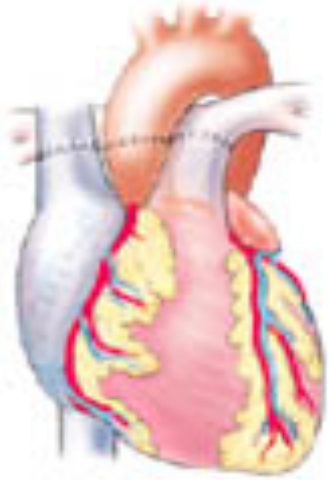
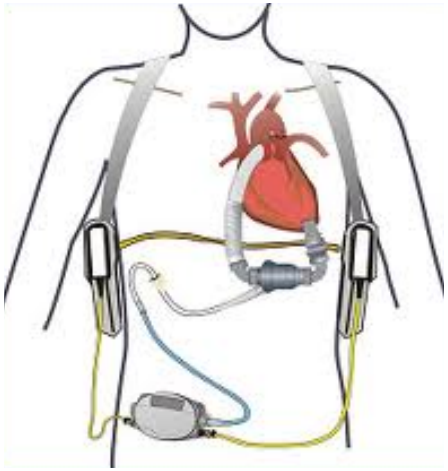
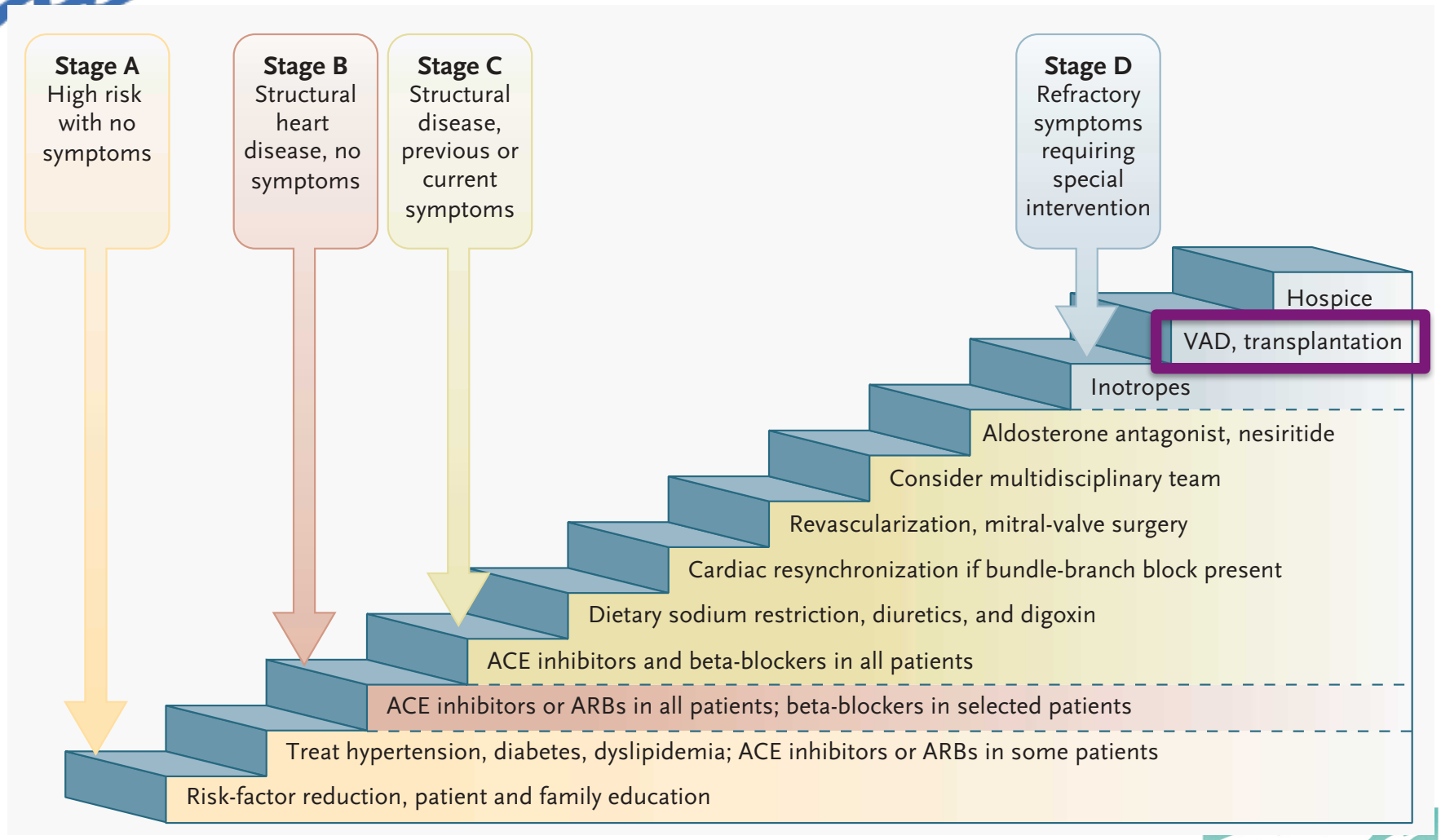
HEART TRANSPLANT AND VADs

CANDIDATE SELECTION



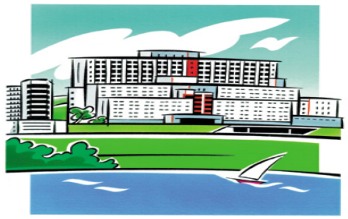



Stage A
High risk with no symptoms
Stage B
Structural heart disease, no symptoms
Stage C
Structural disease, previous or current symptoms
Stage D
Refractory symptoms requiring special intervention
Hospice
VAD, transplantation
Inotropes
Aldosterone antagonist, nesiritide
Consider multidisciplinary team
Revascularization, mitral-valve surgery
Cardiac resynchronization if bundle-branch block present
Dietary sodium restriction, diuretics, and digoxin
ACE inhibitors and beta-blockers in all patients
ACE inhibitors or ARBs in all patients; beta-blockers in selected patients
Treat hypertension, diabetes, dyslipidemia; ACE inhibitors or ARBs in some patients
Risk-factor reduction, patient and family education

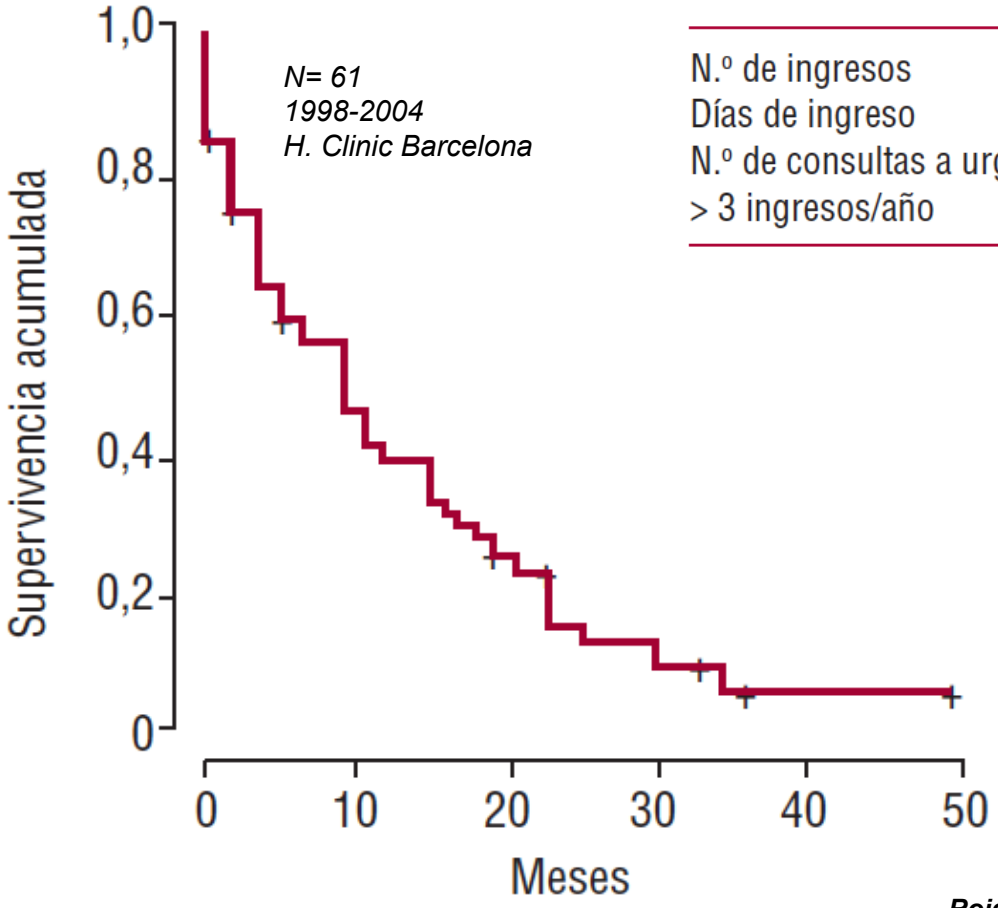
REFRACTORY HF (STAGE D)

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 [5];
   c) High LV filling pressures (mean PCWP > 16 mm Hg, and/or mean RAP > 12 mm Hg by pulmonary artery catheterisation) [6],
   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 [7] or less in females and/or patients aged ≥ 75 years [8]
   c) peak VO_2 < 12 to 14 ml/kg/min [9,10]
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.

Metra M. Eur J Heart Fail 2007.



REFRACTORY HF (STAGE D)



	Antes del PAE	Después del PAE
N.º de ingresos	5,7 ± 0,5	1,9 ± 0,2
Días de ingreso	53 ± 5	19 ± 3
N.º de consultas a urgencias	8,3 ± 1,1	1,2 ± 0,2
> 3 ingresos/año	42 (69%)	7 (11%)

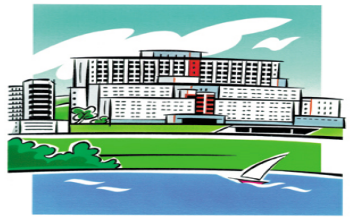
HIGH MORTALITY

POOR QoL

HIGH READMISSION RATES

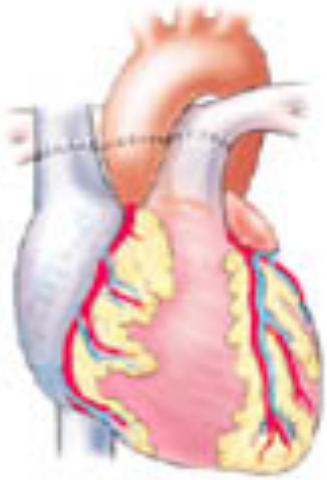
HIGH COSTS

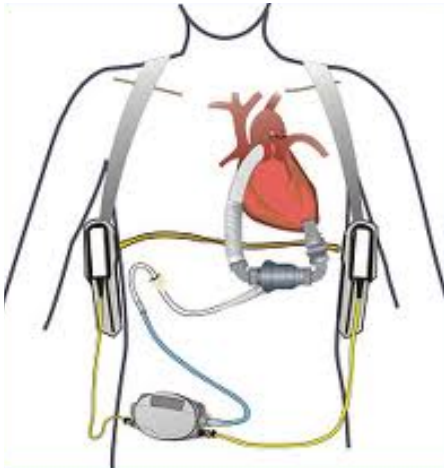
Roig E. Rev Esp Cardiol 2006.



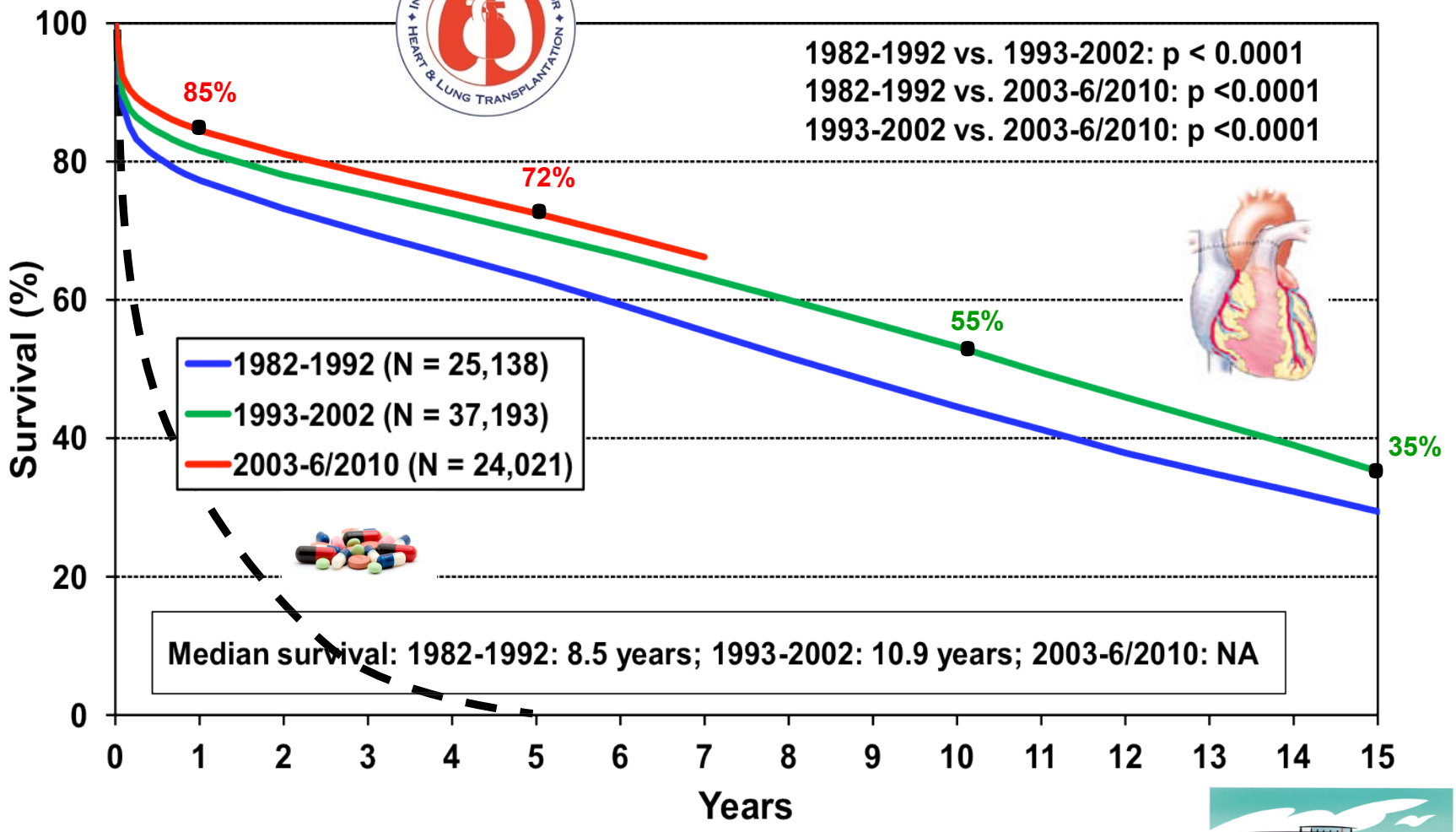
HEART TRANSPLANT AND VADs

OUTCOMES

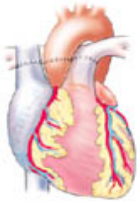




POST-TRANSPLANT SURVIVAL

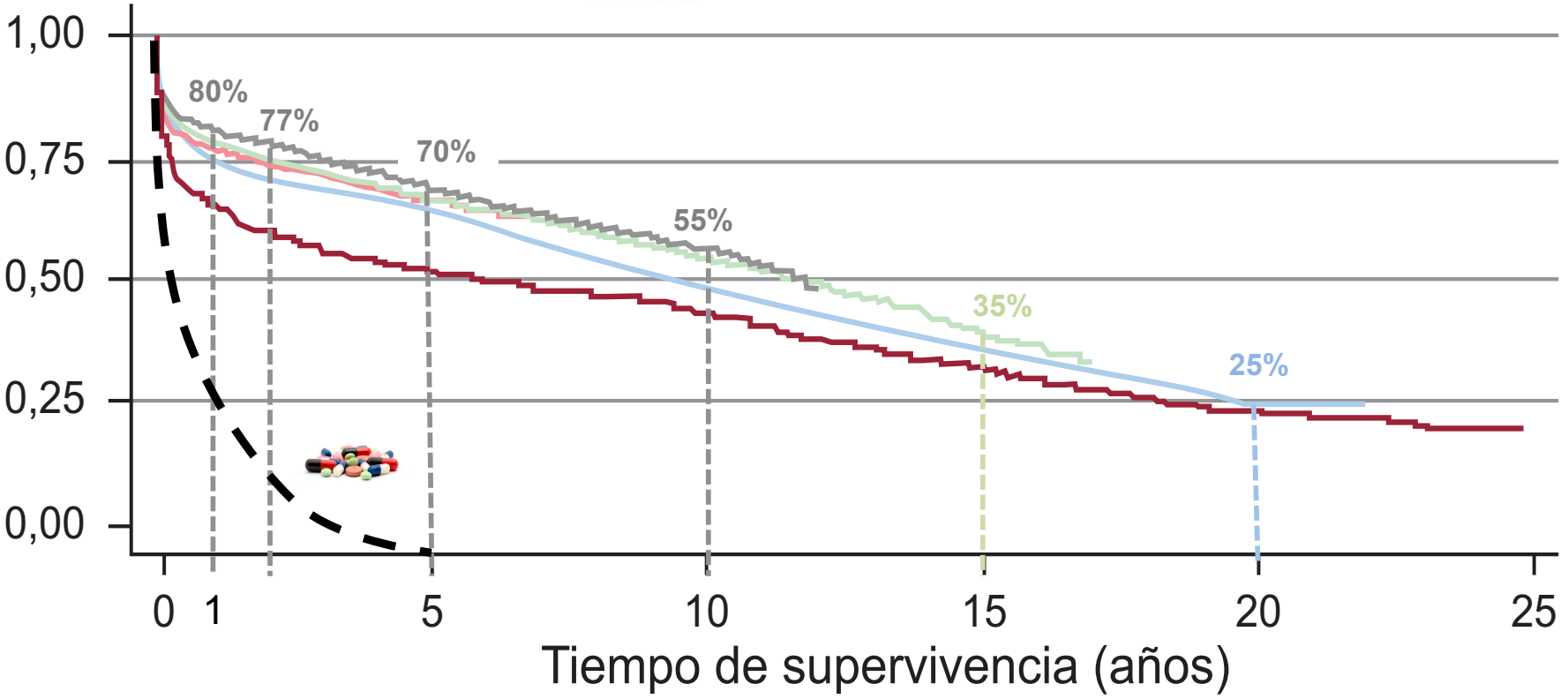


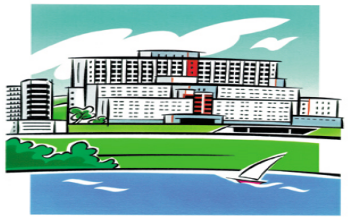
POST-TRANSPLANT SURVIVAL



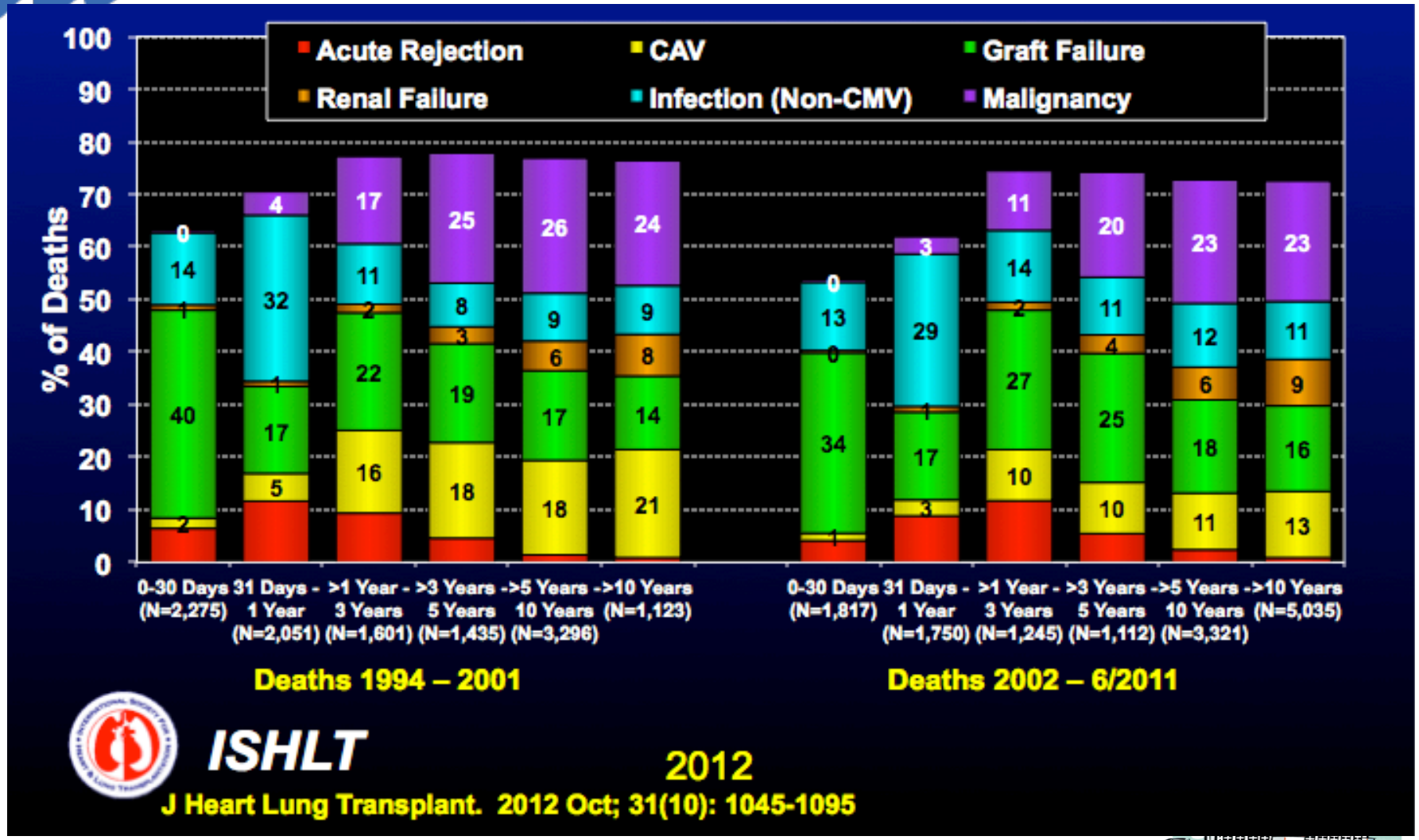
SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA

Sección de Insuficiencia Cardiaca y Trasplante

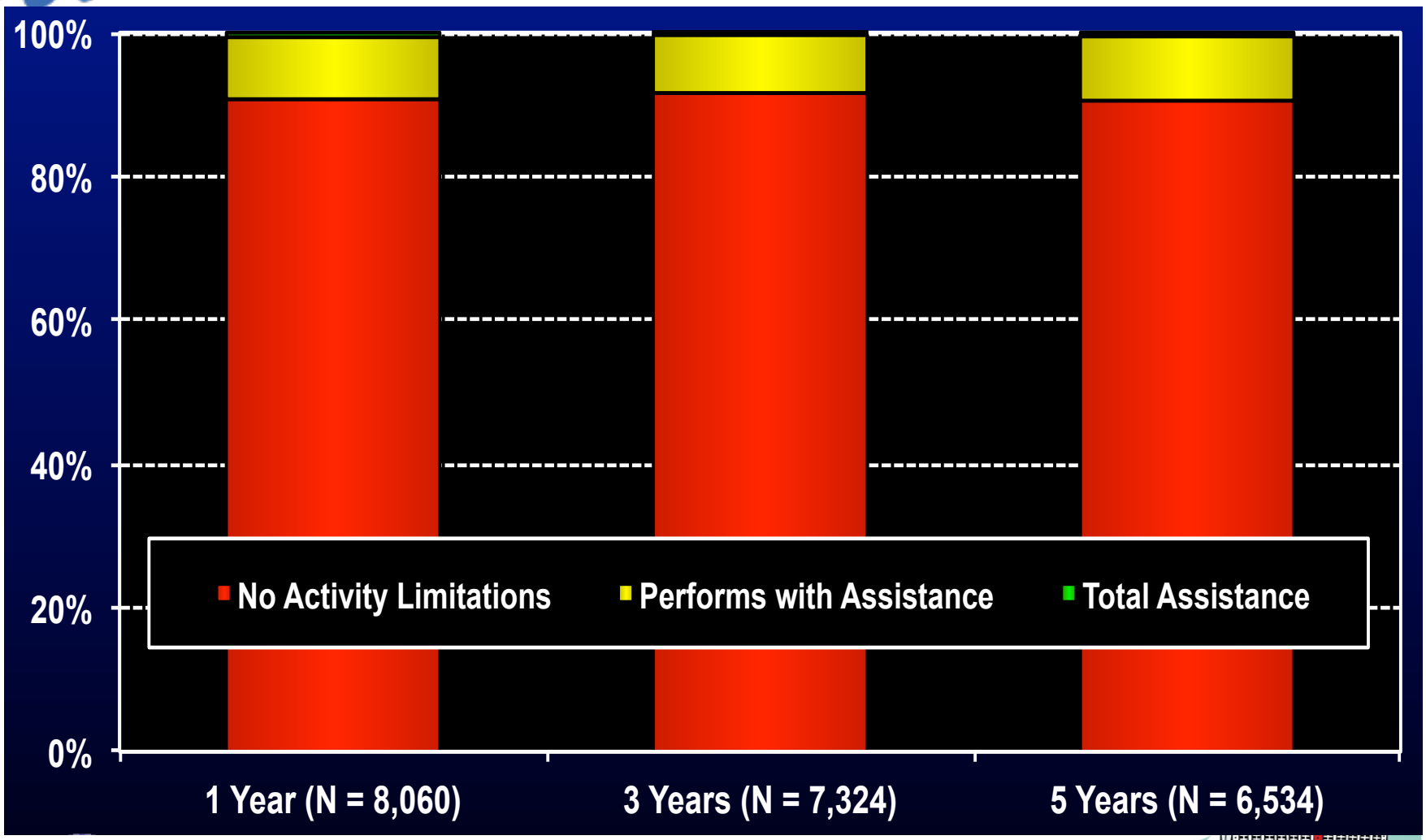




POST-TRANSPLANT COMPLICATIONS

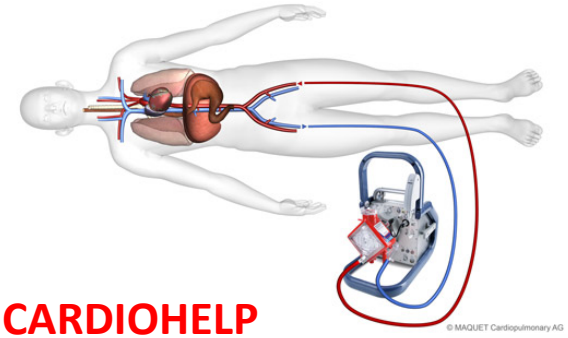


POST-TRANSPLANT QoL



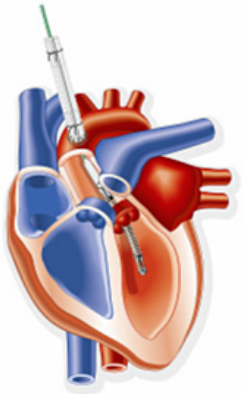
MECHANICAL CIRCULATORY SUPPORT

SHORT-TERM
(EXTRACORPOREAL)



CARDIOHELP

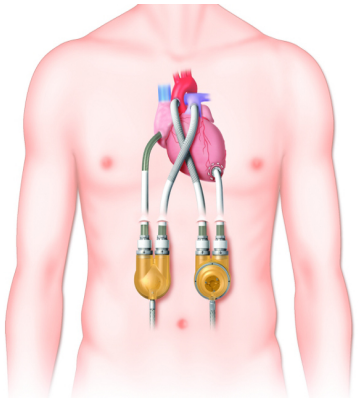
CENTRIMAG



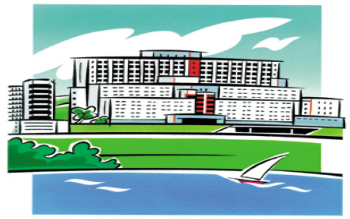
IMPELLA

MID-TERM
(PARACORPOREAL)

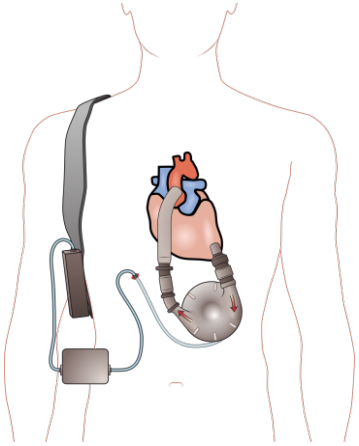
EXCOR



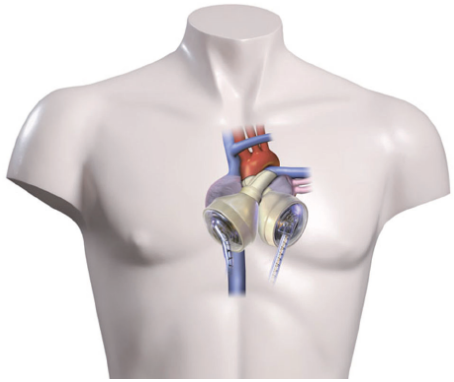
PVAD



PULSATILE FLOW

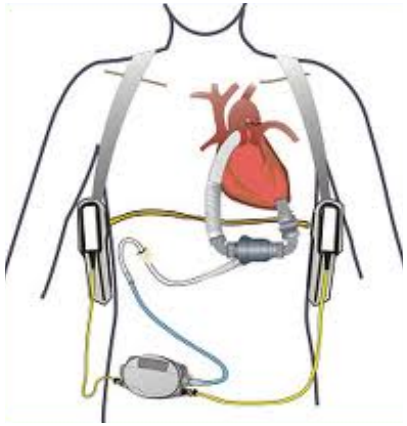


HEARTMATE XVE



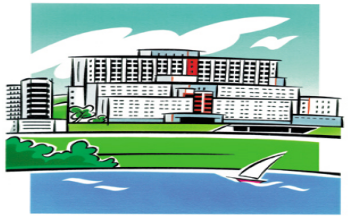
SYNCARDIA

CONTINUOUS FLOW



HEARTMATE 2

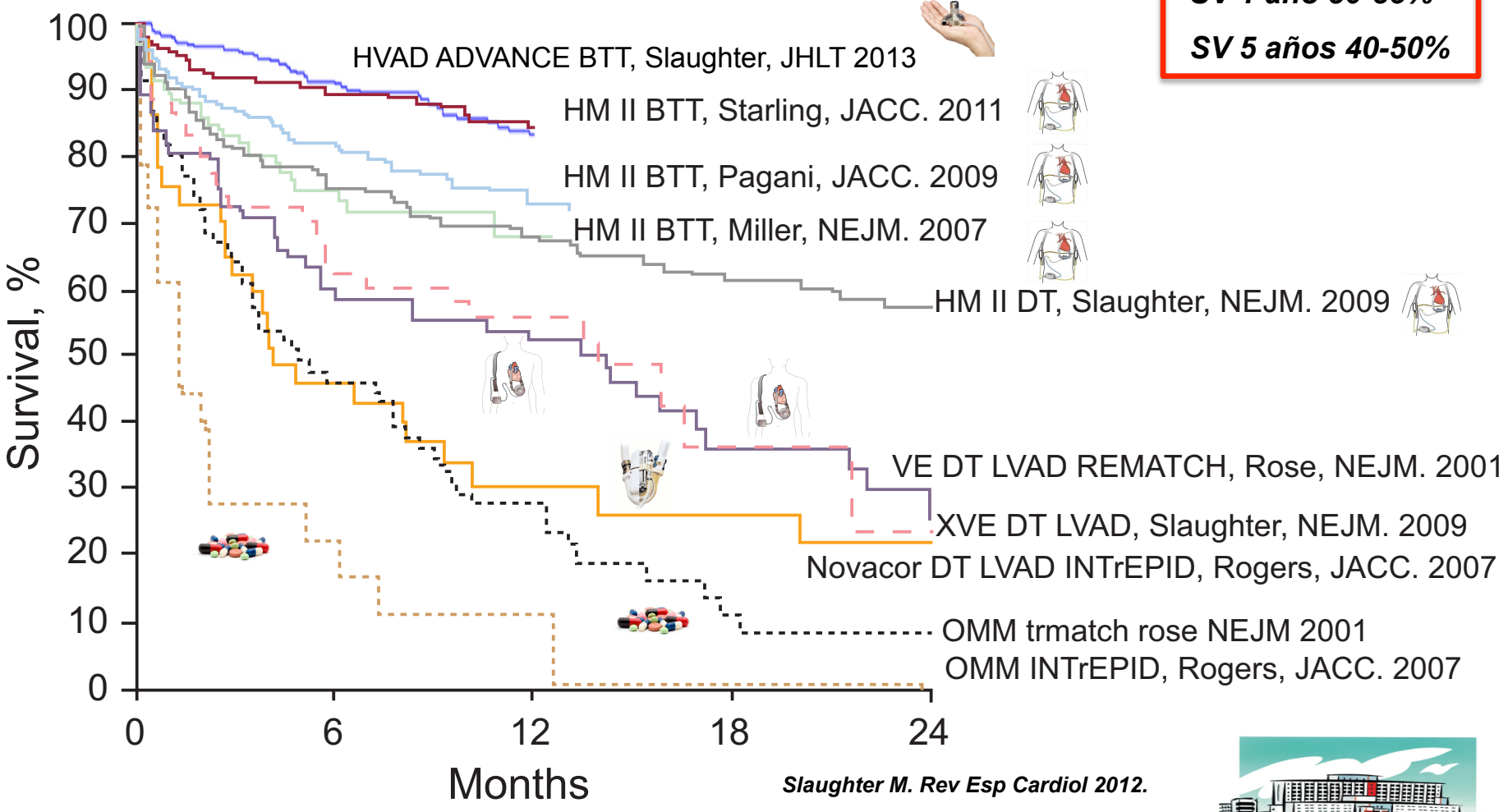
HEARTWARE HVAD



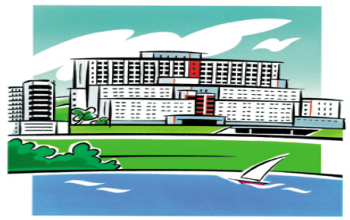
LVADs: SURVIVAL

SV 1 año 80-85%

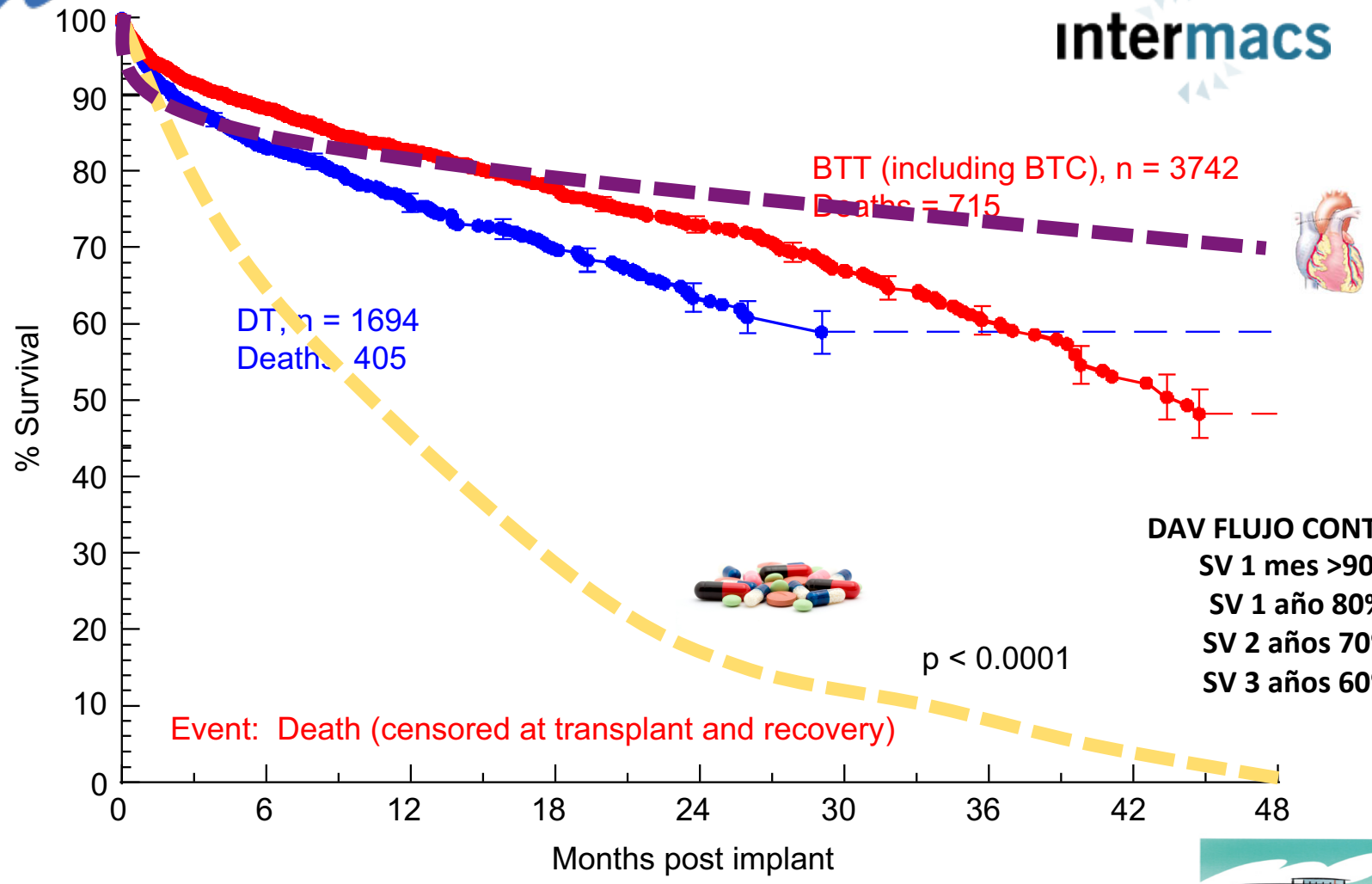
SV 5 años 40-50%



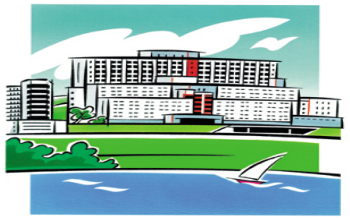
Slaughter M. Rev Esp Cardiol 2012.



LVADs: SURVIVAL



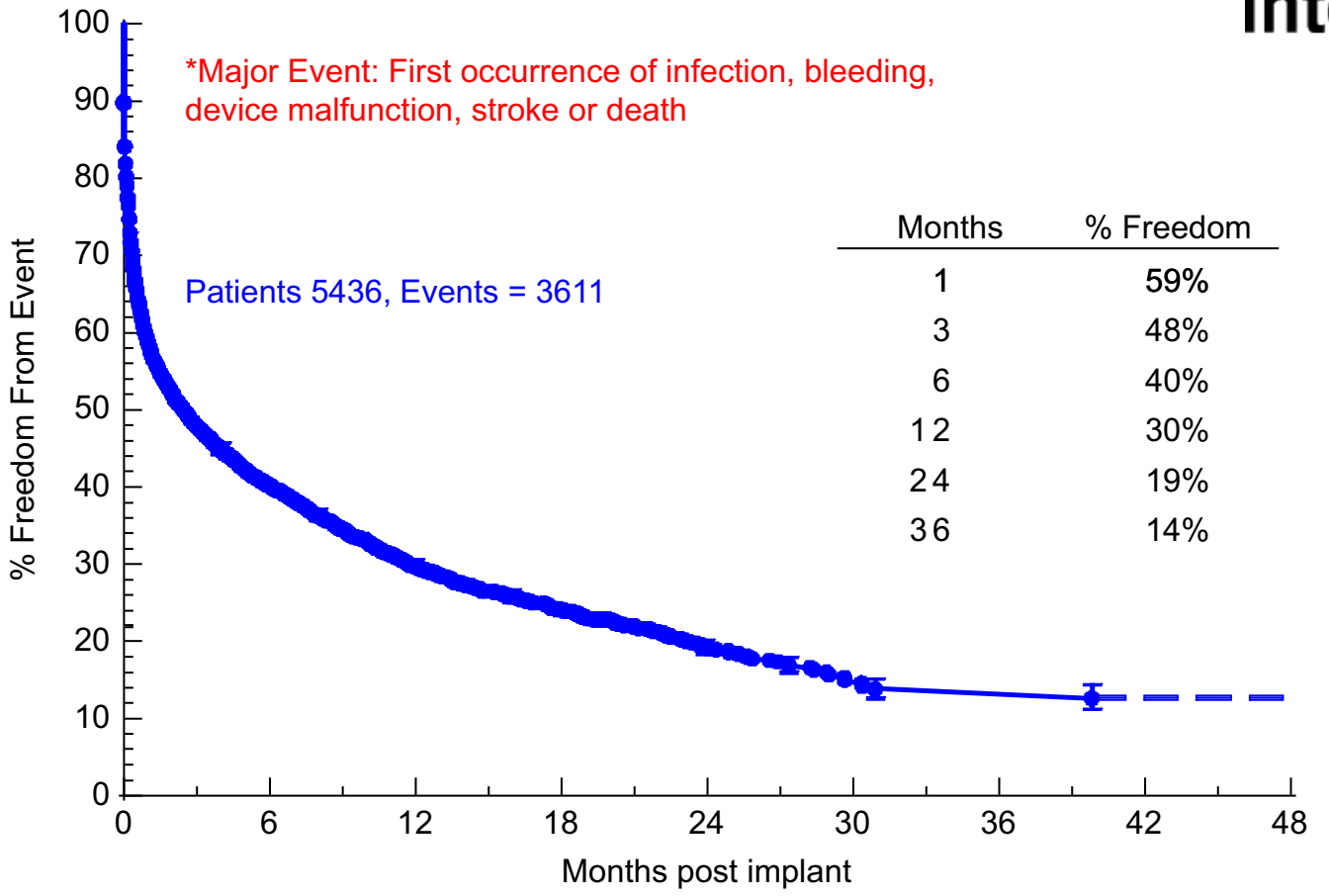
DAV FLUJO CONTINUO
SV 1 mes >90%
SV 1 año 80%
SV 2 años 70%
SV 3 años 60%



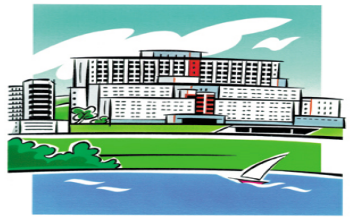
LVADs: COMPLICATIONS

Adult Primary Continuous Flow LVADs & BIVADs, DT and BTT, n = 5436
Implants: June 2006 – June 2012
Time to First Major Event*

intermacs

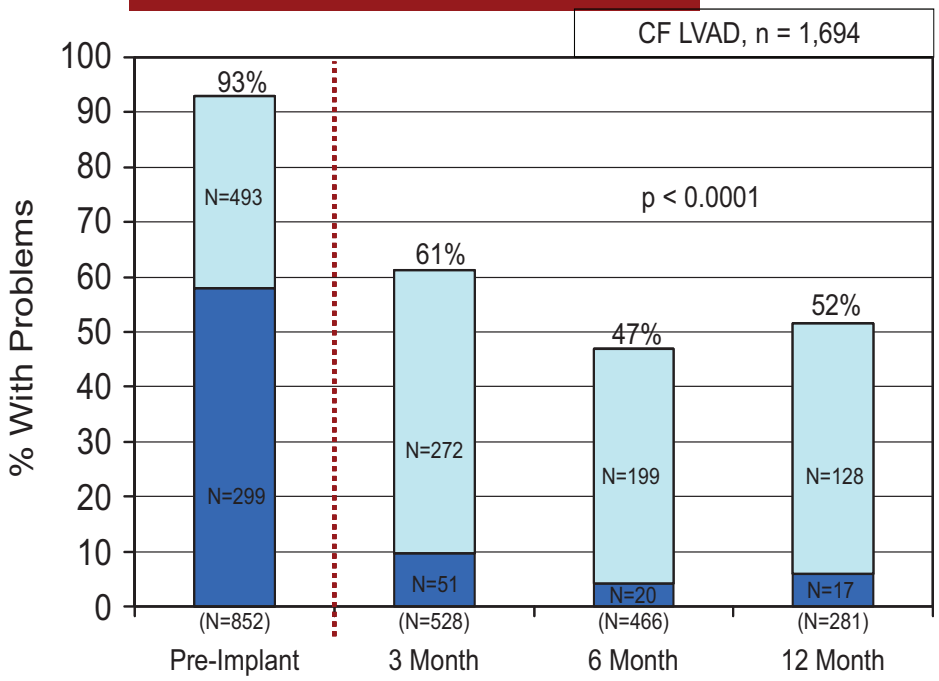


Months	% Freedom
1	59%
3	48%
6	40%
12	30%
24	19%
36	14%

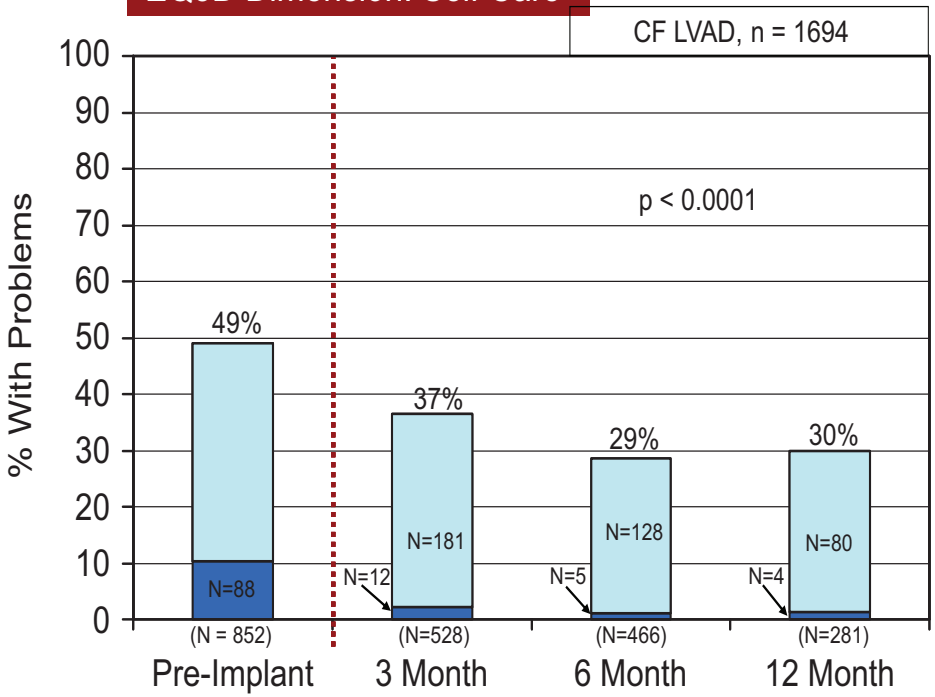


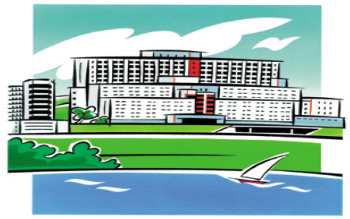
LVADS: QoL

EQ5D Dimension: Usual Activities



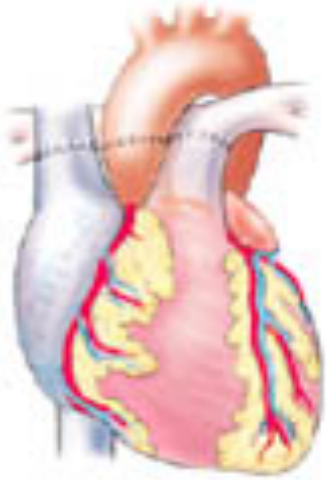
EQ5D Dimension: Self Care

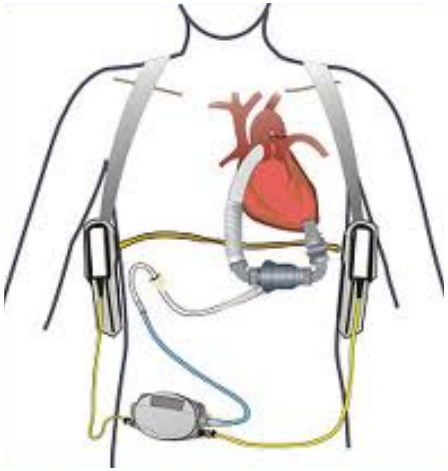




HEART TRANSPLANT AND LVADs

INDICATIONS

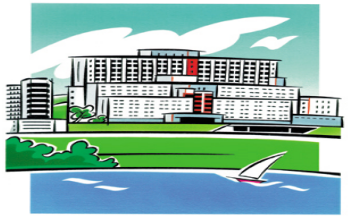




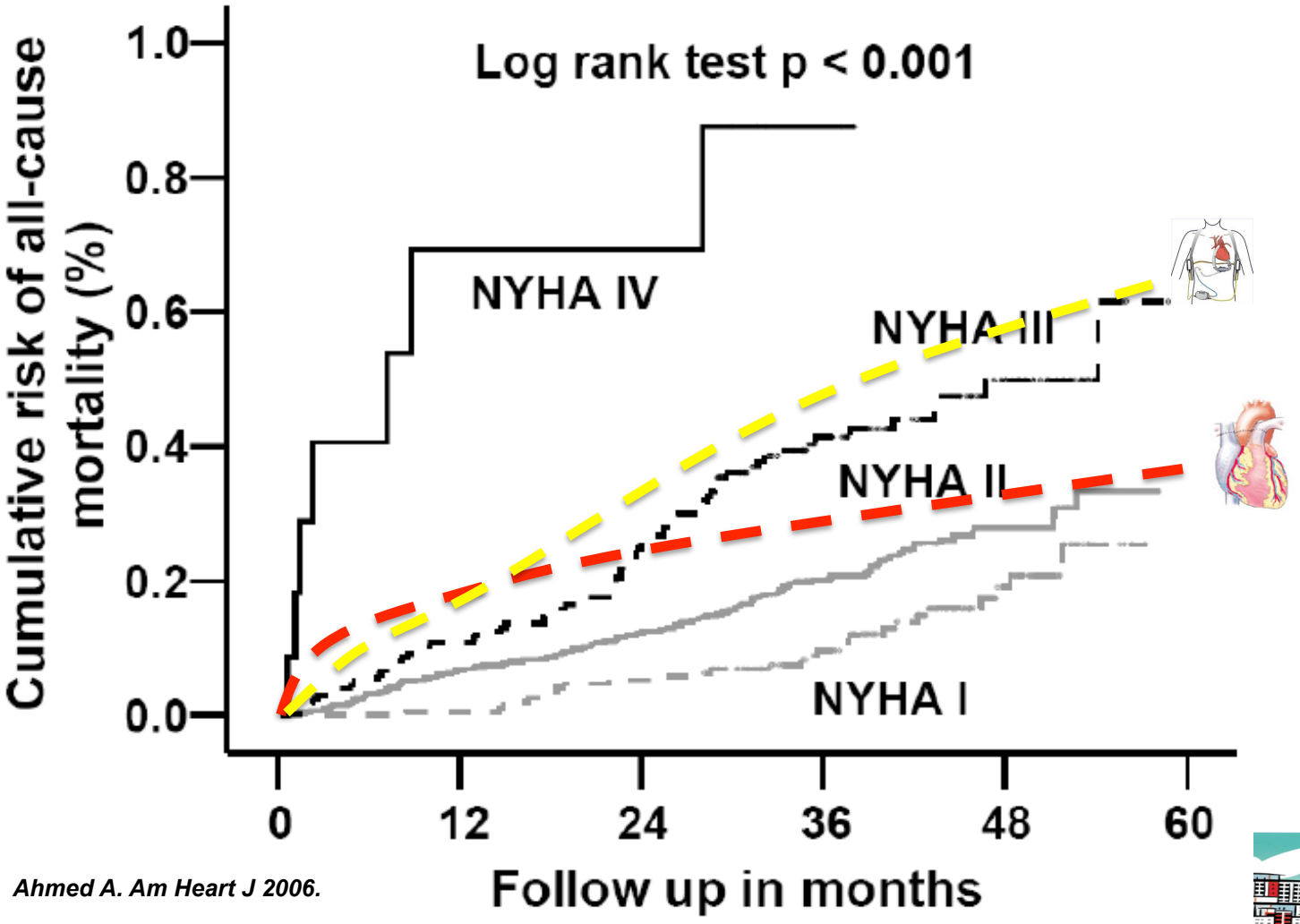
THE GOLDEN RULE OF ADVANCED HF

"HEART TRANSPLANT SHOULD BE CONSIDERED IN HF PATIENTS WITH EXPECTED 1-YEAR MORTALITY >20%"

"IF AN ABSOLUTE CONTRAINDICATION FOR HT EXISTS, LVAD IMPLANTATION MAY BE REASONABLE"

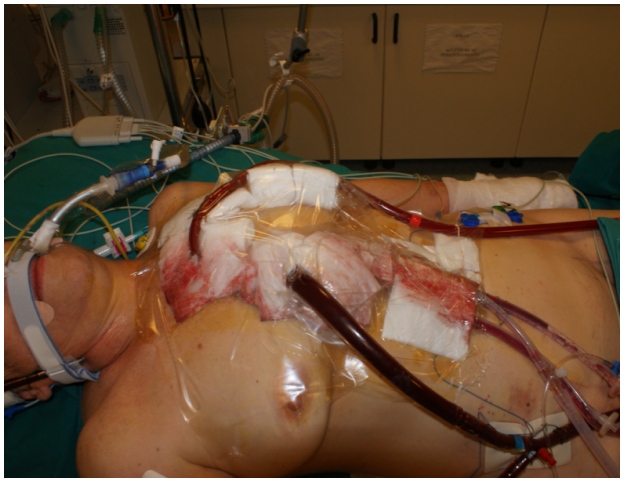


NYHA CLASS: IS IT ENOUGH?



Ahmed A. Am Heart J 2006.

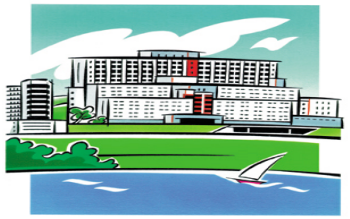
ALL OF THESE ARE NYHA IV PATIENTS…



NYHA CLASS: IS IT ENOUGH?

Intermacs

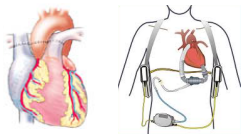
SUPPORTING HEARTS THROUGH KNOWLEDGE



INTERMACS PROFILES

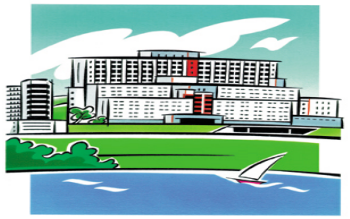
Level[a]	Hemodynamic status	
1 "Crash and burn"	Persistent hypotension despite rapidly escalating inotropic support and eventually IABP, and critical organ hypoperfusion.	HOURS
2 "Sliding on inotropes"	Intravenous inotropic support with acceptable values of blood pressure and continuing deterioration in nutrition, renal function, or fluid retention.	DAYS
3 "Dependent stability"	Stability reached with mild to moderate doses of inotropes but demonstrating failure to wean from them due to hypotension, worsening symptoms, or progressive renal dysfunction.	WEEKS TO MONTHS
4 "Frequent flyer"	Possible weaning of inotropes but experiencing recurrent relapses, usually fluid retention.	
5 "Housebound"	Severe limited tolerance for activity: comfortable at rest with some volume overload and often with some renal dysfunction.	VARIABLE
6 "Walking wounded"	Less severe limited tolerance for activity and lack of volume overload. Fatigue easily.	
7 "Placeholder"	Patient without current or recent unstable fluid balance. NYHA class II or III.	

NYHA IV



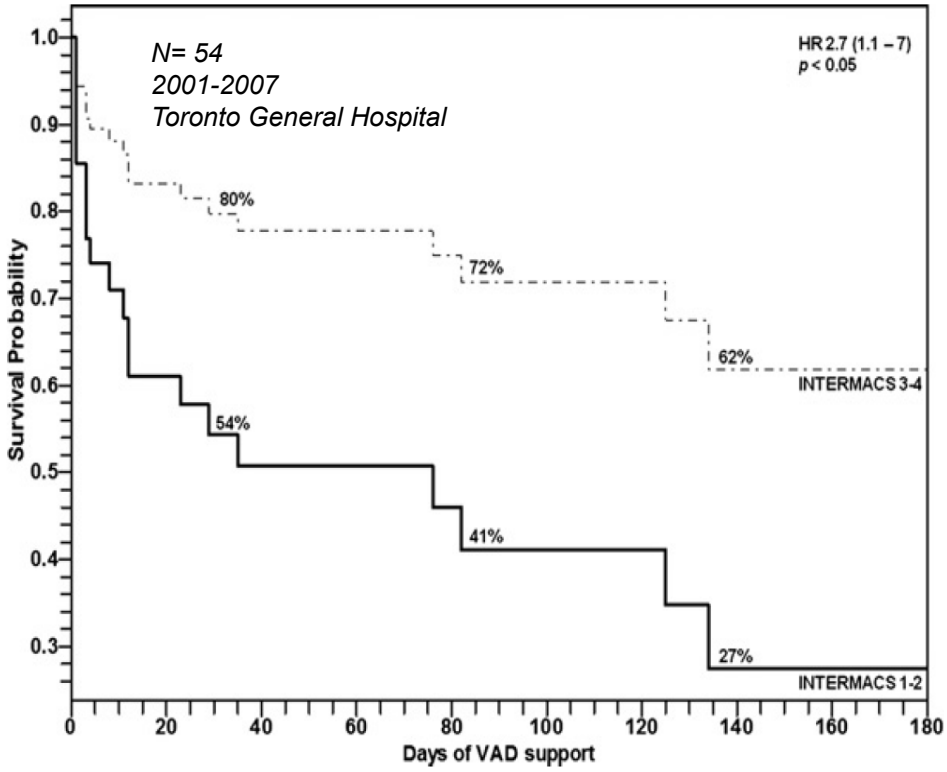
NYHA III

Stevenson L. JHLT 2013.



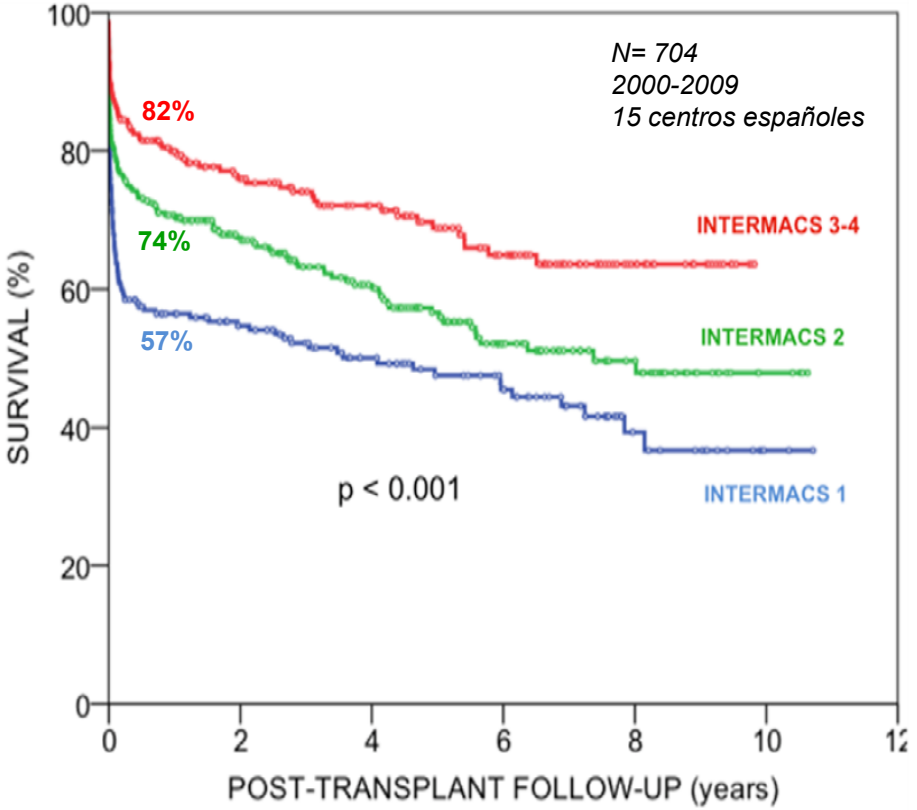
INTERMACS PROFILES: PROGNOSTIC VALUE

LVADs

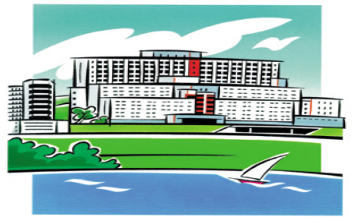


Alba AC. J Heart Lung Transplant 2009.

HEART TRANSPLANT



Barge-Caballero E. Circ Heart Fail 2013.



ESCALA INTERMACS: VALOR PRONÓSTICO

Table 2 Pre-implant Adult Patient Profiles by Year of Implant: June 23, 2006, to June 30, 2011

Patient pre-implant profile	Implant year 2006 No. (%)	2007 No. (%)	2008 No. (%)	2009 No. (%)	2010 No. (%)	2011 (~Jun) No. (%)	Total
1. "Critical cardiogenic shock" (patient has life-threatening hypotension and profound low cardiac output with rapidly escalating inotropic pressor support)	42 (40.8)	155 (45.2)	213 (29.3)	204 (21.5)	186 (12.3)	102 (14.0)	902
2. "Progressive decline" (patient has been demonstrated "dependent" on inotropic support but nonetheless shows signs of continuing deterioration)	40 (38.8)	122 (35.6)	310 (42.7)	443 (46.7)	637 (42.0)	302 (41.4)	1,854
3. "Stable but inotrope-dependent" (patient is clinically stable on mild-moderate doses of intravenous inotropes, or has a temporary circulatory support device, after repeated documentation of failure to wean without symptoms)	8 (7.8)	33 (9.6)	110 (15.2)	162 (17.1)	384 (25.3)	202 (27.7)	899
4. "Resting symptoms" (patient is at home on oral therapy but frequently has symptoms of congestion at rest or with activities of daily living)	6 (5.8)	25 (7.3)	66 (9.1)	94 (9.9)	211 (13.9)	88 (12.1)	490
5. "Exertion intolerant" (patient is comfortable at rest but unable to engage in any activity, living predominantly within the house or household)	0 (0.0)	6 (1.8)	9 (1.2)	22 (2.3)	49 (3.2)	26 (3.6)	112
6. "Exertion limited" (patient is comfortable at rest without evidence of fluid overload, is able to do some mild activity)	2 (1.9)	2 (0.6)	7 (1.0)	16 (1.7)	30 (2.0)	6 (0.8)	63
7. "Advanced NYHA class III" (patient is clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation)	5 (4.9)	0 (0.0)	11 (1.6)	8 (0.8)	19 (1.3)	3 (0.4)	46
Total	103 (100.0)	343 (100.0)	726 (100.0)	949 (100.0)	1,516 (100.0)	729 (100.0)	4,366

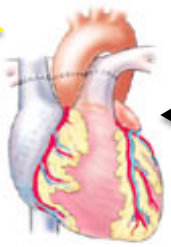
NYHA, New York Heart Association.

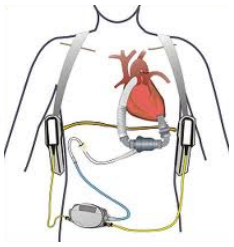
Kirklin J. JHLT 2012.

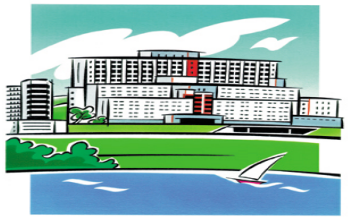
DECISION-MAKING PROCESS

INTERMACS PROFILE-LEVEL
INTERMACS 1
INTERMACS 2
INTERMACS 3
INTERMACS 4
INTERMACS 5
INTERMACS 6
INTERMACS 7

HIGH RISK

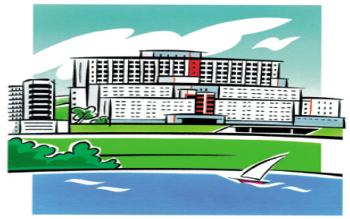






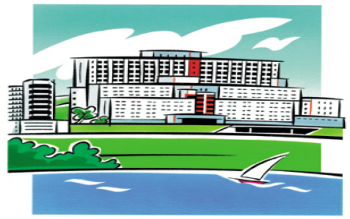
ADVERSE PROGNOSTIC MARKERS

- ✓ Ventricular arrythmya
- ✓ Intolerance to HF medications
- ✓ Low blood pressure
- ✓ Frequent decompensations
- ✓ End-organ dysfunction (kidney, liver)
- ✓ Cardiac caquexia
- ✓ Anemia
- ✓ Biomarkers (NTproBNP, ST2, galectine)
- ✓ Functional parameters
    - VO2 <12 (<14) ml/kg/min if RER > 1.05
    - CI < 2.2 l/min/m2 / CWP > 20 / CVP > 10
    - mPAP > 40 mm Hg / TPG > 12 mm Hg / PVR > 3 UW
    - LVEF < 20%
- ✓ HF risk scores (HFSS, SHFM)

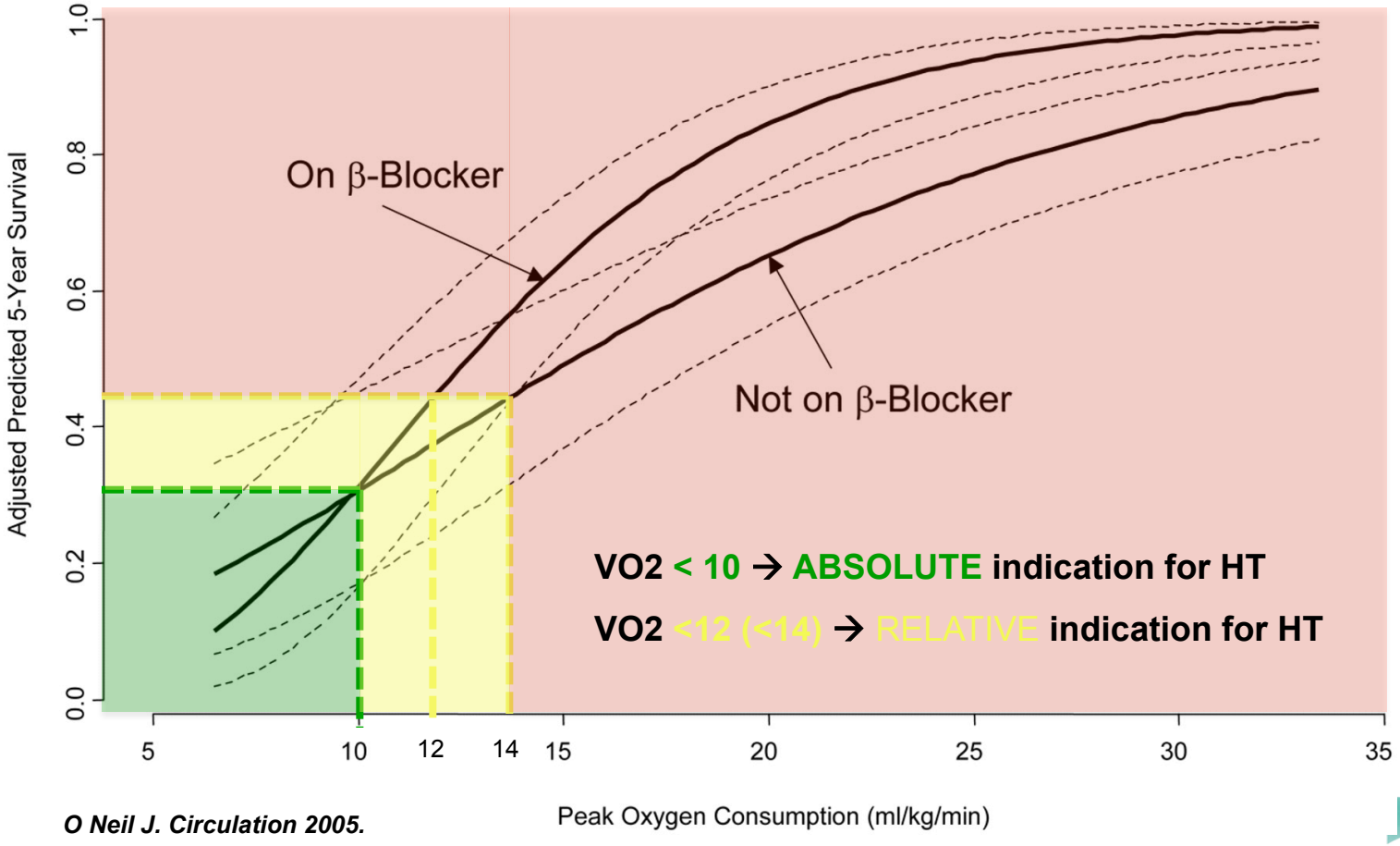


ADVERSE PROGNOSTIC MARKERS

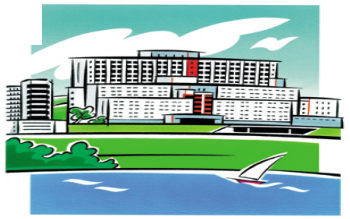
- ✓ Ventricular arrythmya
- ✓ Intolerance to HF medications
- ✓ Low blood pressure
- ✓ Frequent decompensations
- ✓ End-organ dysfunction (kidney, liver)
- ✓ Poor nutrional status
- ✓ Anemia
- ✓ Biomarkers (NTproBNP, ST2, galectine)
- ✓ Functional parameters
  - **VO2 <12 (<14) ml/kg/min if RER > 1.05**
  - CI < 2.2 l/min/m2 / CWP > 20 / CVP > 10
  - mPAP > 40 mm Hg / TPG > 12 mm Hg / PVR > 3 UW
  - LVEF < 20%
- ✓ **HF risk scores (HFSS, SHFM)**



PEAK OXYGEN UPTAKE



O Neil J. Circulation 2005.



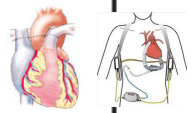
HEART FAILURE SURVIVAL SCORE

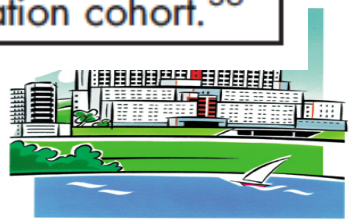
Table I. Calculation of the Heart Failure Survival Score

Risk Factor	Contribution
Left ventricular ejection fraction, %	+Ejection fraction*0.0464
Mean blood pressure, mm Hg	+Blood pressure*0.0255
Peak maximal oxygen uptake, mL/m/kg	+Maximal oxygen uptake *0.0546
Serum sodium, mmol/L	+Sodium*0.0470
Ischemic cardiomyopathy	–0.6931 if yes
Intraventricular conduction delay >120 ms	–0.6083 if yes
Resting heart rate, beats per min	–Heart rate*0.0216

Sum of Risk Factors	Strata of Risk	1-Year Survival, %
≥8.1	Low	93
≥7.2, <8.1	Medium	72
<7.2	High	43

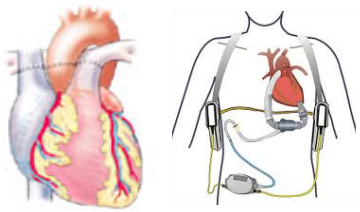
The top portion of the Table depicts the calculation of the risk score while the bottom portion depicts expected 1-year survival without urgent transplantation in the derivation cohort.[36]





SEATTLE HEART FAILURE MODEL

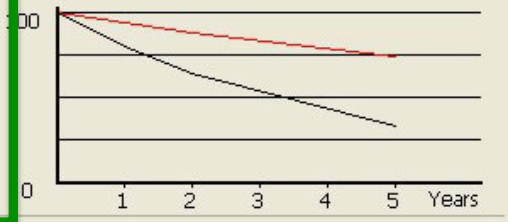
1-YEAR
SV <80%



Seattle Heart Failure Model Calculator

File Info

	Baseline 1 Year	Baseline 2 Year	Baseline 5 Year	Intervention 1 Year	Intervention 2 Year	Intervention 5 Year
Survival	80%	64%	33%	94%	88%	74%
Mortality	20%	36%	67%	6%	12%	26%
Mean life expectancy	4.1 years			9.4 years		



Clinical
Age: 65
Gender: Male
NYHA Class: 3A
Weight (kg): 80
EF: 30
Syst BP: 120
Ischemic

Medications
ACE-I
Beta-blocker
ARB
Statin
Allopurinol
Aldosterone blocker

Diuretics
Furosemide: 80
Bumetanide: 0
Torsemide: 0
Metolazone: 0
HCTZ: 0

Lab Data
Hgb (g/dL): 14
Lymphocyte %: 25
Uric Acid (mg/dL): 8
Total Chol (mg/dL): 190
Sodium: 137
QRS > 120 msec

Devices
None
BiV Pacer
ICD
BiV ICD

Default Values

Interventions
ACE-I ARB Beta-blocker
Statin Aldosterone blocker

Devices
None
BiV Pacer BiV ICD
ICD LVAD

Note: Some devices may be disabled if CMS clinical criteria are not met

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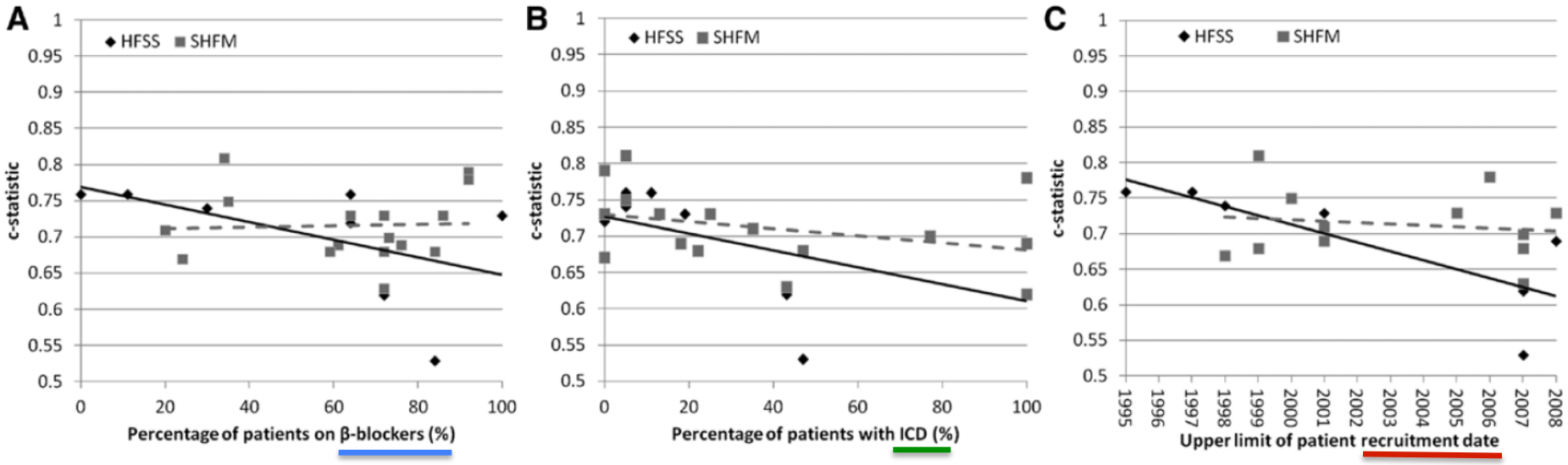
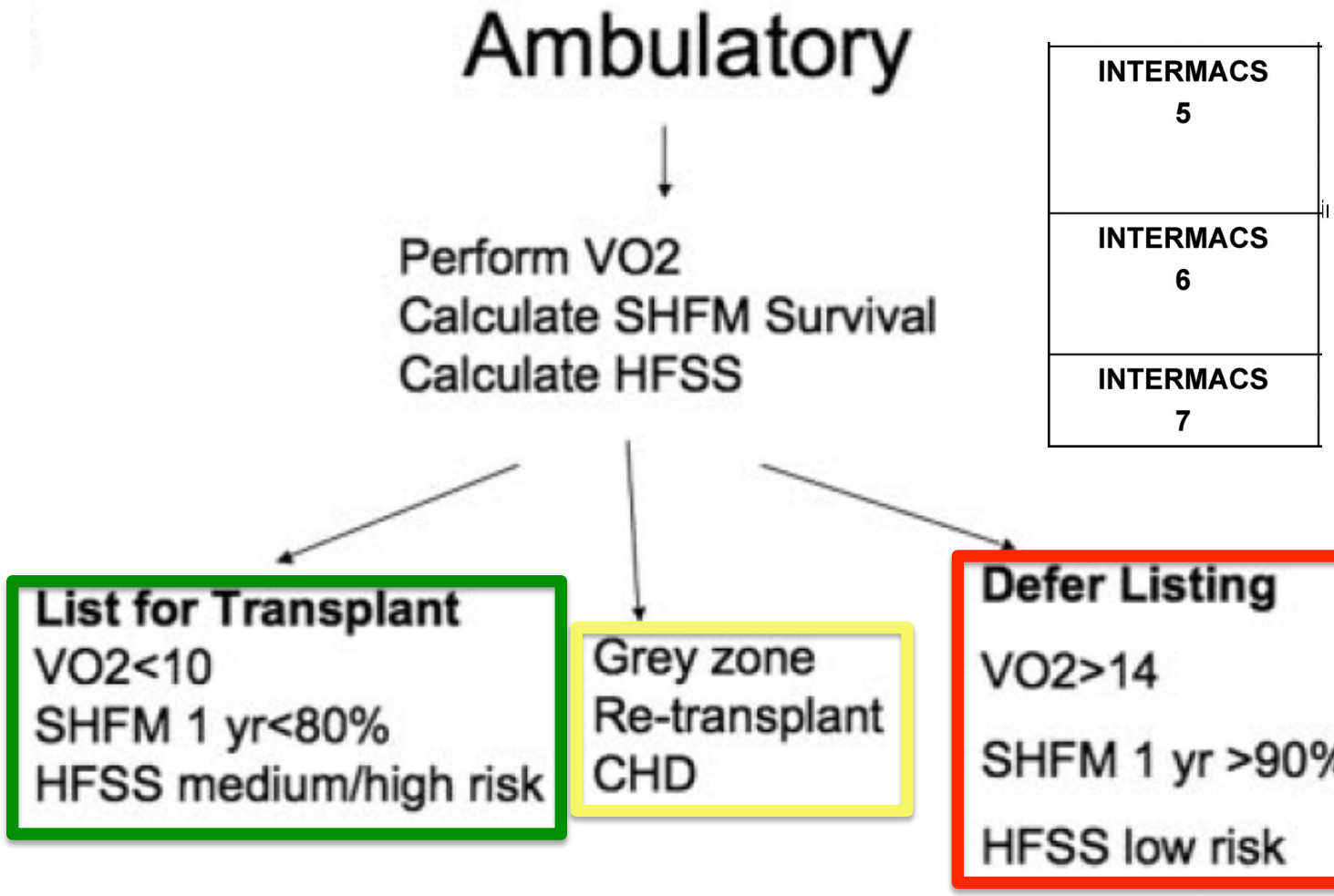
SHFM better than HFSS in contemporary HF populations



C (SHFM) = 0.63-0.81
C (HFSS) = 0.56-0.79

Alba AC. Circ Heart Fail 2013.

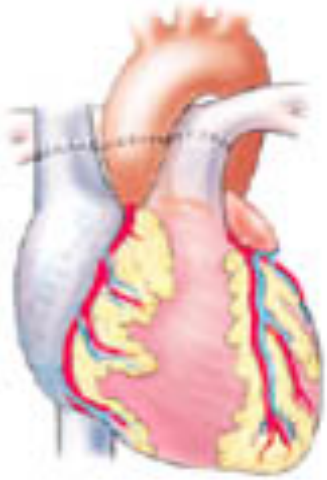
INTERMACS PROFILES 5-7

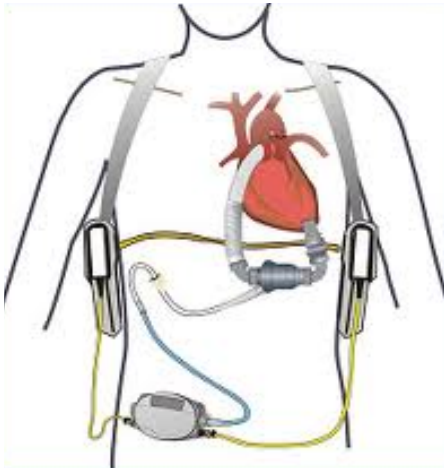


Mancini D. Circulation 2010.

HEART TRANSPLANT AND LVADs

CONTRAINDICATIONS



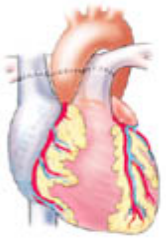


CONTRAINDICATIONS FOR HT

Contraindications	
	Active infection
	Severe peripheral arterial or cerebrovascular disease
	Current alcohol or drug abuse
	Treated cancer in previous 5 years
	Unhealed peptic ulcer
	Recent thrombo-embolism
	Significant renal failure (e.g. creatinine clearance <50 mL/min)
	Significant liver disease
	Systemic disease with multiorgan involvement
	Other serious co-morbidity with poor prognosis
	Emotional instability or untreated mental illness
	High, fixed pulmonary vascular resistance (>4–5 Wood Units and mean transpulmonary gradient >15 mmHg)

EUROPEAN SOCIETY OF CARDIOLOGY®

Table 3. Contraindications to cardiac transplantation.[5]



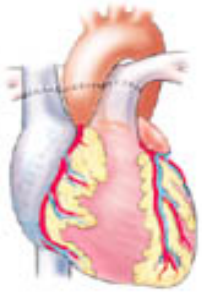
- Pulmonary hypertension (TPG > 15 mm Hg, SPAP > 50 mm Hg, PVR > 4 WU, PVRI > 6)
- Systemic disease (anticipated to limit long-term survival)
- Elevated creatinine (> 200 µmol/L)
- Active infection
- Psychosocial (substance abuse, smoking, medical noncompliance)
- Malignancy (within 5 years)
- Morbid obesity (> 140% ideal body weight)
- Marked cachexia (< 60% ideal body weight)
- Osteoporosis
- Peripheral or cerebrovascular disease
- Diabetes mellitus with end organ damage

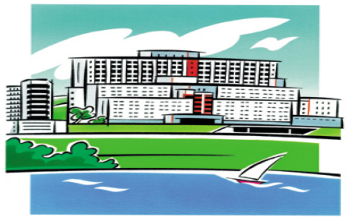
CONTRAINDICATIONS FOR HT

UNOS DONATE LIFE
UNITED NETWORK FOR ORGAN SHARING

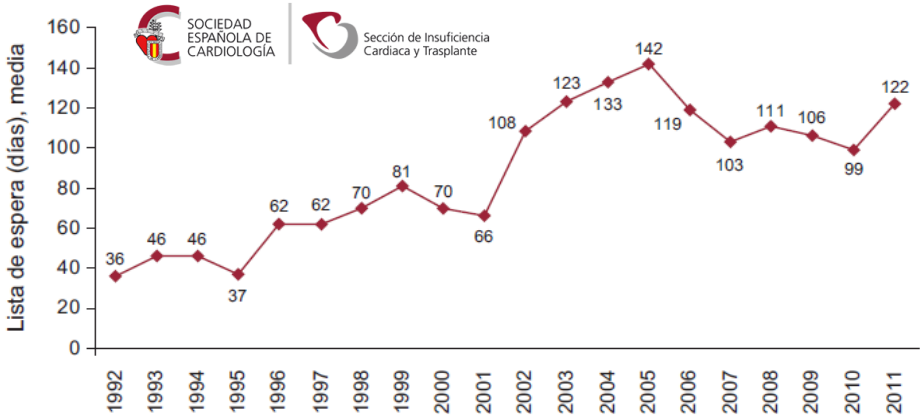
Table 3. Change in Listing Characteristics From 1999 to 2009

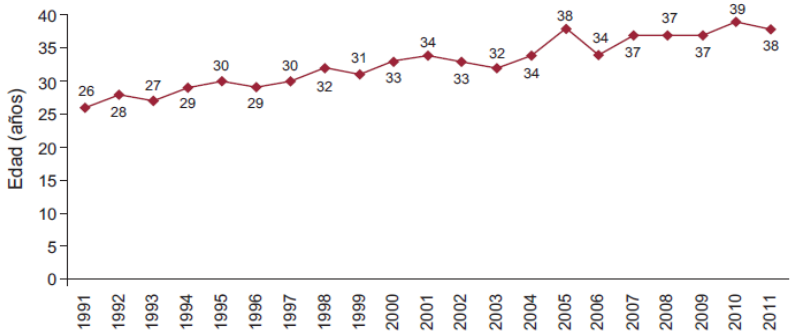
	1999	2009
Age, y	<65	<72
PVR, Wood units	Fixed >6; trial of IV inotropes	Fixed >6; trial inotropes, sildenafil, mechanical assist device
Diabetes mellitus	Minimal end-organ involvement, insulin use	Moderate end-organ involvement, combined transplants
Malignancy	Remote	Bridge with mechanical assist device if malignancy within 2 y; in some low-grade malignancies, proceed after appropriate treatment
PVD	Severe	No change
Infections	Defer	Proceed in setting of device infection
Senitized patient	Pretreat with immunosuppression	Additional option of rituximab

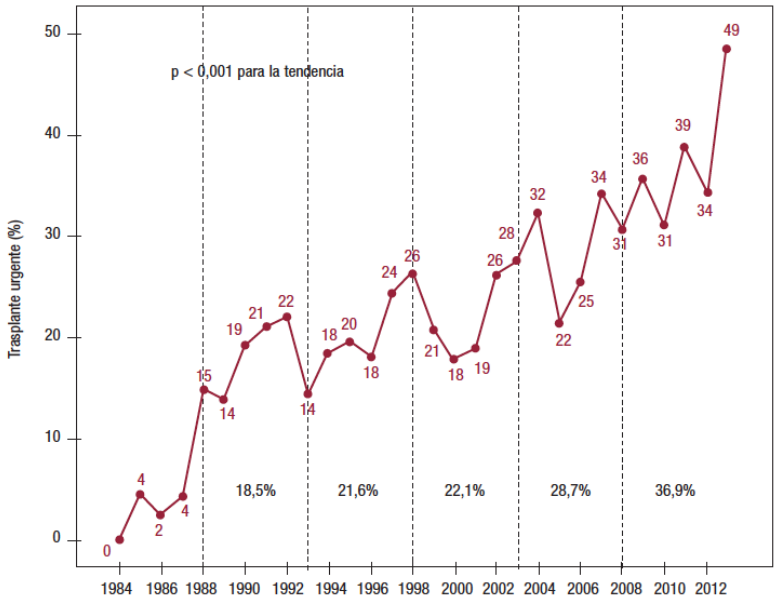


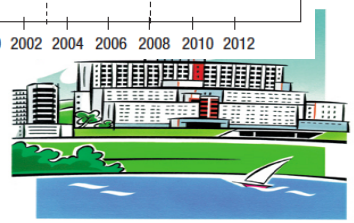


DONOR SCARCITY









CONTRAINDICATIONS FOR LVADs

4.3 Contraindicaciones

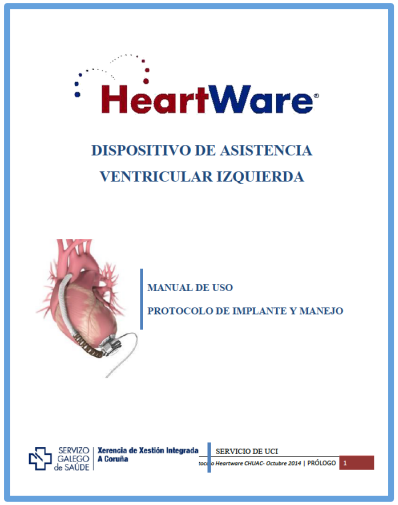
Si bien no son muchas, existen varias condiciones que deben ser consideradas una contraindicación absoluta para el implante de un DAVI:

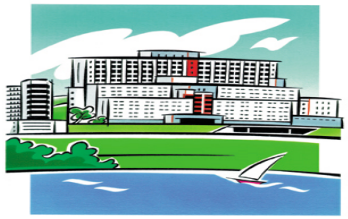
- ✓ Expectativa de vida limitada (<2 años) por comorbilidades extracardiacas.
- ✓ Disfunción severa de ventrículo derecho que requiera asistencia circulatoria a largo plazo.
- ✓ Déficit neurológico irreversible o dudas acerca de su existencia.
- ✓ Disfunción cognitiva avanzada.
- ✓ Neoplasia con metástasis.
- ✓ Fallo multiorgánico.
- ✓ Infección sistémica activa.
- ✓ Diátesis hemorrágica severa.
- ✓ Trombocitopenia severa (<50000).
- ✓ Cirrosis hepática evolucionada.
- ✓ Enfermedad renal crónica avanzada con diálisis permanente.
- ✓ Alteración ventilatoria obstructiva severa (VEMS <1000 ml o < 30-50% predicho o insuficiencia respiratoria crónica)
- ✓ Trastorno psiquiátrico o neurológico severo que interfiera de modo significativo en la cumplimentación del régimen de vida y cuidados recomendados tras el implante.
- ✓ Ausencia absoluta de apoyo social y familiar.

CONTRAINDICATIONS FOR LVADs

Hay que tener en cuenta otras condiciones que aisladamente no constituyen una contraindicación absoluta para DAVI-i, pero sí deben ser consideradas contraindicaciones relativas:

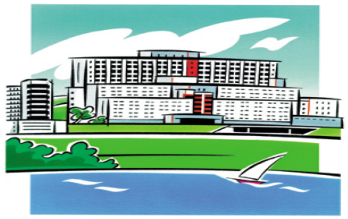
- ✓ Aneurisma de aorta abdominal >5 cm.
- ✓ Alteración ventilatoria obstructiva moderada.
- ✓ Enfermedad renal crónica (GFR < 30 ml/min/m2).
- ✓ Edad > 75 años (terapia de destino) o > 70-72 años (puente a trasplante).
- ✓ Disfunción ventricular derecha no severa.
- ✓ Enfermedad cerebrovascular sintomática.
- ✓ Ateromatosis carotídea con estenosis hemodinámicamente significativas.
- ✓ Tromboembolismo pulmonar reciente.
- ✓ Historia previa de sangrado digestivo.
- ✓ Trombocitopenia inducida por heparina.
- ✓ Hepatopatía crónica.
- ✓ Neoplasia no metastásica.
- ✓ Hipertensión pulmonar no reversible.
- ✓ Hipertensión portal.
- ✓ Ventilación mecánica prolongada (>7 días) con FiO2 > 60%.
- ✓ Inestabilidad hemodinámica severa (perfiles INTERMACS 1 y 2).
- ✓ Antecedentes de incumplimiento terapéutico.
- ✓ Infección localizada o no severa.
- ✓ Enfermedad vascular periférica.
- ✓ Prótesis valvulares mecánicas.





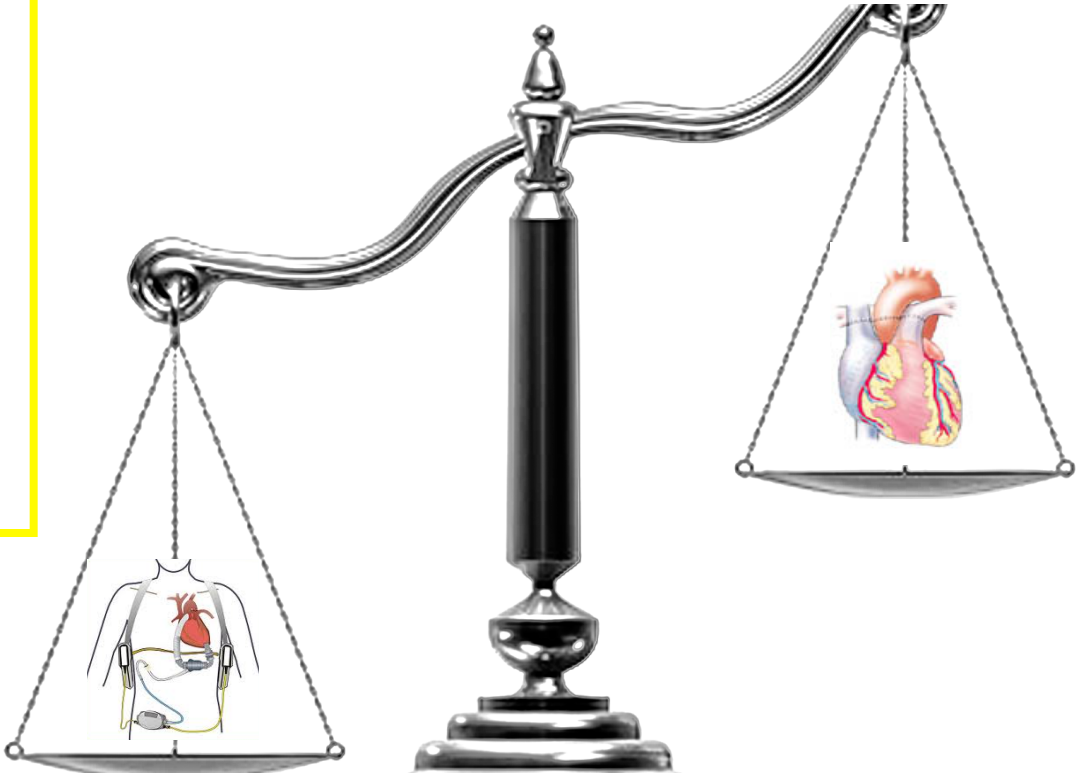
¿TRANSPLANT OR LVADs?

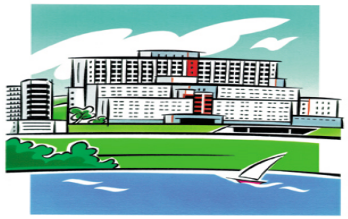
- Age < 70
- Clinically stable
- HT mortality < 15-20%
- Anticoagulation not possible
- RV failure
- Thrombotic diathesis
- GI bleeding
- Mechanical prosthesis
- Aortic regurgitation



¿TRASPLANT OR LVADs?

Age > 70
Comorbidities (DM, CKD, PVD)
Clinically unstable
HT mortality > 15-20%
Neoplasia
Pulmonary hypertension
Donor availability
Waiting list time
Donor quality



CONCLUSIONS

- ✓ Patients with refractory HF present poor quality of life, high rates of readmission and short survival.
- ✓ Both HT and LVADs improve morbidity and mortality in refractory HF patients.
- ✓ INTERMACS profiles are useful to guide the decission-making process.
- ✓ VO2, SHFM and HFSS give us relevant prognostic information in ambulatory individuals.
- ✓ The decission between HT and LVADs is conditioned by several factors like age, comormidities, patient´s preference, social support and donor availability.