Evaluation of Tacrolimus Prescribing Patterns in Post-Operative Heart Transplant Recipients

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Background

- Standard triple drug immunosuppression therapy used to reduce the risk of organ rejection post-transplant includes tacrolimus[1]
- Serious adverse effects from tacrolimus include nephrotoxicity, neurotoxicity, and infection[1]
- Due to the narrow therapeutic range, tacrolimus requires extensive monitoring and dose adjustments[1]
- By exploring current prescribing patterns and barriers to achieving therapeutic levels in the post-transplant period, opportunities for medication optimization may be identified

Objectives

- Determine the average time from heart transplant to the first therapeutic tacrolimus level (TTTL, time to therapeutic tacrolimus level)
- Identify patient specific factors that may impact TTTL
- Assess if a relationship exists between TTTL and clinically significant transplant outcomes

Methods

- Design:
  - Retrospective, single-center chart review
  - Included patients who underwent heart transplantation from January 2020 through March 2023
  - Patients followed for 30 days post-transplant
- Exclusion Criteria:
  - Patients who did not survive index hospitalization
- Primary Outcome:
  - Average time from heart transplant to first therapeutic tacrolimus level, 10-13 ng/mL (TTTL)
- Secondary Outcomes:
  - Assess the impact of the use of induction agents and post-transplant renal function on TTTL
  - Assess the impact of achieving TTTL on development of acute cellular rejection (ACR)

Results

Table 1. Baseline Characteristics (n=28)

Sex – no. (%)	
Male	16 (57.1)
Female	12 (42.9)
Age – years, mean (SD)	
Recipient age	54 (13.8)
Minimum age	23
Maximum age	70
Donor age	32 (9.7)
Minimum age	17
Maximum age	49
Race – no. (%)	
White	24 (85.7)
Black or African American	3 (10.7)
Declined	1 (3.6)
Renal function prior to transplant – no. (%)	
eGFR ≥60	20 (71.4)
eGFR 30-59	6 (21.4)
eGFR 15-29	2 (7.1)
Ventricular assist device prior to transplant – no. (%)	5 (17.9)
Nonischemic cardiomyopathy – no. (%)	19 (67.9)
Induction agent use – no. (%)	
Induction agent utilized	23 (82.1)
Antithymocyte globulin	4 (17.4)
Basiliximab	19 (82.6)

CRRT, continuous renal replacement therapy; eGFR, estimated glomerular filtration rate [mL/min/1.73 m3]

Table 2. Primary and Secondary Post-Transplantation Clinical Endpoints

	Mean TTTL (days)	Standard Deviation (SD)	p-value
Primary Endpoint			
TTTL (10-13 ng/mL)	7.2	3.22	-
Secondary Endpoints			
Induction agent use			
Induction agent used	7.3	3.29	
No induction agent used	6.6	3.13	0.647
Renal function‡			
eGFR ≥60 mL/min/m3	7.3	3.17	
eGFR <60 mL/min/m3 or receiving CRRT	7.1	3.39	0.909
Occurrence of ACR			
Experienced any ACR	7.4	3.43	
Did not experience ACR	7.0	3.11	0.732

‡Renal function at 24-hours post-transplant

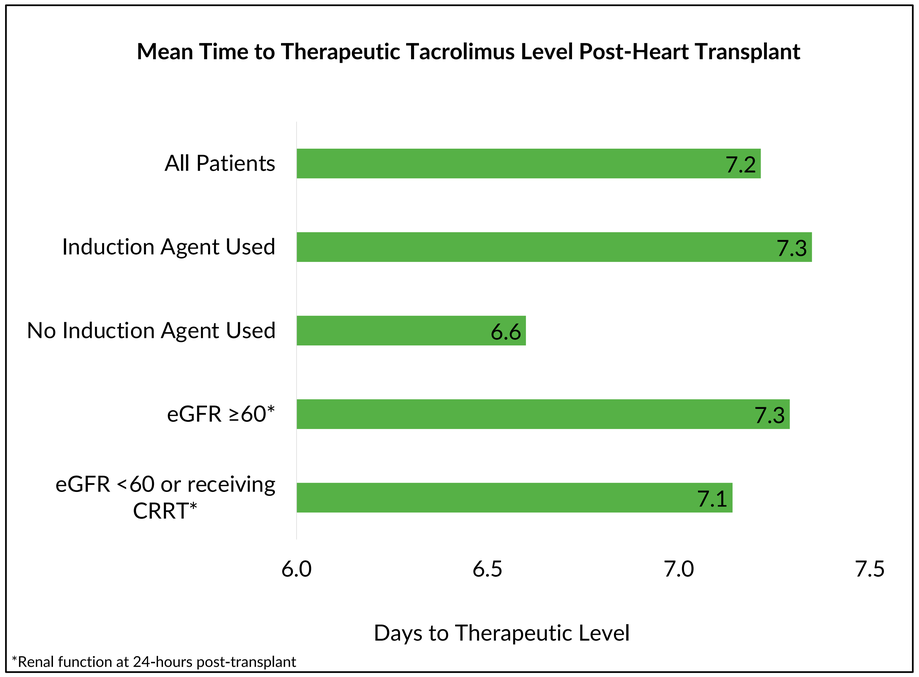

Figure 1. Mean time to therapeutic tacrolimus level (TTTL) amongst various groups.

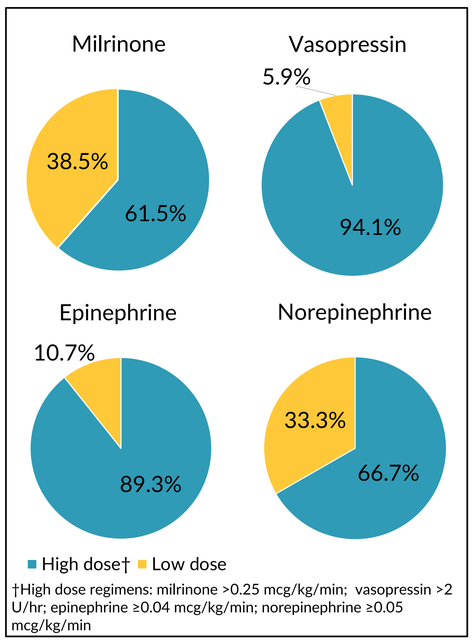

Figure 2. Percentage of high vs. low dose inotrope and vasopressor use 24-hour post-transplant.

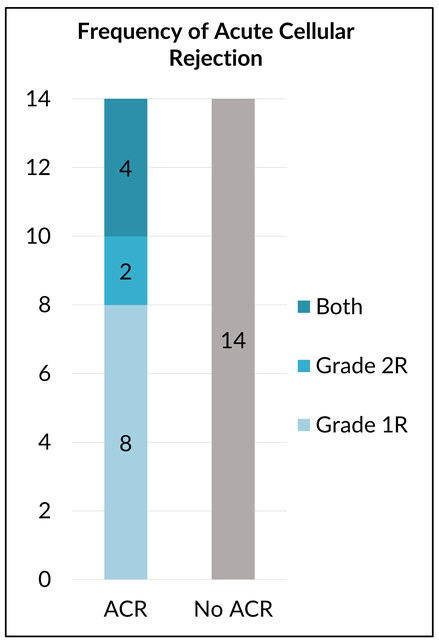

Figure 3. Number of patients who experienced ACR within 30 days post-transplant.

Conclusions

- The average time to therapeutic tacrolimus level was 7.2 days (Table 2)
- Induction immunosuppressive agents and renal function did not appear to impact time to therapeutic tacrolimus level (Table 2)
- The majority of patients (82.1%) received an induction agent, with basiliximab being the most common (Table 1)
- The rate of ACR did not appear to be affected by time to therapeutic tacrolimus level (Table 2)
- At 24 hours post-transplant, 100% of patients were receiving epinephrine, 92.9% milrinone, 75% norepinephrine, and 60.7% vasopressin
- Of those receiving inotropic or vasopressor support at 24 hours post-transplant, the majority required a high-dose regimen (Figure 2)
- In the post-transplant period, 50% of patients experienced ACR (57.1% 1R; 14.3% 2R; 28.6% both 1R and 2R) (Figure 3)

Study Limitations

- Small sample size with limited diversity
- Relatively short trial duration (30 days)

Areas of Further Study

- Assessing outcomes of time in therapeutic tacrolimus range post-transplant
- Assessing prescribing patterns in a larger cohort
- Expanding the scope of the study to evaluate long-term outcomes (1-year post-transplant) of TTTL on post-heart transplant patients

References

1. Kittleson MM, Kobashigawa JA. Management of the ACC/AHA Stage D patient: cardiac transplantation. *Cardiol Clin*. 2014;32(1):95-viii. doi:10.1016/j.ccl.2013.09.004

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