Future Directions and Reflections

Atlantic Transplant Conference
Halifax Nov 4.2016
Miroslaw Rajda MD,FRCP
Director, Heart Transplant Program

Disclosure

- No conflict of interest to report for this presentation

HF: The Fastest Rising Cardiovascular Condition In Canada

- The prevalence of HF has increased over the past few decades[1]
  - More accurate diagnostic algorithms
  - Increasing numbers of elderly and patients with risk factors for HF
  - Improved survival rates of cardiac and other chronic conditions
- An estimated 500,000 Canadians are living with HF and 50,000 new patients are diagnosed each year[2]
  - 1.4 million hospital days per year

1. Johansen H, *et al. Can J Cardiol*. 2003;19(4):430-435 / 2. Ross H, *et al. Can J Cardiol*. 2006;22(9):749-754.

HF: The Fastest Rising Cardiovascular Condition In Canada

- Depending on the severity of symptoms, heart dysfunction, age and other factors, HF can be associated with an annual mortality of between 5% and 50%[3-5]
  - Up to 40% to 50% of people with congestive heart failure die within five years of diagnosis

- 3. Yeung et al., CMAJ 2012: 184 (14): E765-773
- 4. Bhatia RS, et al. N Engl J Med. 2006;355(3):260-269.
- 5. Jong P, et al.. Circulation. 2003;108:184-191.

Oldest Record

Legendary Pien Ch'iao

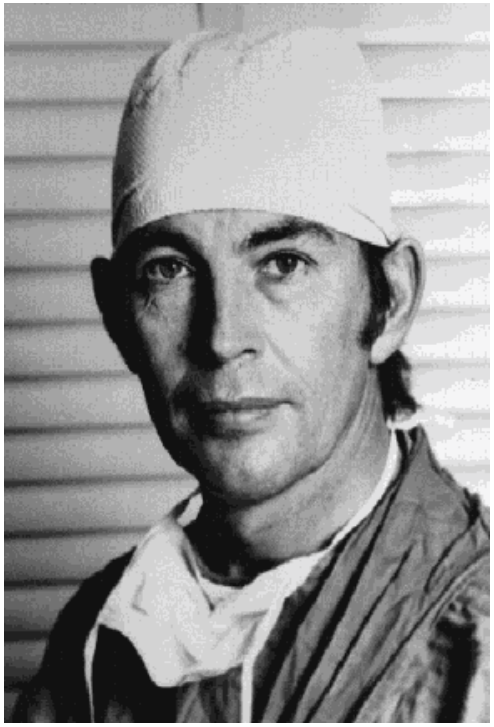
Performed the "Legendary Exchange of Hearts."

Balance between the spirit and the will

Pien Ch'iao, legendary doctor sometimes described as the Chinese God of medicine, c. 255BC, Major, 87-89, KU History of Med. Dept. Aso shows two smaller figures

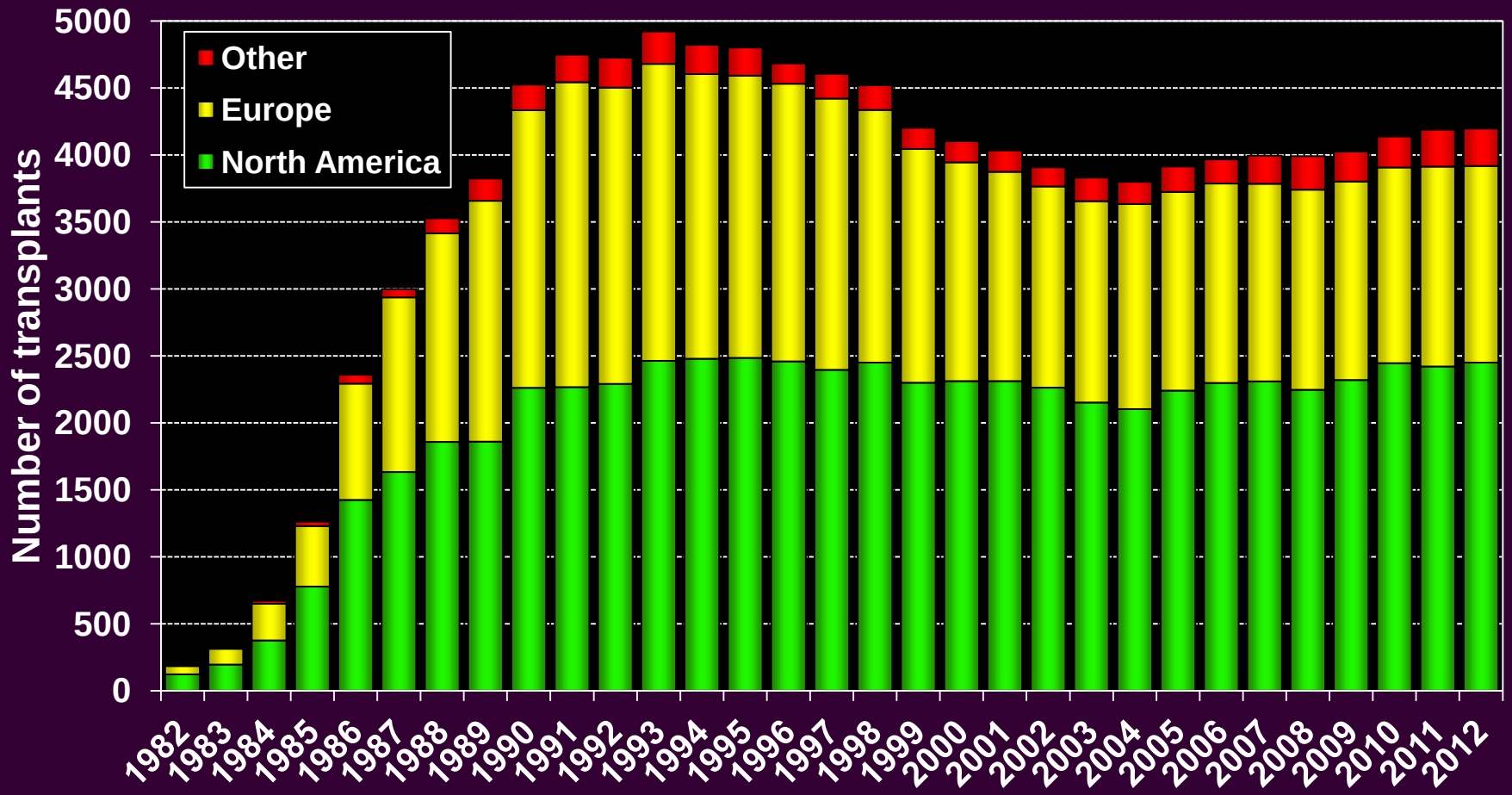
First Heart Transplant

Louis Washkansky



Professor Christiaan Barnard, performed the first heart transplant at Groote Schuur Hospital in Cape Town on December 3rd 1967.

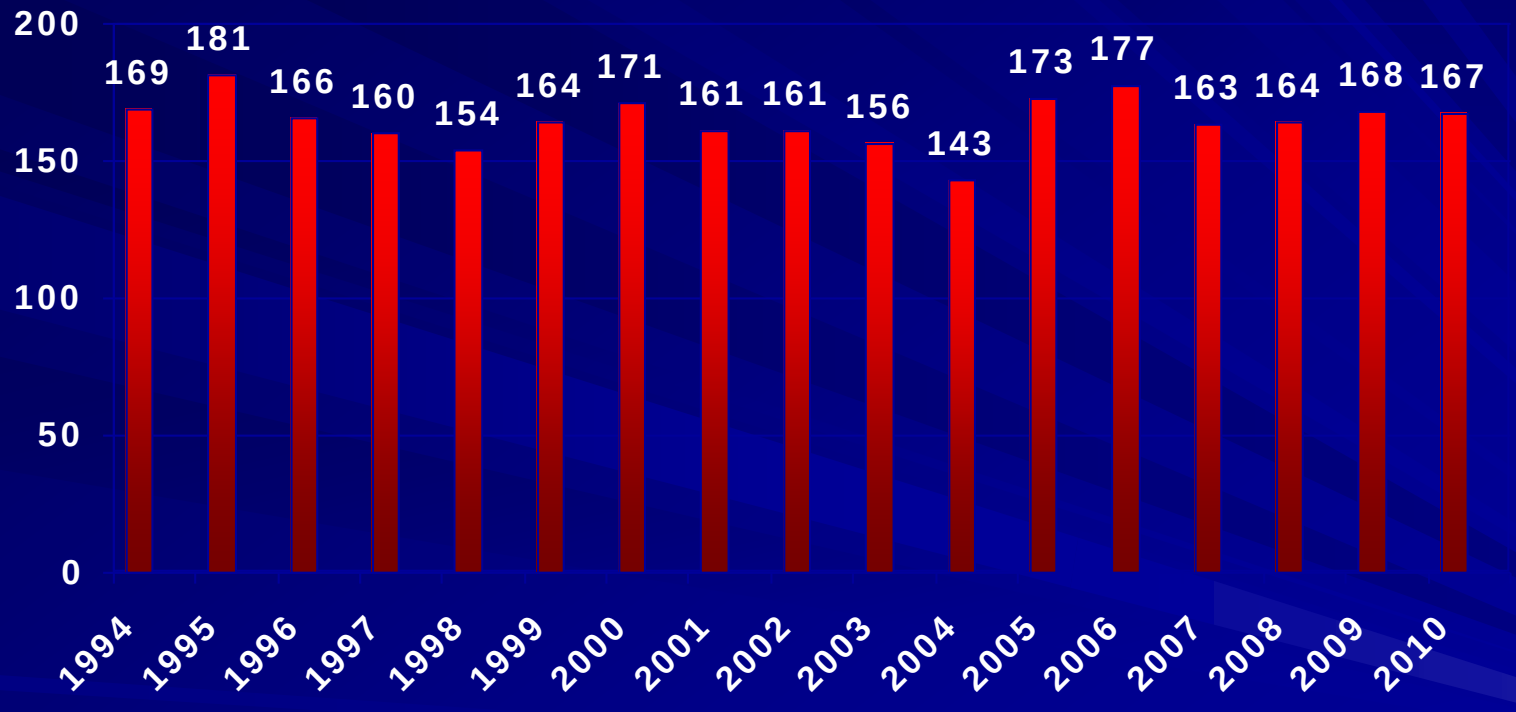
Adult and Pediatric Heart Transplants
Number of Transplants by Year and Location



NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2014
JHLT. 2014 Oct; 33(10): 996-1008

Heart Transplants, Canada



Does not include combination transplants.
Source: Canadian Organ Replacement Register, Canadian Institute for Health Information

First Heart Transplant in Halifax

July 11.1988

VG PERFORMS HEART TRANSPLANT

JUL 13 1988

Region's first operation may launch new program

By LAURENT LE PIERRES
Staff Reporter

The provincial government must soon decide whether to establish a regular heart transplant program at the Victoria General Hospital in Halifax now that the hospital's cardiac team has completed Atlantic Canada's first successful heart transplant, says Health Minister Joel Matheson.

Mr. Matheson said in an interview Tuesday the success of the emergency heart transplant on a 53-year-old Nova Scotia man early Tuesday morning "points out the time is close when we've got to make some firm decisions as to the direction the hospital is going to take."

The patient, whose name has not been released, is in stable condition in the hospital's intensive care unit today after undergoing a three-hour operation to receive the heart of a younger man.

Dr. Philip Belitsky, director of multi-organ transplantation at the VG, said at a press conference Tuesday afternoon the patient's condition had deteriorated so severely it was impossible to send him to a hospital in central Canada to undergo the operation.

The patient suffered from coronary heart disease, and only 11 per cent of his heart was

See VG PERFORMS page 2

Wednesday, July 13, 1988

VG perform

JUL 13 1988

(Continued from page one)

working. The donor heart became available Monday night and the VG team began operating at 3:45 a.m. Tuesday. The cardiac team performed "in a well-oiled fashion" and completed the operation without a hitch, said Dr. Belitsky.

Although the VG has been preparing for heart transplants since 1984, it still does not have the formal approval of the province to conduct them, said Dr. Belitsky. However, because this case was an emergency, the team went ahead with the transplant with the approval of the government and the VG's medical staff.

The board is currently discussing the establishment of a heart transplant unit with the government and a decision is expected to be made by September, said Mr. Matheson. The government and the VG administration want to ensure that opening a

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Wednesday, July 13, 1988

VG performs transplant

JUL 13 1988

(Continued from page one)

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The board is currently discussing the establishment of a heart transplant unit with the government and a decision is expected to be made by September, said Mr. Matheson. The government and the VG administration want to ensure that opening a heart transplant unit will not be to the detriment of other services provided by the hospital, the minister said.

But he said Tuesday's heart transplant demonstrates the ability of the VG to "carry out advanced surgical procedures."

Dr. Belitsky said the VG could begin performing heart transplants on a regular basis immediately because it has the equipment and the expertise. But "the decision is not really ours," he said.

The hospital already has a multi-organ transplant program and is one of the busiest centres for kidney transplants in the country. Its liver transplantation program began in 1985, and the infrastructure — including laboratory investigations and nursing care — is already in place for a heart transplant program.

The VG's cardiac surgeons have also attended international seminars on cardiac transplantation over the past few years. The hospital already has one of the largest cardiac surgery programs in Canada.

Cardiologist Dr. Brian Chandler said about 10 patients are transferred to other major hospitals in Canada for heart transplants every year.

He said the VG's first heart transplant patient is expected to remain in intensive care for the next four or five days. His stay in hospital is expected to last about a month.

The patient, who has been visited by his family since the surgery, was conscious and aware his surgery was over as of 7:30 a.m. Tuesday. He is receiving drugs to prevent his body from rejecting the new heart.

Cardiovascular surgeon Dr. Jeremy Wood said the patient's chances of surviving one year are 85 per cent, and between 50 and 55 per cent for the next five years. The longest any heart transplant patient has ever lived is 18 years.

The man's name is being withheld at the request of his family, and the hospital has a policy of not divulging the identity of the organ donor, said Dr. Belitsky.

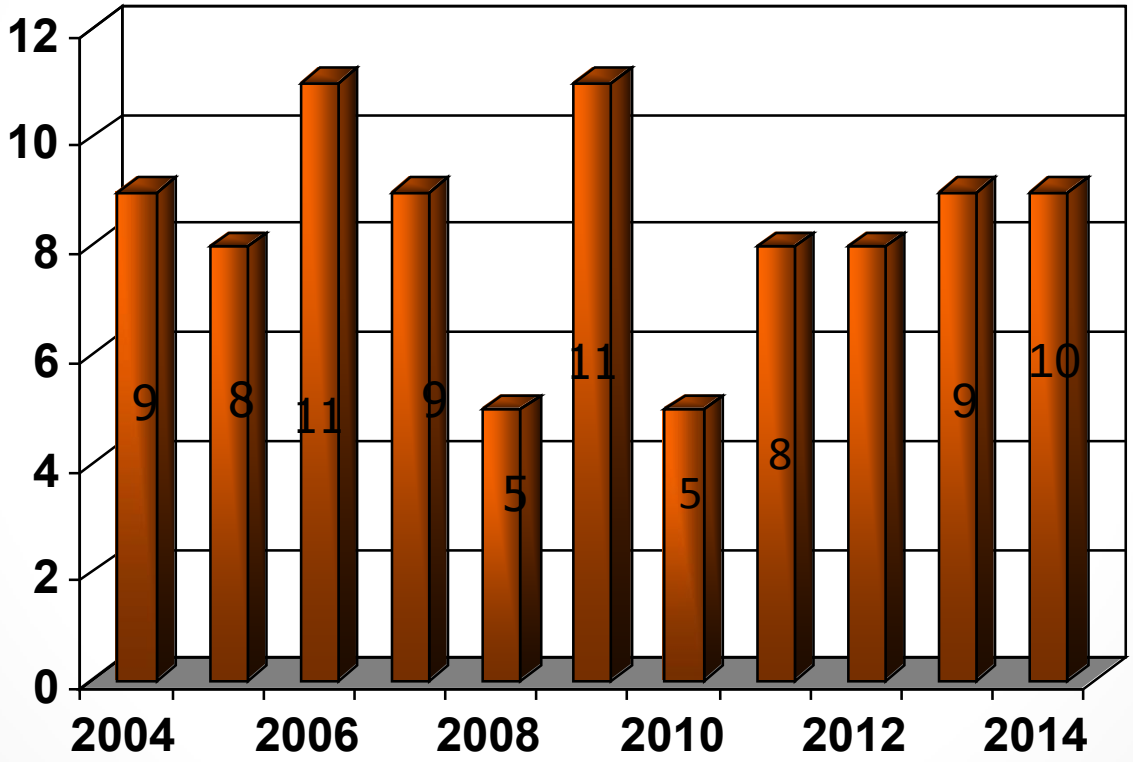
The transplant also under-

Dr. Philip Belitsky

scores the importance of organ donation, he added. The kidneys of the heart donor were transplanted in another patient Tuesday afternoon, he said.

Among the medical experts who performed the operation were Dr. David Murphy, director of cardiovascular surgery, cardiovascular surgeons Dr. John Sullivan and Dr. Jeremy Wood, cardiology chief Dr. Brian Chandler, and staff cardiologist Dr. Lucille Lalonde. Dr. Belitsky was in the operating room but was not at the operating table.

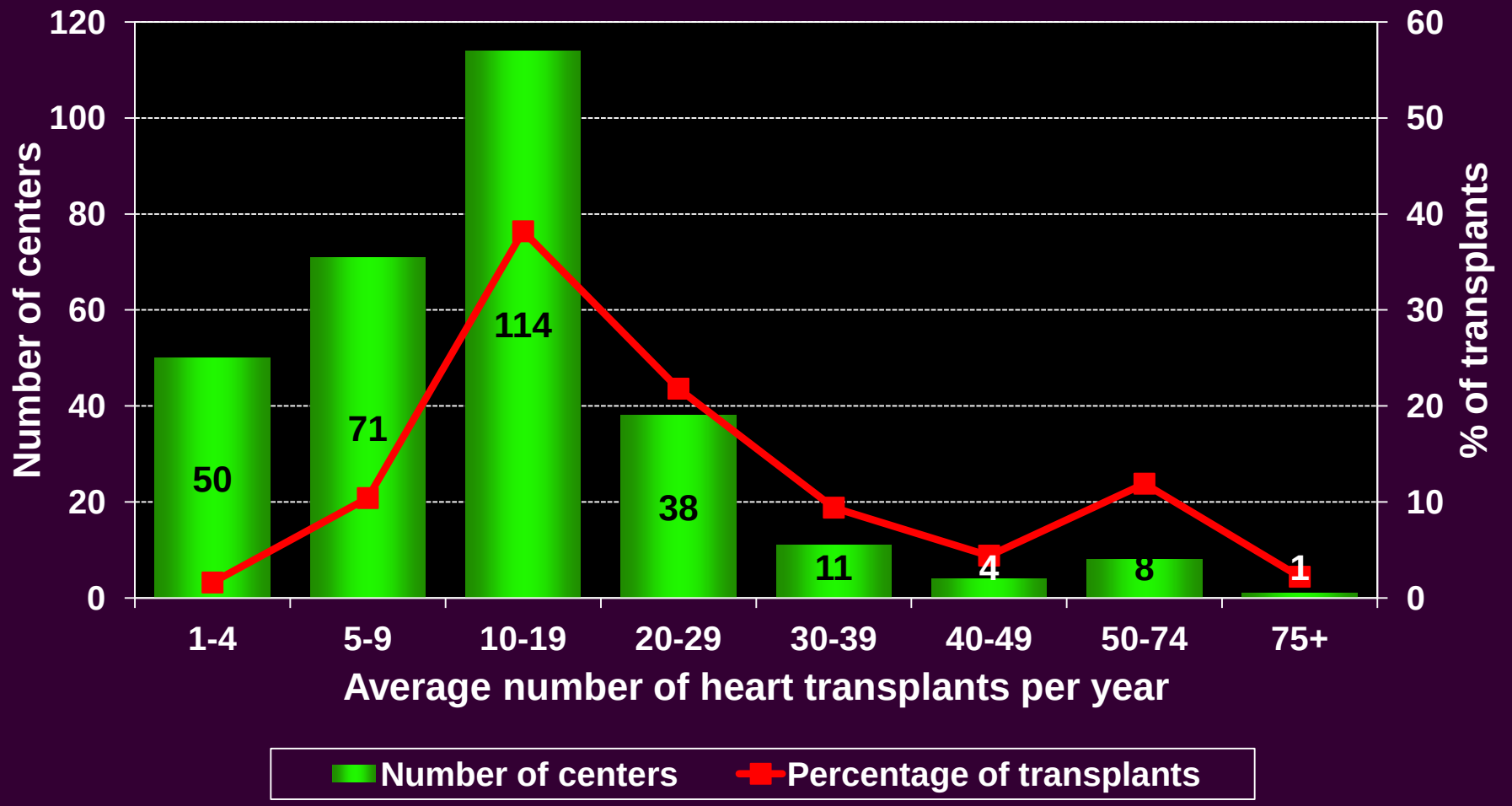
Number of transplants



Number of heart transplant in Canada - 167

Adult and Pediatric Heart Transplants

Average Center Volume (Transplants: January 2006 – June 2013)



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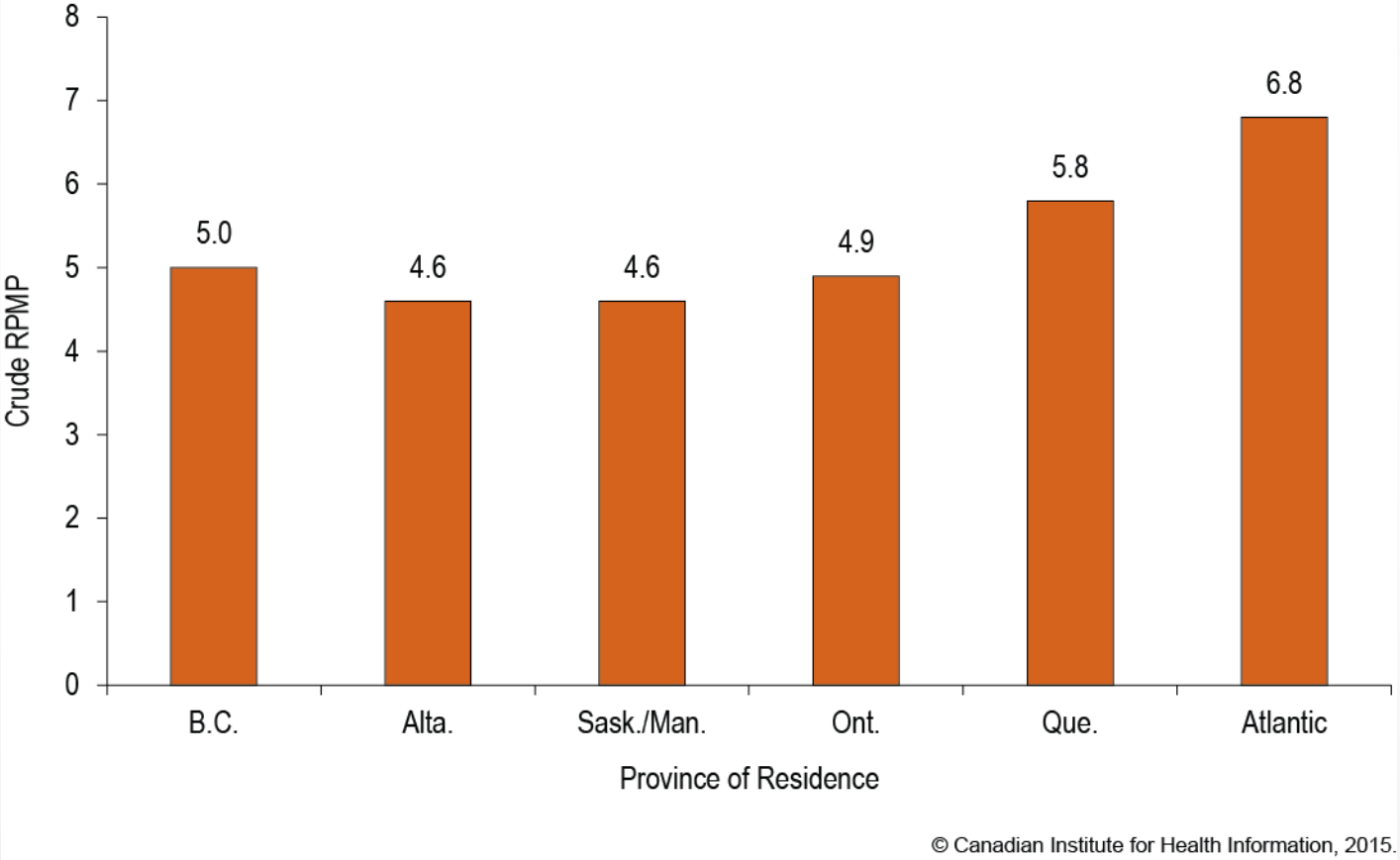
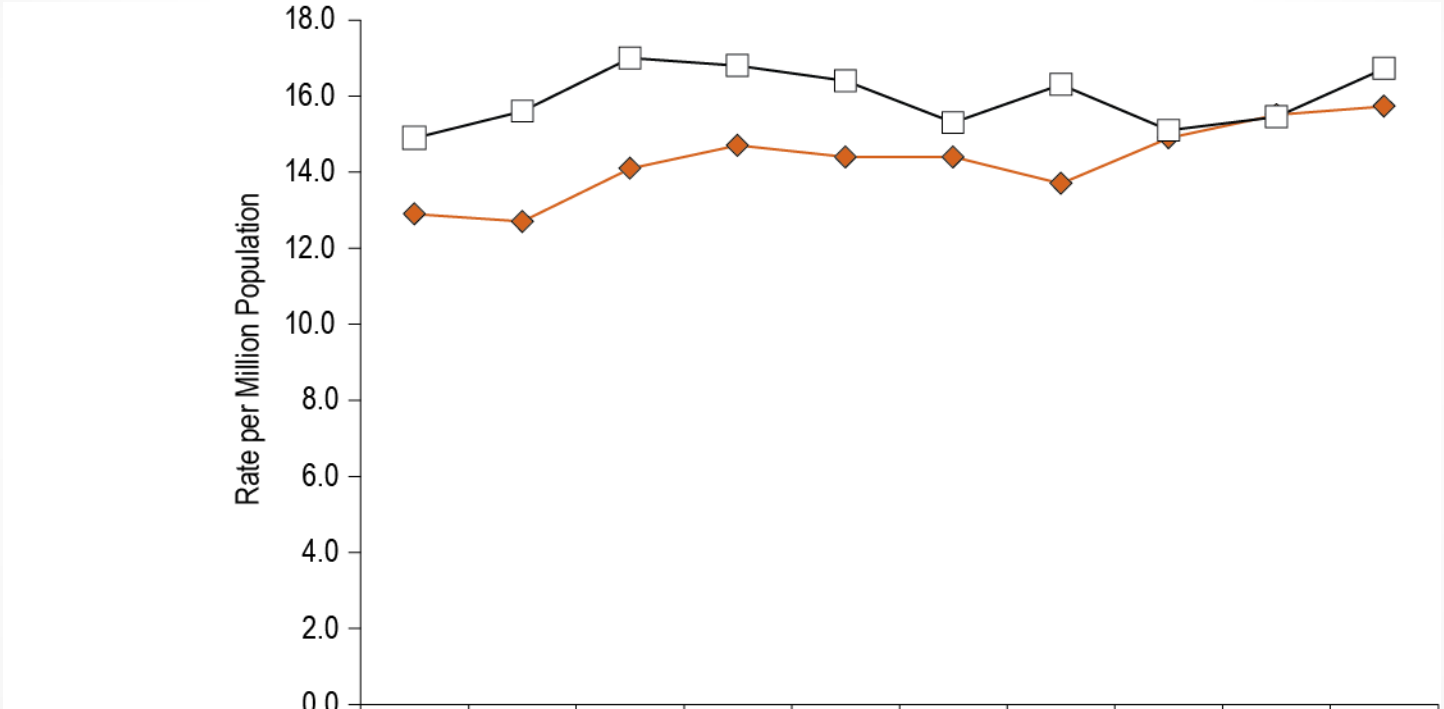
Heart Transplant Recipients by Province of Residence, Canada, 2013 (Crude Rate per Million Population)



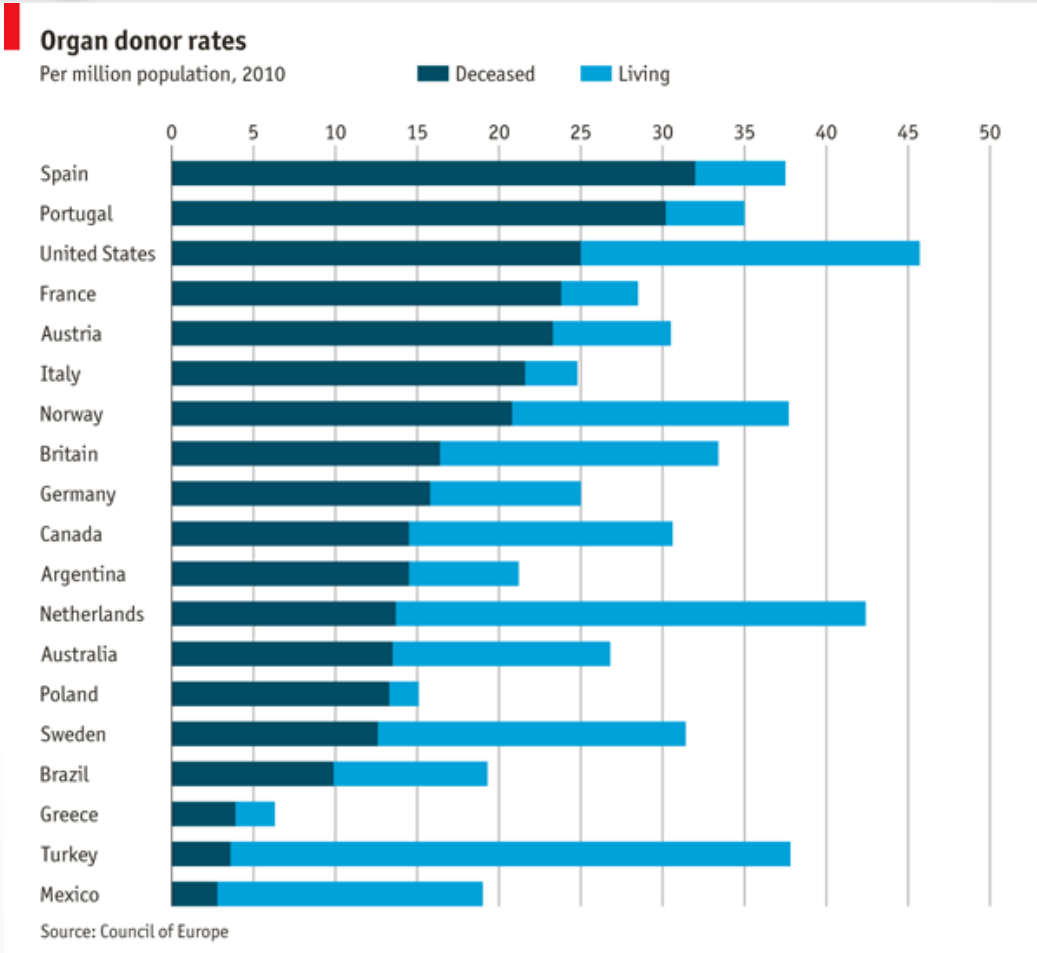
Donor Rate per Million Population, by Donor Source

(Deceased or Living), Canada, 2004 to 2013



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Deceased Donor	12.9	12.7	14.1	14.7	14.4	14.4	13.7	14.9	15.5	15.7
Living Donor	14.9	15.6	17.0	16.8	16.4	15.3	16.3	15.1	15.5	16.7

Organ Donor Rates



2015 Atlantic Canada Donor Total: 33

- **NB had 8 donors**:
  Of the 8: 1) **2** were sent to Toronto (no recipients here)
  2) **6** were determined to be medically unsuitable and were not transplanted
- **NFL had 8 donors:**
  Of the 8: 1) **2** were transplanted here
  2) **5** were determined to be medically unsuitable and were not Transplanted
  3) **1** was an ABO: AB and no recipients found in Canada or eastern USA.

- **NS had 17 donors:**

  Of the 8: 1) **1** were transplanted here

  2) **14** were determined to be medically unsuitable and were not transplanted

  3) **2** were sent away (no recipients here)

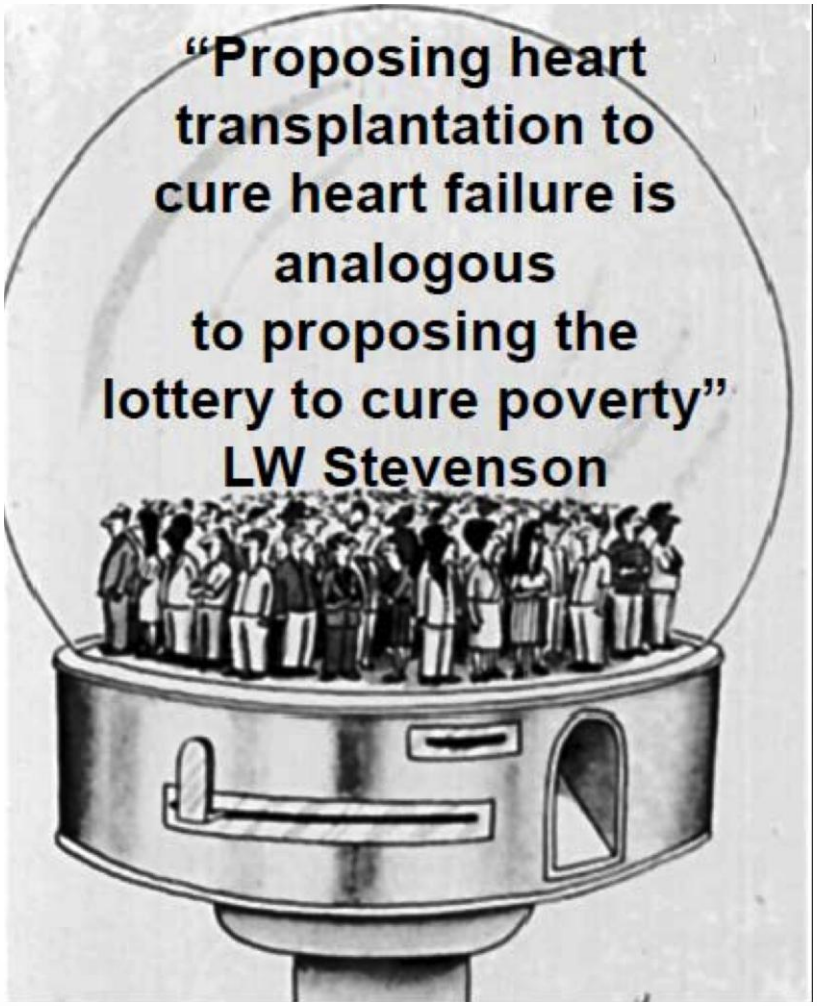
- 2 heart came from the outside Atlantic provinces

Halifax Experience

- In last 5 years – 9 patients with weight >90 kg were transplanted
- Average wait time – 588 days
- 3 patients with weight >100 kg
  1. 117 kg – 2128 days
  2. 105 kg – 979 days
  3. 119 kg – 467 days

So Why is That Happening?

- Decline in heart utilization from 44% to 29%
- Increasing age of the donor population
- Fear of “high risk” hearts
- Avoidance of LVH
- Fear of longer ischemic times
- Avoidance of gender and size mismatching


"Proposing heart transplantation to cure heart failure is analogous to proposing the lottery to cure poverty"
LW Stevenson

Mechanical Circulatory Suppor (MCS)
“VAD”
This is now part of our future

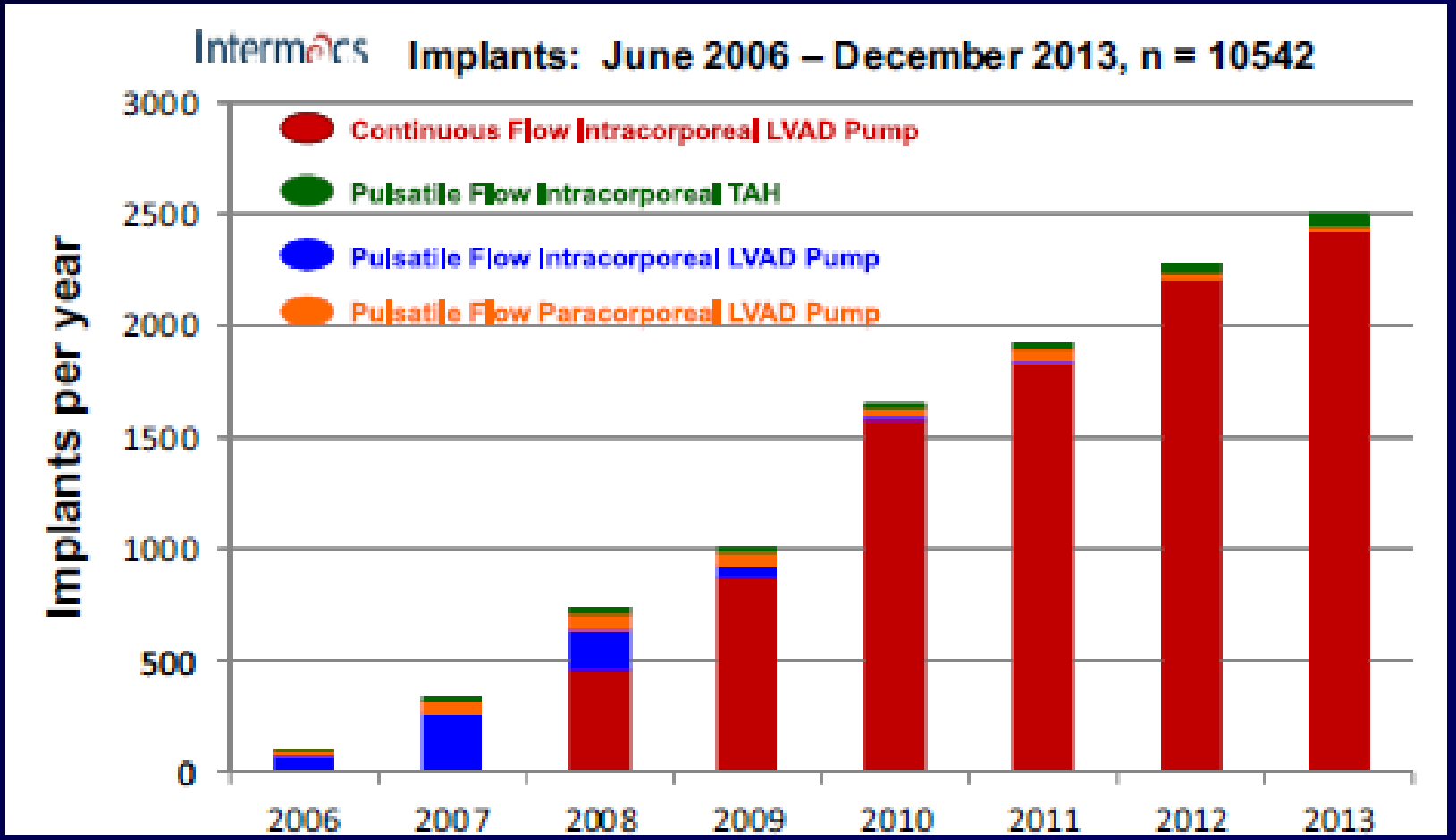
Evolution of long term devices

1990’s 2000’s 2010

Sixth INTERMACS annual report: A 10,000-patient database

J Heart Lung Transplantation 2014

James K. Kirklin, MD,[a] David C. Naftel, PhD,[a] Francis D. Pagani, MD, PhD,[b] Robert L. Kormos, MD,[c] Lynne W. Stevenson, MD,[d] Elizabeth D. Blume, MD,[e] Marissa A. Miller, DVM, MPH,[f] J. Timothy Baldwin, PhD,[f] and James B. Young, MD[g]

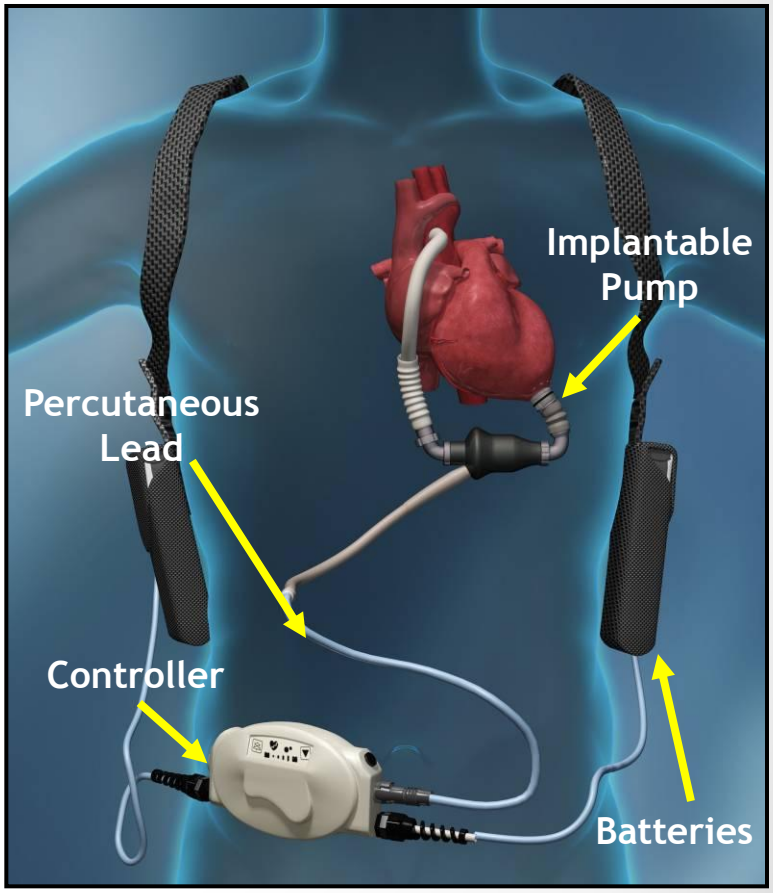


Indications for VAD

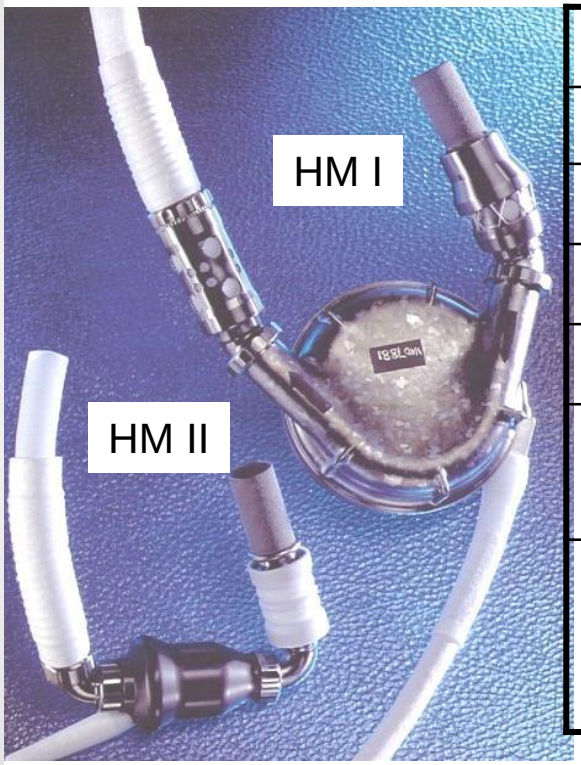
- Bridge to transplant (BTT)
  - most common
  - allow rehab from severe CHF while awaiting donor
- Bridge to recovery (BTR)
  - unload heart, allow "reverse remodeling"
  - can be short- or long-term
- "Destination" therapy (DT)
  - permanent device, instead of transplant
  - currently only in transplant-ineligible patients
- Bridge to candidacy (BTC)/
  Bridge to decision (BTD)
  - when eligibility unclear at implant
  - not true "indication" but true for many pts

HeartMate II® LVAS

- A surgically implanted, rotary continuous-flow device in parallel with the native left ventricle
  - Left ventricle to ascending aorta
- Percutaneous driveline
- Electrically powered
  - Batteries and line power
- Fixed-speed operating mode
- Home discharge with ability to return to activities of daily life (work, school, exercise, hobbies, etc.)



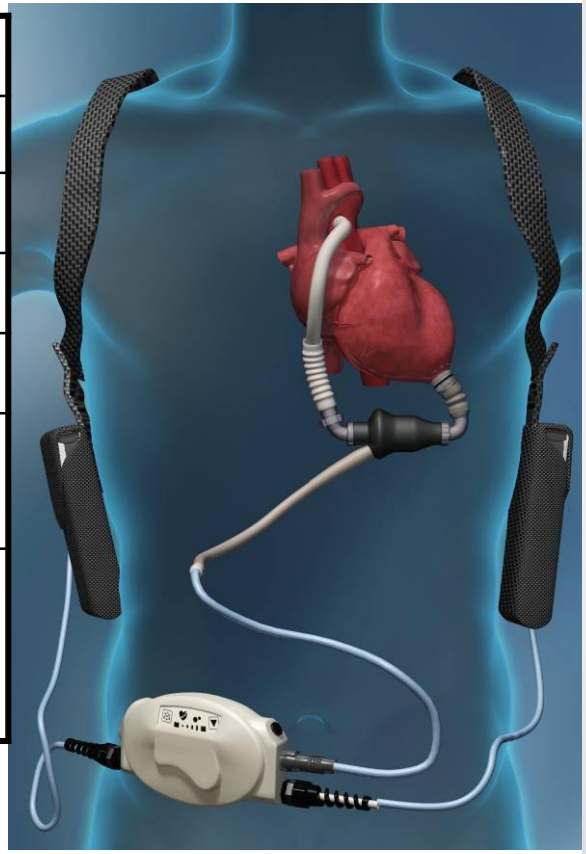
Comparison of HM I (XVE) and HM II



	HM I	HM II
Weight (gm)	1250	280
Volume (ml)	450	63
Noise	Audible	Silent
Moving parts	Many	One
Maximal flow (l/min)*	10	10
Clinical Durability (yr)	1.5	Est. > 5

* at mean pressure=100 mm Hg

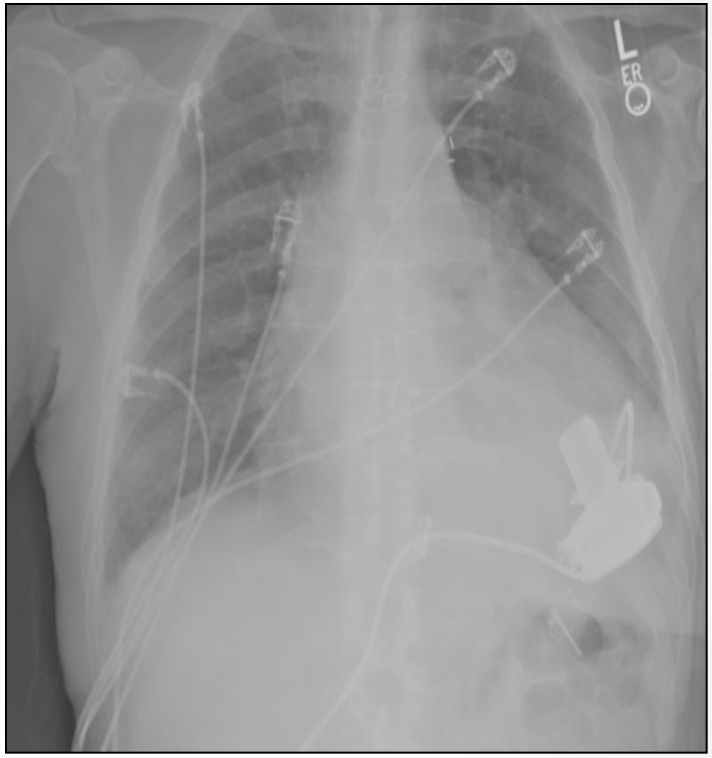
HM II with controller and batteries



Heartware

- Left ventricular assist device only
- Long term use
- BSA must be >1.2
- Centrifugal pump
- Bridge to transplant
- Destination therapy

HeartWare



Next: HeartMate III…

- Magnetically Levitated Rotor (bearingless)
- Transcutaneous charging of implanted battery
- Flow : 2-12 l/min
- Potential extended longevity (>10 yrs)


BOWLARAMA
BOWLARAMA

Worrisome signals: Need to consider MCS

- Hypotension
- Laboratory
  - Renal insufficiency
  - Hepatic dysfunction
  - Hyponatremia
- Pulmonary Hypertension
- RV dysfunction
- Unresponsiveness to CRT
- Need for Inotropes
- Symptoms
  - Refractory
  - At rest
- Recurrent admissions
- Medications
  - Intolerance or lower doses
    - ACE-I/ARBs
    - Beta blockers
  - Increasing diuretic doses

Ideal time for referral

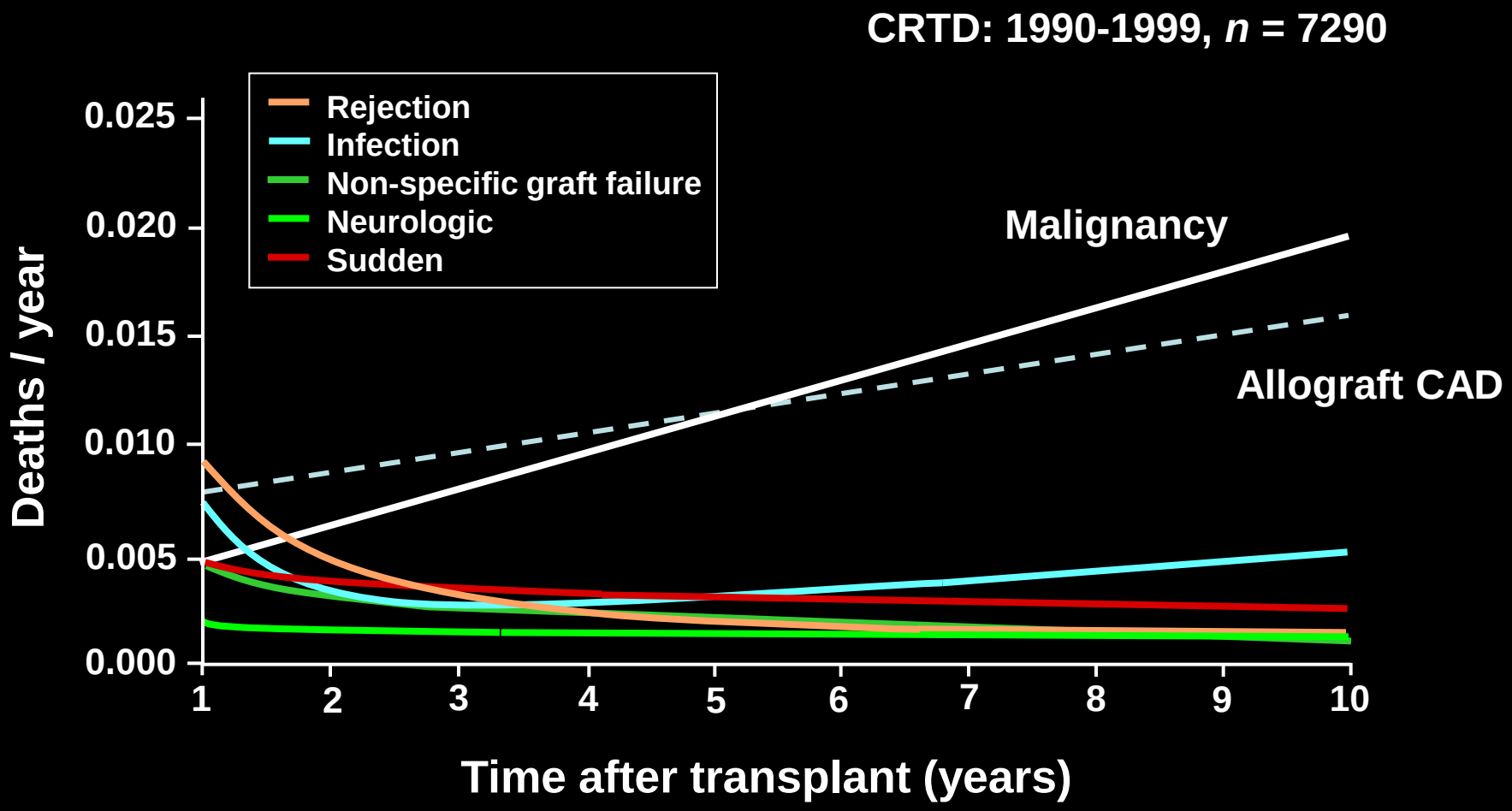
- NYHA III or IV plus one of the following:
  - Inability to walk < 1 block without dyspnea (shortness of breath)
  - Serum sodium < 136 mmol/L
  - BUN > 40mg/dL
  - Intolerant or refractory to ACE-I / ARB / BB
  - Diuretic dose > 1.5mg/kg
  - One or more CHF related hospital admissions within 6 months
  - CRT nonresponder
  - Hematocrit < 35%

Russell SD, Miller LW, Pagani FD. Advanced heart failure: a call to action. *Congest Heart Fail.* 2008;14:316-321

Post-transplant chronic complications

- cellular and antibody mediated rejection
- infection
- malignancy
- immunosuppression toxicity
- graft vascular disease

Specific Causes of Death One Year After Cardiac Transplantation



Kirklin JK, et al. *J Thorac Cardiovasc Surg 2003*; 125:881-90.

Proposed Mechanisms in the Development of Allograft Vasculopathy

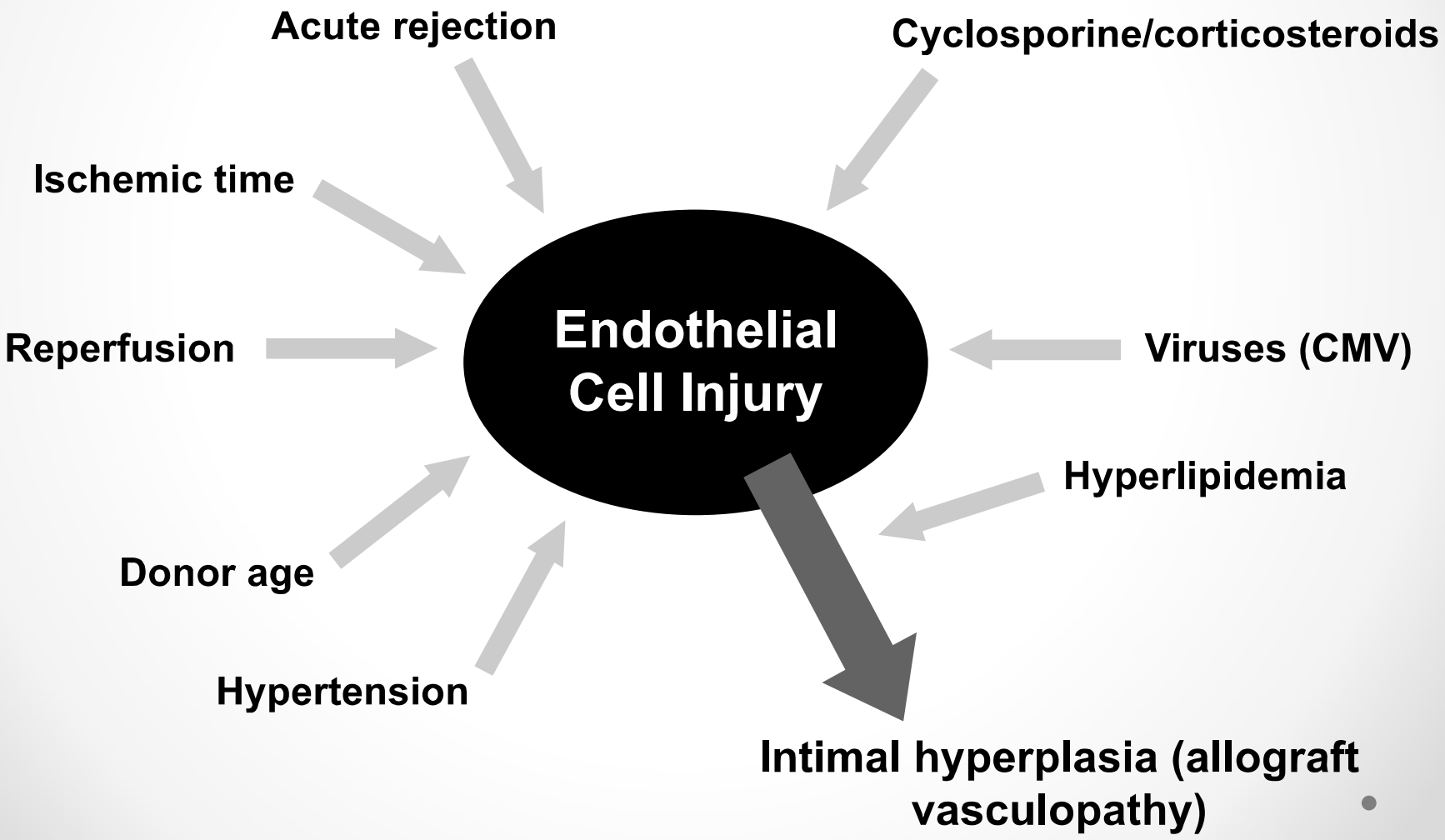
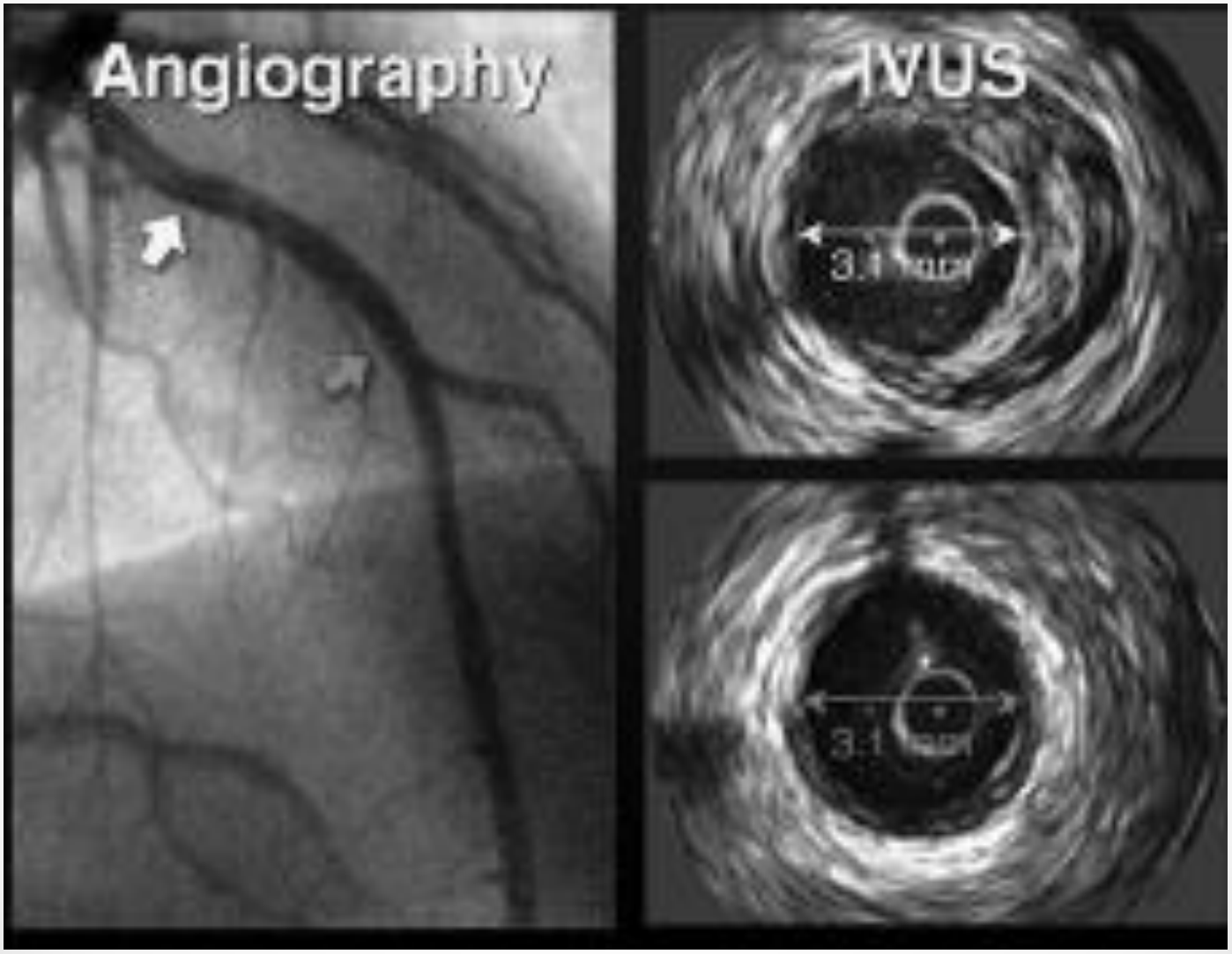
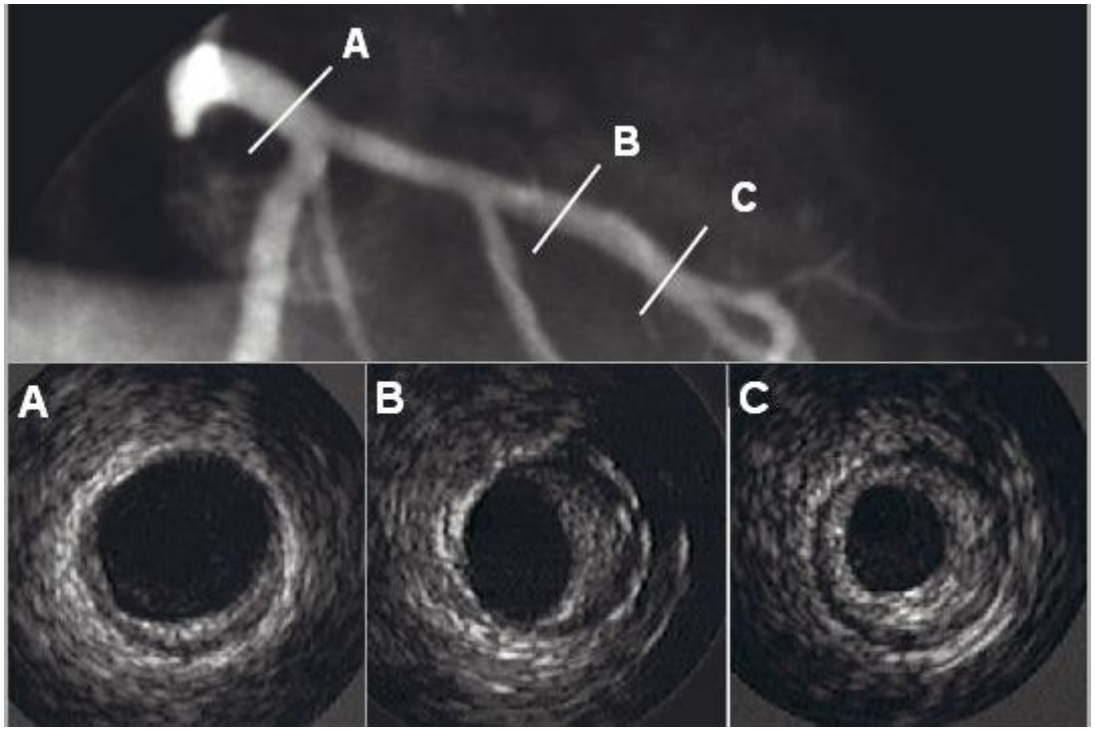
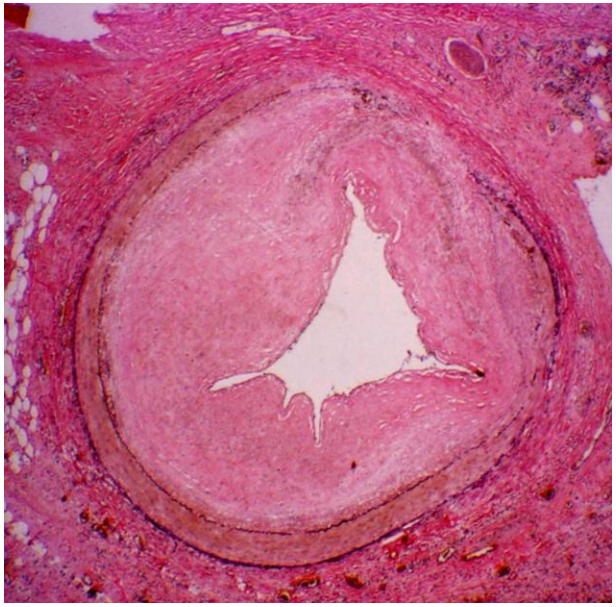


Figure 2. Comparison of Angiography and IVUS in Detecting Intimal Thickening with Compensatory Dilatation



Cardiac Allograft Vasculopathy

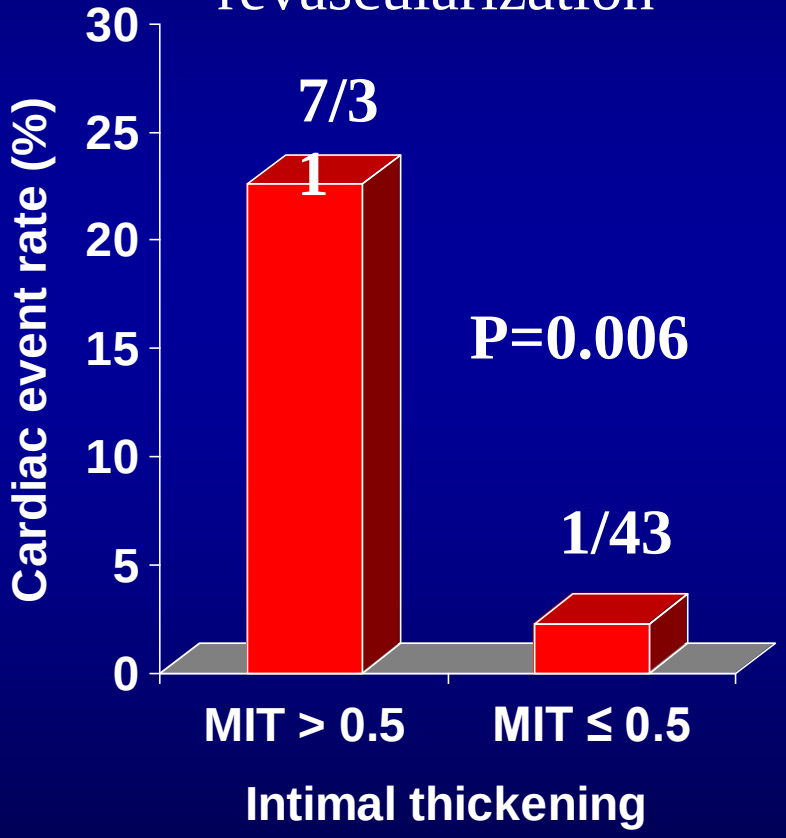


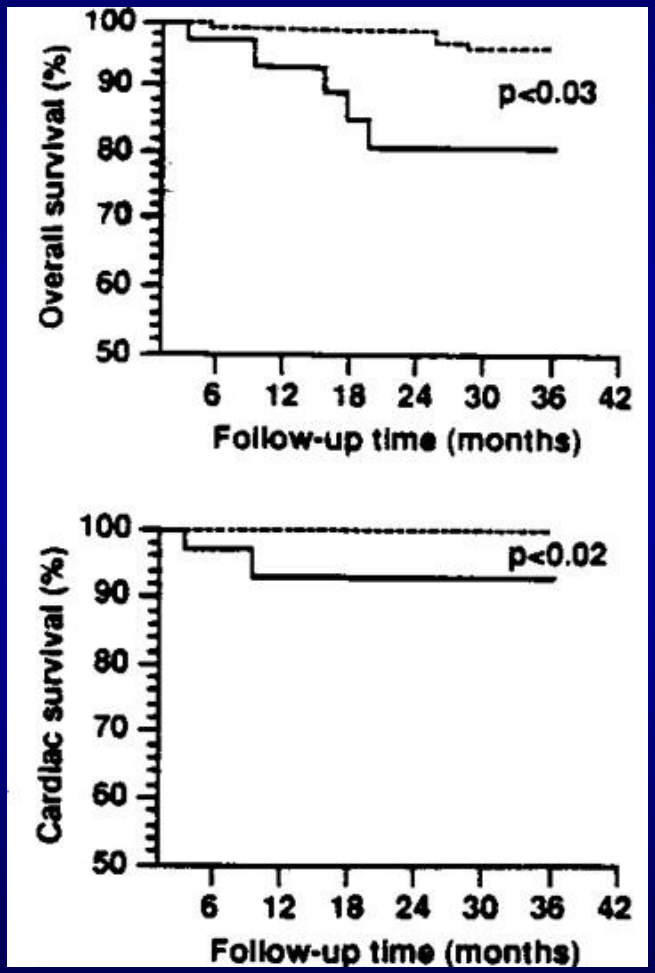


Diagnosis: coronary angiogram, IVUS, Dobutamine stress Echocardiography (DSE), myocardial perfusion imaging (MPS)

Significance of Intimal Thickening

Sudden death, MI, or need for revascularization





1 Mehra et al., JHLT 1995; 2 Rickenbacker et al., Circ 1995

Immunosuppression Regimens

Pre-1980's	Typical	Graft CAD	Renal Sparing
	Cyclosporin Tacrolimus	Cyclosporin Tacrolimus	Sirolimus
Imuran	MMF Imuran	Sirolimus	MMF
Prednisone	Prednisone (month 0-6)		

Current Challenges

- Changing recipient population
- Decreasing donor population
- Increasing recipient sensitization
  - Desensitization protocols
  - Acute cellular rejection
  - Acute humoral rejection

Patient Population

- Better management of advanced heart failure
- Patient population is older and sicker
- Other options to heart transplantation:
  Mechanical Support

Changing Patient Population

- Re-transplantation candidates
- Multiple previous operations
  - Complex congenital patients

- New challenges
  - Sensitized Patients
  - Surgical challenges
  - Ethical issues

Future Directions

- Modulation of donor/recipient interaction
- Improved therapy for rejection
- Earlier detection of rejection and coronary disease
- Earlier implantation of LVADs/smaller devices
- Less reliance on transplantation and more Mechanical Circulatory Support

Thank you