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The Use of the Berlin Heart EXCOR Pediatric in Patients with Functional Single Ventricle

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Disclosures

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Background

- Options for pediatric patients requiring cardiac mechanical assistance improving since 2000
  - Blume Circulation. 2006;113:2313-2319
  - Stein Circ Heart Fail. 2010;682-688
  - Morales The Jnl Hrt and Lung Tplant. Vol 30, No 1, 2011
  - Almond Circulation. 2013 March 2013, Epub

- Berlin Heart EXCOR Pediatric
  - Small pumping chambers, 10 mL
  - Transparent chambers
  - Exchanges at bedside
  - > 1,200 implants in > 34 countries

Berlin Heart EXCOR Pediatric FDA IDE Trial

- Fraser, et al
  - 90% survival
  - Survival rates significantly higher than historical ECMO controls
  - Neurologic dysfunction in 29%
  - Majority of patients who received the device in the US were excluded (> 75%) from the primary cohort
    - Complex Congenital Heart Disease
      - Single Ventricle Lesions

N Engl J Med 367;6 2012

Overall Experience

- Almond et al, 2013
  - 204 US Children, May, 2007- December, 2010
  - 64% of patients transplanted, 6% recovery
  - 70% survival

- Almond et al, 2011
  - ELSO Registry/ECMO for Bridge to Heart Transplant
  - 773 patients (1994-2009)
  - Overall 45% survival
  - Single Ventricle survival 27%

Circulation March 2013;127:1702

Circulation June 2011; 123:2875-84

Study Objectives and Patient Population

- Describe the initial experience for patients with single ventricular anatomy or physiology (SV) treated with Pediatric EXCOR VAD

- Patient Population (n =26)
  - Berlin Heart EXCOR IDE trial database
  - 5/2007-12/2011
  - Implanted under FDA compassionate use regulations at both participating and non participating IDE sites

- Compared to results for 2-ventricle patients treated during the same time period (n=255)
  - Primary Study Cohort + continued access patients
  - Compassionate Use Cohort at IDE and non IDE sites

Methods

- All SV patients were followed until death, explant or transplant
- SAE data
  - All IDE site data were adjudicated
  - SAE Data collected during the CAP and from non IDE sites were not
- Operative Notes
- Personal Communication with surgeons
- Data analyzed using SAS v9.2
  - Continuous variables are described using medians and ranges
  - Statistical Comparisons made using Chi-Square and Fisher's Exact tests for categorical variables
  - Statistical Comparisons made using Kruskal-Wallis test for continuous variables

Patient Characteristics

	n (% of 26)
Primary Anatomic Diagnosis	
HLHS	15 (57.7%)
Unbalanced AV Canal	2 (7.7%)
Tricuspid Atresia, ASD, VDS	1 (3.9%)
Pulmonary Atresia/IVS	1 (3.9%)
DILV, DOLV	1 (3.9%)
Ebstein's, DORV	1 (3.9%)
TGA, Hypoplastic LV	1 (3.9%)
Palliative Stage at Implant	
Stage I	9(34.6%)
Stage II	12(46.1%)
Stage III	5(19.2%)
BiVAD Support	
Stage I	1 (3.9%)
Stage II	1 (3.9%)

Patient Characteristics

Variable	Summary	1-Ventricle (n=26)	2-Ventricle (n=255)	p-value
Age (months)	Median [range]	18.8 [0.2-173.2]	20.6 [0.4 - 239.3]	0.39[1]
Gender	Female	12 (46.2%)	126 (49.4%)	0.75[2]
Weight (kg)	Median [Range]	10.2 [2.8 - 71.0]	10.8 [2.9 - 60.0]	0.24[1]
BSA (m2)	Median [Range]	0.47 [0.19 - 1.75]	0.50 [0.19 - 1.67]	0.23[1]
BSA category	0.19 – 0.70 m^2 0.71 m^2 +	23 (88.5%) 3 (11.5%)	182 (71.4%) 73 (28.6%)	0.06[1]
ECMO pre EXCOR		12 (46.2%)	101 (39.6%)	0.52[2]
Days on ECMO prior to EXCOR	Median [Range]	6.0 [2.0 - 12.0]	6.0 [0.0 - 38.0]	0.53[1]

1. Kruskal-Wallis test 2. Chi-square test

Outcomes and Days of Support

Variable		1-Ventricle (n=26)	2 Ventricle (n=255)	p-value
Successful outcome	Transplant/ Recovery	11 (42.3%)	185 (72.5%)	0.001[1]
	Transplant	11 (42.3%)	179 (70.2%)	
	Recovery	0 (0.0%)	8 (3.1%)	
Treatment Failures	Death on Device	11 (42.3%)	59 (23.1%)	
	Transition to ECMO, Death < 30d	4 (15.4%)	2 (1.2%)	
	Transitioned to ECMO or weaned due to poor prognosis	0 (0.0%)	9 (3.5%)	
Days of Support	Median [Range]	10.5 [0 - 363]	39.0 [0 - 435]	0.01[2]

1. Chi-square test; 2. Kruskal Wallis

Duration of Support by Stage of Palliation

Stage	# patients	Survivors	Days on VAD survivors	Days on VAD non survivors	Days on VAD prior to ECMO	Death on ECMO
Stage I	9	1	57	0,1, 1, 4,10,11,12,17	1*	
Stage II	12	7	5,8,22,52, 59,77,101	1, 270	3,7,7	0,14,30
Stage III	5	3	1,3,229	362,363		

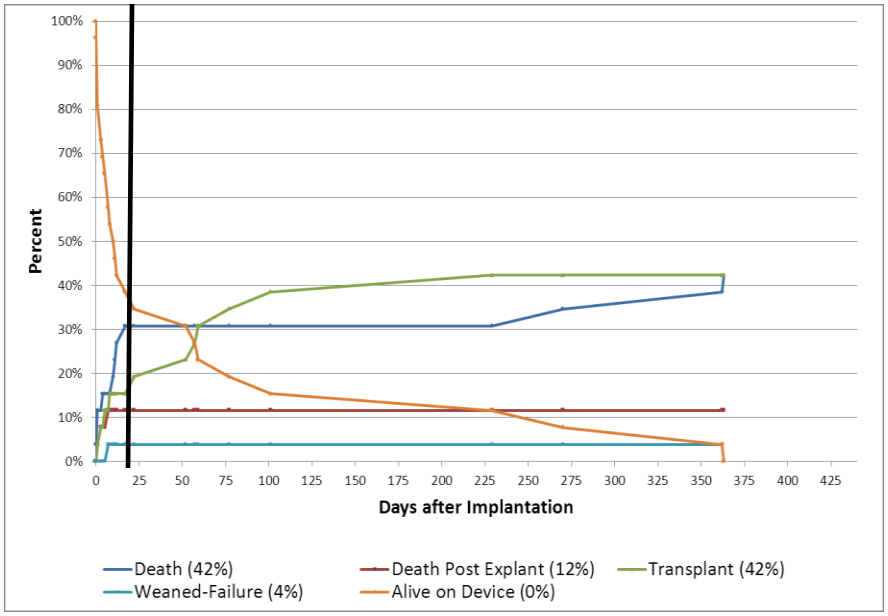
*Transplanted after 8 days of ECMO support

Causes of Death

Stage of Palliation	Causes of Mortality	Secondary Causes of Mortality
Stage I	Pulmonary (3) Cardiovascular: low CO Multi System Organ Failure (2) Circulatory: Hemorrhagic Shock Other	Progressive Hypoxemia Sepsis
Stage II	Multi System Organ Failure (4) Pulmonary	Abd Compartment (1)
Stage III	Multi System Organ Failure Nervous System: Dysfunction	Sepsis

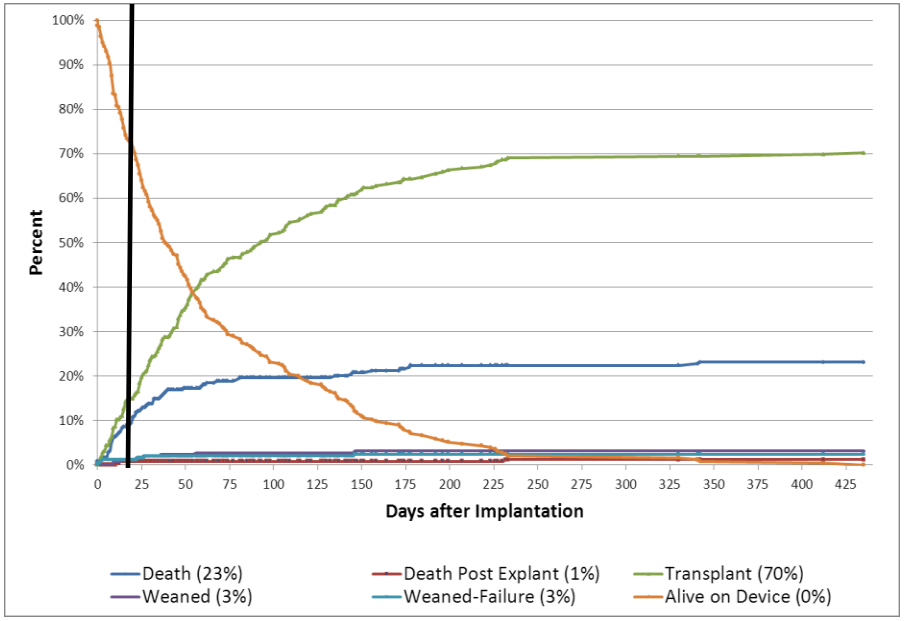
Competing Outcomes

26 Single Ventricle Patients



Days of Support for Survivors
52 days [1-229]

255 Two Ventricle Patients



Days of Support for Survivors
49 days [1 – 435]

Serious Adverse Events

Events occurring while on EXCOR Device Support	1 Ventricle (n=26)		2 Ventricle (n=255)	
	Subject with event (% of 26)	Total Events (Rate per 100 Pt-day)	Subject with event (% of 255)	Total Events (Rate per 100 Pt-day)
Any Serious Adverse Event	19 (73.1%)		211 (82.8%)	
Major Bleeding Event	10 (38.5%)	14 (0.85)	113 (44.3%)	194 (1.15)
Hypertension Event	3 (11.5%)	4 (0.24)	68 (26.7%)	73 (0.43)
Major Infection Event	6 (23.1%)	21 (1.28)	87 (34.1%)	239 (1.42)
Neurological Dysfunction	4 (15.4%)	4 (0.24)	44 (17.3%)	49 (0.29)
Arterial non-CNS thromboembolism	0 (0.0%)	0 (0.00)	7 (2.8%)	7 (0.04)
Venous thromboembolism	0 (0.0%)	0 (0.00)	5 (2.0%)	5 (0.03)
Renal Dysfunction Event-Acute	3 (11.5%)	3 (0.18)	25 (9.8%)	28 (0.17)
Renal Dysfunction Event-Chronic	0 (0.0%)	0 (0.00)	2 (0.8%)	2 (0.01)
Respiratory Failure	11 (42.3%)	15 (0.92)	69 (27.1%)	90 (0.53)
Pump change due to thrombus	7 (26.9%)	21 (1.28)	103 (40.4%)	194 (1.15)

Conclusions

- Patients with SV CHD can be supported with a cardiac mechanical assist device as a bridge to transplantation, though the early results with the EXCOR suggest that success will not be as high as for patients with two ventricles

Conclusions

- Though the initial numbers are small, success following stage II or stage III palliation can be similar to the overall cohort of pediatric patients receiving a VAD

- The EXCOR can allow for long term support of close to one year in patients with partial or total cavo-pulmonary connections

Conclusions

- Currently, outcomes supporting patients following stage I palliation with systemic sources of pulmonary blood flow is dismal, and caution is advised
  - BSA
  - Physiology
  - Age
  - Collateral Flow
  - Technical

Study Limitations

- Small number of patients
- Lack of Randomization
- SAEs not completely adjudicated
- Outcomes for patients who survived to transplant are not collected

Thank you

Ratio of Pump Size to BSA

Variable	1-Ventricle	2-Ventricle	Kruskal-Wallis p-value
All patients	45.4 [26.7 – 67.2] n=26	42.3 [18.9 – 72.9] n=255	0.09
Survivors	52.1 [26.7 – 67.2] n=11	42.9 [23.3 – 73.9] n=185	0.04
Non-Survivors	42.7 [27.5- 61.3] n=15	40.9 [18.9 – 64.0] n=70	0.70

Median [range]

Additional Trends

- Systemic VAD stroke rate and systolic pressure were higher in the SV group when compared to BV patients
  - SR: 85 [65 - 130] vs. 70.0 [40 – 130] p=0.001
  - SP: 200 [160 - 250] vs. 185[100 - 300] p=0.01

- Low BSA is associated with higher mortality in both SV and BV groups, but mortality is higher in SV patients, especially in very small patients [BSA < 0.35 m^2 (75% vs. 46%) p<0.001]