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RESEARCH HOSPITAL


# Il VAD e le decisioni cliniche nel centro Spoke.

## Quali sono i criteri di inclusione e di esclusione?

## Quando devo telefonare al centro Hub?

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*Dr. Alessandro BARBONE*
*UO di Cardiochirurgia*

# Quando devo telefonare al centro Hub?

RegioneLombardia
LA GIUNTA

DELIBERAZIONE N° IX / 4983 Seduta del 07/03/2013

- In alcuni pazienti l'accertamento dell'idoneità al trapianto può essere difficile prima dell'impianto di LVAD […]
- L'indicazione a trapianto può risolversi a distanza dall'impianto di LVAD, così come può sopravvenire per complicanze correlate al sistema di assistenza.

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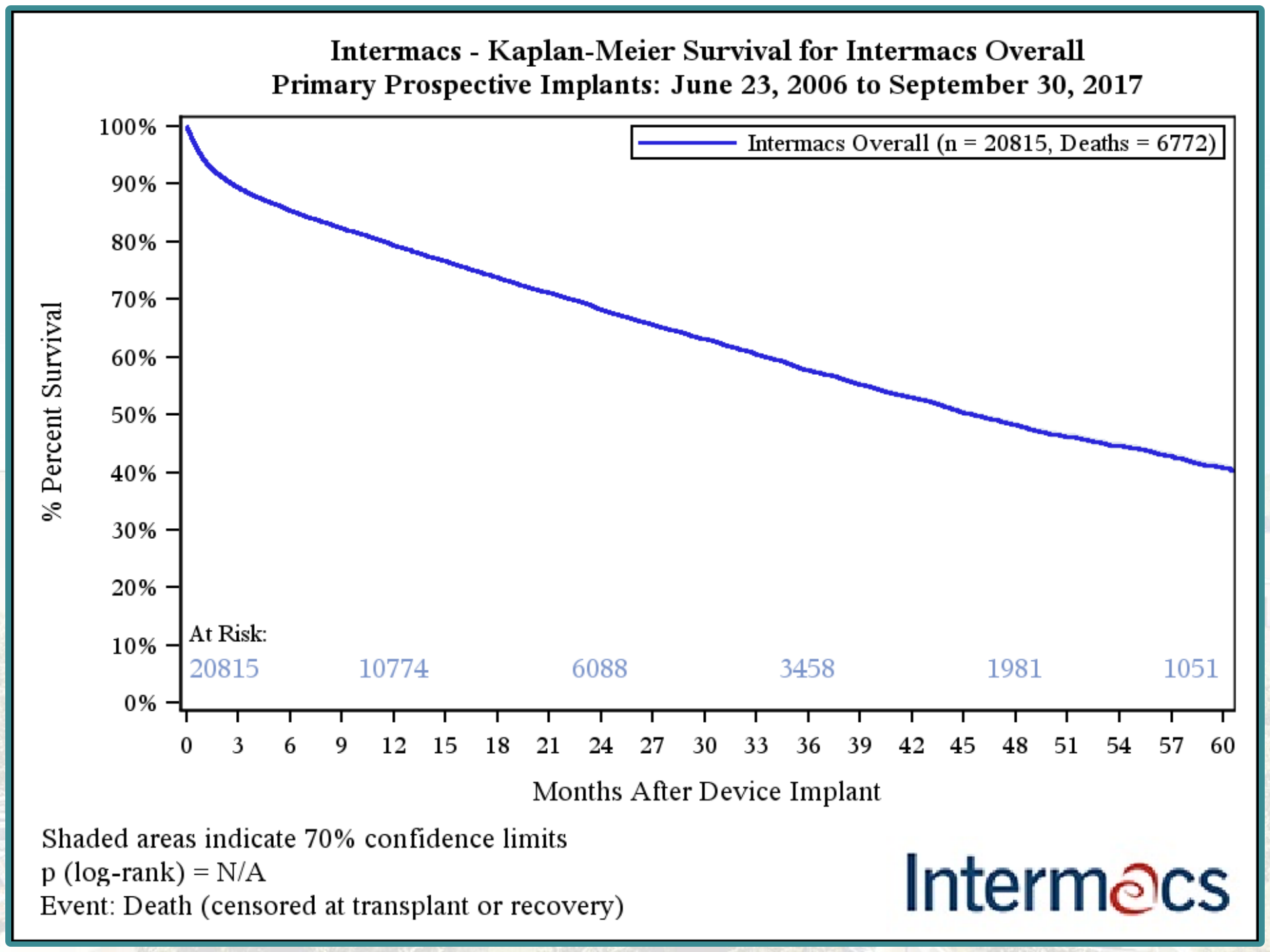
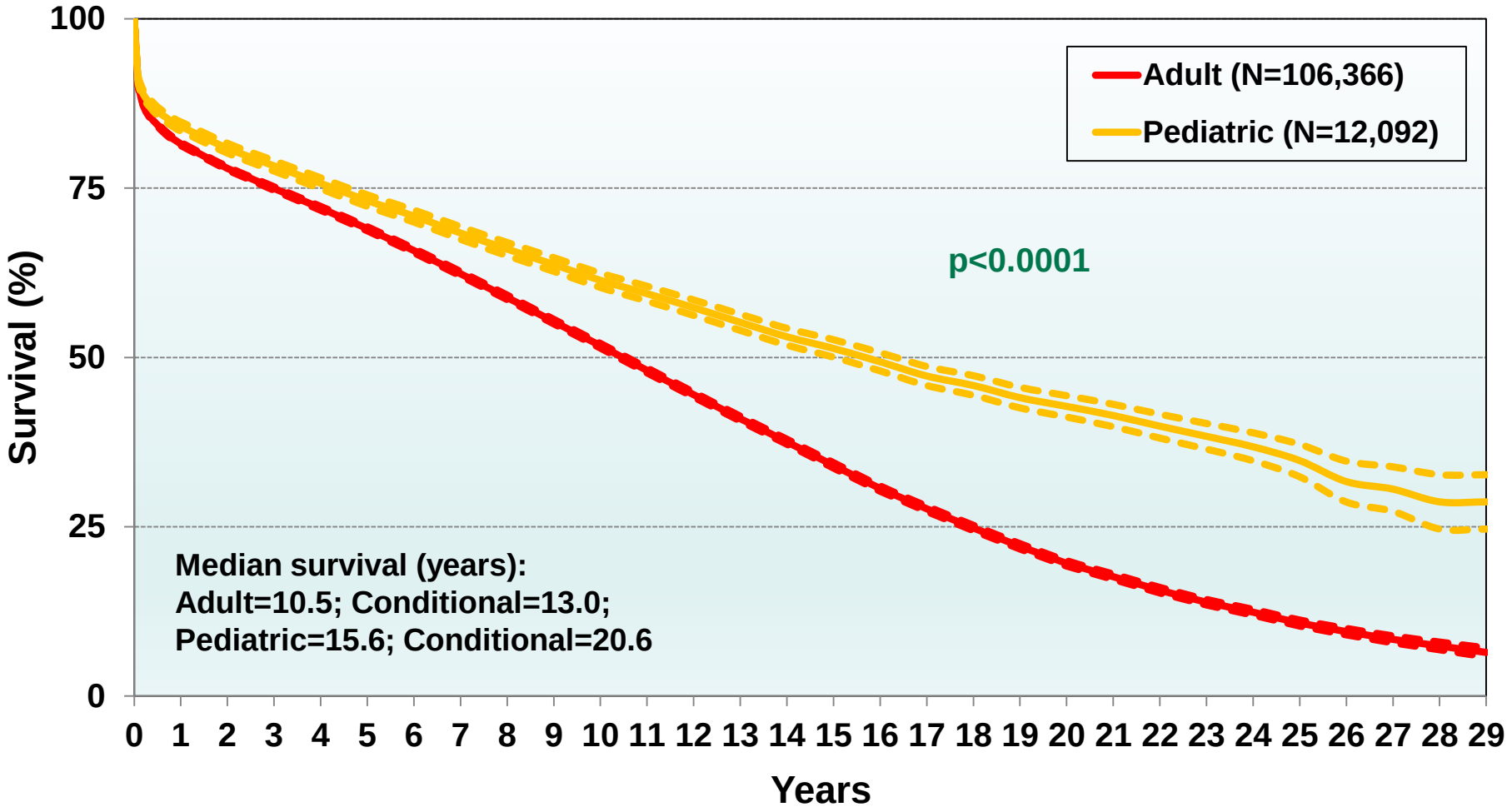

Intermacs - Kaplan-Meier Survival for Intermacs Overall
Primary Prospective Implants: June 23, 2006 to September 30, 2017
Intermacs Overall (n = 20815, Deaths = 6772)
% Percent Survival
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
At Risk:
20815
10774
6088
3458
1981
1051
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Months After Device Implant
Shaded areas indicate 70% confidence limits
p (log-rank) = N/A
Event: Death (censored at transplant or recovery)
Intermacs

# Adult and Pediatric Heart Transplants

## Kaplan-Meier Survival by Age Group

(Transplants: January 1982 – June 2015)

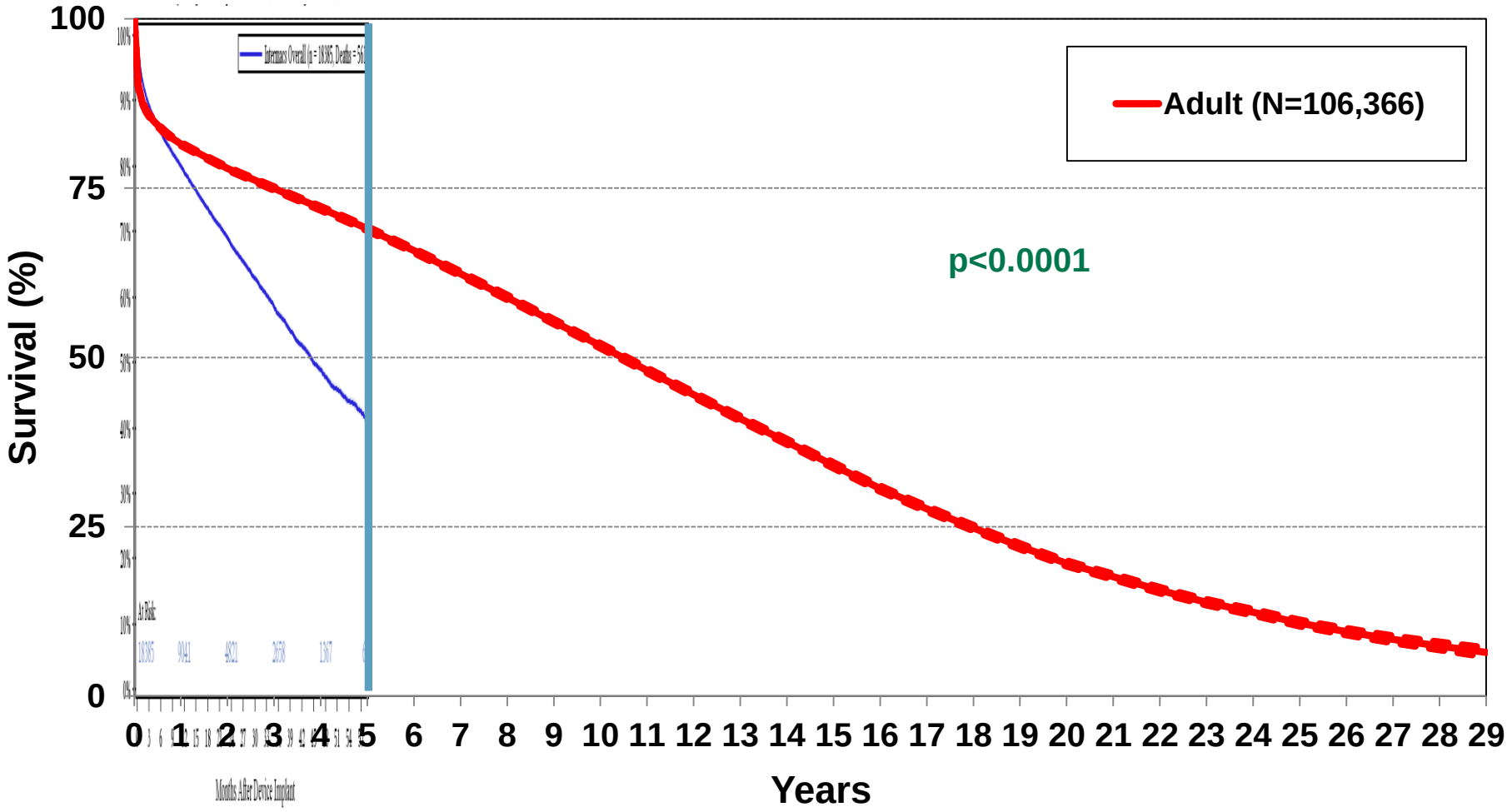



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

# Adult and Pediatric Heart Transplants

## Kaplan-Meier Survival by Age Group

**(Transplants: January 1982 – June 2015)**

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# Quando devo Telefonare al Centro Hub?

- L'eleggibilità a trapianto e a LVAD dei pazienti cronici di età inferiore a 65 anni sarà valutata prima del trattamento, considerando eventuali controindicazioni e fattori di rischio, di concerto con il Centro Trapianto di riferimento, ***che potrà eventualmente prendersi carico del paziente***.

- I pazienti con shock cardiogeno devono essere considerati per supporto short-term prima dell'impianto di LVAD.

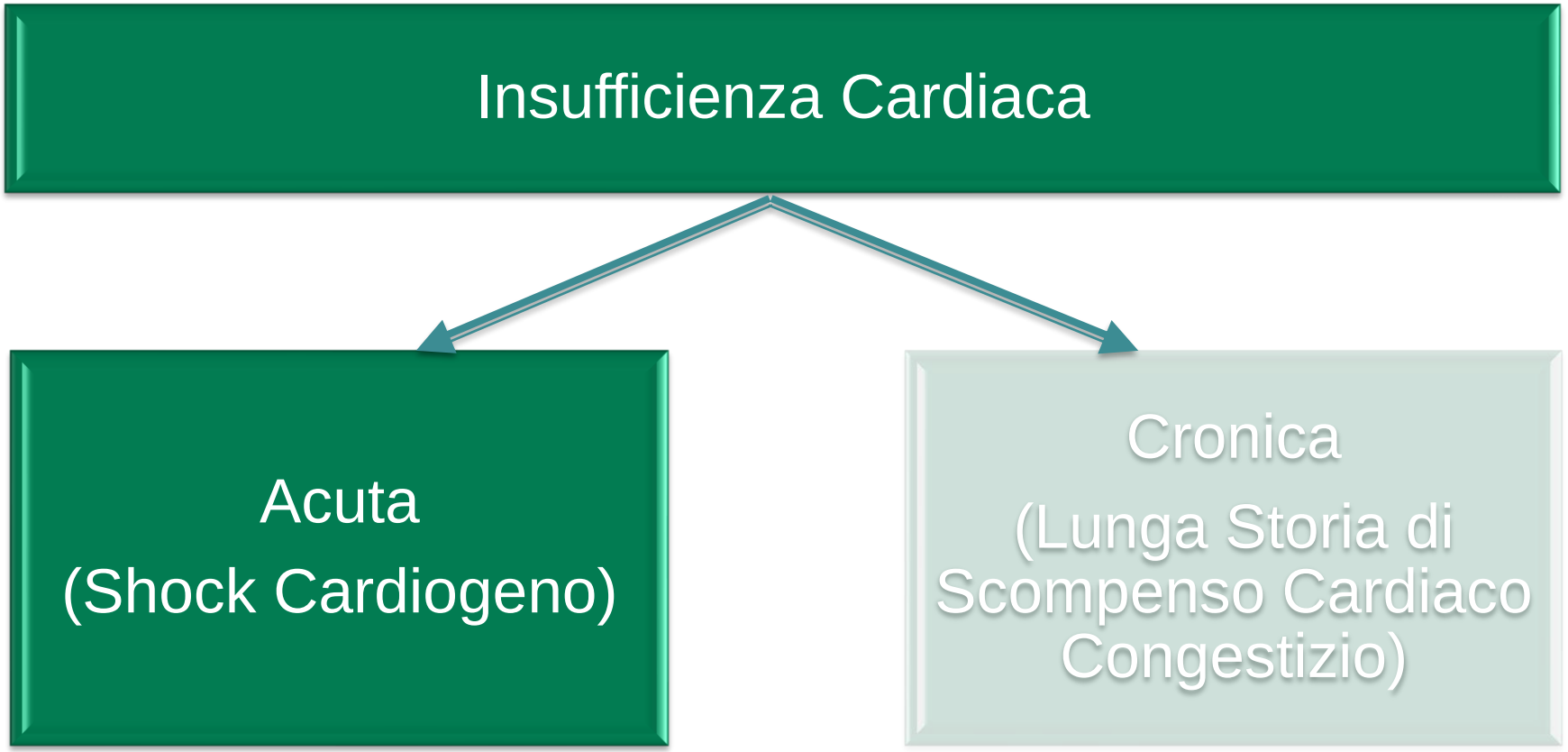
# Quando Devo Telefonare al Centro Hub?

- In sintesi, possono essere trattati con LVAD di lungo periodo presso Centri diversi dai Centri di Trapianto:
  - i pazienti con chiara indicazione DT
  - i pazienti urgenti con incerta idoneità al trapianto (BTC-BTD), che dovranno essere valutati con il Centro di Trapianto di riferimento dopo stabilizzazione.

# Quando devo telefonare al centro Hub?

- Il prima possibile!!!
  - Per così coordinare e valutare il miglior percorso clinico e di trattamento per il paziente

# VAD e Centri Spoke



# *Algoritmo per impianto di Assistenza Ventricolare a Breve Termine in Shock Cardiogeno*

**Modified From: L.E. Samuels et al.**
(Ann Thorac Surg 2001;71:S67–72)

Precardiotomy → Shock Cardiogeno ← Postcardiotomy

Inotropi

**Sindrome da bassa portata con 2 o più farmaci**

**30 min dopo il primo tentativo di svezzamento dalla CEC**

I.A.B.P.

**Sindrome da bassa portata con 2/3 farmaci ad alte dosi**

**1 h dopo il primo tentativo di svezzamento dalla CEC**

VAD a Breve Termine

Assistenza Ventricolare Sinistra

**La maggior parte dei casi può essere superata con la sola assistenza sinistra. Se l'impianto viene ritardatoil rischio di assistenza bieventricolare è aumentato.**

Assistenza Ventricolare Destra

Supporto Bi-Ventricolare

# VAD e Shock Cardiogeno
## Indicazioni

- Funzione ventricolare da considerarsi irrecuperabile
- Funzione ventricolare troppo compromessa per mantenere emodinamica o funzione d'organo
- Se funzione d'organo compromessa ma aspettativa di recupero grazie ad assistenza meccanica
- Assenza di danno d'organo irreversibile

# When is too early –too late?

| | Support Level | | | | | |
|---|---|---|---|---|---|---|
| | Too Early – | Partial Support - | LVAD | BIVAD | TAH | Too Late |
| LVEF (%) | 35 | 30 | 25 | 20 | 15 | <10 |
| LVEDD (mm) | 65 | 70 | 75 | 80 | 85 | >90 |
| Indice Cardiaco (l/min/$m^2$) 1,4 | | 2,4 | 2,2 | 2 | 1,8 | 1,6 |
| PVC | 10 | 12 | 14 | 16 | 18 | >20 |
| APACHE II | <10 | <10 | 11-15 | 11-15 | 16-20 | >20 |
| Inotropi (giorni) | 0 | 0 | 1 | 2-4 | 5-10 | >10 |
| Insufficienza Epatica (bil mg/dl) | <1 | <1.5 | <2 | <3 | <5 | >5 |
| RVF (RVFAC)% | >40 | >40 | >35 | >30 | >25 | <20 |
| Ventilazione (giorni) | 0 | 0 | <1 | 1-3 | 4-6 | >7 |
| Altro supporto meccanico (giorni) | 0 | 0 | <1 | 1-3 | 4-6 | >7 |
| MOF (organs) | 0 | 1 | 1 | 2 | 3 | >3 |

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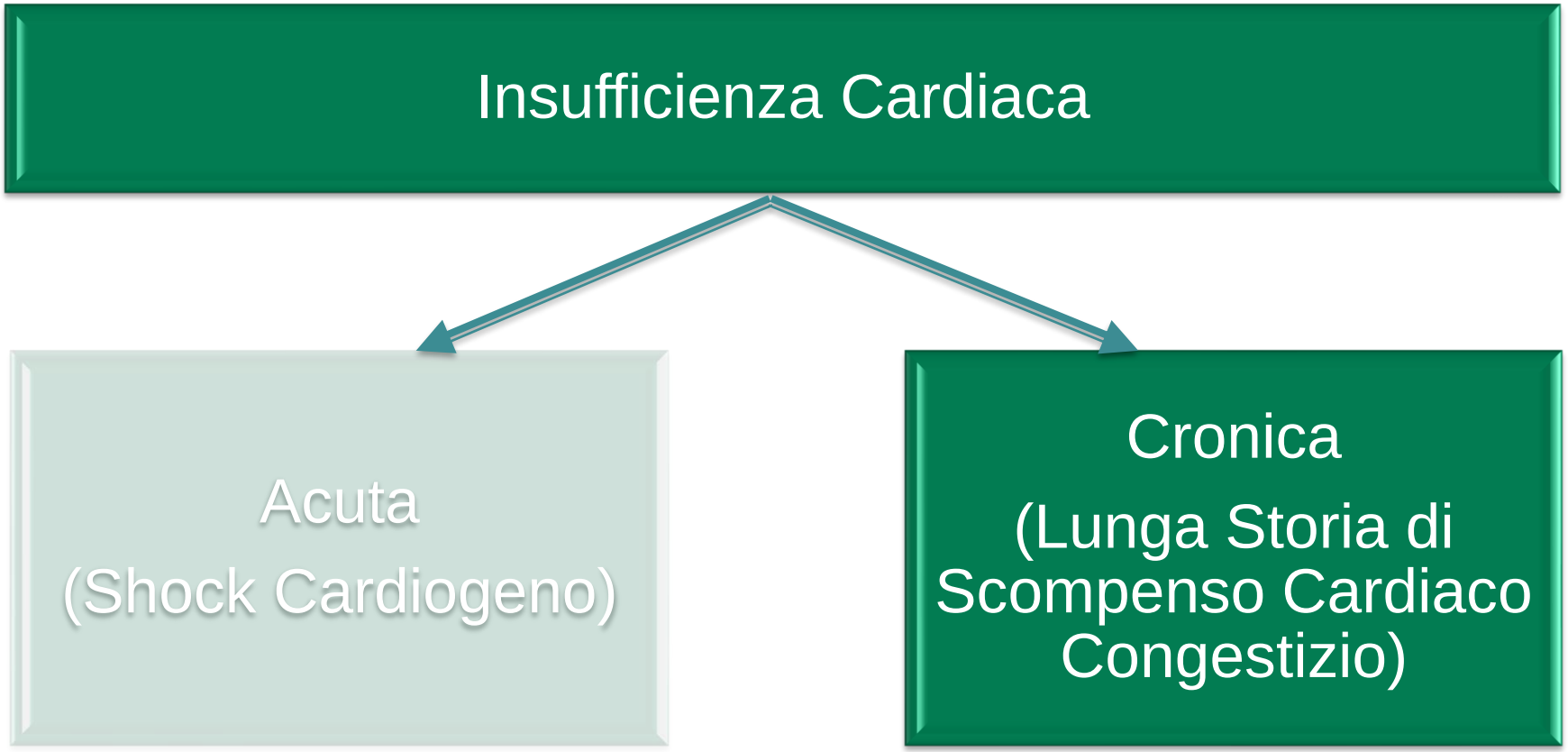
**Riadattato da El Banayosi, Oklaoma City**

# VAD e Centri Spoke

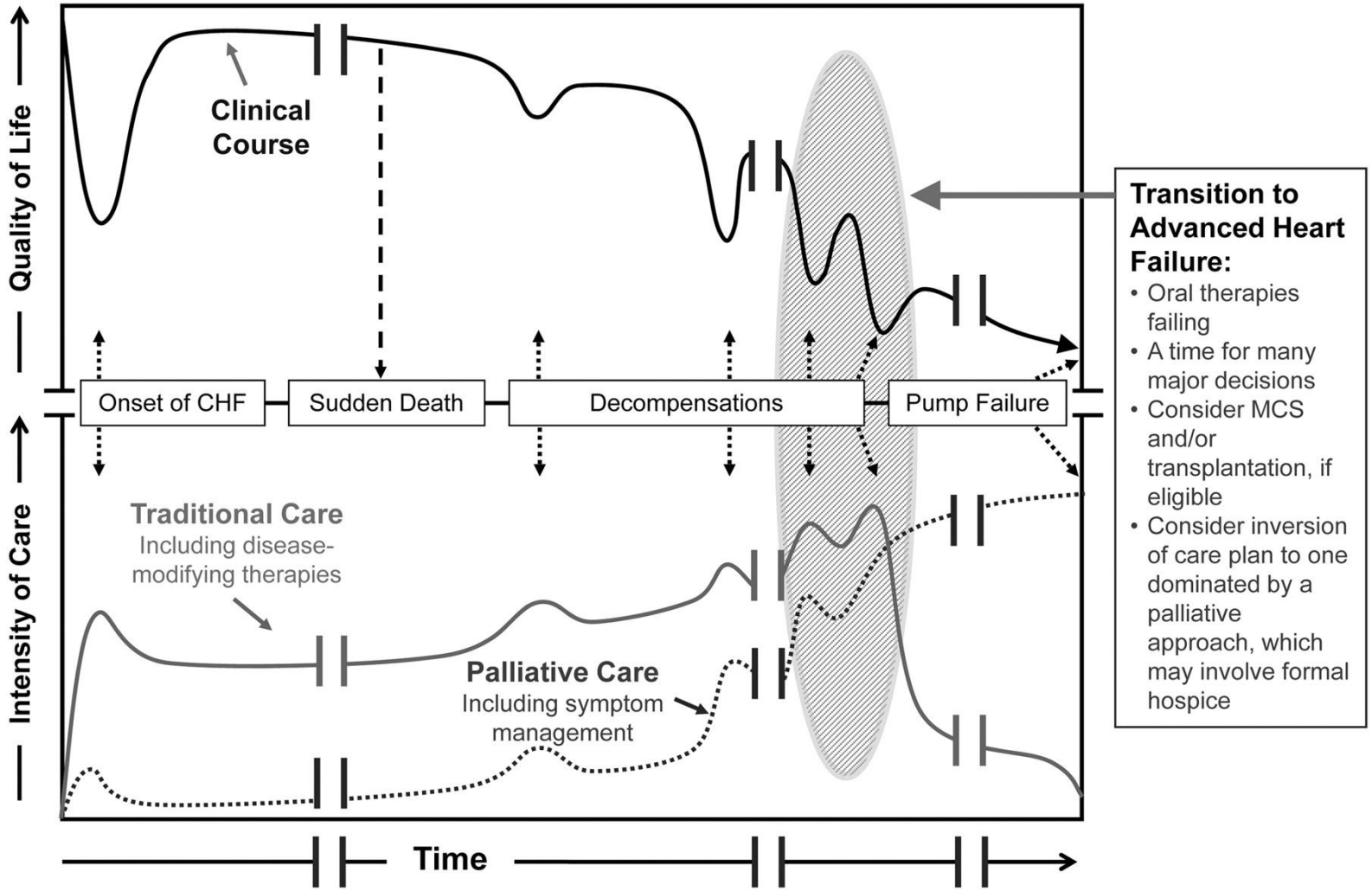


# Criteri di Inclusione/Esclusione

## all'assistenza meccanica al circolo

- Criteri Clinici
  - Prognosi e Sintomi
- Criteri Personali - Psicologici
  - Cambiare una malattia con un'altra
- Criteri Sociali
  - Supporto Sociale e Familiare

**A depiction of the clinical course of heart failure with associated types and intensities of available therapies.**




Larry A. Allen et al. Circulation. 2012;125:1928-1952

American Heart Association.

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# European Society of Cardiology Criteria for Advanced Chronic Heart Failure

1.Sintomi di astenia o dispnea a riposo o per sforzi minimi (NYHA class III or IV)

2.Episodi di Bassa Portata Cardiaca o Scompenso Congestizio

3.Evidenza Obbiettivabile di insufficienza cardiaca per la presenza di almeno 1 dei seguenti criteri:

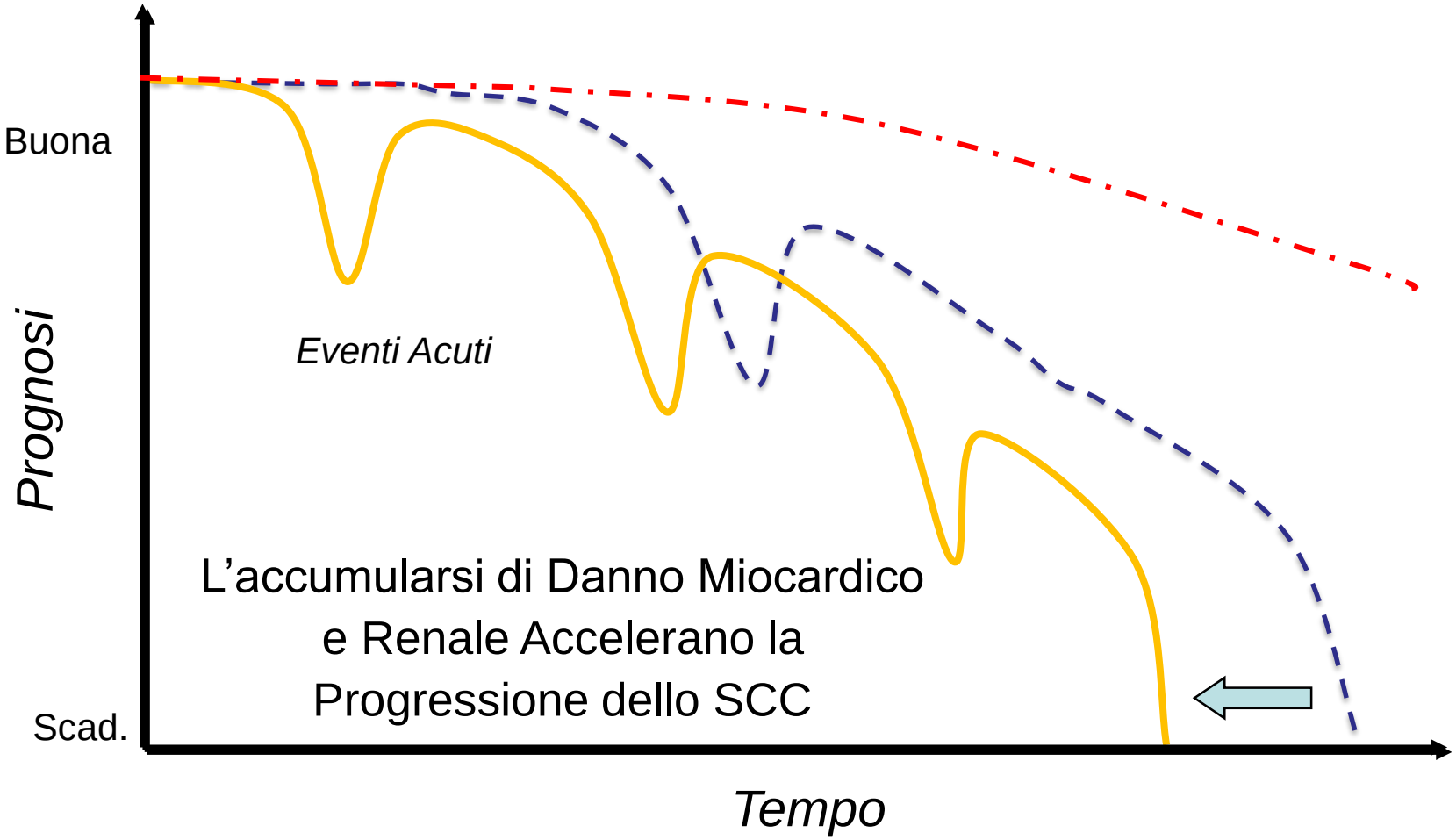
a) Frazione di Ejezione <30%
b) Pattern di flusso transmitralico pseudonormale o restrittivo al Doppler
c) Pressioni di Riempimento del Ventricolo Sinistro e/o Destro aumentate
d) Pepetide Natriuretico Atriale tipo B aumentato

4.Severa Limitazione funzionale come dimostrato dal 6MWT con distanza <300 m o consumo di ossigeno <12 to 14 mL $\cdot$ $g^{-1}$ $\cdot$ $min^{-1}$

5.Storia di almeno 1 episodio di ospedalizzazione negli ultimi 6 mesi

6.I criteri precedenti sono mantenuti nonostante una Terapia Medica Ottimizzata

# Storia Clinica Scompenso

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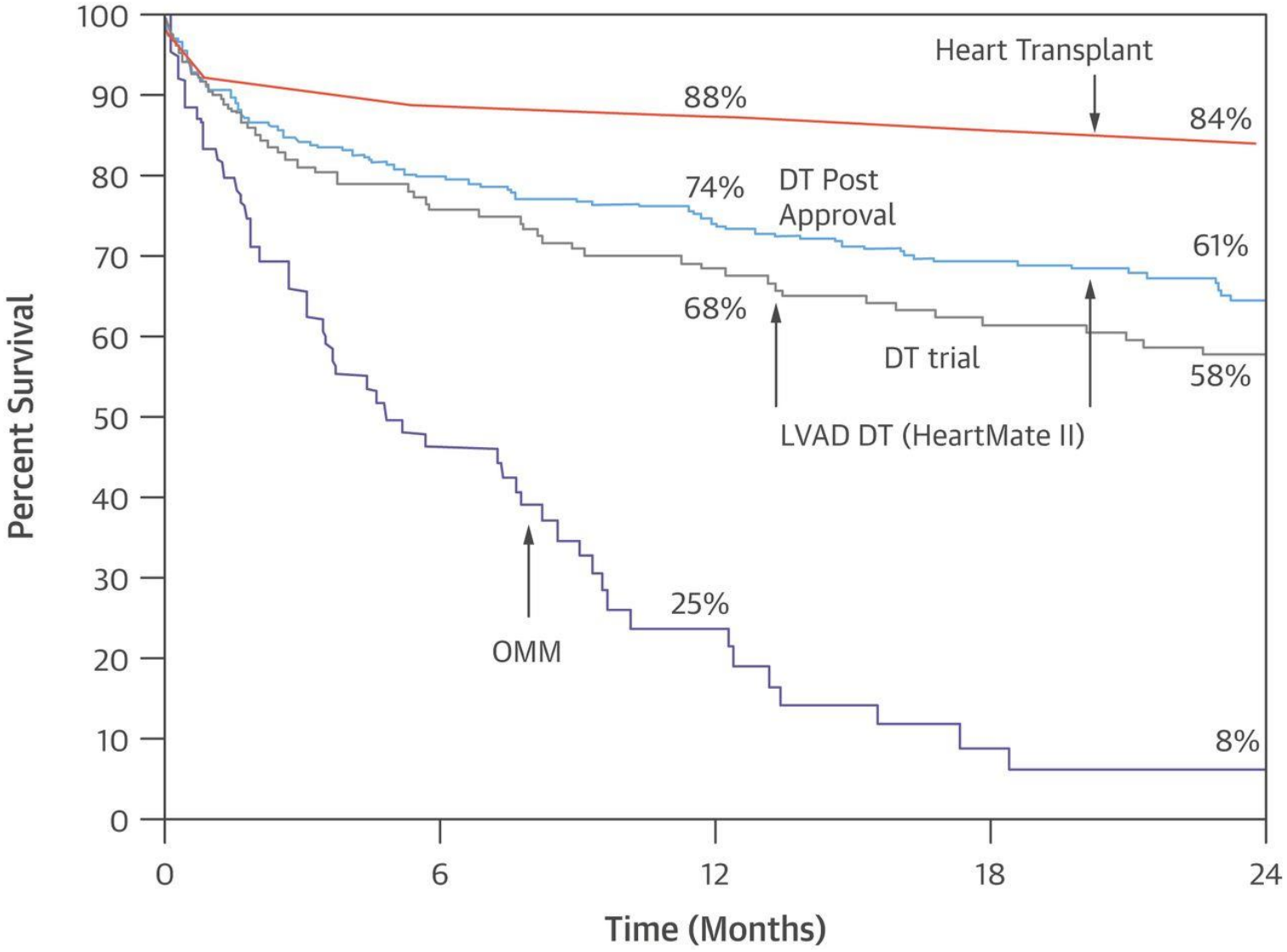
*From Gheorghiade . Am J Cardiol 2005 (mod.)*

# Criteri Clinici

- Cause Di Insufficienza Cardiaca
  - Reversibilità con terapia Medica/Chirurgica
- Terapia Medica
  - Massima Terapia Tollerata
  - Dipendenza da Inotropi (Elevata Mortalità)
- Funzione D'Organo
  - Segni di Declino
    - Non Irreversibilità




**Donna Mancini, and Paolo C. Colombo JACC 2015;65:2542-2555**

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JACC

# Criteri Clinici

**Table 13.3 Patients potentially eligible for implantation of a left ventricular assist device**

| **Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:** |
|---|
| LVEF <25% and, if measured, peak $VO_2$ <12 mL/kg/min. |
| ≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause. |
| Dependence on i.v. inotropic therapy. |
| Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mmHg and SBP ≤80–90 mmHg or CI ≤2 L/min/$m^2$). |
| Absence of severe right ventricular dysfunction together with severe tricuspid regurgitation. |

CI = cardiac index; HF = heart failure; i.v. = intravenous; LVEF = left ventricular ejection fraction; PCWP = pulmonary capillary wedge pressure; SBP = systolic blood pressure; $VO_2$ = oxygen consumption.

# Criteri Clinici

**Table 13.2 INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) stages for classifying patients with advanced heart failure**

| INTERMACS level | NYHA Class | Description | Device | 1y survival with LVAD therapy |
|---|---|---|---|---|
| 1. Cardiogenic shock "Crash and burn" | IV | Haemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critical hypoperfusion of target organs (severe cardiogenic shock). | ECLS, ECMO, percutaneous support devices | 52.6±5.6% |
| 2. Progressive decline despite inotropic support "Sliding on inotropes" | IV | Intravenous inotropic support with acceptable blood pressure but rapid deterioration of renal function, nutritional state, or signs of congestion. | ECLS, ECMO, LVAD | 63.1±3.1% |
| 3. Stable but inotrope dependent "Dependent stability" | IV | Haemodynamic stability with low or intermediate doses of inotropics, but necessary due to hypotension, worsening of symptoms, or progressive renal failure. | LVAD | 78.4±2.5% |
| 4. Resting symptoms "Frequent flyer" | IV ambulatory | Temporary cessation of inotropic treatment is possible, but patient presents with frequent symptom recurrences and typically with fluid overload. | LVAD | 78.7±3.0% |
| 5. Exertion intolerant "Housebound" | IV ambulatory | Complete cessation of physical activity, stable at rest, but frequently with moderate fluid retention and some level of renal dysfunction. | LVAD | 93.0±3.9%[a] |
| 6. Exertion limited "Walking wounded" | III | Minor limitation on physical activity and absence of congestion while at rest. Easily fatigued by light activity. | LVAD / Discuss LVAD as option | - |
| 7. "Placeholder" | III | Patient in NYHA Class III with no current or recent unstable fluid balance. | Discuss LVAD as option | - |

ECLS = extracorporeal life support; ECMO = extracorporeal membrane oxygenation; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; NYHA = New York Heart Association.

[a]Kaplan-Meier estimates with standard error of the mean for 1 year survival with LVAD therapy. Patients were censored at time of last contact, recovery or heart transplantation. Due to small numbers outcomes for INTERMACS levels 5, 6, 7 were combined[610].

## Recommendations for implantation of mechanical circulatory support in patients with refractory heart failure

| Recommendations | Class [a] | Level [b] | Ref [c] |
|---|---|---|---|
| An LVAD should be considered in patients who have end- stage HFrEF despite optimal medical and device therapy and who are eligible for heart transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death (Bridge to transplant indication). | IIa | C | |
| An LVAD should be considered in patients who have end-stage HFrEF despite optimal medical and device therapy and who are not eligible for heart transplantation to, reduce the risk of premature death. | IIa | B | 605, 612, 613 |

HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVAD = left ventricular assist device.

[a]Class of recommendation.

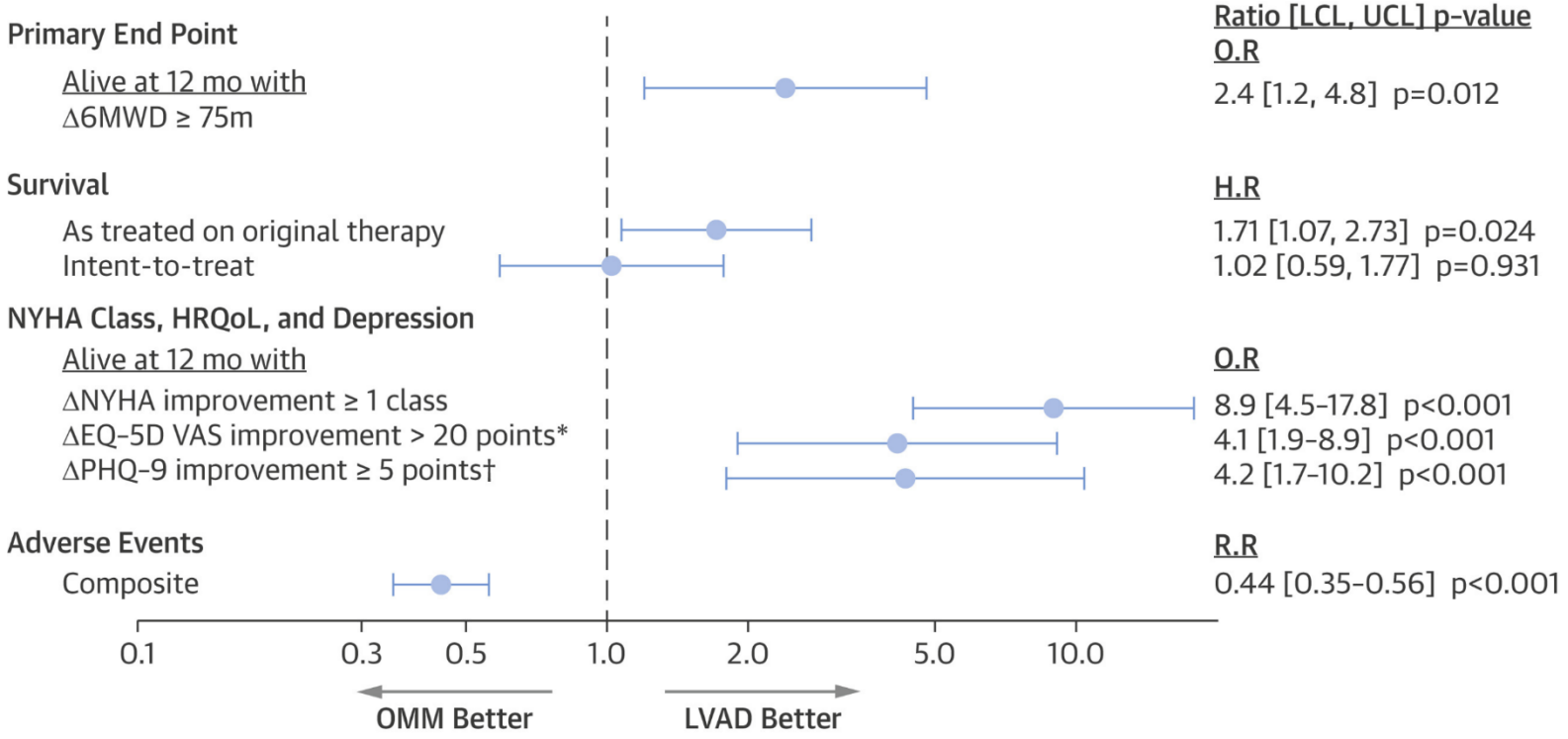
[b]Level of evidence.

[c]Reference(s) supporting levels of evidence.

JACC Journals

## From: Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: Results From the ROADMAP Study

J Am Coll Cardiol. 2015;66(16):1747-1761. doi:10.1016/j.jacc.2015.07.075




### Figure Legend:

**Risk/Benefit Analysis**

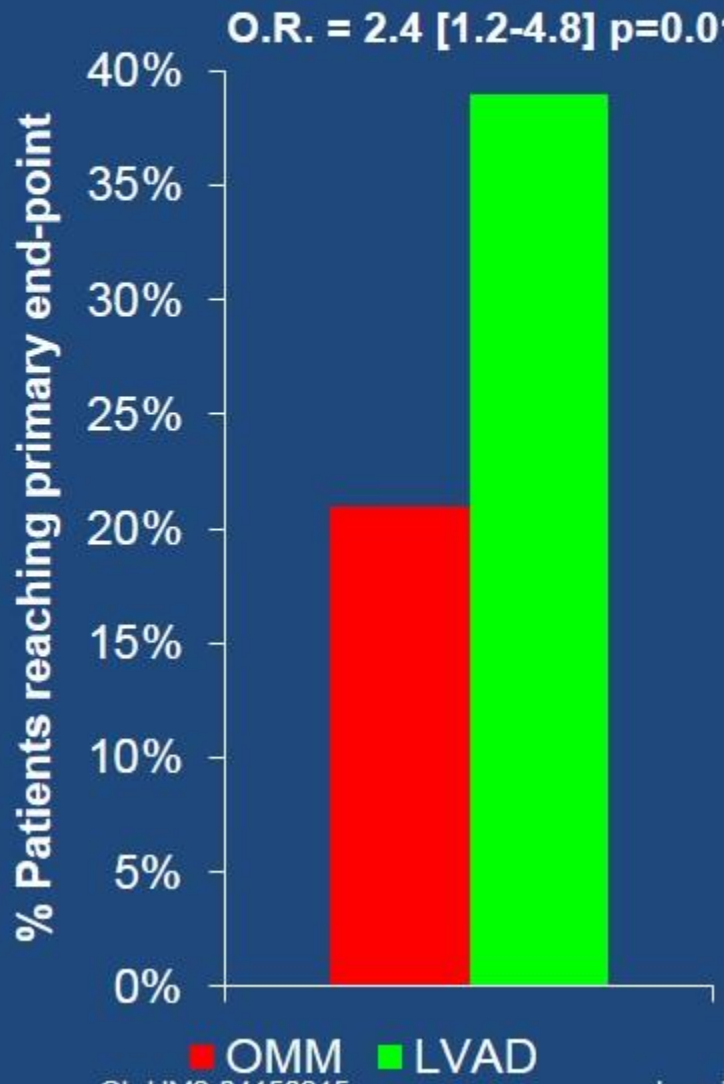
**Survival, changes in functional capacity, health-related quality of life (HRQol), and depression favor LVAD therapy, but the adverse event rate favors OMM. *Includes patients with baseline VAS <68 (lowest 3 quartiles). †Includes patients with baseline PHQ-9 scores >4 (mild or worse depression severity). LCL = lower confidence limit; OR = odds ratio; UCL = upper confidence limit; other abbreviations as in Figures 1, 2, 6, and 7.**

# Criteri Personali

- Intenzione di migliorare qualità di vita
  - Motivazione a guadagnare «tempo di vita»
  - Predisposizione a lottare per stare meglio
  - Attitudine a superare le complicazioni
  - Rassegnazione ad accettare le limitazioni

# Primary Endpoint

## Alive at 12 months on original therapy with increase in 6MWD by 75m




| End Point | OMM (n=81)[1] | LVAD (n=85)[2] |
|---|---|---|
| Alive at 12 months on original therapy with increase in 6MWD by 75m | 17 (21%) | 33 (39%) |
| | | P=0.017 |
| First event that prevented success: | N=64 (79%) | N=52 (61%) |
| Death within 1 year | 17 (21%) | 17 (20%) |
| Delayed LVAD | 18 (22%)[3] | NA |
| Delta 6MWT<75m | 29 (36%) | 33 (39%) |
| Urgent Tx | 0 (0%) | 2 (2%) |

[1]Excluded OMM patients: 9 withdrawn, 13 missing 6MWD
[2]Excluded LVAD patients: 3 withdrawn, 8 missing 6MWD, 1 elective HTx
[3]Including 1 TAH

# Adverse Events

Prevalence:% of patients within 12 months; Incidence: events/pt-yr (eppy) on all data

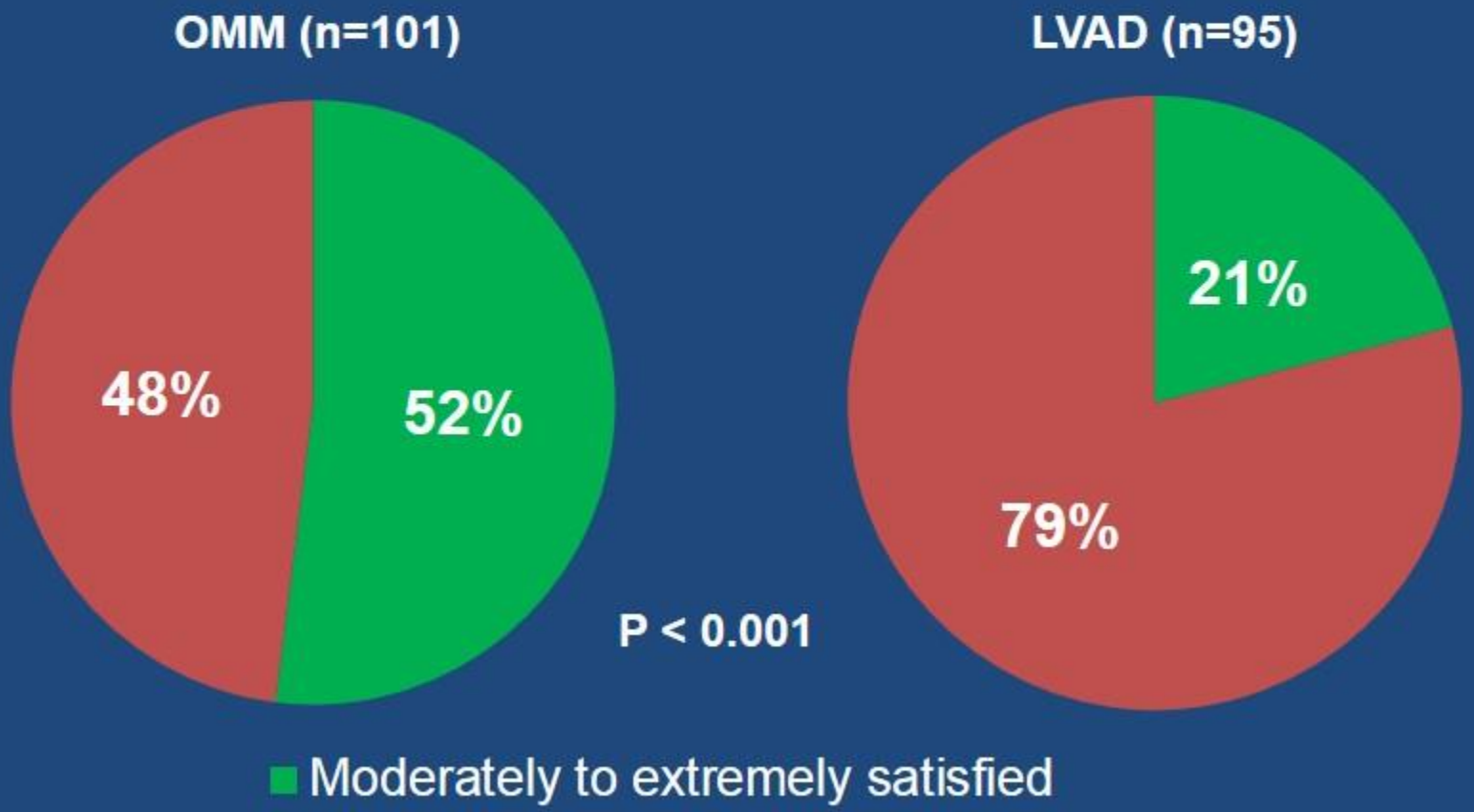
| Adverse Event | OMM (n=103) pts (%) (eppy) | LVAD (n=94) pts (%) (eppy) | DT Trial as reference (eppy) (Park et al)[1] |
|---|---|---|---|
| Bleeding<br>GI bleeding | 1 (1%) (0.02)<br>1 (1%) (0.02) | 44 (47%) (1.22) ***<br>29[2] (31%) (0.76) *** | 1.13<br>NA |
| Driveline Infection | NA | 9 (9.6%) (0.14) *** | 0.22 |
| Pump Thrombus<br>Within 90 days<br>Pump replacement year 1 | NA | 6 (6.4%) (0.08) **<br>1 (1.1%)<br>4 (4.3%) | 0.07[3]<br><br>2.1% |
| Stroke<br>Ischemic<br>Hemorrhagic | 2 (2%) (0.02)<br>1 (1%) (0.01)<br>1 (1%) (0.01) | 9 (9.6%) (0.10) *<br>5 (5.3%) (0.06) *<br>5 (5.3%) (0.04) ns | 0.08<br>0.05<br>0.03 |
| Arrhythmias VT/VF | 6 (5.8%) (0.12) | 17 (18.1%) (0.23) *** | 0.46 |
| Worsening Heart Failure[5] | 36 (35%) (0.68) | 10 (10.6%) (0.12) * | NA |
| Re-hospitalizations | 64 (62%) (1.42) | 75 (79.8%) (2.49) *** | 2.64[4] |
| "Composite" event rate[6] | 39 (38%) (0.83) | 62 (66%) (1.89) *** | 2.09 |
| Relative Risk [95% CI] | OMM/LVAD: 0.44 [0.34, 0.55] *** | | |

[1] Park et al, Circ Heart Failure 2012; 5:241-248
[2] Four patients had 50% of all GI bleeding events
[3] thrombus + hemolysis
[4] Slaughter et al NEJM 2009;361:2241-51
[5] Worsening HF: Symptoms resulting in unexpected hospitalization, ER visit, or urgent clinic visit requiring IV therapy for HF
[6] sum of bleeding, infection, thrombus, stroke, arrhythmias, and worsening HF

*p<0.05 , **p<0.01, ***p<0.001

# Patient Questionnaire at Baseline

Is the patient satisfied with current QoL (at baseline)?



# Patient Questionnaire at Baseline

## Reasons Provided for LVAD or OMM[1]

| LVAD | N (%)[2] |
|---|---|
| It will improve chances to live longer | 81 (85%) |
| It will improve QoL | 79 (83%) |
| It will improve heart failure symptoms | 72 (76%) |
| It will help me return to activities I enjoy | 72 (76%) |

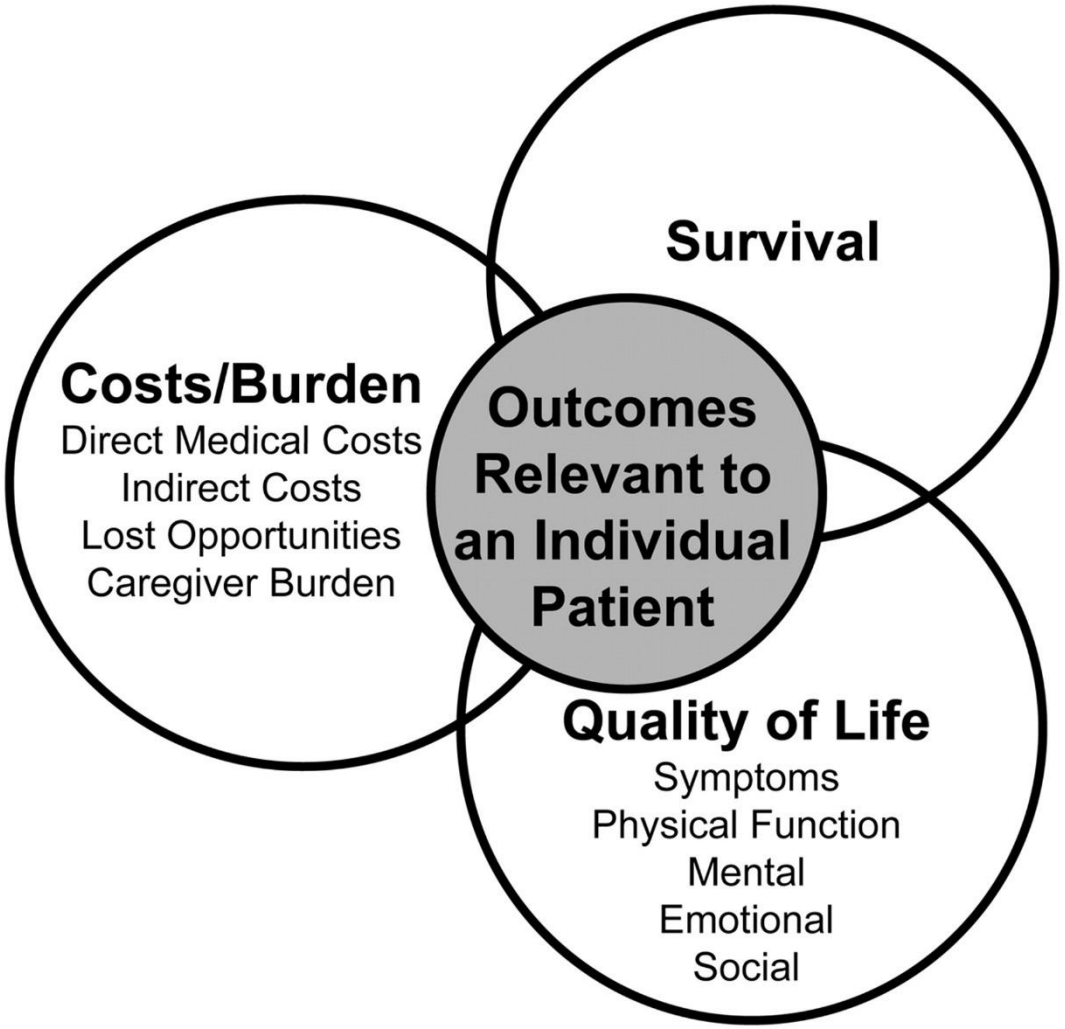
| OMM | N (%)[3] |
|---|---|
| Don't like the idea of major device implantation surgery | 40 (40%) |
| Don't want to depend on a machine | 26 (26%) |
| Don't feel sick enough | 25 (25%) |
| Worried about too many complications with a LVAD | 21 (21%) |
| Don't think a LVAD will improve QoL | 13 (13%) |

[1]Patients could provide multiple reasons
[2]Out of 95 LVAD patients who completed questionnaire
[3]Out of 101 OMM patients who completed questionnaire

# Criteri Sociali

- Paziente completamente dipendente
  - Presenza di Care Giver Dedicato
    - Necessità di Medicazione Driveline
    - Limitazione Funzionale da Pacco Batterie
    - Difficoltà Gestione Accessori

**Prognosis is not only about expectations for survival.**




Larry A. Allen et al. Circulation. 2012;125:1928-1952

American Heart Association.

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# Criteri di Successo


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# Take Home Message

- Criteri di inclusione ed esclusione
  - Clinici
    - Insufficienza Cardiaca Avanzata Acuta e Cronica
    - Segni di Scadimento Emodinamico e/o Danno D'organo non Irreversibile
  - Personali - Psicologici
    - Valutazione Costo/Beneficio Individuale
  - Sociali
- Quando devo telefonare al centro hub?
  - Non appena sospetto che i criteri sono soddisfatti