Favorable Outcomes in Solid Organ Transplant Recipients Treated with Newer Therapies for COVID-19

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Introduction

Little information is available on COVID-19 outcomes in solid organ transplant (SOT) recipients treated with newer therapies including remdesivir, dexamethasone, & convalescent plasma. Theoretical concerns have been raised about safety in this population specifically regarding renal or liver function after remdesivir, infections after dexamethasone, & alloimmunity after convalescent plasma. Our objective in this study was to assess the outcomes of SOT recipients receiving these therapies in regards to renal & liver function, graft function, rejection, secondary infections, & mortality.

Methods

In a single center retrospective study, we included 131 SOT recipients (77 inpatients & 54 outpatients) with COVID-19 between 3/1/20 – 11/30/20 with 30 to 90-day follow-up. We compared recipient outcomes between three 3-month periods based on changing treatment paradigms over time: era 1 from 3/1/20-5/31/20, n=21; era 2 from 6/1/20-8/31/20, n=21; era 3 from 9/1/20-11/30/20, n=35. Patients in eras 2 & 3 received newer therapies such as remdesivir, dexamethasone, & convalescent plasma. Data were collected on demographics, comorbidities, graft dysfunction, infections, WHO severity scores & various lab values including inflammatory markers & tests of organ function. We compared the laboratory trajectory of those treated with remdesivir or plasma to those non-treated to assess the short & long-term post-treatment effects.

Results

	Era 1 (3/1-5/31)	Era 2 (6/1-8/31)	Era 3 (9/1-11/30)	p-value
N	21	21	35	
Gender				0.28
Male	12 (57.1%)	9 (42.9%)	23 (65.7%)	
Female	9 (42.9%)	11 (52.4%)	12 (34.3%)	
Others	0 (0.0%)	1 (4.8%)	0 (0.0%)	
Length of stay, median (IQR)	8 (5, 9) (n=21)	6 (5, 10) (n=21)	6 (3, 10) (n=34)	0.75
Organ category				0.85
Kidney	12 (57.1%)	13 (61.9%)	16 (45.7%)	
Liver	4 (19.0%)	3 (14.3%)	9 (25.7%)	
Heart	2 (9.5%)	1 (4.8%)	2 (5.7%)	
Lung	2 (9.5%)	3 (14.3%)	7 (20.0%)	
Hand	0 (0.0%)	1 (4.8%)	0 (0.0%)	
Simultaneous kidney/liver	1 (4.8%)	0 (0.0%)	1 (2.9%)	
Graft dysfunction	8 (38.1%)	8 (38.1%)	20 (57.1%)	0.25
Baseline MMF use				0.58
None	8 (38.1%)	8 (38.1%)	18 (51.4%)	
Baseline use	13 (61.9%)	13 (61.9%)	17 (48.6%)	
MMF discontinued	13 (100.0%)	13 (100.0%)	17 (100.0%)	
Death	1 (4.8%)	0 (0%)	3 (8.5%)	

- Remdesivir (31.2%), dexamethasone (31.2%), & convalescent plasma (57.1%) were administered to inpatients from 6/2020 onwards.
- Remdesivir & dexamethasone were targeted to patients with hypoxemia (O2 saturation of <94% on room air for >1 hour); renal function did not restrict remdesivir use.
- Over the study period, outcomes were similar across eras; overall inpatient mortality was low, 5.2% died. All who died had pre-admission existing graft dysfunction. Rejection occurred in 2.6% inpatients. No significant differences in secondary infections were observed across eras.
- Pre-existing graft dysfunction was associated with a higher need for inpatient & ICU admission, delayed hospital discharge (sub-hazard ratio $_{0.4}0.6_{0.9}$, p=0.01), higher median WHO score, & poorer survival.
- Acute kidney injury was present on admission in 37.3% overall; renal function improved in most patients (creatinine change median, IQR, from baseline: 0 [-0.2, 0.11]; from admission: -0.1 [-0.5, 0.06]). More rapid improvement in creatinine was seen after receipt of remdesivir
- Patients on convalescent plasma showed no evidence of late allograft dysfunction.

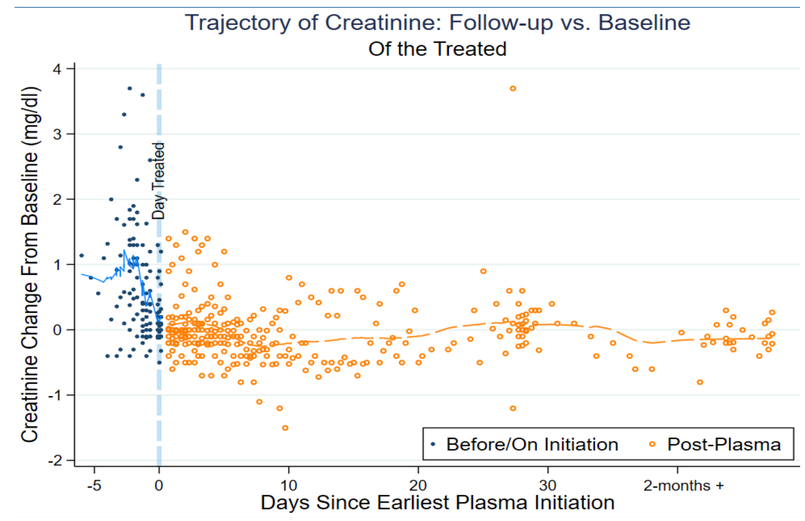

Figure 1: Trajectory of creatinine in patients given plasma.

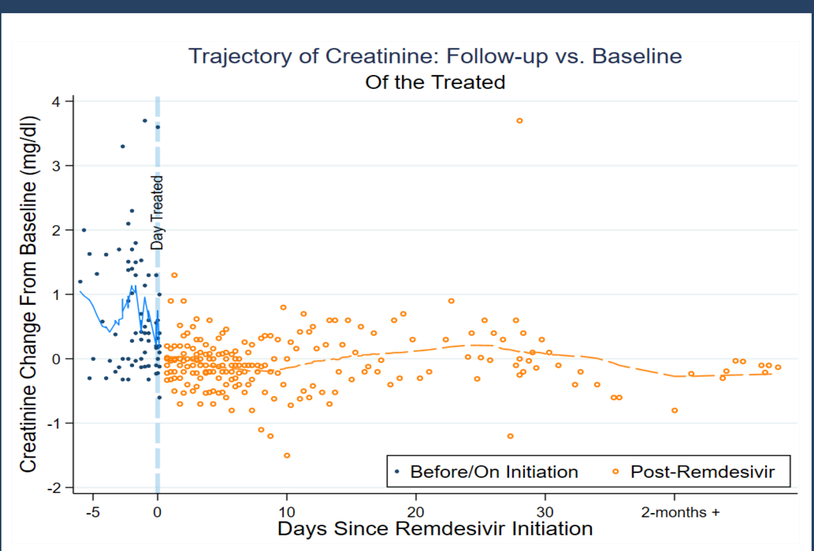

Figure 2: Trajectory of creatinine in patients treated with remdesivir

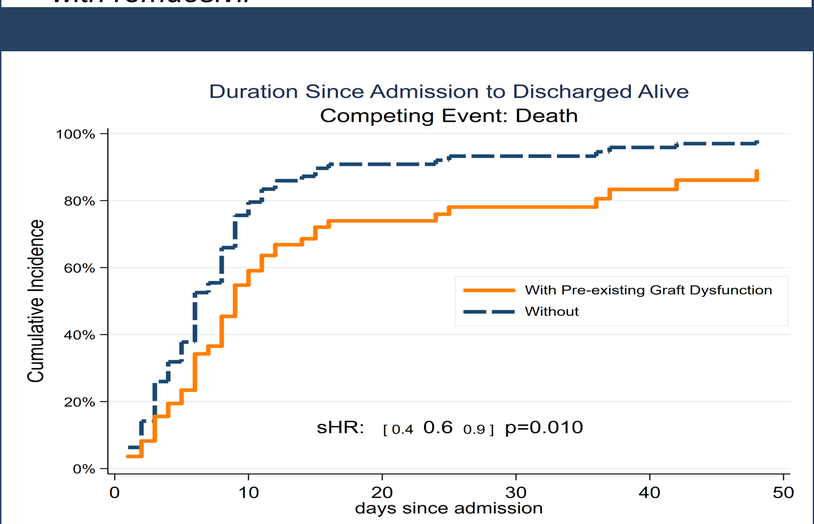

Figure 3: Delayed hospital discharge observed in patients with pre-existing graft dysfunction.

Conclusions

- We found no evidence that newer COVID-19 therapies are associated with worsening kidney or liver function, acute rejection, excess risk for infections or other safety signals, & would encourage the use of these therapies in SOT inpatients who meet appropriate therapeutic criteria.
- Patients who received convalescent plasma showed no evidence of late allograft dysfunction.

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