Heart Failure & Heart Transplant

Everything

you need to know in 15 minutes

- Heart Failure Guidelines – a Concise Summary *MedicineToday* 2019; 20(6): 14-24
- Honoring 50 Years of Clinical Heart Transplantation. In-Depth State-of-the-Art Review *Circulation.* 2018;137:71–87

theAlfred

Dr Peter Bergin. Medical Director, Advanced Heart Failure Service. Alfred Hospital
FRACP. August 29th 2020

COMMON COMORBID FATAL

1 - 2% popul^{n}

38M Worldwide

5-25% Advanced

24% CKD

22% DM

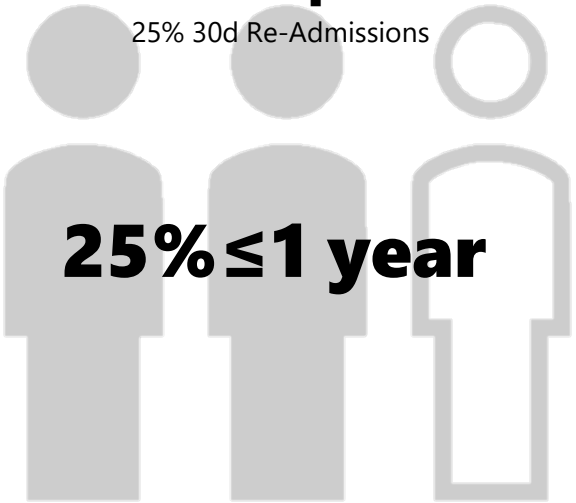
40% AF

67% HT

49% IHD

5% Hospital

25% 30d Re-Admissions



25%≤1 year

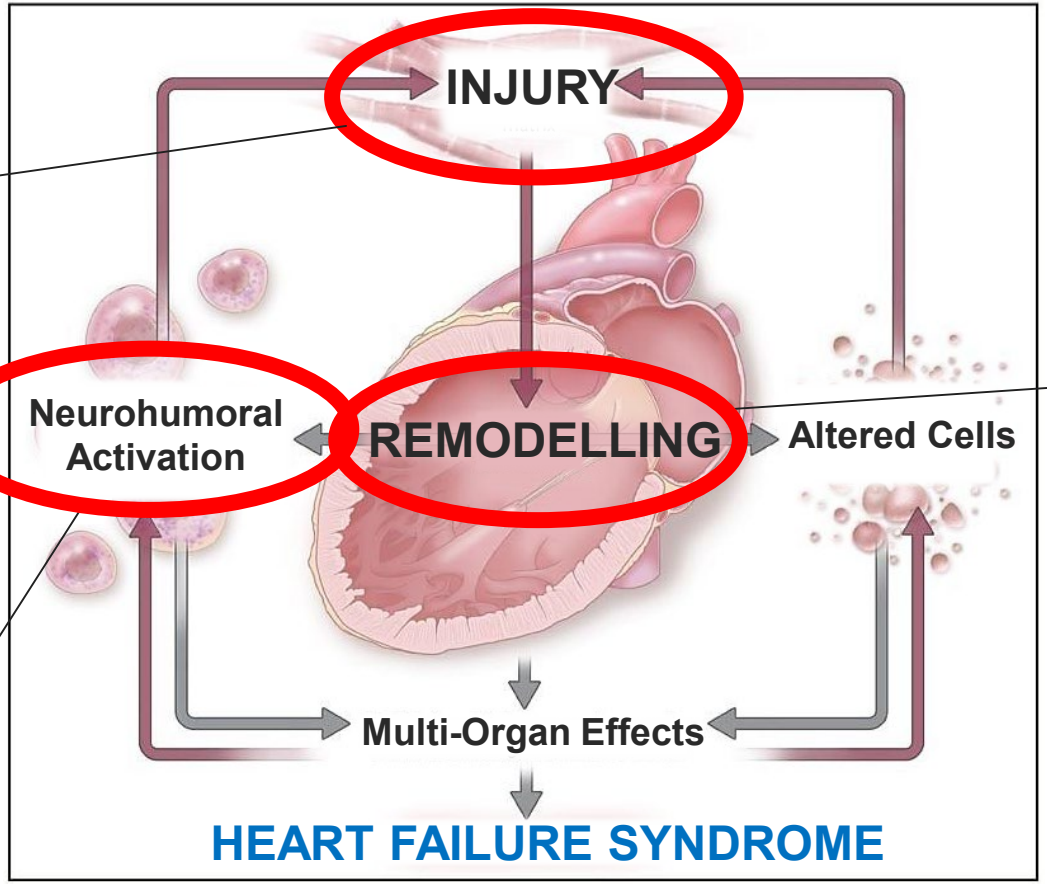
50%≤5 yrs

Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. Lancet 2018;391:572-580

HFrEF Pathophysiology

IHD
HT
DCM

SNS
RAAS
BNP



↑ LV size
Δ LV shape
↑ MR

McMurray J. N Engl J Med 2010;362:228-38.

HF – Essential Clinical

1

Symptoms

Dyspnoea, Fatigue, NYHA

2

Signs

Oedema, JVP, Crackles

3

Investigations

Haemodynamics, Imaging, Complications & Px

4

Treatment

ABCD, HF Team

HF*r*EF

REDUCED

Symptoms ± Signs of HF

LVEF <50%

Dilated LV + Global / Regional Dysfunction

*If LVEF mildly reduced (LVEF 41-49%), additional criteria required (e.g. signs of heart failure; diastolic dysfunction with high filling pressure demonstrated by invasive means or echocardiography or biomarker testing)

HF*p*EF

PRESERVED

Symptoms ± Signs of HF

LVEF ≥50%

Small LV, thick walled, stiff

And Objective evidence of:

- Relevant structural heart disease (LVH, LAE)

And/or Diastolic dysfunction + high filling pressure by any of:

- Cardiac catheterisation or Echocardiography
- Biomarker (elevated BNP or NT proBNP)
- Exercise (invasive or echocardiography)

Guidelines for the prevention, detection and management of HF in Australia 2018.
Atherton J. Heart Lung Circ (2018) 27, 1123–1208

CSANZ Cardiac Society of Australia and New Zealand | Heart Foundation

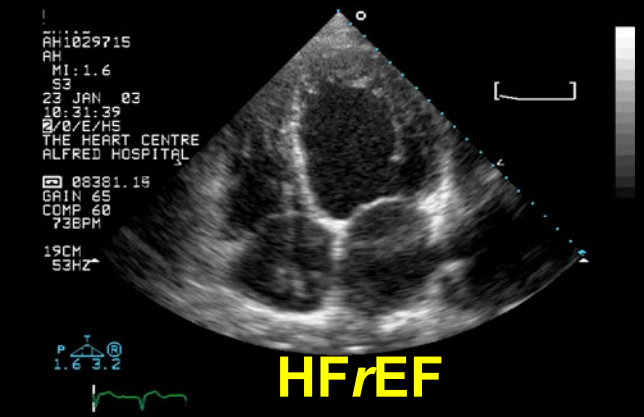
HF Investigations

Echo is the single most useful Ix in suspected HF

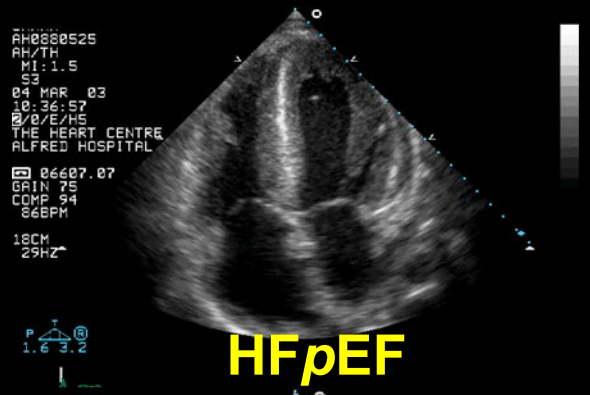
- HFrEF Vs HFpEF Vs Non-Myocardial
- Ischaemic Vs Non-Ischaemic
- Haemodynamics
- Valves

Cardiac MRI is the Critical Add-on

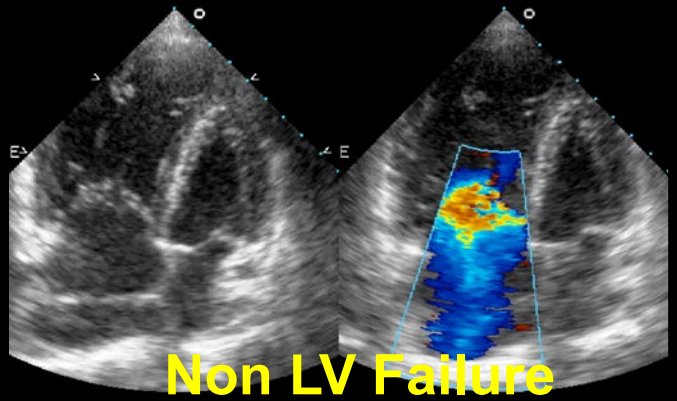
Diverse Disease



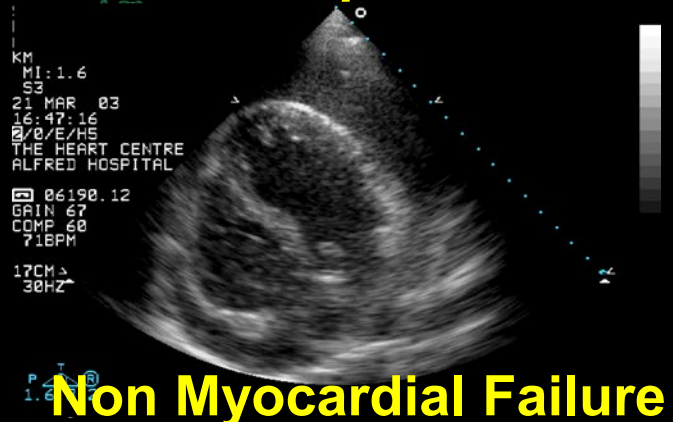
HF*r*EF



HF*p*EF

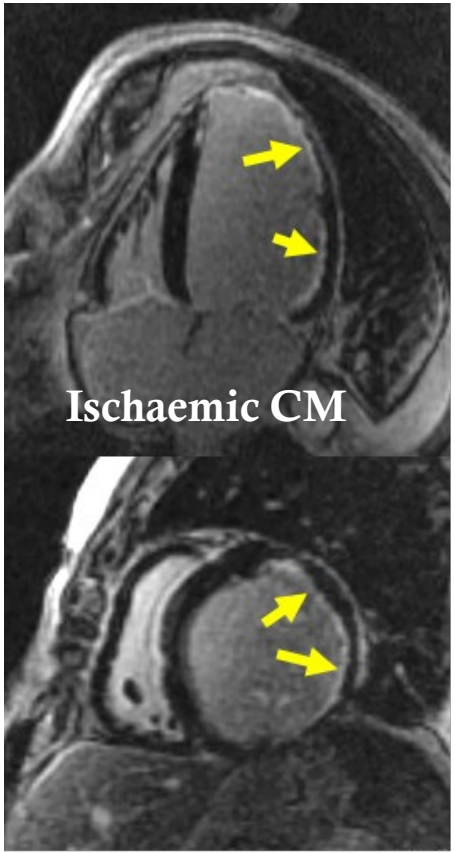


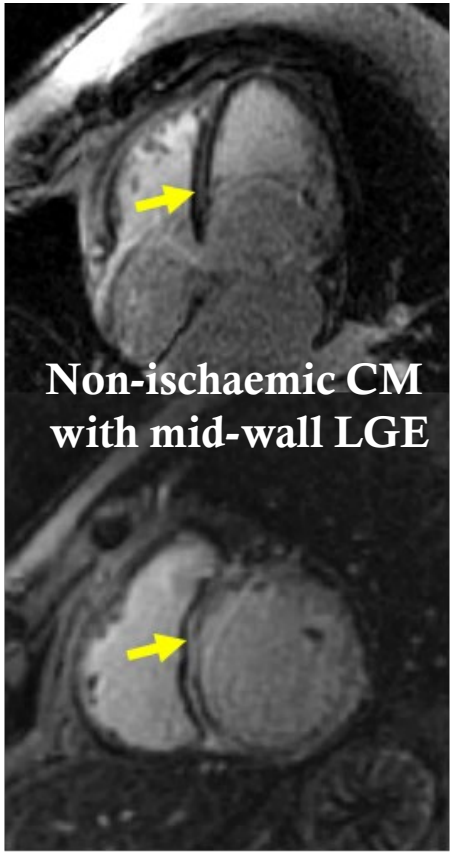
Non LV Failure

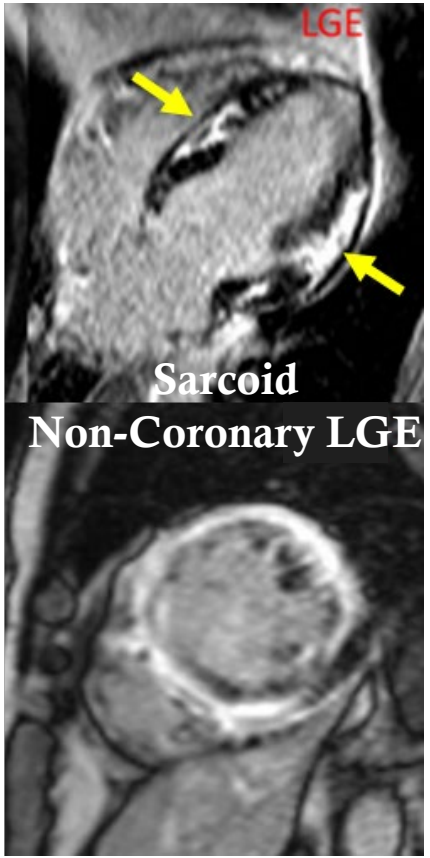


Non Myocardial Failure

Changing Dx AND Px







LGE identifies regional but not diffuse myocardial fibrosis

The Life Savers in Symptomatic HF $_{R}$EF

- ACEi
- βB
- MRA
- ARNI

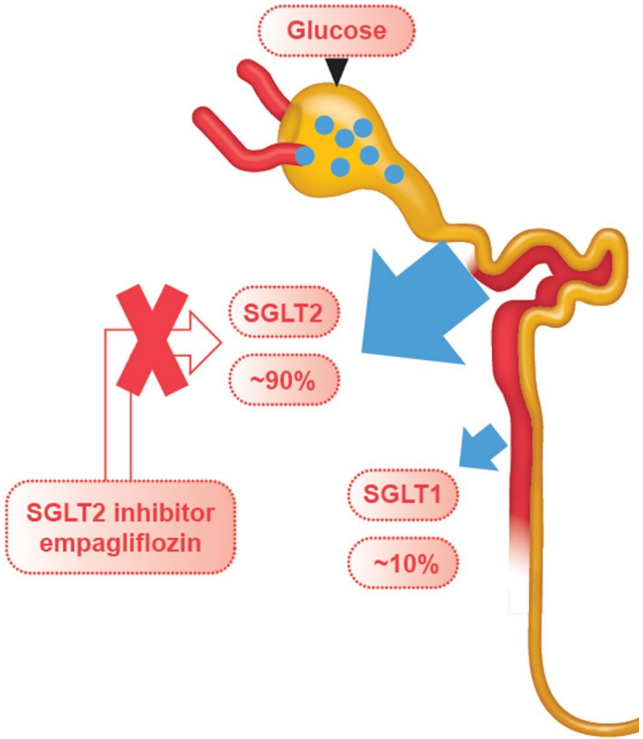
↓ Death
↓ Remodelling
↓ Hospitalis^{n}
↓ Symptoms

UPTITRATE to MAX Tolerated

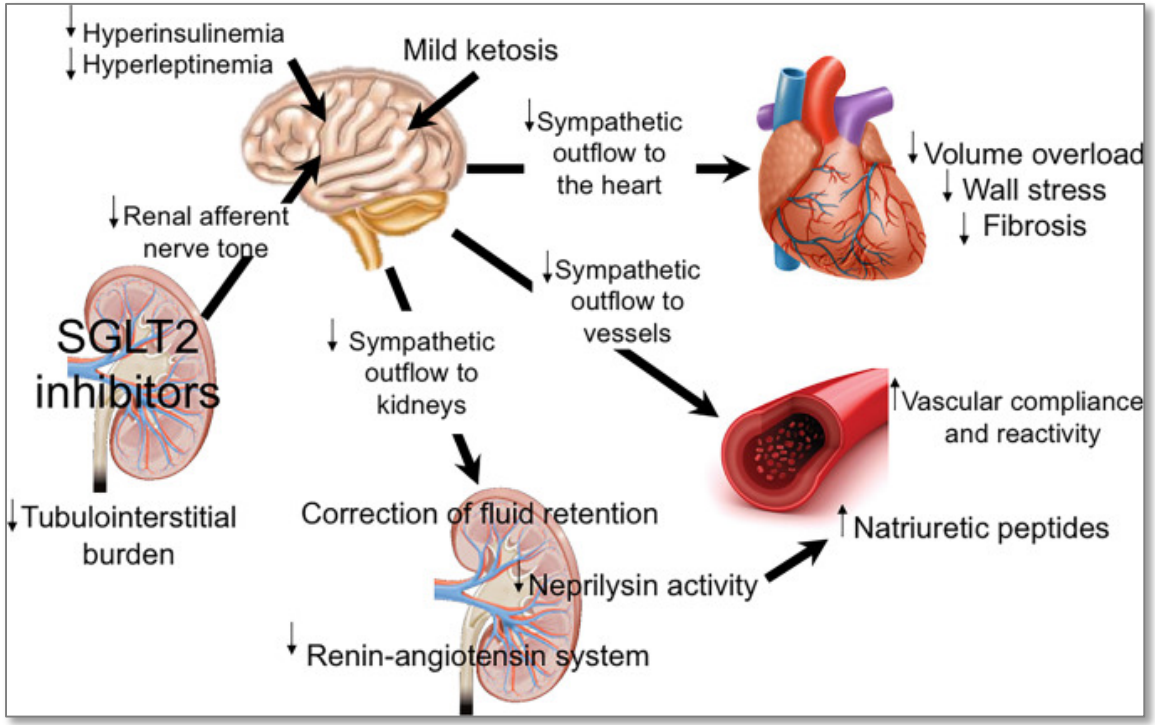
DIURETICS for Euvolaemia
BUT Maintain Organ Perfusion

SGLT2i and the Heart

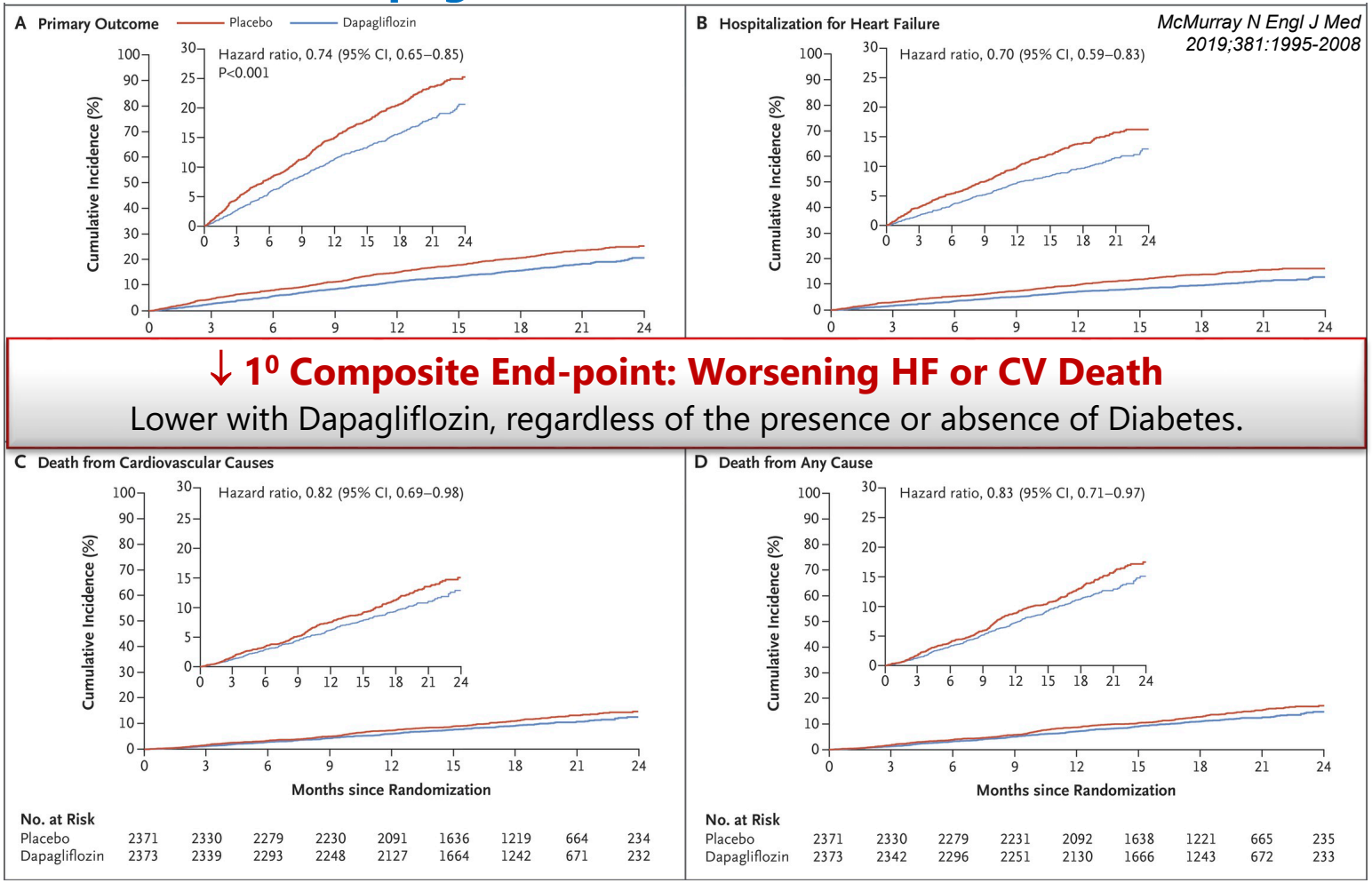
Inhibit Glucose Reabsorption in PCT



?Effects on myocardial metabolism, ion transporters, fibrosis, adipokines, and vascular function



DAPA-HF: Dapagliflozin in Patients with HFrEF - CV



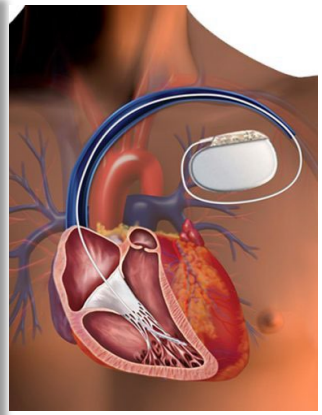
McMurray N Engl J Med 2019;381:1995-2008

↓ 1⁰ Composite End-point: Worsening HF or CV Death

Lower with Dapagliflozin, regardless of the presence or absence of Diabetes.

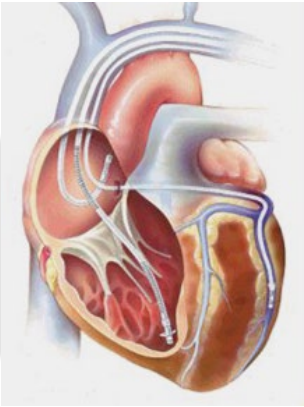
• 1^0 Prevention AICD

Recommendation	GRADE strength	GRADE quality
≥ 1 month post AMI with LVEF ≤ 30%	Strong	High
Ischaemic HFrEF and LVEF ≤ 35%	Strong	Mod
NIDCM HFrEF and LVEF ≤ 35%	Weak	Low

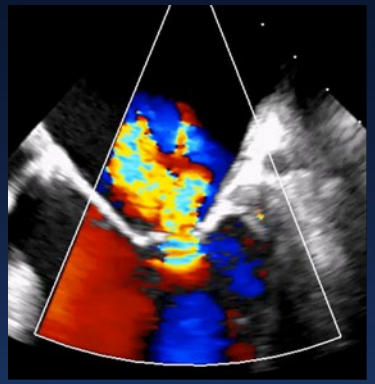


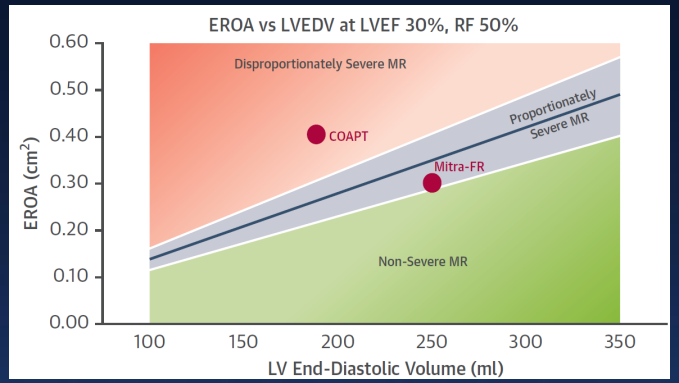
• CRT (BiV) in HFrEF and OMT

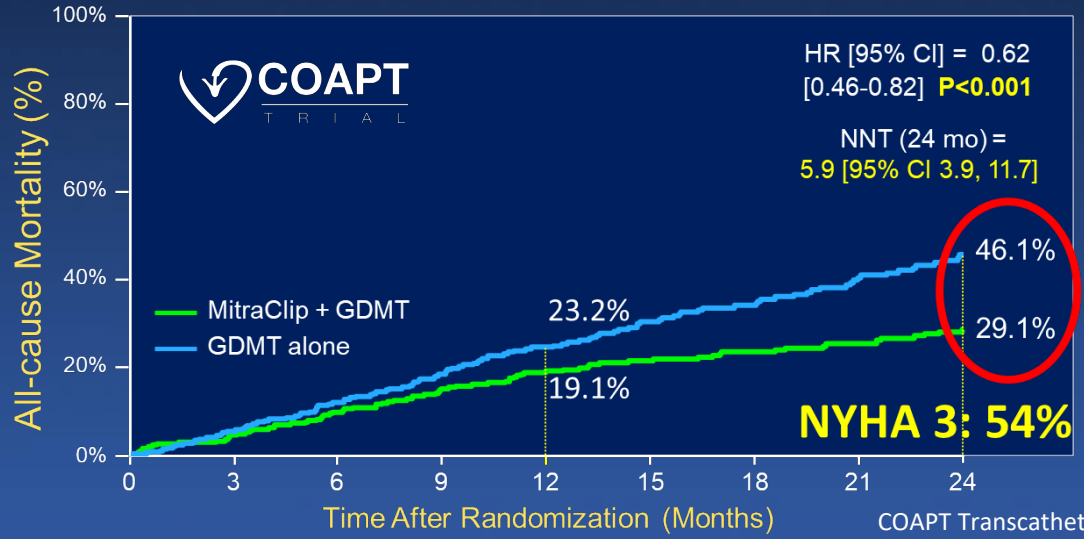
Recommendation	GRADE strength	GRADE quality
Sinus, LVEF ≤ 35%, LBBB, QRS ≥ 150ms	Strong	High



MitraClip in Functional MR







COAPT Transcatheter MV Repair in Heart Failure NEJM 2018

Red Flags for Advanced HF Therapy

CLINICAL FEATURES

- Hypotension
- Persistent ≥ NYHA 3
- Hospitalizations ≥ 2 ≤12 mths
- Recurrent ≥ 2 AICD shocks

MEDICATION

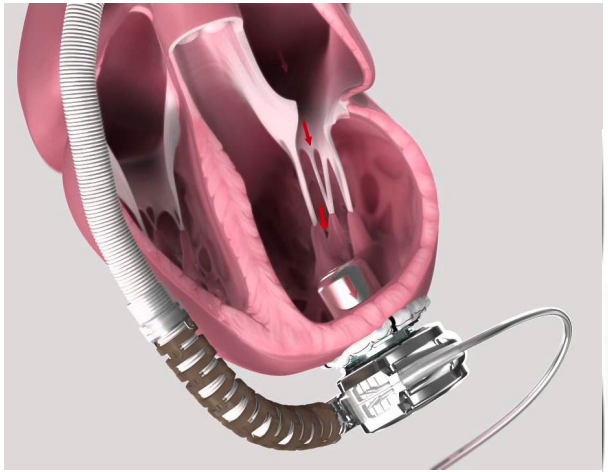
- Down-titration of ACE/ARB, Beta blocker
- Increasing diuretic need
- Prior or ongoing inotrope requirement

INVESTIGATIONS

- End organ dysfn (renal, hepatic)
- LVEF < 20%
- High/rising BNP/NT-proBNP
- Low Serum Na+

Ventricular Assist Device (LVAD)

- **Inflow cannula**
- **Centrifugal Blood pump**
- **Outflow cannula**
- **External**
  - Percutaneous lead
  - Controller
  - Power sources



Indications for VAD

NYHA 3^{+}- 4 HFrEF

(refractory to OMT and conventional surgery)

Ejection fraction <25%

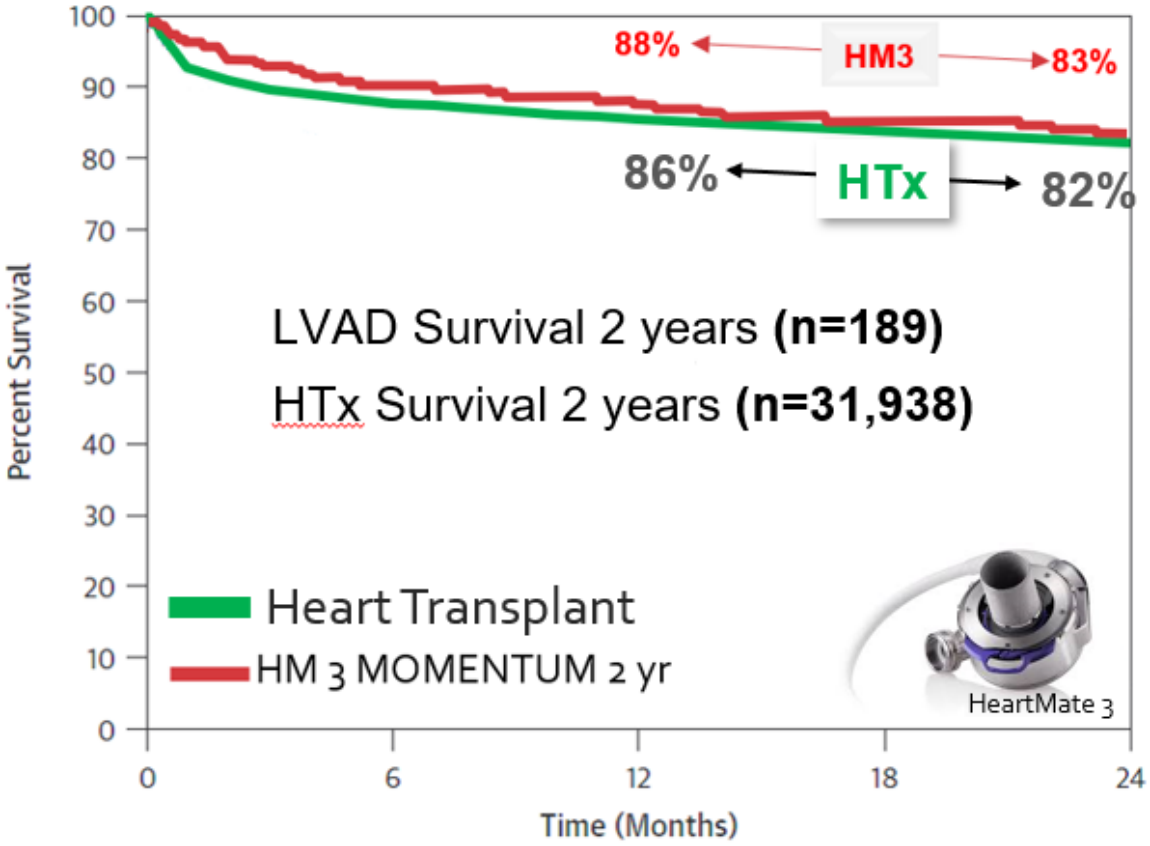
Reduced functional capacity

(with maximal VO2<14 mg/kg/min)

BTT Bridge to Transplant

DT Destination Therapy

Circulation. 2018;138:2841–2851



Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure M.R. Mehra, MOMENTUM 3 Investigators* N Engl J Med 2018;378:1386-95
ISHLT 2019 REGISTRY REPORT JHLT. 2019 Oct; 38(10): 1015-1066
State of the Art LVADs A Rapidly Evolving Alternative to HTx Donna Mancini, Paolo Colombo JACC 2015;65:2542–55)

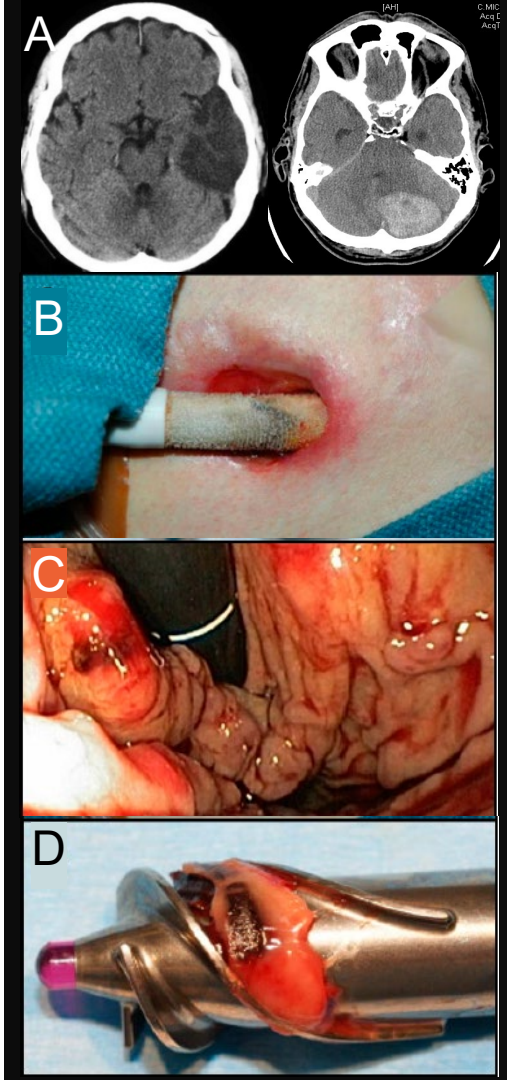
VAD - The Gang of Four

A. Stroke 10%[3]

B. Driveline infections 20%

C. GI bleeding 26%

D. Pump thrombosis 1.4%



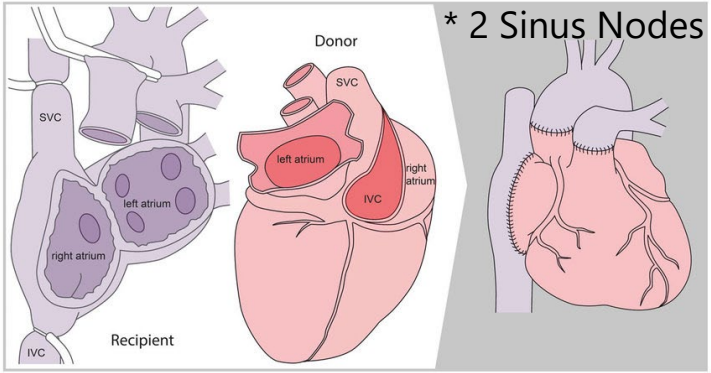
[1]Epidemiology of infection in MCS: IMACS Report. J Heart Lung Transplant 2019;38:364−373
[2]Intermacs database annual report. J Heart Lung Transplant 2019;38:114−126
[3]% are at 2Years

HTx – What Do I Need to Know

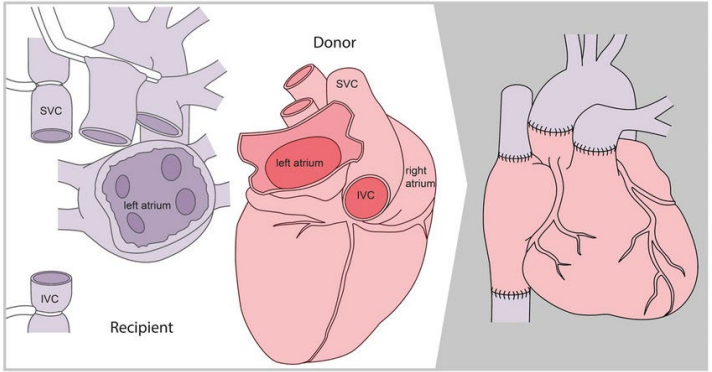
- Donor / Recipient
- Indications / CI
- Outcomes

- Immunotherapy
- Types
- Complications

Biatrial Technique for Heart Transplantation



Bicaval Technique for Heart Transplantation



TTX REGISTRY DATABASE:
Number of Transplants Reported

Organ	1/7/2017 – 30/6/2018	Total Transplants 1982- 30/6/2018
Heart	4,978	146,975
Heart-Lung	70	4,884
Lung	3,936	71,734

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2019
JHLT. 2019 Oct; 38(10): 1015-1066

ANZ DATA | AUSTRALIA & NEW ZEALAND ORGAN DONATION REGISTRY

Australian Donation and Transplant Snapshot

In Australia there were **554** actual deceased solid organ donors in 2018, an increase of 8.6% in the number of donors from 2017 (510 donors);

The deceased organ donors per million population (pmp) was **22.2** donors pmp in 2018, an increase from 20.7 donors pmp in 2017;

there was an 11.4% increase in the number of donors after brain death to **400** and a 2.0% increase in the number of donors after circulatory death to **154** in 2018;

a total number of **897** kidney transplants (**35.9 pmp**)

a total number of **318** liver transplants (**12.7 pmp**)

a total number of **129** heart transplants (**5.2 pmp**)

a total number of **222** lung transplants (**8.9 pmp**)

ANZOD Annual Report 2019

Heart Tx –Donor Criteria

- Satisfy Standard Donation Criteria
- Age < 50 yrs
- No Significant Cardiac Disease
- Not on High Dose Inotropes
- Ischaemic Time < 4 hrs

DBD	Donation after Brain Death
DCD	Donation after Circulatory Death

Heart Tx – Recipient General Indications (despite Optimal Rx)

- Severe symptomatic HF
- Frequent AICD discharges
- Intractable angina (rare)

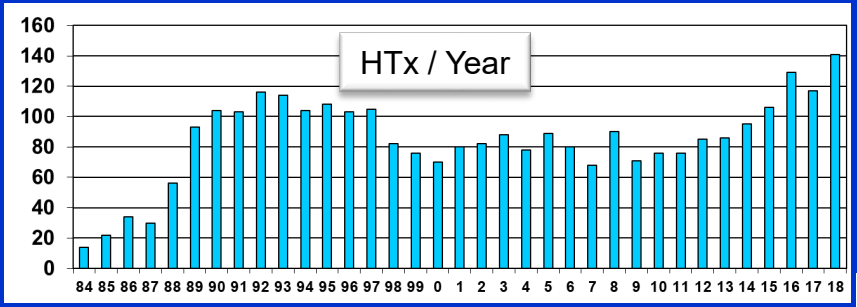
An expected survival benefit, with a reasonable prospect of returning to an active lifestyle

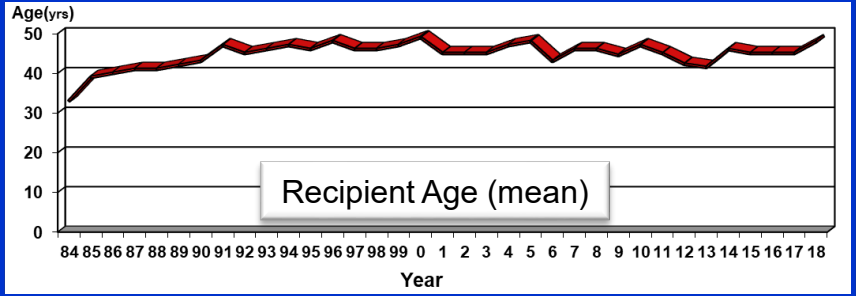
Low EF alone is NOT an Indication

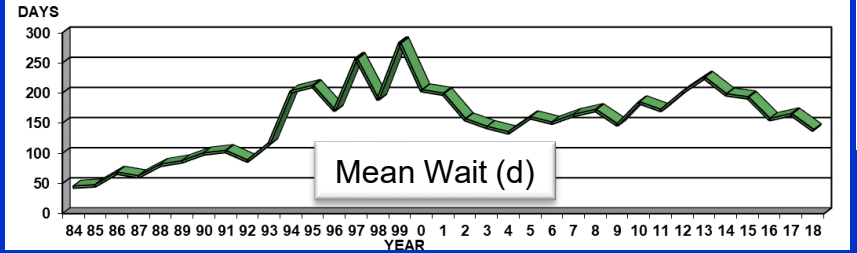
Heart Tx – General Recipient Contraindications

- Age is not by itself a C/I – unlikely over 70 years
- Comorbidities that result in high mortality/morbidity/risk
  - Active malignancy
  - Uncontrolled Infection (??Hep C)
  - Complicated diabetes
  - Obesity (BMI>30 - 35)
  - Lifestyle factors that result in poorer outcomes
  - Substance abuse (alcohol, smoking, illicit drugs)
    - 6 months abstinence recommended before consider listing
- Irreversible damage of other organ systems that preclude rehabilitation

Australia Heart Tx 1984 - 2018

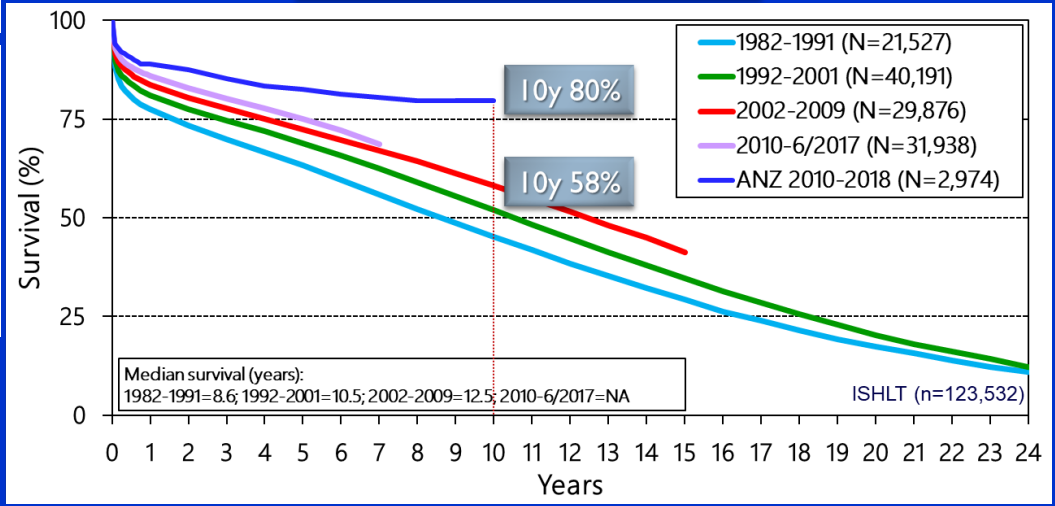






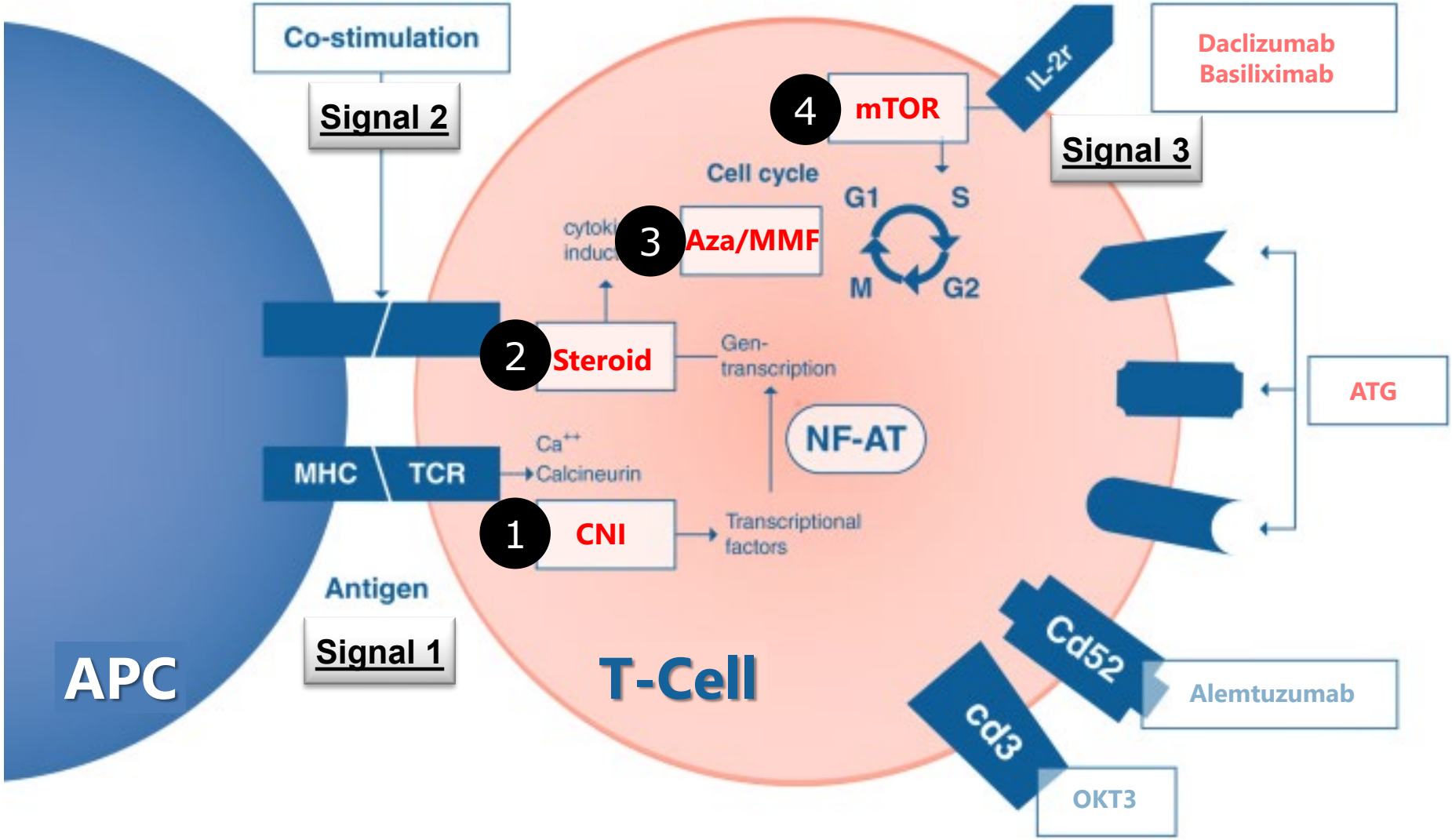
- 50% LVAD pre
- ~50% NIDCM
- ~30% IHD

HTx Survival – ANZ Vs ISHLT



ISHLT 2019

ANZCOTR 2018


Co-stimulation
Signal 2
Antigen
Signal 1
APC
MHC
TCR
T-Cell
4
mTOR
IL-2r
Daclizumab
Basiliximab
Signal 3
Cell cycle
G1
S
M
G2
3
Aza/MMF
2
Steroid
Gen-
transcription
NF-AT
Ca++
Calcineurin
1
CNI
Transcriptional
factors
ATG
Cd52
Alemtuzumab
cd3
OKT3

S I D E F X

Calcineurin inhibitors

Cyclosporine	Renal insufficiency
	Hypertension and dyslipidemia
	Hypokalemia and hypomagnesemia
	Hyperuricemia
	Neurotoxicity (encephalopathy, seizures, tremors, neuropathy)
	Gingival hyperplasia
	Hirsutism
Tacrolimus	Renal dysfunction
	Hypertension
	Hyperglycemia and diabetes mellitus
	Dyslipidemia
	Hyperkalemia
	Hypomagnesemia
	Neurotoxicity (tremors, headaches)

Corticosteroids

Prednisone	Weight gain
	Hypertension, hyperlipidemia, hyperglycemia
	Osteopenia
	Poor wound healing
	Salt and water retention
	Proximal myopathy
	Cataracts
	Peptic ulcer disease

Cell cycle agents

Azathioprine	Bone marrow suppression Remember Allopurinol Interaction
	Hepatitis (rare)
	Pancreatitis
	Malignancy
Mycophenolate mofetil	Gastrointestinal (nausea, gastritis, diarrhea)
	Leukopenia

Proliferation signal inhibitors

Sirolimus	Oral ulcerations
Everolimus	Hypercholesterolemia and hypertriglyceridemia
	Poor wound healing
	Lower extremity edema
	Pulmonary toxicities (pneumonitis, alveolar hemorrhage)
	Leukopenia, anemia, and thrombocytopenia
	Pericardial effusion
	Potentiation of calcineurin inhibitor nephrotoxicity

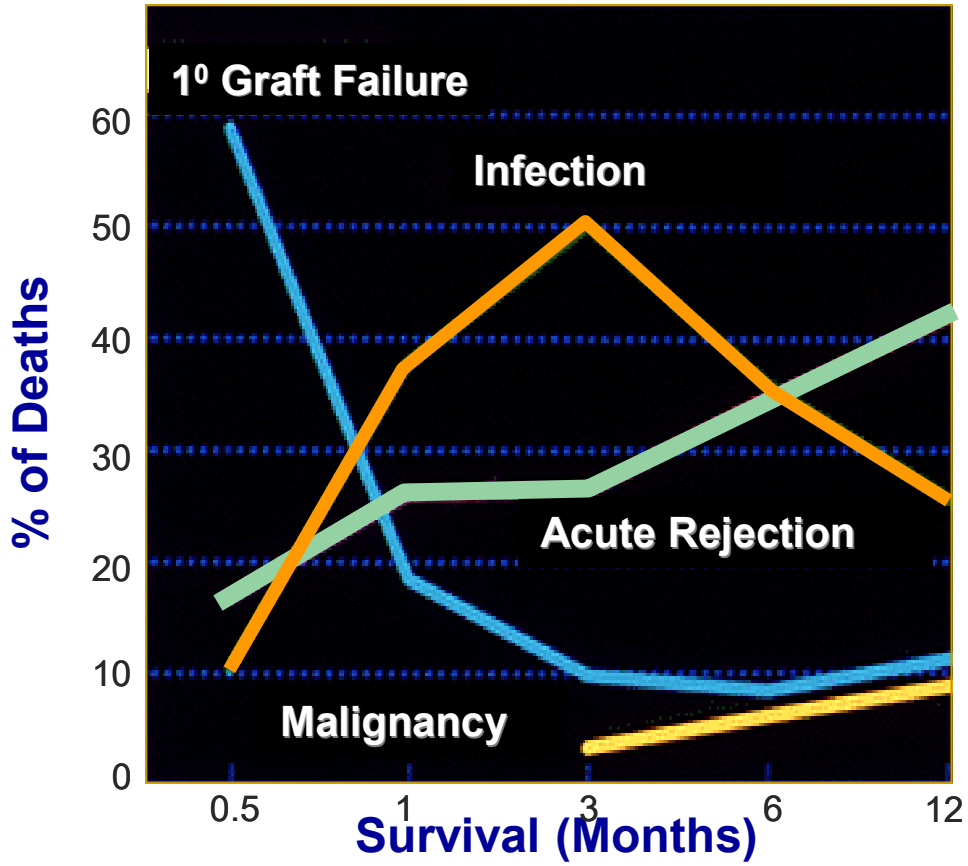
Rejection – Cellular & Humoral (Ab mediated)

- Leading cause of early mortality - 30%
- Early diagnosis essential
  - Biopsy is the current "gold standard"
  - 90% within 6 months.
  - ♀ / young at high risk
- Early Rx (typically Prednisolone) essential

Alternatives

- ECG
- Imaging
  - Echo
  - CMRI
- Biomarkers
  - BNP
  - Troponin
  - CRP
- Cell Free DNA

Early Mortality Post Transplant



Adult Heart Transplants
Cumulative Morbidity Rates in Survivors within 1, 5 and 10 Years Post Transplant (Transplants: January 1995 – June 2017)

Outcome	≤ 1 Year	≤ 5 Years	≤ 10 Years
Cardiac Allograft Vasculopathy	7.7%	29.0%	46.8%
Diabetes[1]	20.0%	33.8%	-
Severe Renal Dysfunction[2]	6.7%	15.7%	22.3%
Creatinine > 2.5 mg/dl (221 µmol/L)	5.1%	12.2%	14.3%
Chronic Dialysis	1.5%	2.9%	6.0%
Renal Transplant	0.1%	0.6%	2.0%
Malignancy (all types combined)	5.1%	16%	27.7%

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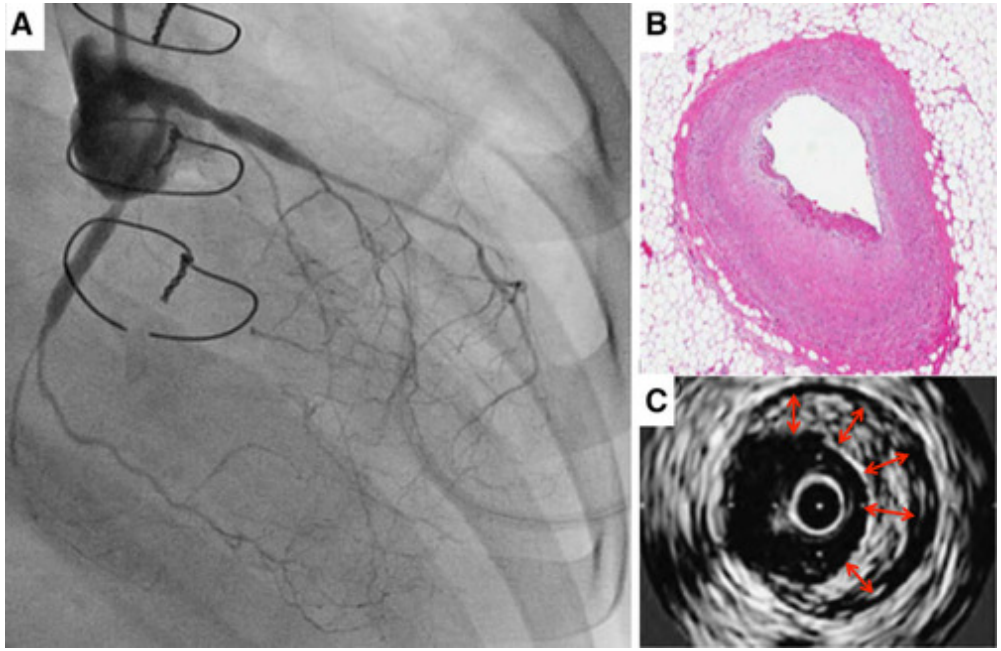
JHLT. 2019 Oct; 38(10): 1015-1066

[1] Data are not available 10 years post-transplant.
[2] Severe renal dysfunction = Creatinine > 2.5 mg/dl (221 µmol/L), dialysis, or renal Tx

Infections

- **Common** is still **Common**
  - usual presentations
  - unusual presentations
- Consider unusual infections
- Remember non-bacterial
  - Viruses especially CMV
  - Fungus
  - Mycobacteria
- Not all fever is infection

Coronary Allograft Vasculaopathy (CAV)



Non - Tx	Tx
Proximal	Distal
Localised	Diffuse
Eccentric	Concentric
Calcified	Non-calcified

CAV = intimal hyperplasia & interstitial fibrosis

Josef Stehlik. Circulation. Honoring 50 Years of Clinical Heart Transplantation in Circulation, Volume: 137, Issue: 1, Pages: 71-87

Take Home: Heart Transplantation

- HTx is highly effective treatment
- Survival in eligible pts without HTx is < 2 yrs
- About 100 - 130 HTx each year in Australia
- ANZ median survival is 14 years
- >1/3 survive more than 20 years