Riya Patel, COL2027

Impact of CMV D+/R- Status on Outcomes after Kidney-Pancreas Transplantation

Riya Patel[1], Leon Chen[1], Srijan Tandukar[1 2], Elizabeth Sonnenberg[3], Ingi Lee[4], Vishnu Potluri[1 2]

[1]University of Pennsylvania, [2]Renal Division, [3]Department of Surgery, [4]Division of Infectious Diseases at the Hospital of the University of Pennsylvania

BACKGROUND AND OBJECTIVES

Simultaneous kidney-pancreas (SPK) transplantation can be a "cure" for diabetes, but it comes at a cost.

- Dual organ transplants require heavier immunosuppression as there is increased risk of rejection.
- Cytomegalovirus (CMV) can cause a host of issues, such as encephalitis, pneumonitis, diarrhea, etc.
- Transplants that are Donor +/Recipient – (D+/R-) for CMV are at highest risk of developing CMV infection

Granular outcomes for CMV D+/R- SPK transplant are unknown in the US.

- Very limited research using highly granular data on outcomes after CMV D+/R- SPK transplants in the US
- Aim: to examine the effect of CMV in the US context, we used detailed chart review and deep phenotyping of cases

METHODS

- Adult CMV D+/R- Kidney-Pancreas transplant recipients at Penn Medicine between 1/1/2010 – 12/31/2022
- Patients who received prior, single, or other multi-organ transplant were excluded from the study

Primary Outcome:

- CMV Viremia: detectable and quantifiable viral load (> 1000 IU/mL) from CMV Quant, regardless of symptoms

Secondary Outcomes:

- Recurrent CMV Viremia: CMV Viremia after two consecutive negative tests OR a positive test 30 days after a negative test result
- Hospitalization: admission to the hospital that was at least 24 hours in length

RESULTS

- 18 (56%) of the 32 CMV D+/R- SPK recipients developed CMV viremia
- Median time between transplant and first instance of viremia was 228 days (IQR 197 – 253)
- All patients who developed CMV viremia had a peak viral load greater than 1000 IU/mL
- 6 (19%) of the 32 recipients lost their grafts; 3 developed viremia prior to graft loss while the other 3 patients did not develop viremia
- One graft loss was directly attributed to CMV
- 4 (12%) of the 32 recipients died, 2 of which had developed viremia
- Out of the 18 patients that developed viremia, 10 (55%) were hospitalized due to CMV
- Median hospitalization stay due to CMV was 3.5 days (IQR 2 – 6)
- 9 (50%) patients of the 18 who developed viremia experienced recurrence
- Median peak viral load for those who were hospitalized (237990 IU/mL) was significantly greater than the peak viral load of those who did not require hospitalization (24700 IU/mL)

TABLE 1: PATIENT CHARACTERISTICS

Variable	N%
Male	20 (62.5%)
Female	12 (27.5%)
Age at Transplant (Median, IQR)	42 (36 – 49)
Race	
White	22 (68%)
African American	7 (21%)
Asian	1 (3%)
Other	2 (9%)
Development of CMV	
Developed CMV	18 (56%)
Did not develop CMV	14 (44%)

TABLE 2: OUTCOMES

	Recipients with Viremia (n = 18)	Recipients without Viremia (n = 14)
Timing of first CMV after transplantation (median and IQR) in days	228 (197 – 253)	
Timing of highest viral load after transplantation (median and IQR) in days	238 (219 – 261)	
Peak Viral Load (IU/mL, median, and IQR)	80850 (8670 – 265600)	
Hospitalizations within five years of transplant	73	50
Hospitalizations due to CMV	10	
Hospitalizations unrelated to CMV	63	
Recurrence of CMV infection	9 (50%)	
Graft Loss	3 (17%)	3 (21%)
Mortality	2 (11%)	2 (14%)
Immunosuppression Dose Reduction	15	
Antimetabolite Stopped	10	
Antimetabolite Reduced by 50%	3	
Some Other Change was Made	2	
No Changes to Immunosuppression	3	

FIGURE 1. DEEPER DIVE INTO GRAFT LOSS

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
CMV Viremia	Yes	Yes	Yes	No	No	No
Graft Lost	Pancreas	Kidney	Kidney	Pancreas	Kidney	Kidney
Cause of Graft Loss	Acute Pancreas Rejection	Kidney torsion	AKI and ARDS in setting of CMV pneumonia	Pancreatitis Thrombosis	Alcoholic Pancreatitis Leading to ARDS and AKI	Chronic allograft injury
Days between Transplant and Graft Loss	2058	57	235	0	3776	2286

HOSPITALIZATION DATA

	Number of Hospitalized Patients (n = 10)
Asymptomatic	2 (20%)
Symptomatic	8 (80%)
Treated with IV Ganciclovir	10 (100%)
Duration of Stay (Median and IQR) in Days	3.5 (2 – 6)

LIMITATIONS

- Single center study
- Not all patients reached five years post-transplant
- Cannot determine the effects of CMV infection on inflammation and subsequent indirect effects leading to graft failure and mortality

CONCLUSIONS

- **CMV infection is common** among CMV D+/R- recipients
- Among patients who developed CMV infection, all had a CMV viral load greater than 1000 IU/mL necessitating antiviral therapy
- CMV infection frequently led to hospitalizations, and there was a high risk of CMV viral recurrence.
- Our study calls for standardizing guidelines to monitor CMV infection following the completion of prophylaxis.
- One graft failure and mortality was due to CMV infection.
- However, reducing immunosuppression for CMV infection did not directly lead to kidney rejection.