Trapianto cardiaco: un miraggio ancora per pochi?

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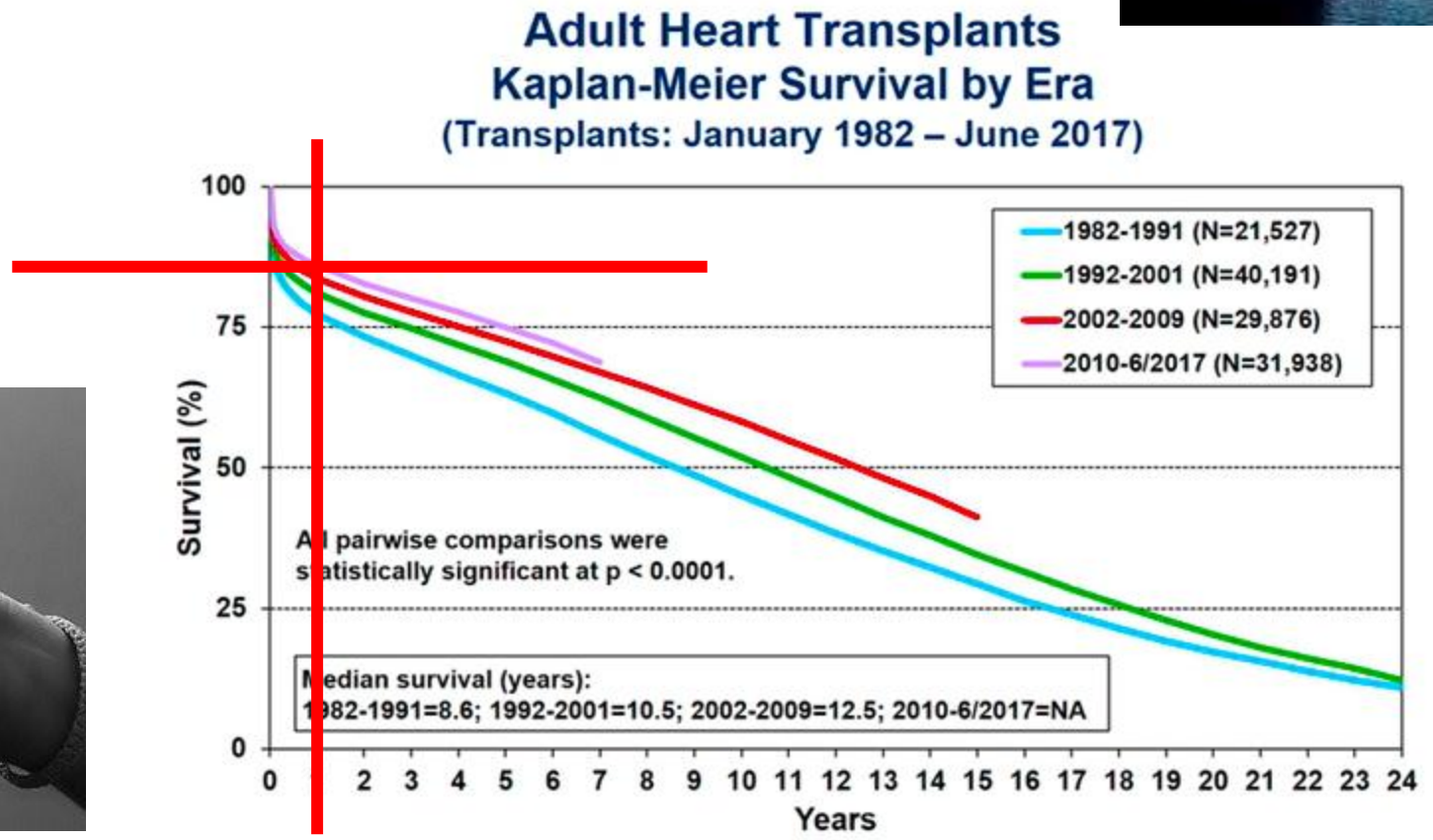
In a perfect world…



ISHLT 2019
INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
JHLT. 2019 Oct; 38(10): 1015-1066

Advanced HF treatment: the reality

Advanced Heart Failure Epidemiology and Outcomes

A Population-Based Study

Of 6386 patients, **only 3.3% patients received an LVAD, and 2.9% patients underwent heart transplantation** during follow-up.

Balance between obtaining the maximum benefit for the patient who needs it most, avoiding futility and wasting the (always scarce) organ.

J Heart Lung Transplant. 1997 Feb;16(2):160-8.

Restrictive criteria for heart transplantation candidacy maximize survival of patients with advanced heart failure

M Frigerio [1], E G Gronda, M Mangiavacchi, B Andreuzzi, T Colombo, C De Vita, F Oliva, E Quaini, A Pellegrini

The patient who needs it the most

- Insufficienza cardiaca avanzata
- Prognosi infausta :
  - Test cardiopolmonare (VO2)
  - Score prognostici (Seattle o HFSS)
- Assenza di controindicazioni

1.1. Cardiopulmonary stress testing to guide transplant listing

A maximal cardiopulmonary exercise test is defined as one with a respiratory exchange ratio (RER) $>$ 1.05 and achievement of an anaerobic threshold on optimal pharmacologic therapy (**Class I, Level of Evidence: B**).

In patients intolerant of a β-blocker, a cutoff for peak oxygen consumption (V_{O_2}) of $\leq$ 14 ml/kg/min should be used to guide listing (**Class I, Level of Evidence: B**).

In the presence of a β-blocker, a cutoff for peak V_{O_2} of $\leq$ 12 ml/kg/min should be used to guide listing (**Class I, Level of Evidence: B**).

In young patients ($<$ 50 years) and women, it is reasonable to consider using alternate standards in conjunction with peak V_{O_2} to guide listing, including percent of predicted ($\leq$ 50%) peak V_{O_2} (**Class IIa, Level of Evidence: B**).

In the presence of a sub-maximal cardiopulmonary exercise test (RER $<$ 1.05), use of ventilation equivalent of carbon dioxide (V_E/V_{CO_2}) slope of $>$ 35 as a determinant in listing for transplantation may be considered (**Class IIb, Level of Evidence: C**).

In obese (body mass index [BMI] $>$ 30 kg/m^2) patients, adjusting peak V_{O_2} to lean body mass may be considered. A lean body mass–adjusted peak V_{O_2} of $<$ 19 ml/kg/min can serve as an optimal threshold to guide prognosis (**Class IIb, Level of Evidence: B**).

Listing patients based solely on the criterion of a peak V_{O_2} measurement should not be performed (**Class III, Level of Evidence: C**).

1.2. Use of heart failure prognosis scores

Heart failure prognosis scores should be performed along with cardiopulmonary exercise test to determine prognosis and guide listing for transplantation for ambulatory patients. An estimated 1-year survival as calculated by the Seattle Heart Failure Model (SHFM) of $<$ 80% or a Heart Failure Survival Score (HFSS) in the high/medium risk range should be considered as reasonable cut points for listing (Class IIb, Level of Evidence: C).

Listing patients solely on the criteria of heart failure survival prognostic scores should not be performed (Class III, Level of Evidence: C).

Avoiding futility

- Absolute contraindications
  - Systemic illness with a life expectancy <2 y despite heart transplantation, including
    - Active or recent solid-organ or blood malignancy within 5 y
    - AIDS with frequent opportunistic infections
    - Systemic lupus erythematosus, sarcoid, or amyloid with active multisystem involvement
    - Irreversible renal or hepatic dysfunction in patients considered for only heart transplantation
    - Significant obstructive pulmonary disease (FEV_1 <1 L/min)
  - Fixed pulmonary hypertension
    - Pulmonary artery systolic pressure >60 mm Hg
    - Mean transpulmonary gradient >15 mm Hg
    - Pulmonary vascular resistance >6 Wood units
- Relative contraindications
  - Age >70 y
  - Any active infection (with exception of device-related infection in VAD recipients)

Times up!

The Journal of
Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

Factors Influencing Access to Transplant, Waitlist Mortality, and Post-Transplant Survival in the Italian National Heart Transplant Database

M. Frigerio • M. Varrenti • C. Santolamazza • ... D. De Angelis • A.D. Milano • M. Valsecchi •

Variable	1-y WL death Univariate, HR (95% CI)	Multivariate, HR (95% CI)	1-y HTX Univariate, HR (95% CI)	Multivariate, HR (95% CI)	post-HTX death Univariate, HR (95% CI)	Multivariate, HR (95% CI)
Gender, M vs F	ns	ns	0.55 (0.47-0.65)***	0.56 (0.45-0.70)***	1.63 (1.19-2.30)**	1.52 (1.05-2.19)*
Age, ≥ vs <55y	ns	ns	0.80 (0.69-0.93)**	ns	1.56 (1.20-2.03)***	1.57 (1.16-2.14)**
BMI, >25-30 vs ≤25	ns	ns	0.64 (0.55-0-76)***	0.71 (0.57-0.89)**	ns	ns
BMI, >30 vs ≤25	ns	ns	0.56 (0.42-0.73)***	0.65 (0.46-0.91)***	1.91 (1.27-2.88)**	1.58 (1.00-2.51)#
Blood type(1), A vs 0	ns	ns	1.71 (1.45-2.03)***	1.85 (1.49-2.30)***	ns	ns
Blood type(1), AB vs 0	ns	ns	2.41 (1.76-3.29)***	2.30 (1.55-3.41)***	ns	ns
Blood type(1), B vs 0	ns	ns	1.87 (1.49-2.35)***	1.77 (1.31-2.38)***	ns	ns
Status(2) 1, vs 2B	6.2 (4.06-9.31)***	6.58 (3.40-12.70)***	5.20 (4.27-6.33)***	2.49 (1.80-3.46)***	1.60 (1.18-2.16)**	ns
Status(2) 2A, vs 2B	1.91 (1.32-2.76)***	2.98 (1.76-5.05)***	1.67 (1.40-2.00)***	2.04.(1.61-2.60)***	ns	ns
Creatinine, > vs ≤1 mg/dl	2.28 (1.50-3.46)***	2.57 (1.42-4.66)**	0.85 (0.72-0.97)*	ns	1.86 (1.36-2.55)***	1.48 (1.05-2.08)*
Bilirubine, > vs ≤1.38 mg/dl	2.23 (1.62-3.06)***	ns	1.35 (1.16-1.58)***	ns	ns	ns
Cardiac Index, > vs ≤1.7 l/min/m²	0.58 (0.40-0.84)**	0.60 (0.40-0.91)*	ns	ns	ns	ns
HR, bpm, continuous	1.02 (1.01-1.03)***	1.02 (1.01-1.03)**	1.02 (1.01-1.02)***	ns	ns	ns
LVAD, vs no MCS	ns	0.37 (0.14-0.85)*	ns	0.47 (0.32-0.69)***	ns	ns
Short term MCS, vs no MCS	3.59 (2.44-5.29)***	2.56 (1.46-4.52)***	2.92 (2.41-3.53)***	ns	1.41 (1.02-1.96)*	ns
Emergency allocation requested, y vs no	1.52 (1.02-2.28)*	0.51 (0.25-1.02)#	2.74 (2.33-3.22)***	1.92 (1.52-2.44)***	1.66 (1.26-2.18)***	ns

Legends. (1): crude incidence of death at 1-y significantly higher in blood type 0 vs others. (2): Status 1: short term MCS, complicated LVAD, ventilator + IABP + inotropes; Status 2A: non complicated LVAD, in-hospital i.v. inotr

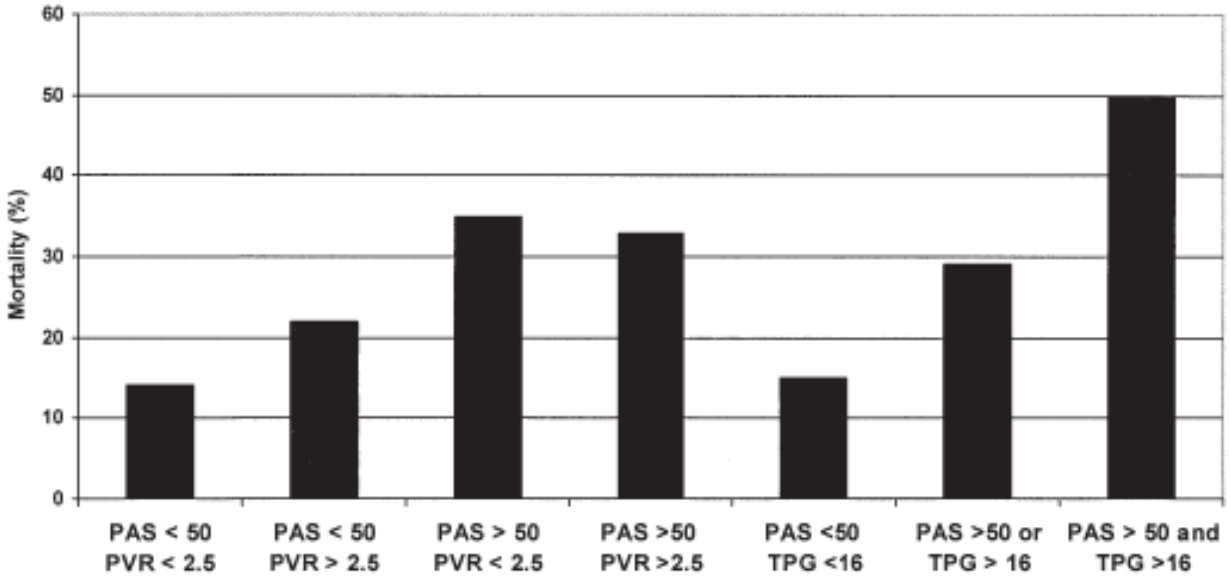
***p<.001; #p<.06

The Journal of Heart and Lung Transplantation, Vol 38, No 4S, April 2019

Times up!

Pre-Transplant Reversible Pulmonary Hypertension Predicts Higher Risk for Mortality After Cardiac Transplantation

Javed Butler, MD, MPH,[a,b,c,d,e] Mark A. Stankewicz, MD,[a] Jack Wu,[a] Don B. Chomsky, MD,[a,d]
Renee L. Howser, RN, MSN,[a] Ghazanfar Khadim, MD,[a] Stacy F. Davis, MD,[a]
Richard N. Pierson, III, MD,[f] and John R. Wilson, MD[a]

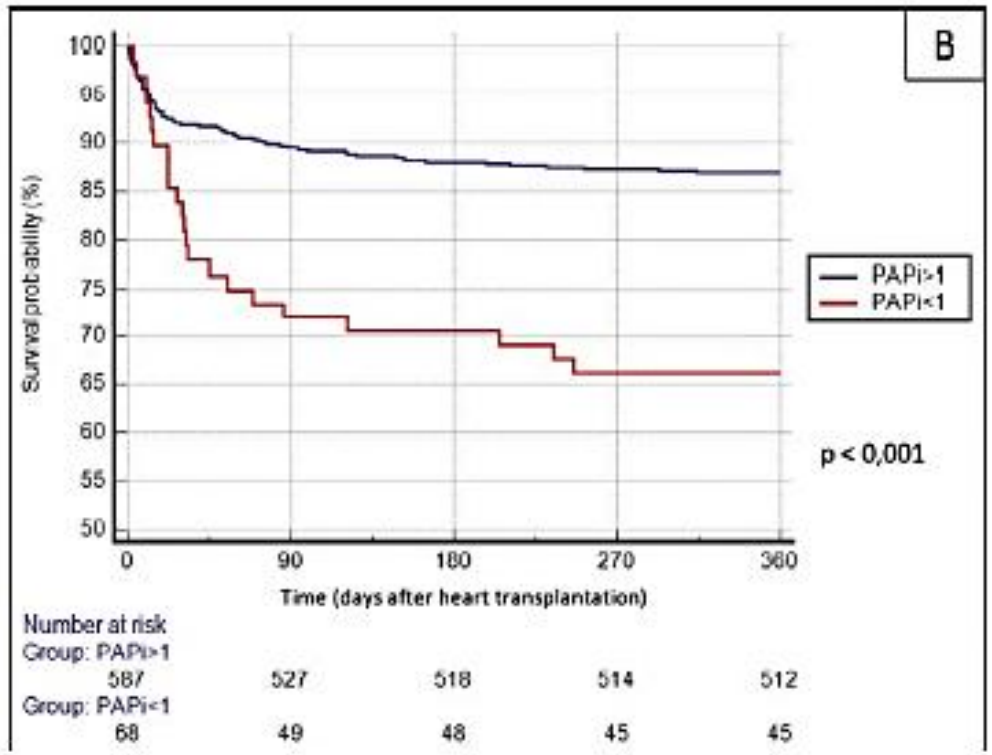


Journal of Cardiac Failure Vol. 00 No. 00 2021

Pretransplant Right Ventricular Dysfunction Is Associated With Increased Mortality After Heart Transplantation: A Hard Inheritance to Overcome

MATTEO BELLETTINI, MD,[1] SIMONE FREA, MD,[1] STEFANO PIDELLO, MD,[1] MASSIMO BOFFINI, MD,[2]
PAOLO BORETTO, MD,[1] GUGLIELMO GALLONE, MD,[1] FEDERICA BONGIOVANNI, MD,[1] MARCO MASETTI, MD, PhD,[3]
MARIO SABATINO, MD,[3] CLAUDIA RAINERI, MD,[1] DAVIDE PACINI, MD, PhD,[3] SOFIA MARTIN SUAREZ, MD, PhD,[3]
ANTONIO LOFORTE, MD, PhD,[3] MAURO RINALDI, MD,[2] LUCIANO POTENA, MD, PhD,[3,§] AND
GAETANO M. DE FERRARI, MD[1,§]

Turin, and Bologna, Italy



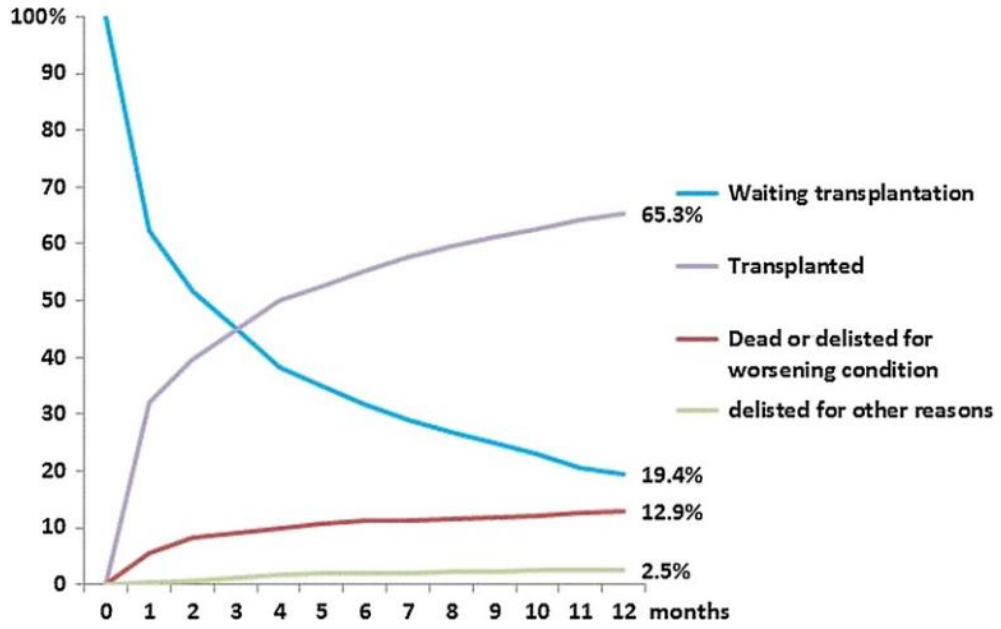
Waiting times

Circulation: Heart Failure

Changing Demographics, Temporal Trends in Waitlist, and Posttransplant Outcomes After Heart Transplantation in the United States: Analysis of the UNOS Database 1991–2019

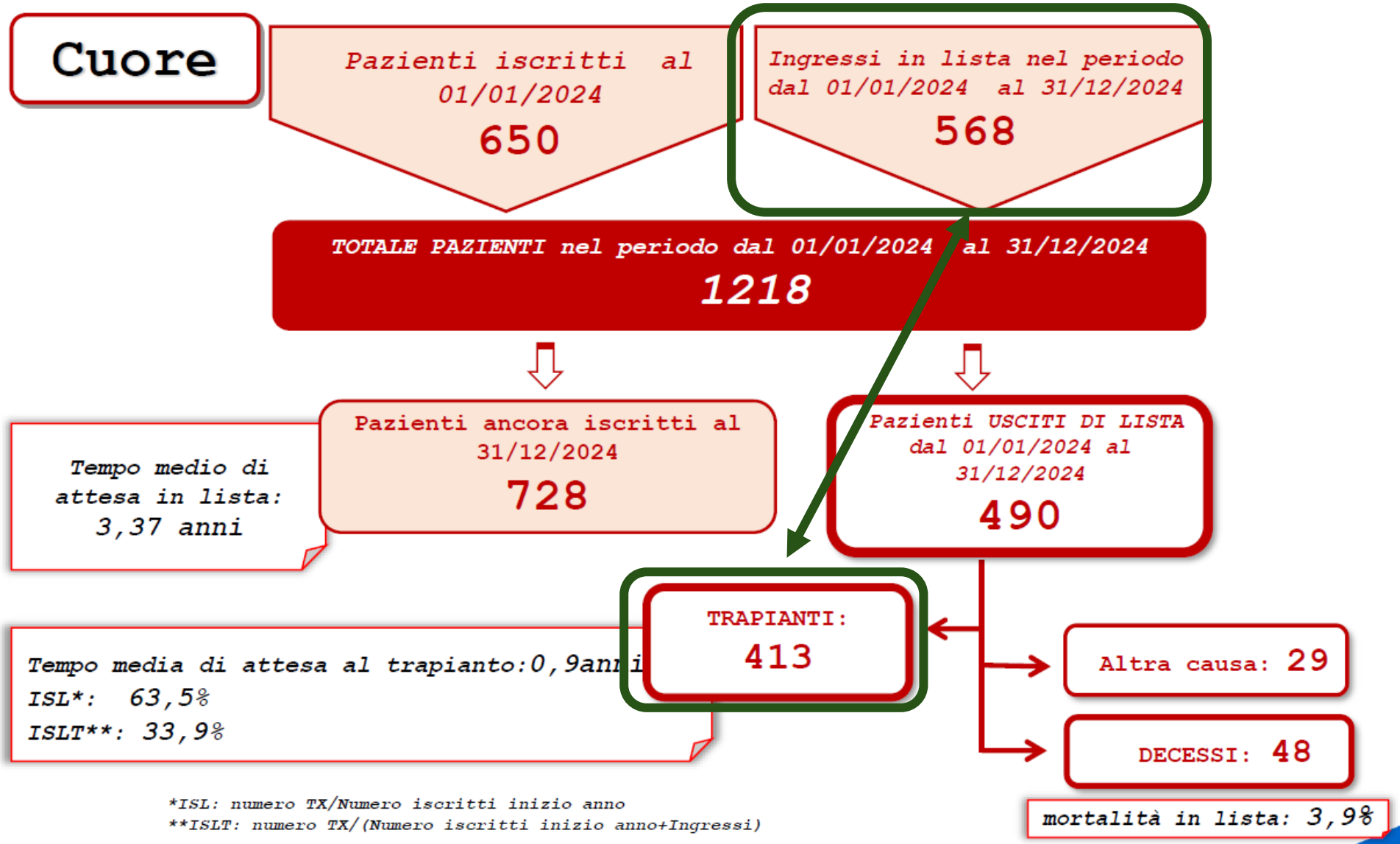
Emmanuel Akintoye, Paulino Alvarez, Doosup Shin, Alexander Egbe, Anthony Panos, Frank Sellke, Alexandros Briasoulis

Originally published 25 Oct 2021 | https://doi.org/10.1161/CIRCHEARTFAILURE.121.008764 |
Circulation: Heart Failure. 2021;0:CIRCHEARTFAILURE.121.008764



Competing outcomes of candidates on the waiting list—derivation cohort, N = 1555.

Flussi Lista di attesa 01/01/2024 – 31/12/2024



*ISL: numero TX/Numero iscritti inizio anno
**ISLT: numero TX/(Numero iscritti inizio anno+Ingressi)

Fonte dati: SIT

Still waiting…

Impact of Recipient Body Mass Index on Organ Allocation and Mortality in Orthotopic Heart Transplantation

Eric S. Weiss, MD, MPH,[a] Jeremiah G. Allen, MD,[a] Stuart D. Russell, MD,[b] Ashish S. Shah, MD,[a] and John V. Conte, MD[a]

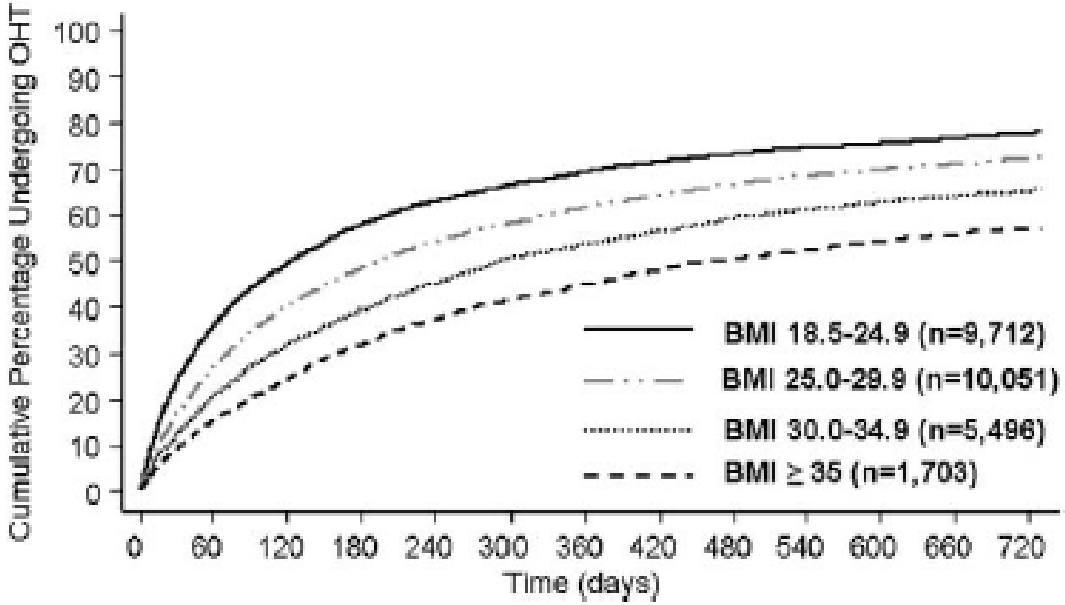


Figure 2. Cumulative incidence of OHT for those patients on the wait list, stratified by BMI at listing (based on OPTN data, May 2008).

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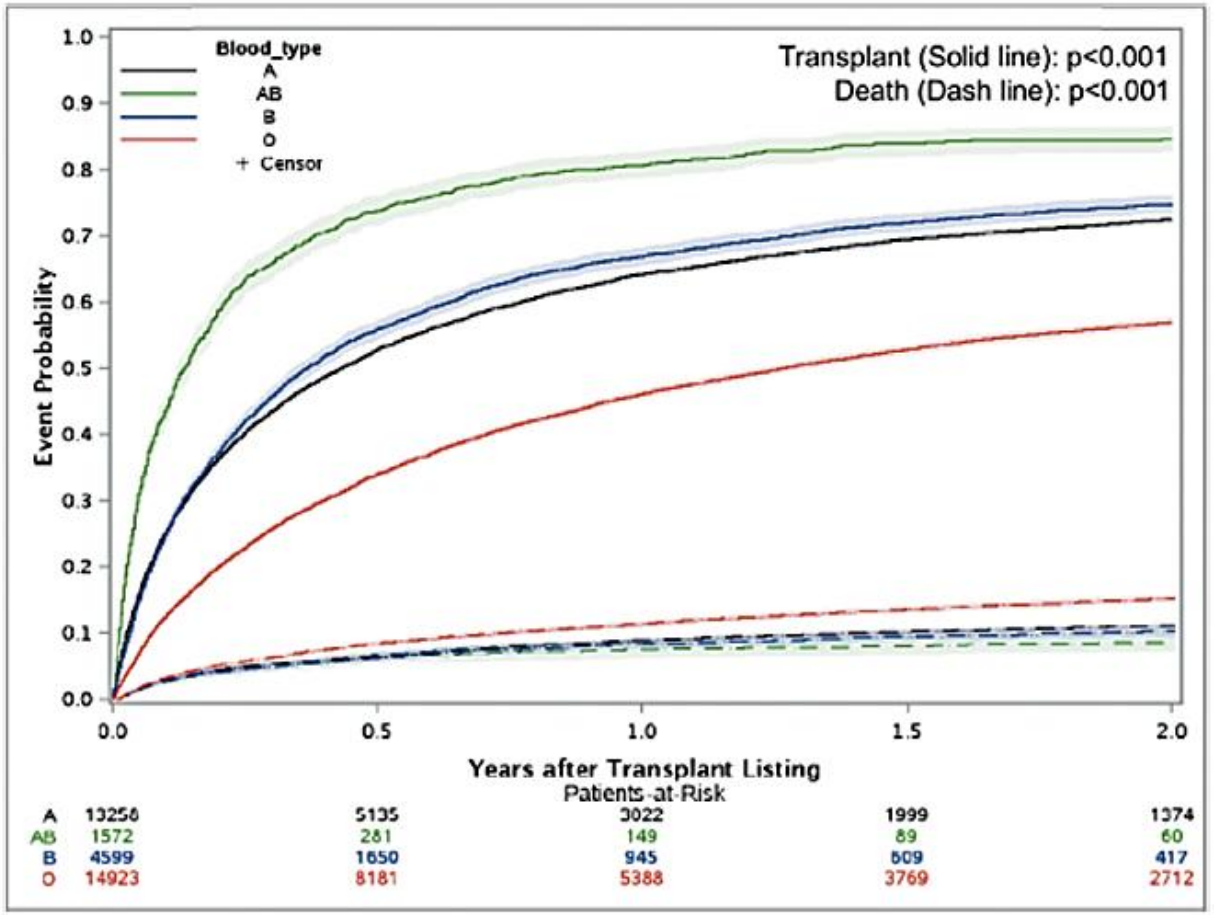
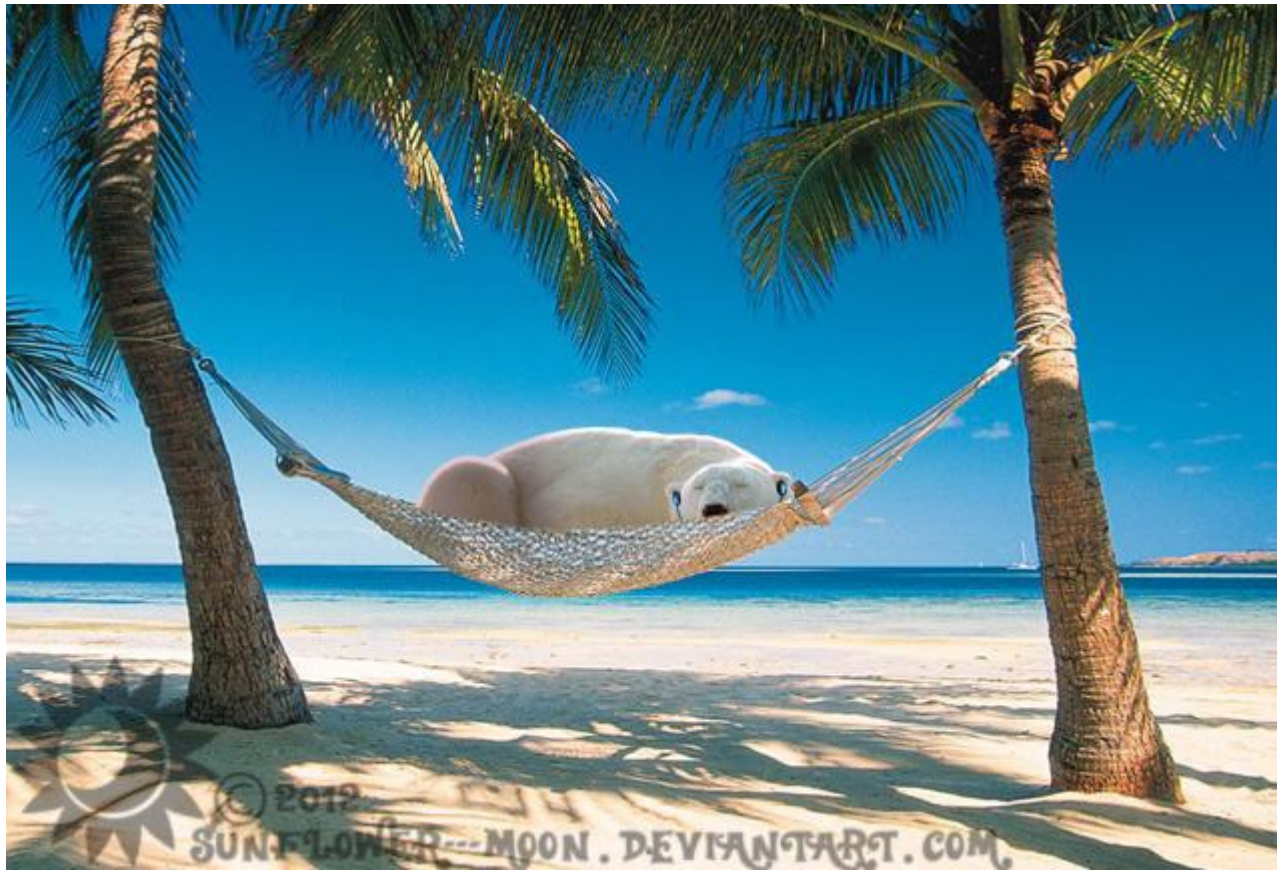
Volume 28, Number 11

Association between recipient blood type and heart transplantation outcomes in the United States

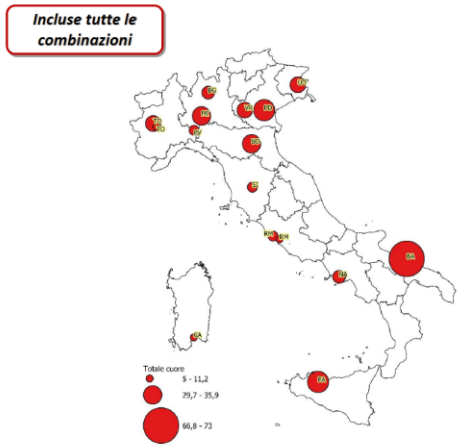


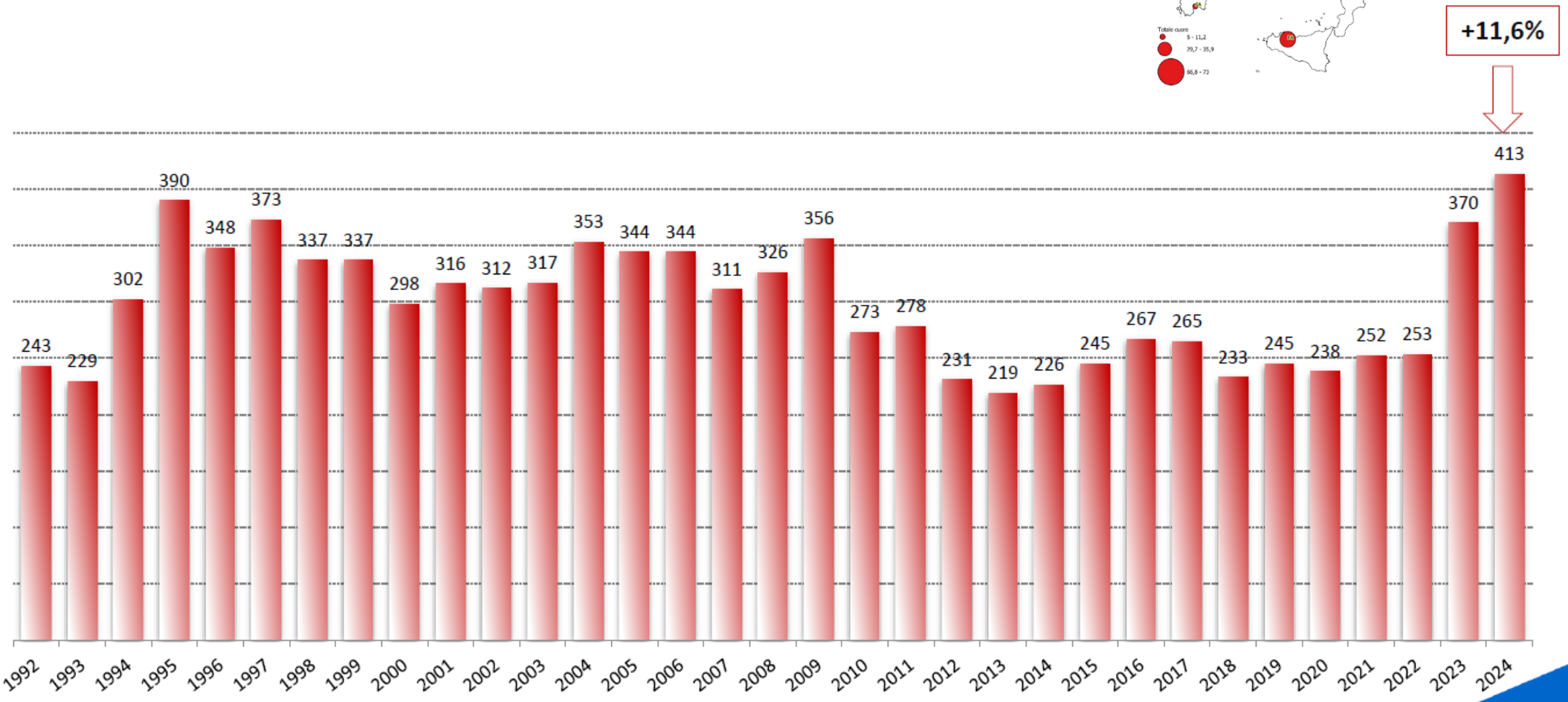
The Journal of Heart and Lung Transplantation, Vol 39, No 4, April 2020

Other perspectives?



Increase the donor pool!





Fonte dati: SIT

Centro Nazionale Trapianti

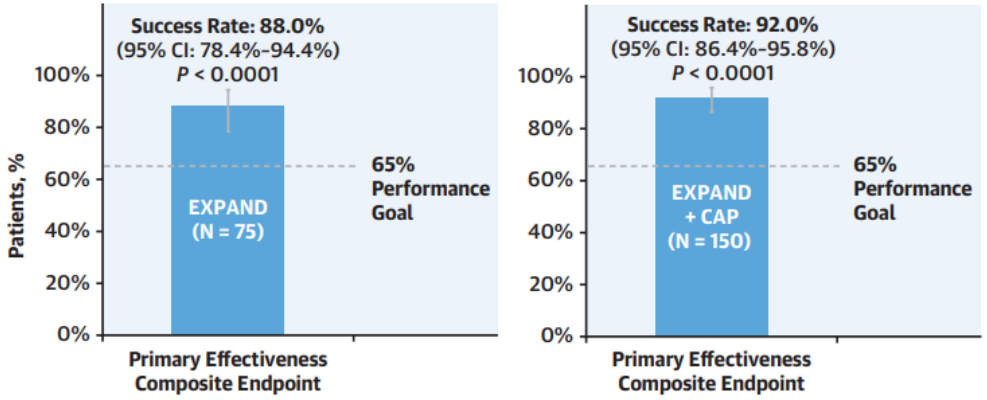
Organ Care System

Patients received extended criteria hearts from brain-dead donors.
Extended criteria hearts were defined by an expected cross-clamp time of ≥4 hours or expected cross-clamp time of ≥2 hours plus ≥1 of the following risk factors:

- Donor age ≥55 years, donor age 45–55 years with no coronary angiogram
- Reported downtime of ≥20 minutes with stable hemodynamics at final assessment
- LV septal or posterior wall thickness of 13–16 mm, LVEF 40%–50%
- Donor angiogram with luminal irregularities with no significant CAD
- History of carbon monoxide poisoning with good cardiac functional final assessment
- History of diabetes combined with negative coronary angiogram for CAD
- Social history of alcoholism with good cardiac function at time of final assessment

150 of 173
Donor Hearts Transplanted After OCS Perfusion and Assessment

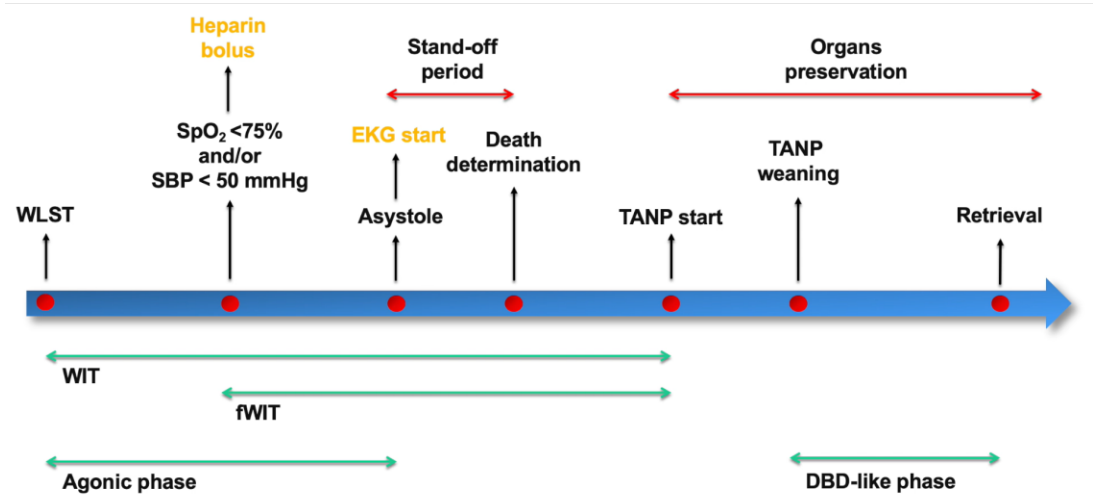
23 of 173
Hearts Turned Down

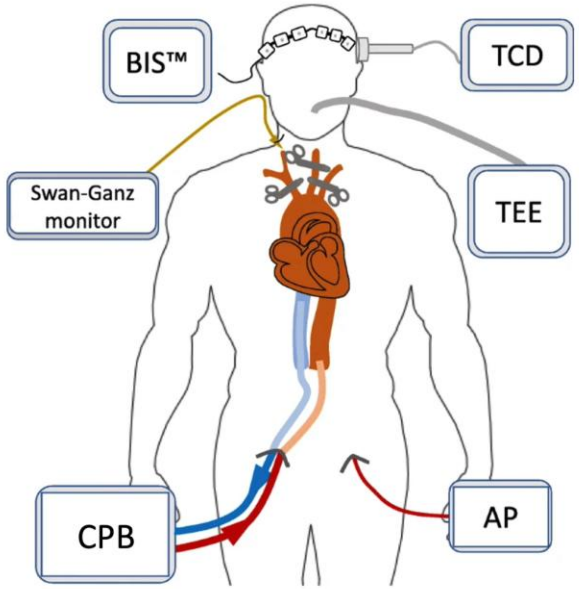


Schroder JN, et al. J Am Coll Cardiol HF. 2024;12(3):438-447.

Donor after Circulatory Death (DCD)

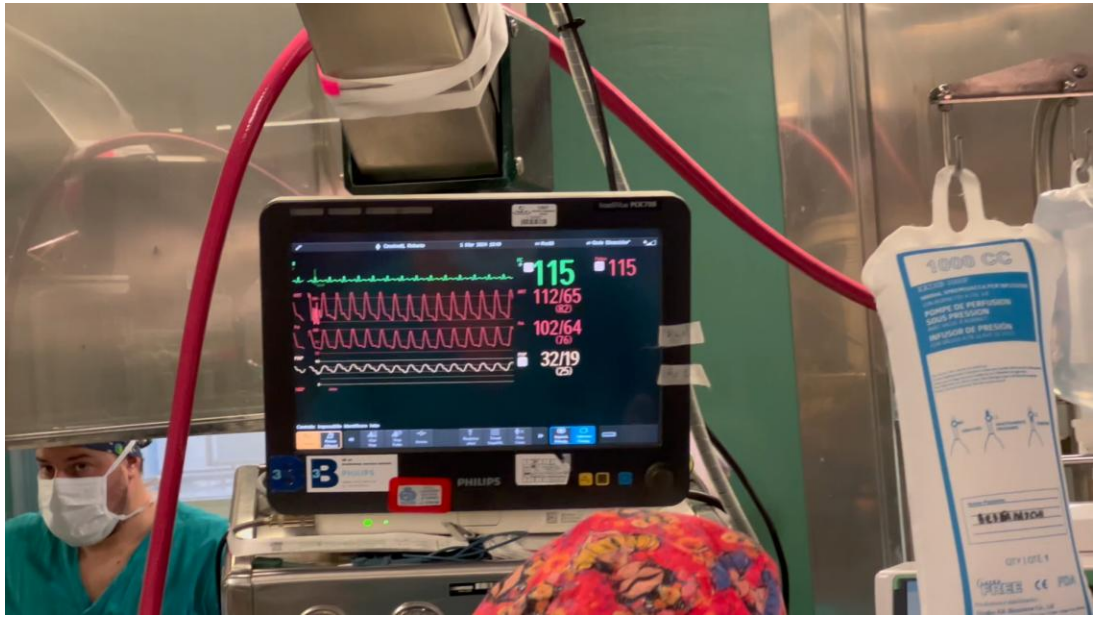
- **Agonic phase**: extubation + analgesia
- **Functional Warm Ischemia**: heparin drip at SBP <50 mmHg and/or SpO_2 <70%
- TEE monitoring of aortic valve opening
- **Stand-off period**: 20 min of EKG registration from asystole





Courtesy of dr. M.Marro

DCD case: before withrawal of treatment

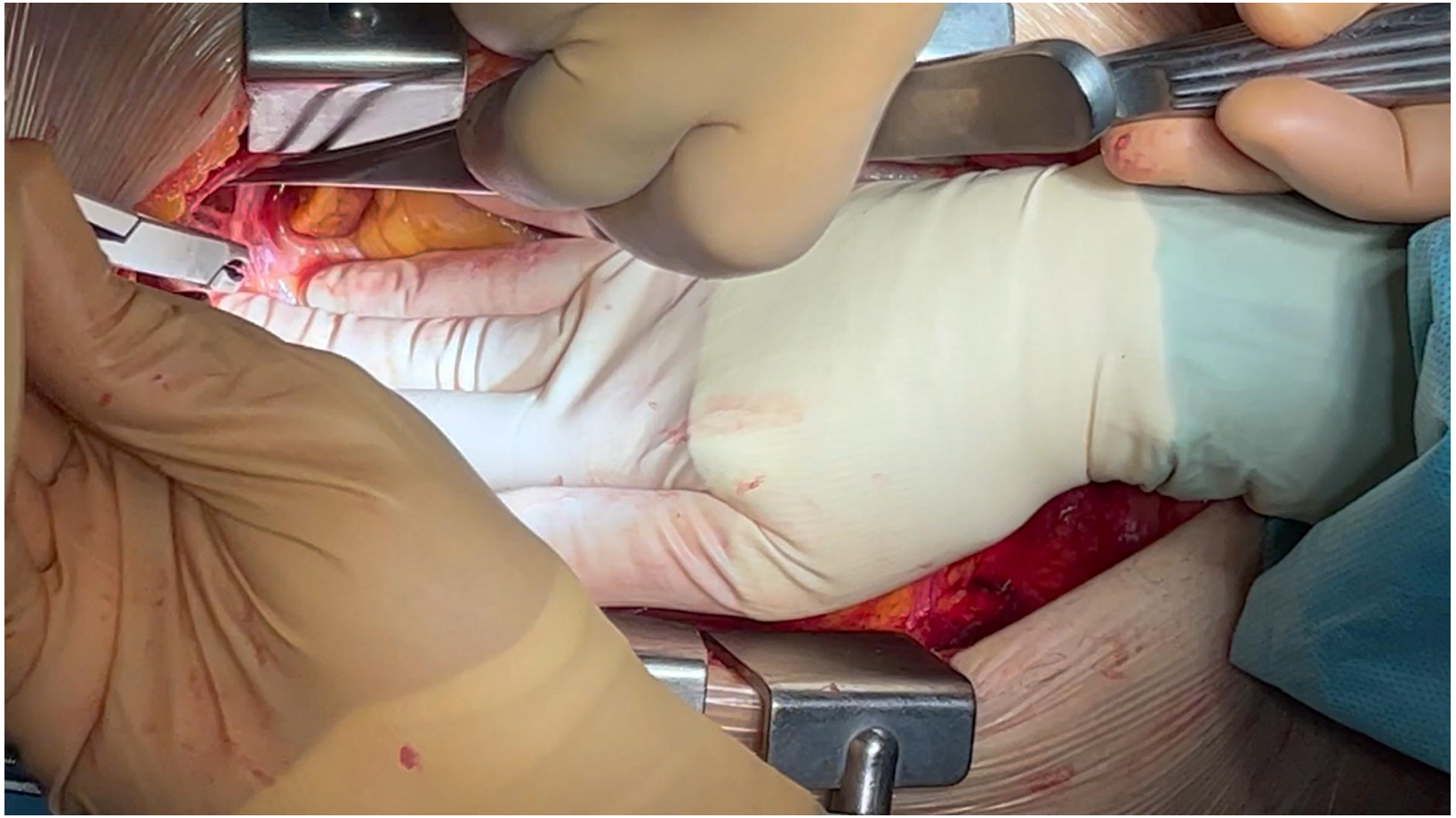


Courtesy of dr. M.Marro

DCD case: death determination

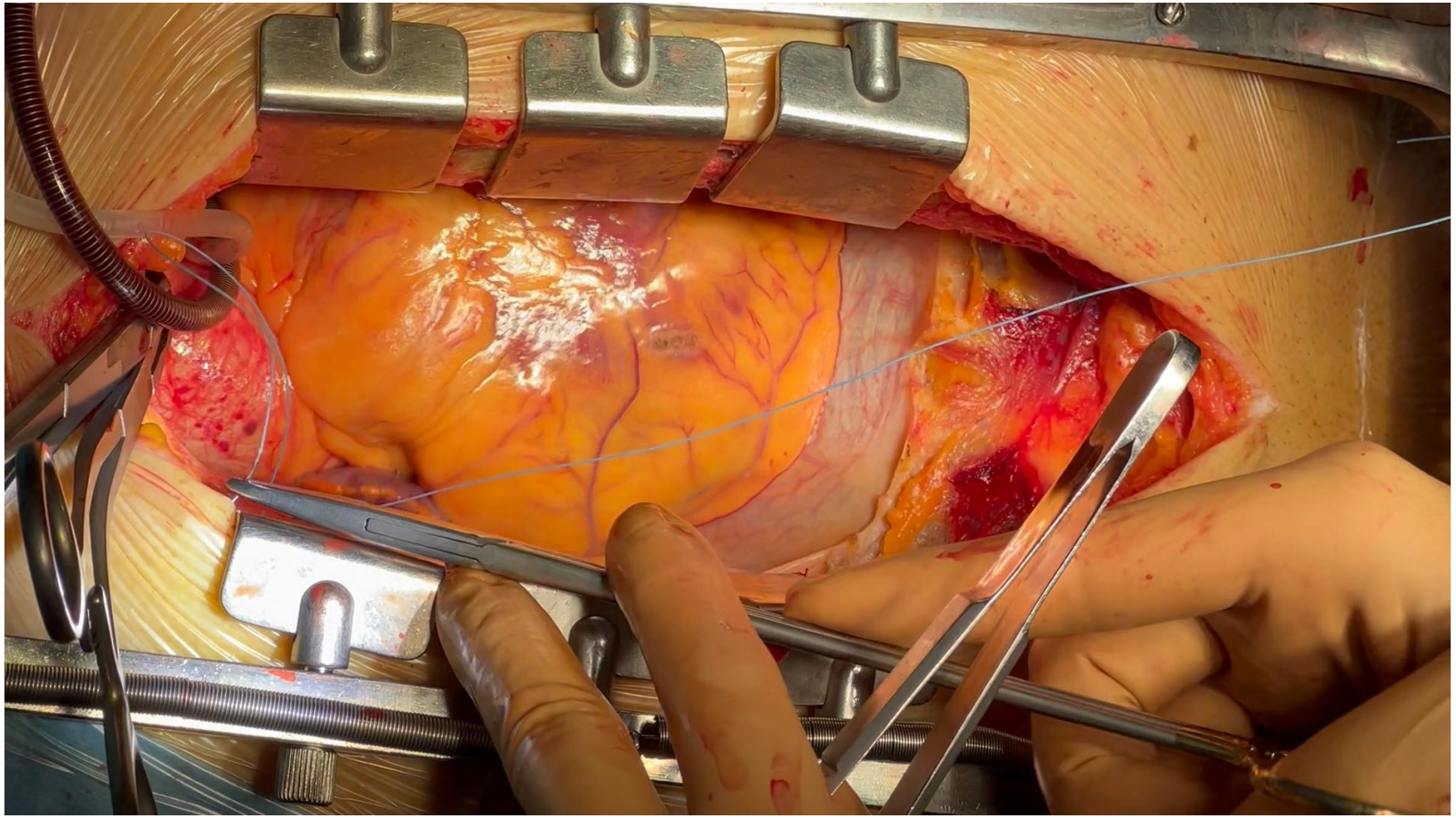
Courtesy of dr. M.Marro

DCD case: ECMO starts



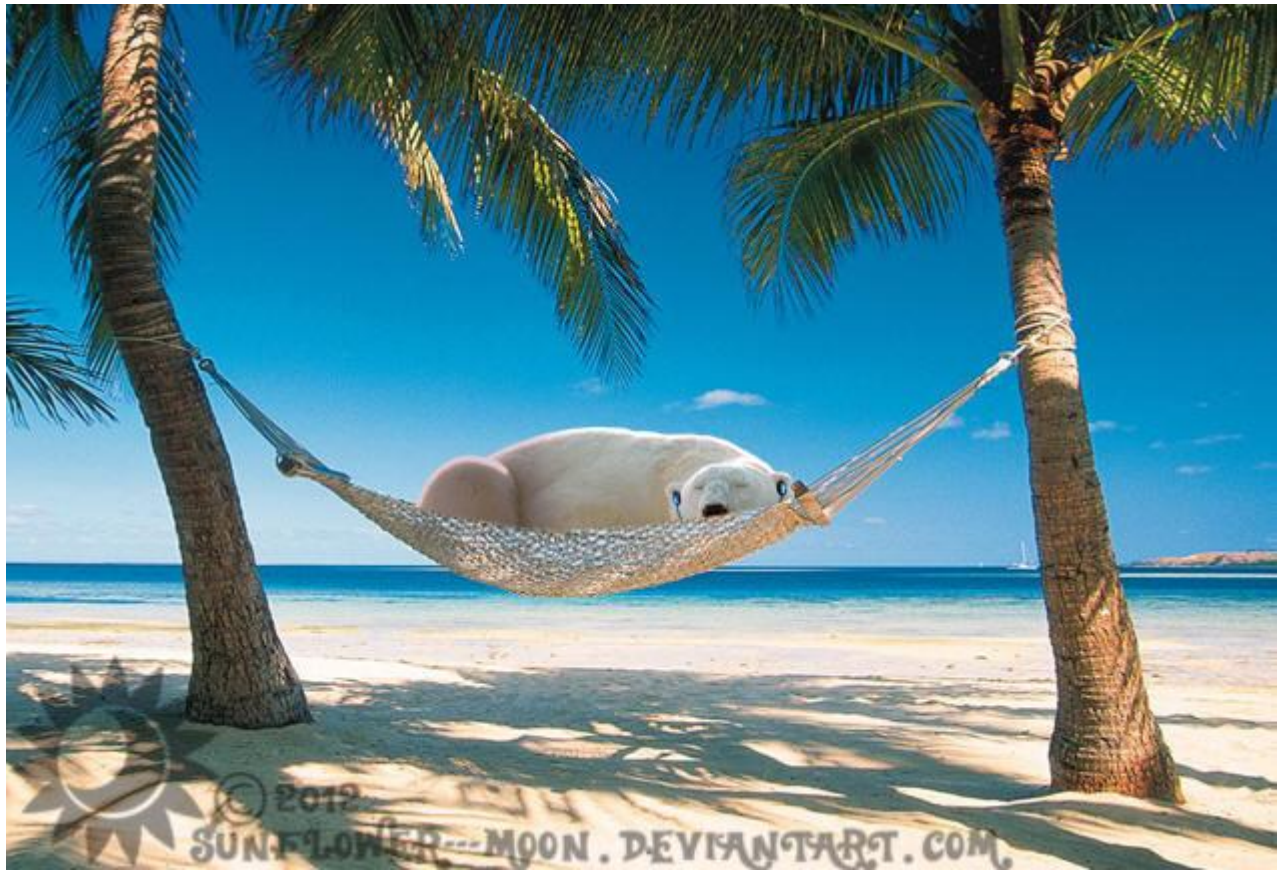
Courtesy of dr. M.Marro

DCD case: organ quality assessment



Courtesy of dr. M.Marro

Other perspectives?

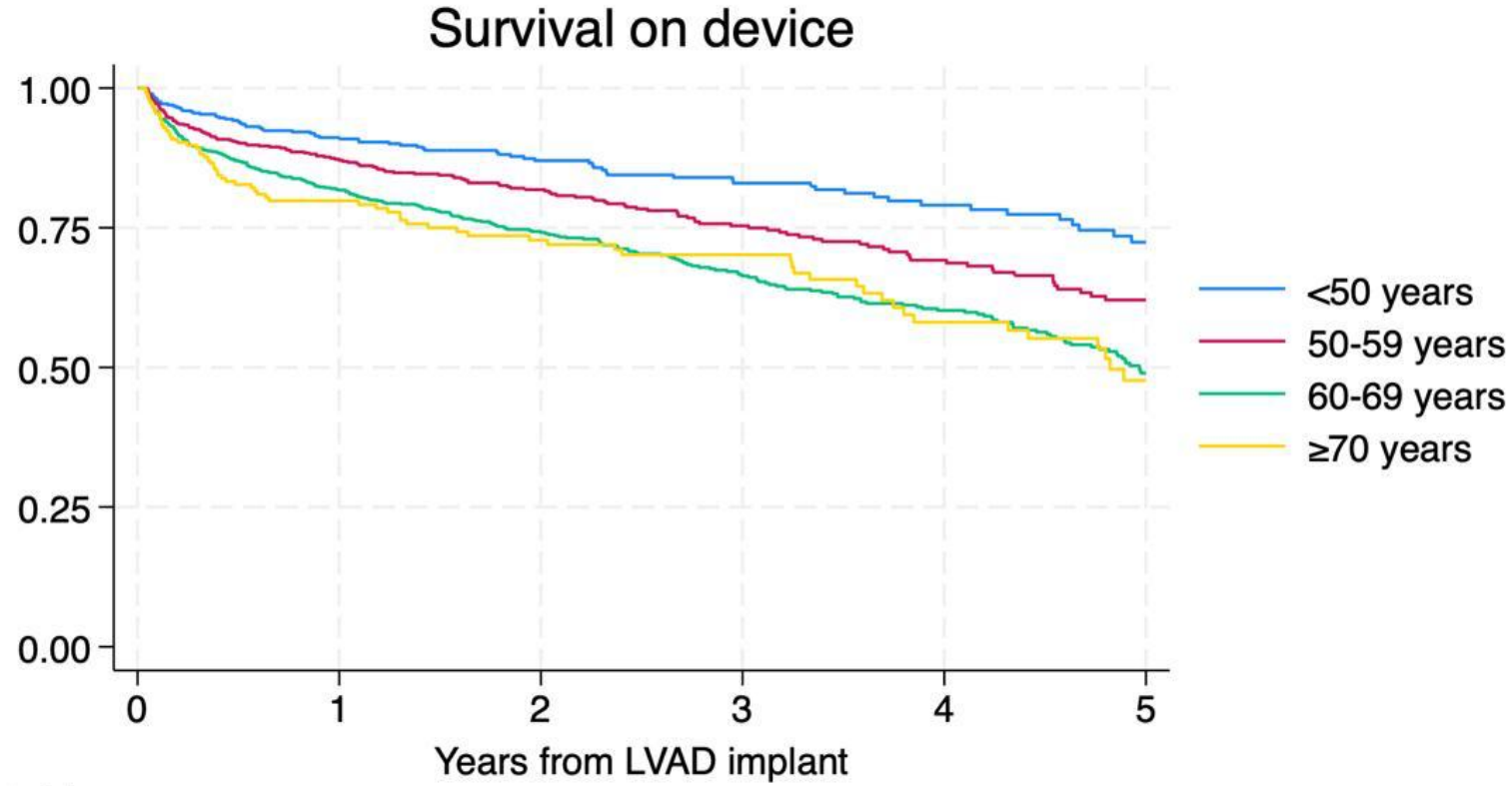


COMPETING TREATMENTS
HM3 vs. HT

Always available vs. uncertain waiting time

Be mindful in
- Inotrope/tMCS-dependent patients
- Obese/large BSA
- Group 0/sensitized patients
- Frequent flyers

EUROMACS



Number at risk

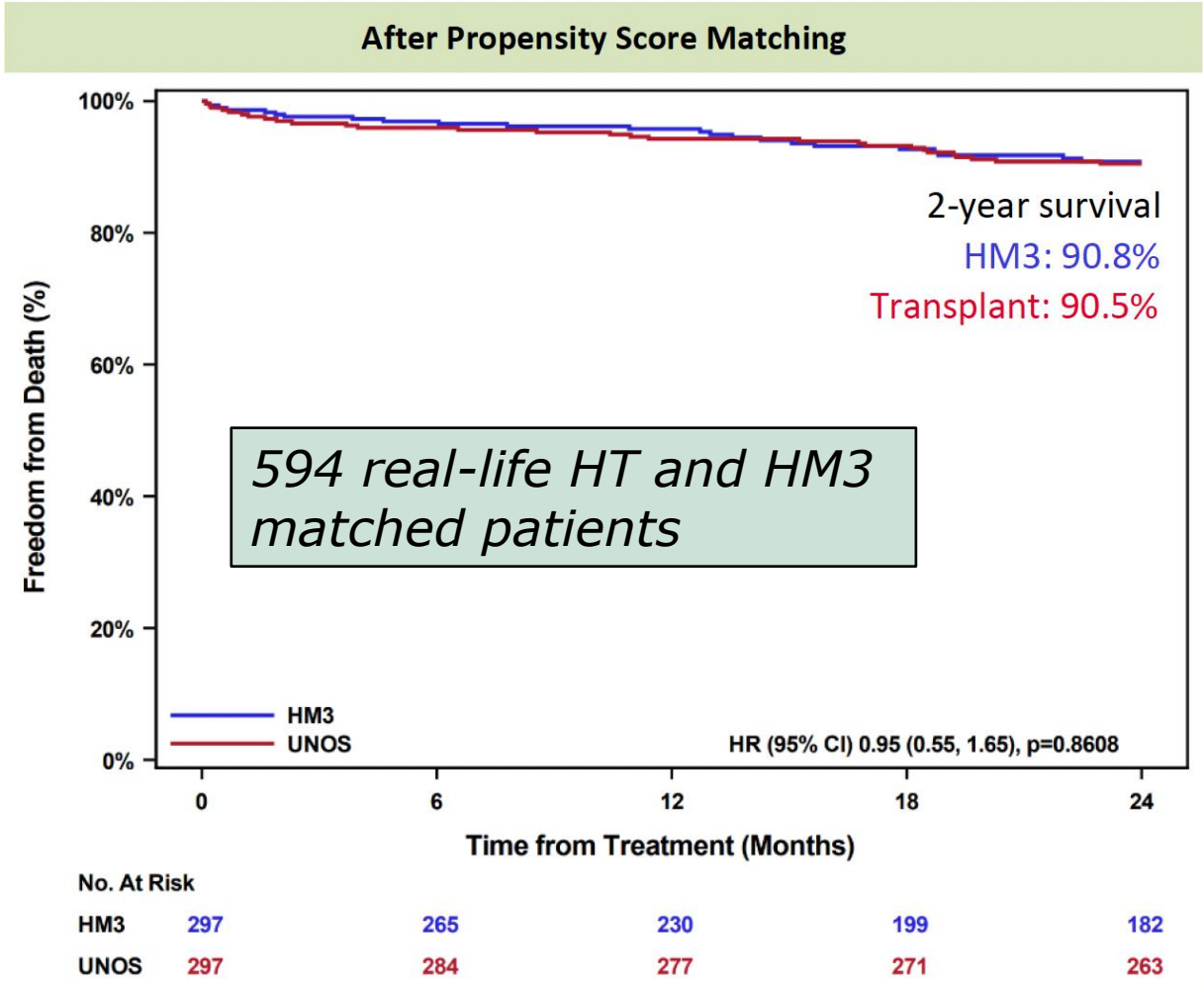
<50 years	504	345	225	162	103	62
50-59 years	651	454	316	196	134	90
60-69 years	879	577	400	258	189	108
≥70 years	197	121	93	66	44	23

Unpublished

HM3 survival is significantly better in young patients

UNIVERSITÀ DI TORINO

Young patients - HM3 vs. HT

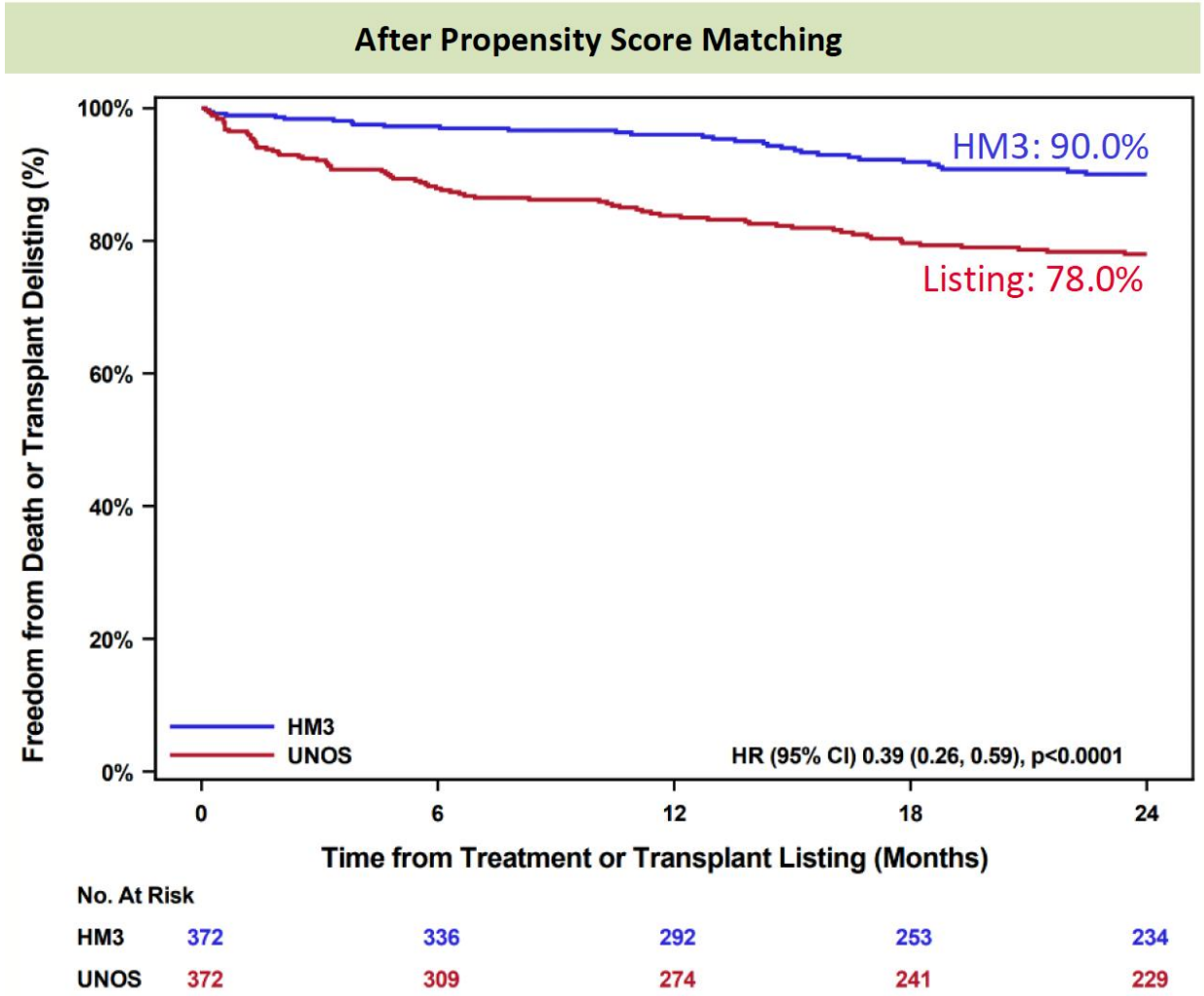


Heart Failure & World Congress on Acute Heart Failure 2025

Uriel et al. ESC HF congress 2025

Similar 2-year survival in HT vs. HM3

Young patients - HM3 vs. HT listing

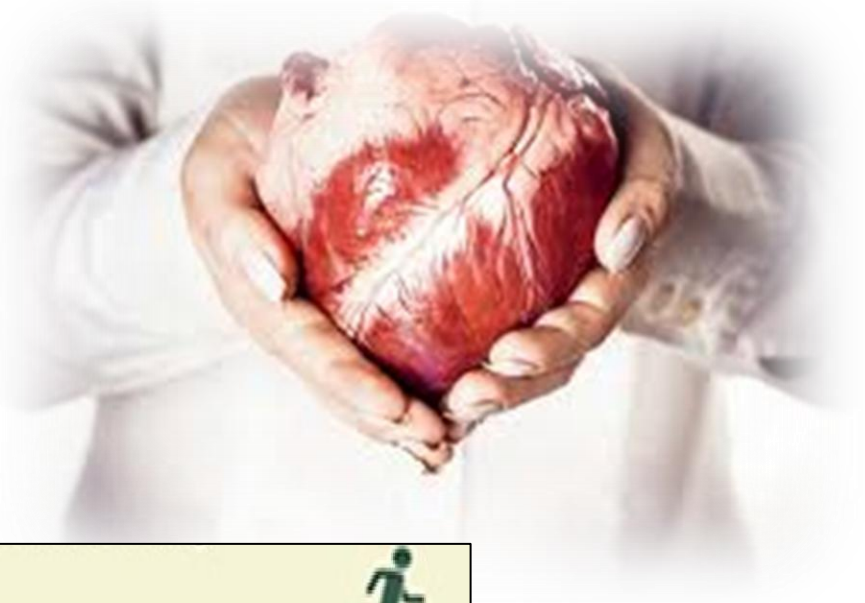


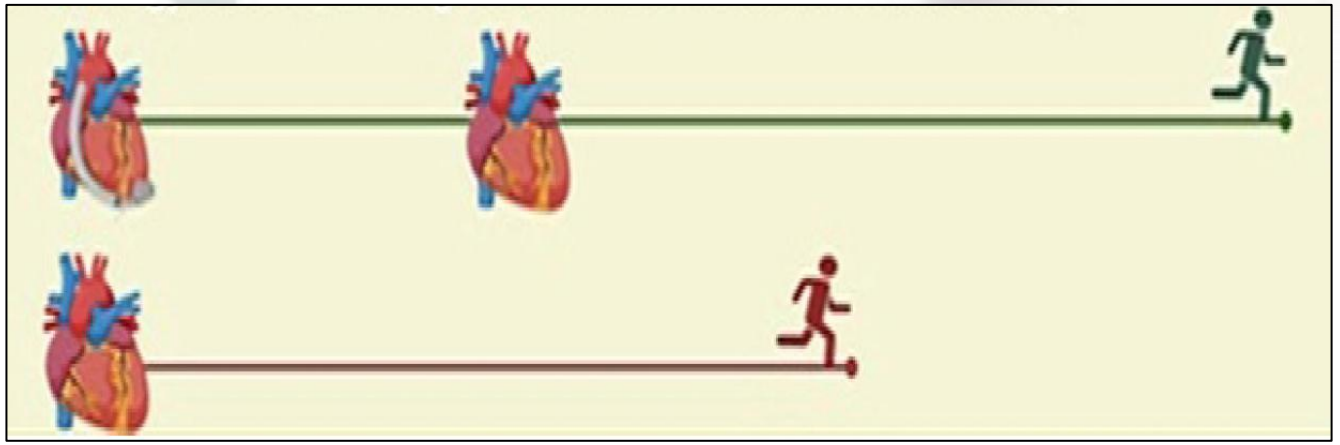
Heart Failure & World Congress on Acute Heart Failure 2025

Uriel et al. ESC HF congress 2025

HM3 has superior survival vs. HT listing

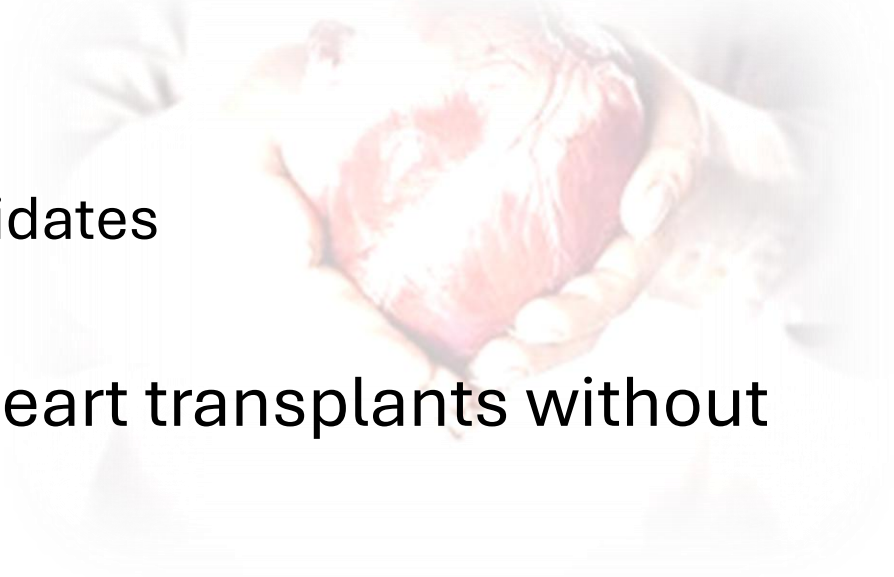
Is an LVAD the best option for this patient?





Conclusions

- Heart transplant is the gold standard treatment in advanced heart failure
  - though its access is still limited
  - though the mandatory selection of candidates



- Increasing the donor pool increases heart transplants without affecting outcomes

- The evolving LVAD technology challenges heart transplant survival, thus raising new horizons in selected patients


Thank you!