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**Review of heart transplantation from hepatitis C-positive donors**

Patel P *et al*. Heart transplantation from hepatitis C-positive donors

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**Abstract**

Significant scarcity of a donor pool exists for heart transplantation (HT) as the prevalence of patients with end-stage refractory heart failure is increasing exceptionally. With the discovery of effective direct-acting antiviral and favorable short-term outcomes following HT, the hearts from hepatitis C virus (HCV) patient are being utilized to increase the donor pool. Short-term outcomes with regards to graft function, coronary artery vasculopathy, and kidney and liver disease is comparable in HCV-negative recipients undergoing HT from HCV-positive donors compared to HCV-negative donors. A significant high incidence of donor-derived HCV transmission was observed with great success of achieving sustained viral response with the use of direct-acting antivirals. By accepting HCV-positive organs, the donor pool has expanded with younger donors, a shorter waitlist time, and a reduction in waitlist mortality. However, the long-term outcomes and impact of specific HCV genotypes remains to be seen. We reviewed the current literature on HT from HCV-positive donors.

**Key Words:** Heart transplant; Hepatitis C-positive donors; Direct-acting antiviral; Coronary allograft vasculopathy; Allograft rejection

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**Core Tip:** Given the favorable preliminary data and ongoing opioid epidemic, the utilization of hepatitis C virus-positive hearts is on the rise, which is aiding in the closure of the gap between heart transplantation candidates and donors. Additionally, with future studies evaluating long-term outcomes and standardization of direct-acting antiviral therapy, more transplant centers will accept hepatitis C virus-positive organs.

**INTRODUCTION**

Heart failure (HF) prevalence is increasing, with 6.2 million adults diagnosed from 2013 to 2016 compared to 5.7 million from 2009 to 2013. The prevalence is estimated to increase to more than 8 million by 2030[1,2]. In 10%-15% of patients, end-stage refractory HF will develop requiring advanced therapies including orthotopic heart transplantation (OHT) or durable mechanical support therapies[2,3]. There is a substantial mismatch between donors and recipients as there is an increasing prevalence of HF over the years with a constant rate of OHTs performed. During 2018, 268 patients died while waiting for OHT with 3883 patients being added to the transplant list and 3440 OHTs performed[4]. Expanding the donor pool with utilization of organs from hepatitis C virus (HCV)-positive individuals is an opportunity to close this gap.

Historically, HCV-positive donors were not considered due to high risk of HCV transmission, ineffective and unsafe HCV treatments, and overall inferior survival following heart transplantation (HT)[5,6]. With the discovery of direct-acting antivirals (DAAs), the donor pool has expanded with the addition of HCV-positive donors due to great success of treating HCV, limited interaction with immunosuppression, and optimal short-term outcomes following HT. Data of long-term outcomes are scarce, and there is a wide variation with the use of different DAA agents and optimal initiation among the studies. Therefore, we reviewed the current literature of HT from HCV-positive donors in HCV-negative recipients and discussed the epidemiology, outcomes of HT in the pre- and post-DAA era, complications, and potential barriers for more widespread utilization of HCV-positive donors.

**MATERIALS AND METHODS**

We searched the terms “heart transplant,” “organ transplant,” “transplant,” and “hepatitis C” in various combinations in Medline through November 2021.

**DONOR HCV STATUS CLASSIFICATION**

HCV infection in donors can be classified using two serological markers: HCV antibodies (Ab), which typically present after 6-8 wk of exposure to HCV[7]; and nucleic acid testing (NAT), which is present during an active infection occurring after 3-4 d of exposure to HCV[8,9].

***HCV Ab-positive NAT-negative***

Donors that are HCV Ab-positive and NAT-negative have spontaneously cleared the virus or were treated with antiretrovirals. There is low to no risk of transmission of the virus to the HT recipient[10,11].

***HCV Ab-positive NAT-positive***

Donors that are HCV Ab-positive and NAT-positive have an ongoing infection or chronic active hepatitis. There is a high risk of HCV transmission to the HT recipient.

***HCV Ab-negative NAT-positive***

Donors that are HCV Ab-negative and NAT-positive have an acute HCV infection without adequate time for Ab production against HCV. There is a high risk of transmission in solid organ transplant recipients.

***HCV Ab-negative NAT-negative***

Donors that are HCV Ab-negative and NAT-negative are in the eclipse period (within a week) of acquisition of HCV when NAT is not detectable with negative HCV Ab. This serological classification typically includes high-risk donors and intravenous drug users (IVDU). The potential of such donors is 32.4 per 10000 in the United States[12].

**EPIDEMIOLOGY AND HCV-POSITIVE DONOR POOL**

HCV, a single-stranded RNA virus, is the most frequent blood-borne infection common among IVDUs[13,14]. The World Health Organization reports that the HCV worldwide prevalence is 71 million with an annual incidence of 50300 in 2018 in the United States and a 3-fold increase from 2009 to 2018 with a rate of 0.3 to 1.2 per 100000 population[15].

The prevalence of HCV infection among IVDUs increased from 28% in 2008 to 40% in 2015 in North America[14,16], and it is estimated to increase by 43% by 2030[17]. The pool of HCV-positive donors is increasing by 10-fold due to the current opioid epidemic in the United States and to the increase in deaths related to overdose since 2000, which is on the rise from 15.1% in 2010 to 26.1% in 2018[18]. In 2020, 81230 deaths due to opioid overdose increased by 38.4% over a 12-mo period from June 2019 to May 2020. These younger victims without significant comorbidities are a potential for prolonged organ survival following HT[19,20]. The United Network of Organ Sharing reported HT from HCV-positive donors is on the rise from 247 to 362 HT from HCV-positive donors from 2018 to 2019. A single center reported doubling their transplant volume by utilizing HCV-positive hearts from 130 to 260 from 2013 to 2018, with a reduced mean waiting period of 4 d[21]. Nationwide utilization of HCV-positive donors can increase the number of HTs resulting in reduction in the waiting period and closing the gap between donors and recipients.

**HCV-POSITIVE TRANSPLANT IN THE PRE-DAA ERA**

Limited data are available on HT from HCV-positive donors in the pre-DAA era (Table 1)[5,22-31]. Studies reported a high transmission rate of HCV with an inferior survival rate of 70% at 1 year compared to 89% in controls[5] and a 10-year survival rate of 25% in the HCV-positive group *vs* 53% in controls[31] due to a higher incidence of cardiac allograft rejections, cardiac allograft vasculopathy, progression to chronic HCV infection, and liver disease[5]. Haji *et al*[30] reported HCV seropositivity as an independent risk factor for overall mortality by 2.8-fold and increased incidence of cardiac allograft vasculopathy by 3-fold. Historically, interferon-based therapy was being utilized for HCV infection, which demonstrated poor tolerability and a risk of interaction with immunosuppressants[32]. Due to these complications and decreased overall survival, the use of HCV-positive donors diminished until recent years following the discovery of DAAs.

**HCV-POSITIVE TRANSPLANT IN THE POST-DAA ERA**

In 2011, DAAs were introduced demonstrating high efficacy in eradicating HCV and achieving remission[33]. In 2013, the combination of sofosbuvir and simeprevir achieved 92% sustained virologic response (SVR) at 12 wk after completion of the antiretroviral regimen without the addition of historical medications such as interferon and ribavirin[34]. In 2014, a four-drug combination was approved for acute HCV infectionwith ombitasvir, paritaprevir, ritonavir, and dasabuvir, which achieved 100% SVR[35]. These DAAs used in post-transplant recipients achieved comparable SVR to non-transplanted patients[11,33,36-38]. The overall survival in HCV-negative recipients receiving hearts from HCV-positive donors is comparable to HCV-negative donors (Table 2)[10,11,21,33,36,37,39-52].

**POTENTIAL COMPLICATIONS OF HT IN HCV-NEGATIVE RECIPIENT FROM HCV-POSITIVE DONOR**

***HCV contraction***

HCV contraction is 82% to 100% from HCV NAT-positive donors. Schlendorf *et al*[11] demonstrated 95.7% of donor-derived HCV from HCV NAT-positive donors, and the risk of acquiring HCV from HCV Ab-positive and NAT-negative donors is low. One study demonstrated no viremia up to 1 year in 10 HCV-negative recipients receiving hearts from NAT-negative donors[11]. The risk of developing HCV is variable across all the studies, but it appears to be reduced with the use of HCV NAT-negative donors compared to HCV NAT-positive donors. All patients with donor-derived HCV achieved SVR across all studies with DAA treatment.

***Cardiac allograft rejection***

Transplant allograft rejection, either cellular or antibody-mediated, is associated with poor allograft survival and increased mortality[53]. In the pre-DAA era, the studies demonstrated an increased rate of allograft rejection in HT recipients from HCV-positive donors, and the risk was directly associated with viremia post-HT[5,27,54]. Two potential pathways are linked with allograft rejection from HCV infection. The first is the activation of lymphocytes, predominately T cells, through direct and indirect pathways affecting the endothelium, and the second is direct allograft injury is mediated by upregulation of interferon-alpha and apoptotic and proliferative genes[55].

The incidence of allograft rejection was 58% in 12 HCV-negative recipients undergoing HT from HCV NAT-positive donors compared to 30% in 13 HCV NAT-negative donors with a mean follow-up of 147 d[56]. Another study demonstrated allograft rejection of 12% and 3% in HCV-negative recipients from HCV Ab-positive NAT-positive compared to HCV Ab-positive NAT-negative donors at 180 d follow-up, respectively. The time to first event of rejection was earlier in recipients with NAT-positive compared to NAT-negative donors demonstrating viremia directly played a role in acute allograft rejection[54]. Schlendorf *et al*[42] reported two events of acute cellular rejection requiring treatment in recipients who became viremic at a mean of 4 d, and the initiation of DAAs was delayed as they were introduced on an outpatient basis at a mean of 33 d. Therefore, early detection and aggressive implementation of DAAs are required to decrease the incidence of allograft rejection. Overall short-term survival in the current era is similar, but the long-term risk of allograft rejection remains to be seen.

***Cardiac allograft vasculopathy***

Cardiac allograft vasculopathy (CAV) is the major cause of morbidity and mortality following HT with an incidence of 8% at 1-year and 50% at 10-year[57], and the risk of CAV is increased by 3-fold in donor-derived HCV recipients[30]. The pathophysiology of CAV is not completely understood but presumed to be immune-mediated endothelial injuries observed with elevated intracellular adhesion molecule-1 in HCV-infected patients[58]. The risk was observed to be further increased with B cell cross-reactivity in HCV-positive heart recipients[30]. CAV has been associated with increased alloimmune response[59,60]. CAV directly affects the longevity of the graft, but treatment with DAAs rapidly clears viremia, and studies have demonstrated no statistically significant risk of CAV at 1 year following HT from HCV-positive donors[11,59]. Zalawadiya *et al*[61] reviewed intracoronary ultrasound of 54 HCV-negative recipients from HCV-positive hearts treated with ledipasvir and sofosbuvir for 12 or 24 wk following HT and up to 1-year follow-up. They found no significant difference in CAV compared to the control group. Schlendrof *et al*[11] also showed that 29 recipients receiving hearts from HCV-positive donors had no statistically significant incidence of CAV compared to HCV-negative donors. All current studies are single centered and small sample size with short-term follow-up of 1 year. However, compared to the pre-DAA era, the evidence shows that there is a decreased reduction in the incidence of CAV secondary to rapid and effective clearance of HCV with DAA-based therapy. Long-term risk of CAV and its impact on graft survival remains to be explored.

***Liver disease***

A higher incidence of liver disease was noted in the pre-DAA era attributing to increased mortality in HCV-positive recipients[31]. HCV is a known cause of progressive liver disease leading to liver cirrhosis and risk of hepatocellular carcinoma (HCC)[62]. Early eradication of HCV reverses the liver damage that is caused by inflammation from HCV and decreases the incidence of downstream effects. Untreated HCV in transplant patients resulted in fulminant liver failure, cholestatic liver disease, and chronic hepatitis[23-25].

Pre-DAA recipients receiving hearts from HCV-positive donors had higher liver-related mortality with a hazard ratio of 5.9[63]. In immunocompromised hosts, the progression to advanced liver disease and cirrhosis was accelerated by a median of 2 years to 10 years compared to 30 years in immunocompetent individuals[64], and the recipients receiving an anti-lymphocyte preparation peritransplant had a higher risk of liver disease[22].

HCV has 6 different genotypes, with 1 to 4 being the most the common worldwide[65,66]. Genotype 1b and 3b are associated with a higher rate of liver disease compared to other genotypes[67,68]. Genotype 2 carriers have an improved overall HCC survival, and other genotypes can lead to progressive liver disease and HCC[69]. Both antiviral therapies, including interferon and DAAs, reduce the risk of HCC following achievement of SVR[70], but DAAs are more tolerable and efficacious compared to interferon[71]. All HCV genotypes can be responsive with various combinations of DAA treatment. However, relapse of HCV has been observed after DAA treatment[72,73].

***DAA in HT recipients***

No data are available on the optimal initiation for DAA-therapies following HT. However, recent studies report an increased risk of rejection with delayed treatment[54]. Empirical initiation of DAAs have decreased the viral load and shown the rapid clearance of HCV in 10 d[74]. Hence, early initiation of DAAs post-transplant while in the hospital should be highly encouraged[11,75]. Fluctuating kidney function following HT limits the use of DAAs as some agents like sofosbuvir may adversely affect kidney function, but DAAs have been used successfully in renal transplant recipients with no impact on renal function[51].

DAAs are well tolerated with no major adverse effects, and recipients typically suffer from self-limiting constitutional symptoms like headaches, fatigue, or insomnia[75]. Overall cost of a 12-wk course of DAAs are expensive, ranging from $80000 to $100000, but recently the cost has been reduced to as low as $30000 in 2020[33,40,49]. This is far less compared to the cost of a mechanical cardiac support device with an average cost of hospitalization of $726000 and a yearly cost ranging from $30000 to $80000 for follow-up and maintenance[32,76]. The burden of caring for durable mechanical support by the patient and their families should also be noted.

***Overall survival***

In the pre-DAA era, the overall mortality was increased by 2-fold in recipients receiving hearts from HCV-positive donors[5,6]. With the effective treatment against HCV with DAAs, the 1-year survival rate is 90.4% in HCV-positive recipients similar to HCV-negative recipients[37,48,61]. However, there is a scarcity of available data beyond 1 year. Larger studies are currently ongoing for evaluating long-term outcomes[11,37]. The average waiting period for HT is reduced and thereby decreasing waiting list mortality[11,37]. Data on multiorgan transplants are limited. McMaster *et al*[50] demonstrated equivalent survival rates in combined heart and kidney transplants with preservation of renal function[48-50].

***Future of HCV-positive donor utilization***

The studies have demonstrated comparable 1-year outcomes following HT from HCV-positive donors compared to HCV-negative donors with a potential for younger donors[47]. Generally, the recipients have an uncomplicated course following HT with rapid clearance of viremia with the use of DAAs with minimal interactions with immunosuppressants and few side effects[77,78]. One-year outcomes of HT recipients from HCV-positive donors are encouraging, but further studies are needed to evaluate the risk of allograft rejection, development of CAV, long-term sequela of liver disease and potential HCC risk, HCV genotype-specific effects, and recurrence of HCV and its impact on morbidity and mortality beyond the 1st year. In 2020, only 28% of the transplant centers were utilizing HCV-positive hearts[21], but with more experience and reassuring long-term outcomes, more transplant centers will begin accept HCV-positive organs.

**CONCLUSION**

As the IVDUs and opioid epidemic is on the rise in the United States, the donor pool, including HCV-positive hearts is going to increase in the coming years. With highly effective DAA therapy and comparable short-term outcomes following HT, it is reasonable to utilize these organs to meet the increasing prevalence of end-stage refractory HF patients. However, a multidisciplinary team approach and close monitoring of these recipients are needed with close observation for long-term sequelae.

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**Table 1 Heart transplantation from hepatitis C virus-positive donors in the pre-direct-acting antivirals era**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Study type** | **Study group** | **Outcome** |
| Pereira *et al*[22], 1991 | Retrospective, observational | 6 HCV-negative recipients underwent HT from HCV Ab-positive donors | 50% of recipients acquired HCV infection and higher incidence of liver disease was noted |
| Hayashi *et al*[23], 1994 | Case Report | 46-yr-old male with end- stage cardiomyopathy receiving HT from HCV Ab-positive donor | Fulminant liver failure and patient died in less than 2 yr |
| Lim *et al*[24], 1994 | Case Report | 51-yr-old male undergoing HT from HCV Ab-positive donor | Fulminant hepatitis, which was treated successfully with interferon-based therapy; Died due to pulmonary aspergillosis |
| Zein *et al*[25], 1995 | Observational | 1 HCV-negative recipient underwent HT from HCV Ab-positive donors | Cholestatic liver disease and liver failure-related mortality |
| Pfau *et al*[26], 2000 | Retrospective | 5 recipients without HCV infection underwent HT with HCV Ab-positive donors | 1 out of 5 recipients became HCV Ab-positive; Elevated liver enzymes were noted and normalized by 12 mo |
| Marelli *et al*[27], 2002 | Retrospective | 20 recipients (10 were status I and 10 were status II) without HCV infection underwent HT from HCV NAT-positive donors | Overall survival was 90% in status I and 80% in status II group; Higher incidence of rejection and CAV were noted |
| File *et al*[5], 2003 | Retrospective | 10 recipients without HCV infection underwent HT from HCV-positive and NAT-positive | All recipients became HCV NAT-positive, 6 out of 9 recipients developed hepatitis and severe liver injury occurring in 2 patients; Inferior survival of 70% was noted |
| Gudmundsson *et al*[28], 2003 | Retrospective | 7 recipients without HCV infection underwent HT from HCV Ab-positive donors | Overall 5-yr survival was 71.4%; 3 developed chronic active hepatitis, 1 died from liver failure |
| Wang *et al*[29], 2004 | Retrospective | 4 recipients without HCV infection underwent HT with HCV Ab-positive donors | 1 recipient became HCV Ab-positive without clinical hepatitis |
| Haji *et al*[30], 2004 | Retrospective | 34 recipients without HCV infection underwent HT from HCV Ab-positive donors and evaluated overall mortality and CAV | 75% of recipients became HCV seropositive; Higher mortality by 2.8-fold and accelerated CAV by 3.0-fold was noted compared to the control group |
| Gasink *et al*[31], 2006 | Retrospective, registry-based, cohort | 261 recipients without HCV infection underwent HT with HCV Ab-positive donor | Overall inferior 1-yr, 5-yr, and 10-yr survival compared to control; Higher incidence of liver disease and CAV were noted |

Ab: Antibodies; CAV: Cardiac allograft vasculopathy; HT: Heart transplant; HCV: Hepatitis C Virus; NAT: Nucleic acid test.

**Table 2 Heart transplantation from hepatitis C virus-positive donors in the post-direct-acting antivirals era**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Study type** | **Study group** | **Outcome** |
| Gottlieb *et al*[33], 2017 | Case report | 1 recipient without HCV infection underwent HT with HCV NAT-positive donor; treated with sofosbuvir/velpatasvir for 12 wk | A recipient acquired HCV infection on day 9, and it was cured at 12 wk |
| Jawad *et al*[39], 2018 | Case report | 1 recipient without HCV infection underwent HT with HCV-positive donor; in 2014, after approval of DAA, the patient was treated with sofosbuvir and daclatasvir for 8 mo | Patient acquired HCV infection in 2010 without any clinical sequelae and with treatment of DAA in 2014 it was eradicated; Progressive CAV was noted |
| Moayedi *et al*[40], 2018 | Single center, single arm  | 2 recipients without HCV infection underwent HT with HCV NAT-positive donors  | Low cost of HCV treatment compared to alternative treatment with mechanical cardiac support; Potential for 300-500 more HT annually noted |
| Moayedi *et al*[41], 2018 | Retrospective, registry-based | From 2013 to 2017, 64 (5%) underwent HT from HCV-positive donors; Total of 1305 HCV-positive donors were recovered during this time period | Comparable survival was noted in recipients of HCV-positive donors to HCV-negative donors |
| Patel *et al*[10], 2018 | Single center, single arm case series | 14 HCV-negative recipients underwent HT in 2017 from HCV Ab-positive and NAT-negative donors | None developed HCV infection |
| Schlendorf *et al*[42], 2018 | Single center, single arm prospective observational case series | 13 HCV-negative (1 was treated) recipients underwent HT from HCV-positive donors and treated with DAA | 69% of these recipients acquired HCV, and all of them achieved SVR following therapy with DAA except 1 who died due to pulmonary embolism |
| McLean *et al*[36], 2019 | Single arm, single centered, prospective case series | 10 HCV-negative recipients underwent HT with HCV NAT-positive donors, treated with elbasvir/grazoprevir after viral detection | Overall 9/10 recipients achieve SVR following DAA; 1 recipient died due to Ab cross-match leading to rejection, graft failure, and multiorgan failure |
| Woolley *et al*[43], 2019 | Non-randomized, single center, prospective trial | 8 HCV-negative recipients underwent HT from HCV NAT-positive donors; Treated with sofosbuvir-velpatasvir for 4 wk; Overall survival was compared to 12 recipients undergoing HT from HCV-negative donors | 100% SVR was noted; Comparable survival rate at 12 mo in both groups |
| Frager *et al*[44], 2019 | Single arm, single center, prospective trial | 6 HCV-negative recipients underwent HT from HCV NAT-positive donors; multiple regimens of DAA were implemented | 4 achieved SVR; 5 with 1R-2R rejection and 2 with stable chronic kidney disease; Decreased time on the waiting list noted |
| Schlendrof *et al*[11], 2019 | Single arm, single center, prospective observational case series with a 1-year follow-up | 80 HCV-negative recipients underwent HT from HCV Ab-positive and/or NAT-negative donors; Multiple DAA regimens utilized | 95.7% of recipients acquired HCV infection from donors with HCV NAT-positive; DAA SVR was achieved in all recipients; No recipients acquired donor-derived HCV from NAT-negative recipients; Comparable 1-yr survival of 90.7% in both groups, and median wait time of 4 d was noted |
| Reyentovich *et al*[37], 2019 | Non-randomized, single center, prospective observational case series | 12 HCV-negative recipients underwent HT with HCV NAT-positive donors treated with glecaprevir/pibrentasvir for 8 wk compared to 13 controls undergoing HT from HCV-negative donors | Equivalent survival rate in both groups; Mean waiting period of 62 d noted |
| Aslam *et al*[45], 2019 | Retrospective, single center, observational | 21 HCV-negative recipients underwent HT with HCV Ab-positive and NAT-negative or positive donors | All recipients of NAT-positive donors acquired HCV infection; With DAA treatment 100% SVR was achieved; All recipients (2/2) were Ab-positive but NAT-negative and did not acquire HCV infection |
| Morris *et al*[46], 2019 | Single center, retrospective | 25 HCV-negative recipients underwent HT from HCV Ab-positive and NAT-positive (*n* = 23) or negative (*n* = 2) donors; DAA regimen was implemented, and outcomes were compared to 37 recipients undergoing HT from HCV- negative donors | 22 of 23 recipients received hearts from HCV viremia acquired HCV infection; No difference in overall survival, rejection, hospitalization, and CAV between 2 groups; Delay in HCV treatment was due to insurance coverage |
| Lebeis *et al*[47], 2019 | Single center, retrospective | 23 HCV-negative recipients underwent HT with HCV-positive donors compared to control group receiving hearts from HCV donors | Recipients receiving preemptive treatment with DAA had preserved early allograft function receiving hearts from HCV-positive donors |
| Gaj *et al*[48], 2019 | Single center, retrospective | Baseline characteristics were assessed in 111 HT; 23 of these organs came from HCV-positive donors | 20% of recipients underwent HT from HCV-positive donors, and the donors were younger with a mean of 37 compared to 40 yr old; Short-term outcomes were similar in both groups |
| Kilic *et al*[21], 2020 | Multicenter, retrospective, registry-based | Of 7889 HT, 343 HCV-negative recipients received hearts from HCV-positive donors | 1-yr survival rate was indifferent between 2 groups; From 2016-2018, 28% of transplant centers utilized HCV-positive donors |
| Zhu *et al*[49], 2020 | Single center, retrospective | 10 HCV-negative recipients underwent HT from HCV-positive donors between 1997-2019 | 1-yr survival was 80%; 4 recipients acquired donor-derived HCV, and 3 of them demonstrated cure with DAA treatment |
| McMaster *et al*[50], 2020 | Single center, retrospective | 12 HCV-negative recipients underwent combined heart and kidney transplant from HCV Ab-positive and 10/12 were NAT-positive donors and were compared to 27 HCV-negative donors | A shorter median waitlist time for HCV-positive organs; Both groups had similar perioperative cardiac and renal function; Creatinine was higher in HCV-positive recipients at 3 mo compared to the control group, but at 1-yr it was similar in both groups; 80% of recipients acquired donor-derived HCV infection, and with DAA treatment 100% SVR was noted |
| Zalawadiya *et al*[51], 2020 | Single center, retrospective | 45 HCV-negative recipients underwent HT between 2016-2018 from HCV Ab-positive and NAT-positive donors; Renal function was assessed following transplantation | Data from 23 recipients were available at 12 wk and 18 recipients at 1 yr; No significant change in renal function up to 1-yr was noted |
| Reyentovich e *et al*[52], 2020  | Single center prospective observational | 22 HCV-negative recipients underwent HT between 2018-2019 from HCV NAT-positive donors; Data were compared to 28 HCV NAT-negative recipients | All recipients acquired donor-derived HCV; 20 recipients achieved 100% SVR following DAA therapy; Comparable outcomes with Ab-mediated rejection in both groups |

Ab: Antibodies; CAV: Cardiac allograft vasculopathy; DAA: Direct acting antiretroviral; HT: Heart transplant; HCV: Hepatitis C Virus; NAT: Nucleic acid test; SVR: Systemic viral response.



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