Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Impact of Donor-Transmitted Hepatitis C Virus on Development of Early Cardiac Allograft Vasculopathy in the Current Era

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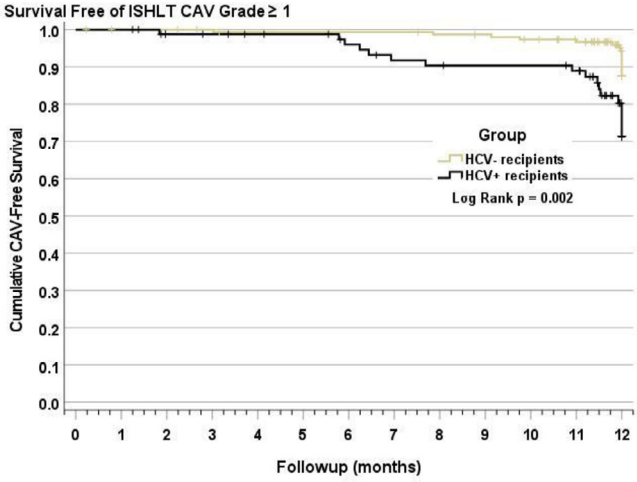
Purpose: Rates of heart transplantation (HT) from hepatitis C virus (HCV)-infected donors have recently increased significantly. While historical data suggest that donor-transmitted HCV (dt-HCV) may be associated with higher rates of cardiac allograft vasculopathy (CAV), the impact of dt-HCV on development of CAV in the current era remains unclear.

Methods: We performed a retrospective review of adults undergoing HT at our institution between September 2016 and December 2020 who had coronary angiography +/- intravascular ultrasound (IVUS) performed at least once for CAV surveillance. Kaplan-Meier and multivariable Cox proportional hazards models tested whether CAV-free survival (ISHLT grade $\geq$ 2 and $\geq$ 1) differed over the first post-HT year between patients transplanted with HCV-infected donors (HCV+ recipients) and those who were not (HCV- recipients). The incidence of rapidly progressive CAV (RPC), defined as increase in maximum intimal thickness $\geq$ 0.5 mm, was compared between groups using Fisher's Exact test.

Results: Among 83 HCV+ recipients compared with 162 HCV- recipients, there were no significant differences in donor age or age at HT. HCV+ recipients were less likely to be treated for rejection within the first post-HT year (16.9% vs. 32.1%, p = 0.014). Survival free of CAV $\geq$ 2 did not differ over the first year (p = 0.555) whereas survival free of CAV $\geq$ 1 was lower among HCV+ recipients (Figure, p = 0.002), even after adjusting for donor age and treated rejection (HR 2.9, 95% CI 1.4 to 5.8). Among 121 patients who underwent IVUS at baseline and 1-year, incidence of RPC was greater among HCV+ than among HCV- recipients (33.9% vs. 16.1%, p = 0.034).

Conclusion: In our single center study, the largest of its kind, HT from HCV-infected donors was associated with higher incidence of RPC and reduced survival free of CAV $\geq$ 1 but similar survival free of CAV $\geq$ 2 over the first post-HT year. Longer-term studies are needed to evaluate the impact of dt-HCV on rates of CAV and survival after the first post-HT year.



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Poke Not Prod: First Canadian Experience Using Donor-Derived Cell Free DNA to Replace Endomyocardial Biopsy During COVID-19

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Purpose: After a heart transplant (HT), non-invasive methods for rejection surveillance minimize the need for endomyocardial biopsies (EMBx). We describe the first experience with combined use of genetic expression profiling (GEP) and donor-derived cell-free DNA (dd-cfDNA) testing in Canada as part of a quality improvement project to minimize patient risk during the COVID pandemic.

Methods: Adult outpatients at least 6 months after HT were screened from May 2021 to July 2021 to have their routine EMBx replaced by a combination of GEP and dd-cfDNA. Demographics, modification of immunosuppression (IS) and outcomes (hospital admission, rejection, and need for EMBx) were collected.

Results: Among 90 patients, 31 (33%) were enrolled, and 37 non-invasive tests were performed. The median time after HT was 2 years and patients were predominantly Caucasian (52%) and male (68%). 53% had a history of acute cellular rejection during the first year and 32% had cardiac allograft vasculopathy. Of the tests performed, 23 (60%) were - GEP / - dd-cfDNA, 10 (27%) were + GEP / - dd-cfDNA, 4 (11%) were - GEP / + dd-cfDNA and none were + GEP / + dd-cfDNA. Being bridged with a VAD (OR = 5.5, p=0.034) and a history of a previously treated CMV (OR = 16.0, p=0.003) were associated with a positive GEP and a negative dd-cfDNA result. Having received a COVID vaccine in the last 3 months did not affect GEP results (GEP was positive in 23.8% after vaccination vs 33.3% in non-vaccinated patients, p=0.690; average GEP score 29.8 vs 30.7, p=0.673). The 4 patients with a + dd-cfDNA (range 0.19 - 0.81%) underwent an EMBx with no significant cellular or antibody mediated rejection, thus avoiding 89% of the EMBx. No unscheduled clinic visits, emergency department or hospital admissions were recorded. After non-invasive testing, the IS was reduced in 16 cases (43.2%). IS was reduced in in 59% of patients with negative concordant tests (- GEP / - dd-cfDNA), 30% in patients with + GEP / - dd-cfDNA and no reduction in IS occurred in those with + dd-cfDNA.

Conclusion: The combination of GEP and dd-cfDNA for rejection surveillance allowed for a marked reduction in EMBx (89%) and for a personalized downtitration of IS without adverse events in the short term. The use of non-invasive rejection surveillance testing was an effective strategy to avoid hospital contact for HT recipients during the COVID-19 pandemic.

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Incidence of mTORi Associated BOOP in Cardiac Transplant Recipients – A Single Center Perspective

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Purpose: The incidence of mammalian target of rapamycin inhibitor (mTORi) associated bronchiolitis obliterans organizing pneumonia (BOOP) varies in the literature. We have previously reported a 24% incidence of BOOP in patients transitioned to sirolimus. This high rate was believed to be related to the full withdrawal of calcineurin inhibitor (CI) therapy. The aim of this study is to compare those results to our current practice of maintaining a low-dose CI with mTORi-based regimens

Methods: This was a single-center retrospective review of adult heart transplant recipients initiated on an mTORi at least six months post-transplant. The primary outcome of the study was incidence of BOOP. Secondary outcomes included timing of mTORi conversion post-transplant and associated tacrolimus concentrations.

Results: During the study period, none of the 61 included heart transplant patients developed BOOP. Late mTORi transition (>1 year post transplant) was more common (72%) than early conversion (6 months - 1 year post transplant; 28%), and sirolimus was more commonly utilized than everolimus (90% vs 10%). Following our centers mTORi conversion policy, all patients were maintained on low-dose tacrolimus at initiation, with 84% of patients continuing concomitant tacrolimus at one year. Of these patients, 46% had an FK goal < 4 mcg/mL and 38% had an FK goal 4-8 mcg/mL.