Review Article

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Recent Trends in the Management of Refractory Heart Failure

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ABSTRACT

Refractory heart failure represents the end stage of heart failure in which hypotension and oliguria, leads to progressive generalized edema. Refractory heart failure is considered the end product of a vicious circle in which reduced cardiac output and impaired salt and water renal excretion have a negative impact on each other. This ongoing vicious cycle leads to frequent hospitalisations and expenditures. With advancing technology, it is important to know the newer approaches for the management of this condition to improve quality of life and attempt to reduce morbidity and mortality.

Heart failure (HF) is a Clinical Syndrome characterized by anasarca due to systemic perfusion which is inadequate to meet body's metabolic demands as a result of impaired function of Cardiac Pump.

Refractory Heart Failure is defined as advanced structural heart disease and marked symptoms of heart failure at rest despite dietary modification, salt restriction and maximal medical therapy.[1-3] It forms stage IV of New York Heart Association (NYHA) classification of heart failure

It is important to recognise the precipitating causes for worsening heart failure which is refractory to standard therapy and initiating specific therapy (aggressive) at the earliest.[4-6]

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The precipitating causes can be:

- Dietary and / or pharmacologic non-compliance;
- Negative ionotropes, antiarrhythmics and first generation calcium channel blockers;
- NSAIDs increasing salt and water retention and worsening of renal function;
- Damage to the myocardium by Adriamycin, Alcohol and/ or Cocaine;
- Myocardial Infarction, Myocarditis;
- Increased myocardial workload as in Anemia, Hypoxia, Infection and Pulmonary Embolism;
- Worsened Valvular Dysfunction ;
- Arrhythmias;

Meticulous control of fluid retention is recommended in patients with refractory end-stage HF. Limiting patient's intake to 2 g/day of dietary sodium and 2 L/day of fluid will lessen congestion and decrease the need for diuretics. Referral of patients with refractory end-stage HF to a HF program with expertise in the management of refractory HF will be useful. Options for end-of-life care should be discussed with the patient and family.[7,8]

APPROACHES IN THE MANAGEMENT OF PATIENTS WITH REFRACTORY HEART FAILURE

- Implantable Device
  - Implantable cardiac Defibrillator
  - Cardiac Resynchronization Therapy (CRT)
  - Combination of CRT and ICD (Combo devices)
- Percutaneous Therapy
  - Coronary Intervention in revascularizable anatomy
  - Intra-aortic balloon counterpulsation
  - Implantable assist devices (Impella Recover system, Tandem heart system)
  - Percutaneous valve repair
  - Percutaneous reshaping devices - Annuloplasty, edge-to-edge repair, and ventricular reshaping
  - Percutaneous stem cell delivery
- Surgical therapy
  - Coronary artery bypass surgery in selected patients
  - Coronary revascularisation surgeries
  - Ventricular remodelling / restoration
  - Aneurysmal segment linear closure by Cooley
  - Aneurysmal resection and intrication Jaten
  - Cardiomyoplastyor "Dynamic Cardiomyoplasty,"
  - Mitral valve repair or replacement
  - Left Ventricular reshaping surgeries
    - Batisa Procedure "Partial Left Ventriculectomy."
    - Dor Technique "Endoventricular Circular Patch Plasty" or EVCPP.
  - Stem cells
  - Left Ventricular assist devices (LVAD)
  - Cardiac Transplantation

In this review article of recent trends in the management of refractory heart failure, we would like to detail some of the above recent trends.

IMPLANTABLE CARDIAC DEFIBRILLATOR (ICD)

Approximately 50% of patients with heart failure die suddenly. Implantation of an ICD can be superior to antiarrhythmic drug therapy in preventing sudden death.[5-8]

Indications For ICD

1. Cardiac arrest survivor
2. Sustained ventricular tachycardia
3. Inducible ventricular tachycardia
4. Ischemic cardiomyopathy with an Left Ventricular Ejection Fraction (LVEF) ≤35%
5. Dilated cardiomyopathy with an LVEF ≤35%

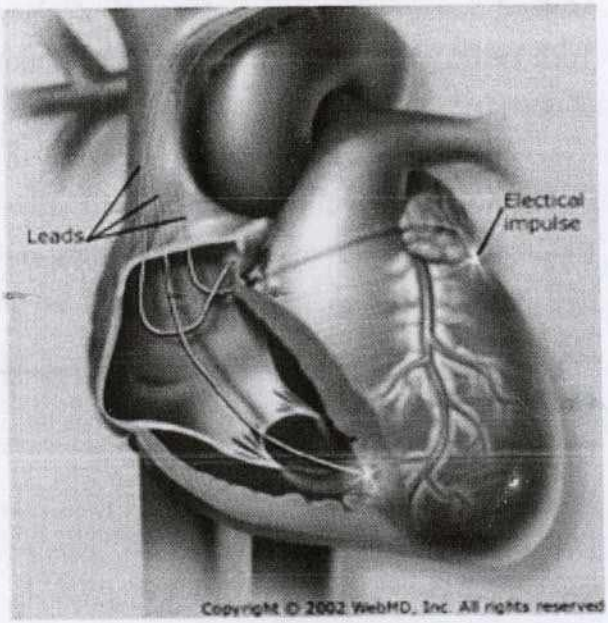

Fig 1: (Pacemaker leads are implanted in the RA, RV and Left Cardiac vein via the coronary sinus)

with symptoms

CARDIAC RESYNCHRONISATION THERAPY (CRT)

Patients with systolic heart failure due to ischemia or dilated cardiomyopathy often show significant cardiac dyssynchrony. Resynchronizaion of the myocardial contraction can be done by pacing the right ventricle and left ventricle (thro a lead in the coronary sinus) with the implantation of biventricular pacemakers.

Indications for CRT - NYHA Class III or IV heart failure symptoms; LVEF $\leq$ 35%; wide QRS > 120ms ; Evidence of dyssynchrony (LBBB, Intraventricular conduction delay)

Pacemaker leads are implanted in the RA, RV and left cardiac vein via the coronary sinus

Symptomatic improvement is achieved in approximately 70% of patients because of improved ventricular contraction, ventricular reverse-remodeling, and reduction of mitral regurgitation.

INTRA-AORTIC BALLOON COUNTER-PULSATION (IABP)

IABP is used as bridge LVAD implant and in heart transplantation. IABP is a mechanical device that increases myocardial oxygen perfusion by increasing cardiac output, increasing coronary blood flow and therefore myocardial oxygen delivery. It consists of a cylindrical polyethylene balloon that sits in the aorta, approximately 2 centimeters from the left subclavian artery and counterpulsates. That is, it actively deflates in systole, increasing forward blood flow by reducing after load. It actively inflates in diastole, increasing blood flow to the coronary arteries. These actions combine to decrease myocardial oxygen demand and increase myocardial oxygen supply.[9-11]

Indications for IABP

1. Left Ventricular failure or cardiogenic shock - Myocardial infarction (MI), Myocarditis, Cardiomyopathy, Severe myocardial contusion, septic shock and Drug induced
2. Mechanical complications of acute MI
3. Post MI ventricular irritability
4. Unstable angina refractory to medical therapy
5. Severe HF with cardiac index< 1.5 l/min.
6. Not responding to pharmacological treatment
7. Unfit for LVAD / cardiac transplantation
8. Failed PTCA

Duration of use is 48 to 72 hours, and for a maximum 27 days

Complications of IABP

- Vascular loss of distal pulse, ischemic pain at the site, thrombus emboli and neuropathy.
- Infections- focal, disseminated bacteremia and fever

CORONARY REVASCULARIZATION PROCEDURES

Coronary artery disease is common in patients with advanced heart failure, with some studies suggesting a prevalence of 50%-70%.[12] Coronary revascularization with coronary artery bypass surgery or percutaneous coronary interventions appropriate should be considered in patients with heart failure and suitable coronary anatomy presenting with significant angina, or acute coronary syndrome.[1-3]

VENTRICULARASSIST DEVICE (VAD)

VAD is a single system device that is surgically attached to the left ventricle of the heart and to the aorta for left ventricular support. For right ventricular support, the device is attached to the right atrium and to the pulmonary artery. It can be used for the left (L VAD), right (R VAD), or both ventricles (Bi VAD). The pump output can be pulsatile or non-pulsatile.

Indications for VADs

1. Bridge to Transplant (BTT)
   a. Most common
   b. Allows rehabilitation from severe CHF while awaiting donor
2. Bridge to Recovery (BTR)
   a. Unloads the heart and allows for 'reverse remodelling'
   b. Can be short term / long term
3. "Destination" therapy (DT)
   a. Permanent device, instead of a transplant
   b. Currently used only in transplant-ineligible patients
4. Bridge to Candidacy (BTC) / Bridge to Decision (BTD)
   a. When eligibility is unclear at implant
   b. Not true "indication" but true for many patients.

CARDIAC TRANSPLANTATION

Class I Indications for Cardiac Transplantation

- Cardiogenic shock requiring mechanical assistance.
- Refractory heart failure with continuous inotropic infusion.
- NYHA functional class 3 and 4 with a poor 12 month prognosis.
- Progressive symptoms with maximal therapy.
- Severe symptomatic hypertrophic or restrictive cardiomyopathy.
- Medically refractory angina with unsuitable anatomy for revascularization.
- Life-threatening ventricular arrhythmias despite aggressive medical and device interventions.
- Cardiac tumors with low likelihood of metastasis.
- Hypoplastic left heart and complex congenital heart disease.

Absolute Contraindications to Cardiac Transplantation - Any systemic illness that will

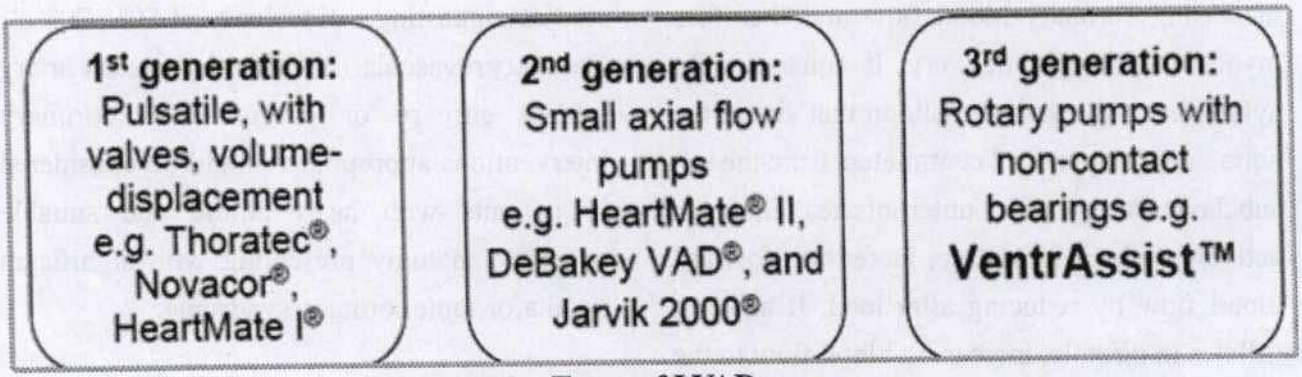

Fig 2: Types of LVAD

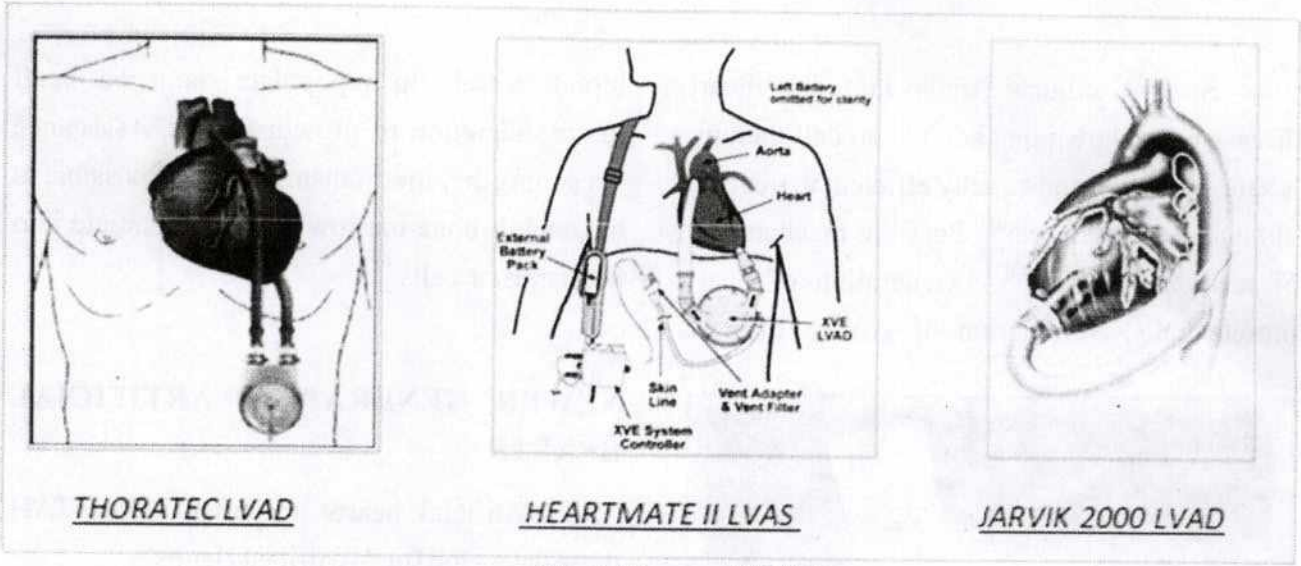

Fig 3: Types of LVAD

limit survival despite heart transplant Neoplasm, HIV / AIDS (CD4<200); Active SLE or sarcoid with dissemination; Any systemic process with a high probability of recurring in the transplanted heart; Fixed Pulmonary Hypertension; age> 70 years.

• ORTHOTOPIC IMPLANTATION is the most common. It involves complete explantation of the native heart.

• HETEROTOPIC IMPLANTATION is an alternative technique in which the donor heart functions in parallel with the recipient's heart. This procedure can be considered if the donor heart is small enough to fit into the mediastinum without physical restriction of function.

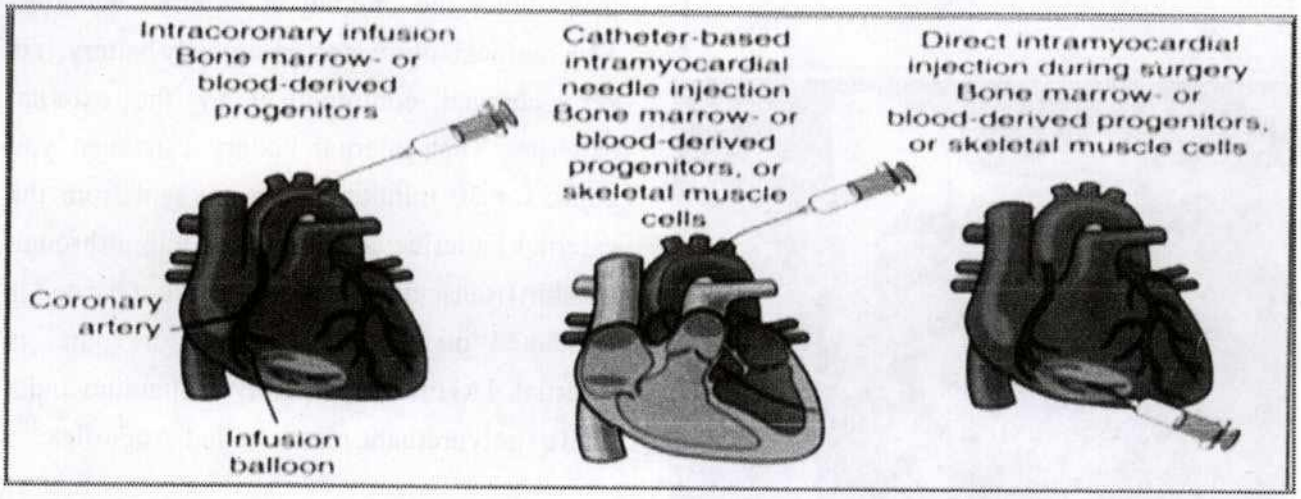

Fig 4: STEM CELL THERAPY

Cardiac Donor- Brain death is necessary for any cadaveric organ donation. If brain death is uncertain, confirmation tests using EEG, cerebral flow imaging, or cerebral angiography are indicated.

Surgical Transplantation Techniques

STEM CELL THERAPY

Several clinical trials targeting heart disease have shown that adult stem cell therapy is safe, effective, and equally efficient in treating old and recent infarcts.[13] Possible mechanisms of recovery include[14] - Generation of heart muscle cells, Stimulation of growth of new blood vessels to repopulate damaged heart tissue, Secretion of growth factors, Assistance via some other mechanism. It may be possible to have adult bone marrow cells differentiate into heart muscle cells.[14]

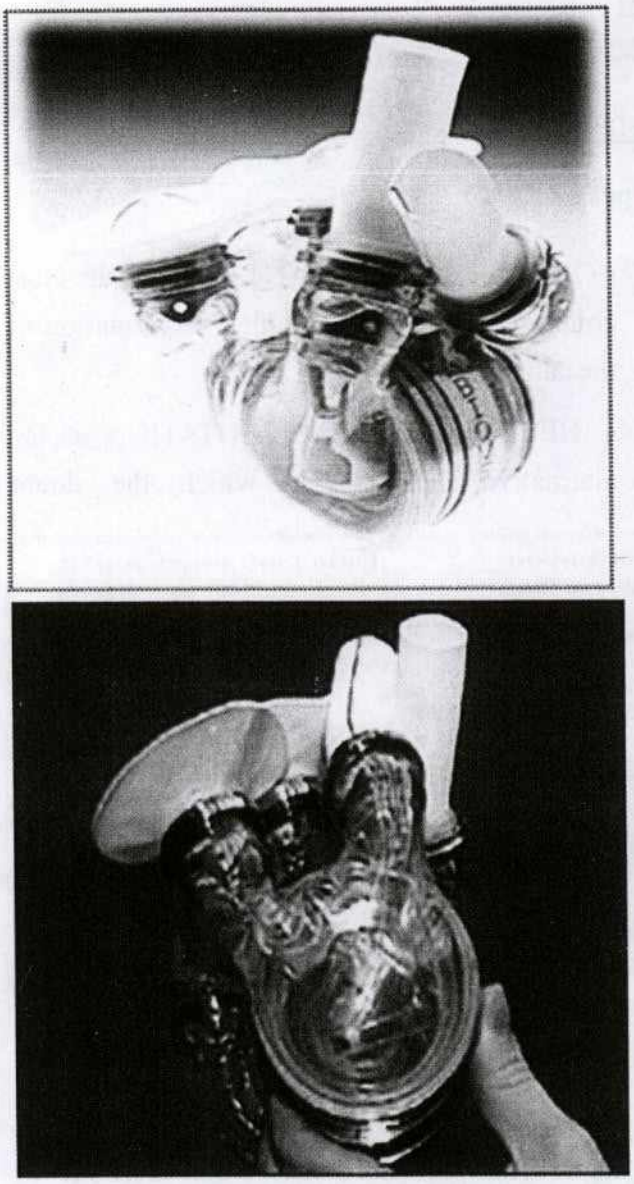

Fig 5: The Abiocor™ Artificial Heart

NEWER GENERATION ARTIFICIAL HEARTS

Artificial hearts are often called TAH these days - for Total Artificial Hearts.

The Abiocor™ TAH is designed to fit completely inside the body, with no wires or tubes poking through skin. It is implanted into stomach area. It monitors and controls the TAH, changing the pumping speed of the heart to handle changing activity levels. It uses energy from either the internal or external batteries. The internal battery is an emergency battery. It is kept charged continuously by the external batteries. That internal battery can keep you going for 30 minutes. Power is sent from the external batteries to the internal pump through the skin (transcutaneous), using coils. One coil is implanted inside the body and the other is external. TAH is made mainly of titanium and a kind of polyurethane plastic called Angioflex.[15]

NEWER DRUGS - MEDICAL THERAPY

Milrinone- A phosphodiesterase inhibitor that enhances contractility. Milrinone is useful for patients with low-output heart failure and

Milrinone dose

DOSE	ADVERSE EFFECT
Bolus: 50 µg/kg bolus over 10 to 30 min Infusion: 0.375 to 0.75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (dose adjustment necessary for renal impairment)	Ventricular arrhythmias Hypotension Cardiac ischemia Torsade des pointes

pulmonary hypertension.

Nesiritide- A synthetic BNP, an arterial and venous vasodilator with modest diuretic and natriuretic properties.[16] Nesiritide increases cardiac output by afterload reduction without increasing heart rate or oxygen consumption. It modulates the vasoconstrictor and sodium-retaining effects of other neurohormones.

Levosimendan - A novel inotropic agent that can be administered intravenously in the treatment of acute decompensated heart failure. It is a pyridazinone-dinitrile derivative. Levosimendan has two important mechanisms of action. Its primary action is to enhance cardiac contractility. Levosimendan has an important secondary action - vasodilation of vascular smooth muscle. It acts upon ATP-sensitive potassium channels found in the myocardium, peripheral blood vessels and coronary arteries.[16,17] This widespread vasodilation has the beneficial effect, in the failing heart, of reducing cardiac pre-load and afterload in addition to improving coronary flow, reducing ischaemia and improving renal blood flow. Dose-dependent hypotension may occur, however.

CONCLUSION:

Refractory heart failure can be treated with better prognosis. Now many specific therapies suitable to the individual patient are available at higher cardiac centres.

OUR RECOMMENDATIONS:

- ✓ Early recognition is the key to effective therapy;
- ✓ Amending /correcting precipitating causes ;
- ✓ Referral to higher centre where specific treatment is possible.

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