Society for Heart Failure and Transplantation

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EDITOR'S NOTE

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Greetings dear Readers of The Revival,

This issue on Heart Transplant in Congenital Heart Disease – Who and When - by our guest author Dr Swati Garekar carries an important message – "Timely Referral for Heart Transplant". There is a Golden Window of Referral which avoids the innate risks of permanent end organ dysfunction. Dr Garekar has emphasised that a patient with CHD (Repaired, palliated or unrepaired) with Heart Failure should be referred to the Heart Failure team when they reach early Stage C. A Stage D referral will be too late. Dr Swati goes on to enumerate the indications and the favourable outcomes of transplants in this subset. Dr Julius Punnen, President, Society for Heart Failure and Transplantation, in his note has highlighted the essential role of a multidisciplinary team of cardiologists, congenital heart surgeons, transplant physicians and mental health professionals in providing comprehensive care for patients with CHD and Heart Failure.

I thank our Guest Author for this informative article and wish you dear Readers, Happy Reading!!!

Dr Manoj Durairaj
Editor "The Revival"

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Dr Talha Meeran

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Dear Colleagues,

This edition of REVIVAL features an excellent summary of the indications of cardiac transplant in congenital heart defects by Dr Swati Garekar. Dr Swati had previously written about post-transplant care of pediatric cardiac transplant recipients. This article serves as a good follow-up to the first one wherein she has described each group of congenital heart defects which can possibly lead to transplant. Of particular note are the Eisenmenger's syndrome patients which are extremely common in our daily clinical practice. The enlisted clinical findings and echo findings for Eisenmenger's are a useful guide to guide timing for transplant referral.

Sincerely,
Dr Talha Meeran
Sub Editor "The Revival"

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Special thanks to Dr Swati Garekar for authoring this month's article.

Designed by Maithili Kulkarni

PRESIDENTIAL MESSAGE

Dr Julius Punnen

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Dear Members and Colleagues,

In this issue of The Revival, Dr Swati Garekar has addressed a very important topic, and today, we focus our attention on those who face the unique challenges presented by congenital heart conditions. In adults, the indications and timing for referral, listing and choosing the type of transplant needed is straightforward, but in children these decisions are not so easy particularly when the heart and/or lung function seem preserved. In our country there is a shortage of trained heart failure cardiologists and when it comes to paediatric heart failure the shortage is even more pronounced. Dr Garekar also brings out an important aspect of the definition of Stage D heart failure, where other therapy no longer works in stage C and they need to have heart transplantation or MCS and therefore the importance of early referral to a heart failure specialist team. This would be applicable to both paediatric and adult patients.

Congenital heart disease is a complex group of conditions that affect the structure and function of the heart since birth. While advances in medical and corrective / palliative surgical treatment have significantly improved the quality of life for many with congenital heart disease, there comes a point for some where heart transplantation becomes a life-saving option. The question we often face is, "Who should receive a heart transplant, and when is the right time?"

The decision to pursue heart transplantation in individuals with congenital heart disease is a delicate balance of medical expertise, ethical considerations, and the patient's unique circumstances. Several key factors come into play:

1. Severity of Congenital Heart Disease: The degree of complexity and severity of the congenital heart condition is a crucial determinant. For some patients, successful surgical interventions can provide a long and fulfilling life. However, for those with advanced heart failure despite medical and surgical therapies, transplantation may be the only viable option.

2. Functional Status: Evaluating the patient's functional status and quality of life is vital. Patients who struggle with day-to-day activities, experience severe symptoms, or have frequent hospitalizations due to their congenital heart disease may benefit from transplantation to regain a better quality of life.

3. Timing: The timing of transplantation is another critical consideration. Waiting too long can lead to irreversible organ damage, making transplantation less effective. On the other hand, performing the transplant too early may subject the patient to unnecessary risks.

4. Ethical and Psychological Factors: It is essential to involve patients and their families in the decision-making process. Ethical discussions should revolve around the allocation of scarce donor organs, the patient's understanding of the procedure, and their willingness to commit to the lifelong care required post-transplant.

5. Multidisciplinary Care: Complex cases of congenital heart disease require a multidisciplinary team of experts, including cardiologists, congenital heart surgeons, transplant physicians, and mental health professionals, to provide comprehensive care and support.

In conclusion, heart transplantation in congenital heart disease is a multifaceted issue that demands careful consideration. As we continue our journey to advance the field of heart transplantation, it is our responsibility to ensure that those with congenital heart disease receive the best care possible. We must prioritize collaboration, research, and education to refine our understanding of when and for whom transplantation is most beneficial.

With warm regards,

Dr Julius Punnen

President, Society for Heart Failure and Transplantation

HEART TRANSPLANTS IN CONGENITAL HEART DEFECTS: WHO AND WHEN?

ABOUT THE AUTHOR

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Dr Swati Garekar is a pediatric cardiologist practising at Fortis hospital, Mulund, Mumbai.
She completed her MBBS from Seth GS Medical college and KEM Hospital, Mumbai after which she did her MD pediatrics at the Children's Hospital of Michigan, Detroit. She went on to complete her 3 year pediatric cardiac fellowship at the same institution. She is interested in echocardiography, fetal echo, 3D printing of hearts, and heart failure/transplants.

Introduction

Care of patients with congenital heart defects (CHD) is getting better by the year. From the simplest to the most complex, there is a specific reparative or a palliative intervention available for all. And for those where disease specific intervention is not a good option or has failed, our speciality can now offer heart/ heart-lung/ heart-liver transplantation. The ISHLT data shows that the outcomes of heart transplantation for CHD are as good or better in adult recipients conditional to survival upto 60days. In the pediatric age group, the outcomes are slightly better in recipients with a primary diagnosis of cardiomyopathy versus those with CHD.

This writeup is a summary which patients with a CHD get a heart transplant and when is the best time to get it as per the current literature.

It is worthwhile noting that heart failure secondary to CHD (repaired, palliated or unrepaired) usually presents in adulthood. The American college of Cardiology/American heart association has classified stage C of heart failure as where patients are significantly symptomatic. Stage D of heart failure is where drug (or surgical/device intervention) therapy no longer helps for stage C patients and is associated with a 6 fold increase in mortality. Stage D heart failure is certainly an indication for heart transplant or MCS. But patients with CHD need to be referred to the heart failure team when they reach early Stage C; stage D referral may be too late. Patients with CHD tend to have higher sensitization to HLA antigens, complex anatomies and low tolerance to marginal donor hearts; hence the waiting time on the list is longer.

Patients with CHD who need a heart transplant

1. Fontan failure or Glenn failure
2. Systemic ventricle being a right ventricle and failing
3. Tetralogy of Fallot (certain situations)
4. Certain subtypes of Hypoplastic left heart syndrome (HLHS); hypoplastic right heart syndrome, Ebstein's anomaly, Shone complex
5. Eisenmenger syndrome (with lung transplant)

Fontan Failure

The Fontan palliative surgery is a staged 2 step palliation for hearts where biventricular repair is not an option. At the end of the final (Fontan) step, the vena cavae are diverted and flow passively to the pulmonary arteries while the ventricle receives pulmonary venous blood (and coronary sinus), pumping it out to

the aorta. The anatomies include uni-ventricles, tricuspid atresia, HLHS, complex double outlet right ventricle (DORV), unbalanced AV canal defects and complex ccTGA. In patients with too less of pulmonary or systemic blood flow or too much of pulmonary flow, an additional step (BTT shunt/PDA stent/PA band) is required as a neonate/early infancy. The Fontan population is thus very heterogenous. The anatomy, state of pulmonary arteries, the timing of surgeries and associated syndromes are highly variable.

The top concerns with the Fontan circulation are

- Low cardiac output (limited preload variability) as pulmonary circulation has no pump in it.
- Elevated CVP (probable reasons are elevated PVR/PA stenosis/ventricular dysfunction/ AV valve regurgitation).
- Chronic low arterial saturation (fenestration, coronary sinus draining into the atrium; systemic veins to pulmonary venous collaterals)
- By the time a patient with Fontan circulation enters the 3rd/4th decade of life, there is chance of encountering complications:
- Ventricular dysfunction.....more likely if the ventricle is the right ventricle.
- Gut wall leakiness.... Protein losing enteropathy
- Liver congestion.....Fontan Associated Liver Disease (FALD)
- Lymphatic abnormalities.....Plastic bronchitis
- Non pulsatile flow in pulmonary circuit..... Thromboembolism

Ventricular dysfunction: This may be systolic or diastolic and may be difficult to assess in preclinical stages unless one has serial follow up of echocardiographic parameters. The other tools are cardiac MRI, exercise stress testing, 6MWT and serum NT pro BNP (or BNP) levels (serial follow up). In rare patients of single ventricle, post Glenn palliation, ventricular dysfunction may be seen; manifest as elevated EDP on cardiac catheterization and mild systolic dysfunction on echo. Early referral for transplant is warranted.

Protein Losing Enteropathy (PLE): It refers to protein loss in the gut which may be clinical (diarrhea and peripheral edema) or subclinical. The incidence is 3-5% post Fontan. There are various theories of causation including elevated central venous pressure, dysfunctional lymphatic system and intestinal wall inflammation. The onset of PLE is at a mean of 5 years post Fontan surgery. Various medical and transcatheter options are available but have low effectiveness overall and PLE is considered progressive. The chances of surviving without transplant at 5years post diagnosis is 70%. Heart transplant offers a good chance of cure from the PLE and early counselling is advisable.

FALD: This is a spectrum of liver pathology ranging from chronic passive congestion and hepatomegaly to fibrosis to cirrhosis to hepatocellular carcinoma. Although almost all patients post Fontan will have some degree of congestion and fibrosis, the rate of progression to advanced stages (decompensated) is unknown. Further, there is no uniform staging of fibrosis or cirrhosis. The gold standard of diagnosing cirrhosis is a liver biopsy and is recommended 10-15years after Fontan completion in all patients. Blood tests and imaging modalities are often unreliable. The algorithm for management of patients with FALD is complex and a multi-disciplinary team should be involved. An early referral to the heart failure team is advisable. A combined heart and liver transplantation has been done in <50 Fontan patients worldwide and the results are encouraging.

Most studies indicate that the key to a reduce mortality post heart transplant for a failing Fontan is to decrease the time between detection of failure and the transplant. Leg varicosities and veno-venous collaterals are also predictors of mortality post heart transplant. Efforts to identify Fontan failure and refer early are ongoing. A recent German study proposed a 15 point scale where a score of 4 or less is against the diagnosis of a failing Fontan while a score from 5 to 15 is in favour of failing Fontan. Some of the parameters they included were NT pro BNP, RDW, VO2 peak, pulse oximetry reading, mean PA pressure, grade of AV valve regurgitation, eGFR, Ejection fraction and end diastolic pressure of the ventricle.

Failing Systemic Right ventricle

There are 2 diseases where the systemic ventricle is the right ventricle:

ccTGA (uncorrected or those with physiologic repair)

dTGA s/p atrial switch.

The population of patients with atrial switch in India is likely to be less than what is seen in the Western world; in proportion to the patients with ccTGA. The right ventricle is unsuitable for sustained support of the systemic circulation and shows temporal decline. Hence in people with a simple ccTGA with no associated lesion, 33% of them will have ventricular failure by the time they turn 50 years old. The other 2 top complications seen in ccTGA are progressive tricuspid valve regurgitation and complete heart block. Attempts may be made to address these complications by heart failure medications (very few studies with small numbers), tricuspid valve replacement (repair is infrequent), pulmonary artery banding (septal shift improves the TR degree) or pacemaker insertion (cardiac resynchronization therapy or dual chamber pacing).

It is challenging to identify the patient who will need advanced heart failure referral. Some parameters that are examined are:

- NYHA class
- Number of hospitalizations (congestion, life threatening arrhythmias)
- Echocardiographic parameters of right ventricular function
- Cardiac MRI findings of fibrosis of the RV myocardium
- Exercise stress testing: serial follow up of results. Absolute

cut off values are ineffective.

- NT pro BNP
- 6MW test
- Annual screening of end organ health (liver and renal function tests).

Tetralogy of Fallot (certain subtypes)

For the purpose of this write up, tetralogy of Fallot can be studied as

- unrepaired tetralogy of Fallot

- tetralogy of Fallot with pulmonary atresia with multiple aorto-pulmonary collaterals (TOF/PA)(unrepaired)

While rare in the Western world, it is not uncommon for us to see the unrepaired adult with tetralogy of Fallot; presenting with florid biventricular failure after decades of living with cyanosis and its aftereffects. Heart transplant is a valid option in this situation.

Tetralogy of Fallot with pulmonary atresia

This subset is unrepaired when the branch PAs appear unsalvageable. The native branch PAs may be hypoplastic or absent. The MAPCAs may be multiple and small instead of a few and large. The pulmonary vasculature may be protected or may be hypertensive in some lung segments, depending on the size of the MAPCA. Over the past some decades, surgical management plans have evolved to accommodate staged surgery for many of these patients. Therefore when such a patient is referred to the advanced heart failure team for heart or heart/lung combined transplant, every effort must be made to ensure that a single or a staged repair is not feasible. The standard approach is a detailed cardiac catheterization for a pressure and angiographic study of each collateral to determine operability.

Certain subtypes of Hypoplastic left heart syndrome (HLHS); hypoplastic right heart syndrome, Ebstein's anomaly, Shone complex

HLHS is palliated with the Norwood-Fontan pathway. If the tricuspid valve is dysplastic and regurgitant then heart transplant maybe a better option. Some centres adopt a hybrid approach with bilateral branch PA bands and atrial septectomy and then list for heart transplant. Similarly, in the case of pulmonary atresia with an intact ventricular septum with right ventricle dependant coronary circulation, heart transplant maybe be better.

Ebsteins anomaly is much amenable to repair. Occasionally, it is accompanied by significant non-compaction of the right ventricular and left ventricular myocardium. This may be a precursor to ventricular dysfunction. A heart transplant becomes a valid option in such a situation. Failed repairs or Ebsteins anomaly accompanied by other major heart defects are also indication for heart transplant.

Eisenmenger syndrome (ES)

This condition of large shunts leading to pulmonary vascular obstructive disease requires lung (plus/minus heart) transplantation as a primary surgery. The current results of lung (or heart lung) transplant are encouraging. A recent paper (2020) found 5-year, 10-year and 15-year survival rates of 83%, 67% and 50%, respectively subject to surviving upto the first year after transplant in pts with ES. The most common post transplant complications encountered were haemorrhage, rejection, cancer, renal insufficiency, coronary allograft vasculopathy and bronchiolitis obliterans.

The natural history of Pre tricuspid shunts with ES is worse compared to post tricuspid shunts. Clinically, the patient manifests with signs and symptoms of chronic cyanosis and heart failure. Although survival upto the 4-5th decade of life has been described, the morbidity is tremendous. Currently there are multiple medications for pulmonary hypertension that can be used alone or in combination . These medications, along with correction of relative iron deficiency show some potential in delaying the need for transplant.

It is recognised that as long as the right ventricular function is preserved, clinical stability will be maintained; however when dysfunction begins, it is a bad sign.

The echo parameters for an adult with ES that signal referral for transplant are TAPSE <15mm, right atrial area >25cm2 (or RA/LA area ratio >1.5) and systolic/diastolic duration (from spectral Doppler of Tricuspid valve regurgitation) >1.5. A baseline pulse oximeter reading of <85% or an increase of NT proBNP by >25% from baseline or values staying above 630pg/ml or 6minute walk test distance of <350m are also indications of referral.

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