Provider Attitudes toward the Use of Hepatitis C Virus-Positive Organs in Kidney Transplantation

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Keywords

Hepatitis C · Organ allocation · Kidney transplantation · Provider education

Abstract

Background: Direct-acting antivirals have changed the landscape of hepatitis C virus (HCV) care. While transplantation with HCV-positive donor organs is increasing, little is known about providers' attitudes toward this topic. The aim of this study is to determine providers' attitudes toward HCV-positive kidney transplantation. **Methods:** Willing transplant and nontransplant nephrologists, transplant surgeons, and mid-level providers completed an online survey from April through May 2018. The survey asked about HCV knowledge and willingness to transplant HCV-positive antibody, nucleic acid testing-positive kidneys into HCV-negative recipients. Descriptive analyses including mean and median for continuous variables and frequencies for categorical variables were calculated. **Results:** Seven-hundred surveys were emailed and 99 providers (62 transplant nephrologists, 28 nontransplant nephrologists, 7 transplant surgeons, and

2 advanced practice providers) completed the survey (participation rate 14.1%). All providers knew that HCV was curable, with 60% believing that it had no effect on transplant success and 32% thinking it reduced transplant success. Providers were significantly more likely to offer a HCV-positive organ to HCV-positive recipients compared to HCV-negative recipients in all queried circumstances ($p < 0.005$ in all cases), especially with increasing impact on patient's quality of life. While only 39% of providers would offer a HCV-positive organ for transplant to a patient without HCV if it reduced the waitlist time by 1 year, 92% would offer a HCV-positive organ if it reduced the waitlist time by 4 years. However, only 47% thought that the use of HCV-positive kidneys should be for routine care, while 38% believed it should be reserved for research purposes only. There were no significant differences between transplant and nontransplant nephrologists in attitudes toward HCV-positive kidney transplantation. Providers believed that donor organs from those who were obese, >50 years old, or had died from a cardiac arrest were

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significantly more likely to reduce the likelihood of a successful transplant 1-year posttransplant when compared with a HCV-positive organ ($p < 0.005$ in all cases). Eighty-six percent of providers had concerns about HCV curability posttransplant. **Conclusion:** Although 92% of providers were willing to offer a HCV-positive kidney for transplant as patient waitlist time increases, less than half supported offering HCV-positive transplantation for routine care rather than for research. The results underscore the need for further education and data about the efficacy and safety of HCV-positive kidney transplantation.

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Introduction

Donor organ scarcity remains a significant issue facing transplant medicine today. In the last 30 years, the kidney transplant (KT) waitlist size has increased by 600% in the absence of a corresponding increase in donations [1]. According to the 2016 Organ Procurement Transplant Network/Scientific Registry of Transplant Recipients annual report on KT, 30,869 adult patients were newly added to the transplant list in 2016. While inequities exist in KT rates across donation service areas, as little as 9.1% of KT candidates are transplanted within 5 years. Mortality rates for KT candidates on the waitlist range from 0 to 2.7 per 100,000 patient-years [2].

To improve donor graft shortages, hepatitis C virus (HCV)-positive donor grafts are being used across all solid organ transplantation [3]. In the direct-acting antiviral (DAA) era, HCV treatments are well tolerated, and most regimens have nearly 100% cure rates. HCV positivity affects 1–2% of the U.S. population, an estimated 1.8–8% of KT recipients, and 4–18% of potential organ donors [3–5]. Prior to the DAA era in 2014, HCV cure rates using interferon-based regimens were approximately 50% and even lower (18–34%) for KT recipients [6, 7]. In addition, in the pre-DAA era, HCV-positive kidneys were often not transplanted due to the near certainty of HCV transmission during transplant, as well as increased risk of mortality and graft loss in HCV-positive patients after KT. Between 2005 and 2014, 4,144 HCV antibody-positive kidneys, most of which were of good quality, were discarded [8]. These kidneys, however, may have not had active HCV and were only antibody positive as nucleic acid testing (NAT) status, a more accurate marker of active infection, was not routinely assessed [8]. The advent of DAA therapy has led to a reduction in HCV-positive organ discard rate, from 28% in 2010 to 11% in 2015 for HCV-

positive livers [9–15]. HCV-positive KT recipients who receive HCV-positive grafts have been shown to have shorter waitlist times and improved graft survival compared to HCV-positive recipients who receive HCV-negative grafts [16, 17]. The efficacy and safety of treating HCV-positive KT patients with DAA therapy have been shown in several studies [7, 12].

HCV-positive KT for HCV-negative patients, however, has been less studied and raises ethical questions of known infection transmission, informed consent, and DAA insurance coverage posttransplant. Small trials of HCV NAT-positive KT into HCV-negative recipients, either with DAA treatment very early post-KT or prophylactic pre-KT showed 100% SVR rates [18, 19]. One trial showed similar graft and patient survival rates for HCV antibody-positive KT recipients regardless of whether they received an HCV-positive or HCV-negative graft [20]. Despite the efficacy of HCV treatment, HCV-positive organs may not be routinely offered to patients. Little is known about provider attitudes toward HCV-positive KT, particularly in the DAA era. Given the ongoing interest in HCV-positive KT, we examined nephrologists', transplant surgeons', and transplant advanced practice providers' beliefs on this topic.

Methods

This study enrolled nephrologists, transplant surgeons, and advanced practice providers in transplant nephrology at academic medical centers in the United States and Canada. These providers were identified through online searches of nephrology and transplant departments in North America. Scripted emails inviting potential participants to complete a survey were sent to the providers listed on the academic medical centers' websites. If potential participants did not respond to the initial email, identical second and if necessary third emails, over a period of 2 months, were sent inviting the providers to participate. If willing to participate, providers completed an electronic survey.

The survey used the web-based REDCap and was designed with the assistance of the University of Chicago Survey Lab. It consisted of 5 parts: transplant provider status, knowledge of HCV and transplantation, beliefs toward offering HCV NAT-positive kidney grafts to HCV-positive and HCV-negative patients, attitudes toward the doctor-patient relationship, and demographics, including age, gender, time spent performing research and/or clinical care, and United Network for Organ Sharing (UNOS) practice region. Unless otherwise stated, for the remainder of the manuscript, "HCV-positive" denotes HCV NAT positivity.

Example survey questions and statements include the following, with answer choices in parentheses:

- What do you expect the rate of cure to be of HCV for posttransplant patients who acquire active HCV (antibody positive, NAT positive) through the receipt of an infected organ? (much

lower than the general rate; somewhat lower than the general rate; about the same as the general rate; somewhat better than the general rate; much better than the general rate)

- Does a donor with active HCV (positive antibody and viral load) likely reduce, not affect, or improve the odds of a successful transplant (at 1-year posttransplant), all other factors equal? (reduces likelihood of success; no effect on likelihood of success; improves likelihood of success)
- Despite obtaining prior written informed consent, do you worry HCV might not be curable after transplant if offering patients without HCV an active HCV organ? (not a worry; small worry; moderate worry; agree; large worry)

The entire survey can be found in online supplement 1 (see www.karger.com/doi/10.1159/000502049). Providers received a USD 10 Amazon Gift Card for their participation. The study was approved by the Institutional Review Board at the University of Chicago.

Descriptive analysis including mean and median for continuous variables and frequencies for categorical variables was performed. Student *t* test and one-way analysis of variance (continuous data) and Fisher's Exact test (categorical data) were used to compare differences between groups.

Results

Demographics

The survey was sent to 700 providers; 99 providers (65 males, 34 females) responded (14.1% participation rate) and were included in the study (Table 1). The median age was 44 years (range 32–73). The majority (90.9%) were nephrologists with 62.6% of total providers transplant nephrologists, and 7.1% transplant surgeons. The majority of providers exclusively cared for adults (90.9%) and reported being primarily clinicians (59.6%). The median years spent in practice were 15 (range 1–41).

Attitudes toward HCV-Positive KT

All of the surveyed providers reported that HCV was a curable disease. Table 1 shows provider attitudes toward the use and success of HCV-positive organs. Three quarters (74.7%) of participants believed that the cure rate posttransplant of HCV acquired from an infected transplanted organ was about the same as the general rate. Most (59.6%) respondents thought that a HCV-positive graft had no effect on the odds of a successful KT 1-year posttransplant, with 32.3% of providers thinking that a HCV-positive graft reduced transplant success at 1-year posttransplant. Nearly half (47.5%) of providers thought that the use of HCV-positive kidney grafts should be for routine care only, while 38.4% believed it should be reserved for research purposes only; of the 14 providers who chose "other," 5 wrote that HCV-positive KT should

be performed for both routine care and research purposes.

Compared to providers who believed the HCV cure rate was lower than the general rate, providers who believed that the HCV cure rate posttransplant was similar were significantly more likely to believe that HCV had no effect on the 1-year success of KT (68.9 vs. 22.7% respectively; $p < 0.005$). They were also significantly more likely to believe that HCV-positive KT should be used for routine care as opposed to research purposes only (55.4 vs. 27.3%, respectively; $p = 0.03$).

Attitudes toward Organ Donor Sources

The survey asked about attitudes concerning other types of organ donors. Donor organs from those who were obese, >50 years old, or had died from a cardiac arrest were thought to significantly reduce the likelihood of success 1-year post KT compared with a HCV-positive organ ($p < 0.005$ in all cases, Fig. 1). Grafts from a donor <50 years old who died accidentally were thought to significantly improve the likelihood of success 1-year posttransplant compared with a HCV-positive organ ($p < 0.005$, Fig. 1).

Attitudes toward Scenarios Involving HCV-Positive and HCV-Negative Kidney Grafts

Providers were asked whether or not they would offer a HCV-positive kidney to both HCV-positive and HCV-negative patients in 5 different clinical contexts: (1) patient who is pre-dialysis with a glomerular filtration rate <20 mL/min/1.73 m²; (2) patient who has been on dialysis for a year with an expected 5 year waitlist time before KT and is happy with their quality of life; (3) similar patient on HD but is unhappy with their quality of life; (4) patient who has been on HD for 4 years and is running out of HD access options; and (5) patient who is >65 years old with diabetes mellitus and coronary artery disease who has recently initiated dialysis. Providers were significantly more likely to offer a HCV-positive organ to HCV-positive patients compared to HCV-negative patients in all queried circumstances ($p < 0.005$ in all cases), especially with increasing impact on patient's quality of life.

Attitudes toward HCV-Positive KT and Waitlist Time

About two-fifths (39.4%) of participants reported that they would offer a HCV-positive organ to a HCV-negative patient if it reduced their waitlist time by 1 year. This percentage increased for every year reduction in waitlist time, with 91.9% of respondents reporting they would of-

Table 1. Demographic, practice, and attitudes toward HCV-related kidney transplantation data among all participants

	All respondents (<i>n</i> = 99)
<i>Demographic variables</i>	
Age, years, mean, median (range)	46.4, 44.0 (32–73)
Gender, female, <i>n</i> (%)	34 (34.3)
Provider, <i>n</i> (%)	
Transplant surgeon	7 (7.1)
Transplant nephrologist	62 (62.6)
Nontransplant nephrologist	28 (28.3)
Mid-level provider	2 (2.0)
Type of practice, <i>n</i> (%)	
Adult	90 (90.9)
Pediatrics	1 (1.0)
Adult and pediatrics	8 (8.1)
Years in practice, mean, median (range)	16.1, 15.0 (1–41)
UNOS Region, <i>n</i> (%)	
1	6 (6.2)
2	5 (5.2)
3	15 (15.5)
4	1 (1.0)
5	17 (17.5)
6	12 (12.4)
7	6 (6.2)
8	7 (7.2)
9	11 (11.3)
10	4 (4.1)
11	14 (14.4)
<i>Provider attitudes toward HCV-positive KT</i>	
HCV is a curable disease, <i>n</i> (%)	99 (100)
HCV cure rate of KT recipient who acquires HCV	
NAT + donor organ, <i>n</i> (%)	
Lower than the general rate	22 (22.3)
About the same as the general rate	74 (74.7)
Better than the general rate	3 (3.0)
HCV + transplantation for which purposes, <i>n</i> (%)	
Routine care only	47 (47.5)
Research purposes only	38 (38.4)
Other	14 (14.1)
HCV-infected organ affecting the odds of a successful transplant at 1-year post KT, <i>n</i> (%)	
Reducing likelihood	32 (32.3)
No effect	59 (59.6)
Improving likelihood	8 (8.1)
Would offer HCV-infected organ to a patient without HCV if reduced waitlist time by, year, <i>n</i> (%)	
1	39 (39.4)
2	61 (61.6)
3	82 (82.8)
4	91 (91.9)
HCV, hepatitis C virus; KT, kidney transplantation; NAT, nucleic acid testing.	

Fig. 1. Providers' attitudes toward donor sources and/or donor characteristics improving, reducing, or having no effect on transplant success within 1 year after transplant. Asterisks indicate answers that the literature primarily supports. HCV, hepatitis C virus; IVDU, intravenous drug user.

Fig. 2. Increasing willingness of providers to offer HCV NAT-positive KT to HCV-negative patients based upon waitlist reduction time. The providers are stratified according to their beliefs regarding HCV NAT-positive KT on transplant success. KT, kidney transplant.

fer HCV-positive KT to HCV-negative patients if it reduced waitlist time by 4 years (Fig. 2). Providers who believed that HCV-positive KT had no effect on transplant success were not more likely to offer a HCV-positive organ if waitlist time decreased compared to providers who believed that HCV-positive KT reduced transplant success ($p = 0.201$).

Concerns Associated with HCV-Positive KT

The most frequently cited concern among providers regarding HCV-positive KT for HCV-negative recipients was that HCV may not be curable after transplant, with only 14.1% of providers not worried about this possibility. 62.6% of providers reported worrying about patients' feeling "soiled" by receiving a diseased, although curable,

organ, 62.6% were concerned about violating the "do no harm" medical ethic, and 59.6% were worried about the risk of a malpractice lawsuit.

When asked whether they viewed their role as a provider primarily in terms of a medical expert, who provides the best course of treatment according to their training and science, or primarily in terms of a collaborator, who works with a patient to devise plans that take into account patient preferences, beliefs, and practical constraints, even when these run counter to science of best medical practice, 28.3% of providers viewed themselves in the former category while 71.7% classified themselves as the latter. When these 2 groups were compared, there were no significant differences when asked about provider responsibility toward a patient refusing treatment that will

reduce morbidity and mortality as well as refusing a HCV-positive graft if they were HCV negative ($p = 0.548$, $p = 0.208$, respectively). There were no significant differences between transplant and nontransplant nephrologists in any queried attitudes toward HCV-positive organ transplantation.

Discussion

To the best of our knowledge, this is the first study to assess providers' attitudes specifically toward HCV NAT-positive KT for HCV-negative patients in the DAA era. Although 91.9% of providers were willing to offer a HCV-positive kidney to a HCV-negative patient if doing so reduced waitlist time by 4 years, less than half of providers believed in offering HCV-positive KT for routine care rather than for research. Approximately one-third of providers thought that a HCV-positive organ reduced transplant success at 1-year posttransplant, and the surveyed providers were more willing to offer HCV-positive kidney grafts to HCV-positive patients compared to HCV-negative patients. This reinforces the need for further data regarding the efficacy and safety of HCV NAT-positive kidney transplantation in the DAA era and highlights the need for increased efforts at provider education.

Utilization rates for HCV-positive kidney grafts in the pre- and post-DAA eras have been consistently shown to be lower than HCV-negative kidney grafts. From 1995 to 2009, HCV antibody-positive kidney grafts were 2.6 times more likely to be discarded compared to HCV-negative kidney grafts for HCV-positive patients [21]. In a retrospective analysis of more than 9,000 patients who had HCV antibody and NAT data, HCV antibody-positive or NAT-positive kidney grafts were significantly less likely to be transplanted than their negative counterparts due to their HCV positivity [22]. Slightly less than half (47.5%) of respondents believed that HCV-positive KT should be performed as routine care, while 38.4% of providers reported that this practice should be limited to research purposes only. Given that the majority of providers believed that HCV was highly curable post-KT, perhaps rather than doubting DAA effectiveness post-KT, providers would prefer to see more efficacy and safety data before offering HCV-positive KT routinely. Performing high-quality trials comparing outcomes for donor HCV NAT positive/recipient HCV NAT negative (D+/R-) KT to HCV NAT D+/R+, D-/R+, and D-/R- KT should be a priority for the transplant community.

A majority of providers in our study believed that the HCV cure rate post KT from a HCV-positive donor was about the same as the general rate (74.7%) and that a HCV-infected organ had no effect on the odds of a successful transplant at 1-year posttransplant (59.6%). These beliefs are likely secondary to the documented high SVR rates for KT patients in the DAA era – both for KT recipients with chronic HCV infection and for KT recipients who acquired acute HCV from a HCV-positive kidney [7, 18, 19]. In addition, a 2017 study reported that KT recipients who received HCV antibody-positive kidney grafts had the same graft and survival rates as those who received HCV-negative kidney grafts; of note, only 29.6% of KT recipients who received HCV-positive kidney grafts were HCV-positive before KT [20].

Some providers, however, reported that the HCV cure rate posttransplant was less than the average rate (22.3%). Those who believed this were significantly more likely to believe that a HCV-positive organ reduced the odds of a successful transplant at 1-year posttransplant compared to those who believed the cure rate was similar to the general rate. These differences in provider attitudes may suggest that patients may receive varying information on posttransplant outcomes as well as discrepant offers for HCV-positive grafts, depending on provider beliefs.

While initial data are positive regarding efficacious SVR rates and outcomes for HCV-positive KT recipients – both who acquired HCV before or from KT – few clinical trials have been conducted specifically examining these issues. Two open label, nonrandomized pilot trials, each with ten HCV-negative patients who underwent HCV NAT-positive KT, demonstrated 100% SVR rates [18, 19]. These trials have led to a surge in interest in HCV D+/R- KT and may herald a paradigm shift in transplant medicine. Given the low utilization rates of HCV-positive kidney grafts, increased provider education on the efficacious HCV SVR rates and preliminary outcome and safety data may lead to increased use of these grafts.

Little data exist regarding provider attitudes toward Public Health Service (PHS) increased risk (IR) organ donation, including for HCV-positive KT, both into HCV-positive and HCV-negative patients. From 2005 to 2008, PHS IR kidney grafts were 8.2% less likely, compared to non-PHS IR kidneys, to be used for KT, even though posttransplant survival rates were equivalent between the 2 groups at 2-year follow-up [23]. Similarly, a study examining patients from 2010 to 2013 showed that PHS IR kidney grafts were used at a lower rate than non-PHS IR

kidneys (76.7 and 83.7%, respectively) [24]. A 2014 survey of 87 nonphysician transplant providers, 64% of whom were registered nurses, found that 56% of respondents felt uncomfortable discussing informed consent for PHS IR kidney grafts [25]. In this study, 99% of those surveyed also wanted supplemental education on PHS IR kidney donation.

Although some respondents expressed concerns about HCV positivity on transplant success, the participants were more likely to view obesity, a kidney from a donor >50 years old, or a kidney from a donor who died of cardiac arrest as more likely to reduce posttransplant success than a HCV-positive kidney graft. A potential explanation for these differences includes the previously discussed equivalent patient and graft survival rates as well as high SVR rates for HCV-positive KT recipients in the DAA era. Other reasons may be that HCV-positive donors have been shown to be younger and have less comorbidities than non HCV-positive donors [20, 26–28]. In addition, kidney grafts from those who are older and who have died from cardiac arrest have been shown to lead to worse posttransplant outcomes [29, 30]. Intravenous drug user donor grafts have been shown to have equivalent outcomes to nonintravenous drug user grafts, and controversy exists regarding whether donor obesity affects KT outcomes positively or negatively [31, 32].

Providers were also more likely to offer HCV D+/R+ KT compared to HCV D+/R– KT. This belief coincides with the most frequently cited provider concern: HCV curability, with 85.9% citing this as a worry they had regarding HCV-positive KT. Although the vast majority of providers had this concern, 79.8% of providers reported that the general cure rate of HCV was greater than 90%, and approximately 3-quarters of them believed that the HCV cure rate post-KT was the same as the general rate. In addition to rare SVR failures, obtaining insurance approval for these sometimes costly DAA therapies could be potential reasons for this concern [20, 33].

There are several limitations to our study. The response rate was 14.1%, resulting in potential selection bias. Because the survey lacked questions that identified individuals, it is impossible to compare participants' and nonparticipants' demographic information, gender, profession, and UNOS region, which may have aided in results analysis and mitigated potential downsides to the response rate. Future studies on provider attitudes should link participants' identity to their responses in order to analyze these potential differences. The online survey format may have contributed to the response rate seen as multiple studies have documented a lower response rate

for online surveys of 17.9–22%, including ongoing declines in online survey participation each year, compared to traditional written surveys [34–36]. Another limitation is the paucity of transplant surgeon and mid-level provider representation in our study. Further studies analyzing these providers' attitudes – particularly transplant surgeons – are necessary given the essential role they play in KT care and the transplant consent process. Generalizability of our results, both across the United States as well as worldwide, may be a limitation. All UNOS regions are represented in our survey; however, given the number of participants, 6 regions each have less than ten percent of those surveyed. In addition, overseas provider attitudes of HCV-positive KT may differ, given the divergent incidence of HCV in different countries and the known varying cultural beliefs toward HCV in general [37–39].

In addition, although this study reports providers' beliefs concerning HCV-positive KT, these attitudes are not coupled with providers' actions or patient beliefs. Although outside the scope of this survey study, a robust study linking attitudes and clinical practice would shed light on if provider beliefs toward HCV-positive KT are influencing their clinical practice. A 2019 study examining solid organ (primarily kidney) transplant candidates' attitudes toward HCV NAT-positive KT showed that 46% of patient were willing to receive a HCV NAT-positive kidney, 30% were unsure, and 24% were unwilling [40]. The candidates amenable to HCV NAT-positive KT had significantly higher levels of trust in their physicians [40]. These data reinforce the need for greater provider and patient education toward HCV NAT-positive KT.

In summary, less than half of providers surveyed reported that HCV-positive KT should be performed for clinical purposes only. However, a majority of providers in our study believed that the cure rate posttransplant of HCV acquired from an infected transplanted organ was about the same as the general rate and that a HCV-infected organ had no effect on the odds of a successful transplant at 1-year posttransplant. HCV-positive KT was more appealing to providers than grafts from obese donors, those >50 years old, and donors who died from cardiac arrest. Increasing waitlist times were also associated with increased provider willingness to offer HCV-positive KT. More research on the safety and efficacy, as well as standardization of protocols, of DAA therapy post-KT will likely influence providers' beliefs toward HCV-positive KT. Provider education regarding the high HCV cure rates post-KT may result in an increase in routine HCV-positive KT.

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Statement of Ethics

Subjects have given their written informed consent. The study protocol has been approved by the University of Chicago Medical Center's committee on human research. No animal experiments were performed in the course of this research.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

T.C.: acquisition of data; interpretation of data; drafting of manuscript. J.K., K.S., and A.N.: acquisition of data. H.Y.: critical revision of manuscript for important intellectual content. R.C.: study concept and design; critical revision of manuscript for important intellectual content. S.P.: study concept and design; interpretation of data; drafting of manuscript; critical revision of manuscript for important intellectual content.

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