

EDITOR'S NOTE



Dr. Manoj Durairaj

Heart Transplant Surgeon, MS,MCh. (AIIMS, New Delhi), FACC. Director, Marian Cardiac Centre and Research Foundation. Program Director, Department of Heart and Lung Transplantation, Sahyadri Hospitals, Pune.

Dear Colleagues,

Greetings. This is the second issue of The Revival – The Newsletter of the Society for Heart Failure and Transplantation. This issue delves into the finer nuances of Paediatric Heart Transplantation by Dr Ganapathy Subramaniam, an accomplished paediatric heart transplant surgeon. He has shared very lucidly his experience in this exciting field and I'm sure the readers will be enlightened by his brilliant article.

Some tips which I would like to share regarding this topic is that all paediatric patients undergoing transplant should have a CT angiogram to delineate any anatomical anomalies like left superior vena cava and interruption of the Inferior vena cava and abnormal connections. CT angiogram also helps in measuring the diameters of the vessels which need to be anastomosed. This helps to plan for any disparity in size between the donor and the recipient. 2 D echo measurement of the recipient heart size is also imperative so as to match the donor heart size. The length of the heart (Roof of Left Atrium

to LV apex), transverse diameter (diameter of the heart at the level of tricuspid and mitral valves) and the antero-posterior diameter should be noted. Sometimes a donor is available who is maybe twice the age of the recipient but with the exact heart size matching. These measurements will help in going ahead with paediatric transplantation with adequate size matching. Extra donor tissue like pericardium, arch and descending thoracic aorta can also be harvested, just in case there may be a requirement of fashioning new connections.

I would like to thank Dr V Nandakumar, President, Dr Jabir Abdullakutty, Secretary, Dr Talha Meera, Sub Editor and the Executive Committee of the Sfhft for their enthusiastic support for The Revival.

- Dr. Manoj Durairaj
Editor "The Revival"

SUB EDITOR



Dr. Talha Meeran

MBBS, MD, FACC, Consultant Cardiologist, Dept of Advanced Cardiac Sciences and Cardiac Transplant, Sir HN Reliance Foundation Hospital, Mumbai.

Dear Colleagues,

I am again thrilled to be part of the editorial team of this second issue of the "Revival". This issue contains an excellent commentary by Dr Ganapathy detailing the surgical challenges in the field of pediatric cardiac transplant and pediatric mechanical circulatory support. Dr Ganapathy discusses the unique challenges facing pediatric cardiac transplant right from the shortage of donors, pre-transplant immunological workup, donor harvesting techniques to post transplant complications. I am sure all readers will learn something new after reading this issue.

Sincerely,
Dr. Talha Meeran
Sub Editor "The Revival"

PRESIDENTIAL MESSAGE



Prof. (Dr) V. Nandakumar

Director & Chief, Division of Cardio Vascular/ Thoracic Surgery & Cardiac Transplantation, Metromed International Cardiac Centre, Calicut, Kerala.

Dear Colleagues,

Greetings from the Society for Heart Failure and Transplantation.

We are bringing out the second issue of our news letter. In this edition, emphasis is given to the challenges in Paediatric Heart Transplantation for congenital heart disease. When heart transplantation is

done for complex congenital heart disease, it is technically demanding. Various aspects of paediatric heart transplantation with technical details of its complexity are dealt with in this article. I am sure this will give you a lot of information on this topic. Your valuable comments and suggestions will be greatly appreciated .

Thanks to the great efforts by Dr Manoj and Dr Talha Meeran in bringing out this edition on time.

- Prof. (Dr) V. Nandakumar
President

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Special thanks to
Dr K Ganapathy Subramaniam for
authoring this month's article.

Designed by Maithili Kulkarni

SECRETARY'S NOTE

SFHFT ACTIVITIES MARCH 2021



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FRCP Senior Consultant
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It's a great pleasure to see the second edition of THE REVIVAL, the newsletter of the Society for Heart Failure and Transplantation. I take this opportunity to appreciate the tremendous efforts taken by our Editor Dr. Manoj Durairaj and sub-editor Dr. Talha Meeran in publishing this newsletter with suitable scientific content on time.

It's the duty of all working in Heart failure to Stem the Tide of Heart Failure, which has a high mortality, morbidity, and is the cause for a poor quality

of life for the affected patients. There has been tremendous progress in understanding the optimal treatment of heart failure with reduced ejection fraction garnered from well-designed randomized controlled trials over the last three decades. Accumulation of evidence alone is not sufficient to translate this to clinical practice. This requires extraordinary effort on implementation strategies to provide the patients with the best evidence-based therapies.

SfHFT has started a series of webinars to disseminate knowledge regarding the state of the art medical therapy in Heart failure titled **"TO STEM THE TIDE"**. The first webinar took place on 5th March with Dr. Scott D Solomon as the speaker on the topic **NEW PARADIGMS OF HF-ARE SGLT2 INHIBITORS OPENING NEW DOORS**. There was a panel discussion on SGLT2 inhibitors in HF - Challenge in translating evidence to practice. The national faculty included Dr. V K Chopra, Dr. P S Banerjee, Dr. Ambuj Roy, Dr. V K Ajithkumar, Dr. S S S Iyengar, and Dr. P B Jayagopal, Dr. Abraham Oommen, Dr. Amit Malavya. And Dr. P V Girish. The meeting was well attended.

We are planning to bring in a series of webinars to promote the best therapy in Heart failure, and I request all to make this programme a success. Our motto is to promote **"RIGHT DRUG FOR RIGHT PATIENT AT RIGHT TIME FOR THE BEST OUTCOME" IN Heart Failure.**

- Dr. Jabir Abdullakutty,
Secretary

Society for Heart Failure and Transplantation
Webinar Series 1

TO STEM THE TIDE

Topic ————

NEW PARADIGMS OF HF - ARE SGLT 2 INHIBITORS OPENING NEW DOORS

📅 5th March 2021 ⌚ 7:30 -9:00 PM IST

International Speaker ————

Prof Scott D Solomon
Director, Non Invasive Cardiology Brigham and Women's Hospital Department of Medicine, Boston

Chairpersons

Dr Ambuj Roy Dr Ajit Kumar V K

Panellists

Dr Abraham Oommen Dr Amit Malviya

Panel Discussion on **SGLT 2 inhibitors challenges in translating evidence to practice**

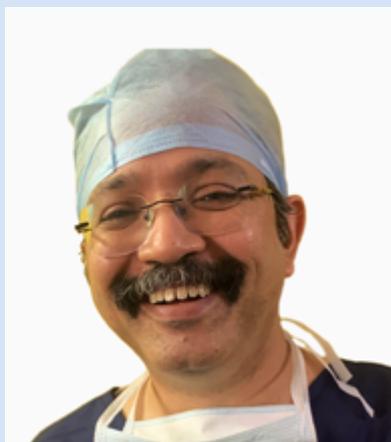
👉 [Click here to Join Video Meeting](#)

Dr V Nandakumar President Dr Jabir A Secretary Dr Girish P V Organising Secretary

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HEART FAILURE AND HEART TRANSPLANTATION IN CHILDREN AND FOR CONGENITAL HEART DISEASE: CURRENT SCENARIO



Dr K Ganapathy Subramaniam

Dr K. Ganapathy Subramaniam is senior consultant cardiac surgeon at MGM Healthcare and visiting consultant at Institute of Child Health, Egmore. He finished his M.Ch (Cardiac Surgery) at AIIMS (New Delhi) and Pediatric Cardiac Training at Dr. K. M. Cherian unit at Frontier Lifeline and Sydney, Australia. He looks after the Pediatric and Congenital heart disease program at MGM Healthcare, and is a part of the Heart and Lung transplant Unit at MGM Healthcare under the leadership of Dr K.R. Balakrishnan.

His areas of interest include complex congenital and neonatal cardiac surgeries. Heart transplantation. Lung transplantation in Pediatric patients and in patients with Congenital heart disease and Mechanical Circulatory support

He has played an active role in setting and helping transplant programs across the country and was involved in the developing transplant program in Pune, Kolkata,

Bangalore. Hyderabad, Jaipur and Vijaywada. He works along with Aishwarya Trust to make Pediatric Cardiac Surgery accessible to underprivileged people.

History and Prevalence

Heart transplantation is an accepted modality of treatment for children with heart failure refractory to medical therapy. The first Pediatric transplant for an Ebstein's anomaly was attempted by Adrian Kantrowitz in 1967 on Dec 6 (within 3 days of the first heart transplant) and the child survived for 6.5 hrs. In 1984, Leonard Bailey and his team at Loma Linda did the first Xenotransplantation in much publicized Baby Fae. She received a baboon heart for Hypoplastic Left heart syndrome and survived for 18 days.

According to registry of International society for Heart and Lung Transplantation, pediatric cardiac transplants represent about 10-15% of total transplants performed world wide which range between 500-700 procedures.

Indications

The indications vary according to the age. In infants, it is congenital heart disease which cannot be palliated surgically. This includes, Hypoplastic Left Heart Syndrome with severe ventricular dysfunction or tricuspid regurgitation, severe form of Ebstein's anomaly and congenital cardiomyopathy. In older children dilated and various forms of cardiomyopathy form the common indication. In an older age group, an increasing number of heart failure children, are the ones with previous palliation, especially those with a failing Fontan circulation. The youngest child in our series of 102 transplants was 12 months old. Dilated and restrictive cardiomyopathy form close to 75% of the indication for transplantation. Congenital heart disease form 11% (12/102) of the patients and majority are patients with single ventricle physiology.

Selection and Timing of Surgery

Selection of patients and timing of transplantation is crucial, but what is even more important is the selection of the donor. Worsening activity levels not improving with medical therapy, feed intolerance, recurrent admissions for heart failure symptoms with need for inotropes for stabilization and increasing Brain Natriuretic Peptide (BNP) levels (which are usually increased more than 10 times the recommended upper normal limit at the time of transplantation) can be used for deciding about timing for transplantation. Worsening abdominal pain due to hepatic congestion is a common complaint in pediatric population.

In failing single ventricle physiology patients – worsening cyanosis, protein losing enteropathy (PLE) and single ventricle dysfunction with worsening arrhythmias and valve regurgitation are indications. The failing single ventricle palliation with normal ventricular function is a high risk subset due to our lacunae in understanding of the altered circulatory and lymphatic physiology. Fortunately, all patients with PLE respond to transplantation with normalization in 3-4 weeks.

An early Fontan failure (<6 months) is a particularly high risk subset and these patients are better managed by taking down the Fontan to a Glenn stage and then transplanting them. The best subsets for transplantation are the single ventricle physiology patients with protected pulmonary circulation with ventricular dysfunction with no previous palliation. The patients with single ventricle and ventricular dysfunction tend to perform better following transplantation than those with normal ventricular function at least in the short term. The problem of sensitization due to: previous surgeries (redo sternotomy), transfusion, homograft use and difficulties in hemodynamic evaluation of pulmonary vascular resistance (PVR) are other challenges in this subgroup.

Evaluation of the Donor

Evaluation of potential donor is done usually with the help of transthoracic echocardiography. While blood group matched donor is necessary for older children, ABO incompatible cardiac transplants with results comparable to blood group matched donors are possible in neonatal and infant population. In presensitized individuals with high Panel Reactive Antibody levels, a negative Complement



Dependent Cytotoxicity (CDC) cross match is preferred prior to transplantation. The use of older and heavier donors, whose heart can fit into the pericardial cavity of the recipient is frequently used. This is not always a disadvantage as these hearts can pump against the higher pulmonary vascular resistance compared to age and weight matched donors. Cutting down on the pericardium on the left side and opening the pleura widely, leaving the

chest open till the donor heart adapts and leaving a small atrial communication are other maneuvers which can be used while using oversized donors. Custodiol (HTK) cardioplegia is used routinely and the median cold ischemic time is 200 minutes and the maximum is 330 min with good outcome in our experience.

While assessing the donor left ventricular function is easy, what we need is to identify if the donor right ventricle heart can pump against the increased pulmonary resistance of the recipient. A conductance catheter which can generate pressure volume loops of the donor can help decide the suitability of the heart particularly in patients with borderline elevated PVR. This is a study in progress.

A particular problem with the use of oversized hearts in pediatric population is the 'Big heart Syndrome'- they can present with hypertension, poor sensorium, seizures, cortical blindness and other neurological symptoms, which requires aggressive control of blood pressure in the postoperative period to prevent neurological morbidity. With preemptive management of increasing blood pressure in the immediate postoperative period, this syndrome has become uncommon of late.

Preoperative Stabilization

Preoperative stabilization of the recipient is paramount. Mechanical circulatory support (MCS) should be considered if there is end organ dysfunction setting in not responding to inotropes. Waiting time death rate, before the organ is available after listing for transplantation, is between 15-30 % and efforts should be made to reduce this using priority allocation and use of MCS.

Extracorporeal membrane oxygenation is the most easily available temporary mechanical support in our setting. ECMO can be converted to ventricular assist device without the oxygenator using extracorporeal centrifugal pumps. We have bridged 10 of our patients with MCS with 70 % 5 year survival rate. The results in patients whose end organs are functioning normally with decreased pulmonary resistance are understandably better, though bleeding and sepsis could be of concern. Long term pumps though available for use in grown up children are prohibitively expensive for most of our population. We have experience with HVAD (Medtronic, Minneapolis) and Berlin Excor and have used Virtual Reality and 3-D printing to size and site the inflow cannula prior to surgical implantation.

Technical Aspects of Pediatric Heart Transplantation

The technical aspects of transplantation need close attention. Gentle handling of the donor heart, preventing distension are as important as the implantation of the organ. Extended donor organ harvest including the arch, branch pulmonary arteries, innominate vein and donor pericardium may be needed depending on the anatomic needs of the recipient. While explanting the recipient heart, the dictum is to stay close to the myocardium. Leaving a large cuff of recipient tissue can help manage systemic venous anomalies. An orienting suture on the anterior most aspect of the donor and recipient heart can help avoid twisting of the anastomosis. It should be ensured that there is enough adventitia on the recipient and donor aorta particularly in the area between the aorta and the pulmonary artery. Bleeding can be troublesome, if suturing is done only to the media devoid of adventitia of either the aorta or the PA. Discrepancies in size and abnormal relationship of the great vessels can be overcome by careful suturing and having extra length of great vessels. The dictum is to keep the PA as short as possible and leave the aorta long. We usually measure the PA and Left atrial pressure on the table before going on bypass of the recipient. If the transpulmonary gradient (Mean PA pressure – LA pressure) is high (> 12 mmHg) a small atrial communication is left in the donor heart to help in the management of posttransplant RV dysfunction.

Fontan patients have a condition which is opposite to a typical patient with cardiomyopathy. They have smaller hearts, large and dilated aortas and small and thin walled pulmonary arteries and left atrial wall, which is contrary to what happens in a typical dilated cardiomyopathy patient. Oversizing in Fontan patients has been done extreme cautiously as the pericardial cavity is usually small and cutting down on the pericardium and pleura may not be possible because of adhesions. Handling stented pulmonary arteries, multiple redo surgeries and bleeding can make this subset extremely challenging.

Immunosuppression and Posttransplant surveillance

Immunosuppression is by using induction with Basiliximab

(12mg/m²) 30 min before initiation of cardiopulmonary bypass along with Inj. Methylprednisolone (20 mg/kg) given at the time of initiation of CPB and during aortic cross clamp release. Maintenance therapy is with Tacrolimus started on 2nd postoperative day at a dose of 0.5- 1mg(0.05 – 0.3mg/kg depending on tacrolimus metabolizer status) aiming for a trough level of 8-12ng/ml, mycophenolate mofetil (10-20mg/kg/dose twice daily and Prednisone, which is tapered and stopped by 6 months.

Endomyocardial biopsies (EMB) for rejection surveillance is done prior to discharge and once yearly in our unit as recommended protocol biopsies by western centres, are not possible due to financial and logistic reasons. Any drop in ventricular function or new onset valve regurgitation should be aggressively investigated and anti-rejection measures initiated. Donor derived cell free DNA can be used to perform liquid biopsy and limit the number of EMB in the future.

Outcomes

The outcomes of pediatric transplantation in our unit are comparable to the survival reported in literature with 89% 90 day survival and 5 year survival of 73%. Severely elevated Right atrial pressure (> 18mm Hg), presence of ascites, elevated creatinine (>1.5mg/dl), lower INTERMACS category

(very sick patients), presence of Pulmonary artery stenting were risk factors for mortality. The duration of cold ischemia and Preoperative PVR did not have effect on short or long term survival.

Early mortality in our experience is mostly due to right ventricular dysfunction and sepsis. A falling urine output, increasing central venous pressures, falling pulmonary artery pressures and worsening liver function are indicators of RV dysfunction, can be initially managed with inotropes, inhaled Nitric Oxide, but may necessitate institution of ECMO to support failing RV. Long term mortality may be due to infection, unrecognized rejection or graft vasculopathy.

Summary

The children with successful outcomes have very good quality of life and demonstrate rapid catchup growth. The renewed zeal towards life which the children show after successful transplantation needs to be seen to be believed. More awareness needs to be created about organ donation in pediatric hospitals and patients need to be referred reasonably early. Pediatric heart failure and its comprehensive management including patients with previously operated congenital heart disease requires dedicated specialized team and our country has the talent and skill to provide it.

SALIENT POINTS:

1. Pediatric Cardiac Transplantation is a proven modality for managing endstage heart failure and for managing Congenital heart disease where further palliation is not possible.
2. There is a need to increase awareness regarding pediatric organ donation and to refer early for consideration of transplantation.
3. ABO incompatible transplants are possible in neonates and infants with comparable outcomes.
4. An affordable durable mechanical circulatory support for pediatric population is the need of the hour.
5. Oversized hearts can be safely used for pediatric population.
6. Failing Single Ventricle physiology are particularly challenging subsets where liver and renal dysfunction and sensitization can adversely influence outcomes.
7. PLE resolves following heart transplantation.
8. Panel reactive antibody levels, Endomyocardial biopsies, immunosuppression should be tailored to our needs.
9. Good early outcomes and acceptable mid term outcomes are possible even in our set up.
10. Xenotransplantation, Immune tolerance, Donation after circulatory death, Organ care and transport systems , increasing number of adults with single ventricle physiology will make Cardiac Transplantation for pediatric and congenital heart disease an exiting area of study.

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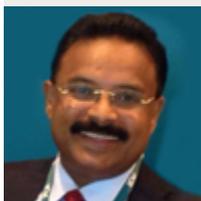


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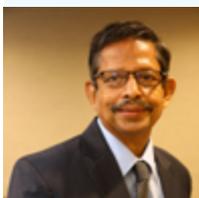
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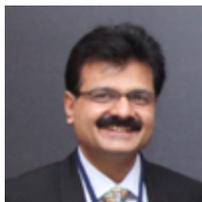
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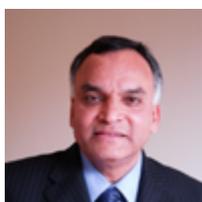
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