Lo Scompenso Cardiaco Avanzato:
la riparazione transcatetere della valvola mitrale,
l’assistenza meccanica,
e....altro.

Francesco Santini

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University of Genova Medical School, Italy
Advanced chronic heart failure: A position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology

Marco Metra a,*, Piotr Ponikowski b, Kenneth Dickstein c, John J.V. McMurray d, Antonello Gavazzi e, Claes-Hakan Bergh f, Alan G. Fraser g, Tiny Jaarsma h, Antonis Pitsis i, Paul Mohacsi j, Michael Böhm k, Stefan Anker l, m, Henry Dargie n, Dirk Brutsaert o, Michel Komajda p on behalf of the Heart Failure Association of the European Society of Cardiology

Definition of ACHF

1. Severe symptoms of HF with dyspnoea and/or fatigue at rest or with minimal exertion (NYHA functional class III or IV)
2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral oedema) and/or of reduced cardiac output at rest (peripheral hypoperfusion)
3. Objective evidence of severe cardiac dysfunction, shown by at least one of the following:
   a) A low LVEF (<30%),
   b) A severe abnormality of cardiac function on Doppler-echocardiography with a pseudonormal or restrictive mitral inflow pattern
   c) High LV filling pressures (mean PCWP>16 mm Hg, and/or mean RAP>12 mm Hg by pulmonary artery catheterisation)
   d) High BNP or NT-ProBNP plasma levels, in the absence of non-cardiac causes.
4. Severe impairment of functional capacity shown by one of the following:
   a) Inability to exercise,
   b) 6-MWT distance<300 m or less in females and/or patients aged ≥75 years
   c) peak VO₂ < 12 to 14 ml/kg/min
5. History of ≥1 HF hospitalisation in the past 6 months
6. Presence of all the previous features despite “attempts to optimise” therapy including diuretics, inhibitors of the renin–angiotensin–aldosterone system, and beta-blockers, unless these are poorly tolerated or contraindicated, and CRT, when indicated.
A group of patients for whom symptoms limit daily life despite usual recommended therapies and for whom lasting remission into less symptomatic disease is unlikely.

Selected Prognostic Models in HF

Heart Failure Survival Score

Seattle Heart Failure Model

EVEREST Risk Model

EFFECT

ADHERE

ESCAPE Discharge Score
Left ventricular systolic dysfunction
Each year cardiovascular disease (CVD) causes over 4 million deaths in Europe and over 1.9 million deaths in the European Union (EU).

Just under half of all deaths from CVD in both men and women are from CHD. One in five men (20%) and over one in five women (22%) die from the disease; From the: European Cardiovascular Disease Statistics (2012 ed.) British Heart Foundation Health Promotion Research Group - Department of Public Health, University of Oxford.
Comparison of Coronary Artery Bypass Grafting Versus Medical Therapy on Long-Term Outcome in Patients With Ischemic Cardiomyopathy (A 25-Year Experience from the Duke Cardiovascular Disease Databank)

Christopher M. O'Connor, MD, Eric J. Velazquez, MD, Laura H. Gardner, BSHH, Peter K. Smith, MD, Mark F. Newman, MD, Kevin P. Landolfo, MD, Kerry L. Lee, PhD, Robert M. Califf, MD, and Robert H. Jones, MD

FIGURE 4. Event-free survival curves for CABG versus medical therapy.

FIGURE 5. Hazard ratios (95% confidence interval) for mortality in subgroups defined by baseline characteristics. EF = ejection fraction; MED = medical; NYHA = New York Heart Association.
Preoperative evaluation of myocardial viability in this group of patients using PET scanning or dobutamine echocardiography might additionally improve outcomes of this surgical approach.
Algorithms for identifying and treating patients with CAD and chronically dysfunctional but viable myocardium
### Table 1. Results of Different Imaging Modalities to Predict Recovery of Global LV Function After Revascularization

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Patients, n</th>
<th>Sensitivity, Mean (95% CI)</th>
<th>Specificity, Mean (95% CI)</th>
<th>PPV, Mean (95% CI)</th>
<th>NPV, Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional nuclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Tc-sestamibi $^{63}$</td>
<td>19</td>
<td>71 (51–91)</td>
<td>40 (18–62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT FDG$^{63,70}$</td>
<td>94</td>
<td>86 (79–93)</td>
<td>93 (88–98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{111}$In-oxine, reinjection$^{12,62,63,65}$</td>
<td>211</td>
<td>84 (79–89)</td>
<td>70 (64–76)</td>
<td>97 (92–100)</td>
<td>93 (96–100)</td>
</tr>
<tr>
<td>$^{201}$Tl rest redistribution + FDG$^{66}$</td>
<td>47</td>
<td>86 (76–96)</td>
<td>92 (84–100)</td>
<td>90 (81–99)</td>
<td>89 (80–98)</td>
</tr>
<tr>
<td>Total</td>
<td>371</td>
<td>84 (80–88)</td>
<td>77 (73–81)</td>
<td>94 (89–98)</td>
<td>91 (85–97)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE$^{73,62,63,65,66,72}$</td>
<td>408</td>
<td>76 (71–80)</td>
<td>81 (77–85)</td>
<td>84 (77–91)</td>
<td>91 (85–96)</td>
</tr>
<tr>
<td>DSE + strain rate$^{66}$</td>
<td>55</td>
<td>67 (55–79)</td>
<td>89 (81–97)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic wall thickness$^{66}$</td>
<td>43</td>
<td>63 (49–77)</td>
<td>68 (54–82)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>506</td>
<td>74 (70–77)</td>
<td>81 (77–84)</td>
<td>84 (77–91)</td>
<td>91 (85–96)</td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG$^{63,70}$</td>
<td>205</td>
<td>81 (75–86)</td>
<td>65 (59–72)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>205</td>
<td>81 (75–86)</td>
<td>65 (59–72)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FPV indicates positive predictive value; NPV, negative predictive accuracy.

*Circulation.* 2008;117:103-114
5.3 Detection of myocardial viability

Non-invasive assessment of myocardial viability has been used to guide the management of patients with chronic ischaemic systolic LV dysfunction. Multiple imaging techniques, including PET, SPECT, and dobutamine stress echocardiography, have been evaluated for assessment of viability and prediction of clinical outcome after myocardial revascularization. In general, nuclear imaging techniques have a high sensitivity, whereas techniques evaluating contractile reserve have a somewhat lower sensitivity but higher specificity. MRI has a high diagnostic accuracy for assessing the transmural extent of myocardial scar tissue and can also assess contractile reserve, but its ability to detect viability and predict recovery of wall motion is no better than other imaging techniques. The differences in performance between the various imaging techniques are small, and experience and availability commonly determine which technique is used. The evidence is mostly based on observational studies or meta-analyses. One RCT, relating to PET imaging, showed that patients with a substantial amount of dysfunctional but viable myocardium are likely to benefit from myocardial revascularization.
Symptoms and/or signs of congestive heart failure with abnormal left ventricular function (clinical examination and echocardiography)

CAD+
- Assess myocardial viability with technique available
  - No evidence of viability or viability in <25% of LV
    - Medical treatment, CRT, ICD, LVAD
  - Presence of significant viability in segments subtented by stenotic coronaries
    - Coronary revascularization by PCI or CABG

CAD-
- Investigate alternative aetiologies (DCM, valve disease, etc.)
Symptoms and/or signs of congestive heart failure with abnormal left ventricular function (clinical examination and echocardiography)

CAD+

Assess myocardial viability with technique available

Presence of significant viability in segments subtented by stenotic coronaries

Coronary revascularization by PCI or CABG

Circulation. 2008;117:103-114
Off-pump CABG

To perform coronary surgery on a beating heart

Heart-lung machine not used
Stabilizer / Shunts
Less overall “trauma”

? Complete revascularization
Ischemic Cardiomyopathy

Improvement in:

- LVEF
- NYHA FC
- disabling angina
- freedom from recurrence of HF
- “hospitalization for HF exacerbations
- overall quality of life
Secondary (functional) Mitral Regurgitation:
The mitral valve structure is normal and valve incompetence is related to severe LV dysfunction (Ischemic / Non-Ischemic).

- Annular dilatation
- Loss of systolic annular contraction
- Increased LV size
- PM dysfunction
- PM migration
A “ventricular disease” masquerading as a valvular disease

Otsuji Y. et al.; J Am Coll Cardiol 2001;37:641-648
Type IIIb: Restricted leaflet motion during systole
Geometric deformity after anterior and inferior MI

Three-dimensional images of the mitral annulus in normal control patients, patients with inferior MI, and anterior MI. Upper panel, vertical view from left atrium; lower panel, horizontal view.

MR begets MR

Persistent MR is associated with a poor prognosis
Predictors of Improvement of Unrepaired Moderate Ischemic Mitral Regurgitation in Patients Undergoing Elective Isolated Coronary Artery Bypass Graft Surgery

Martin Penicka, MD, PhD; Hana Linkova, MD; Otto Lang, MD, PhD; Richard Fojt, MD; Viktor Kocka, MD; Marc Vanderheyden, MD; Jozef Bartunek, MD, PhD

Circulation 2009;120:1474-1481

viable myocardium (reverse LV remod)

papillary muscle dyssynchrony (<60msec)

< MV coaptation depth
Beneficial effect of **concomitant** CABG and MVR:

Acceptable perioperative mortality of 0.8% to 11%, and declining.

5-year survival between 51% - 83%, and improving.

Concomitant CABG and MVR achieve superior reduction in MR than CABG alone in moderate to severe MR.

Concomitant CABG and MVR have been associated with improved:
- LVEF
- LVESV/LVEDV, LV sphericity index
- NYHA and QoL

….no studies, however, have shown a clear **survival benefit**.
Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

**Table 13** Indications for mitral valve surgery in chronic secondary mitral regurgitation

<table>
<thead>
<tr>
<th>Indication</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is indicated in patients with severe MR&lt;sup&gt;a&lt;/sup&gt; undergoing CABG, and LVEF &gt;30%.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in patients with moderate MR undergoing CABG&lt;sup&gt;a&lt;/sup&gt;</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in symptomatic patients with severe MR, LVEF &lt;30%, option for revascularization, and evidence of viability.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Surgery may be considered in patients with severe MR, LVEF &gt;30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

European Heart Journal (2012) 33, 2451–2496
Rick A. Nishimura, Catherine M. Otto, Robert O. Bonow, Blase A. Carabello, John P. Erwin III, Robert A. Guyton, Patrick T. O'Gara, Carlos E. Ruiz, Nikolaos J. Skubas, Paul Sorajja, Thoralf M. Sundt III and James D. Thomas

### Recommendations

<table>
<thead>
<tr>
<th></th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

### Stages of Progression of VHD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk</td>
<td>Patients with risk factors for development of VHD</td>
</tr>
<tr>
<td>B</td>
<td>Progressive</td>
<td>Patients with progressive VHD (mild-to-moderate severity and asymptomatic)</td>
</tr>
</tbody>
</table>
| C     | Asymptomatic severe | Asymptomatic patients who have the criteria for severe VHD:  
  C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated  
  C2: Asymptomatic patients with severe VHD, with decompensation of the left or right ventricle |
| D     | Symptomatic severe | Patients who have developed symptoms as a result of VHD |

VHD indicates valvular heart disease.
1. Annular dilatation and flattening
2. Papillary muscle (PM) dysfunction
3. Leaflet tethering
4. LV dysfunction, dilatation, and free wall kinetic abnormalities
5. Closing forces
Undersized (or ‘restrictive’) annuloplasty
- complete, rigid, 3-D, asymmetric rings
- coaptation length of at least 8 mm

Resection of the secondary chordae

Repositioning of the papillary muscle

Leaflet augmentation

Concomitant LV restoration procedure

MV repair
Functional mitral regurgitation: a 30-year unresolved surgical journey from valve replacement to complex valve repairs

Francesco Onorati · Francesco Santini · Rajesh Dandale · Andrea Rossi · Esther Campopiano · Konstantinos Pechlivanidis · Daniele Calzaferri · Aldo Milano · Alessandro Mazzucco · Giuseppe Faggian

Heart Fail Rev 2013
Anteroseptal MI, dilated LV (EDVi < 100mL/m2), depressed LVEF (<20%), LV regional dyskinesia or akinesis > 30% of ventricular perimeter, angina, heart failure, arrhythmias, inducible ischemia.
The STICH trial design

hypothesis 1: added value of revascularization over OMT

hypothesis 2: the benefit of adding SVR to CABG

issue 3: the impact of determining myocardial viability prior to revascularization
Predictors of MR after repair

- Mild annular dilatation
- Complex multiple regurgitant jets
- Advanced LV remodeling
- Excessive tethering (coaptation depth >1.5 cm)
- Posterior mitral leaflet angle >45°
- Distal anterior mitral leaflet angle >25°
- Systolic tenting area >2.5 cm²
- Endsystolic interpapillary muscle distance >20 mm
- Systolic specificity index >0.7

Nat. Rev. Cardiol. 9, 133–146 (2012)
Mitral Valve Replacement

Types of Prostheses: the choice has to be individualized

Excellent durability;
Good overall performance (avoiding physical hazards)
✓ Age group 40 – 65 years

Life-long anticoagulation (complication rate 0.3-6.8/100 pt-yr)
Thromboembolic events, perivalv. leakage, hemolysis, endocarditis
Risk of chronic warfarin

Elderly patients (>65 yrs) [in sinus rhythm (...)]
Freedom from anticoagulation
Thromboembolic events, perivalvular leakage, endocarditis
Controindicated in chronic renal failure
Limited durability [SVD] (more rapid degeneration < 45 yrs)
Randomized Trial of Partial Versus Complete Chordal Preservation Methods of Mitral Valve Replacement

A Preliminary Report

Kwok L. Yun, MD; Colleen F. Sintek, MD; D. Craig Miller, MD; Gregg T. Schuyler, MD; Alden D. Fletcher, MD; Thomas A. Pfeffer, MD; Gary S. Kochamba, MD; Siavosh Khonsari, MD; Michael R. Zile, MD

Reduced systolic wall stress
Mitral valve repair or replacement for ischemic mitral regurgitation? The Italian Study on the Treatment of Ischemic Mitral Regurgitation (ISTIMIR)

CONCLUSIONS

We observed no significant difference in left ventricular reverse remodeling or survival at 12 months between patients who underwent mitral-valve repair and those who underwent mitral-valve replacement. Replacement provided a more durable correction of mitral regurgitation, but there was no significant between-group difference in clinical outcomes. (Funded by the National Institutes of Health and the Canadian Institutes of Health; ClinicalTrials.gov number, NCT00807040.)
Nonischemic Cardiomyopathy

Improvement in:

- LVEF
- NYHA FC
- MR grade
- ventricular sphericity
- 6-minute walk time
Percutaneous mitral valve repair using the MitraClip® device
Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes.
Class IIIb

3. Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for HF (426). (Level of Evidence: B)


Patient eligibility for transcatheter mitral valve repair (TMVR) with MitraClip® therapy is determined by the following criteria:

<table>
<thead>
<tr>
<th>Degenerative MR</th>
<th>✓</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant mitral regurgitation (MR ≥3+)</td>
<td>✓</td>
</tr>
<tr>
<td>Symptomatic (NYHA functional class III or IV)</td>
<td>✓</td>
</tr>
<tr>
<td>Prohibitive risk criteria, including any of the following:</td>
<td>✓</td>
</tr>
<tr>
<td>- 30-day STS predicted operative mortality risk score of</td>
<td>✓</td>
</tr>
<tr>
<td>- ≥8% (mitral valve replacement)</td>
<td>✓</td>
</tr>
<tr>
<td>- ≥6% (mitral valve repair)</td>
<td>✓</td>
</tr>
<tr>
<td>- Porcelain aorta or extensively calcified ascending aorta</td>
<td>✓</td>
</tr>
<tr>
<td>- Frailty (assessed by in-person cardiac surgeon consultation)</td>
<td>✓</td>
</tr>
<tr>
<td>- Hostile chest</td>
<td>✓</td>
</tr>
<tr>
<td>- Severe liver disease / cirrhosis (MELD Score &gt;12)</td>
<td>✓</td>
</tr>
<tr>
<td>- Severe pulmonary hypertension (systolic pulmonary artery pressure &gt;2/3 systemic pressure)</td>
<td>✓</td>
</tr>
<tr>
<td>- Unusual extenuating circumstance, such as right ventricular dysfunction with severe tricuspid regurgitation, chemotherapy for malignancy, major bleeding diathesis, immobility, AIDS, severe dementia, high risk of aspiration, internal mammary artery at high risk of injury, etc.</td>
<td>✓</td>
</tr>
</tbody>
</table>

For optimal results, the following anatomic patient characteristics should be considered:

| The primary regurgitant jet is non-commissural. If a secondary jet exists, it must be considered clinically insignificant | ✓ |
| Mitral valve area ≥4.0cm² | ✓ |
| Minimal calcification in the grasping area | ✓ |
| No leaflet cleft in the grasping area | ✓ |
| Flail width <15 mm and flail gap <10 mm | ✓ |
| LVEF >20% or LVESD <60mm | ✓ |

TMVR is contraindicated for degenerative MR patients with the following conditions:

| Patients who cannot tolerate procedural anticoagulation or post procedural antiplatelet regimen | ✗ |
| Active endocarditis of the mitral valve | ✗ |
| Rheumatic mitral valve disease | ✗ |
| Evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus | ✗ |
### Recommendations

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG or percutaneous intervention is indicated for HF patients on GDMT with angina and suitable coronary anatomy, equivalent</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>CABG to improve survival is reasonable when dysfunction and significant multivessel myocardium is present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG or medical therapy is reasonable when severe LV dysfunction (EF &lt; 35%) and a predicted surgical mortality of no greater than 10%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit and should only be considered after careful candidate selection and with a background of GDMT (854–857). *(Level of Evidence: B)*
OUTCOMES BY DMR AND FMR CAUSES

Both FMR and DMR causes were represented, with FMR present in the majority of patients (70.1%). DMR patients were older, on average, than FMR patients (by 9 years), but the 2 groups were otherwise comparable. Safety outcomes were similar between the 2 groups, and both of the groups experienced improvements in effectiveness measures.
COAPT

RESHAPE-HF 2

MITRA-France

MATTERHORN (F MR)

HIRIDE (D MR)
Improvements:
- IM grade
- NYHA Class
- LV remodeling
- QoL
• Patient selection
• Interdisciplinary Heart Team
• Timing
• Environment
• Learning Curve
• Hospital Center
• Scientific Registries
A new report on an era of medical failure

The Tragic Record of Heart Transplants

Six recipients of transplants, shown here against a backdrop of the heart, were all dead within eight months of being photographed together.
Heart Transplantation is the “gold standard” treatment for CHF ... albeit its inability to serve to the current demand.
Completamento dell'anastomosi atriale destra (tecnica standard)
The increasing routine use of ventricular assist devices (VADs) to keep patients alive until heart transplantation paved the way to their clinical use as an established treatment for end-stage heart failure (DT).
Patient Criteria - DT

- Refractory NYHA Class IV Heart Failure
- Life Expectancy <2 years
- Non-candidate for heart transplantation
- LVEF< 25%
- Failed optimal medical management for 60 of previous 90 days
- VO2<12 mL/kg/min or need for inotropes
  - Hypotension, renal dysfunction, pulmonary congestion
- BSA>1.5 m2
- Absence of comorbidities limiting survival
- Dependence on inotropes for 2 weeks

http://www.cms.hhs.gov/
European Society of Cardiology (ESC) guidelines for the use of LVAD therapy

<table>
<thead>
<tr>
<th>Table 1 Indication for LVAD implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular function 25% and aVO2 peak &lt;12 mL/kg/min</td>
</tr>
<tr>
<td>≥3 hospitalizations within the previous 12 month</td>
</tr>
<tr>
<td>Inotropic support dependent patient</td>
</tr>
<tr>
<td>Secondary progressive hepatic and/or renal failure</td>
</tr>
<tr>
<td>Increased left ventricular filling (post capillary wedge pressure ≥ 20 mmHg; systolic blood pressure 80-90 mmHg)</td>
</tr>
<tr>
<td>Cardiac index &lt;2 L/min/qm</td>
</tr>
<tr>
<td>Right ventricle dysfunction</td>
</tr>
<tr>
<td>Modified from ESC guidelines 2012 by McMurray et al. LVAD, left ventricular assist device.</td>
</tr>
</tbody>
</table>
The *Destination Therapy* SAGA

- Device technology continues to evolve
- Patient Survival is improving
- Many Device Complications remain
- Future clinical trials will identify those patients who benefit more from device therapy
The **Interagency Registry for Mechanically Assisted Circulatory Support** (Intermacs) is a North American registry established in 2005 for patients who are receiving mechanical circulatory support device therapy to treat advanced heart failure.

Intermacs was established as a joint effort of:

National Heart, Lung and Blood Institute (NHLBI),
Food and Drug Administration (FDA),
Centers for Medicare and Medicaid Services,
Clinicians,
Scientists,
Industry representatives.

*University of Alabama at Birmingham*

www.uab.edu/medicine/intermacs
## INTERMACS Profiles of Advanced Heart Failure: The Current Picture

Lynne Warner Stevenson, MD, Francis D. Pagani, MD, James B. Young, MD, Mariell Jessup, MD, Leslie Miller, MD, Robert L. Kormos, MD, David C. Naftel, PhD, Karen Ulisney, MSN, CRNP, Patrice Desvigne-Nickens, MD, and James K. Kirklin, MD

### Categorization of patients as per the indication of ventricular assist implantation according to the US-Based Interagency Registry for Mechanical Circulatory Support (INTERMACS)

<table>
<thead>
<tr>
<th>Level of Indication for VAD Implantation</th>
<th>Definition: Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>&quot;Crash and burn&quot;: patients with hypotension refractory to conventional treatments with signs of hypoperfusion of organs requiring implantation of a cardiocirculatory support system suitable within a few hours</td>
</tr>
<tr>
<td>Level 2</td>
<td>&quot;Sliding on inotropes&quot;: patients with worsening of cardiac function despite inotropic treatment, which require implantation of a cardiocirculatory support system within a few days</td>
</tr>
<tr>
<td>Level 3</td>
<td>&quot;Dependent stability&quot;: stable patients with intravenous inotropic support that cannot be discontinued, which require implantation of a cardiocirculatory support system within a few weeks</td>
</tr>
<tr>
<td>Level 4</td>
<td>&quot;Frequent flyer&quot;: patients requiring elective implantation of a cardiocirculatory assist device within months and before conventional treatment becomes inadequate to treat acute events with recovery of the underlying condition, including nutritional status</td>
</tr>
<tr>
<td>Level 5</td>
<td>&quot;Housebound&quot;: patients with limiting of everyday household activities. The &quot;timing&quot; appropriate for the implant is variable and depends on the maintenance of nutritional status, the function of organs, and the quality of life of the subject</td>
</tr>
<tr>
<td>Level 6</td>
<td>&quot;Walking wounded&quot;: asymptomatic patients capable of outdoor daily activities. The &quot;timing&quot; appropriate for the implant is variable and depends on the maintenance of nutritional status, organ function, and exercise tolerance</td>
</tr>
<tr>
<td>Level 7</td>
<td>&quot;Too well&quot;: clinically stable patients with medical therapy and only moderately limited physical activity. Support with a VAD is not indicated</td>
</tr>
</tbody>
</table>
Between June 23, 2006 and June 30, 2015, 161 hospitals participated in Intermacs and, of these, 156 hospitals actively contributed information on a total of 14746 patients. Cumulative patient accrual and the number of participating hospitals over this time period are displayed.
Intermacs - Implants per Year by Device Strategy
Primary Prospective Implants: June 23, 2006 to June 30, 2015

Number of Patients

Year


1. Approved Durable Devices

<table>
<thead>
<tr>
<th>Company</th>
<th>Device Brand List</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablomed, Inc.</td>
<td>AbioCor TAH</td>
<td>TAH</td>
</tr>
<tr>
<td>Berlin Heart, Inc.</td>
<td>Berlin Heart EXCOR Pediatric</td>
<td>L/R</td>
</tr>
<tr>
<td>Micromed Technology, Inc.</td>
<td>MicroMed DeBakey VAD – Child</td>
<td>L</td>
</tr>
<tr>
<td>SynCardia Systems, Inc.</td>
<td>SynCardia</td>
<td>TAH</td>
</tr>
<tr>
<td>Thoratec Corporation</td>
<td>HeartMate II LVAS</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td>HeartMate IP</td>
<td>L/R</td>
</tr>
<tr>
<td></td>
<td>HeartMate VE</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td>HeartMate XVE</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td>Thoratec IVAD</td>
<td>L/R</td>
</tr>
<tr>
<td></td>
<td>Thoratec PVAD</td>
<td>L/R</td>
</tr>
<tr>
<td>HeartWare, Inc.</td>
<td>NovaCor PC</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td>NovaCor PCq</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td>HeartWare HVAD</td>
<td>L/R</td>
</tr>
</tbody>
</table>

Legend:
- Bridge to Transplant - Listed
- Bridge to Candidacy
- Destination Therapy
- Bridge to Recovery
- Other
Intermacs - Kaplan-Meier Survival for Continuous Flow LVADs (with or without RVAD implant at time of LVAD operation) by Implant Era
Primary Prospective Implants: June 23, 2006 to June 30, 2015

Implant Era
- < 2010 (n = 1326, Deaths = 434)
- 2010-2011 (n = 3417, Deaths = 1358)
- 2012-2015 (Jan-Jun) (n = 8716, Deaths = 1944)

% Percent Survival

At Risk:
- 8716
- 3417
- 1326

3852
2019
630

1582
1430
371

1050
568
244

340
168
123

57
54
51
48
45
42
39
36
33
30
27
24
21
18
15
12
9
6
3
0

Months After Device Implant

Shaded areas indicate 70% confidence limits
p (log-rank) = 0.0739
Event: Death (censored at transplant or recovery)

Intermacs
Intermacs - Kaplan-Meier Survival for Continuous Flow LVADs (with or without RVAD implant at time of LVAD operation) by Pre-Implant Patient Profile

Primary Prospective Implants: June 23, 2006 to June 30, 2015

% Percent Survival

At Risk:

<table>
<thead>
<tr>
<th>Months After Device Implant</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>15</th>
<th>18</th>
<th>21</th>
<th>24</th>
<th>27</th>
<th>30</th>
<th>33</th>
<th>36</th>
<th>39</th>
<th>42</th>
<th>45</th>
<th>48</th>
<th>51</th>
<th>54</th>
<th>57</th>
<th>60</th>
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</thead>
<tbody>
<tr>
<td>Pre-Implant Patient Profile</td>
<td>Level 1 - Critical Cardiogenic (n = 2006, Deaths = 605)</td>
<td>574</td>
<td>1838</td>
<td>4005</td>
<td>4974</td>
<td>2006</td>
<td>855</td>
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<td>Level 2 - Progressive Decline (n = 4974, Deaths = 1457)</td>
<td>323</td>
<td>971</td>
<td>1976</td>
<td>425</td>
<td>195</td>
<td>225</td>
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<td>Level 3 - Stable but Inotrope (n = 4005, Deaths = 995)</td>
<td>522</td>
<td>1014</td>
<td>1219</td>
<td>225</td>
<td>465</td>
<td>225</td>
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<tr>
<td></td>
<td>Level 4 - Resting Symptoms (n = 1838, Deaths = 515)</td>
<td>113</td>
<td>245</td>
<td>586</td>
<td>110</td>
<td>272</td>
<td>60</td>
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</tr>
<tr>
<td></td>
<td>Levels 5, 6, 7 - All Others (n = 574, Deaths = 154)</td>
<td>39</td>
<td>110</td>
<td>205</td>
<td>39</td>
<td>110</td>
<td>30</td>
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</tr>
</tbody>
</table>

Shaded areas indicate 70% confidence limits
p (log-rank) = <.0001
Event: Death (censored at transplant or recovery)
Varying the rate can increase flow/output and change ventricular dimension and volume.
Varying the speed of the rotor can increase flow/output and change ventricular dimension and volume.
Main differences between ventricular assist devices (VAD) with pulsatile flow and VADs with continuous flow

Advantages of continuous-flow VADs versus pulsatile-flow VADs
Smaller dimensions (better compliance and easier implantation)
Simple structure with fewer moving parts (less risk of mechanical failure)
No filling chamber (less chance of stasis and thromboembolic events)
Reduced energy consumption (smaller batteries and greater autonomy)

Hypothetical disadvantages (with negative clinical implications – unproven)
A certain degree of hemolysis, usually well tolerated by patients
The long-term effects of systemic non-pulsatile flow are still not known
Control mechanisms (feedback) of the speed of the pump, and therefore, the flow generated are complex and not yet optimized
Heart Mate III (HM II) (Thoratec Inc. USA/St Jude)
Berlin Heart Incor (Berlin Heart AG, Germany)
DuraHeart (Terumo, USA)
HeartWare Ventricular Assist System (HeartWare Inc. USA)
HeartWare HVAD® System

- Miniaturized implantable blood pump
- Pericardial placement – no pump pocket
- Provides full support
- Centrifugal design, continuous flow
- Hybrid magnetic / hydrodynamic impeller suspension
- Optimizes flow, pump surface washing and hemocompatibility
- Thin, flexible driveline with fatigue resistant cables
Third-generation Blood Pumps With Mechanical Noncontact Magnetic Bearings

*Hideo Hoshi, †Tadahiko Shinshi, and *Setsuo Takatani

*Department of Artificial Organs, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Tokyo; and †Precision and Intelligence Laboratory, Tokyo Institute of Technology, Yokohama, Japan
Next Generation VADs
Heartmate III

- Fully Magnetically Levitated
- Large pump gaps designed to reduce blood trauma
- Artificial pulse
- Textured blood contacting surfaces
- Wide range of operation
- Full support (2 - 10 L/min)
- Advanced Design for Surgical Ease
HeartMate III: Full MagLev Technology

Key Design Benefits: Fluid Dynamics

- The HeartMate III rotor and volute have been designed to minimize shear and avoid stasis over the entire range of operation (2 to 10 L/min).
- The relatively large secondary flow paths facilitate smooth flow transitions, generous washing, and low shear.
- Impressively low hemolysis has been demonstrated in both in vitro and in vivo (plasma-free hemoglobin always <10 mg/dL) studies.

*In development. Not approved for sale.*
HeartMate III: Artificial Pulse

Key Potential Benefits

- Artificial Pulse
  - Full Magnetic Bearing permits sharp spectral changes and ability to implement an artificial pulse
  - Potential clinical advantages / reduced adverse events¹-⁴
    - Aortic insufficiency
    - Bleeding
    - Thrombosis & stroke

Clinical Study Protocol

- 5 US centers; 10 patients/center
- 1:1 Randomization between HMII vs HMIII
- No distinction between BTT or DT patients
- Inclusion Criteria
  - Age≥18 yrs; BSA >1.2 m²
  - NYHA Class IIIIB or 4; LVEF ≤25%
  - Inotrope dependent or CI<2.2 L/min/m² on OMM or IABP for 7 days

¹. Pantalos et al. Effect of continuous and pulsatile flow left ventricular assist on pulsatility in a pediatric animal model of left ventricular dysfunction: pilot observations. ASAIO 2007;53:385-91.

*In development. Not approved for sale.
Long Term Complications

- Infection (driveline, pump)
- CVAs
- Device Thrombosis
- Bleeding Acquired von Willebrand’s disease
- Aortic Insufficiency
- Right Heart Failure
- Line fractures/mechanical failure
# Right-ventricular failure following left ventricle assist device implantation

## The Interagency Registry for Mechanically Assisted Circulatory Support definition and severity scale of right-ventricular failure following left-ventricular assist device implantation

<table>
<thead>
<tr>
<th>INTERMAC</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic criteria for RV Failure</strong></td>
<td>Symptoms and signs of persistent right ventricular dysfunction, central venous pressure (CVP) &gt;18 mmHg with a cardiac index (CI) &lt;2.01/min.m²</td>
</tr>
<tr>
<td></td>
<td>In the absence of elevated left atrial/pulmonary capillary wedge pressure &gt;18 mmHg, tamponade, ventricular arrhythmias or pneumothorax</td>
</tr>
<tr>
<td></td>
<td>Requiring RVAD implantation; or requiring inhaled nitric oxide or inotropic therapy for duration of more than 1 week at any time after LVAD implantation.</td>
</tr>
</tbody>
</table>

## Severity scale

<table>
<thead>
<tr>
<th>Severity</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>Need for RVAD</td>
</tr>
<tr>
<td>Moderate</td>
<td>Need for inotrope or intravenous or inhaled pulmonary vasodilator (e.g. prostaglandin E or inhaled nitric oxide)</td>
</tr>
<tr>
<td>Mild</td>
<td>Meets 2 of the 4 clinical criteria listed below</td>
</tr>
<tr>
<td></td>
<td>• CVP &gt; 18 mmHg or mean RA pressure &gt; 18 mmHg</td>
</tr>
<tr>
<td></td>
<td>• CI &lt; 2.31/min/M² (using a pulmonary artery catheter)</td>
</tr>
<tr>
<td></td>
<td>• Ascites or evidence of moderate to worse peripheral edema</td>
</tr>
<tr>
<td></td>
<td>• Evidence of elevated CVP by echo (dilated inferior vena cava without collapse), physical exam (signs of increased jugular venous pressure)</td>
</tr>
</tbody>
</table>
In recent series using continuous flow devices the incidence of RVF is between 20 and 40%.

Evaluation of pre-operative risk factors for post-operative RHF.

Risk scoring systems:

**Matthews’ score**

**Fitzpatrick’s score**

**Drakos’ score**
Patient with end-stage heart failure requiring mechanical support

Assessment of risk for RV failure

High risk
- Consider TAH

Moderate
- Optimize HF and choose right timing of LVAD
- Consider periop inhaled pulmonary vasodilators or PDI
- Monitoring for RV dysfunction

Low
- Monitoring for RV dysfunction

Management of RV failure post LVAD

Intraoperative
- Short term RH bypass
- Consider inhaled pulmonary vasodilators
- If CI < 2.0 l/min/m² and CVP > 20 mmHg, consider temporary RVAD

Post-operative
- Consider inhaled pulmonary vasodilators
- Consider inotropic agents
- Change pump speed to optimize preload
- Cardioversion if in atrial arrhythmia
- Avoid autopeep and acidosis
- If CI < 2.0 l/min/m² and CVP > 20 mmHg, consider temporary RVAD (percutaneous or paracorporeal)
Intermacs - Competing Outcomes for Continuous Flow LVADs (without RVAD implant at time of LVAD operation)
Primary Prospective Implants: June 23, 2006 to June 30, 2015

- Alive (device still in place): 62.2%
- Death (before transplant): 19.1%
- Transplant: 17.8%
- Explanted (recovery): 0.7%

Months after Device Implant

Proportion of Patients
Intermacs - Competing Outcomes for Continuous Flow LVADs with RVAD implant at time of LVAD operation

Primary Prospective Implants: June 23, 2006 to June 30, 2015

- Alive (device still in place)
- Death (before transplant)
- Transplant
- Explanted (recovery)

Months after Device Implant:
- 0 months: 100%
- 12 months: 40.7%
- 24 months: 39.3%
- 36 months: 20.0%
- 48 months: 0.0%
Total Artificial Heart

It is mostly used as a “bridge to transplant”. The indications are reserved for patients waiting for a heart transplant for which any other type of assistance is excluded.
Find the appropriate time to discuss and evaluate preferences, compliance, prognosis, and medical options with your patients;

Periodical systematic “heart failure review” with HF-patients should include discussion of current and potential therapies for both anticipated and unanticipated events, in a multidisciplinary fashion;

Intercept HF progression, since a timely indication is the key to success!

Prof. Francesco Santini  
Divisione e Cattedra di Cardiochirurgia  
Università degli Studi di Genova  
francesco.santini@unige.it