2016	1.22 (0.85-1.76)	.281	1.21 (1.04-1.42)	.017
2017	1.32 (0.93-1.91)	.126	1.27 (1.08-1.48)	.003
2018	1.01 (0.69-1.48)	.961	0.94 (0.80-1.11)	.494
2019	1.00 (0.66-1.51)	.995	1.03 (0.86-1.23)	.722
Region				
1	Ref (Ref)	Ref	Ref (Ref)	Ref
2	1.19 (0.53-3.19)	.701	2.20 (1.35-3.78)	.003
3	1.33 (0.59-3.55)	.529	4.23 (2.62-7.23)	<.001
4	1.30 (0.57-3.48)	.566	2.33 (1.43-4.02)	.001
5	0.93 (0.42-2.49)	.880	0.65 (0.39-1.12)	.102
6	1.15 (0.46-3.26)	.782	0.72 (0.40-1.35)	.289
7	0.68 (0.28-1.89)	.414	3.02 (1.86-5.20)	<.001
8	1.30 (0.54-3.62)	.589	2.16 (1.29-3.79)	.005

(Continued)

TABLE 3. Continued

Factor	30-d mortality		Acute rejection before discharge	
	HR (95% CI)	P value	HR (95% CI)	P value
9	0.41 (0.14-1.28)	.108	4.81 (2.94-8.34)	<.001
10	1.07 (0.46-2.92)	.887	2.95 (1.81-5.08)	<.001
11	0.99 (0.44-2.67)	.982	4.03 (2.50-6.91)	<.001

Bold indicates *P* values less than .05. *HR*, Hazard ratio; *CI*, confidence interval; *F* > *M*, female to male; *HLA*, human leukocyte antigen; *BMI*, body mass index; *LVEF*, left ventricular ejection fraction; *HCV*, hepatitis C virus; *NAT*, nucleic acid testing; *MELD-XI*, Model for End-stage Liver Disease excluding INR; *ECMO*, extracorporeal membrane oxygenation; *VAD*, ventricular assist device. *Under the new allocation system (status 1-6).

HCV-viremic donors.⁵ The percentage of donors with a history of cocaine or other drug use was >2-fold higher in the HCV NAT⁺ cohort; however, over time, this proportion increased significantly in the HCV NAT⁻ cohort as well. The donor population differences did not lead to a difference in organ quality (using left ventricular ejection fraction as a measure of quality). Notwithstanding, the long-term effects of donor substance use—particularly cocaine use—warrant further investigation.

Shifting Paradigms in HCV⁺ Heart Utilization

Although the number of active listings for heart transplantation has consistently increased each year,¹⁸ the number of HCV-negative transplantations has remained stagnant since 2016. With up to 400 deaths on the waitlist

each year,¹⁸ the use of HCV viremic hearts has added >100 hearts per year, a significant advance in closing the gap between demand and donor availability. Despite this increase, the use of HCV⁺ organs remains a largely untapped resource, with approximately 300 donor hearts discarded yearly for reasons unrelated to graft quality.¹⁹ Several UNOS regions do not routinely accept HCV viremic hearts, and even in regions that accept hearts from HCV⁺ donors, this resource is underutilized. Region 1 performs 15.9% of HCV NAT⁺ heart transplantations, the third highest in the nation, but a recent study showed that only 8 out of 100 viable HCV⁺ donor hearts were accepted in this region.¹⁹ A recent study by Moayed and colleagues¹⁹ demonstrated that only 5% of viable HCV⁺ hearts were transplanted in the era of DAA therapy and that a large

FIGURE 3. Regional and institutional variation in acceptance of hepatitis C virus (*HCV*) viremic hearts. A and B, Regional acceptance and transplantation of hearts from HCV nucleic acid testing (*NAT*)⁺ donors (A) and HCV NAT⁻ donors (B) reported based on United Network for Organ Sharing (*UNOS*) region. Comparisons note the contribution of a single region as a percentage of the total number of HCV NAT⁺ transplants performed. C, Institutional variation is reported by number of transplantation centers per UNOS region that have performed HCV NAT⁺ transplants, as a percentage of total number of centers in the region.

FIGURE 4. Post-transplantation survival for patients who received hepatitis C virus (HCV) nucleic acid testing (NAT)⁺ versus HCV NAT⁻ heart transplantations. A, Unadjusted time to all-cause mortality for patients who received HCV NAT⁺ versus HCV NAT⁻ heart transplantations. Time 0 is defined as the time of heart transplantation. B, Propensity-matched time to all-cause mortality for patients who received HCV NAT⁺ versus HCV NAT⁻ heart transplantations. Time 0 is defined as the time of heart transplantation.

number of donor hearts were rejected between 2014 and 2017 for reasons unrelated to structural abnormalities of donor medical comorbidities. Unfortunately, the UNOS database contains a limited amount of granular information on declined donor organs. A future study focusing on all HCV viremic deceased donors, reasons for decline, and characteristics of organs that were recovered and rejected

may be warranted, although this is outside the scope of this study, which focuses on trends in completed heart transplantations.

The utilization of HCV NAT⁺ hearts varies considerably on both regional and institutional levels (Figure 5). Across regions, the number of HCV NAT⁺ hearts transplanted differed, with <25% of HCV NAT⁺ heart transplantations

FIGURE 5. Trends in the use of hepatitis C virus (HCV) viremic donor hearts. This study examined trends in heart transplantation using organs from HCV viremic donors. A retrospective analysis of the United Network for Organ Sharing (UNOS) database was performed, examining adult heart transplantation recipients from 2015 to September 2019. HCV viremic donor organs are increasingly used in the era of direct-acting antiviral (DAA) therapy. Regional and center-specific trends demonstrate significant variation in the use of HCV viremic hearts, despite comparable outcomes to date. NAT, Nucleic acid testing.

performed outside of the Northeast or Region 11. Interestingly, when examining this in a center-specific manner, the proportion of transplantation centers that perform

VIDEO 1. Regional and institutional trends in use of hepatitis C virus (HCV) viremic hearts over time. The utilization of HCV viremic hearts differs significantly among regions and individual centers. This variation decreases over time as the practice of HCV viremic heart transplantation becomes increasingly accepted. Video available at: [https://www.jtcvs.org/article/S0022-5223\(20\)32640-4/fulltext](https://www.jtcvs.org/article/S0022-5223(20)32640-4/fulltext).

HCV NAT⁺ transplantations also varies across regions. Some regions demonstrate a relatively uniform acceptance of this practice, with 66.7% and 71.4% of transplantation centers in Regions 1 and 9 using HCV NAT⁺ hearts. In contrast, only one-third of transplantation centers in Region 11 used hearts from HCV⁺ donors. However, this region performed the most HCV NAT⁺ heart transplantations overall due to a single institution performing 20.9% of all HCV NAT⁺ heart transplantations. This likely reflects significant differences in transplantation center practices as well as available resources and support systems for postoperative care. A multidisciplinary team, including hepatologists and infectious disease specialists, is essential for preoperative and postoperative care, and smaller institutions might not have the personnel or equipment to manage these patients. In this case, these patients may be selectively funneled to a larger institution, accounting for the significant variation within the region.

Outcomes and Seroconversion

Early analysis of the UNOS database before DAA therapy demonstrated increased mortality rates that were observable as early as 30 days after transplantation and persisted in long-term outcomes.⁴ In this study, we

reevaluated 30-day mortality rates with HCV viremic hearts (2.5%) compared with HCV⁻ donation (3.3%) and found no significant difference. Overall survival by Kaplan–Meier analysis also did not differ, as reflected in similar 1-year survival rates in the single-center trials as well.^{7,8}

Although early data have been optimistic, we continue to await long-term results. It is expected that donor hearts with good functionality will have adequate short-term outcomes. The primary concern in the use of organs from HCV viremic donors centers on seroconversion and the downstream implications on infection, rejection, and long-term survival, for which there remain little data. In the present study, we observed an 11.7% seroconversion rate among recipients of HCV NAT⁺ hearts, although less than one-half of the recipients underwent testing at follow-up visits. Within this group, coronary artery disease was noted in 14.3% of the seroconverted patients, slightly increased compared with 10.3% in seronegative recipients of HCV NAT⁺ hearts. Previously reported 1-year rates of coronary vasculopathy were 7.8% overall²⁰ and 10% to 25% in recipients of HCV-seropositive hearts.¹⁵ Despite the increased rates of coronary vasculopathy, graft function remained adequate in this study, with the lowest recorded ejection fraction at 49% among seroconverted patients. Hospitalization rates for infection were lower in the seroconverted group (7.9% vs 13.1%), and the rate of admission for rejection was unchanged (10.9% of seroconverted patients vs 10.3% of seronegative patients). One-year survival rates were similarly unaffected (97.4% seroconverted vs 93.7% seronegative), although longer follow-up is needed to further understand the implications of seroconversion.

The management of seroconversion, including the optimal regimen and treatment time of DAA combinations remains unknown and has not yet been standardized. Our institution and others have explored preemptive DAA treatment in all recipients of HCV viremic organs,⁹ whereas other centers initiate treatment on initial detection of viremia at follow-up. The use of prophylactic DAA therapy is also influenced by insurance coverage, which differs across states, contributing to the regional variation that we observe. The duration of treatment varies widely as well, ranging from 4 to 24 weeks. In all cases to date, all surviving patients across multiple series have reached viral clearance with no relapses after DAA therapy.²¹ Although there remains no consensus on the timing of DAA therapy or management of seroconversion, our center implements an 8-week regimen of glecaprevir/pibrentasvir given preemptively to all patients on acceptance of an HCV viremic organ. Our previous study demonstrated that such a regimen was well-tolerated and lead to a sustained virologic response at 12 weeks after completion in all recipients.

Limitations

This retrospective study carries with it the usual limitations of selection bias and differences in baseline cohort characteristics. Additional limitations of this study include skewed sample sizes, with a significantly smaller cohort for recipients of HCV viremic hearts, which we attempt to account for with propensity matching. The use of HCV viremic hearts remains relatively recent, and median follow-up times differed significantly between the 2 cohorts. In addition, the study period includes transplantations performed using both the old and the new heart allocation systems, with the latter being implemented in October 2018. As such, effects on waitlist times, travel distance, and ischemic times may be affected in the analyses. To mitigate this, we attempted to account for temporal changes in policies such as this by controlling for year of transplantation. Finally, the UNOS database is missing large amounts of more granular data and follow-up regarding serology and nucleic acid testing, coronary vasculopathy, and additional outcomes, which need to be ascertained in alternative studies.

CONCLUSIONS

The transplantation of HCV viremic hearts expands the donor pool with comparable post-transplantation outcomes in the modern era. This study adds to the growing body of evidence that supports the use of HCV viremic organs with promising short-term survival and graft outcomes. We observe increased organ availability with this practice, and as this strategy becomes more widely adopted across all UNOS regions, we expect this trend to continue and ultimately, for waitlist mortality to decline. However, the downstream effects of seroconversion and potentially increased rates of coronary vasculopathy remain unclear, and ongoing investigation is required to fully understand the implications of HCV viremia on long-term outcomes (Video 1). HCV viremic organ transplantation opens a field of additional questions to be addressed, and although ongoing investigation is necessary, we encourage the consideration of HCV viremic organs in the present to address the current need.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: heart transplantation, hepatitis C viremic donor, regional variation, trends in use of donors with hepatitis C

TABLE E1. Trends in HCV NAT⁺ transplantation characteristics over time

Characteristic	2015-6 (N = 4359)	2017 (N = 2503)	2018 (N = 2498)	2019 (N = 1707)	P value
Recipient					
Age, y, mean (SD)	57.92 (5.71)	53.71 (10.85)	56.16 (12.18)	54.54 (12.50)	.439
Male sex, n (%)	10 (76.9)	41 (83.7)	104 (75.9)	95 (74.8)	.651
Ethnicity, n (%)					.658
White	10 (76.9)	37 (75.5)	97 (70.8)	79 (62.2)	
Asian	0 (0.0)	2 (4.1)	4 (2.9)	3 (2.4)	
Black	3 (23.1)	5 (10.2)	23 (16.8)	34 (26.8)	
Hispanic	0 (0.0)	4 (8.2)	11 (8.0)	9 (7.1)	
Other	0 (0.0)	1 (2.0)	2 (1.5)	2 (1.6)	
Education, n (%)					.665
None	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.8)	
Grade school (0-8)	0 (0.0)	0 (0.0)	4 (2.9)	2 (1.6)	
High school (9-12)	5 (38.5)	25 (51.0)	43 (31.4)	51 (40.2)	
College/technical school	3 (23.1)	10 (20.4)	41 (29.9)	32 (25.2)	
Associate/bachelor degree	3 (23.1)	10 (20.4)	30 (21.9)	26 (20.5)	
Post-college degree	2 (15.4)	4 (8.2)	17 (12.4)	10 (7.9)	
Unknown	0 (0.0)	0 (0.0)	1 (0.7)	5 (3.9)	
Primary payment, n (%)					.583
Private insurance	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)	
Public insurance	7 (53.8)	25 (51.0)	60 (43.8)	53 (41.7)	
Other (self, donation, foreign government)	6 (46.2)	24 (49.0)	77 (56.2)	72 (56.7)	
At the time of transplantation					
Creatinine, mg/dL, mean (SD)	1.27 (0.40)	1.36 (0.46)	1.27 (0.40)	1.20 (0.37)	.118
Total bilirubin, mg/dL, mean (SD)	1.02 (0.92)	0.81 (0.50)	0.93 (0.78)	0.94 (0.86)	.735
MELD-XI score, mean (SD)	10.65 (5.88)	10.50 (5.48)	10.11 (4.79)	9.41 (5.68)	.541
ECMO, n (%)	0 (0.0)	0 (0.0)	3 (2.2)	6 (4.7)	.29
IABP, n (%)	0 (0.0)	5 (10.2)	14 (10.2)	25 (19.7)	.048
VAD, n (%)	10 (76.9)	19 (38.8)	60 (43.8)	58 (45.7)	.101
Inotropic support, n (%)	1 (7.7)	13 (26.5)	41 (29.9)	47 (37.0)	.115
HCV seropositive, n (%)	3 (23.1)	2 (4.1)	8 (5.8)	5 (3.9)	.037
Diabetes, n (%)	4 (30.8)	10 (20.4)	35 (25.5)	43 (34.1)	.244
Previous heart transplantation	0 (0.0)	2 (4.1)	7 (5.1)	1 (0.8)	.193
Status at transplantation, n (%)					.002
High (1A or 1-2*)	8 (61.5)	24 (49.0)	74 (54.0)	44 (34.6)	
Intermediate (1B or 3-4*)	1 (7.7)	6 (12.2)	10 (7.3)	4 (3.1)	
Low (2 or 5-6*)	4 (30.8)	19 (38.8)	53 (38.7)	79 (62.2)	
Donor					
Age, y, mean (SD)	32.62 (6.01)	32.04 (7.71)	33.59 (8.08)	33.66 (7.36)	.597
Male sex, n (%)	11 (84.6)	42 (85.7)	101 (73.7)	86 (67.7)	.079
Ethnicity, n (%)					.727
White	12 (92.3)	40 (81.6)	111 (81.0)	107 (84.3)	
Asian	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)	
Black	1 (7.7)	6 (12.2)	11 (8.0)	6 (4.7)	
Hispanic	0 (0.0)	2 (4.1)	12 (8.8)	10 (7.9)	
Other	0 (0.0)	1 (2.0)	3 (2.2)	2 (1.6)	
History of smoking, n (%)	7 (53.8)	27 (55.1)	68 (49.6)	63 (49.6)	.907
History of cocaine use, n (%)	8 (61.5)	31 (64.6)	80 (59.3)	63 (52.1)	.44
History of other drug use, n (%)	13 (100.0)	40 (83.3)	119 (87.5)	115 (91.3)	.251
Current alcohol abuse, n (%)	3 (23.1)	10 (20.8)	29 (22.1)	21 (17.2)	.787
Inotropic support, n (%)	6 (46.2)	19 (38.8)	35 (25.9)	38 (29.9)	.217
LVEF <45%, n (%)	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.6)	.747
Donor-recipient sex mismatch (F > M), n (%)	1 (7.7)	4 (8.2)	14 (10.2)	17 (13.4)	.713
ABO compatible, n (%)	2 (15.4)	11 (22.4)	20 (14.6)	15 (11.8)	.363

(Continued)

TABLE E1. Continued

Characteristic	2015-6 (N = 4359)	2017 (N = 2503)	2018 (N = 2498)	2019 (N = 1707)	P value
HLA mismatch, n (%)					.156
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
1	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	
2	0 (0.0)	3 (7.1)	3 (2.6)	2 (1.8)	
3	2 (20.0)	2 (4.8)	25 (21.6)	10 (9.2)	
4	1 (10.0)	11 (26.2)	30 (25.9)	24 (22.0)	
5	3 (30.0)	17 (40.5)	40 (34.5)	47 (43.1)	
6	4 (40.0)	9 (21.4)	18 (15.5)	25 (22.9)	
BMI discrepancy >20%, n (%)	7 (53.8)	16 (32.7)	65 (47.4)	52 (40.9)	.252
Distance, mi, mean (SD)	353.23 (285.14)	303.04 (247.20)	280.85 (216.28)	311.54 (246.43)	.6
Ischemic time, h, mean (SD)	3.63 (0.70)	3.47 (0.88)	3.51 (1.05)	3.53 (0.95)	.958
Region, n (%)					<.001
1	3 (23.1)	8 (16.3)	22 (16.1)	14 (11.0)	
2	2 (15.4)	9 (18.4)	3 (2.2)	17 (13.4)	
3	0 (0.0)	0 (0.0)	6 (4.4)	7 (5.5)	
4	1 (7.7)	1 (2.0)	7 (5.1)	4 (3.1)	
5	0 (0.0)	6 (12.2)	11 (8.0)	16 (12.6)	
6	0 (0.0)	0 (0.0)	3 (2.2)	4 (3.1)	
7	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.4)	
8	0 (0.0)	0 (0.0)	0 (0.0)	5 (3.9)	
9	1 (7.7)	3 (6.1)	30 (21.9)	16 (12.6)	
10	0 (0.0)	0 (0.0)	21 (15.3)	15 (11.8)	
11	6 (46.2)	22 (44.9)	34 (24.8)	26 (20.5)	

SD, Standard deviation; MELD-XI, Model for End-stage Liver Disease excluding INR; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; VAD, ventricular assist device; HCV, hepatitis C virus; LVEF, left ventricular ejection fraction; F > M, female to male; HLA, human leukocyte antigen; BMI, body mass index. *Under the new allocation system (status 1-6).

TABLE E2. Trends in HCV NAT⁺ transplantation characteristics over time

Characteristic	2015-6 (N = 4359)	2017 (N = 2503)	2018 (N = 2498)	2019 (N = 1707)	P value
Recipient					
Age, y, mean (SD)	53.42 (12.61)	53.41 (12.91)	53.77 (12.84)	52.71 (13.24)	.073
Male sex, n (%)	3223 (73.9)	1826 (73.0)	1785 (71.5)	1236 (72.4)	.156
Ethnicity, n (%)					.073
White	2780 (63.8)	1604 (64.1)	1636 (65.5)	1109 (65.0)	
Asian	170 (3.9)	80 (3.2)	92 (3.7)	64 (3.7)	
Black	954 (21.9)	588 (23.5)	530 (21.2)	335 (19.6)	
Hispanic	397 (9.1)	208 (8.3)	210 (8.4)	180 (10.5)	
Other	58 (1.3)	23 (0.9)	30 (1.2)	19 (1.1)	
Education, n (%)					<.001
None	2 (0.0)	5 (0.2)	5 (0.2)	3 (0.2)	
Grade school (0-8)	146 (3.3)	65 (2.6)	74 (3.0)	63 (3.7)	
High school (9-12)	1661 (38.1)	941 (37.6)	899 (36.0)	627 (36.8)	
College/technical school	1209 (27.7)	692 (27.6)	731 (29.3)	453 (26.6)	
Associate/bachelor degree	882 (20.2)	529 (21.1)	506 (20.3)	339 (19.9)	
Post-college degree	388 (8.9)	236 (9.4)	219 (8.8)	162 (9.5)	
Unknown	71 (1.6)	35 (1.4)	64 (2.6)	59 (3.5)	
Primary payment, n (%)					.002
Private insurance	16 (0.4)	11 (0.4)	9 (0.4)	19 (1.1)	
Public insurance	2000 (45.9)	1186 (47.4)	1162 (46.5)	828 (48.5)	
Other (self, donation, foreign government)	2343 (53.8)	1306 (52.2)	1327 (53.1)	860 (50.4)	
At the time of transplantation					
Creatinine, mg/dL, mean (SD)	1.27 (0.85)	1.23 (0.51)	1.23 (0.46)	1.21 (0.48)	.009
Total bilirubin, mg/dL, mean (SD)	0.91 (1.25)	0.93 (1.52)	0.96 (1.83)	1.00 (1.90)	.225
MELD-XI score, mean (SD)	9.57 (5.47)	9.30 (5.42)	9.27 (5.39)	9.23 (5.73)	.041
ECMO, n (%)	42 (1.0)	19 (0.8)	42 (1.7)	89 (5.2)	<.001
IABP, n (%)	327 (7.5)	207 (8.3)	227 (9.1)	498 (29.2)	<.001
VAD, n (%)	2206 (50.6)	1268 (50.7)	1169 (46.8)	608 (35.6)	<.001
Inotropic support, n (%)	1623 (37.2)	878 (35.1)	810 (32.4)	641 (37.6)	<.001
HCV seropositive, n (%)	83 (1.9)	49 (2.0)	71 (2.8)	32 (1.9)	.045
Diabetes, n (%)	1243 (28.5)	689 (27.5)	690 (27.6)	440 (25.8)	.205
Previous heart transplantation	87 (2.0)	56 (2.2)	65 (2.6)	57 (3.3)	.017
Status at transplantation, n (%)					<.001
High (1A or 1-2*)	2926 (67.1)	1674 (66.9)	1608 (64.4)	965 (56.5)	
Intermediate (1B or 3-4*)	1329 (30.5)	772 (30.8)	799 (32.0)	681 (39.9)	
Low (2 or 5-6*)	104 (2.4)	57 (2.3)	91 (3.6)	61 (3.6)	
Donor					
Age, y, mean (SD)	31.98 (11.22)	31.83 (11.04)	32.43 (10.73)	32.88 (11.43)	.007
Male sex, n (%)	3026 (69.4)	1721 (68.8)	1734 (69.4)	1221 (71.5)	.267
Ethnicity, n (%)					.718
White	2786 (63.9)	1646 (65.8)	1571 (62.9)	1090 (63.9)	
Asian	80 (1.8)	35 (1.4)	43 (1.7)	23 (1.3)	
Black	721 (16.5)	390 (15.6)	415 (16.6)	272 (15.9)	
Hispanic	703 (16.1)	388 (15.5)	424 (17.0)	292 (17.1)	
Other	69 (1.6)	44 (1.8)	45 (1.8)	30 (1.8)	
History of smoking, n (%)	2035 (46.7)	1111 (44.4)	1120 (44.8)	708 (41.5)	.003
History of cocaine use, n (%)	918 (21.3)	580 (23.4)	639 (26.1)	456 (27.0)	<.001
History of other drug use, n (%)	2308 (53.4)	1369 (55.0)	1444 (58.5)	989 (58.3)	<.001
Current alcohol abuse, n (%)	713 (16.7)	420 (17.1)	444 (18.2)	299 (18.0)	.408
Inotropic support, n (%)	1738 (40.0)	928 (37.2)	936 (37.6)	679 (39.8)	.056
LVEF <45%, n (%)	29 (0.7)	5 (0.2)	12 (0.5)	12 (0.7)	.049
Donor-recipient sex mismatch (F > M), n (%)	592 (13.6)	354 (14.1)	327 (13.1)	186 (10.9)	.015
ABO compatible, n (%)	614 (14.1)	332 (13.3)	346 (13.9)	259 (15.2)	.37

(Continued)

TABLE E2. Continued

Characteristic	2015-6 (N = 4359)	2017 (N = 2503)	2018 (N = 2498)	2019 (N = 1707)	P value
HLA mismatch, n (%)					.784
0	4 (0.1)	1 (0.0)	3 (0.1)	3 (0.2)	
1	19 (0.5)	11 (0.5)	10 (0.4)	4 (0.3)	
2	116 (2.9)	48 (2.1)	64 (2.8)	43 (2.8)	
3	453 (11.3)	243 (10.5)	234 (10.2)	166 (10.7)	
4	1026 (25.6)	602 (26.1)	573 (24.9)	370 (23.9)	
5	1476 (36.9)	875 (37.9)	877 (38.1)	600 (38.8)	
6	909 (22.7)	530 (22.9)	538 (23.4)	360 (23.3)	
BMI discrepancy >20%, n (%)	1678 (38.5)	991 (39.6)	971 (38.9)	712 (41.8)	.128
Distance, mi, mean (SD)	149.81 (195.86)	152.50 (194.03)	169.97 (202.41)	264.75 (235.39)	<.001
Ischemic time, h, mean (SD)	3.06 (1.03)	3.04 (1.07)	3.05 (1.03)	3.39 (1.01)	<.001
Region, n (%)					<.001
1	184 (4.2)	121 (4.8)	135 (5.4)	107 (6.3)	
2	514 (11.8)	284 (11.3)	252 (10.1)	167 (9.8)	
3	504 (11.6)	326 (13.0)	299 (12.0)	192 (11.2)	
4	509 (11.7)	262 (10.5)	245 (9.8)	155 (9.1)	
5	731 (16.8)	363 (14.5)	398 (15.9)	292 (17.1)	
6	162 (3.7)	95 (3.8)	103 (4.1)	52 (3.0)	
7	358 (8.2)	212 (8.5)	233 (9.3)	180 (10.5)	
8	279 (6.4)	175 (7.0)	189 (7.6)	122 (7.1)	
9	231 (5.3)	128 (5.1)	154 (6.2)	113 (6.6)	
10	360 (8.3)	198 (7.9)	175 (7.0)	136 (8.0)	
11	527 (12.1)	339 (13.5)	315 (12.6)	191 (11.2)	

SD, Standard deviation; MELD-XI, Model for End-stage Liver Disease excluding INR; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; VAD, ventricular assist device; HCV, hepatitis C virus; LVEF, left ventricular ejection fraction; F > M, female to male; HLA, human leukocyte antigen; BMI, body mass index. *Under the new allocation system (status 1-6).

TABLE E3. Institutional differences in HCV NAT⁺ heart transplants

Region	Transplantation center	HCV NAT ⁺ transplantations (N = 326)	
		n	% of total
Region 1	1	26	8.0
	2	13	4.0
	3	5	1.5
	4	3	0.9
Region 2	5	11	3.4
	6	8	2.5
	7	5	1.5
	8	4	1.2
	9	1	0.3
	10	1	0.3
	11	1	0.3
Region 3	12	7	2.1
	13	2	0.6
	14	2	0.6
	15	1	0.3
	16	1	0.3
Region 4	17	11	3.4
	18	1	0.3
	19	1	0.3
Region 5	20	22	6.7
	21	6	1.8
	22	3	0.9
	23	2	0.6
Region 6	24	7	2.1
Region 7	25	3	0.9
Region 8	26	3	0.9
	27	2	0.6
Region 9	28	19	5.8
	29	9	2.8
	30	9	2.8
	31	8	2.5
	32	5	1.5
Region 10	33	24	7.4
	34	12	3.7
Region 11	35	68	20.9
	36	17	5.2
	37	1	0.3
	38	1	0.3
	39	1	0.3

HCV, Hepatitis C virus; NAT, nucleic acid testing.

TABLE E4. Baseline characteristics for unmatched and propensity matched cohorts

Characteristic	Total sample			Matched (3:1)		
	HCV NAT ⁻ (N = 11,067)	HCV NAT ⁺ (N = 326)	P	HCV NAT ⁻ (N = 783)	HCV NAT ⁺ (N = 261)	P
Sex mismatch (F > M), n (%)	1459 (13.2)	36 (11.0)	.066	0.15 (0.35)	0.11 (0.31)	.103
ABO identical, n (%)	9516 (86.0)	278 (85.3)	.02	698 (89.1)	223 (85.4)	.111
HLA mismatch, n (%)	5.66 (1.07)	5.58 (1.07)	.072	4.65 (1.09)	4.58 (1.07)	.063
BMI discrepancy >20%, n (%)	4352 (39.4)	140 (42.9)	.073	0.44 (0.50)	0.44 (0.50)	.008
Donor						
Age, y, mean (SD)	32.18 (11.11)	33.35 (7.67)	.122	33.43 (10.26)	33.46 (7.95)	.004
Ethnicity, n (%)						
White	7093 (64.1)	270 (82.8)	.434	616 (78.7)	212 (81.2)	.064
Asian	181 (1.6)	2 (0.6)	.097	0 (0.0)	1 (0.4)	.088
Black	1798 (16.2)	24 (7.4)	.278	80 (10.2)	21 (8.0)	.075
Hispanic	1807 (16.3)	24 (7.4)	.28	71 (9.1)	21 (8.0)	.037
Other	188 (1.7)	6 (1.8)	.011	16 (2.0)	6 (2.3)	.018
History of smoking, n (%)	4974 (44.9)	165 (50.6)	.114	0.45 (0.50)	0.48 (0.50)	.049
History of cocaine use, n (%)	2593 (23.8)	182 (57.4)	.73	0.54 (0.50)	0.56 (0.50)	.046
History of other drug use, n (%)	6110 (55.7)	287 (88.9)	.798	0.91 (0.29)	0.90 (0.31)	.03
Current alcohol abuse, n (%)	1876 (17.3)	63 (20.1)	.07	0.25 (0.43)	0.19 (0.39)	.143
LVEF <45%, n (%)	58 (0.5)	3 (0.9)	.047	0.01 (0.07)	0.01 (0.09)	.032
Recipient						
Age, y, mean (SD)	53.39 (12.83)	55.23 (11.93)	.149	54.80 (11.89)	55.08 (11.50)	.023
Ethnicity, n (%)						
White	7129 (64.4)	223 (68.4)	.085	521 (66.5)	170 (65.1)	.03
Asian	406 (3.7)	9 (2.8)	.051	24 (3.1)	7 (2.7)	.023
Black	2407 (21.7)	65 (19.9)	.045	172 (22.0)	58 (22.2)	.006
Hispanic	995 (9.0)	24 (7.4)	.059	59 (7.5)	21 (8.0)	.019
Other	130 (1.2)	5 (1.5)	.031	7 (0.9)	5 (1.9)	.087
At time of transplantation						
Creatinine, mg/dL, mean (SD)	1.24 (0.65)	1.26 (0.40)	.023	1.23 (0.42)	1.28 (0.42)	.107
Total bilirubin, mg/dL, mean (SD)	0.94 (1.57)	0.92 (0.78)	.014	0.99 (1.92)	0.93 (0.72)	.043
MELD-XI score, mean (SD)	9.39 (5.48)	9.92 (5.30)	.098	9.59 (5.18)	10.28 (5.30)	.132
ECMO, n (%)	192 (1.7)	9 (2.8)	.069	0.03 (0.17)	0.03 (0.18)	.022
VAD, n (%)	5251 (47.4)	147 (45.1)	.047	0.44 (0.50)	0.41 (0.49)	.067
HCV seropositive, n (%)	235 (2.1)	18 (5.5)	.178	0.05 (0.22)	0.06 (0.23)	.022
Diabetes	2.01 (21.20)	4.65 (55.19)	.063	1.56 (0.91)	5.39 (61.68)	.088
Previous heart transplant	265 (2.4)	10 (3.1)	.041	0.03 (0.16)	0.04 (0.19)	.073
Status at transplantation						
High (1A or 1-2*)	7173 (64.8)	150 (46.0)	.385	373 (47.6)	120 (46.0)	.033
Intermediate (1B or 3-4*)	3581 (32.4)	155 (47.5)	.314	362 (46.2)	122 (46.7)	.01
Low (2 or 5-6*)	313 (2.8)	21 (6.4)	.173	48 (6.1)	19 (7.3)	.046
Distance, mi, mean (SD)	172.70 (207.40)	299.03 (235.51)	.569	296.31 (281.14)	305.79 (243.61)	.036
Ischemic time, h, mean (SD)	3.10 (1.04)	3.52 (0.97)	.409	3.44 (1.14)	3.46 (0.98)	.026
Year of transplantation, n (%)						
2015	1824 (16.5)	1 (0.3)	.61	4 (0.5)	1 (0.4)	.019
2016	2535 (22.9)	12 (3.7)	.59	29 (3.7)	9 (3.4)	.014
2017	2503 (22.6)	49 (15.0)	.195	115 (14.7)	41 (15.7)	.028
2018	2498 (22.6)	137 (42.0)	.425	334 (42.7)	110 (42.1)	.01
2019	1707 (15.4)	127 (39.0)	.548	301 (38.4)	100 (38.3)	.003
Region						
1	547 (4.9)	47 (14.4)	.325	17 (2.2)	4 (1.5)	.047
2	1217 (11.0)	31 (9.5)	.049	104 (13.3)	31 (11.9)	.042
3	1321 (11.9)	13 (4.0)	.297	30 (3.8)	11 (4.2)	.019

(Continued)

TABLE E4. Continued

Characteristic	Total sample			Matched (3:1)		
	HCV NAT ⁻ (N = 11,067)	HCV NAT ⁺ (N = 326)	P	HCV NAT ⁻ (N = 783)	HCV NAT ⁺ (N = 261)	P
4	1171 (10.6)	13 (4.0)	.256	33 (4.2)	12 (4.6)	.019
5	1784 (16.1)	33 (10.1)	.178	94 (12.0)	32 (12.3)	.008
6	412 (3.7)	7 (2.1)	.093	29 (3.7)	7 (2.7)	.058
7	983 (8.9)	3 (0.9)	.375	4 (0.5)	3 (1.1)	.07
8	765 (6.9)	5 (1.5)	.27	12 (1.5)	4 (1.5)	<.001
9	626 (5.7)	50 (15.3)	.32	120 (15.3)	44 (16.9)	.042
10	869 (7.9)	36 (11.0)	.109	100 (12.8)	34 (13.0)	.008
11	1372 (12.4)	88 (27.0)	.373	240 (30.7)	79 (30.3)	.008

The threshold for significant difference was defined as standardized mean difference (SMD) >0.2. *HCV*, Hepatitis C virus; *NAT*, nucleic acid testing; *HLA*, human leukocyte antigen; *BMI*, body mass index; *SD*, standard deviation; *LVEF*, left ventricular ejection fraction; *MELD-XI*, Model for End-stage Liver Disease excluding INR; *ECMO*, extracorporeal membrane oxygenation; *VAD*, ventricular assist device. *Under the new allocation system (status 1-6).