



Transplantation

Listing practices and graft utilization of hepatitis C–positive deceased donors in liver and kidney transplant



Catherine E. Kling, MD^{a,b}, James D. Perkins, MD^{a,b}, Scott W. Biggins, MD^{b,c,d}, Christopher K. Johnson, MD^{b,e}, Ajit P. Limaye, MD^{b,f}, Lena Sibulesky, MD^{a,b,*}

^a Division of Transplant Surgery, Department of Surgery, University of Washington, Seattle, WA

^b Clinical and Bio-Analytics Transplant Laboratory (CBATL), University of Washington, Seattle, WA

^c Divisions of Gastroenterology and Hepatology, Department of Medicine, University of Washington, Seattle, WA

^d Center for Liver Investigation Fostering DiscovERY (C-LIFE), University of Washington, Seattle, WA

^e Division of Nephrology, Department of Medicine, University of Washington, Seattle, WA

^f Division of Infectious Disease, Department of Medicine, University of Washington, Seattle, WA

ARTICLE INFO

Article history:

Accepted 15 March 2019

Available online 6 May 2019

ABSTRACT

Background: The opioid epidemic has resulted in increasing the incidence of hepatitis C virus in the general population and more deceased organ donors with hepatitis C in the United States. We aim to describe how the changing donor landscape affects patterns of liver and kidney transplantation among donors, waitlist candidates, and transplanted recipients.

Methods: Using data supplied by the United Network for Organ Sharing, we examined donor hepatitis C virus antibody (Ab) and nucleic acid testing (NAT) status, center waitlist patterns, and liver and kidney transplants and discards between 2015 and 2017 by 6-month periods.

Results: We observed an increase in donors with any marker of the hepatitis C virus ($n = 283$ [6.2%] in period 1 to $n = 384$ [7.4%] in period 5, $P = .008$) and antibody positive nucleic acid testing negative donors ($n = 81$ [1.8%] in period 1 to $n = 131$ [2.5%] in period 5, $P < .001$). We observed a significant increase in aviremic recipients of liver transplants from antibody positive nucleic acid testing negative donors ($n = 1$ [1.7%] in period 1, to $n = 27$ [31.0%] in period 5, $P = .005$) and a significant decrease in the antibody positive nucleic acid testing positive liver discard rate ($P = .01$). By the end of the study, 75.8% ($n = 97$) of recipients of antibody positive nucleic acid testing negative kidneys were hepatitis C virus negative, an increase from 10.6% ($n = 5$) in period 1.

Conclusion: The number of donors with the hepatitis C virus is increasing. We observed a concomitant increase in the transplantation of kidneys and livers from aviremic donors, and the recipient population of these organs is increasingly hepatitis C virus negative.

© 2019 Elsevier Inc. All rights reserved.

Introduction

After decades of declining incidence, the past decade has been marked by a rising incidence of the hepatitis C virus (HCV) in the population.^{1,2} Although there has been a paradigm shift in HCV care with the ability to cure HCV using direct acting antivirals (DAAs), there has also been an increase in the incident cases of HCV among people who inject drugs in the setting of the opioid epidemic.² The number of new HCV infections in the United States increased 3.5-fold between 2010 and 2016, from 850 to 2,967.³ This has had a direct

impact on transplantation, with the Organ Procurement and Transplantation Network (OPTN) reporting a 3-fold increase in drug overdose as a cause of death among deceased donors during the past decade.⁴ The HCV donor population characteristics are also changing, with the median age of viremic HCV donors decreasing by 12 years between 2012 and 2016 (from 47 years to 35 years of age).⁵

It is in this setting—more young viremic HCV donors, with likely recent infections and the opportunity for a cure using DAAs—that the transplant community has begun to report the transplantation of viremic and aviremic organs from HCV donors into aviremic recipients. Recently, successful use of organs from viremic and aviremic HCV donors for heart,^{6–12} lung,^{12,13} liver,^{14–18} and kidney^{19–22} transplant have been reported. In addition, clinicaltrials.gov lists trials that are actively recruiting recipients for inclusion into studies involving both viremic and aviremic HCV donors in all four organs.²³

* Reprint requests: Lena Sibulesky, MD, Department of Surgery, 1959 NE Pacific St., Box 356410, Seattle, WA 98195-6410.

E-mail address: lenasi@uw.edu (L. Sibulesky).

In this study we describe how the increasing number of donors with markers of HCV infection affects patterns of liver and kidney transplantation, including among donors, waitlist candidates, and transplanted recipients.

Materials and Methods

Data source

We conducted a retrospective cohort analysis of donors, using OPTN data released December 1, 2017, by the United Network for Organ Sharing (UNOS) based on data collected through September 30, 2017. UNOS, which is the contractor for the OPTN, supplied these data. The interpretation and reporting of these data are the responsibility of the authors and in no way should be viewed as an official policy of or interpretation by the OPTN or the US government. This study was exempt from review by the University of Washington Institutional Review Board (Seattle, WA).

Study population

We examined all potential kidney and liver deceased donors and recipients who underwent liver or kidney transplantation for the 2.5-year study period from April 1, 2015 through September 30, 2017. The start date for this period was selected based on research²⁴ demonstrating 99.5% donor HCV nucleic acid testing (NAT) reporting after April 1, 2015, in anticipation of the August 10, 2015, mandated HCV NAT reporting date. The study was divided into the following 5 periods, each of 6 months' duration:

- period 1: April 1, 2015–September 30, 2015;
- period 2: October 1, 2015–March 31, 2016;
- period 3: April 1, 2016–September 30, 2016;
- period 4: October 1, 2016–March 31, 2017; and
- period 5: April 1, 2017–September 30, 2017.

Nomenclature

HCV nomenclature has changed through the years, and these changes have resulted in much confusion. In this report, donors were characterized according to HCV antibody (Ab) and NAT status as follows: Ab– NAT–, Ab– NAT+, Ab+ NAT– and Ab+ NAT+. Donors who were NAT+ are referred to as “viremic.” The term “aviremic” is used in the context of NAT negativity but presence of antibodies to HCV (ie, Ab+ NAT–). Donors who were positive for either Ab or NAT are referred to as “donors with any marker of HCV infection” (identified as any HCV+ in the Tables and Figures). Recipient HCV status is characterized in the OPTN database as “positive,” “negative,” or “unknown”—distinction is not given to Ab or NAT status among ‘positive’ recipients—hence we have used the same terminology in this report. Similarly, the waitlist database lists recipients as either accepting an “HCV-positive” organ or not, without further definition of HCV positivity (ie, Ab and NAT status).

Donor population

Donors were placed into four groups according to HCV Ab and NAT status and included all donors, even if all the organs were refused donation. UNOS donor characteristics were compared among the four HCV categories using the χ^2 or Fisher exact test for categorical values, and continuous variables were compared with ANOVA for a parametric distribution or the Wilcoxon test or Krushal-Wallis test, as appropriate, for nonparametric distributions. Because there were very few donors in the Ab– NAT+

category, this population was excluded from the waitlist and organ transplantation analysis. Donor HCV status was examined over the five periods and across UNOS regions using χ^2 .

Listing practices

Because a listed recipients' acceptance of an HCV-positive organ can change during the period of their listing, we characterized patients based on their acceptance at the time of the final waitlist status—eg, transplanted, died, lost to follow-up, or the end of the study (September 30, 2017). The proportion of a center's waitlist listed as accepting an HCV-positive liver or HCV-positive kidney was described.

Discards and transplantation

Discard rates were examined over time, using linear regression within each HCV donor group and between groups, using the *t* test. Recipients were then classified according to their HCV status (positive or negative), and transplantation over time compared.

Statistical analysis

Analyses were conducted using JMP Pro 13.0.0 (SAS Institute Inc, Cary, NC) statistical software. Some graphics were created in Stata 12.1 (StataCorp, College Station, TX) or Microsoft Excel 14.6.9 (Microsoft, Redmond, WA). Results with a *P* value less than .05 were considered significant.

Results

Donor population

Of the 24,554 potential donors during the study period, 22,889 (93.2%) were Ab– NAT–, 50 (0.2%) were Ab– NAT+, 542 (2.2%) were Ab+ NAT–, and 1,073 (4.4%) were Ab+ NAT+ (Table I). Donors with any marker of HCV infection were more likely to be white, have died of anoxia, be classified as Public Health Service increased risk, and less likely to be a donation after circulatory death donor.

During the study period, there was a statistically significant increase in the number of donors with any marker of HCV, from 283 (6.2%) in period 1 to 384 (7.4%) in period 5 (*P* = .008; Fig 1). The number of Ab+ NAT– donors also increased significantly from 81 (1.8%) in period 1 to 131 (2.5%) in period 5 (*P* < .001), but there was no change in Ab+ NAT+ donors (*n* = 192 [4.2%] in period 1 to *n* = 240 [4.6%] in period 5 [*P* = .84]). During the study, the total mean proportion of donors with any marker of HCV infection (either Ab+ or NAT+) was 6.8%, with significant UNOS region variability from 4.0% in region 4 to 14.0% in region 1 (Table II). We also observed UNOS region variability based on donor type, with Ab+ NAT– donors prevalence ranging from 1.2% (region 8) to 4.3% (region 2), and Ab+ NAT+ donor prevalence ranging from 2.2% (region 7) to 9.6% (region 1).

Listing practices

The median proportion of a center's waitlist listed to accept an HCV-positive liver was 9.7% (interquartile range [IQR] 2.2%–16.7%, range 0%–99.2%), with 28 centers (19.4%) with no recipients listed as accepting a HCV-positive liver (Fig 2, A). The median proportion of a center's waitlist list to accept an HCV-positive kidney was 0.81% (interquartile range 0%–2.4%, range 0%–97.4%), with 87 centers (36.0%) with no recipients listed as accepting an HCV-positive kidney (Fig 2, B). We observed no correlation between regional HCV prevalence and waitlist acceptance of HCV Ab+ livers

Table I
Donor characteristics by HCV status

	HCV groups				P
	Ab- NAT-	Ab- NAT+	Ab+ NAT-	Ab+ NAT+	
n (%)	22,889 (93.2%)	50 (0.2%)	542 (2.2%)	1,073 (4.4%)	
Female	9,073 (39.6%)	27 (54%)	272 (50.2%)	372 (34.7%)	< .001
Age (y ± SD)	39.7 ± 17.7	30.8 ± 9.8	40.9 ± 12.8	36.9 ± 11	< .001
Race					< .001
Asian	620 (2.7%)	0	2 (0.37%)	7 (0.65%)	
Black	3,730 (16.3%)	2 (4%)	41 (7.6%)	103 (9.6%)	
Hispanic	3,133 (13.7%)	3 (6%)	48 (8.9%)	86 (8%)	
Other	438 (1.9%)	0	6 (1.1%)	16 (1.5%)	
White	14,968 (65.4%)	45 (90%)	445 (82.1%)	861 (80.2%)	
Cause of death					< .001
Anoxia	8,865 (38.7%)	36 (72%)	363 (67%)	700 (65.2%)	
CNS tumor	83 (0.36%)	1 (2%)	0	0	
CVA	6,523 (28.5)	3 (6%)	93 (17.2%)	164 (15.3%)	
Head trauma	6,764 (29.6%)	7 (14%)	76 (14%)	187 (17.4%)	
Other	654 (2.9%)	3 (6%)	10 (1.9%)	22 (2.1%)	
Donation after circulatory death	4080 (17.8%)	6 (12%)	55 (10.2%)	91 (8.5%)	< .001
Public health service increased risk	4,727 (20.7%)	43 (86%)	382 (70.5%)	855 (79.7%)	< .001
KDPI groups					< .001
0–20	4,515 (19.7%)	22 (44%)	1 (0.18%)	12 (1.2%)	
21–85	14,059 (61.4%)	27 (54%)	389 (71.8%)	881 (82.1%)	
> 85	4,315 (18.9%)	1 (2%)	152 (28%)	179 (16.7%)	
KDPI Groups minus HCV					< .001
0–20	4,515 (19.7%)	26 (52%)	55 (10.2%)	205 (19.1%)	
21–85	14,059 (61.4%)	23 (46%)	441 (81.4%)	808 (75.3%)	
> 85	4,315 (18.9%)	1 (2%)	46 (8.5%)	60 (5.6%)	

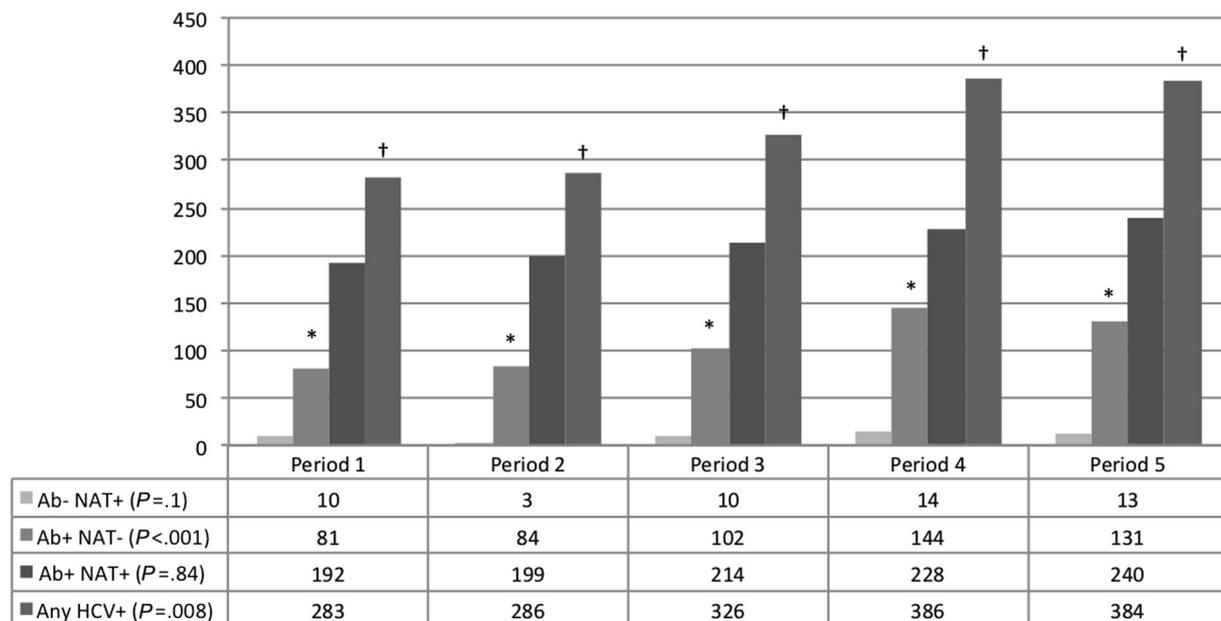


Fig 1. Change in donor HCV status over time. There was a significant increase in the proportion of Ab- NAT+ donors and donors with any marker of HCV positivity ($^*P < .001$ and $^\dagger P = .008$, respectively).

($R^2 = 0.068$) or kidneys ($R^2 = 0.00$). For those centers with both kidney and liver transplant programs, there was no correlation between waitlist HCV Ab+ liver and kidney acceptance ($R^2 = 0.106$).

Discards and transplantation: Liver

Discards

For liver donors, there was no difference in the discard rate between HCV donor groups in any period, with overall discard rates of 33.2% for Ab- NAT- donors, 30.1% for Ab+ NAT- donors, and 37.9% for Ab+ NAT+ donors. However, during the study, there was a

significant decrease in the overall discard rate from 37.9% to 36.7% for Ab+ NAT+ donors ($P = .01$), but not for the other donor groups (Table III).

Transplantation

For recipients of Ab- NAT- livers, there was a decrease in the proportion of HCV-positive recipients and concomitant increase in HCV-negative recipients during the study period ($P = .01$ and $P = .04$, respectively; Table III). We observed a significant increase in the number of HCV-negative recipients of Ab+ NAT- livers from (1.7%) in period 1 to 27 (31.0%) in period 5 ($P = .005$; Fig 3). We

Table II
Donor HCV status and wait list HCV acceptance by UNOS region

Region	Donor HCV category				Any HCV+
	Ab- NAT-	Ab- NAT+	Ab+ NAT-	Ab+ NAT+	
1	774 (86.0%)	4 (0.4%)	36 (4.0%)	86 (9.6%)	900 (14.0%)
2	2,778 (88.2%)	12 (0.4%)	134 (4.3%)	227 (7.2%)	3,151 (11.8%)
3	3,577 (93.9%)	7 (0.2%)	71 (1.9%)	153 (4.0%)	3,808 (6.1%)
4	2,548 (96.0%)	4 (0.2%)	37 (1.4%)	66 (2.5%)	2,655 (4.0%)
5	3,459 (95.6%)	5 (0.1%)	48 (1.3%)	108 (3.0%)	3,620 (4.4%)
6	914 (95.7%)	1 (0.1%)	16 (1.7%)	24 (2.5%)	955 (4.3%)
7	1,889 (95.9%)	4 (0.2%)	32 (1.6%)	44 (2.2%)	1,969 (4.1%)
8	1,630 (95.4%)	4 (0.2%)	21 (1.2%)	53 (3.1%)	1,708 (4.6%)
9	991 (92.2%)	2 (0.2%)	32 (3.0%)	50 (4.7%)	1,075 (7.8%)
10	1,939 (90.1%)	2 (0.1%)	65 (3.0%)	146 (6.8%)	2,152 (9.9%)
11	2,390 (93.3%)	5 (0.2%)	50 (2.0%)	116 (4.5%)	2,561 (6.7%)
Total	22,889 (93.2%)	50 (0.2%)	542 (2.2%)	1073 (4.4%)	24,554 (6.8%)

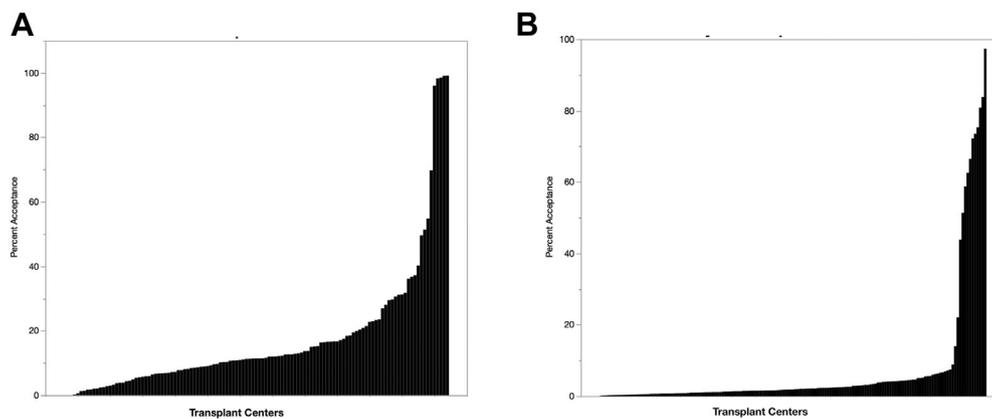


Fig 2. Center-level percentage of wait list patients listed to receive (A) an HCV-positive liver or (B) a kidney.

observed no significant change in the recipient HCV status for Ab+ NAT+ livers, although there were more HCV-negative recipients in period 5 ($n = 22$) than the first 4 periods combined ($n = 19$). To examine whether HCV-negative recipients were classified as such attributable to treatment and cure of an earlier HCV infection, we assessed the underlying etiology of liver failure. For recipients who were HCV negative, only 34.1% of Ab+ NAT+ liver recipients and 9.0% Ab+ NAT- liver recipients had HCV listed as the cause of their cirrhosis.

Discards and transplantation: Kidney

Discards

For kidney donors, discard rates were significantly higher overall for Ab+ NAT- donors (34.7%) and Ab+ NAT+ donors (36.5%) than Ab- NAT- donors (13.5%) in every period ($P < .001$). We observed no significant change in discard rate over time for any HCV donor group, although there was a trend toward significance in the Ab+ NAT- group (decrease from 42.0% to 22.4%, $P = .12$).

Transplantation

For recipients of Ab+ NAT- kidneys, there was a significant increase in the number of HCV-negative recipients, from a minority in period 1 ($n = 5$ [10.6%]) to more than 75% in period 5 ($n = 97$ [75.8%]; $P = .02$; Fig 3). For recipients of Ab+ NAT+ kidneys, there was a significant decrease in the proportion of HCV-positive recipients ($P = .01$), and a trend toward significance for an increase in HCV-negative recipients ($P = .08$; Fig 3).

Discussion

In this nationwide cohort of deceased donors, we found that during a 2.5-year period there was an increase in both the overall number of donors with 1 or more markers of HCV infection and an increase in Ab+ NAT- donors. Recipients of these Ab+ NAT- livers and kidneys are increasingly HCV negative. For Ab+ NAT+ donors, there was a decrease in the liver discard rate and perhaps the start of a trend toward transplantation of these livers into HCV-negative recipients. In addition, there was large variability in waitlist practices at the center level with regard to listing potential recipients for organs from donors with HCV. These data suggest a changing landscape in the listing and transplantation practice of organs with markers of any HCV infection, likely attributable to both the opioid epidemic and availability of DAAs.

Given that organs from donors with HCV are now likely to be of better quality (ie, younger, more likely to be brain dead, and presumed shorter time period with active HCV infection), these data are not all that surprising. Although only one subpopulation demonstrated a significant increase in the proportion of donors over time (Ab+ NAT- donors) and only one subpopulation showed a significant decrease in the discard rate (Ab+ NAT+ liver donors), there is an overall transition from an almost exclusively HCV-positive recipient population to an increasingly HCV-aviremic recipient population. For example, in period 1 there were 18 recipients of all Ab+ organs combined compared with 164 in period 5.

In an earlier study, we predicted potential gains in the number of liver and kidney transplants performed per year if Ab+ NAT- and

Table III
Transplantation of livers and kidneys by donor and recipient (R) HCV status

Liver						
Ab- NAT-	Period 1	Period 2	Period 3	Period 4	Period 5	P
Donors	4,305	4,370	4,660	4,754	4,800	
R HCV-	1,907 (44.3%)	2,078 (47.6%)	2,346 (50.3%)	2,469 (51.9%)	2,443 (50.9%)	.04
R HCV+	880 (20.4%)	733 (16.8%)	695 (14.9%)	666 (14.0%)	633 (13.2%)	.01
R HCV unknown	53 (1.2%)	71 (1.6%)	100 (2.1%)	35 (0.7%)	180 (3.8%)	.32
Discard n (%)	1,465 (34.0%)	1,488 (34.1%)	1,519 (32.6%)	1,584 (33.3%)	1,544 (32.2%)	.12
Ab+ NAT-						
Donors	81	84	102	144	131	
R HCV-	1 (1.7%)	7 (11.9%)	14 (20.3%)	29 (27.6%)	27 (31.0%)	.005
R HCV+	55 (93.2%)	52 (88.1%)	55 (79.7%)	75 (71.4%)	59 (67.8%)	.002
R HCV unknown	3 (5.1%)	0	0	1 (0.95%)	1 (1.2%)	.35
Discard n (%)	22 (27.2%)	25 (29.8%)	33 (32.4%)	39 (27.1%)	44 (33.6%)	.34
Ab+ NAT+						
Donors	192	199	214	228	240	
R HCV-	2 (1.7%)	6 (4.9%)	7 (5.3%)	4 (2.8%)	22 (14.5%)	.16
R HCV+	112 (96.6%)	114 (92.9%)	125 (94.7%)	138 (96.5%)	122 (80.3%)	.39
R HCV unknown	2 (1.7%)	3 (2.4%)	0	1 (0.7%)	8 (5.3%)	.46
Discard n (%)	76 (39.6%)	76 (38.2%)	82 (38.3%)	85 (37.3%)	88 (36.7%)	.01
Kidney						
Ab- NAT-	Period 1	Period 2	Period 3	Period 4	Period 5	P
Donors	6,535	6,611	7,030	7,153	7,351	
R HCV-	5,476 (83.8%)	5,511 (83.4%)	5,846 (83.2%)	5,968 (83.4%)	6,210 (84.5%)	.06
R HCV+	213 (3.3%)	182 (2.8%)	208 (3.0%)	195 (2.7%)	192 (2.6%)	.09
Discard n (%)	846 (12.9%)	918 (13.9%)	976 (13.9%)	990 (13.8%)	949 (12.9%)	.97
Ab+ NAT-						
Donors	81	96	89	139	165	
R HCV-	5 (10.6%)	4 (6.9%)	6 (12.2%)	27 (30.0%)	97 (75.8%)	.02
R HCV+	42 (89.4%)	54 (93.1%)	43 (87.8%)	63 (70.0%)	31 (24.2%)	.08
Discard n (%)	34 (42.0%)	38 (39.6%)	40 (44.9%)	49 (35.3%)	37 (22.4%)	.12
Ab+ NAT+						
Donors	220	213	246	248	237	
R HCV-	10 (6.9%)	9 (6.6%)	18 (11.4%)	22 (13.7%)	18 (13.0%)	.08
R HCV+	134 (93.1%)	128 (93.4%)	140 (88.6%)	139 (86.3%)	121 (87.1%)	.01
Discard n (%)	76 (34.5%)	76 (35.7%)	88 (35.8%)	87 (35.1%)	98 (41.4%)	.15

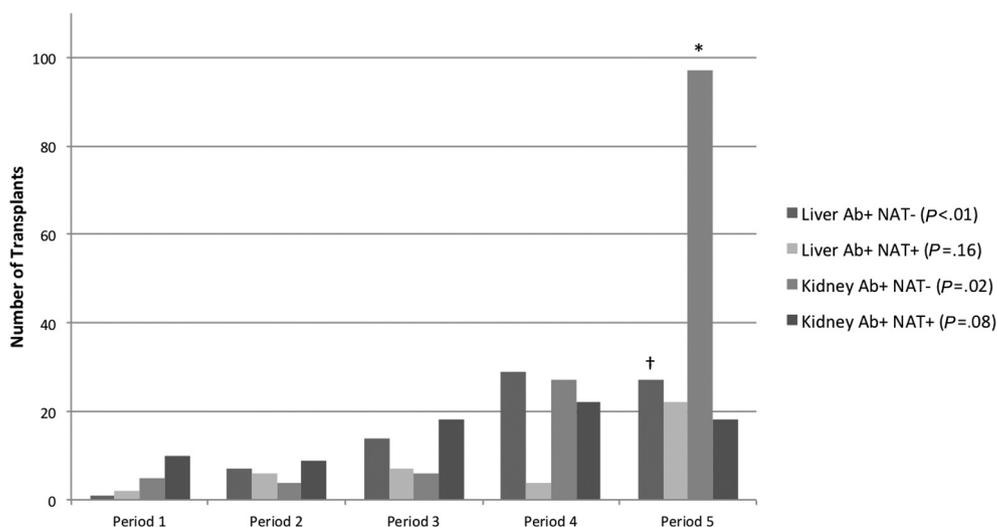


Fig 3. Transplantation of organs from Ab+ NAT- and Ab+ NAT+ donors into HCV-negative recipients (* $P = .02$, † $P < .01$).

Ab+ NAT+ organs were used at the same rate as Ab- NAT- organs.²⁴ In the last year of this study (periods 4 and 5 combined), the number of liver transplants from Ab+ NAT- donors ($n = 192$) far exceeded that predicted by our model ($n = 131$, range 125–136), as did the number of kidney transplants ($n = 218$ in this study versus predicted 124, range 118–130). This is likely attributable to

the increased number of Ab+ NAT- donors during the study period, which was unaccounted for in the original study. Although the rate of drug overdose deaths continued to increase by 12% between 2016 and 2017,²⁵ the most recent data for the 12 months leading up to June 2018 show a plateau or perhaps a slight decrease in drug overdose deaths.²⁶ This could alter the availability of organs

with any marker of HCV over time, although the trajectory of this epidemic is currently unknown.

The transplantation of HCV-viremic and HCV-aviremic donors into aviremic recipients is vastly underreported in the liver and kidney literature, potentially in part because of delays from reporting to publication and considering the practice as an extension of the current standard of care rather than novel and worthy of publication. The first case report of transplantation of an HCV NAT+ liver donor into an aviremic recipient was submitted in 2017 and published in 2018,¹⁸ although based on our data, this practice has been occurring since as early as 2015. Only in recent months have there been case series of use of HCV Ab+ NAT- kidneys into aviremic recipients in the kidney literature,^{19,20} although our data show this is currently now more than 75% of these kidneys are utilized.

Despite increasing evidence of the successful use of organs from donors with HCV, few centers are listing patients for such organs. It is interesting that there is no correlation between a center's kidney and liver waitlist acceptance of HCV-positive organs, perhaps signaling risk tolerance differences between the two programs within the same institution. There appears to be more acceptability of use of HCV-positive organs in the liver than in kidney population, possibly attributable to the lack of liver dialysis. Of note, a minority of these waitlisted patients willing to accept an HCV-positive organ have HCV as a diagnosis for both livers and kidneys. We also found that donor HCV prevalence does not correlate with waitlist HCV organ acceptance, perhaps suggesting that the aggressive centers are driven by the concept rather than availability of organs.

How should these data change your practice? We suggest the transplantation of livers from HCV-viremic donors into HCV-naïve recipients with acute liver failure, hepatocellular cancer, or those who are "sicker than lab model for end-stage liver disease" after a thorough discussion and consent process, as suggested by Saberi et al.¹⁸ Furthermore, consideration should be given to transplanting an HCV-viremic liver into recipients with a model for end-stage liver disease of ≥ 20 , which was life prolonging in a study using a Markov-based mathematical model.²⁷ We suggest considering the transplantation of Ab+ NAT- livers and kidneys into any consenting recipient, with the acknowledgment that the rate of de novo HCV infection is unknown, but likely higher for liver recipients ($n = 5/55$ [9.1%] in the largest liver study¹⁴) than kidney recipients ($n = 1/57$ [1.7%], combining the two kidney studies^{19,20}). All recipients of aviremic organs should undergo posttransplant surveillance.

Although the authors do support the transplantation of HCV-positive organs into HCV-negative recipients, we acknowledge there are certain limitations and knowledge gaps in this practice, particularly regarding long-term outcomes. Early data have shown no statistically significant difference in 1-year patient or graft survival for kidneys recipients (aviremic donors into HCV-negative recipients)²⁸ and 2-year graft survival for liver recipients (viremic and aviremic donors into HCV-negative recipients)²⁹ compared with HCV-negative donors. However, longer-term outcomes are not yet available and should be systematically analyzed. Obtaining insurance approval for DAAs is a programmatic issue that transplant centers must address, and the optimal timing of DAA treatment has not been defined. Highlighting these issues is a recent study that described a case of HCV-induced membranous nephropathy within 3 weeks of liver transplant from a NAT+ donor into a HCV-naïve recipient who was initially denied DAA coverage by his insurance company.³⁰ Of note, there are differing opinions about whether such studies should be performed as a clinical trial, as suggested by Levitsky et al.,⁵ or as an extension of clinical care requiring informed consent but not as part of a trial, as has been done in many studies^{6,8–20} and in the real world, as reported here. Furthermore, cost-effectiveness studies are starting to emerge that suggest either cost

neutrality³¹ or potential cost savings³² in transplanting HCV NAT+ kidneys into aviremic recipients.

Our study demonstrated that there has been an increase in number of donors with markers of HCV infection, which has resulted in a change in how these organs are used in liver and kidney transplant recipients, with more organs being transplanted into HCV-aviremic recipients. The transplantation of livers and kidneys from donors with markers of HCV infection is both more prevalent than being described in the literature and, in our opinion, potentially still underutilized. Although we acknowledge that there are still a lot of unknowns associated with this practice, we encourage increased consideration of the use of organs from donors with HCV infection and more common reporting of experiences.

Conflict of interest

The authors have indicated that they have no conflict of interest regarding the content of this article.

References

- Daniels D, Grytdal S, Wasley A, Centers for Disease Control and Prevention (CDC). Surveillance for acute viral hepatitis—United States, 2007. *MMWR Surveill Summ*. 2009;58:1–27.
- Zibbell JE, Asher AK, Patel RC, et al. Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004 to 2014. *Am J Public Health*. 2018;108:175–181.
- Centers for Disease Control and Prevention. Surveillance for viral hepatitis—United States, 2016 Web site. <https://www.cdc.gov/hepatitis/statistics/2016surveillance/commentary.htm>. Accessed September 4, 2018.
- Goldberg DS, Blumberg E, McCauley M, Abt P, Levine M. Improving organ utilization to help overcome the tragedies of the opioid epidemic. *Am J Transplant*. 2016;16:2836–2841.
- Levitsky J, Formica RN, Bloom RD, et al. The American Society of Transplantation Consensus Conference on the use of hepatitis C viremic donors in solid organ transplantation. *Am J Transplant*. 2017;17:2790–2802.
- Gottlieb RL, Sam T, Wada SY, et al. Rational heart transplant from a hepatitis C donor: New antiviral weapons conquer the Trojan horse. *J Card Fail*. 2017;23:765–767.
- McLean R, Reese PP, Acker M, Abt P, Sicilia A, Hornsby N, et al. Early results from USHER: A pilot trial of transplanting HCV-infected hearts into HCV-negative recipients followed by anti-viral therapy Web site. <https://atcmeetingabstracts.com/abstract/early-results-from-usher-a-pilot-trial-of-transplanting-hcv-infected-hearts-into-hcv-negative-recipients-followed-by-anti-viral-therapy/>. Accessed August 20, 2018.
- Miller TE, Michell E, DeVore A, Schroder J, Patel CB. Breaking the viral spiral: Changing how you C hepatitis. *J Heart Lung Transplant*. 2018;37:S77.
- Patel SR, Saeed O, Sims D, et al. Cardiac transplantation from non-viremic hepatitis C donors. *J Heart Lung Transplant*. 2018;37:S137.
- Schlendorf K, Zalawadiya S, Shah A, et al. Early outcomes using hepatitis C-exposed donors for cardiac transplantation in the era of effective direct-acting antiviral treatments. *J Heart Lung Transplant*. 2018;37:S341.
- Wettersten N, Tran H, Pretorius V, Aslam S, Adler E. Case of combined heart-kidney transplant from hepatitis C (+) donor to a HCV (–) recipient. *J Heart Lung Transplant*. 2018;37:S139.
- Wooley AE, Singh SK, Mallidi HR, et al. Transplanting thoracic organs from hepatitis C positive donors to hepatitis C uninfected recipients. *J Heart Lung Transplant*. 2018;37:S142.
- Mulvihill MS, Cox ML, Watson J, ElLaissi L, Wolfe CR, Gray A, et al. Early experience with the use of hepatitis C antibody-positive, nucleic acid testing-negative donors in lung transplantation. *J Heart Lung Transplant*. 2018;37:S77.
- Luckett K, Kaiser T, Bari K, et al. Use of hepatitis C AB-positive donor liver in hepatitis C nonviremic liver transplant recipients. *J Am Coll Surg*. 2019;228:560–567.
- Campos-Varela I, Agudelo EZ, Sarkar M, Roberts JP, Terrault NA. Use of a hepatitis C virus (HCV) RNA-positive donor in a treated HCV RNA-negative liver transplant recipient. *Transpl Infect Dis*. 2018. <https://doi.org/10.1111/tid.12809>.
- Martins P, Movahedi B, Ahearn A, Bozorgzadeh A. Intentional transplantation of hepatitis C positive livers into hepatitis negative recipients—Report of the first case-series in the world Web site. <https://atcmeetingabstracts.com/abstract/intentional-transplantation-of-hepatitis-c-positive-livers-into-hepatitis-negative-recipients-report-of-the-first-case-series-in-the-world/>. Accessed August 20, 2018.
- Mitchell RA, Hussaini T, Yau AH, et al. Transplantation of a liver allograft from a hepatitis C virus seropositive donor with previous sustained virologic response

- to an uninfected recipient suffering steroid refractory acute graft rejection with no evidence of HCV transmission. *Transplant Direct*. 2018;4:e347.
18. Saberi B, Hamilton JP, Durand CM, et al. Utilization of hepatitis C virus RNA-positive donor liver for transplant to hepatitis C virus RNA-negative recipient. *Liver Transpl*. 2018;24:140–143.
 19. Dao A, Cuffy M, Kaiser T, et al. Use of HCV Ab+/NAT– donors in HCV naïve renal transplant recipients Web site. <https://atcmeetingabstracts.com/abstract/use-of-hcv-ab-nat-donors-in-hcv-naive-renal-transplant-recipients/>. Accessed August 20, 2018.
 20. de Vera ME, Volk M, Ncube Z, et al. Transplantation of hepatitis C virus (HCV) antibody positive, nucleic acid test negative donor kidneys to HCV negative patients frequently results in seroconversion but not HCV viremia. *Am J Transplant*. 2018;18:2451–2456.
 21. Durand CM, Bowring MG, Brown DM, et al. Direct-acting antiviral prophylaxis in kidney transplantation from hepatitis C virus-infected donors to noninfected recipients: An open-label nonrandomized trial. *Ann Intern Med*. 2018;168:533–540.
 22. Reese PP, Abt PL, Blumberg EA, et al. Twelve-month outcomes after transplant of hepatitis C-infected kidneys into uninfected recipients: A single-group trial. *Ann Intern Med*. 2018;169:273–281.
 23. NIH US National Library of Medicine. Clinicaltrials.gov 2018 Web site. <https://www.clinicaltrials.gov>. Accessed July 19, 2018.
 24. Kling CE, Perkins JD, Landis CS, Limaye AP, Sibulesky L. Utilization of organs from donors according to hepatitis C antibody and nucleic acid testing status: Time for change. *Am J Transplant*. 2017;17:2863–2868.
 25. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep*. 2018;67:1419–1427.
 26. Centers for Disease Control and Prevention. Vital statistics rapid release: Provisional drug overdose death counts Web site. <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. Accessed February 7, 2019.
 27. Chhatwal J, Samur S, Bethea ED, et al. Transplanting hepatitis C virus-positive livers into hepatitis C virus-negative patients with preemptive antiviral treatment: A modeling study. *Hepatology*. 2018;67:2085–2095.
 28. Sibulesky L, Kling CE, Blosser C, et al. Are we underestimating the quality of aviremic hepatitis C-positive kidneys? Time to reconsider. *Am J Transplant*. 2018;18:2465–2472.
 29. Cotter TG, Paul S, Sandıkçı B, et al. Increasing utilization and excellent initial outcomes following liver transplant of HCV-viremic donors into HCV-negative recipients. *Hepatology*. 2019. <https://doi.org/10.1002/hep.30540>.
 30. Wadei HM, Pungpapong S, Cortese C, et al. Transplantation of HCV-infected organs into uninfected recipients: Advance with caution. *Am J Transplant*. 2019;19:960–961.
 31. Trotter PB, Summers DM, Ushiro-lumb I, et al. Use of organs from hepatitis C virus-positive donors for uninfected recipients: A potential cost-effective approach to save lives? *Transplantation*. 2018;102:664–672.
 32. Kadatz M, Klarenbach S, Gill J, Gill JS. Cost-effectiveness of using kidneys from hepatitis C nucleic acid test-positive donors for transplantation in hepatitis C-negative recipients. *Am J Transplant*. 2018;18:2457–2464.