Society for Heart Failure and Transplantation

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THE REVIVAL

Promoting Academics to Improve Clinical Outcomes.

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EDITOR'S NOTE

Dr. Manoj Durairaj

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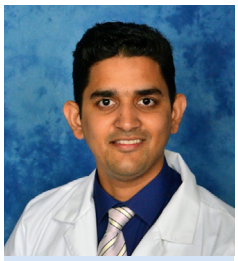
Dear Colleagues,

This issue presents a brilliant article by a young dynamic Paediatric Cardiologist who is doing pioneering work in the field of Pulmonary Hypertension in India. Dr Prashant Bobhate is heading the one of its kind Pulmonary Hypertension Clinic at Kokilaben Dhirubhai Ambani Hospital, Mumbai. Dr Bobhate has eloquently and concisely addressed the topic of Right Heart Failure in Pulmonary Hypertension from the pathophysiology, clinical presentation, evaluation and current medical and surgical management. His centre has the performed 20 Potts Shunts for PH patients and also has 24 patients on prostacyclin therapy.

Editor's Tip: The key to treating RVF due to PH is aggressive early diagnosis and starting the appropriate medical management. With the availability of Macitentan, the prognosis looks better, and once Prostacyclin analogues are available at an affordable cost in our country, it will provide us additional ammunition against this ailment. A reverse Potts shunt has recently emerged as a promising strategy for improving the functional class, reversing the echo parameters and reduction in the medication load in patients with PH and RV failure.

- 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,

This edition of REVIVAL focuses on the often forgotten Right Ventricle and management of RV failure in Pulmonary Hypertension. PAH was once considered to be a certain death sentence, but the advent of newer therapeutic options (both medical and surgical) offers a glimmer of hope to our PH patients. Using his vast personal experience of treating PAH patients, Dr Bhobate has elegantly summarized this topic in a nutshell. The favourable results with surgical reversed Potts shunt with a near identical life expectancy as lung transplants certainly adds another major bridging treatment option to lung transplant for end-stage PAH patients.

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.

August issue of the news letter 'The Revival' covers various aspects of Right Heart Failure in Pulmonary Hypertension. Right ventricle plays an important role in circulation. It cannot handle pressure overload compared to volume overload. RV dysfunction is an important indicator of poor prognosis in heart failure. Widespread use of echocardiography has resulted in the detection of early RV dysfunction before it becomes clinically evident and hence remedial measures can be instituted early in the course of the disease with better outcomes.

Dr.Prashant Bobhate gives a vivid picture of right heart failure in pulmonary hypertension - its evaluation,pathophysiology and management. I am sure this will be a knowledge booster to all readers

- Prof. (Dr) V. Nandakumar
President

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Special thanks to
Dr. Prashant Bobhate for authoring this month's article.

Designed by Maithili Kulkarni

RIGHT HEART FAILURE IN PULMONARY HYPERTENSION

Dr. Prashant Bobhate
MD (Peds), FNB (Peds Card), FPVRI

Dr. Prashant Bobhate is a Paediatric Cardiologist and Pulmonary Hypertension specialist working as Consultant Paediatric Cardiologist and heading the pulmonary hypertension clinic at Kokilaben Dhirubai Ambani hospital, Mumbai. After completion of MBBS from Lokmanya Tilak Municipal Medical college and MD Paediatrics from Seth GS medical college and KEM hospital Mumbai, he did his Fellowship in Paediatric Cardiology at Fortis Escorts Heart Institute, New Delhi.
He has done Fellowship in Pulmonary Hypertension at Mazankoski Heart Institute, Stollery Children's Hospital at University of Alberta, Edmonton, Canada. He has played a pivotal role in setting up a one of its kind Pulmonary Hypertension Clinic in Western India. Apart from the routine investigation and management of patients with PH, this clinic has performed 19 Potts shunt (Highest Single Centre experience in the World) and has 24 patients on prostacyclin therapy. The clinic also has a dedicated Cardiopulmonary Rehabilitation Centre, which helps in rehabilitation of the patients with PH. He is current Convenor of the "Pulmonary Vascular Research Institute" in India and heads their Indian Taskforce since 2018. Along with his clinical work, Dr. Prashant takes keen interest in clinical research and has published more than 20 original articles in national and international peer reviewed journals and 6 chapters in textbooks of paediatric cardiology, cardiology and pulmonary hypertension.

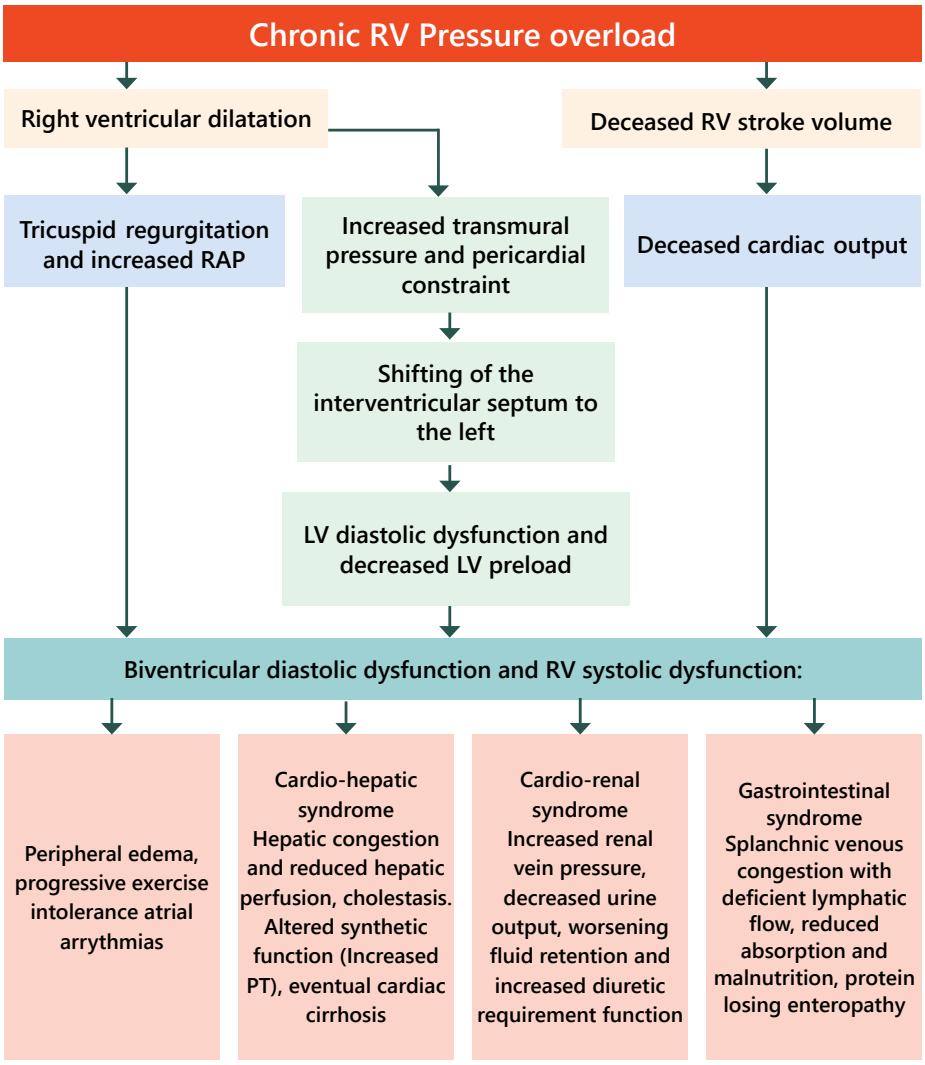
Right heart failure in pulmonary hypertension:

Advanced pharmacological management of PAH has renewed the current interest in the evaluation and management of right ventricular dysfunction (RVD) and right heart failure (RVF). RVD is defined as an abnormal structure or function of the right ventricle, whereas RHF is a clinical syndrome with signs and symptoms of heart failure.

Normal RV ejection fraction (RVEF) is determined by adequate preload (systemic venous return), native contractility of the right ventricular wall, afterload (PAP and PVR), and pericardial compliance. Ejection of blood into a highly compliant and low resistance pulmonary circulation ensures that the energy expenditure required for normal RV output is much less as compared to the left ventricle. Thus RVEF is highly sensitive to afterload, and minimal increase in the afterload has detrimental effects on RVEF. (1) Patients in RHF generally exhibit elevated right-sided filling pressures (right atrial pressure >8 mm Hg) and reduced cardiac index (<2.5 L/(min " m2).

Pathophysiology and clinical manifestations:

Although RV failure can be acute or chronic, in pulmonary hypertension, it is usually chronic secondary to persistently increased afterload. An initial compensatory phase of myocyte hypertrophy and remodeling is gradually replaced by a decompensated



phase associated with myocyte loss and fibrosis. The decompensated phase is usually associated with elevated right atrial pressures and PVRi with a decrease in cardiac output. Decreasing mean Pap with persistently elevated PVR is an ominous sign of end stage RHF.(2)

Clinical manifestations:

- Increased mortality
- Decreased functional capacity
- Cardio-hepatic and cardiorenal syndromes
- Malnutrition and cachexia
- Coagulopathy

Symptoms:

- Exertional Dyspnea, fatigue
- Peripheral edema
- Abdominal fullness or ascites
- Exertional chest pain (angina)
- Presyncope and syncope

Examination:

- Elevated JVP
- RV S3
- Loud P2 (pulmonary hypertension)
- TR murmur which increases on inspiration (Carvello sign)
- Right ventricle heave

Evaluation of right heart failure:

Imaging:

Cardiac echocardiography is the first line of imaging in a patient with right heart failure. It is widely available and enables a rapid assessment of RV size and function. Parameters suggestive of pulmonary hypertension are: septal flattening, RV dilation, dilated and non collapsing IVC, high RVSP estimated from tricuspid regurgitation jet, dilatation of pulmonary artery, decreased pulmonary artery acceleration time. Two important parameters of RV function assessment by 2 D echo are fractional area change (FAC) and TAPSE. FAC < 34% and TAPSE < 17 mm suggest RV dysfunction. 3D echo and speckle tracking/strain imaging are more reliable estimates of RV function. MRI is the gold standard in the assessment of RV function. It also helps in the assessment of RV fibrosis with late gadolinium enhancement. High cost and accessibility is the limitation of MRI.(3)

Biomarker:

There is a long list of biomarkers, but most of them lack specificity. BNP/NTproBNP levels correlated with hemodynamic parameters, echocardiographic indices of RV overload, New York Heart Association functional class, and mortality in patients with PH and RVF. (5). More recently, circulating endothelial cells and micro-RNAs have also been identified as biomarkers in PAH, with possible implications on outcomes. (4)

Treatment:

Treatment of RHF is supportive and symptomatic and revolves around decreasing preload, afterload and improve contractility.

Preload optimization: (Diuretics, salt, and fluid restrictions): The goal of optimal fluid management in chronic RHF is to maintain sufficient preload for adequate cardiac filling while providing relief from right ventricular volume overload, interventricular dependence, and congestion. Loop diuretics and a combination of diuretics like loop diuretics and thiazides may be helpful to augment natriuresis via sequential nephron blockage. Sodium restriction (<3g/day) and fluid restriction (<1.5-2l/day) are reasonable in patients with PAH and RHF. (2)

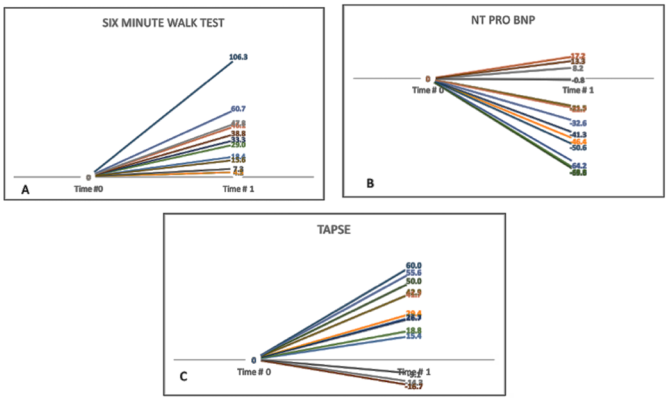
Afterload reduction: Afterload reduction is the cornerstone in the treatment of RV failure with pulmonary hypertension. For patients with group 1 PAH, therapies include PDE (phosphodiesterase)- 5 inhibitors, endothelin receptor antagonists, activators of soluble guanylate cyclase, and prostacyclin analogs. There are no approved therapies for groups 2, 3, and 5 PH beyond treating the underlying disease.

PDE5 inhibitors: Phosphodiesterase 5 inhibitors like sildenafil and tadalafil are established, effective, and well-tolerated in patients with group 1 PAH. Improvement in pulmonary vascular remodelling, right ventricular contractility, and antiproliferative effects have been demonstrated after the use of PDE5 inhibitors. This results in an improvement in functional capacity and reduced clinical events. (5)

Endothelin receptor antagonist: Endothelin -1 has been implicated in the pathogenesis of PAH. ET receptor antagonists (Bosentan, Ambresentan, and Macitentan) have been demonstrated to improve heart failure symptoms, exercise capacity, and clinical worsening in patients with PAH. Although due to superior clinical study design, Macitentan is the only oral, pulmonary vasodilator that has demonstrated mortality benefit in PAH. Elevation in hepatic transaminases, peripheral edema, and anemia are common side effects of these medications. (6)

Prostacyclin analogues: Prostacyclin analogues were one of the first medications which were approved by the US FDA for use in PAH. (7) Unfortunately, they are not yet marketed in India. These can be imported by patients for

their personal use. We currently have 22 patients who are on inhaled iloprost, two patients on subcutaneous treprostinil, and one on oral selexipag. All these patients were started on prostacyclin analogues as add-on therapy on an existing combination of PDE5 inhibitors and endothelin receptor antagonists. Improvement in functional class, decrease in NT pro-BNP, and improvement in echocardiographic parameters have been demonstrated with the use of these medications. (Figure)



Interventional palliative bridge therapy:

Patients who remain in the high-risk category despite maximal medical treatment or deteriorate on the same would be candidates for interventional therapies such as atrial septostomy or a Potts shunt as a bridge to transplant.

Atrial septostomy

Atrial septostomy or the creation of a non-restrictive interatrial communication decompresses the right atrium. It has been shown to improve cardiac output in patients with severe PAH at the expense of causing desaturation. Beneficial effects of the same have been shown to improve functional class and decrease the incidence of syncope in PAH. Relative contraindications for atrial septostomy include mean right atrial pressure of more than 20 mm Hg, resting arterial oxygen saturation < 90%, and patients with impending death. Interatrial communication is known to decrease in size over time, decompresses the right ventricle only in diastole, and has not been demonstrated to reduce the need for pulmonary vasodilators.

Reverse Potts shunt

Decompressing the right ventricle by creating an unrestricted communication between the left pulmonary artery and the descending aorta has recently emerged as a promising management strategy for patients with PAH.

The advantage of a reverse Potts shunt is that it provides high oxygen saturated blood to the coronary arteries and the central nervous system and only causes the lower body's desaturation. Another benefit arises from its effect on pulmonary hemodynamics by the relief of RV pressure overload in systole and diastole pressure, with a subsequent reduction in PA pressure and shifting of the interventricular septum towards the left ventricle with an improvement in systolic and diastolic ventricular performance In our own experience, a reversed Potts shunt was performed in 20 patients with significant improvement in the functional class, echocardiographic parameters, and reduction in medications. (8)

Lung transplant

Bilateral lung transplant or heart and lung transplant may be an option for some children with PH. However, despite improvement in immunosuppression medications, the overall survival after lung transplant remains limited. Besides, it is limited by its availability and financial constraints in low and medium-income countries such as India. Among all causes for a lung transplant, the patients with PAH as an indication for transplant have the worst survival. Median survival after lung transplantation has been reported to be 4.9 years. (9)

Conclusion:

- Pulmonary hypertension is a chronic progressive disease eventually leading to right heart failure
- Suspicion and early diagnosis is important for good long term outcomes
- With current medications survival has improved significantly in patients with PAH
- Upfront combination therapy with PDE5 inhibitors and endothelin receptor antagonist significantly improves morbidity as well as mortality
- Prostacyclin analogues are the need of the hour, currently they are not marketed in India but can be imported, early institution of prostacyclin analogues helps improve functional class, right ventricular function and survival
- Palliative procedures like reversed Potts shunt and atrial septostomy can be used a bridge to transplant
- Lung/ heart and lung transplant needs to be considered in treatment refractory patients.

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