ISHLT ID AND HEART TRANSPLANTATION. NOVEMBER '21
JOURNAL WATCH

Rebecca N. Kumar, MD
Georgetown University Medical Center

TON VAN-KHUE, M.D.
EDITOR
ISHLT.ORG

Genuardi M.V., *et al*. Coronavirus disease 2019 in heart transplant recipients: Risk factors, immunosuppression, and outcomes.

JHLT. 2021; 40:926-935

Clinical Question

1° What is the clinical course and outcomes of heart transplant recipients with confirmed COVID-19?
2° Is there an association between immunosuppressive regimen and outcomes?

Methods

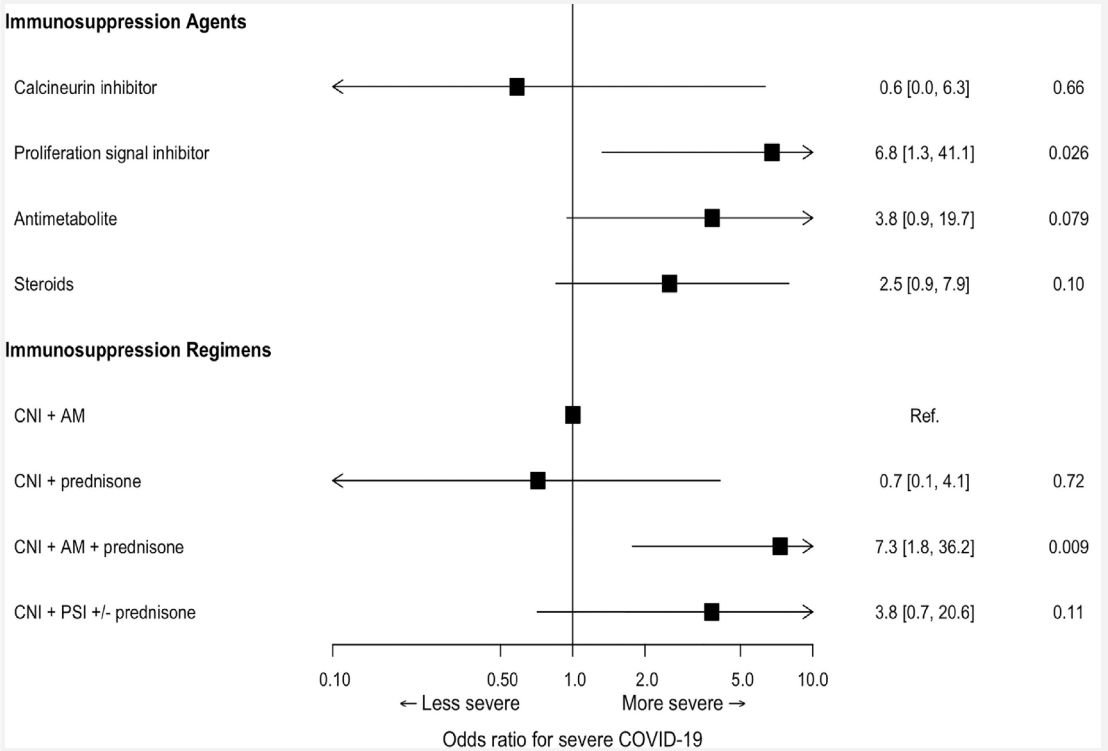
- Multicenter (11) registry enrolled patients from April – October 2020; data collected until January 2021
- Heart transplant recipients 18 years or older with a confirmed COVID-19 diagnosis included
- Data collected via chart review: demographics, pmhx, immunosuppression, labs, COVID-19 course, hospitalization, death
- Student's t-test, χ^2 test, and logistic regression

Results

- 99 patients → 7 asymptomatic so excluded
- 63 of the 92 patients included were hospitalized → 24 developed severe disease
- Factors associated with severe disease ($p<0.05$): HTN, DM, OSA, COPD, respiratory rate ≥20, hypoxia <92%, abnormal neutrophil count, elevated Cr, elevated AST, elevated CRP, elevated ferritin, and elevated troponin
- Mortality rate: 16% among symptomatic patients

Results Cont.

Logistic regression analysis adjusting for age and time since transplant resulted in the following odds ratios:



Similarly, logistic regression adjusting for age and time since transplant found that an immunosuppression regimen of calcineurin inhibitor, antimetabolite therapy, and prednisone was associated with increased odds of death (17.8, 95% CI: 2.1-245)

Reviewer's Impression

The landscape has changed since the introduction of vaccines, but this study shows the natural history of COVID-19, as well as risk factors for severe disease, in heart transplant patients.
Although not discussed in this paper, monoclonal antibodies may also have an impact on outcomes in heart transplant recipients with COVID-19

ISHLT ID AND HEART TRANSPLANTATION. NOVEMBER '21
JOURNAL WATCH

Rachel Sigler, DO, MPH
University of California, San Diego, CA, USA

TON VAN-KHUE, M.D.
EDITOR
ISHLT.ORG

Y. Peled, *et al.* Third dose of the BNT162b2 vaccine in heart transplant recipients: immunogenicity and clinical experience. JHLT. 2021.
doi: 10.1016/j.healun.2021.08.010. [Epub ahead of print]

STUDY HIGHLIGHTS

Objective: Investigating the safety and immunogenicity of a third, booster, dose of the Pfizer BNT162b2 vaccine in heart transplant patients.

Methods: Cohort of 96 adult heart transplant patients received a third homologous dose of BNT162b2 vaccine 168 days after the second dose. Vaccine-induced antibody responses of receptor-binding domain IgG and neutralizing antibodies were assessed in all patients. T cell response studied in a subset of patients.

Results:

Tolerability: Low rate of adverse events, mostly mild and local. No episodes of rejection.

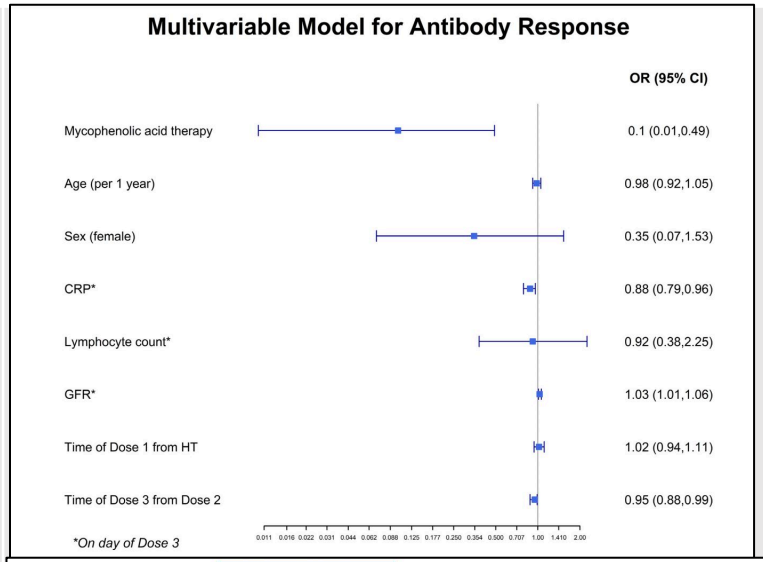
Antibody response: At 18 days following third dose of vaccine, positive antibody response increased from 23% to 67%

-Neutralization antibody geometric mean titer increased from 3.05 to 27.25 (95% CI, 15.7 to 47.3)

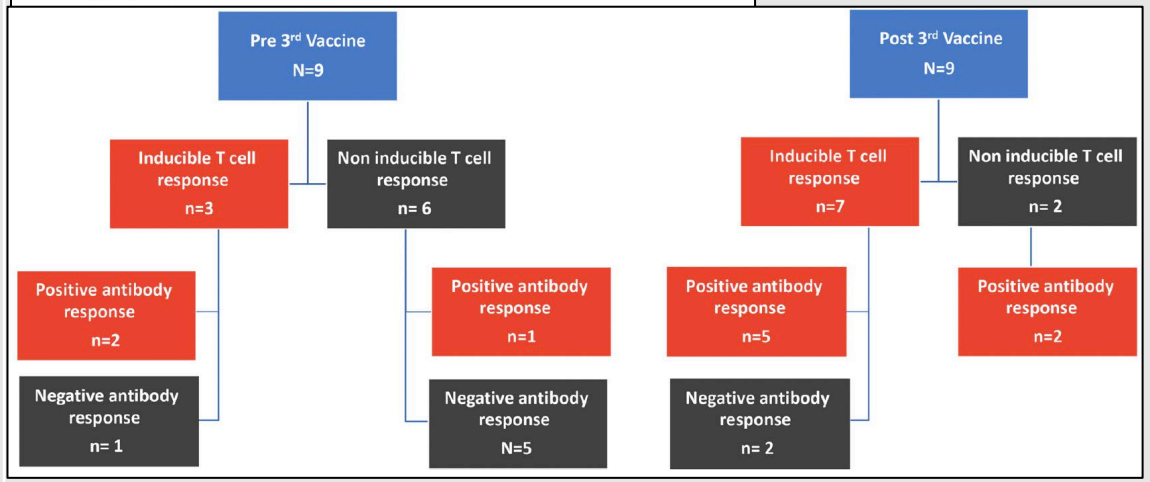
-Neutralization titers >9-fold and IgG receptor binding domain antibodies >3-fold that of the first two doses.

T-cell response: T cell immune response tested in 15 patients. 12 patients (80%) had response. 22% had T cell response before the 3rd dose, increased to 78% after.

CENTRAL FIGURES



-Multivariate regression revealed mycophenolate use independently associated with decreased likelihood of positive antibody response (OR= 0.1, 95% CI 0.01-0.49, p=0.01)



T-cell responses before and 19 days after third dose of the vaccine.

REVIEWER'S COMMENTS

-Demonstrates cellular responses in absence of measurable antibodies

-Noted association between mycophenolate use for immunosuppression and decreased antibody response.

Limitations:

-Single center study

-No established threshold for effective vaccination response

-Small number of patients in T-cell investigation group

Questions raised:

-What is optimal interval between doses?

-Would changes in immunosuppression result in improved outcomes for vaccination in transplant recipients?

-Would booster dose of heterogenous vaccine elicit same response?

ISHLT ID AND HEART TX. NOVEMBER '21
JOURNAL WATCH

Sonya Trinh, MD, MPH
Ochsner Health, New Orleans, LA, USA

TON VAN-KHUE, M.D.
EDITOR
ISHLT.ORG

Heim, C *et al*. **Cytomegalovirus Donor Seropositivity Negatively Affects Survival After Heart Transplantation.**
Transplantation. Sept 2021. doi: 10.1097/TP.0000000000003961

STUDY HIGHLIGHTS

Aim: Compare post-transplant survival in different cytomegalovirus (CMV) donor:recipient serologic combinations

Design: Retrospective cohort study of ISHLT Thoracic Transplant Registry

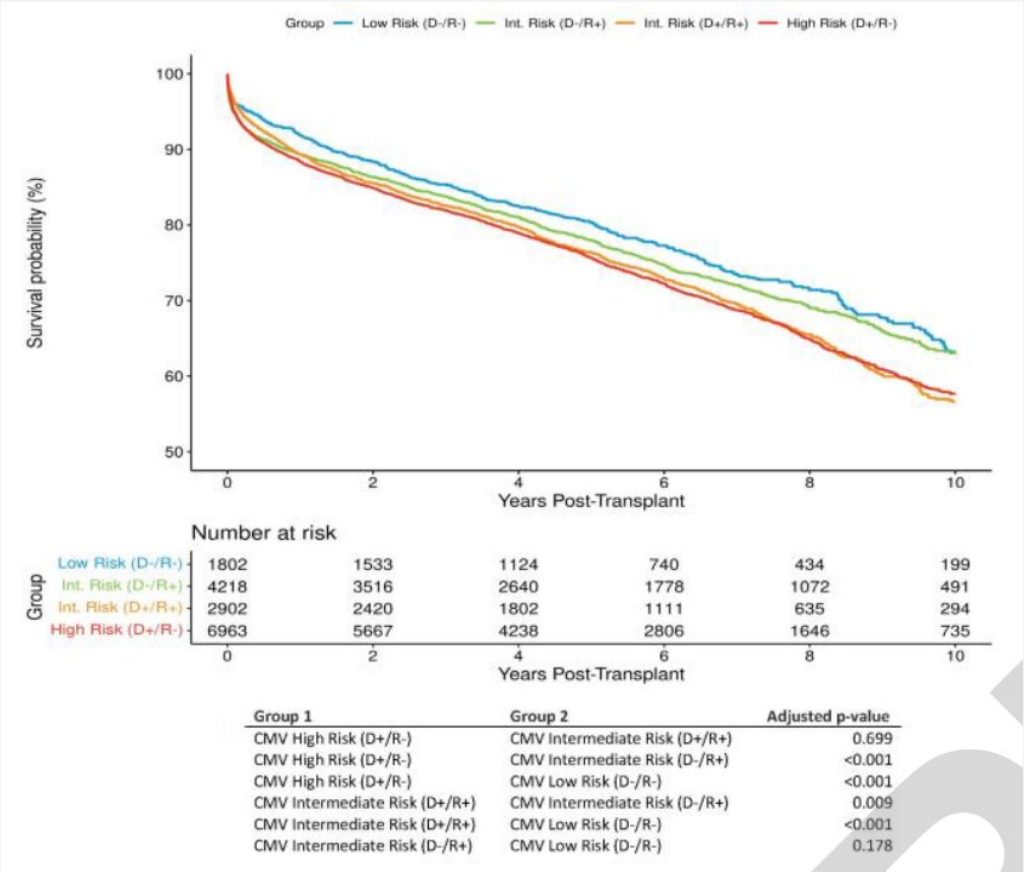
Inclusion: Adult primary heart transplant recipients with known CMV serologic status from 7/2004-6/2014 (n=15,885)

Outcomes: Post-transplant survival and risk of developing cardiac allograft vasculopathy (CAV)

Results: Significantly worse survival for both CMV D+ groups as compared to CMV D-R- group (D+R+ 56.61% vs. D-R- 63.09% p<0.01; D+R- 57.69% vs. D-R- p<0.001). The risk of CAV was not significantly increased in D+ groups as compared to D- groups.

CENTRAL FIGURE

Patient survival and number at risk for Kaplan-Meier estimates of mortality within 10 years



Group 1	Group 2	Adjusted p-value
CMV High Risk (D+/R-)	CMV Intermediate Risk (D+/R+)	0.699
CMV High Risk (D+/R-)	CMV Intermediate Risk (D-/R+)	<0.001
CMV High Risk (D+/R-)	CMV Low Risk (D-/R-)	<0.001
CMV Intermediate Risk (D+/R+)	CMV Intermediate Risk (D-/R+)	0.009
CMV Intermediate Risk (D+/R+)	CMV Low Risk (D-/R-)	<0.001
CMV Intermediate Risk (D-/R+)	CMV Low Risk (D-/R-)	0.178

REVIEWER'S COMMENTS

- CMV serostatus was associated with increased risk for mortality, but not CAV.

- Findings lead to more questions about possible mechanisms given the following study limitations:
--- No information in registry about rates of symptomatic CMV infection and treatment
--- Association between CMV and CAV possibly missed as CAV reported as yes or no versus standardized ISHLT definitions

- Study also leads to more questions about how to mitigate mortality risk associated with CMV serostatus.

Limitations:
- Possible selection bias as only included patients from a third of participating centers with donor and recipient CMV serostatus

Cytomegalovirus donor seropositivity negatively affects survival after heart transplantation

ISHLT Transplant Registry

44,516
heart transplant recipients 2004-14

15,885
10 year follow up: CMV serostatus constellation

Groups based on donor and recipient CMV serostatus

D+ R-	D+ R+	D- R+	D- R-
n=6,963	n=2,902	n=4,218	n=1,802

CMV +ve

D+ groups exhibit ↓ 10 year survival

No significant difference in CAV development

Anti viral therapy for D+ R-: ↓ graft failure

Conclusion: Despite comparable baseline characteristics, donor CMV seropositivity was associated with reduced survival after heart transplantation.

Heim et al. *Transplantation*. August 2021

Transplantation®

@TransplantJrnl