Trends and three-year outcomes of hepatitis C virus–viremic donor heart transplant for hepatitis C virus–seronegative recipients

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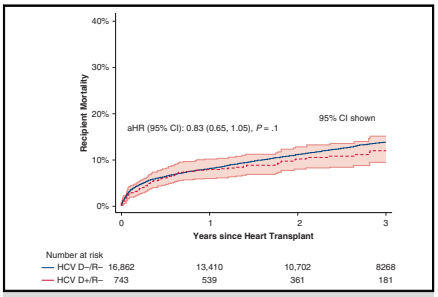
ABSTRACT

Objective: Heart transplants (HTs) from hepatitis C virus (HCV)-viremic donors to HCV-seronegative recipients (HCV D+/R–) have good 6-month outcomes, but practice uptake and long-term outcomes overall and among candidates on mechanical circulatory support (MCS) have yet to be established.

Methods: Using the Scientific Registry of Transplant Recipients, we identified US adult HCV-seronegative HT recipients (R–) from 2015 to 2021. We classified donors as HCV-seronegative (D–) or HCV-viremic (D+). We used multivariable regression to compare post-HT extracorporeal membranous oxygenation, dialysis, pacemaker, acute rejection, and risk of post-HT mortality between HCV D+/R– and HCV D–/R–. Models were adjusted for donor, recipient, and transplant characteristics and center HT volume. We performed subgroup analyses of recipients bridged with MCS.

Results: From 2015 to 2021, the number of HCV D+/R– HT increased from 1 to 181 and the number of centers performing HCV D+/R– HT increased from 1 to 60. Compared with HCV D–/R– recipients, HCV D+/R– versus D–/R– recipients overall and among patients bridged with MCS had similar odds of post-HT extracorporeal membranous oxygenation, dialysis, pacemaker, and acute rejection; and mortality risk at 30 days, 1 year, and 3 years (all $P > .05$). High center HT volume but not HCV D+/R– volume (<5 vs >5 in any year) was associated with lower mortality for HCV D+/R– HT.

Conclusions: HCV D+/R– and D–/R– HT have similar outcomes at 3 years' posttransplant. These results underscore the opportunity provided by HCV D+/R– HT, including among the growing population bridged with MCS, and the potential benefit of further expanding use of HCV+ allografts. (JTCVS Open 2022;12:269-79)



Mortality among US recipients of HCV-viremic and HCV-seronegative heart transplants.

CENTRAL MESSAGE

Heart transplants from donors with and without HCV viremia into recipients without HCV, including MCS-bridged recipients, have similar perioperative outcomes and survival at 3 years posttransplant.

PERSPECTIVE

Hepatitis C virus (HCV)-viremic donors represent a growing portion of the donor pool, mostly due to the ongoing opioid epidemic. Understanding the long-term outcomes of heart transplants from HCV-viremic donors into HCV-seronegative recipients, including MCS-bridged recipients, is critical to encourage uptake of this practice, which will further expand the donor pool and access to transplantation.

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Abbreviations and Acronyms

aHR = adjusted hazard ratio
aOR = adjusted odds ratio
D+ = HCV-viremic donor
D– = HCV-seronegative donor
DAAs = direct-acting antivirals
DCD = donation after circulatory death
ECMO = extracorporeal membranous oxygenation
HCV = hepatitis C virus
HT = heart transplant
IABP = intra-aortic balloon pump
IQR = interquartile range
LVAD = left ventricular assist device
MCS = mechanical circulatory support
R– = HCV-seronegative recipient
SRTR = Scientific Registry of Transplant Recipients

The number of candidates on the heart transplant (HT) waitlist in the United States has grown 34% over the past decade,[1] underscoring the need to expand the organ donor pool to meet demand. The introduction of direct-acting antivirals (DAAs) to cure hepatitis C virus (HCV) infection in 2013[2,3] created the possibility of transplanting hepatitis C–viremic donors (HCV D+) organs into HCV-seronegative recipients (HCV R–), with subsequent cure of the HCV infection. Given the rise in hepatitis C–viremic donors due to the ongoing opioid epidemic,[4,5] these donors could provide a safe and possibly growing expansion of the organ donor pool.

Early, single-center results of HCV D+/R– transplants in the United States showed a dramatic decrease in waitlist time,[6-8] with Schlendorf and colleagues[6] reporting a mean time to HT after consenting to consider HCV-viremic organs of 11 days. All patients in these studies were cured of HCV viremia with the use of DAAs,[6-10] with no adverse impact on renal function.[11] The landmark pilot trial of 44 HCV D+/R– heart and lung transplants by Woolley and colleagues[12] in 2019 similarly found that administering DAAs posttransplant cleared HCV viremia and that all patients were alive with excellent graft function and no detectable HCV infection 6 months' posttransplant. While these early results were encouraging, longer-term results of HCV D+/R–transplants are needed to determine whether greater use of these HCV-viremic donor organs is warranted.

Of note, in the study by Woolley and colleagues,[12] 86% of HT recipients were on mechanical circulatory support (MCS) with a ventricular assist device pretransplant. While the percentage of HT recipients bridged with left ventricular assist devices (LVADs) decreased from 47.8% in 2017 to 33.4% in 2020, the use of other MCS devices such as intra-aortic balloon bump (IABP), right ventricular assist devices, and extracorporeal membrane oxygenation (ECMO) have increased, with an overall increase in the total percentage of recipients who were on pretransplant MCS.[1,13,14] Given that more than one-half of HT recipients are bridged with MCS, and that these represent the sickest patients on the waitlist, careful evaluation of the outcomes of HCV D+/R– transplants in this population is needed.

Using national registry data, we evaluated trends in the annual number of HCV D+/R– transplants and the number of transplant centers performing HCV D+/R– HT. We also compared outcomes including acute rejection and mortality out to 3 years post-HT for HCV D+/R– versus HCV D–/R– transplants. We performed subgroup analyses of these outcomes among HT recipients bridged with different types of MCS.

METHODS

Data Source

This study used data from the United States Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the activities of the Organ Procurement and Transplantation Network and SRTR contractors. These data have been described elsewhere.[15]

Study Population

Using SRTR data, we identified all HCV-seronegative adult (≥18 years old) HT recipients (R–) in the United States between January 2015 and December 2021. We classified recipients as seronegative if they had a negative HCV antibody test. Similarly, donors were classified as seronegative (D–) or viremic (D+) if they had a reactive HCV nucleic acid test. We excluded recipients of multiorgan transplants and those coded as receiving heterotopic HTs. This study was deemed exempt for the need for institutional review board approval by the Johns Hopkins Institutional Review Board (NA_00042871, October 28, 2010).

Temporal Trends in the Use of Heart Allografts From HCV-Viremic Donors for Transplant

We quantified the number of heart transplants from HCV-viremic donors to HCV-seronegative recipients (HCV D+/R–) performed each year from 2015 to 2021. We also quantified the number of transplant centers performing HCV D+/R– heart transplants during each year of the study period. Transplant centers were classified as high-volume if they performed an average of 20 HTs or more per year during the study period. Given the dynamic number of HCV D+/R– HTs by center during the time period, transplant centers were defined as high-volume for HCV D+/R– HT if they performed at least 5 HCV D+/R– HTs in any year from 2015 to 2021.

Donor and Recipient Characteristics

We compared the donor, recipient, and transplant characteristics of HCV D+/R– transplants and HCV-negative donor with HCV-negative recipient (HCV D–/R–) transplants using χ^2 and Wilcoxon rank-sum tests.

Posttransplant Outcomes

We studied incidence of posttransplant outcomes including acute rejection, ECMO, posttransplant incident dialysis, posttransplant pacemaker,

and mortality. We included dialysis as an outcome as the result of reports of a glomerulonephritis-type picture attributed to de novo HCV infection in kidney transplant recipients.[16] We included posttransplant pacemaker as an outcome as the result of previous literature suggesting that HCV infection might be associated with greater risk of arrhythmia, and that treatment with DAAs could interact with certain antiarrhythmic agents, such as amiodarone, causing significant arrhythmia.[17-20] In SRTR, mortality is reported by individual transplant centers, and ascertainment is supplemented through linkage to the Social Security Master Death File. We also compared the length of stay between HCV D+/R– and D–/R– transplants using rank-sum testing.

We used multivariable logistic regression to compare the adjusted odds of binary posttransplant outcomes including acute rejection and post-HT ECMO, incident dialysis, and pacemaker placement between HCV D+/R– and HCV D–/R– HT recipients. Models were adjusted for donor age, sex, and race; recipient age, sex, race, and pre-HT ECMO, IABP, and bilirubin; ischemic time, and high-volume (>20 HT/year) center. Our threshold for identifying high-volume centers as those performing more than 20 heart transplants per year was based on previous studies.[21,22] When selecting covariates for our multivariable analysis, we a priori included donor age, sex, and race and recipient age, sex, and race as covariates in our multivariable model. Additional covariates were included if they met the threshold for significance at $P < .1$ in univariate analysis.

For mortality, we performed time-to-event analysis and visualized the incidence of each outcome using Kaplan–Meier curves. We used multivariable Cox regression to compare risk of post-HT mortality between HCV D+/R– and HCV D–/R–, adjusting for donor age, sex, and race; recipient age, sex, race, and pre-HT ECMO, IABP, and bilirubin; ischemic time, and high-volume (>20 HT/year) center. We followed recipients until the outcome of interest or administrative censorship on February 22, 2022.

Characteristics of centers performing HCV D+/R– HT and centers performing no HCV D+/R– HT were compared. We used rank-sum testing to compare median transplant volume as well as median waitlist time among HT recipients. We used Fisher exact testing to compare whether they were high-volume liver transplant centers. We defined high-volume liver transplant centers as those performing at least 80 liver transplants, on average, per year of the study period based on previous literature and because this fell at approximately the 90th percentile for liver transplant center volume.[23-25]

Characteristics of high-adopter centers compared with low-adopter centers were compared. For this analysis, we limited the study period to 2019 to 2021 based on when the majority of centers that currently perform HCV D+/R– transplants adopted this practice. High-adopter centers were defined as programs with ≥15% of total HT from 2019 to 2021 being HCV D+/R– transplants (n = 14). Low-adopter centers were defined as all other centers who had performed at least 1 HCV D+/R– HT (n = 60). We used χ^2 testing to compare primary recipient source of payment, recipient education status, donation after circulatory death (DCD) transplants, organ sharing, and United Network for Organ Sharing region. We used rank-sum testing to compare median donor age, median ischemic time, and median days on the waitlist.

Subgroup Analyses of Patients Bridged With MCS

We performed subgroup analyses of recipients bridged to HT with MCS. We categorized recipients bridged with MCS into 4 groups based on support device present immediately before transplantation: (1) durable LVAD (consisting of HeartMate II, HeartMate 3, and HeartWare HVAD); (2) IABP; (3) ECMO; and (4) temporary ventricular assist devices (consisting of TandemLife ProtekDuo, TandemHeart, CentriMag, and Impella CP/RP/2.5/5.0). However, due to limited sample size for ECMO (N = 13) and temporary ventricular assist devices (N = 21) devices, subgroup analyses for these types of devices were not performed. We compared baseline recipient, donor, and transplant characteristics and posttransplant outcomes between HCV D+/R– and HCV D–/R– transplants as described previously. For the LVAD and IABP groups, models were adjusted for donor age, sex, and race; recipient age, sex, race, and bilirubin; ischemic time, and high-volume (≥20 HT/year) center. All analyses were performed using Stata 16.1/SE for Windows (StataCorp).

RESULTS

Use of HCV D+/R– HTs

The first HCV D+/R– HT was performed in 2015; only 1 HCV D+/R– HT was performed that year, compared with 2098 HCV D–/R– HT. In 2021, 181 HCV D+/R– HT were performed, compared with 2433 HCV D–/R– HT; the maximum annual number of HCV D+/R– transplants to date is 204 HT performed in 2019. From 2019 to 2021, 557 HCV D+/R– HT transplants were performed, accounting for 7.5% of all HTs performed during those years (Figure 1, *A*). The number of transplant centers performing HCV D+/R– HT also increased over the study period, from 1 in 2015 to 60 in 2021 (Figure 1, *B*). In 2021, 48.8% of all the centers that performed HTs were performing HCV D+/R– HTs. Among high-volume HT centers, 57/73 (78.1%) performed at least 1 HCV D+/R– HT during the study period. Among low-volume HT centers, 18 of 67 (26.9%) performed at least one HCV D+/R– HT.

Study Population

Donors in HCV D–/R– HTs were older (median 33 vs 31 years old, $P < .001$) and more likely to be male (75.2% vs 70.7%, $P = .01$) and of White race (83.0% vs 63.0%, $P < .001$, Table 1) than donors in HCV D+/R– HT. Recipients in HCV D+/R– HTs were older (median 58 vs 57 years old, $P < .001$) and more likely to be male (77.7% vs 73.2%, $P = .006$), of White race (67.2% vs 63.1%, $P = .02$), and of blood type O (47.5% vs 39.2%, $P < .001$). Cardiomyopathy diagnosis distribution was similar between the 2 groups. Of the total study population, 60.4% were bridged to HT with MCS, with a similar frequency of pretransplant ventilator, ECMO, IABP, and VAD between the 2 groups. Median (interquartile range [IQR]) waitlist time was similar between HCV D+/R– and HCV D–/R– transplant recipients (69 [13-241] vs 68 [17-257] days, $P = .18$). A similar percentage of HCV D+/R– and D–/R– recipients received DCD HTs (1.6% vs 1.5%, $P = .87$). Ischemic time was longer for HCV D+/R– HT than for HCV D–/R– HT (median 3.47 vs 3.25 hours, $P < .001$).

Of the 138 transplant centers who performed at least 1 HT during the study period, 74 (54%) performed at least 1 HCV D+/R– HT. Compared with centers that performed no HCV D+/R– HT, centers that performed at least one

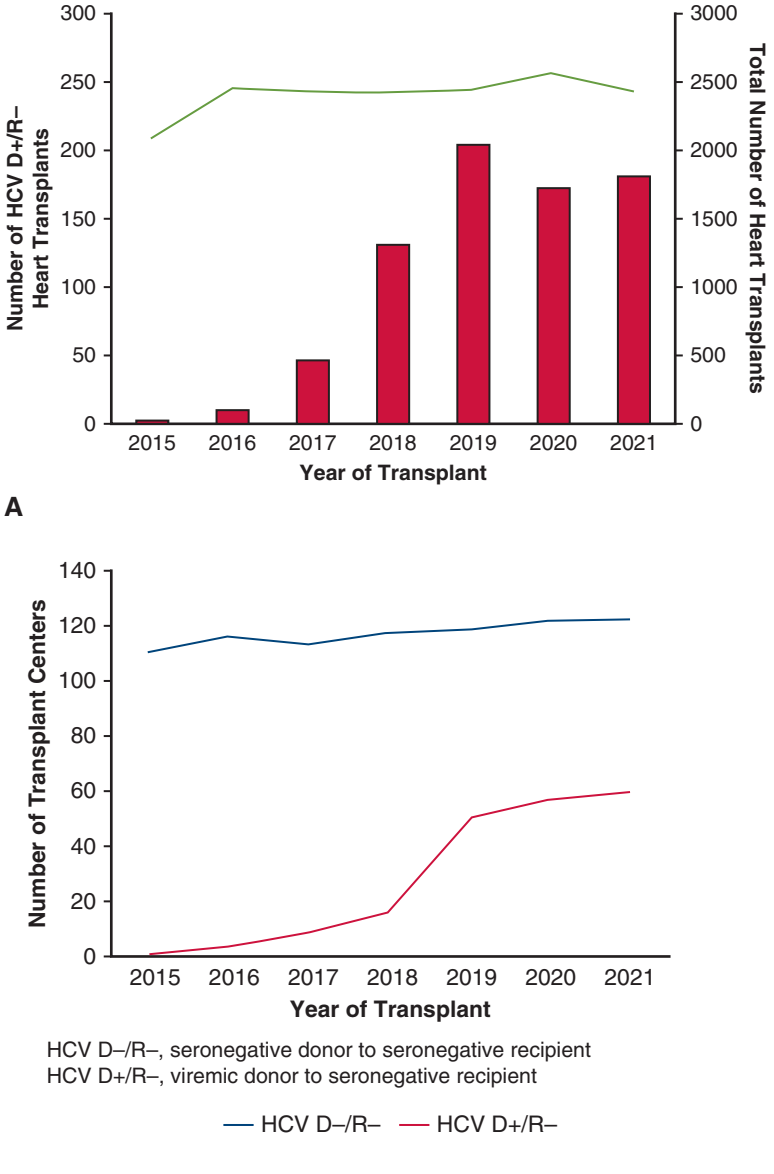

FIGURE 1. Number of (A) transplants and (B) transplant centers by donor and recipient HCV status. *HCV*, Hepatitis C virus; *HCV D+/R–*, viremic donor to seronegative recipient; *HCV D–/R–*, seronegative donor to seronegative recipient.

HCV D+/R– HT had greater overall HT volumes during the study period (median [IQR] 163 [108-238] vs 30 [4-96] transplants, $P < .001$) but similar median (IQR) waitlist times for recipients (205 [149-280] vs 229 [148-398] days, $P = .11$). Centers that performed at least 1 HCV D+/R– HT during the study period were more likely than centers who performed no HCV D+/R– HT to also be a high-volume liver transplant center (17.6% vs 1.5%, $P = .001$).

Between 2019 and 2021, 74 centers performed at least 1 HCV D+/R– HT. Of these, 14 (18.9%) were high-adopter centers with HCV D+/R– transplants making up 19.5% of total HT, and 60 (81.1%) were low-adopter centers with HCV D+/R– making up 6.5% of HT (Table 2). Recipients at high-adopter centers were more likely to be supported by public payer insurance (56.6% vs 49.2%, $P < .001$). High-adopter centers were also more likely to perform transplants using DCD donors (6.2% vs 3.8%, $P < .001$) and nationally shared organs (81.8% vs 75.2%, $P < .001$). Recipients at high-adopter centers had significantly shorter waitlist times (23 [6-149] vs 30 [9-157] days, $P = .002$).

Overall Transplant Outcomes

Post-HT, HCV D+/R– recipients had similar adjusted odds of post-HT ECMO (adjusted odds ratio [aOR], 0.62;

TABLE 1. Donor, recipient, and transplant characteristics by donor and recipient HCV status

Characteristic	HCV D–/R–	HCV D+/R–	*P* value
N (%)	16,862	743	
Donor characteristics			
Age, y, median (IQR)	31 (23-40)	33 (29-39)	<.001
Male sex	11,923 (70.7%)	559 (75.2%)	.01
White race	10,619 (63.0%)	617 (83.0%)	<.001
Recipient characteristics			
Age, y, median (IQR)	57 (46, 63)	58 (49, 64)	<.001
Male sex	12,337 (73.2%)	577 (77.7%)	.006
White race	10,641 (63.1%)	499 (67.2%)	.02
BMI, kg/m^2, median (IQR)	27.5 (24.1-31.3)	28.0 (24.6-32.0)	.002
Creatinine, median (IQR)	1.15 (0.92-1.41)	1.19 (0.98-1.44)	.09
Bilirubin, median (IQR)	0.70 (0.49-1.00)	0.70 (0.40-1.00)	.82
Blood type			<.001
O	6609 (39.2%)	353 (47.5%)	
A	6724 (39.9%)	274 (36.9%)	
B	2611 (15.5%)	95 (12.8%)	
AB	918 (5.4%)	21 (2.8%)	
Cardiomyopathy diagnosis			.13
Dilated	14,170 (84.0%)	632 (85.1%)	
Restrictive	694 (4.1%)	35 (4.7%)	
Ischemic	415 (2.5%)	23 (3.1%)	
Nonischemic	1582 (9.4%)	53 (7.1%)	
Pretransplant characteristics			
On ventilator	238 (1.4%)	10 (1.3%)	.88
On ECMO	364 (2.2%)	10 (1.3%)	.13
On IABP	1699 (10.1%)	87 (11.7%)	.15
On VAD	5240 (31.1%)	228 (30.7%)	.82
Waitlist time, d, median (IQR)	68 (17-257)	69 (13-241)	.18
Donation after circulatory death (DCD)	260 (1.5%)	12 (1.6%)	.87
Heart allograft ischemia time, h, median (IQR)	3.25 (2.52-3.85)	3.47 (2.95-4.02)	<.001

HCV, Hepatitis C virus; *HCV D–/R–*, seronegative donor to seronegative recipient; *HCV D+/R–*, viremic donor to seronegative recipient; *IQR*, interquartile range; *BMI*, body mass index; *ECMO*, extracorporeal membranous oxygenation; *IABP*, intra-aortic balloon pump; *VAD*, ventricular assist device.

95% confidence interval [CI], 0.30-1.25), dialysis (aOR, 0.89; 95% CI, 0.71-1.12), pacemaker (aOR, 0.96; 95% CI, 0.58-1.60), and acute rejection (aOR, 0.84; 95% CI, 0.69-1.03) compared with HCV D–/R– recipients, accounting for donor, recipient, and transplant characteristics. Median (IQR) hospital length of stay was similar for HCV D+/R– and HCV D–/R– recipients (16 [12-24] vs 16 [11-24] days, $P = .54$).

The risk of mortality for HCV D+/R– versus HCV D–/R– HT was similar at 30 days (adjusted hazard ratio [aHR], 0.78; 95% CI, 0.51-1.20), 1 year (aHR, 0.90; 95% CI, 0.68-1.17), and 3 years (aHR, 0.83; 95% CI, 0.65-1.05) posttransplant after adjusting for donor, recipient, and transplant characteristics (Figure 2). Mortality was not significantly different for HCV D+/R– versus D–/R– HT recipients at centers by overall HT volume (high vs low HT volume: aHR, 0.63; 95% CI, 0.32-1.22, $P = .2$) or by HCV D+/R– HT volume (high vs low HCV HT volume: aHR, 0.86; 95% CI, 0.54-1.39, $P = .5$). All-cause graft failure was also similar for HCV D+/R– and HCV D–/R– HT recipients (aHR, 0.81; 95% CI, 0.64-1.02, $P = .07$).

Subgroup Analysis of Recipients Bridged With Durable LVADs

Of the 6448 (36.6%) total study population recipients bridged with LVADs, 270 (4.2%) were HCV D+/R– transplants. Baseline recipient, donor, and transplant characteristics are shown in Table 3. After we adjusted for donor, recipient, and transplant characteristics, the risk of mortality (Figure 3) for HCV D+/R– versus HCV D–/R– HT bridged with LVAD was similar at 30 days (aHR, 0.67; 95% CI, 0.33-1.35), 1 year (aHR, 0.79; 95% CI, 0.51-1.22), and 3 years (aHR, 0.68; 95% CI, 0.46-1.01)

TABLE 2. Center characteristics of high- and low-adopter programs, 2019-2021

Characteristic	Low-adopter program	High-adopter program	*P* value
N	5433	1035	
HCV D+/R– transplants	355 (6.5%)	202 (19.5%)	<.001
Primary source of recipient payment			<.001
Private insurance	2710 (49.9%)	448 (43.3%)	
Public insurance	2674 (49.2%)	585 (56.6%)	
Self	28 (0.5%)	1 (0.1%)	
Other	21 (0.4%)	0 (0.0%)	
Recipient educational attainment			.058
High school or less	2078 (38.3%)	425 (41.1%)	
Attended college/technical school	1440 (26.5%)	254 (24.6%)	
Associate/bachelor's degree	1173 (21.6%)	222 (21.5%)	
Postcollege graduate degree	534 (9.8%)	82 (7.9%)	
Unknown	207 (3.8%)	51 (4.9%)	
Donor age, y, median (IQR)	32 (25-40)	32 (26-40)	.027
Donation after circulatory death	208 (3.8%)	64 (6.2%)	<.001
Organ shared nationally	4087 (75.2%)	847 (81.8%)	<.001
Ischemic time, h, median (IQR)	3.5 (2.8-4.1)	3.5 (2.9-3.9)	.13
Total days on waitlist, median (IQR)	30 (9-157)	23 (6-149)	.002
UNOS region			<.001
1	371 (6.8%)	45 (4.3%)	
2	398 (7.3%)	158 (15.3%)	
3	689 (12.7%)	122 (11.8%)	
4	342 (6.3%)	0 (0.0%)	
5	929 (17.1%)	8 (0.8%)	
6	155 (2.9%)	0 (0.0%)	
7	491 (9.0%)	38 (3.7%)	
8	533 (9.8%)	0 (0.0%)	
9	392 (7.2%)	141 (13.6%)	
10	359 (6.6%)	148 (14.3%)	
11	774 (14.2%)	375 (36.2%)	

High-adopter program (n = 14) defined as centers with ≥15% of transplants being HCV D+/R– between 2019 and 2021. Low-adopter program (n = 60) defined as all other centers performing at least one HCV D+/R– heart transplant. *HCV*, Hepatitis C virus; *HCV D+/R–*, viremic donor to seronegative recipient; *IQR*, interquartile range; *UNOS*, United Network for Organ Sharing.

posttransplant. In recipients bridged with LVAD, HCV D+/R–versus HCV D–/R– HT had similar adjusted odds of postoperative dialysis (aOR, 0.98; 95% CI, 0.69-1.40), pacemaker (aOR, 0.72; 95% CI, 0.29-1.78), and acute rejection (aOR, 1.02; 95% CI, 0.75-1.39), as well as similar median (IQR) lengths of stay (16 [13-24] vs 17 [12-26] days; $P = .8$).

Subgroup Analysis of Recipients Bridged With IABP

Of the 3079 (17.5%) recipients bridged with IABP, 152 (4.9%) were HCV D+/R– transplants. Baseline recipient, donor, and transplant characteristics are shown in Table E1. The risk of mortality (Figure 3) for HCV D+/R– versus HCV D–/R– HT was similar at 30 days (aHR, 0.81; 95% CI, 0.25-2.59), 1 year (aHR, 1.10; 95% CI, 0.60-2.03), and 3 years (aHR, 1.25; 95% CI, 0.76-2.06) posttransplant after adjusting for donor, recipient, and transplant characteristics. In recipients bridged with IABP, HCV D+/R– versus HCV D–/R– HT had similar adjusted odds of postoperative dialysis (aOR, 1.06; 95% CI, 0.66-1.72), pacemaker (aOR, 1.79; 95% CI, 0.70-4.60), and acute rejection (aOR, 0.71; 95% CI, 0.46-1.10), as well as median (IQR) length of stay (16 [12-22] vs 17 [12-24] days; $P = .1$).

DISCUSSION

In this national study of trends in use and 3-year outcomes of HCV D+/R– HT, we found that the number of individuals receiving and centers performing HCV D+/R– HT has risen substantially from 2015 to 2021. Compared with HCV D–/R– HT, HCV D+/R– transplants had similar

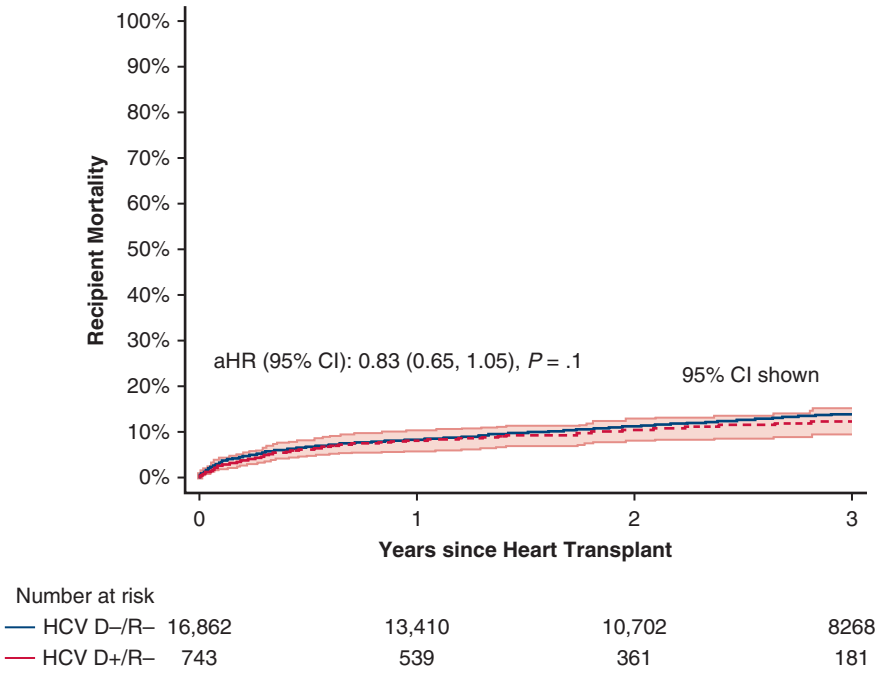

FIGURE 2. Mortality by time since heart transplant. *HCV*, Hepatitis C virus; *HCV D–/R–*, seronegative donor to seronegative recipient; *HCV D+/R–*, viremic donor to seronegative recipient; *CI*, confidence interval; *aHR*, adjusted hazard ratio.

risk of posttransplant ECMO, dialysis initiation, pacemaker placement, acute rejection, and mortality, as well as similar hospital length of stay (all $P > .05$). This was true for HT recipients overall as well as for the 60.6% of recipients who were bridged to transplant with various types of MCS. These findings of similar outcomes among HCV D+/R– and D–/R– HT support the uptake of this practice by transplant centers (Figure 4).

Our finding that waitlist time was similar among recipients of HCV D+/R– and D–/R– transplants contrasts with previously published literature, which showed dramatic decreases in waitlist time with acceptance of HCV-viremic organs.[6,7] This is likely due to data limitations; we can only evaluate a recipient's total waitlist time, not the amount of time that was spent on the waitlist after deciding to consider HCV-viremic organ offers. Additionally, the increases in the number of centers and patients receiving HCV-viremic donor organs that we observed highlights increased competition for these organs, reducing the individual-level effect of these organs on waitlist time. At a center level, however, high-adopter programs had significantly shorter waitlist times. Aggressiveness with other donor factors may also be contributing to shorter waitlist times, but our finding suggests that high-adopter centers are providing their candidates with greater access to transplant without compromising outcomes.

The increased competition for these organs is justified by our finding that HCV D+/R– transplants remain safe and effective at 3 years, as evidenced by similar mortality, acute rejection, and incidence of other posttransplant outcomes compared with HCV D–/R– transplants. Our findings confirm those published in both the landmark pilot study and previous single-center studies[6-8,10,12] and expands upon the work by Li and colleagues[26] in a national population to include transplants that have occurred in more recent years; this increased sample size confirms the excellent outcomes of HCV D+/R– transplants. Although the pilot study Woolley and colleagues[12] provided important data on 6-month outcomes, the small HT population studied (N = 8) limited power to detect differences in outcomes as well as generalizability to the HT recipient population. Our study of more than 700 HCV D+/R– HT recipients provides the strongest evidence to date that these transplants have excellent outcomes.

Finally, our subgroup analysis of patients bridged with MCS provides the first dedicated evidence of the excellent outcomes of HCV D+/R– transplants in this growing HT recipient population. We found that more than 60% of patients from 2015 to 2021 were bridged with MCS. Although the majority of patients in the pilot trial of HCV D+/R– transplants were bridged with MCS, they appear to have had durable MCS devices. In recent years, there has been

TABLE 3. Donor, recipient, and transplant characteristics for patients bridged with left ventricular assist device

Characteristic	HCV D–/R–	HCV D+/R–	*P* value
N	6178	270	
Donor characteristics			
Age, y, median (IQR)	31 (23-40)	33 (28-38)	<.001
Male sex	4710 (76.2%)	207 (76.7%)	.9
White race	4035 (65.3%)	228 (84.4%)	<.001
Recipient characteristics			
Age, y, median (IQR)	56 (47-63)	58 (50-64)	.001
Male sex	4914 (79.5%)	223 (82.6%)	.2
White race	3847 (62.3%)	171 (63.3%)	.7
BMI, kg/m^2, median (IQR)	29.0 (25.6-32.7)	29.7 (26.2-33.6)	.05
Creatinine, median (IQR)	1.19 (0.97-1.43)	1.21 (1-1.49)	.07
Bilirubin, median (IQR)	0.6 (0.4-0.9)	0.6 (0.4-0.8)	.03
Blood type			.01
O	2699 (43.7%)	141 (52.2%)	
A	2350 (38.0%)	97 (35.9%)	
B	900 (14.6%)	28 (10.4%)	
AB	229 (3.7%)	4 (1.5%)	
Cardiomyopathy diagnosis			.2
Dilated	5799 (93.9%)	254 (94.1%)	
Restrictive	62 (1.0%)	4 (1.5%)	
Ischemic	141 (2.3%)	9 (3.3%)	
Nonischemic	175 (2.8%)	3 (1.1%)	
Transplant characteristics			
Waitlist time, d, median (IQR)	218 (66-517)	220 (70-475)	1.0
Donation after circulatory death (DCD)	101 (1.6%)	6 (2.2%)	.5
Heart allograft ischemia time, h, median (IQR)	3.18 (2.43-3.82)	3.47 (2.97-4.07)	<.001

HCV, Hepatitis C virus; *HCV D–/R–*, seronegative donor to seronegative recipient; *HCV D+/R–*, viremic donor to seronegative recipient; *IQR*, interquartile range; *BMI*, body mass index.

a notable increase in the use of temporary MCS devices to bridge patients to transplant, particularly following the allocation policy change in 2018.[1,13,14] The outcomes of HCV D+/R– transplants in this vitally important and sicker population are critical to evaluating the outcomes of HCV D+/R– heart transplants overall.

Our ability to evaluate outcomes of HCV D+/R– and D–/R– HT was limited by the information available in the national registry database. As mentioned previously, this information lacks granularity regarding when an individual recipient began to consider HCV D+/R– organ offers, limiting our comparison of waitlist time between groups. Additionally, the decision to consider HCV-viremic donor organ offers is an individualized decision based on input from the transplant center, providers, and candidate. Using national registry data, we are unable to ascertain reasons for accepting or not accepting HCV-viremic organs. Additionally, important outcomes such as cardiac allograft vasculopathy are not differentiated as unique variables; we instead had to use graft failure as a surrogate measure. Finally, the relative novelty of HCV D+/R– transplants means that the use of these organs remains dynamic. Ongoing evaluation of the use of these organs and outcomes of these transplants is needed.

In conclusion, HCV D+/R– HT are as safe and effective as HCV D–/R– HT at 3 years' posttransplant. The increased use of HCV-viremic heart allografts is an effective way to expand the donor pool and improve access to heart transplantation without compromising outcomes.

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.

The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the US Government.

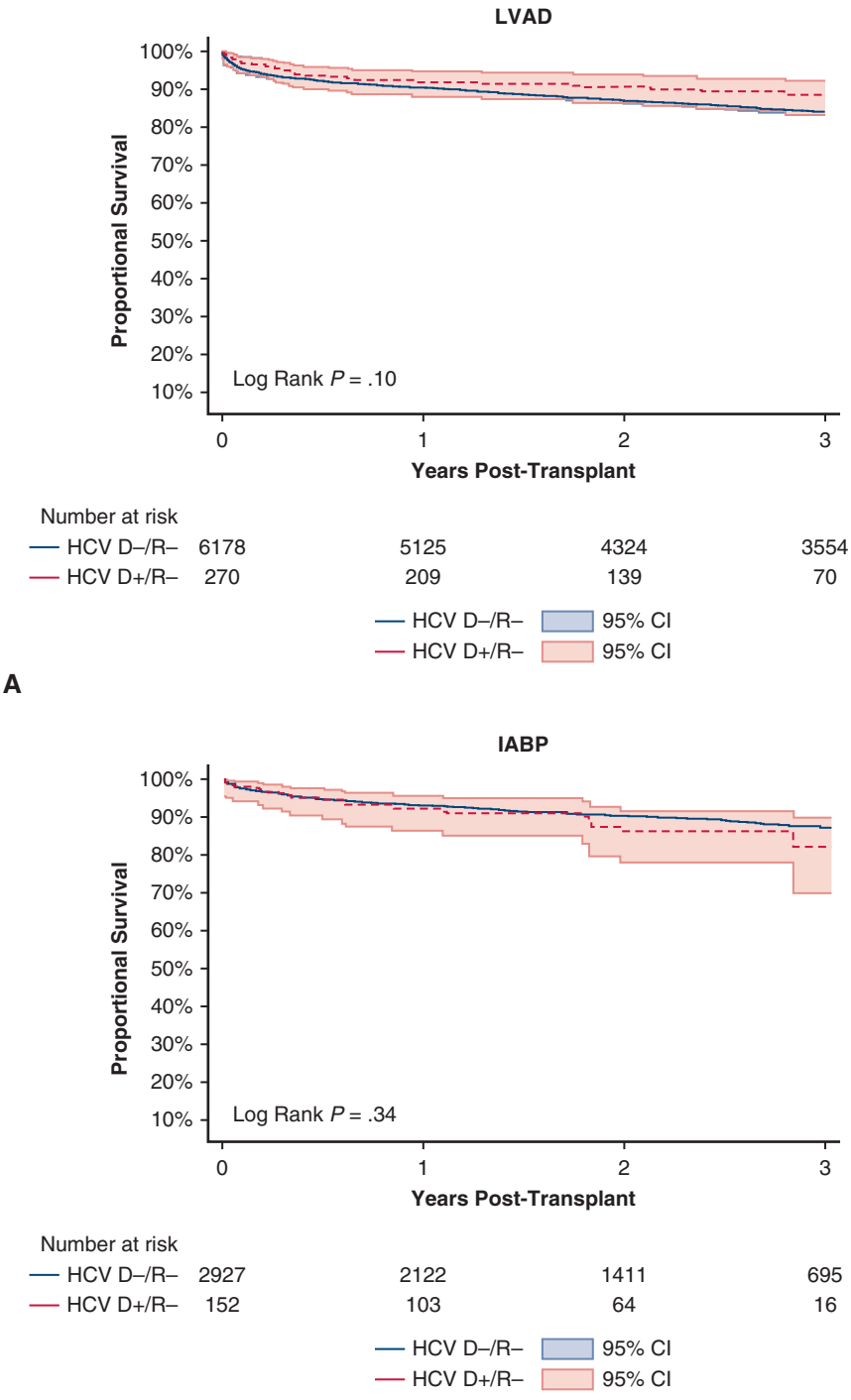

FIGURE 3. Kaplan–Meier survival curves of HCV D–/R– versus HCV D+/R– heart transplants in recipients bridged with (A) LVAD and (B) IABP. *LVAD*, Left ventricular assist device; *HCV*, hepatitis C virus; *HCV D–/R–*, seronegative donor to seronegative recipient; *HCV D+/R–*, viremic donor to seronegative recipient; *IABP*, intra-aortic balloon pump; *CI*, confidence interval.

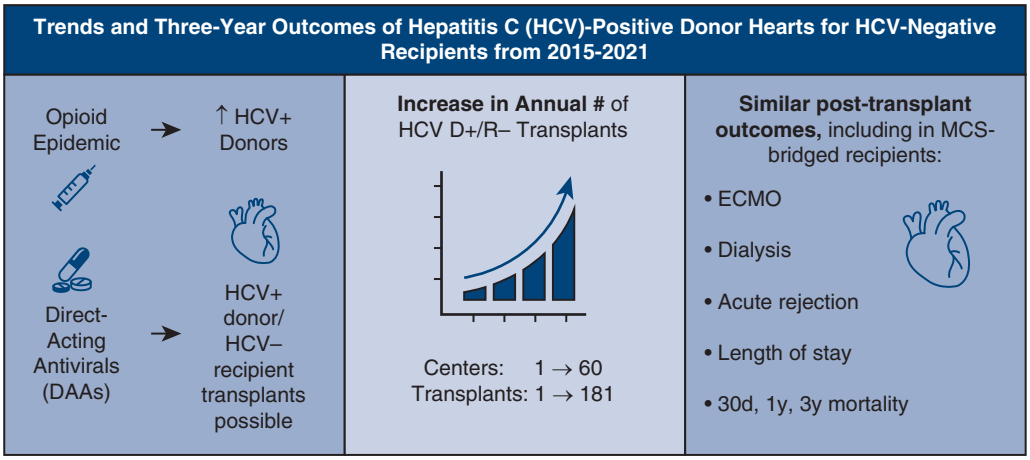

FIGURE 4. Heart transplants from donors with and without HCV viremia into recipients without HCV have similar risk of acute rejection and mortality at 3 years' posttransplant. *HCV*, Hepatitis C virus; *HCV D+/R–*, viremic donor to seronegative recipient; *MCS*, mechanical circulatory support; *ECMO*, extracorporeal membranous oxygenation.

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Key Words: heart transplant, hepatitis C, outcomes, donor pool

TABLE E1. Donor, recipient, and transplant characteristics for patients bridged with IABP

Characteristic	HCV D–/R–	HCV D+/R–	*P* value
N	2927	152	
Donor characteristics			
Age, y, median (IQR)	30 (23-39)	33 (28.5-38)	.001
Male sex	2206 (75.4%)	120 (78.9%)	.3
White race	1744 (59.6%)	126 (82.9%)	<.001
Recipient characteristics			
Age, y, median (IQR)	57 (48-64)	57 (46-65)	1.0
Male sex	2186 (74.7%)	116 (76.3%)	.7
White race	1758 (60.1%)	98 (64.5%)	.3
BMI, kg/m^2, median (IQR)	26.4 (23.3-30.2)	27.0 (23.6-30.6)	.1
Creatinine, median (IQR)	1.12 (0.9-1.4)	1.1 (0.95-1.35)	.7
Bilirubin, median (IQR)	0.7 (0.5-1.2)	0.85 (0.6-1.4)	.004
Blood type			.05
O	1204 (41.1%)	79 (52.0%)	
A	1121 (38.3%)	50 (32.9%)	
B	460 (15.7%)	20 (13.2%)	
AB	142 (4.9%)	3 (2.0%)	
Cardiomyopathy diagnosis			.7
Dilated	2484 (84.9%)	126 (82.9%)	
Restrictive	134 (4.6%)	7 (4.6%)	
Ischemic	94 (3.2%)	4 (2.6%)	
Nonischemic	215 (7.3%)	15 (9.9%)	
Transplant characteristics			
Waitlist time, d, median (IQR)	17 (7-55)	13 (6-39)	.01
Donation after circulatory death (DCD)	27 (0.9%)	0 (0.0%)	.6
Heart allograft ischemia time, h, median (IQR)	3.43 (2.87-3.95)	3.58 (3.08-3.98)	.01

HCV, Hepatitis C virus; *HCV D–/R–*, seronegative donor to seronegative recipient; *HCV D+/R–*, viremic donor to seronegative recipient; *IQR*, interquartile range; *BMI*, body mass index; *IABP*, intra-aortic balloon pump.