



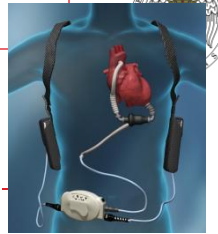
HIPERTENSIÓN PULMONAR EN LA INSUFICIENCIA CARDÍACA AVANZADA

Opciones terapéuticas

Dra. Bravo

HGUGM 2011





IC AVANZADA

- ▶ IC: síndrome clínico de rango epidémico en Occidente.
- ▶ Prev 10.000/millón hab, 10% de los >65 años. 1º causa de ingreso >65 años. Causa de mortalidad similar a Ca en España.
- ▶ **IC avanzada:** NYHA III-IV a pesar de tto óptimo con IECA/ARAII, BB, espironolactona, diuréticos y digoxina. IC terminal si 50% mortalidad a 6 meses.
- ▶ Candidatos a alternativas especializadas: DAI-TRC, inotrópicos, asistencia circulatoria, TxC.



TRASPLANTE CARDÍACO

- ▶ Tratamiento de elección de la IC en pacientes sin más opciones médicas/quirúrgicas.
- ▶ Aporta la mayor supervivencia a largo plazo en poblaciones muy seleccionadas. 85% a 1 año, 73% a 5 años.

TABLA 1. Indicaciones para trasplante cardiaco. ACC/AHA Practice Guidelines, 2005

I. Indicaciones absolutas:

Por compromiso hemodinámico debido a insuficiencia cardiaca

Shock cardiogénico resistente

Dependencia demostrada de soporte inotrópico intravenoso para mantener la perfusión adecuada de los órganos

$VO_{2max} < 10$ ml/kg/min habiendo alcanzado el umbral anaeróbico

Isquemia miocárdica severa con limitación de la actividad habitual y no susceptible de cirugía de revascularización o angioplastia percutánea

Arritmias ventriculares sintomáticas recurrentes resistentes a todas las modalidades terapéuticas

II. Indicaciones relativas:

VO_{2max} entre 11 y 14 ml/kg/min (o el 55% del previsto) y limitación importante de la actividad funcional

Isquemia inestable y recurrente no susceptible de otra intervención

Inestabilidad recurrente del equilibrio hídrico/función renal no debida a incumplimiento del régimen terapéutico

III. Indicaciones insuficientes:

Baja fracción de eyección del ventrículo izquierdo

Historia previa de clase funcional III o IV de la NYHA

Arritmias ventriculares previas

$VO_{2max} > 15$ ml/kg/min (mayor del 55% del previsto) sin otras indicaciones

ACC: American College of Cardiology; AHA: American Heart Association; NYHA: New York Heart Association; VO_{2max} : consumo máximo de oxígeno obtenido en ergometría con análisis de intercambio de gases.



TABLA 3. Factores de riesgo asociados a mayores morbilidad y mortalidad para trasplante cardiaco

Contraindicaciones absolutas

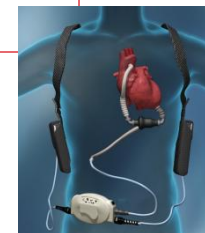
- Enfermedades sistémicas concomitantes con mal pronóstico
- Neoplasias malignas con posibilidades de recidiva
- Diabetes mellitus con afección orgánica (retinopatía, nefropatía o neuropatía)
- Enfermedad aterosclerótica severa cerebral o vascular periférica
- Hipertensión arterial pulmonar severa e irreversible
- Enfermedad pulmonar severa ($FEV_1 < 40\%$; $CVF < 50\%$)
- Infección activa no controlada
- Enfermedad ulcerosa y diverticular activas
- Muy alto riesgo de falta de cumplimiento terapéutico por motivos psiquiátricos, psicosociales o de abuso de drogas
- Edad biológica avanzada con una expectativa de vida menor de 5 años con independencia de su cardiopatía

Contraindicaciones relativas mayores

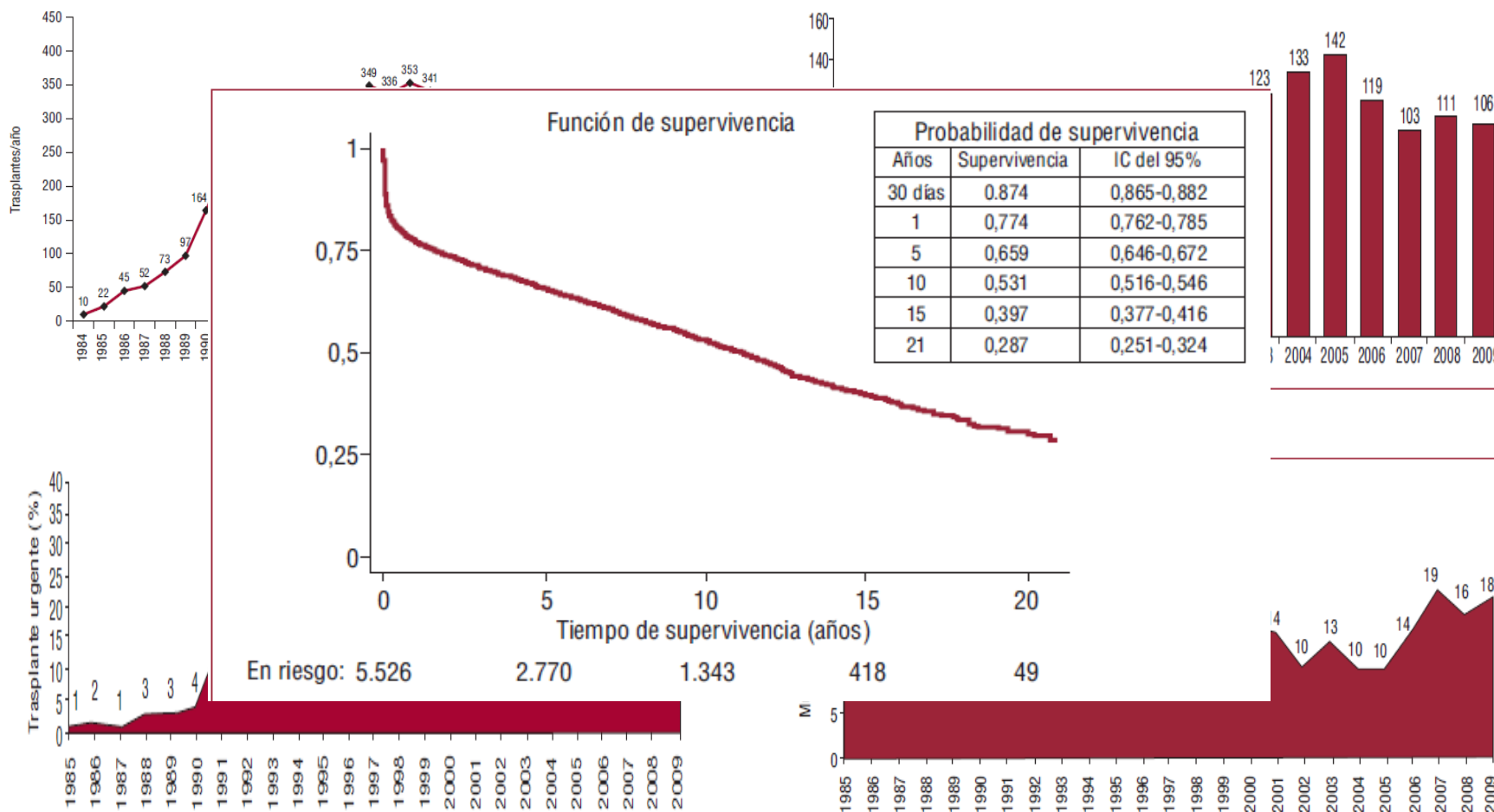
- Peso $> 150\%$ del peso ideal
- Virus de la inmunodeficiencia humana positivo
- Diabetes mellitus sin afección orgánica (retinopatía, nefropatía o neuropatía)
- Enfermedad aterosclerótica ligera-moderada cerebral o vascular periférica
- VHC de alto riesgo
- Insuficiencia renal en hemodiálisis (posibilidad de trasplante combinado)
- Cirrosis (posibilidad de trasplante combinado)
- Edad biológica > 65 años

Contraindicaciones relativas menores

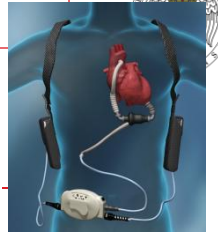
- Peso del 120 al 150% del peso ideal
- Neoplasias con baja probabilidad de recidiva
- Osteoporosis
- Enfermedad pulmonar no severa ($FEV_1 > 40\%$ del predicho; $CVF > 50\%$ del normal)
- VHC o VHB de bajo riesgo
- Afección renal no severa sin hemodiálisis
- Afección hepática no severa sin cirrosis
- Riesgo de falta de cumplimiento terapéutico por motivos psiquiátricos, psicosociales o de abuso previo de drogas
- Abuso de tabaco y/o de alcohol



IC AVANZADA



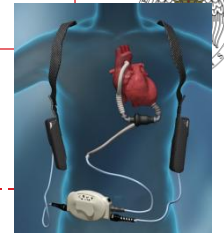
HTP EN IC AVANZADA



- ▶ 60% de IC sistólica y 70% de IC diastólica.
- ▶ Def.: PAPM > 25 mmHg y PCP > 15 mmHg.
- ▶ HTP pasiva (GTP < 12) → reactiva reversible (VD) → reactiva fija.
- ▶ Disf diastólica + valvulop. mitral + remodelado AI → daño endotelial → ↓ NO y ↑ ET.
- ▶ Implicaciones funcionales (postcarga VD en ejercicio, ventilación ineficiente, hiperpnea).
- ▶ Variable independiente de mortalidad (disf VD).



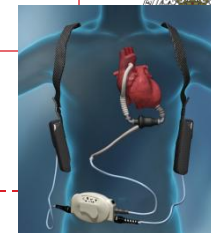
TRATAMIENTO DE LA HTP EN IC AVANZADA



1. **TRATAMIENTO DE LA IC** (fármacos, TRC, inotrópicos).

2. **VASODILADORES PULMONARES “selectivos”:**

- PGs: ↑ mortalidad (estudio FIRST).
- NO inh.: ↑ PCP. Más útil para tratar IC dcha postCCV.
- **Bosentan** y otros ARE: no mejoran síntomas/px (RITZ, REACH-1, ENABLE, EARTH, ...) ¿?
- **Sildenafil**: ↓ PAPM y RVP, PCP=. Mejora síntomas.



TRATAMIENTO DE LA HTP EN IC AVANZADA

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The Effects of Phosphodiesterase-5 Inhibition
With Sildenafil on Pulmonary Hemodynamics and
Diffusion Capacity, Exercise Ventilatory Efficiency,
and Oxygen Uptake Kinetics in Chronic Heart Failure

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Cesare Fiorentini, MD,* Maurizio D. Guazzi, MD, PhD‡

Milan, Italy

modo DVI variable

-CF II-III

-Bien tratados

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart
Association® 
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Sildenafil Improves Exercise Capacity and Quality of Life in Patients With
Systolic Heart Failure and Secondary Pulmonary Hypertension

Gregory D. Lewis, Ravi Shah, Khurram Shahzad, Janice M. Camuso, Paul P.
Pappagianopoulos, Judy Hung, Ahmed Tawakol, Robert E. Gerszten, David M.
Systrom, Kenneth D. Bloch and Marc J. Semigran

Circulation 2007;116:1555-1562; originally published online Sep 4, 2007;

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Heart Failure

**Long-Term Use of Sildenafil
in the Therapeutic Management of Heart Failure**

Marco Guazzi, MD, PhD, FACC,* Michele Samaja, PhD,† Ross Arena, PhD,‡ Marco Vicenzi, MD,*
Maurizio D. Guazzi, MD, PhD, FESC§

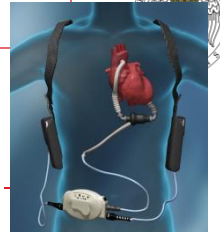
Milan, Italy; and Richmond, Virginia

Mejoría P y síntomas

No descompensación IC

No datos de supervivencia

TRATAMIENTO DE LA HTP EN IC AVANZADA



3. PACIENTE PRETRASPLANTE: la HTP es factor de **morbimortalidad posTxC** (disfunción VD). **Riesgo** si $GTP > 12$ y $RVP > 2.5uW$ tras prueba de VD.

- *Test vasodilatador* si $GTP \text{ basal} > 15$ o $RVP > 3uW$.
- Asegurar $PCP < 25$ durante/después del test y $TAS > 85\text{mmHg}$.
- “*Condicionamiento vasodilatador*”:
inotrópicos+vasodilatadores, hasta test +.
- La HTP reversible continúa teniendo riesgo: protección VD posTxC.



TRATAMIENTO DE LA HTP EN IC

3. PACIENTE PRETRASPLANTE: AVANZADA

RVP > 5, GTP > 16-20, PSAP > 60 → Contraindicación relativa.

Class IIb:

1. If medical therapy fails to achieve acceptable hemodynamics and, if the left ventricle cannot be effectively unloaded with mechanical adjuncts, including an ~~intra-aortic balloon pump (IABP)~~ and/or left ventricular assist device (LVAD), it is reasonable to conclude that the pulmonary hypertension is irreversible (*Level of Evidence: C*).



IC AVANZADA Y ASISTENCIAS

ASISTENCIA VENTRICULAR

- Años 60: Programa corazón artificial (NHLBI), 1ª asistencia postcardiotomía eficaz (**punte a la recuperación**).
- Años 70: 1ª asistencia **punte a trasplante** (corto plazo).
- Años 80: 1ª “ ” “ (largo plazo).
- Años 90: paciente ambulatorio.
- 2001: REMATCH, **terapia definitiva**.
- Año 2011: **punte a la decisión**.



IC AVANZADA Y ASISTENCIAS

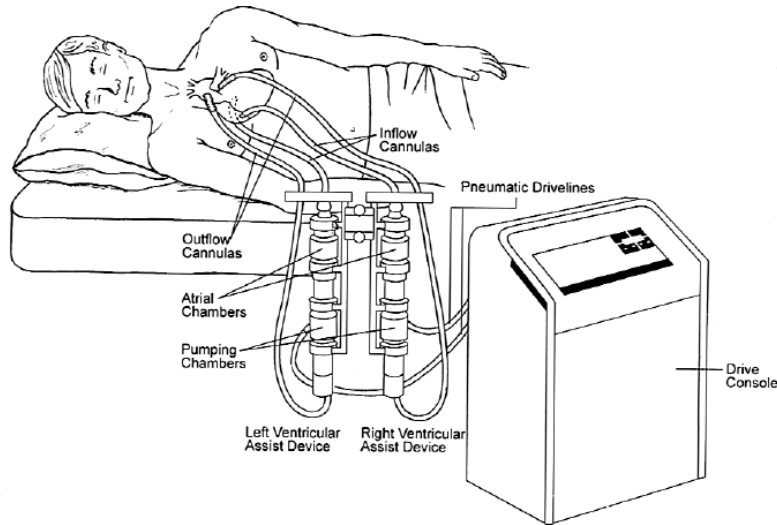
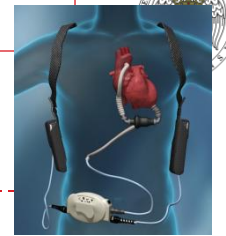


Fig. 7 ABIOMED BVS 5000® circulatory support system. (Courtesy of Texas Heart Institute)

- ✓ Corto-largo plazo.
- ✓ Pulsátil-continua.
- ✓ Bi-univentriculares.

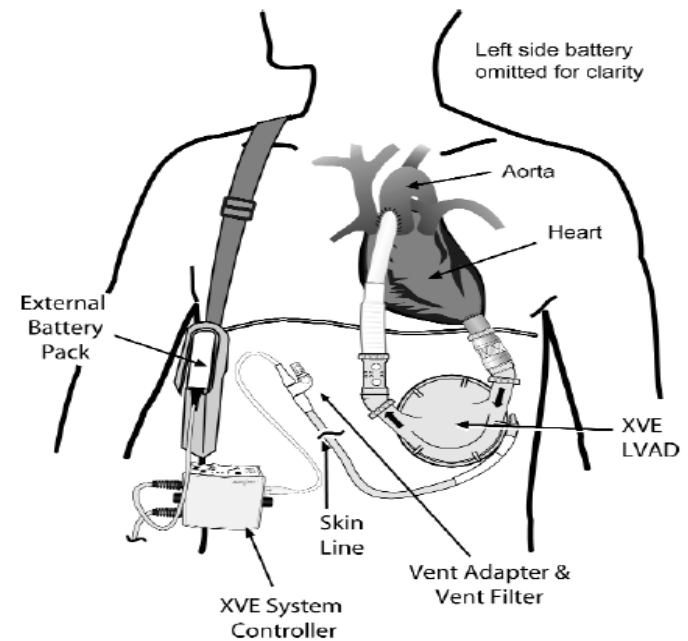
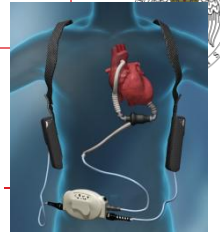


Fig. 2 HeartMate® extended vented electric (XVE) left ventricular assist system. (Courtesy of Texas Heart Institute)



IC AVANZADA Y ASISTENCIAS

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NUMBER 20



LONG-TERM USE OF A LEFT VENTRICULAR ASSIST DEVICE
FOR END-STAGE HEART FAILURE

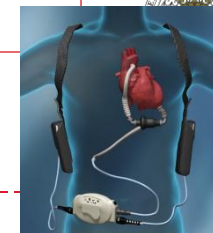
ERIC A. ROSE, M.D., ANNETINE C. GELJINS, PH.D., ALAN J. MOSKOWITZ, M.D., DANIEL F. HEITJAN, PH.D.,
LYNNE W. STEVENSON, M.D., WALTER DEMBITSKY, M.D., JAMES W. LONG, M.D., PH.D., DEBORAH D. ASCHEIM, M.D.,
ANITA R. TIERNEY, M.P.H., RONALD G. LEVITAN, M.Sc., JOHN T. WATSON, PH.D., AND PAUL MEIER, PH.D.,
FOR THE RANDOMIZED EVALUATION OF MECHANICAL ASSISTANCE FOR THE TREATMENT OF CONGESTIVE HEART FAILURE
(REMATCH) STUDY GROUP*

pacientes con IC terminal,
no transplantables.

-Aleatorizados a asistencia vs
tto médico óptimo.

- ▶ **Supervivencia Asistencia: 2x tto médico a 1 año (52% vs 25%); 23% vs 8 % a 2 años.**
- ▶ Mejoría más marcada en pacientes en tto inotrópico.
- ▶ Complicaciones Asistencia: 2x tto médico (pero mejor calidad de vida).
- ▶ Complicaciones: sepsis, sangrado, ictus, disfunción VD.

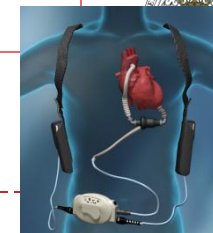




IC AVANZADA Y ASISTENCIAS

TABLE 2. What Is Meaningful Benefit in End-Stage Disease?

| Study (Therapy) | | Control vs Therapy, % of patients | Relative Benefit, % | Absolute Benefit (Year 1 = No. Patients/100) | | |
|---------------------------------------|---|-----------------------------------|---------------------|--|------|-----------------|
| TABLE 1. Profiles of Severe HF | | | | | | |
| SOLVD (ACE inhibitor) ²³ | | | | | | |
| | COI Mortality at 1 y | 14 vs 11 | 21 | 3 | Tx I | REMATCH Medical |
| Age, y | Survival at 1 y | 86 vs 89 | 3 | | 51 | 68 |
| SBP, mm Hg | CONSENSUS (ACE inhibitor) ²² | | | | † | 103 |
| LVEF, % | Mortality at 1 y | 62 vs 45 | 27 | 17 | 17 | 17 |
| Sodium, meq/L | Survival at 1 y | 38 vs 55 | 45 | | 135 | 135 |
| Creatinine, mg/dL | COPERNICUS (β-blocker) ⁶ | | | | | |
| Mortality at 6 mo, % | Mortality at 1 y | 18.5 vs 11 | 41 | 7.5 | 1.4 | 1.8 |
| | Survival at 1 y | 81.5 vs 89 | 10 | | 40† | 48 |
| | RALES (spironolactone) ¹⁵ | | | | | |
| | Mortality at 1 y | 25 vs 17 | 32 | 8 | | |
| | Survival at 1 y | 75 vs 83 | 11 | | | |
| | <u>REMATCH-inotropic (LVAD)</u> | | | | | |
| | Mortality at 1 y | 76 vs 51 | 37 | 25 | | |
| | Survival at 1 y | 24 vs 49 | 104 | | | |

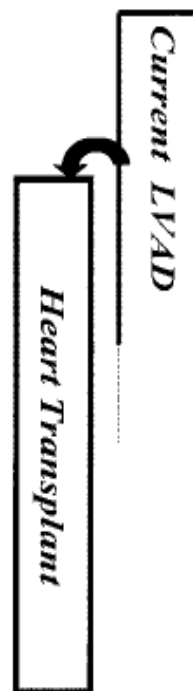


IC AVANZADA Y ASISTENCIAS

ASISTENCIAS: PARA QUIÉN Y CUÁNDO

Potential Populations for Support

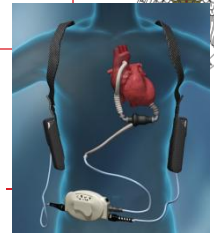
- Acute cardiogenic shock
- Chronic CHF into low output state with organ dysfunction
- CHF Class IV inotrope-dependent
- CHF IV ACEI-intolerant due to symptomatic hypotension or progressive renal dysfunction
- Class IV on ACEI therapy
Plus additional risk factors, e.g.
 - Cachexia
 - Peak oxygen uptake < 10 ml/kg/min
 - Hyponatremia
 - Progressive renal dysfunction
- CHF IV on oral therapy including ACEI
- Class IV stabilized to Class III



Estimated 50% Mortality

- Imminent
1 month, without reversible factors
- 3-6 months
- About 6 months
- ? 6-12 months
- ± 12 months
- > 24 months

Definition of heart failure populations with decreasing estimated mortality. As cardiac transplantation is associated with <20% 1-year mortality and ≈50% 10-year survival, survival benefit is anticipated even in the absence of imminent mortality. Benefit of LVAD for bridging to transplantation is accepted. Initial data on LVAD as permanent “destination” therapy demonstrate survival benefit in patients with 6-month mortality in the range of 50%. Improving results with assist devices will expand the population in whom benefit is expected.



ESCALA INTERMACS

| Patient Profile† | Patient Characteristics | Time Frame Until Intervention |
|------------------|--|---|
| 1 | Critical cardiogenic shock despite escalating support | Within a few hours |
| 2 | Progressive decline with inotrope dependence | Within a few days |
| 3 | Clinically stable with mild to moderate inotrope dependence | Elective implantation over the next few weeks |
| 4 | Recurrent, not refractory, advanced heart failure that can be stabilized with intervention | Elective implantation over weeks to months |
| 5 | Exertion intolerant but is comfortable at rest and able to perform activities of daily living with slight difficulty | Variable; depends on nutrition, organ function, and activity |
| 6 | Exertion limited; is able to perform mild activity, but fatigue results within a few minutes of any meaningful physical exertion | Variable, depends on nutrition, organ function, and activity |
| 7 | Advanced NYHA functional class III | At this time, mechanical circulatory support is not indicated |

NYHA indicates New York Heart Association.

*Adapted from Stevenson et al.¹⁵

†Arrhythmia modifier (A), recurrent ventricular tachyarrhythmias (may be added to any INTERMACS level except 7).

▶ Score predictor de supervivencia y complicaciones.



REGISTRO INTERMACS

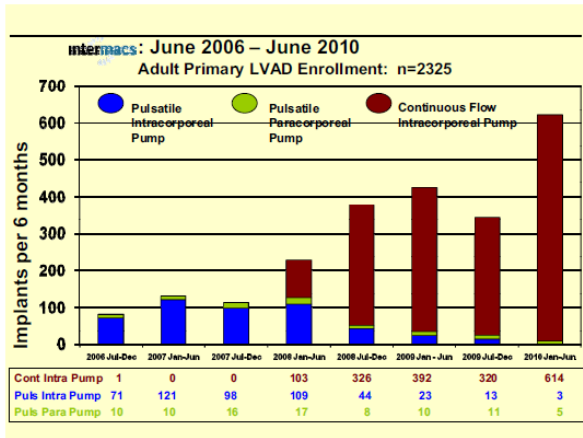


Table 2 Strategy for Device Implant—Adult Primary Implants: INTERMACS, June 2006–June 2010

| Strategy | Jun 2006–Jun 2010 No. (%) (N = 2,680) |
|------------------------------|---|
| Bridge to transplant, listed | 1,161 (43.3) |
| Bridge to candidacy | 1,131 (42.2) |
| Likely | 759 (28.3) |
| Moderate | 280 (0.4) |
| Unlikely | 92 (3.4) |
| Destination therapy | 309 (11.5) |
| Bridge to recovery | 48 (1.8) |
| Rescue therapy | 22 (0.8) |
| Other | 9 (0.3) |
| Total | 2,680 (100) |

INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

Table 7 Transplant Contraindications—Adult Primary Implants: INTERMACS, June 2006–June 2010

| Contraindications | No. (%) (N = 385) |
|-----------------------------------|----------------------|
| Modifiable | |
| Renal dysfunction | 86 (22) |
| High body mass index | 62 (16) |
| Pulmonary hypertension | 45 (12) |
| Still smoking | 27 (7) |
| Limited social support | 20 (5) |
| Severe diabetes | 20 (5) |
| Repeated non-compliance | 16 (4) |
| Illicit drug use | 14 (4) |
| Alcohol abuse | 13 (3) |
| Patient refuses transplant | 11 (3) |
| Limited cognition/understanding | 8 (2) |
| Contraindication to immunotherapy | 7 (2) |
| Risk of recurrent infection | 5 (1) |
| Severe depression | 4 (1) |
| Current infection | 3 (1) |
| Malnutrition/cachexia | 3 (1) |
| Musculoskeletal limitations | 3 (1) |

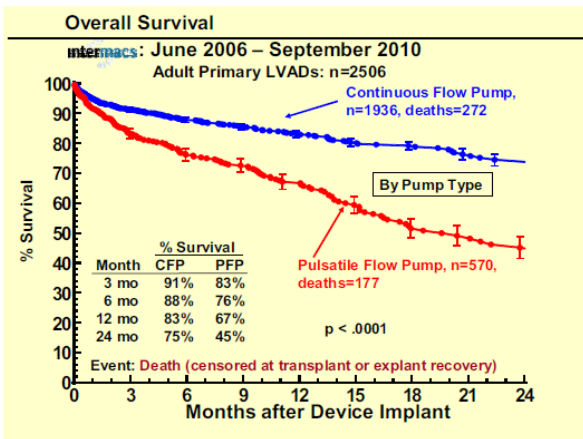


Table 4 Patient Profile Level—Adult Primary Implants: INTERMACS, June 2006–June 2010

| Level | June 2006–Dec 2008 No. (%) (N = 1,138) | Jan 2009–June 2010 No. (%) (N = 1,542) |
|----------------------------------|--|--|
| 1. Critical cardiogenic shock | 395 (34.7) | 267 (17.3) |
| 2. Progressive decline | 457 (40.2) | 697 (45.2) |
| 3. Stable but inotrope-dependent | 148 (13.0) | 300 (19.5) |
| 4. Recurrent advanced HF | 96 (8.4) | 178 (11.5) |
| 5. Exertion intolerant | 15 (1.3) | 51 (3.3) |
| 6. Exertion limited | 11 (1.0) | 32 (2.1) |
| 7. Advanced NYHA class III | 16 (1.4) | 17 (1.1) |
| Total | 1,138 (100) | 1,542 (100) |

HF, heart failure; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; NYHA, New York Heart Association. $P < 0.0001$.



IC AVANZADA Y ASISTENCIAS

CLINICAL HEART TRANSPLANTATION

Improved Survival After Heart Transplantation in Patients With Bridge to Transplant in the Recent Era: A 17-year Single-center Experience

Satoru Osaki, MD, PhD,^a Niloo M. Edwards, MD,^a Maryl R. Johnson, MD,^b Mauricio Velez, MD,^b Alejandro Munoz, PhD,^a Lucian Lozonschi, MD,^a Margaret A. Murray, MSN,^a Amy K. Proebstle, RN, BSN,^a and Takushi Kohmoto, MD, PhD^a

Conclusions: Post-transplant survival has improved in recent BTT patients. Indeed, recent outcome for OHT after BTT has become equivalent to that for OHT without VAD. These data suggest that advances in device technology and our institutional multidisciplinary program have improved survival and allow BTT candidates to have an outcome equivalent to that of non-VAD patients in the recent era. *J Heart Lung Transplant* 2009;28:591-7. Copyright © 2009 by the International Society for Heart and Lung Transplantation.





TRATAMIENTO DE LA HTP EN IC AVANZADA



-Asistencia en pac con y sin HTP

The Journal of Heart and Lung Transplantation
<http://www.jhltonline.org>

-Normalización P pre y postTxC

- Superv postTxC igual

-Disfunción VD igual

-Pac HTP: + tto vasodilatador

Impact of fixed pulmonary hypertension on post-heart transplant outcomes in bridge-to-transplant patients

Ana Carolina Alba, MD,^a Vivek Rao, MD, PhD,^a Heather J. Ross, MD, MHSc,^a Annette S. Jensen, MD,^b Kaare Sander, MD, DMSc,^b Finn Gustafsson, MD, PhD,^b and Diego H. Delgado, MD^a

From the ^aDivision of Cardiology and Heart Transplantation, University Health Network, Toronto, Ontario, Canada; and ^bThe Heart Centre, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark.

556. EXPERIENCIA INICIAL CON ASISTENCIA VENTRICULAR ELECTIVA COMO ESTRATEGIA PREVIA AL TRASPLANTE CARDIACO

Manuel Gómez Bueno, M^a Dolores García-Cosío Carmena, Javier Segovia Cubero, Patricia Mabel Avellana, Elena Pérez Pereira, Santiago Serrano Fiz García, Juan Ugarte Basterrechea, Luis Alonso-Pulpón, Unidad de Trasplantes Cardiacos del Hospital Universitario Puerta de Hierro, Majadahonda (Madrid).



MECHANICAL CIRCULATORY SUPPORT

Right Heart Failure After Left Ventricular Assist Device Implantation in Patients With Chronic Congestive Heart Failure

Nicholas C. Dang, MD, Veli K. Topkara, MD, Michelle Mercado, BS, Joy Kay, BS, Kurt H. Kruger, ScB, Michael S. Aboodi, Mehmet C. Oz, MD, and Yoshifumi Naka, MD, PhD

*Fallo D en 15-20% asistencias

*Distorsión VD+citocinas

* >mort periopx; <tasa TxC

* Mujeres; PVC elevada intraopx





CONCLUSIONES

- ▶ La insuficiencia cardíaca es una de las principales causas de morbimortalidad en los países desarrollados.
- ▶ Disponemos de armas terapéuticas que aumentan la esperanza y calidad de vida, debido a lo cual vez es mayor la proporción de pacientes que llega a la fase terminal de la enfermedad.
- ▶ El trasplante cardíaco continúa siendo el tratamiento con mejores resultados a corto y largo plazo en pacientes seleccionados.
- ▶ La hipertensión pulmonar secundaria a insuficiencia cardíaca es una condición de aparición frecuente, con implicaciones funcionales y pronósticas negativas. Los tratamientos farmacológicos en desarrollo aún no han mostrado un perfil favorable de eficacia.
- ▶ Los dispositivos de asistencia ventricular están en camino de convertirse en una opción terapéutica real para pacientes con IC avanzada, ofreciendo una clara ventaja frente al tratamiento farmacológico a corto plazo.





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