Cardiac Transplant in Pediatrics

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I. History of pediatric cardiac transplant:

The history of human attempts at organ transplantation dates to ancient days, with legends of limb or organ transplants for injured army or nation leaders. The scientific basis of organ procurement, preservation and eventually heterotopic or orthotopic transplantation was initiated and advanced through the groundbreaking work of Dr. Alexis Carrel, the 1912 Nobel Laureate. However, the first clinical heart transplant was the landmark achievement of Dr. Christian Barnard in South Africa on December 3rd 1967. The success (though short lived) of this operation triggered a worldwide enthusiasm and explosion of heart transplants. However, this experience was rapidly curbed by the unacceptable early mortality due to rejection. It was not until 1983 with the application of Cyclosporine and other immunosuppressant that heart transplant had a resurgence of interest where it is currently an acceptable and viable option for children and adults with end-stage heart disease.

The accepted indications for listing a child for heart transplant are an expected survival of less than a year, and significant limitation of activity. Patients are listed as Status 1A, B and II depending on the level of decompensation, in-hospital status and mechanical circulatory support.

II. Demographics of the pediatric heart transplant candidate:

Heart failure in children is a growing medical problem. This is due to the improving survival of patients with congenital heart disease, as well as to growing awareness of cardiomyopathy in children. Heart failure represented over 15,000 hospitalizations in children in 2006, a 25% increase compared to just 5 years earlier. The International Registry of Pediatric Heart Transplant report in 2009 recorded over 450 transplants in 2009, with 27% < 1 year, 35% 1-10 years and 43% 11-17 years old. The most common indication changes with age (CHD in < year, Cardiomyopathy in older children).

Cardiomyopathy can be dialated (DCM), restrictive (RCM) or hypertrophic (HOCM), with special physiologic characteristics to each type. The most common CHD leading to heart failure that requires transplantation are lesions with a single ventricular physiology.

III. Limitations of pediatric heart transplant:

The survival of children on the heart transplant waiting list is a significant issue resulting in a 14% 30 day mortality. This is compounded with the difficulty in identifying appropriate donors, obtaining consent and adequate national allocation
of organs. The most important medical and ethical objective is the appropriate
determination of brain death in a donor. Exclusion and correction of conditions that
confound the diagnosis of brain death (electrolyte abnormalities, intoxication,
hypothermia, and drugs) are essential. No recent doses of sedative hypnotics or
neuromuscular blockers should be delivered to the potential donor. Neurologic
exam should aim at determining three principal findings or criteria of brain death:
coma, apnea and absence of brain stem reflexes. Confirmatory tests can include an
EEG, radionuclide scans, intracranial pressure monitors and cerebral angiograms.

IV. Management goals:

In the pre-transplant period the recipient has significant peripheral vasoconstriction
and peripheral hypoperfusion with possible end organ failure. They have down-
regulation of B-receptors and a blunted response to inotropes. Rapid sequence
induction and full-stomach precautions should be considered even in patients who
have been fasting, due to significant slowing of gastric emptying. The pulmonary
vascular resistance is elevated in most patients, and studies to identify the reactivity
of the pulmonary vascular bed to O2, nitrates and iNO should be reviewed.
The management strategy will vary according to the underlying heart failure
etiology (single ventricle, DCM, RCM) with different goals in heart rate, systemic
and pulmonary vascular resistance and filling volumes.
The survival of children following heart transplant is 85% in the first year, 75% in 5
years and 65% in 10 years. The survival varies with age at transplant with the
average conditional survival of 15 years for teenagers and nearly 19 years for those
transplanted between 1-10 years.
The most important determinants for survival are pre-transplant degree of support,
renal function, recipient/donor ration and gender match, ischemic transplant (>4
hours) of the donor organ and pulmonary vascular resistance in the donor and
recipient.
Transplant morbidity is mostly related to immunosuppressive regimens, acute and
chronic rejection episodes (>36%), allograft coronary vasculopathy (34% within 5
years) and lymphoproliferative disease.
Heart transplant is not a cure for heart disease in children but an attempt at
providing a better quality of life and a more manageable medical condition with
known demands and complications.

V. Alternatives:

The future of heart failure management in children is dependent on advances and
alternatives to cardiac transplantation. Better donor recruitment, allocation and
shorter ischemic times may improve the outcomes. Advances in
immunosuppression, early rejection diagnosis and therapy, and healthier life-styles
of recipients will improve the results. The use of ABO-incompatible organs for
transplant especially in neonates and infants will broaden the donor pool. However,
the more important advances are the breakthroughs in assist device technology,
with the goal of a total implantable long-term artificial heart, bio-engineering of
new hearts through stem-cell biology and the possibility of xenotransplants. The
dream of organ replacement is a long way from complete fulfillment.
VI. References: