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# TTS 2024

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## Association between target CD3 count levels and early acute rejection in rATG induction therapy for heart transplantation

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- The authors have no potential conflict of interest to report





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## Background and Purpose

- The incidence of acute rejection among adult HTx recipients was 20%-30% in 2021.
- Approximately 50% of HTx recipients received induction therapy to prevent rejection.
  - According to the guidelines of the ISHLT, the target CD3 count ranges **from 25 to 50 cells/mm<sup>3</sup>**.
  - The medical center in this study broadened the CD3 count range since the strict target might cause **cytopenia** or other adverse effects.
- This study aimed to assess the association between CD3 count levels and BPAR **at 3 months** post-HTx among patients receiving rATG induction therapy.



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rATG: rabbit antithymocyte globulin  
BPAR: biopsy-proven acute rejection  
HTx: heart transplant  
ISHLT: International Society for Heart and Lung Transplantation



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## Methods

- Patients selection and grouping:  
Patients **over 20 years old** who underwent their **first HTx** and **received rATG induction therapy** were included.

2016/01-2022/12 adult HTx in a medical center: 117 pts

Exclusion: re-HTx: 3, not use rATG: 2,  
suspected rATG allergy: 2, no T-cell  
data: 6 pts

104 pts

Subgroup Analysis  
Logistic Regression Analysis

T cell < 50/mm<sup>3</sup>:  
77 pts (74.0%)

150/mm<sup>3</sup>>T cell >50/mm<sup>3</sup>:  
22 pts (21.2%)

T cell >150/mm<sup>3</sup>:  
5 pts (4.8%)

High Intensity group (HI)

Low Intensity group (LI)

rATG: rabbit antithymocyte globulin  
BPAR: biopsy-proven acute rejection  
HTx: heart transplant  
HI: high intensity  
LI: low intensity  
ROC curve: Receiver operating characteristic curve

- BPAR and cytopenia were compared between groups.
  - **Multivariate logistic regression models** were used to assess the association between BPAR and rATG induction.
  - **ROC curve analysis** was conducted to determine a cut-off point of cumulative rATG dose for cytopenia.
- End points:
  - The difference in **the rejection proportions** between HI group and LI group.
  - The difference in the incidence of **side effects** and the **dosage of rATG**.



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## Results

**Table 1. Baseline characteristics in study population**

	Total n=104	HI n = 77	LI n = 22	P value
<b>Patient index</b>				
Age, yrs	49.6 (9.8)	50.2 (9.7)	48.1 (9.8)	0.331
Sex, female (%)	16 (15.4)	14 (18.2)	0 (0.0)	0.035
Body mass index, BMI, kg/m <sup>2</sup>	23.4 (4.1)	23.4 (4.1)	24.2(4.3)	0.314
<b>Diagnosis before HTx</b>				
DCMP	47 (45.2)	37 (48.1)	8 (36.4)	0.332
ICMP	45(43.3)	29 (37.7)	13 (59.1)	0.073
Acute myocarditis	6 (5.8)	5 (6.5)	1 (4.6)	1.000
<b>Mechanical support and Inotropes before HTx</b>				
IABP	12 (11.5)	9 (11.7)	2 (9.1)	1.000
ECMO	21 (20.2)	14 (18.2)	5 (22.7)	0.759
VAD	64 (61.5)	43 (55.8)	16 (72.7)	0.155
Inotrope using n(%)	45 (43.3)	36 (46.8)	7 (31.8)	0.213
<b>Lab Data before HTx</b>				
Scr, mg/dL	1.55 (1.09)	1.45 (0.83)	1.99 (1.66)	0.374
Dialysis using n (%)	24 (23.1)	18 (23.4)	5 (22.7)	0.949
ALT, U/L	44.2 (57.5)	47.6 (63.3)	33.2 (36.0)	0.114
T-bil, mg/dL	2.07 (2.42)	2.29 (2.68)	1.14 (1.02)	<b>0.004*</b>
Crossmatch n (%)	17 (16.4)	11 (14.3)	4 (18.2)	0.737

**Table 2. Rejection, dosage, and ADR between HI and LI**

	HI n = 77	LI n = 22	P value
<b>Cumulative rATG, mg/kg</b>	1.57 (0.53)	1.32 (0.51)	<b>0.023*</b>
<b>BPAR at 3 months post-HTx</b>			
Any grade	16 (20.8)	2 (9.1)	0.347
Grade 1	15 (19.5)	1 (4.6)	0.112
≥Grade 2	1 (1.3)	1 (4.6)	0.397
<b>Cytopenia</b>	33 (42.9)	6 (27.3)	0.223

- The mean cumulative **rATG dosage** was significantly higher in the HI group compared to the LI group ( $1.57 \pm 0.53$  mg/kg vs  $1.32 \pm 0.51$  mg/kg, **P=0.02**).
- The overall rate of **any grade BPAR** at 3 months post-transplant was 18.2%, with 16 patients (20.8%) in the HI group and 2 patients (9.1%) in the LI group (**P=0.35**).
- The proportions of **≥ grade 2 BPAR** were comparable between the HI and LI groups (1.3% vs 4.6%, **P=0.40**).

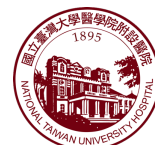
Baseline characteristics did not significantly differ between the two groups.

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rATG: rabbit antithymocyte globulin, DCMP: Dilated cardiomyopathy, ICMP: Ischemic cardiomyopathy  
IABP: Intraaortic balloon pumping, ECMO: Extracorporeal Membrane Oxygenation  
VAD: Ventricular Assist Device, HTx: heart transplant  
BPAR: biopsy-proven acute rejection

Data are represented as the number of patients (%). \*Statistically significant (p < 0.05)





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## Results



**Table 3.**  
Multivariate logistic regression of  $\geq$  Grade 2 BPAR

Rejection	OR	95% CI	P value	
Age, yrs	0.97	0.83-1.14	0.517	
T cell	<50 cells/ mm <sup>3</sup>	0.94	0.01-6.78	0.426
	50-150 cells/mm <sup>3</sup>	1	-	-
Crossmatch	8.26	0.33-208.02	0.200	
T-bil, mg/dL	1.09	0.58-2.06	0.792	
Mean FK level 0-3 months post-HTx, ng/ml	0.75	0.37-1.51	0.420	

In the multivariate logistic regression model, the intensity of rATG induction was not associated with  $\geq$  grade 2 BPAR at 3 months post-transplant. So were the age, crossmatch, T-bil, and mean FK levels.

**Table 4.**  
ROC curve analysis of rATG cumulative dosage

	Achieved T cell < 50 cells/mm <sup>3</sup>	Cytopenia
ROC curve		
p-value	<b>0.008*</b>	<b>0.041*</b>
AUC	0.613 (0.530-0.696)	0.572 (0.503-0.641)
cut-off point (mg/kg)	1.21	0.91
Sensitivity (%)	44.1	71.3
Specificity(%)	78.1	46.8

A cumulative rATG dosage exceeding 0.91 mg/kg was likely to increase the risk of cytopenia (71.3% sensitivity and 46.8% specificity, P=0.04).



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rATG: rabbit antithymocyte globulin  
BPAR: biopsy-proven acute rejection  
HTx: heart transplant  
ROC: Receiver operating characteristic  
T-bil: total bilirubin



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## Conclusion

- There was **no significant difference** in BPAR at 3 months post-heart transplant between patients with CD3 counts  $< 50$  cells/mm<sup>3</sup> and those with counts between 50 and 150 cells/mm<sup>3</sup> when using rATG induction therapy.



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