ISHLT JOURNAL WATCH
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Cytomegalovirus Immunity Assays Predict Viremia but not Replication Within the Lung Allograft

Li J et al., *Transplantation Direct*. 2023. doi: 10.1097/TXD.0000000000001501

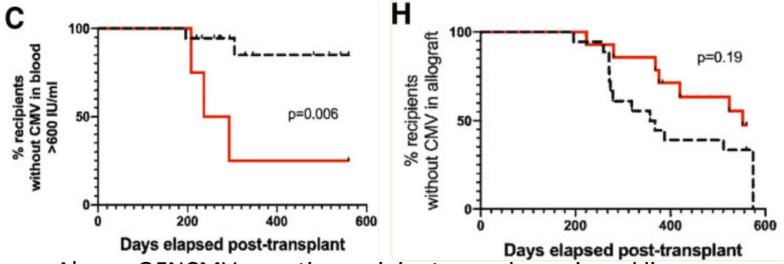
Study Highlights

Question: Can QuantiFERON-CMV (QFCMV) & T-Track CMV (ELISPOT) predict CMV reactivation in the blood or bronchoalveolar lavage fluid (BAL) in lung transplant recipients (LTxR)?

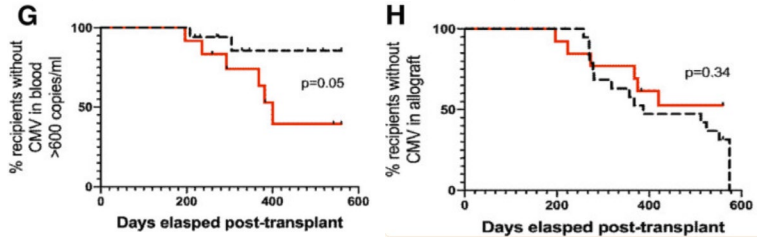
Methods:

- Prospective observational study of 32 LTxR (19% CMV D+R-, 81% R+)
  - CMV antiviral prophylaxis x 5 or 11 months
- Diagnostic Intervention:
  - One QFCMV per patient collected 126-196d post-Tx
  - One T-Track CMV per patient collected 91-245d post LTx
- Comparisons:
  - QFCMV pos vs. neg LTxRs
  - T-Track CMV pos vs. neg LTxRs
- Outcomes: proportion of patients with CMV activation in blood (any vs. > 600 IU/mL) and allograft

Results



- Above, QFNCMV-negative recipients are shown in red lines, and QFNCMV–positive recipients are shown in black lines
- Negative QFCMV was associated with CMV in the blood (graph C) in patients on ppx for 5 months only
- Negative QFCMV not association with allograft (graph H)



- ELISPOT-negative recipients are shown in red lines and ELISpot-positive recipients are shown in black lines.
- Negative ELISASPOT was associated with CMV in the blood (graph G) but not allograft (graph H)

Reviewer Comments

This study demonstrates correlation between two CMV-specific cell-mediated immune assays and control of viraemia. CMV reactivation in the allograft was not found to be associated with either assay. T-Track CMV result was more generalizable than QFCMV.

The consistent finding of prediction of high blood viral load with negative tests suggests possible clinical application**.** However, it is unclear the clinical significance of this finding, especially given the lack of association with reactivation in the graft itself.

This study is limited by its size and its use of a single timepoint for prediction. However, it highlights the need for a usable and reliable tool to predict CMV reactivation in the lung transplant population, especially given the association of CMV with chronic lung allograft dysfunction. Future large cohort studies including clinical outcomes are needed for future investigation and validation.

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Clinical outcomes of ventricular assist device support by HIV infection status: An STS-INTERMACS analysis

Birk S et al, *The Journal of Heart and Lung Transplantation*. 2023. doi:10.1016/j.healun.2023.04.014

Study Aim

- Evaluate all-cause mortality and clinical outcomes in HIV+ and HIV- receiving ventricular assist device (VAD)

Design

- Retrospective data from the STS-INTERMACS database
- Patients undergoing VAD implant from January 2012 through June 2020
- Analysis:
  - Kaplan-Meier survival analysis
  - Univariate and multivariate Cox proportional hazards regression
  - Propensity-matched analysis of 3 HIV –: 1 HIV+ patients matched on 21 preimplant characteristics, separate analysis conducted for 2012-2017 and 2018-2020 (introduction of HeartMate III in August 2017)

Results

- 85 HIV+ patients (39 from 2018-2020), 21,980 HIV- patients (7,157 from 2018-2020)
- Viral load <50-400 copies/mL in all HIV+ patients
- No significant difference in 6-month, 1-year, and 2-year survival (Fig. 1), even with stratified analysis (2012-2017 and 2018-2020).
- HIV+ not a predictor of mortality (univariate HR = 1.1, p =0.53, multivariate HR = 1.4, p=0.09).
- Propensity-matched survival analysis showed significantly higher mortality in HIV+ from 2012-2017 at 6 (22% vs 9%, p=0.02) and 12 months (28% vs 12%, p< 0.01), but not in the 2018-2020 cohort at 6 (10% vs 14%, p=0.58) and 12 months (13% vs 15%, p=0.79)

Results Continued

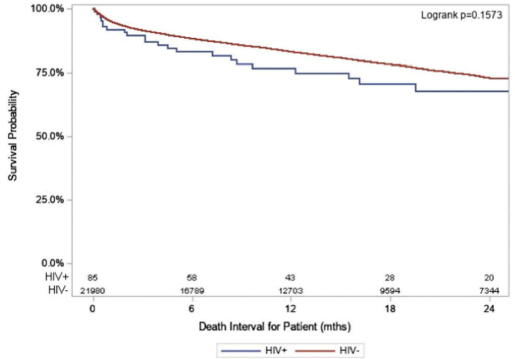

Fig. 1 Kaplan Meier Survival curves for 24 months postimplantation in all patients. Caption: A Kaplan-Meier curve showing the death interval for all HIV+ and HIV- patients in the dataset (implant year between 2012 and 2020). The difference between morality at 24 months between HIV+ and HIV- patients following implantation with ventricular assist devices is not statistically significant ($p = 0.16$).

- In matched and unmatched cohorts, there was no increase in major bleeding, stroke, or VAD-related and non-VAD related major infections. HIV+ had higher rate of rehospitalization for fluid overload

Reviewer Comments

- VAD implantation is a viable option for HIV+ patients with end-stage heart failure. In earlier years of VAD implantation there may have been a trend toward increased mortality for HIV+ patients, but this does not appear to be true in the era of HeartMate III
- Many VAD complications, including major infections, did not appear increased in HIV+ patients.

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Secondary Prophylaxis With Inhaled Colistin to Prevent Recurrence of *Pseudomonas aeruginosa* and ESBL Enterobacterales Pneumonia in ICU After Lung Transplantation: A Before-and-after Retrospective Cohort Analysis

A. Tran-Dinh, et al. *Transplantation* Nov 2022 doi.org/10.1097/tp.0000000000004187

Study Highlights

Background: *Pseudomonas aeruginosa* and ESBL Enterobacterales (ESBL-PE) organisms are frequent causes of pneumonia in lung transplant recipients.

Methods: The effect of inhaled colistin in addition to standard of care antibiotics was examined in lung transplant recipients in the ICU diagnosed with a pneumonia secondary to *pseudomonas aeruginosa* or ESBL-PE. Primary objective: Compare the proportion of patients with ≥1 recurrence of P aeruginosa or ESBL-PE pneumonia in the standard of care (SOC) and SOC+ inhaled colistin periods.

Results: A total of 271 lung transplants were included (125 in the SOC period and 146 in the SOC + inhaled colistin period). The patients were predominately male (64.2%) with a median age of 57 y and received double LTx (67.9%) for COPD/emphysema (36.2%) or interstitial lung disease (48.3%). The proportion of patients who experienced ≥1 recurrence of P aeruginosa or ESBL-PE pneumonia was significantly lower in the intervention period (n=1, 0.7%) than in the observation period (n=9, 7.2%) (p = 0.007).

Conclusion: This study suggests a potential benefit of secondary prophylaxis with IC to prevent the recurrence of *P aeruginosa* or ESBL-PE pneumonia in the intensive care unit after LTx.

Table 2: (modified) Comparison of characteristics and outcomes of patients with *P aeruginosa* or ESBL-PE pneumonia (n=52) before (observation period or SOC) and after (intervention period or SOC + inhaled colistin)

	Observation period (n = 23)	Intervention period (n = 29)	*P*
General characteristics			
Age, y	57 (47.5–60)	56 (49–61)	0.59
Female sex	5 (21.7)	9 (31)	0.54
Cause			
Emphysema	9 (39.1)	10 (34.5)	0.73
Interstitial lung disease	12 (52.2)	14 (48.3)	0.78
Others	2 (8.7)	5 (17.2)	0.44
Pretransplant coronary angioplasty and stent	6 (4.8)	5 (3.4)	0.57
eGFR, mL/min/1.73 m2	90 (80–90)	90 (80–90)	0.85
Pretransplant mPAP, mm Hg	28 (25–32)	25 (19.5–28.5)	0.06
ECMO as bridge-to-transplant	1 (4.3)	4 (13.8)	0.37
High-emergency lung allocation	2 (8.7)	8 (27.6)	0.16
Lung transplant surgery			
Type of LTx			
Single LTx	9 (39.1)	8 (27.6)	0.38
Double LTx	14 (60.9)	21 (72.4)	0.55
Maximum graft ischemic time, min	330 (278–390)	334 (270–435)	0.37
Intraoperative ECMO	18 (78.3)	22 (75.9)	0.84
Postoperative ICU stay			
SAPS II at admission	43 (39–48)	48 (42–60)	0.13
SOFA score at admission	9 (7–10)	8 (6–10)	0.25
Acute kidney injury (KDIGO 3)	9 (39.1)	6 (20.7)	0.15
Renal replacement therapy	6 (26.1)	4 (13.8)	0.31
Duration of mechanical ventilation, d	27 (10.5–42)	25 (5–55)	0.68
Duration of vasopressor, d	3 (1–6.5)	4 (2–9)	0.15
ECMO in ICU	9 (39.1)	15 (51.7)	0.41
Duration of ECMO in ICU, d	0 (0–2)	1 (0–3)	0.38
Tracheotomy	13 (56.5)	18 (62.1)	0.69
Recurrence of pneumonia due to *P aeruginosa* and ESBL-PE	9 (39.1)	1 (3.4)	0.003
Recurrence of pneumonia due to *P aeruginosa*	7 (30.4)	1 (3.4)	0.01
Recurrence of pneumonia due to ESBL-PE	4 (17.4)	0 (0)	0.03
Grade 3 primary graft dysfunction	10 (43.5)	10 (34.5)	0.51
Length of stay, d	37 (19–89)	45 (26–55)	0.90
Mortality			
ICU mortality	5 (21.7)	5 (17.2)	0.68
30-d mortality	0 (0)	1 (3.4)	1
90-d mortality	3 (13)	4 (13.8)	1

Reviewer's Comments

- This study uncovered an effect of inhaled colistin in addition to SOC antibiotics in preventing a recurrence of pneumonia due to *P. aeruginosa* or ESBL-PE in post-lung transplant ICU patients
- Groups before and after intervention were well matched, although the intervention group had longer ischemic times and were "sicker"
- No clinically significant differences (mortality, renal replacement therapy, length of stay) were noted between the observation and intervention group

Limitations

- Variations in drug resistance and post-transplant protocols may impact generalizability
- A small number of patients developed a recurrence due to *P. aeruginosa* or ESBL-PE (n=10, 9 in observation and 1 in intervention)
- A small percentage had pre-transplant colonization n=4 or <2% or bronchiectasis (n=23 or <10%).
- Resistance to colistin was not assessed
- Outcomes only assessed to 90 days