Insights into Protein Losing Enteropathy and Heart Transplantation: A Single Center's 24 Year Experience

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Introduction

- Protein Losing Enteropathy(PLE) is an ominous complication of Fontan palliation with > 50% mortality within 5 years of diagnosis[1]. Heart Transplantation(HTx) is the only palliation that can offer a longer and improved quality of life.
- However, HTx for PLE is associated with high mortality - prior studies have demonstrated a 36% 90 day mortality rate after HTx[2].
- **Aims:**
  1. Determine if there is a difference in survival between patients with Failed Fontan physiology transplanted with PLE versus without PLE.
  2. Determine rate of resolution of PLE symptoms after HTx.
- **Hypothesis:** HTx for PLE is associated with high mortality from infection and bleeding; yet , there is also increased risk of rejection due to allosensitization.

Methods

- **Study design:** Retrospective, descriptive single center cohort study
- **Inclusion criteria:** All patients with previous Fontan operation who underwent HTx at our institution from 5/1998 to 10/2012.
- **Primary outcome variable:**
  - Survival to latest follow-up
- **Secondary outcome variables:**
  - Infection and rejection rate the first year after HTx
  - Rate of improvement of Albumin and IgG levels
  - Rate of resolution of enteric protein losses
- **Statistical Methods:**
  Kaplan-Meier survival curves were constructed and survival and freedom from rejection, and infection were compared using the log-rank test.

Results

- **Of 190 HTx recipients, 21 patients (15%) had HTx for failed Fontan physiology - 14 had PLE, 6 had ventricular dysfunction, 1 had plastic bronchitis (Tables 1 & 2).**

Disclosure

- None

Results

Table 1. Pts with Fontan Physiology	Pts with PLE (n=14)	Non PLE Pts (n=7)
Median Age	12 (4-39)	11(0.4 – 47)
Gender(M:F)	5:9	5:2
Underlying Single Ventricle Lesion - RV dominant: LV Dominant	5:9	5:2
Number of prior Sternotomies	5 (3-7)	4 (3-4)
PVR at HTx listing (Wood units)	2.4 (0.94-5.7)	1.6 (0.3.-2.5)
Average Days on Wait List	63 (4-335)	199 (108-289)
Listing Status at time of HTx 1A 1B	 13 1	 6 1
PRA (>10%)	10	0

Table 2. Pts with PLE	
Mean Duration of Symptoms prior to HTx (months)	27.4 (6-72)
PRA(>10%) Mean HLA Class I PRA Mean HLA Class II PRA	 64 % (0-100) 36 % (0-99)
Mean IgG Level (mg/dL)	141(82-263)
Mean Stool Alpha 1 Antitrypsin Level (mg/dL)	775 (158-1391)
Mean Albumin Level (g/dL)	2.0 (1.2-2.5)
Flow Cytometry Mean Absolute CD3 (cells/mm^3) Mean Absolute CD19(cells/mm3)	 195(7-319) 356(69-709)

- Age at Htx did not make a difference in outcome.
- PLE patients had greater incidence of allosensitization.
- PLE patients received basiliximab or thymoglobulin for induction depending on CD3 counts.

Table 3. Outcomes After HTx	Pts with PLE (n=14)	Non PLE Pts (n=7)
Mortality Perioperative Within 6 months Late	 2 2 1	 1 0 2
Positive Crossmatch	4	0
Patients with Rejection in the 1st year Antibody Mediated Rejection Cellular Rejection (grade ≥ 1B)	 6 5	 0 2
Patients with Infection in the 1st Year	5	0
Mean Graft Survival Time(months)	29(0-128)	79(0-158)

- Four deaths occurred early in PLE patients:
  1 due to coagulopathy & graft failure
  3 due to infections (H1N1,*Bacteroides*, & *Enterobacter*).
- PLE patients had greater incidence of significant rejection events in 1st year:
  6 episodes of Grade 2 cellular rejection
  2 episodes of pAMR1
  4 episodes of pAMR2.
- Five PLE patients required plasmapheresis post HTx.

Results

- Thirty day, 1 and 5 year survival in PLE group were 79%,71%, and 53% respectively.
- One late death occurred at 55 months post HTx due to CAV.

Figure 1. Freedom from death or re-transplant

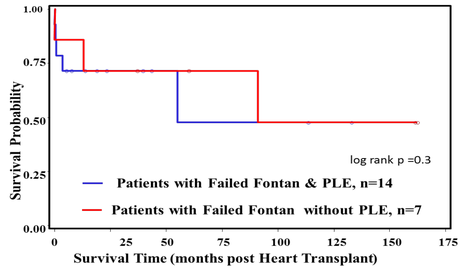
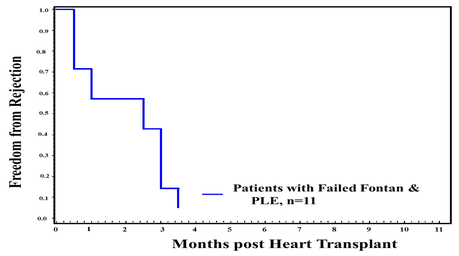


Figure 2. Freedom from rejection the first year post HTx



- Albumin, IgG, and stool protein losses normalize.

Figure 3. Albumin trends post HTx

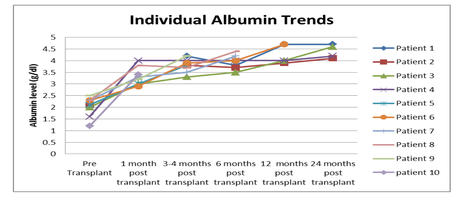
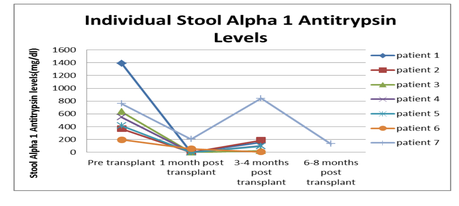


Figure 4. Alpha 1 Antitrypsin levels post HTx



Conclusion

1. **Highest mortality after HTx for PLE occurs early from infection; however, rejection is also common.**
2. **Pts with PLE appear to have a tendency to higher mortality and morbidity than non PLE pts; but statistical significance limited by small cohort size.**
3. **Resolution of PLE symptoms occurs rapidly after HTx.**
4. **With earlier referral and immune monitoring post HTx, outcome may improve .**

[1]Mertens, et al. *Journal of Thoracic Cardiovascular Surgery*, 1998; 115: 1063-1073
[2] Davies, et al. *The Journal of Cardiothoracic and Cardiovascular Surgery*, 2012; 143: 1183-1192