Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Fraser CD Jr, Jaquiss RDB, Rosenthal DN, et al. Prospective trial of a pediatric ventricular assist device. N Engl J Med 2012;367:532-41. DOI: 10.1056/NEJMoa1014164

Prospective Trial of a Pediatric Ventricular Assist Device

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Supplementary Appendix

Table of Contents

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Table S1 – Inclusion and Exclusion Criteria.

Inclusion criteria

- Severe NYHA Functional Class IV (or Ross Functional Class IV for subjects ≤ 6 years) heart failure refractory to optimal medical therapy, and has met at least one of the following criteria:
  a. INTERMACS profile status 1 or 1A, i.e. critical cardiogenic shock
  b. INTERMACS profile status 2 or 2A AND at least one of the following criteria
     i. Decline in renal function as defined by a 50% reduction in estimated GFR despite optimization of subject volume status
     ii. Decline in nutritional status as defined b a sustained (≥7 days) inability to tolerate an enteral nutritional intake sufficient to provide at least 75% of the prescribed caloric needs for the subject, or signs of nutritional compromise despite appropriate intervention
     iii. Decline in mobility/ambulation as defined by sustained bed confinement (≥7 days without prospect for improvement) attributable to heart failure symptoms or its treatment
  c. Support with extra-corporeal membrane oxygenation or other mechanical circulatory support device OR
  d. Unable to separate from cardiopulmonary bypass (must be listed for heart transplant at time of transfer to the operating room)
- Listed for cardiac transplantation
- Two-ventricle circulation, including cardiomyopathy, repaired structural heart disease or acquired heart disease
- Age 0 to 16 years; corrected gestational age ≥ 37 weeks
- Weight ≥ 3 kg and ≤ 60 kg
- Written informed consent

Exclusion criteria

- Support on Extracorporeal membrane oxygenation ≥10 days
- Cardiopulmonary resuscitation duration ≥30 min within 48 hours prior to device implantation
- Presence of a mechanical aortic valve
- Unfavorable or technically challenging cardiac anatomy (including single ventricle physiology, restrictive cardiomyopathy)
- Evidence of intrinsic hepatic disease (total bilirubin level or AST/ALT >5 times the upper limit of normal for age – except in association with acute heart failure as

determined by the principal investigator)

- Evidence of intrinsic renal disease (serum creatinine > 3 times the upper limit of normal for age - except in association with acute heart failure as determined by the principal investigator)
- Hemodialysis or peritoneal dialysis (not including dialysis or Continuous Veno-Venous Hemofiltration for volume removal)
- Evidence of intrinsic pulmonary disease (chronic lung disease, respiratory distress syndrome) as defined by need for chronic mechanical ventilation - except in association with acute heart failure as determined by the principal investigator
- Moderate or severe aortic and/or pulmonary valve insufficiency considered technically challenging to repair at the time of the device implantation as determined by the principal investigator
- Apical ventricular septal defect or other hemodynamically significant lesion considered technically challenging to repair at the time of device implantation as determined by the principal investigator
- Documented heparin induced thrombocytopenia or idiopathic thrombocytopenia or other contraindication to anticoagulant/antiplatelet therapy
- Documented coagulopathy (e.g. Factor VIII deficiency, disseminated intravascular coagulation) or thrombophilic disorder (e.g. Factor V Leiden mutation)
- Hematologic disorder causing fragility of blood cells or hemolysis (e.g. sickle cell disease)
- Active infection within 48 hours of implant demonstrated by a) positive blood culture OR b) temperature >38°C and white cell count >15 000/ml
- Documented human immunodeficiency virus infection or acquired immunodeficiency syndrome
- Evidence of recent or life-limiting malignant disease
- Stroke within past 30 days prior to enrollment, or congenital central venous malformation associated with increased risk of bleeding (e.g. arteriovenous malformation, Moyamoya disease)
- Psychiatric or behavioral disease (e.g. antisocial disorder) with high likelihood for non-compliance
- Currently participating in another investigational device or drug trial and has not completed the required follow-up period for that study
- Subject is pregnant or nursing

Figure S1 – Size Options for the Study Device.

The Berlin Heart Excor Pediatric ventricular assist device pump is available in sizes ranging from 10 mL to 60 mL. Size selection of the pumps and cannulas was based on the size of the patient as detailed in the Manufacturers Instruction for Use.

Figure S2 – 10 mL Pump in Place in a Small Infant.

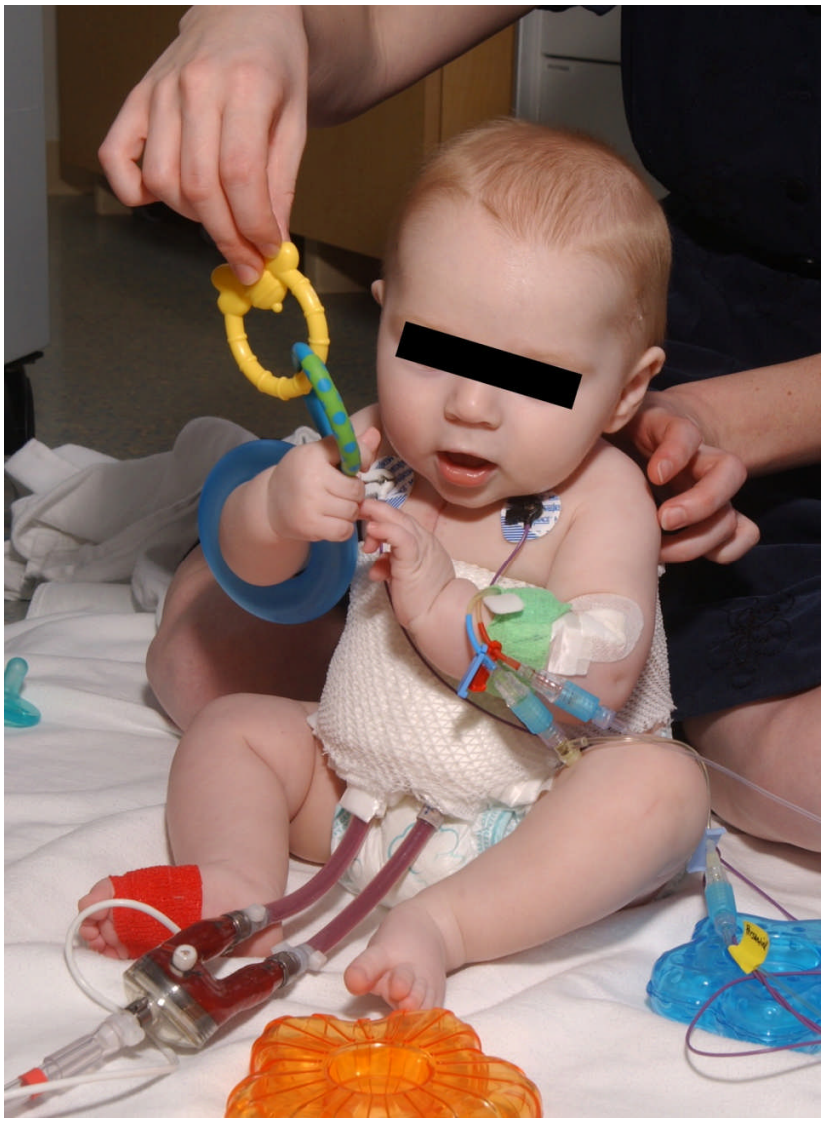
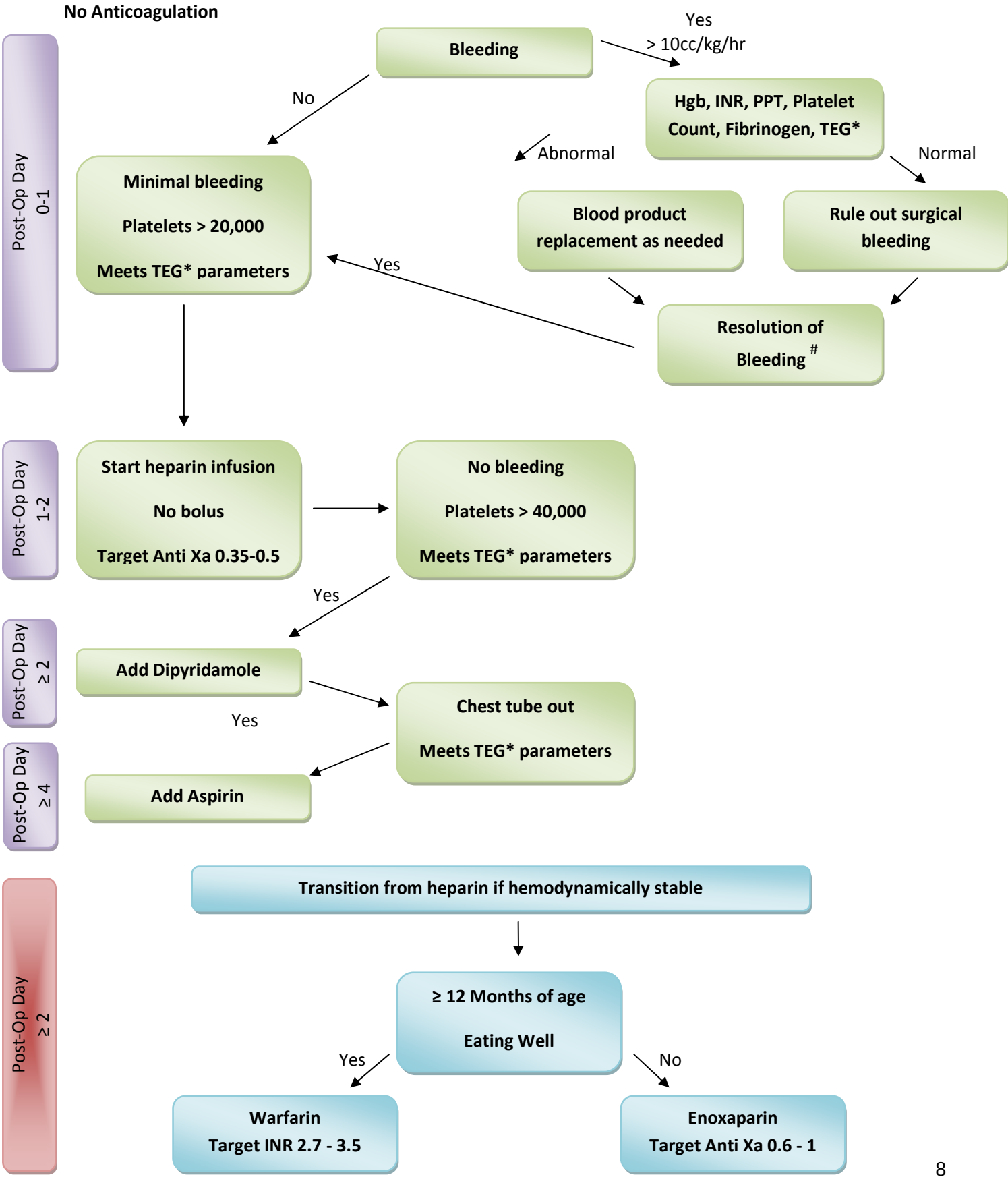


Figure S3 – Postoperative Antithrombotic Therapy Guideline.



* TEG = thromboelastogram

\# Bleeding or clotting issues recurring during therapy are addressed in an individualized manner dependent on etiology and laboratory and clinical parameters.

Selection of the Control Group

A historical group of patients supported by ECMO was selected as a control from the Extracorporeal Life Support Organization (ELSO) registry (Ann Arbor, MI). The ELSO registry is a multicenter, voluntary database that enrolls patients who receive ECMO. It provided a resource for identifying patients who were similar to the study participants, but who had received ECMO support rather than ventricular assist device support.

There are limitations with the ELSO registry. The ELSO registry relies on voluntary reporting and unmonitored data collection. Serious adverse events are not clearly defined nor are the reported adverse events monitored or adjudicated. Outcomes data in the ELSO database are incomplete and limited to mortality with minimal discharge information. Data regarding heart transplantation were not collected until recently, and were not available in the dataset used for the propensity matching.

The control patients were selected based on a pre-specified propensity analysis strategy for matching ELSO patients (control group) to the Excor Pediatric participants (treatment group). A propensity score (PS) analysis was performed by a blinded, independent statistician to match each study participant to two control patients from the ELSO database. The study design consisted of a treatment group, 48 participants who received the Excor Pediatric, and a control group, 96 patients who received extracorporeal membrane oxygenation (ECMO). The propensity matching was performed separately and independently for each of the ventricular assist device cohorts.

A logistic regression analysis was performed for the event “participant received the Excor Pediatric device”. The pre-specified variables for the propensity analysis were age, weight, diagnosis, ventilator status, inotrope use and prior cardiac arrest. Variables were retained in the model regardless of significance level. Based on the logistic analysis, the probability of receiving a ventricular assist device was calculated for each ventricular assist participant and each ECMO patient. The two ECMO patients who most closely matched a ventricular assist device participant based on the predicted probability were chosen to be matches. This sampling method proceeded in a random order of the ventricular assist device participants, and the ECMO patients were selected without replacement.

The details of the propensity matching process were as follows:

1. Obtain patients from the ELSO Registry who met the inclusion criteria of: age between 0 and 16 years, weight greater than 3 kg, ECMO for cardiac support, and ECMO support initiated between 2000 and 2007. Patients with complex congenital diagnosis or trauma were excluded. This resulted in 747 patients.

2. Data management processes removed patients with missing data or inconsistent data. This reduced the ELSO group of patients to 670.

3. Pool of ELSO patients: The pool of 670 ELSO patients to be used in the propensity analyses for each of the cohorts were further refined depending on age.

A. Cohort 1 (small participants): For the cohort 1 matching, the ELSO patients were restricted to those patients who were less than 10 years of age and this resulted in 640 ELSO patients.

B. Cohort 2 (larger participants): For the cohort 2 matching, the ELSO patients were restricted to those patients who were greater than 30 days of age and this resulted in 503 ELSO patients.

4. Perform the propensity analysis using logistic regression.

For cohort 1, the group for the logistic regression included the 24 Excor participants and the 640 ELSO pool patients. The event variable was "participant received an Excor device". The following variables were specified to be included in the regression analysis: age, weight, diagnosis, ventilator status, inotrope use and prior cardiac arrest. All variables were to be included in the model regardless of the statistical significance.

5. Based on the logistic regression model, the predicted probability of receiving the Excor device was calculated for the 24 Excor participants and the 640 ELSO patients. The propensity score was defined to be the predicted probability.

6. The matching process proceeded with the following steps: An Excor participant was chosen at random. The 2 ELSO patients whose probability (propensity score) most closely matched the Excor probability (propensity score) were selected as the 2 controls for the selected Excor participant. This process continued until all 24 Excor participants received 2 matched ELSO patients. Once an ELSO patient was selected as a match, then this ELSO patient was no longer available for subsequent matching.

7. Steps 4 through 6 were repeated for cohort 2.

8. The resultant ELSO controls were statistically comparable to the Excor participants. See Table 2 below.

9. To assess the adequacy of the matching process, the correlation of the predicted probabilities (propensity scores) for the Excor participants and their matched ELSO controls were calculated for each cohort. The correlation coefficient for the matched propensity scores was 0.97 ($p < .0001$) for cohort 1 and was 0.96 ($p<.0001$) for cohort 2.

Table S2 – Results of the Propensity Match.

The comparability of the ELSO controls to the EXCOR participants based on the pre-specified variables in the propensity matching strategy.

	Cohort 1: Comparisons		**Cohort 2: Comparisons**	
	Entire ELSO (p-value)	**Matched ELSO (p-value)**	**Entire ELSO (p-value)**	**Matched ELSO (p-value)**
Age group	0.007	0.21	0.0001	0.001
Weight group	0.07	0.72	0.0001	0.02
Diagnosis group	0.0001	0.32	0.0001	0.51
Ventilator status group	0.80	0.42	0.0001	0.50
Inotrope use group	0.40	0.78	0.84	0.64
Prior cardiac arrest group	0.90	0.99	0.41	0.56

Neurological Assessment and PSOM

A standardized neurological protocol, including imaging and examination using the Pediatric Stroke Outcome Measure (PSOM) [1,2], was used to evaluate the neurological status of study participants. The PSOM is a standardized neurological exam performed by a pediatric neurologist who rates findings in a "Final Summary of Impression" on a scale of 0 (normal) to 10 (maximal deficit). Scores of 0.5-1.0 were considered mild, 1.5 - 2.0 moderate, and $\geq$ 2.5 severe deficits. An unacceptable neurological outcome was defined as presence of a comatose state, or in non-comatose survivors the presence of profound sensory, motor, language or cognitive impairment as measured by PSOM scores on the Final Summary of Impression domains as follows: a score of 3 or 4 (maximal score 4) on Part A (sensory-motor), or a score of 3 or 4 (maximal score 4) in Parts B and C combined (language comprehension and language production), or a score of 2 (maximal score 2) in Part D (Cognitive or behavioral deficit).

Computed tomography (CT) imaging of the brain was performed at baseline, and for evaluation of new neurologic symptoms or deficits. Adverse neurologic events were ascertained through routine assessment of neurologic status by bedside caregivers as part of standard clinical care at all sites. The occurrence of new neurologic symptoms or deficits while on device led to standard clinical neurological consultation and treatment, with completion of a PSOM. The timing of neurologic events was determined based on the dates that symptoms were observed as documented in the clinical records and imaging reports. Post-explant neurological evaluation took place at 30 days or at hospital discharge, whichever was longer.

1. deVeber GA, MacGregor D, Curtis R, Mayank S. Neurologic outcome in survivors of childhood arterial ischemic stroke and sinovenous thrombosis. J Child Neurol 2000;15:316-24.
2. Kitchen L, Friefeld S, Anderson P, Sofranas M, Domi T, DeVeber GA. A validation study of the Pediatric Stroke Outcome Measure. Stroke 2003;34:316 (Abstract #P31).

Table S3 – INTERMACS Adverse Event Definitions.

Adverse event definitions according to INTERMACS version 2.2 standards.

Adverse Event	**Definition**
Major Bleeding	An episode of internal or external bleeding that results in death, the need for re-operation or hospitalization; or necessitates transfusion of red blood cells as follows: Within any 24 hour period: 1. ≥ 4U packed red blood cells (PRBC) within any 24 hour period during the first 7 days post-implant 2. Any transfusion of packed red blood cells (PRBC) after 7 days following implant with the Investigator recording the number of units given. For subjects < 50 kg: 1. ≥ 20cc/kg packed red blood cells (PRBC) within any 24 hour period during the first 7 days post-implant 2. Any transfusion of packed red blood cells (PRBC) after 7 days following implant with the Investigator recording the number of units given. **NOTE:** Hemorrhagic stroke is considered a neurological event and not as a separate bleeding event.
Cardiac Arrhythmias	Any documented arrhythmia that results in clinical compromise (e.g., diminished VAD flow, oliguria, pre-syncope or syncope) that requires hospitalization or occurs during a hospital stay. Cardiac arrhythmias are classified as 1 of 2 types: 1. Sustained ventricular arrhythmia requiring defibrillation or cardioversion. 2. Sustained supraventricular arrhythmia requiring drug treatment or cardioversion.
Pericardial Fluid Collection	Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage. This event will be subdivided into those with clinical signs of tamponade (e.g. increased central venous pressure and decreased cardiac/VAD output) and those without signs of tamponade. **Note:** For those without signs of tamponade, please record the reason for percutaneous drainage.
Device Malfunction	Device malfunction denotes a failure of one or more of the components of the EXCOR® Pediatric system which either directly causes or could potentially induce a state of inadequate circulatory support (low cardiac output state) or death. The manufacturer must confirm device failure. A failure that was iatrogenic or recipient-induced will be classified as an Iatrogenic/Recipient-Induced Failure. Device failure should be classified according to which components fails as follows: 1. Pump failure (blood contacting components of pump and any motor or other pump actuating mechanism that is housed with the blood contacting components). In the special situation of pump thrombosis, thrombus is documented to be present within the device or its conduits that result in or

	could potentially induce circulatory failure. **Note:** Blood pump replacement due to suspected thrombus is not included in this definition. The replacements will be reported separately on the follow-up form. 2. Non-pump failure (e.g., external pneumatic drive unit, electric power supply unit, batteries, controller, interconnect cable, compliance chamber) **Note:** Low cardiac output is defined as a multifaceted syndrome of persistent hypotension, inadequate tissue perfusion, oliguria and rising lactate that is clinically defined by an estimated CI less than 2.0 L/min/m^2 that is persisting for greater than 60 minutes despite optimization of medical therapy.
Early Hemolysis	Early Hemolysis is defined by clinical signs associated with hemolysis (e.g. anemia, low hematocrit, hyperbilirubinemia) occurring within the first 72 hours post-implant. Hemolysis related to documented non-device-related causes (e.g. transfusion or drug) is excluded from this definition.
Hemolysis	A plasma-free hemoglobin value that is greater than 40 mg/dl, in association with clinical signs associated with hemolysis (e.g., anemia, low hematocrit, hyperbilirubinemia) occurring after the first 72 hours post-implant. Hemolysis related to documented non-device-related causes (e.g. transfusion or drug) is excluded from this definition.
Hepatic Dysfunction	An increase in any two of the following hepatic laboratory values – total bilirubin – aspartate aminotransferase/AST – alanine aminotranferease/ALT) to a level greater than three times the upper limit of normal for the hospital, beyond 14 days post-implant (or if hepatic dysfunction is the primary cause of death) .
Hypertension	New onset blood pressure elevation greater than or equal to 140 mm Hg or 90 mm Hg diastolic in subjects under 18 years of age weighing < 50 kg, hypertension is defined as systolic, diastolic, or mean blood pressure greater than the 95th percentile for age which requires the addition of iv or oral drug therapy for management.
Major Infection	A clinical infection accompanied by pain, fever, drainage and/or leukocytosis that is treated by anti-microbial agents (non-prophylactic). A positive culture from the infected site or organ should be present unless strong clinical evidence indicates the need for treatment despite negative cultures. The general categories of infection are listed below: **Localized Non-Device Infection** Infection localized to any organ system or region (e.g. mediastinitis) without evidence of systemic involvement (see sepsis definition), ascertained by standard clinical methods and either associated with evidence of bacterial, viral, fungal or protozoal infection, and/or requiring empirical treatment.

	Percutaneous Site and/or Pocket Infection A positive culture from the skin and/or tissue surrounding the drive line or from the tissue surrounding the external housing of a pump implanted within the body, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis. **Internal Pump Component, Inflow or Outflow Tract Infection** Infection of blood-contacting surfaces of the VAD documented by positive center culture. (There should be a separate data field for paracorporeal pump that describes infection at the percutaneous cannula center, e.g. Thoratec PVAD). **Sepsis** Evidence of systemic involvement by infection, manifested by positive blood cultures and/or hypotension.
Myocardial Infarction	Two categories of myocardial infarction will be identified: **Peri-Operative Myocardial Infarction** The clinical suspicion of myocardial infarction together with CK-MB or Troponin > 10 times the local hospital upper limits of normal, found within 7 days following VAD implant together with ECG findings consistent with acute myocardial infarction. (This definition uses the higher suggested limit for serum markers due to apical coring at the time of VAD placement, and does not use wall motion changes because the apical sewing ring inherently creates new wall motion abnormalities.) **Non-Perioperative Myocardial Infarction** The presence at > 7 days post-implant of two of the following three criteria: a) Chest pain which is characteristic of myocardial ischemia, b) ECG with a pattern or changes consistent with a myocardial infarction, and c) Troponin or CK (measured by standard clinical pathology/laboratory medicine methods) greater than the normal range for the local hospital with positive MB fraction (≥ 3% total CK). This should be accompanied by a new regional LV or RV wall motion abnormality on a myocardial imaging study.

Neurological Dysfunction	Any new, temporary or permanent, focal or global neurological deficit ascertained by a standard neurological examination (administered by a neurologist and documented with appropriate diagnostic tests and consultation note). The examining physician will distinguish between a transient ischemic attack (TIA), which is fully reversible within 24 hours (and without evidence of infarction), and a stroke, which lasts longer than 24 hours (or less than 24 hours if there is evidence of infarction). The neuromotor assessment must be re-administered at 30 and 60 days following the event to document the presence and severity of neurological deficits. Each neurological event must be subcategorized as: 1) Transient Ischemic Attack (acute event that resolves completely within 24 hours with no evidence of infarction) 2) Ischemic or Hemorrhagic Cerebrovascular Accident/CVA (event that persists beyond 24 hours or less than 24 hours associated with infarction on an imaging study. In addition, to above, for subjects < 6 months of age, any of the following: 3) New abnormality of head ultrasound 4) EEG positive for seizure activity with or without clinical seizure
Psychiatric Episode	Disturbance in thinking, emotion or behavior that causes substantial impairment in functioning or marked subjective distress requiring intervention. Intervention is the addition of new psychiatric medication, hospitalization, or referral to a mental health professional for treatment. Suicide is included in this definition.
Renal Dysfunction	Two categories of renal dysfunction will be identified: **Acute Renal Dysfunction** Abnormal kidney function requiring dialysis (including hemofiltration) in subjects who did not require this procedure prior to implant, or a rise in serum creatinine of greater than 3 times baseline or greater than 5 mg/dL (in children, creatinine greater than 3 times upper limit of normal for age) sustained for over 48 hours. **Chronic Renal Dysfunction** An increase in serum creatinine of 2 mg/dl or greater above baseline, or requirement for hemodialysis sustained for at least 90 days.
Respiratory Failure	Impairment of respiratory function requiring reintubation, tracheostomy or (for subjects older than age 5 years) the inability to discontinue ventilatory support within six days (144 hours) post-VAD implant. This excludes intubation for re-operation or temporary intubation for diagnostic or therapeutic procedures.
Right Heart Failure	Symptoms and signs of persistent right ventricular dysfunction [central venous pressure (CVP) > 18 mmHg with a cardiac index <2.0 L/min/m^2 in the absence of elevated left atrial/pulmonary capillary wedge pressure (greater than 18 mmHg), tamponade, ventricular arrhythmias or pneumothorax] requiring either RVAD implantation or inotropic therapy; or requiring inhaled nitric oxide or inotropic therapy for a duration of more than 1 week at any time after LVAD implantation.

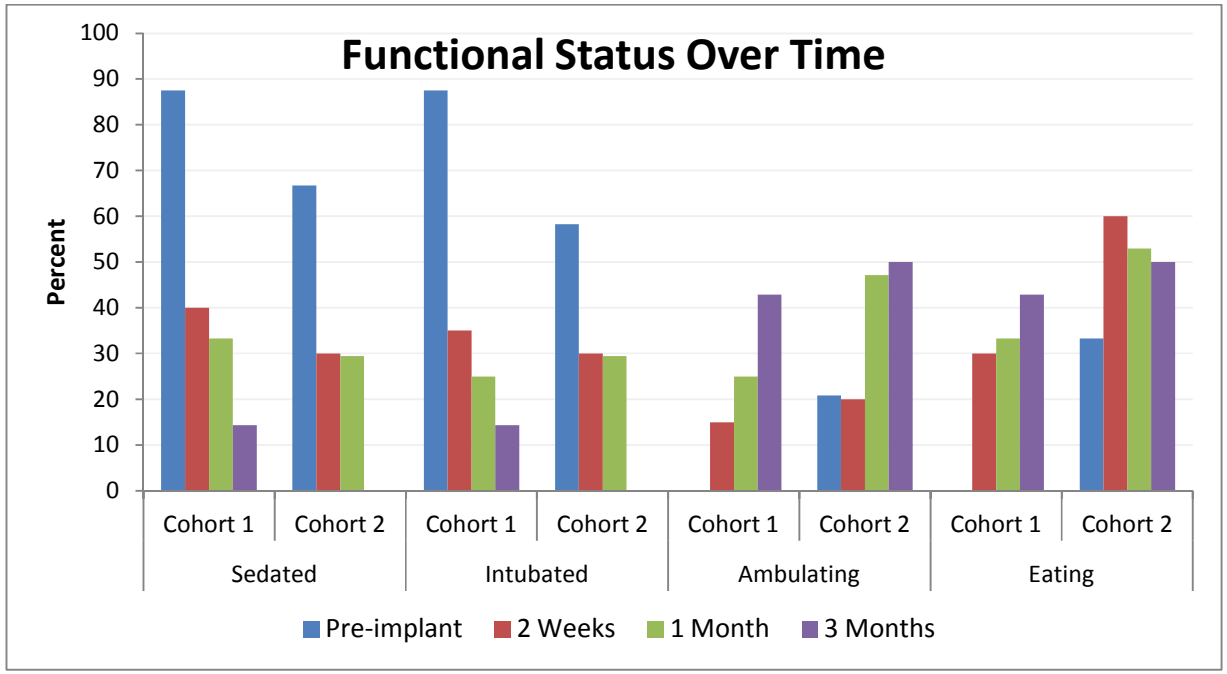
Arterial Non-CNS Thromboembolism	An acute systemic arterial perfusion deficit in any non-cerebrovascular organ system due to thromboembolism confirmed by one or more of the following: 1) Standard clinical and laboratory testing 2) Operative findings 3) Autopsy findings This definition excludes neurological events.
Venous Thromboembolism Event	Evidence of venous thromboembolic event (e.g. deep vein thrombosis, pulmonary embolism) by standard clinical and laboratory testing.
Wound Dehiscence	Disruption of the apposed surfaces of a surgical incision, excluding infectious etiology, and requiring surgical repair.
Other	An event that causes clinically relevant changes in the subject's health (e.g. cancer). In addition to the above, events not classified in the above categories were classified as "other", e.g. global hypoxic injury and CNS/non-CNS thromboembolic event.

Functional Status

Prior to implantation the majority of participants were sedated (87.5% cohort 1, 66.7% cohort 2) and mechanically ventilated (87.5% cohort 1, 58.3% cohort 2) and few were ambulatory (0% cohort 1, 20.8% cohort 2) or able to take nutrition by mouth (0% cohort 1, 33.3% cohort 2). Within two weeks of implantation fewer participants were sedated (40% cohort 1, 30% cohort 2) and mechanically ventilated (35% cohort 1, 30% cohort 2). Increasing proportions of participants were ambulatory (15% cohort 1, 20% cohort 2) and eating (30% cohort 1, 60% cohort 2). Continued improvement occurred over time. For participants requiring support for three months, a further decrease in proportions requiring sedation (14.3% cohort 1, 0% cohort 2) and intubation (14.3% cohort 1, 0% cohort 2), and an increase in proportions of ambulatory participants (42.9% cohort 1, 50% cohort 2) and participants eating (42.9% cohort 1, 50% cohort 2), was observed. None of these changes reached statistical significance, however, when compared to preimplantation status (see Figure 4 below).

Figure S4 – Functional Status Over Time.

Changes in parameters of functional status in Cohort 1 and Cohort 2. Each bar represents the proportion of participants exhibiting each marker of functional status before implantation and 2 weeks, 1 month, and 3 months after implantation in those participants remaining on the device.



Deaths and Adverse Neurologic Outcomes

Two Cohort 1 participants died during support. The first death occurred on the day of implantation secondary to respiratory failure. The second death occurred after multiple ischemic strokes, after 38 days of Excor Pediatric support. One additional participant in Cohort 1 sustained a significant neurologic injury and was weaned from support after 146 days, but remained alive 30 days after explant. This event was classified by the Clinical Events Committee as "other: global hypoxic ischemic brain injury" and not as a stroke. Two Cohort 2 participants died. One death occurred after 19 days of support in a participant who sustained hemorrhagic conversion of a large ischemic stroke. The other death occurred at 144 days in a participant who sustained a fatal multisystem thromboembolic event.

In the total study population, 17 strokes occurred in 14 participants. Of the 14 participants with stroke, 7 were on ECMO or other VAD support prior to implantation of the Excor Pediatric, and two died after being withdrawn from support due to severe neurological injury. One additional participant was temporarily removed from transplant candidacy. PSOM data were available post-explant for all 12 participants (range 17-357 days) experiencing a stroke who survived and for 40 of the 44 (90.9%) survivors in the combined cohorts. Among the 12 participants who survived their stroke, at a median follow-up of 164 days (range 53-449 days) after device implant, the median latest PSOM score was 1.25 (range 0-10, with higher scores indicating greater deficits). Deficits were mild (PSOM 0.5-1.0) in 4, moderate (PSOM 1.5-2.0) in 2, and severe (PSOM > 2.5) in 4 children. No deficits (PSOM 0) were reported in 2 participants. For surviving participants who did not sustain a stroke, at a median follow-up of 69 days (range 7-482 days), the median latest PSOM score was 0.5.

The 14 participants who had a neurological dysfunction event had the following outcomes at last-follow-up, which occurred at a median of 43 days post explant. In cohort 1, 1 participant was normal with no deficit, 3 had mild/moderate deficits, 2 had severe deficits, and 1 child had support withdrawn due to the insult. In cohort 2, 1 participant was normal with no deficit, 3 had mild/moderate deficits, 2 had severe deficits, and 1 child had support withdrawn due to the insult. Therefore, the proportion of participants with severe neurological dysfunction was 12.5% in Cohorts 1 and 2 (see Tables 4, 5, and 6 below).

Fourteen subjects in Cohorts 1 and 2 had neurologic events. Eight of these 14 had 17 pump changes (4 participants > 1). Eight pump changes occurred in five participants before the neurologic event, and 11 pump changes occurred in 5 participants following a neurologic event. There was no identifiable association between pump changes and neurological events. This was screened using both univariate and multivariate models.

Table S4 – Outcome in Participants with Neurologic Dysfunction.

PSOM at last follow-up* post-explant in participants with neurological dysfunction.

Cohort	Normal	Mild/Moderate	Severe/Support withdrawn
Cohort 1	1	3	3
Cohort 2	1	3	3

*Median time to PSOM assessment = 43.5 days post-explant.

Table S5 – Cohort 1 Detailed Neurologic Outcomes.

ID	Neuro Days Post Implant	PSOM At time of event	Highest PSOM Reported	Latest PSOM	PSOM Category	Latest Verbal Report
007-101	20 d	0.5 (7 d)	1.5 (pre)	0.0 (17 post tx)	No Deficit	Doing well from cardiac status 970 days post explant
006-102	15 d	Unable (7 d)	7.0 (5 post tx)	1.0 (221 post tx)	Mild 0.5-1.0	Alive, delayed, speech and OT therapy 1157 days post explant
010-106	60 d	3.0 (31 d)	6.0 (pre)	0.5 (23 post tx)	Mild 0.5-1.0	Doing fabulously, riding horses 571 days post explant
004-101	37 d	4.5 (31 d)	5 (19 d)	1.5 (82 post tx)	Mod 1.5-2.0	Survived 341 days post transplant then expired
004-105	13 d	Unable (13 d)	3.5 (90 d)	3.0 (34 post tx)	Severe > 2.0	Doing well, no focal deficits 630 days post explant
006-105	20 d	Unable (14 d)	10 (20 post tx)	4.0 (54 post tx)	Severe > 2.0	Survived 181 days post transplant then died from sudden cardiac death
008-101	26 d	Unable (8 d)	Unable	N/A	N/A	Withdrawn from support

Table S6 – Cohort 2 Detailed Neurologic Outcomes.

ID	Neuro Days Post Implant	PSOM At time of event	Highest PSOM Reported	Latest PSOM	PSOM Category	Latest Verbal Report
006-101	1 d	Unable (pre)	0.5 (30 d)	0.0 (50 post tx)	No Deficit	Survived 419 days post transplant then expired.
006-104	6 d	0.0 (pre)	6.0 (37 d)	0.5 (49 post tx)	Mild 0.5-1.0	Awake, alert and eating, receives physical, occupational and speech therapy [08/18/08] 49 days post explant
007-107	8 d	Unable (pre)	5.0 (9 d)	1.0 (27 post tx)	Mild 0.5-1.0	Wechsler evaluation average IQ; currently uses left hand to write, increased strength in right hand [04/27/11] 393 days post explant
009-101	14 d	Unable (14 d)	6.0 (80 d)	2.0 (357 post tx)	Mod 1.5-2.0	Overall been well since transplant; residual neurologic abnormalities with hypertonic left leg; cheerful, interactive, and attends school full-time [04/01/11] 947 days post explant
006-111	12 d	Unable (12 d)	10 (29 post tx)	10 (29 post tx)	Severe > 2.0	Multiple residual problems: non verbal with right-sided hemiparesis but responding well to PT; in general very happy and energetic in appearance [12/10/10] 340 days post explant
007-105	30 d	Unable (28 d)	10 (38 post tx)	10 (38 post tx)	Severe > 2.0	12 month post explant, PSOM 4/6/11; severe delay [05/01/11] 386 days post explant
010-107	16 d	3 (16 d)	4.5 (pre)	N/A	N/A	Support withdrawn

Table S7 – Serious Adverse Events during VAD Support

SAE	Cohort 1		Cohort 2	
	# events	# participants with an Event (% of 24)	# events	# participants with an Event (% of 24)
Any SAE	96	22 (91.7%)	107	19 (79.2%)
Major Bleeding	15	10 (41.7%)	22	12 (50.0%)
Infection	35	15 (62.5%)	24	12 (50.0%)
Infection-Localized Non-Device	25	12 (50.0%)	18	10 (41.7%)
Infection-Site or Pocket	4	4 (16.7%)	0	0 (0.0%)
Infection-Sepsis	6	5 (20.8%)	6	6 (25.0%)
Infection-Internal pump	0	0 (0.0%)	0	0 (0.0%)
Neurological Dysfunction Ischemic Hemorrhagic	8 8 0	7 (29.2%)	9 7 2	7 (29.2%)
Hypertension	12	12 (50.0%)	8	8 (33.3%)
Respiratory Failure	3	3 (12.5%)	9	6 (25.0%)
Cardiac Arrhythmia-Sustained VT	1	1 (4.2%)	2	2 (8.3%)
Cardiac Arrhythmia-Sustained SVT	0	0 (0.0%)	4	3 (12.5%)
Pericardial Fluid -W/Tamponade	1	1 (4.2%)	2	2 (8.3%)
Pericardial Fluid -W/out Tamponade	2	2 (8.3%)	2	2 (8.3%)
Renal Dysfunction-Acute	3	2 (8.3%)	2	2 (8.3%)
Right Heart Failure	2	2 (8.3%)	3	3 (12.5%)
Hemolysis-Late	1	1 (4.2%)	1	1 (4.2%)

SAE	Cohort 1		Cohort 2	
	# events	# participants with an Event (% of 24)	# events	# participants with an Event (% of 24)
Hepatic Dysfunction	1	1 (4.2%)	1	1 (4.2%)
Psychiatric Episode	0	0 (0.0%)	1	1 (4.2%)
Renal Dysfunction-Chronic	0	0 (0.0%)	2	2 (8.3%)
Arterial Non-CNS Thromboembolism	1	1 (4.2%)	0	0 (0.0%)
Venous Thromboembolism Event	1	1 (4.2%)	0	0 (0.0%)
Device Malfunction	0	0 (0.0%)	0	0 (0.0%)
Early hemolysis	0	0 (0.0%)	0	0 (0.0%)
Myocardial infarction	0	0 (0.0%)	0	0 (0.0%)
Wound dehiscence	0	0 (0.0%)	0	0 (0.0%)
Other	10	6 (25.0%)	15	6 (25.0%)