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

Jessica M. Ruck, MD, a Alice L. Zhou, MS, a Laura B. Zeiser, ScM, a Diane Alejo, BA, a Christine M. Durand, MD, b Allan B. Massie, PhD, MHS, c Dorry L. Segev, MD, PhD, c,d Errol L. Bush, MD, a and Ahmet Kilic, MD a

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.

From the aDivision of Cardiac Surgery, Department of Surgery, and bDivision of Infection Disease, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Md; cDivision of Transplant Surgery, Department of Surgery, NYU Langone Health, New York, NY; and dScientific Registry of Transplant Recipients, Minneapolis, Minn.

This work was supported by grant number F32-AG067642091A1 (Dr Ruck) from the National Institute of Aging (NIA) and K24-AI144954-08 (Dr Segev) from the National Institute of Allergy and Infectious Disease (NIAID). The analyses described here are the responsibility of the authors alone and do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products or organizations imply endorsement by the US Government.

Received for publication July 21, 2021; revisions received Oct 17, 2022; accepted for publication Oct 24, 2022; available ahead of print Nov 24, 2022.

Address for reprints: Ahmet Kilic, MD, Department of Surgery, Johns Hopkins Medical Institutions, Sheikh Zayed Tower, Suite 7107, 1800 Orleans St, Baltimore, MD 21287 (E-mail: Akilic2@jhmi.edu).

Copyright © 2022 The Author(s). Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

https://doi.org/10.1016/j.xjon.2022.10.007
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 membrane 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 20132,3 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 Schledendorf and colleagues6 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 colleagues12 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 pump (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 χ² 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.\(^1\) 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 antihypertrophic 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.\(^11,21\) 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, 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 >50% of total HT from 2019 to 2021 being HCV D+/R− transplants (\(n = 14\)). Low-adopter centers were defined as all other centers who performed at least 1 HCV D+/R− HT (\(n = 60\)). We used \(\chi^2\) 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, 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, 37/73 (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
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;
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 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      | 0.001     |
| Donor 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     |
| Male sex     | 12,337 (73.2%) | 577 (77.7%) | .006      |
| White race   | 10,641 (63.1%) | 499 (67.2%) | .02       |
| Bilirubin, median (IQR) | 7.5 (24.1-31.3) | 28.0 (24.6-32.0) | .002      |
| Blood type   | 0.70 (0.49-1.00) | 0.70 (0.40-1.00) | .82       |
| Cardiomyopathy diagnosis | 14,170 (84.0%) | 632 (85.1%) | .13       |
| Dilated      | 6609 (39.2%) | 353 (47.5%) | <.001     |
| Restrictive  | 6724 (39.9%) | 274 (36.9%) | <.001     |
| Ischemic     | 2611 (15.5%) | 95 (12.8%) | .02       |
| Nonischemic  | 918 (5.4%) | 21 (2.8%) | <.001     |
| Pretransplant characteristics | 238 (1.4%) | 10 (1.3%) | .88       |
| On ventilator | 364 (2.2%) | 10 (1.3%) | .82       |
| On ECMO      | 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 (DAD) | 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.
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, 0.95-1.78), 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
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 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
a notable increase in the use of temporary MCS devices to bridge patients to transplant, particularly following the allocation policy change in 2018. 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.

| TABLE 3. Donor, recipient, and transplant characteristics for patients bridged with left ventricular assist device |
|-------------------------------------------------------|-------------------------------------------------------|------------------|
| Characteristic                                      | HCV D–/R–                                      | HCV D+/R–            |
| 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/m², 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                                          |                                               |                   |
| O                                                    | 2699 (43.7%)                                   | 141 (52.2%)        | .01   |
| A                                                    | 2350 (38.0%)                                   | 97 (35.9%)         |       |
| B                                                    | 900 (14.6%)                                    | 28 (10.4%)         |       |
| AB                                                   | 229 (3.7%)                                     | 4 (1.5%)           |       |
| Cardiomyopathy diagnosis                           |                                               |                   |
| Dilated                                             | 5799 (93.9%)                                   | 254 (94.1%)        | .2    |
| 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.
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.

References

1. Colvin M, Smith JM, Ahn Y, Skeans MA, Messick E, Bradbrook K, et al. OPTN/SRTR 2020 Annual data report: heart. *Am J Transplant*. 2022;22:350-437.

2. US Food and Drug Administration. Approval of incivek (telaprevir) a direct-acting antiviral (DAA) to treat hepatitis C virus (HCV) infection. Accessed September 1, 2022. http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varAppNo¼201917

3. US Food and Drug Administration. Approval of vicriviroc (boceprevir) a direct-acting antiviral drug (DAA) to treat hepatitis C virus (*HCV*). Accessed September 1, 2022. http://www.fda.gov/VXX

4. Durand CM, Bowring MG, Thomas AG, Kucirka LM, Massie AB, Cameron A, et al. The drug overdose epidemic and deceased-donor transplantation in the United States: a national registry study. *Ann Intern Med*. 2018;168:702-11.

5. Alsthuler PJ, Helmers MR, Schiavazza AR, Hu R, Han JJ, Herbst DA, et al. HCV-positive allograft use in heart transplantation is associated with increased access to overdose donors and reduced waitlist mortality without compromising outcomes. *J Card Fail*. 2022;28:32-41.

6. Schlendorf KH, Zalawadiya S, Shah AS, Wigger M, Chung CY, Smith S, et al. Early outcomes using hepatitis C-positive donors for cardiac transplantation in the era of effective direct-acting anti-viral therapies. *J Heart Lung Transplant*. 2018;37:763-9.

7. Geminhofer YK, Brambatti M, Greenberg BH, Adler E, Aslam S, Pretorius V. The impact of using hepatitis C virus nucleic acid test-positive donors hearts on heart transplant waitlist time and transplant rate. *J Heart Lung Transplant*. 2019;38:1178-88.

8. Aslam S, Yumul I, Mariski M, Pretorius V, Adler E. Outcomes of heart transplantation from hepatitis C virus-positive donors. *J Heart Lung Transplant*. 2019;38:1259-67.

9. McMaster WG Jr, Rahaman ZM, Shipe ME, Quintana EN, Sandhaus EM, Smith SS, et al. Early outcomes of multivisceral transplant using hepatitis C-positive donors. *Annu Thorac Surg*. 2021;112:511-8.

10. Smith DE, Chen S, Fargnoli A, Lewis T, Galloway AC, Kon ZN, et al. Impact of early initiation of direct-acting antiviral therapy in thoracic organ transplantation from hepatitis C virus positive donors. *Semin Thorac Cardiovasc Surg*. 2021;33:407-15.

11. Zalawadiya SK, Lindenfeld J, Shah A, Wigger M, Danter M, Brinkley DM, et al. Trends in renal function among heart transplant recipients of donor-derived hepatitis C virus. *ASAIO J*. 2020;66:553-8.

12. Woolley AE, Singh SK, Goldberg HJ, Mallidi HR, Givertz MM, Mehra MR, et al. Heart and lung transplants from HCV-infected donors to uninfected recipients. *N Engl J Med*. 2019;380:1606-17.

13. Cogswell R, John R, Estep JD, Duval S, Tedford RJ, Pagani FD, et al. An early investigation of outcomes with the new 2018 donor heart allocation system in the United States. *J Heart Lung Transplant*. 2020;39:1-4.

14. Javitz OK, Fedim M, Raman V, Breyer BS, DeVore AD, Mentz RJ, et al. Reassessing recipient mortality under the new heart allocation system: an updated UNOS registry analysis. *JACC Heart Fail*. 2020;8:548-56.

15. Massie AB, Kucirka LM, Kuricka DL, Segev DL. Big data in organ transplantation: registries and administrative claims. *Am J Transplant*. 2014;14:1723-30.

16. Javitz OK, Fedim M, Raman V, Breyer BS, DeVore AD, Mentz RJ, et al. Reassessing recipient mortality under the new heart allocation system: an updated UNOS registry analysis. *JACC Heart Fail*. 2020;8:548-56.

17. Wu VC-C, Chen T-H, Wu M, Huang CH, Chen SW, Cheng CW, et al. Risk of cardiac arrhythmias in patients with chronic hepatitis B and C infections—a 13-year nationwide population-based study. *J Cardiovasc Electrophysiol*. 2019;30:533-8.

18. Yang YH, Chiang HJ, Yip HK, Chen KJ, Chiang JY, Lee MS, et al. Risk of new-onset atrial fibrillation among Asian chronic hepatitis C virus carriers: a nation-wide population-based cohort study. *J Am Heart Assoc*. 2019;8:e012914.

19. Karimi-Sari H, Rezaee-Zareakh MS. Non-atherosclerotic cardiac manifestations of chronic hepatitis C virus infection in the era of direct-acting antiviral agents. *Atherosclerosis*. 2020;298:70-90.

20. Rubin R. Warning for hepatitis C treatments given with amiodarone. *JAMA*. 2015;313:1704.

21. Pettit SJ, Hulsd PS, Hawkins NM, Gardner RS, Haj-Yahia S, McMurray JJ, et al. How small is too small? A systematic review of center volume and outcome after cardiac transplantation. *Circ Cardiovasc Qual Outcomes*. 2012;5:783-90.

22. Fiedler AG, Smith JW, Raza F, Hernsen JL, Dhirgara R. Differences in heart transplant volume growth and outcomes among low and high volume centers. *J Heart Lung Transplant*. 2020;39:S268.

23. Axelrod DA, Guidinger MK, McCullough KP, Leichtman AB, Punch JD, Merson RM. Association of center volume with outcome after liver and kidney transplantation. *Am J Transplant*. 2004;4:920-7.

24. Northup PG, Pruett TL, Stakenborg GJ, Berg CL. Survival after adult liver transplantation does not correlate with transplant center case volume in the MELD era. *Am J Transplant*. 2006;6:2455-62.

25. Reese SR,€ tire H, Thomasson AM, Shults J, Markmann JF. Transplant center volume and outcomes after liver retransplantation. *Am J Transplant*. 2009;9:309-17.

26. Li SS, Osho A, Moonsamy P, D’Alessandro DA, Lewis GD, Villavicencio MA, et al. Trends in the use of hepatitis C viremic donor hearts. *J Thorac Cardiovasc Surg*. 2022;163:1873-85.e7.

**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/m², 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.