PRA Is Not Associated with Rejection in Combined Heart and Liver Transplantation

Juan M. Ortega-Legaspi[1], Maria R. Molina[1], Ylenia A. Quiaoit[1], K. E. Gerrity[1], Nicole L. Casciello[1], Pavan Atluri[2], Marisa Cevasco[2], Lee Goldberg[1], Stuart B. Prenner[1], Michael Genuardi[1], Edo Y. Birati[1], Yuli Y Kim[3], Joyce Wald[1]

[1]Heart Failure and Transplant Section, University of Pennsylvania, Philadelphia, PA,
[2]Division of Cardiothoracic Surgery, University of Pennsylvania, Philadelphia, PA,
[3]Division of Cardiovascular Medicine, Adult Congenital Heart Disease Section, University of Pennsylvania, Philadelphia, PA

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Disclosures

- Dr Lee Goldberg reports personal fees from Abbott and Novartis. The institution as well as himself receive fees from Respircardia.

- All other authors have nothing to disclose.

Introduction

- Combined heart liver transplantation (CHLT) is relatively rare with approximately 250 cases from 1988-2018 nationally.

- However, the number of cases is rising each year due to increasing need in the adult congenital heart disease and cardiac amyloid populations with excellent survival.

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Introduction

- CHLT outcomes have potential immunological benefits compared to heart transplant alone.

- Liver allografts have long been observed to be more tolerant to HLA mismatch while showing some degree of immune protection in combined organ transplantation.

Study question and aim

- Sensitization as defined by a high level of calculated panel of reactive antibodies (cPRA) to the human leukocyte antigen (HLA) is a known risk factor for worse outcomes in heart transplant recipients.

- Outcomes in larger cohorts of CHLT recipients and the immunological consequences are not well known.

- Therefore, we aimed to explore the relationship between level of sensitization and outcomes in our cohort of CHLT recipients.

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Hypothesis

- We hypothesized that those with elevated cPRA would have no significant difference in outcomes in CHLT compared to those with no or low-moderate cPRA.

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Methods

- A retrospective analysis from a single center experience of CHLT between 1997 and 2019 was performed.
- The data was extracted directly from the electronic medical record.
- The retrospective data collection and analysis was approved by our Institutional Review Board.
- Outcomes of patients who had pre-transplant elevated cPRA >50% were compared to those with 0% and those with a low to moderate cPRA (1-50%).
- The hypothesis was tested with the Fisher's exact test.

Results: Clinical characteristics of the CHLT at the Hospital of the University of Pennsylvania

Age range	42.4 years +/- 10
Race	
➢ White	26
➢ Black	7
➢ Latino	3
➢ Asian	1
Sex	
➢ Female	11
➢ Male	26

<u>Indication for heart transplant</u>	
➢ Congenital heart disease	
○ Fontan physiology	10
○ Tetralogy of Fallot	1
➢ Hypertrophic cardiomyopathy	9
➢ Idiopathic dilated cardiomyopathy	6
➢ Arrhythmogenic right ventricular cardiomyopathy	5
➢ Ischemic cardiomyopathy	4
➢ Cardiac sarcoidosis	1
➢ Left ventricular non-compaction	1
<u>Indication for liver transplant</u>	
➢ Cardiac cirrhosis	26
➢ Liver fibrosis from congestive hepatopathy	7
➢ Autoimmune hepatitis	2
➢ Hepatitis C	1
➢ Cryptogenic cirrhosis	1

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Results: Clinical characteristics of patients who underwent CHLT by cPRA level.

	cPRA 0% N= 27 (72.9%)	cPRA 1-50% N= 6 (16%)	cPRA 51-99% N= (10.8%)	p
History of				
➢ Fontan	8 (21.6%)	2 (5.4%)	0	0.694
➢ PLE	8 (21.6%)	2 (5.4%)	0	0.694
➢ Diabetes	0	0	1 (2.7%)	0.111
➢ Hypertension	9 (24.3%)	1 (2.7%)	2 (5.4%)	0.536
➢ CKD	6 (16.2%)	1 (2.7%)	1 (2.7%)	1.000
➢ Sternotomy	8 (21.6%)	2 (5.4%)	0	0.686
Death				
➢ Overall	6 (21.6%)	2 (5.4%)	0	0.639
➢ < 1 year	3 (13.5%)	2 (5.4%)	0	0.164
ACR				
➢ Heart	0	1 (2.7%)	1 (2.7%)	0.08
➢ Liver	2 (5.4%)	1 (2.7%)	1 (2.7%)	0.291
DSA	2 (5.4%)	1 (2.7%)	0	0.669
LVEF< 50%				
➢ 1 month post	2 (5.4%)	0	0	1.000
➢ 1 year post	2 (5.4%)	0	0	1.000
LOS > 30 days	12 (32.4%)	4 (10.8 %)	1 (2.7%)	0.507
Post-transplant				
➢ Diabetes	17 (45.9%)	6 (16.2%)	3 (8.1%)	0.231
➢ Hypertension	11 (29.7%)	4 (10.8%)	3 (8.1%)	0.363
➢ AKI or CKD	17 (45.9%)	5 (13.5%)	3 (8.1%)	0.668

CHLT = combined heart and liver transplant, cPRA = calculated panel reactive antibody, ACR = acute cellular rejection, DSA = donor specific antibodies, PLE = protein losing enteropathy, CKD = chronic kidney disease, LVEF = left ventricular ejection fraction, LOS = length of stay at index admission, AKI = acute kidney injury

Results

- There was no statistical significance at baseline between PRA and:
  - History of Fontan physiology
  - Protein losing enteropathy
  - Prior sternotomy
  - Diabetes
  - Hypertension
  - Renal disease

- There was no correlation between cPRA and:
  - Death
  - Rejection of either organ
  - Presence of donor specific antibodies
  - Ejection fraction below 50% (1 mo and 1 year)
  - Length of stay over 30 days
  - Post-transplant:
    - Hypertension
    - Diabetes
    - Renal disease
- Additionally, there were no episodes of antibody mediated rejection.

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Conclusions

- The degree of allosensitization was not associated with worse outcomes in the CHLT population.

- Given the likelihood of an increased patient population requiring evaluations for CHLT, it is relevant to further understand the mechanisms and variables that impact outcomes in this highly complex group of patients.

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Conclusions

- While the sample is small, these data is intended to contribute to further understanding the immune protection conferred by the liver in patients requiring a transplant of both organs.

- Further, a multicentre analysis of this cohort is necessary in the future.

- The findings hereby presented give reassurance that may change the perception of risk when planning a CHLT in a highly sensitized patient.

Perelman School of Medicine
University of Pennsylvania

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Thank you!