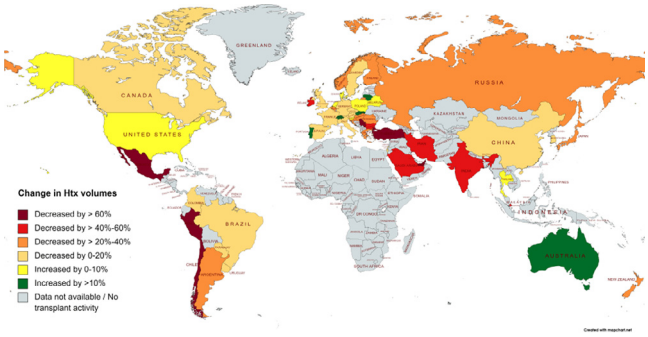
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.



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Predictors of Humoral Response to COVID-19 Vaccination in Heart Transplant Recipients

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Purpose: A reduced formation of IgG antibodies after COVID-19 vaccination has been reported in immunosuppressed heart transplant (HT) recipients. However, predictors of decreased humoral response in patients after heart transplantation remain elusive.

Methods: In 68 HT recipients who previously received two doses of a COVID-19 vaccine, anti-SARS-CoV-2 spike IgG (anti-spike IgG) were quantified (LIAISON® SARS-CoV-2 TrimericS IgG assay) during routine visits. IgG concentrations at or above 33.8 BAU/ml were considered positive, as defined by the manufacturer. Clinical characteristics including the immunosuppressive regimen were assessed. We performed regression analyses to identify predictors of humoral response.

Results: Of 68 HT recipients (44 (65%) male, median age 54 years (IQR 41-64), median time since HT 7.4 years (1.7-13.0)), 56 patients (82%) were treated with calcineurin-inhibitors, 35 (51%) with mycophenolate mofetil, 47 (69%) with everolimus, and 33 (49%) with prednisolone.

60 patients (88%) received two doses of an mRNA vaccine (50 patients BNT162b2, 10 mRNA-1273) and 8 patients (12%) two doses of the vector vaccine AZD1222. Two patients (2.9%) reported a prior COVID-19 infection. The median interval between the two vaccine shots was 41.5 days (35.0, 42.0). A positive humoral response 40 days after the second dose was detected in 26 patients (38%). Comparing the two types of vaccines used, antibody positivity rates were not significantly different ($p = 0.10$). Upon multivariate analysis, older patient age (p=0.006), shorter time since HT (p=0.022), male sex in combination with time since HT (p=0.023 for interaction effect), and use of prednisolone ($p<0.001$ in a tobit linear regression) were associated with lower log-transformed COVID-19 antibody titers. There was no detectable effect of vaccine type or of other immunosuppressive agents.

Conclusion: Older age, shorter time since transplantation, and treatment with prednisolone appear to be associated with lower anti-spike IgG concentrations after COVID-19 vaccination in HT patients. Overall humoral response rates were low (38%), regardless of the type of vaccine used or type of non-prednisolone immunosuppressive agent. Further studies are needed to determine the clinical effectiveness of COVID-19 vaccination in HT recipients and the need for specific booster vaccinations in this vulnerable population.

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Effect of CMV Viremia on HeartCare

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Purpose: CMV infection post-heart transplantation presents complex challenges affecting changes in immunosuppression and antiviral therapy that have both short- and long-term consequences. AlloMap gene expression profiling (AM), a non-invasive method to detect acute cellular rejection was affected by the presence of CMV infection. The aim of this study was to evaluate the impact of CMV infection on donor derived cell free DNA (AS) in patients post heart transplantation (HT).

Methods: The Surveillance Using HeartCare Outcomes Registry (SHORE) is a multicenter study for post-heart transplant patients followed with AM/AS for 5 years following heart transplantation. Patients enrolled in the SHORE registry were analyzed based on CMV infection. AM/AS were evaluated before, at the time, and following the viremic episodes. Both individual trends and the differences between the median AS and AS levels were studied. Nonparametric tests were used to assess categorical and longitudinal variables.

Results: 1702 patients were included, 1245 (73%) male, median age 57, 1156 (68%) white. CMV infection was diagnosed in 360 (21%) patients occurring at a mean time of 229 days after HT. CMV(-) patients had similar demographics to those patients CMV(+ve), but CMV(+) were older (p=0.025). CMV(+ve) patients had an increase in both AS (0.07% v. 0.05%, $p<0.001$) and AM (34 v. 30, $p<0.001$) compared to those without CMV [Figure 1a]. Levels returned to baseline within 5 weeks following the infection [Figure 1b]. The threshold to discriminate CMV infection with a NPV of 95% with GEP is 34 and dd-cfDNA is 0.12% .

Conclusion: AS does not seem to be confounded by CMV, but the presence of CMV infection may be associated with an elevated AS if there is allograft injury. Recovery from CMV infection was associated with normalization of AS and AM. This study points to the need to evaluate CMV in the presence of an increased AS, with further work to compare PCR titers and AS levels planned.

Figure 1a.

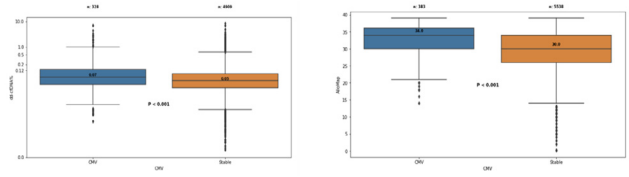
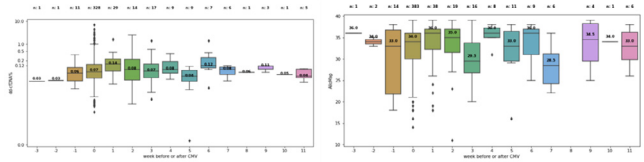


Figure 1b.



(256)

Using Donor-Derived Cell-Free DNA for Assessment of Myocardial Injury in Heart Transplant Recipients After SARS-CoV2 Infection

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Purpose: A link between SARS-CoV2 infection and myocardial injury has been described. Our center utilizes non-invasive surveillance with gene expression profiling and donor-derived cell-free DNA (dd-cfDNA) in heart transplant (HTx) patients who are either stable or in whom invasive surveillance is contraindicated. We evaluated whether HTx recipients diagnosed with SARS-CoV2 infection demonstrated evidence of myocardial allograft injury using dd-cfDNA.
Methods: HTx recipients were included if they had dd-cfDNA testing (AlloSure; CareDx Inc., Brisbane, CA) within 60 days of their initial SARS-CoV2 diagnosis. Data on hospitalization, therapy, and clinical outcomes was captured. Dd-cfDNA results at the assay limit of detection (LOD, <0.12%) were set equal to the LOD.
Results: Between 3/2020 and 6/2021, we identified 12 HTx recipients with SARS-CoV2 and dd-cfDNA results within the specified time period; median age was 55 (IQR 28 - 64.5) with infection occurring 506.5 days (IQR 176 - 803.5) after transplant. Mean dd-cfDNA was 0.13 ± 0.03%, assessed 26 (IQR 20 - 35) days after infection. Prior results, available for 9 patients and obtained a median of 33 (IQR 27 - 59) days prior to infection, did not differ from post-infection values (0.13 ± 0.02%, p = 0.66). Following diagnosis, 8 (67%) patients were hospitalized; 5 had mycophenolate held, 2 received steroids, 2 received convalescent plasma, 4 received remdesivir, and 1 received monoclonal Ab therapy. At a median follow-up time of 304 (IQR 212.5 - 331) days after diagnosis, all twelve patients were alive with good allograft function (mean ejection fraction 59 ± 4.8%); interval clinically-relevant immunologic outcomes included one episode of rejection (pAMR1) and three (25%) findings of de novo donor-specific antibodies (dnDSA).
Conclusion: In this single-center pilot study assessing myocardial injury among HTx recipients within 2 months of SARS-CoV2 infection, the majority of patients had low dd-cfDNA results (<0.15%) and demonstrated good intermediate-term (6-12 months) graft function. While limited by sample size and protocol-based inclusion criteria, our findings suggest that sustained myocardial injury in HTx recipients after SARS-CoV2 infection may not be common. The impact of SARS-CoV2 infection on immunologic outcomes including rejection and dnDSA in this population merit further study.

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Heart Transplantation in Chagas Cardiomyopathy: Long-Term Follow-Up in a Referral Center

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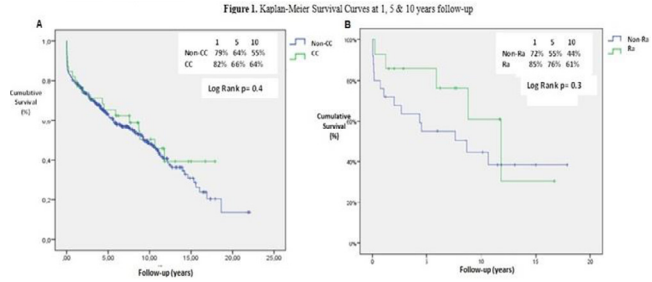
Purpose: Chagas disease affects approximately 6 million people in Latin America.; 25% to 35% of these patients progress to Chagas cardiomyopathy (CC). A therapeutic option in its advanced stages is heart transplantation (HT). The aim of the study was to compare the survival of HT patients due to CC against other etiologies and to analyze the incidence and impact on survival of Chagas disease reactivation (Ra) in this subgroup of patients.
Methods: Between August 1998 and March 2021, HT patients were retrospectively evaluated. Survival was analyzed using Kaplan-Meier curves and Log Rank test. The Ra diagnosis was performed using molecular methods, Strout test in peripheral blood, myocardial and/or skin tissue.
Results: Out of 511 HT patients, 39 (7.6%) had CC. Median follow-up 4.4 years (IQR 1.2-8.6). Chagas cardiomyopathy subgroup age 51 years (IQR 45-60). Men 28 patients (72%). Survival 1, 5 and 10 years HT by CC versus HT by other causes: 82%, 66% and 64% versus 79%, 64% and 55% (p = 0.4). Ra was documented in 38.5% of the patients. Survival 1, 5 and 10 years of HT CC with Ra versus non-Ra: 85%, 76% and 61% versus 72%, 55% and 44% (p= 0.3).
Conclusion: In our series, no statistically significant difference was found in the survival of heart transplant patients due to Chagas' Cardiomyopathy compared to those transplanted for other causes, nor between the patients who reactivated Chagas disease and those who did not.



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The Widening Care Gap in VAD Therapy: An Analysis of the STS Intermacs and Pedimacs Database

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Purpose: The removal of the HVAD (HW) due to inferior outcomes cf. to Heartmate 3 (HM3) in adults has created a care gap for younger patients (pt). It is unclear if HW survival differs by age and if the initial experience with HM3 can bridge the gap.
Methods: Using the STS Intermacs/Pedimacs registry, durable implants between 09/12-08/21 where identified. Young adults (YA) were <40yrs old. Pt were excluded with an isolated RVAD or implanted as DT. Survival analysis by Kaplan Meier (KM) and Competing Outcomes Curves (COC) were performed and 1-year survival is reported.
Results: The Intermacs cohort consisted of 11569 pt with 1817 (15.7%) YA [HW n=817; HM3 n=372]. The median age of YA was 31.2 yrs (IQR 26.5-36.2) and wt 83Kg (IQR 68-104Kg). Most had cardiomyopathy (CM) (92.2%). The Pedimacs cohort was 660 pt [median age 9.4yrs (IQR 1.8-14.3), wt 27 Kg (IQR 10-57.2), CM (70.3%)]. Device breakdown included: HW (n=328), EXCOR (n=275) and HM3 (n=57). Fig 1 shows distribution of devices by wt.
HW survival in adults differed by age, with YA fairing better (88.9% vs 79.4% at 1 yr, p<0.0001). YA survival was also better compared to Pedimacs pt (88.9 vs 83.7%, p=0.0002) but when competing events were analyzed, mortality was similar to YA (9.2% vs 9.5%, p=0.1) with a higher proportion undergoing transplant in Pedimacs (74% vs 31.2 %, p<0.0001). Survival by device did differ between HW and HM3 in YA (88.9% vs 95%, p=0.0006), but the difference was less than in older adults (79.4% vs 86.9%, p<0.001). This difference in survival was not seen in children (73.9% vs 84.8%, p=0.56), despite 31.7% of the HW implanted in pt <10 yrs compared to 14% of the HM3 (p=0.03).
Conclusion: The removal of the HW device may result in a care gap in younger pt whose survival outcomes do not mirror that of adults. The HM3 can fill a portion of this gap but there remains a subset of pediatric pt that based on initial HM3 use may no longer have access to intracorporeal support. However, it is likely with ongoing experience that a better understanding of the lower weight limit for HM3 will be determined.