30-Year Journey of Heart Transplantation in Asan Medical Center

Jae-Joong Kim, MD

Asan Medical Center, Republic of Korea

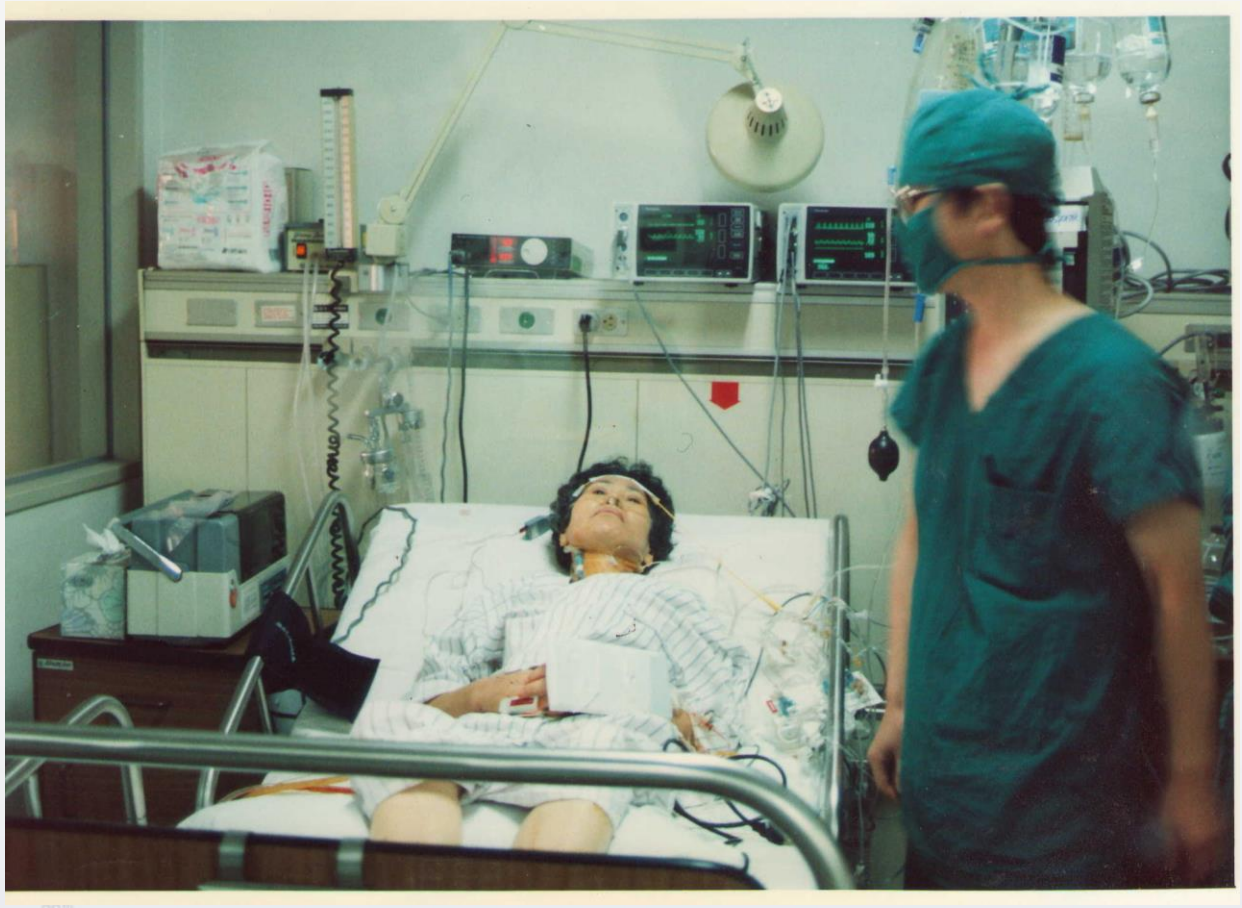
Disclosure

- I have nothing to disclosure.

The 1st Heart TPL in AMC

The 1st heart transplantation in Korea

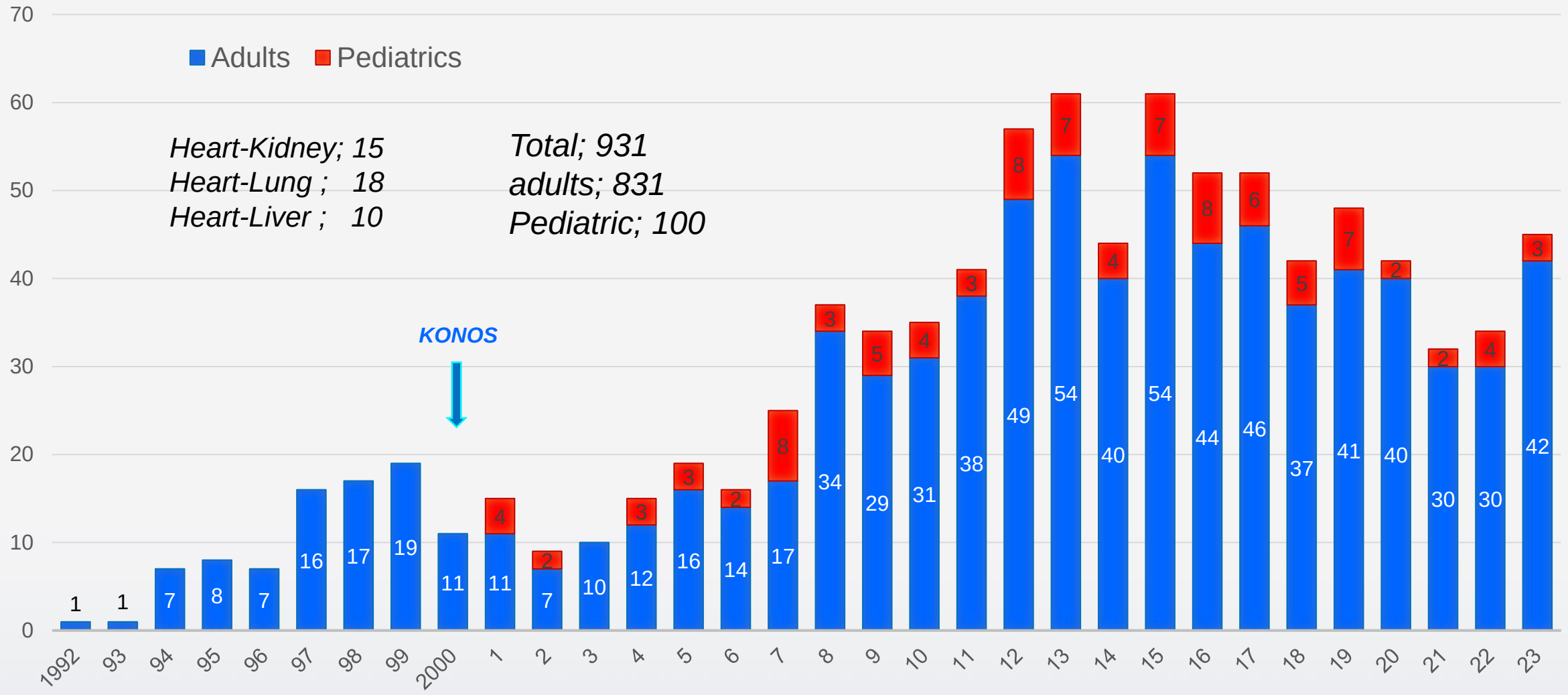
1992.11.11 F/51 DCMP, M/24 TA



1992.11.11 ~ 2016.08.24

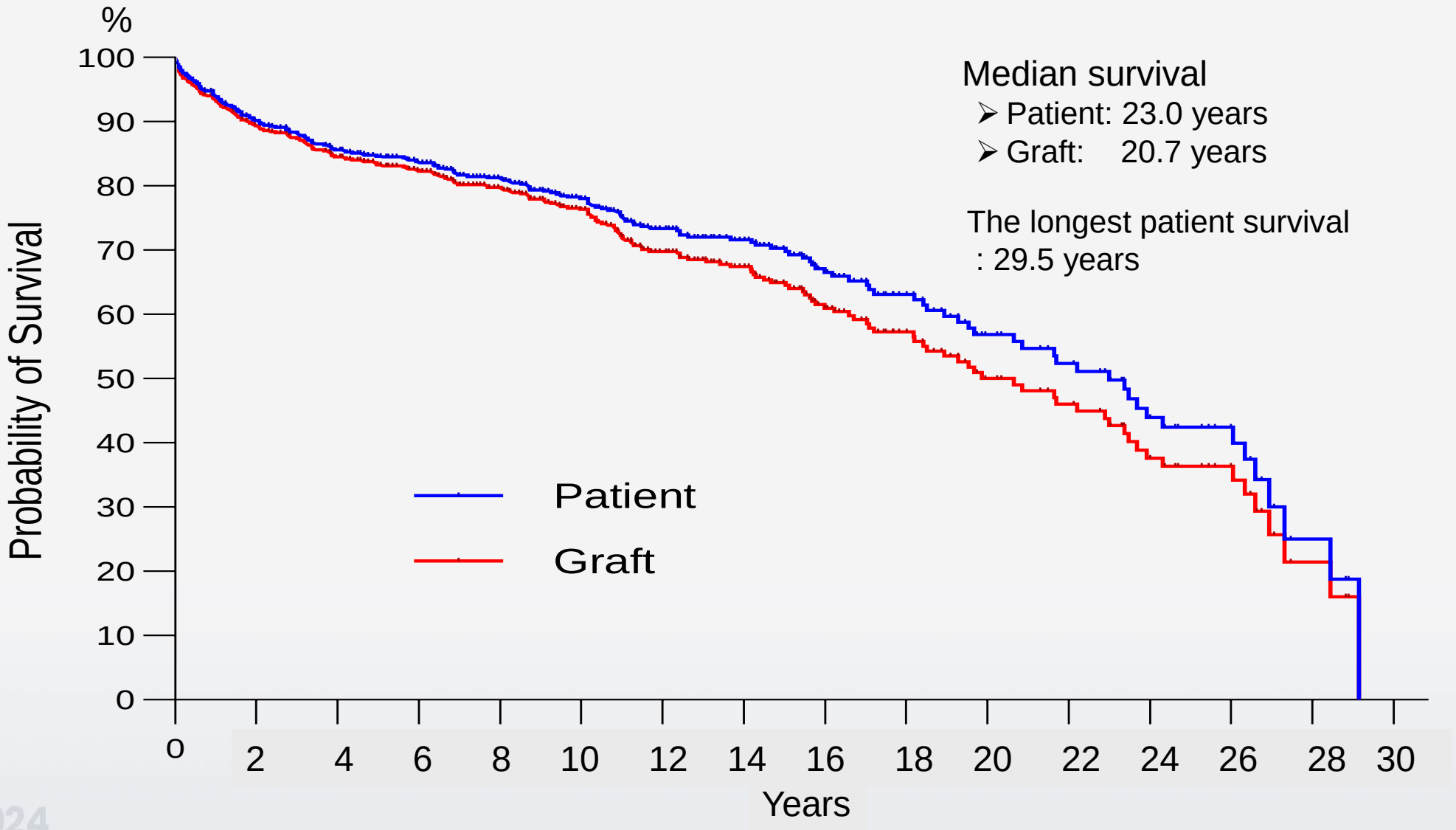
Heart Transplants in AMC

Number of Transplants by Year



Survival of Heart Transplants in AMC

Adults Heart Transplantation



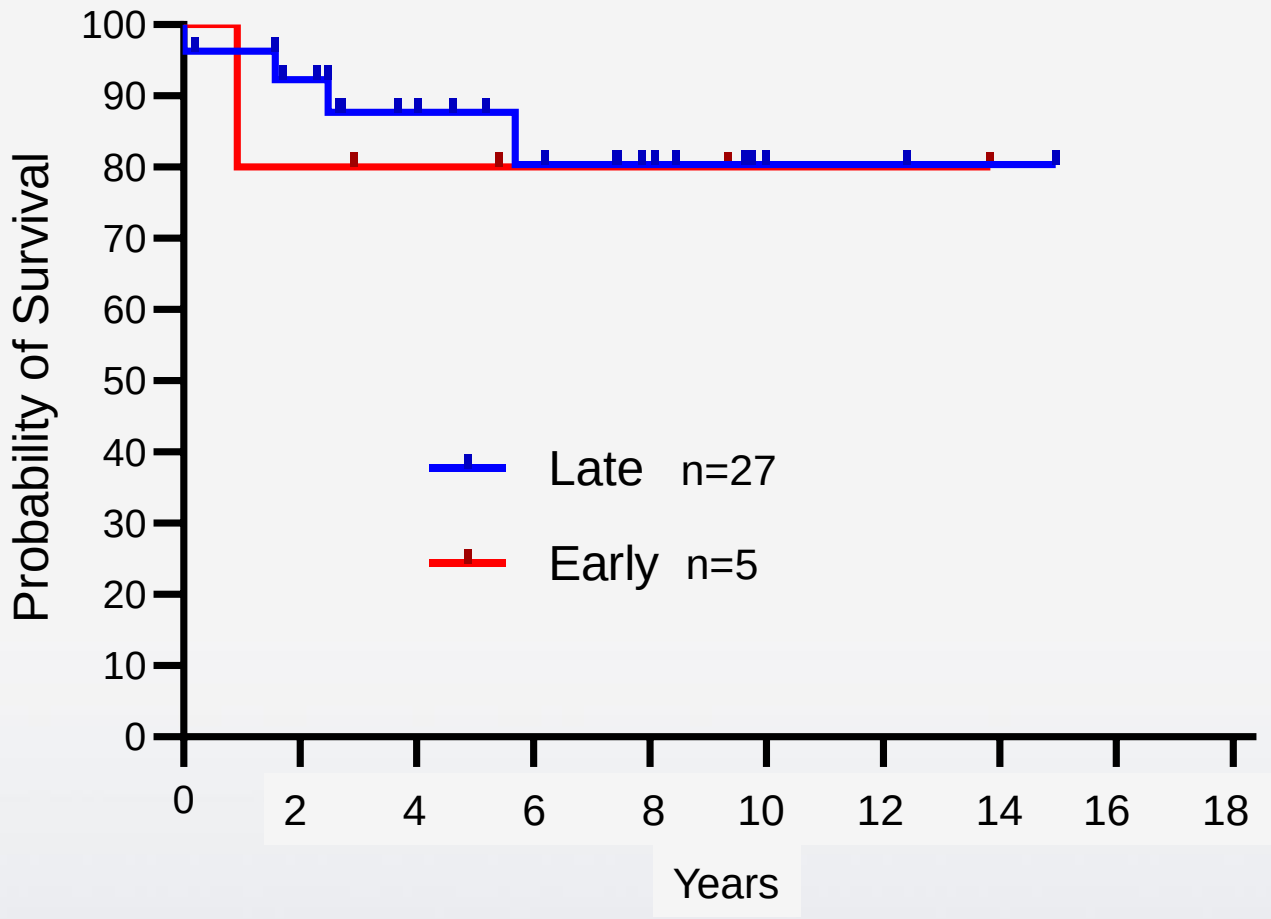
Median survival
- Patient: 23.0 years
- Graft: 20.7 years

The longest patient survival
: 29.5 years

Survival of Heart Transplants in AMC

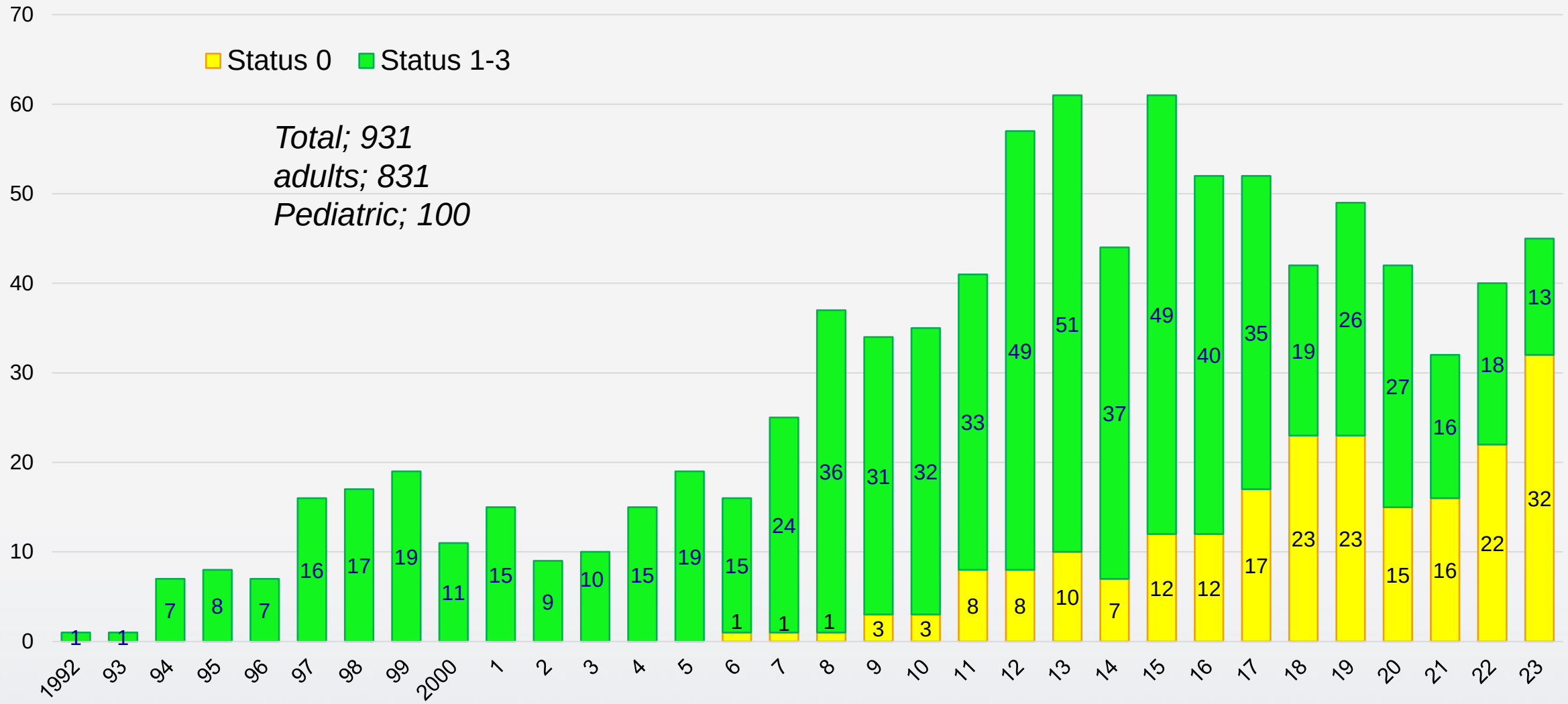
Adults Retransplantation

- Total 32/831 patients (3.6%)
- Early ReTPL (within 1 year)
  - N=5, 10.6(3-18) days
  - Severe PGF in 3
  - RV failure d/t high PVR in 2
- Late ReTPL (later than 1 year)
  - N=27, 137.9(17.1 - 274.7) mos
  - CAV in 24
  - Graft failure with fibrosing constrictive pericarditis in 1
  - Unknown graft failure in 2
    - Diffuse fibrosis in 1
    - Multifocal myocardial degeneration in 1



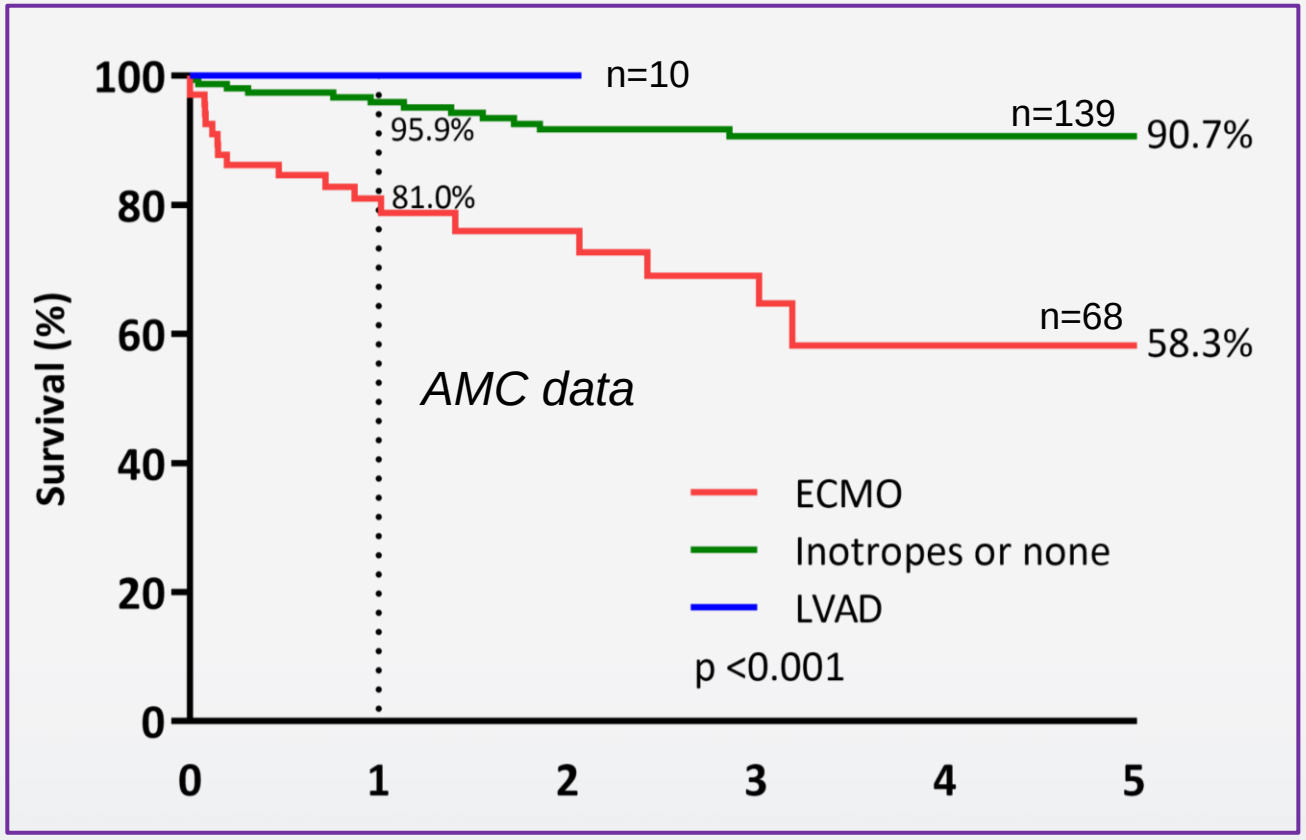
Heart Transplants in AMC

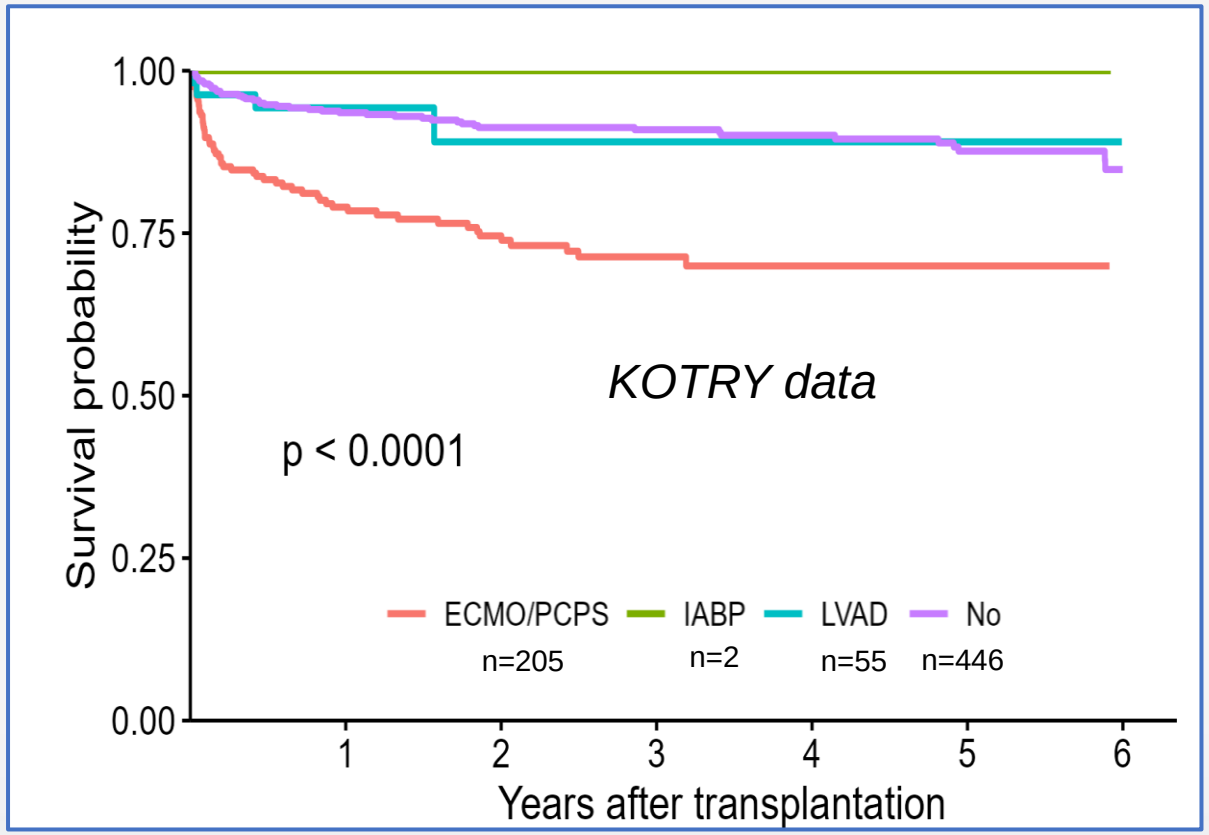
Number of Transplants by Year



Survival of Adult Heart Transplantation

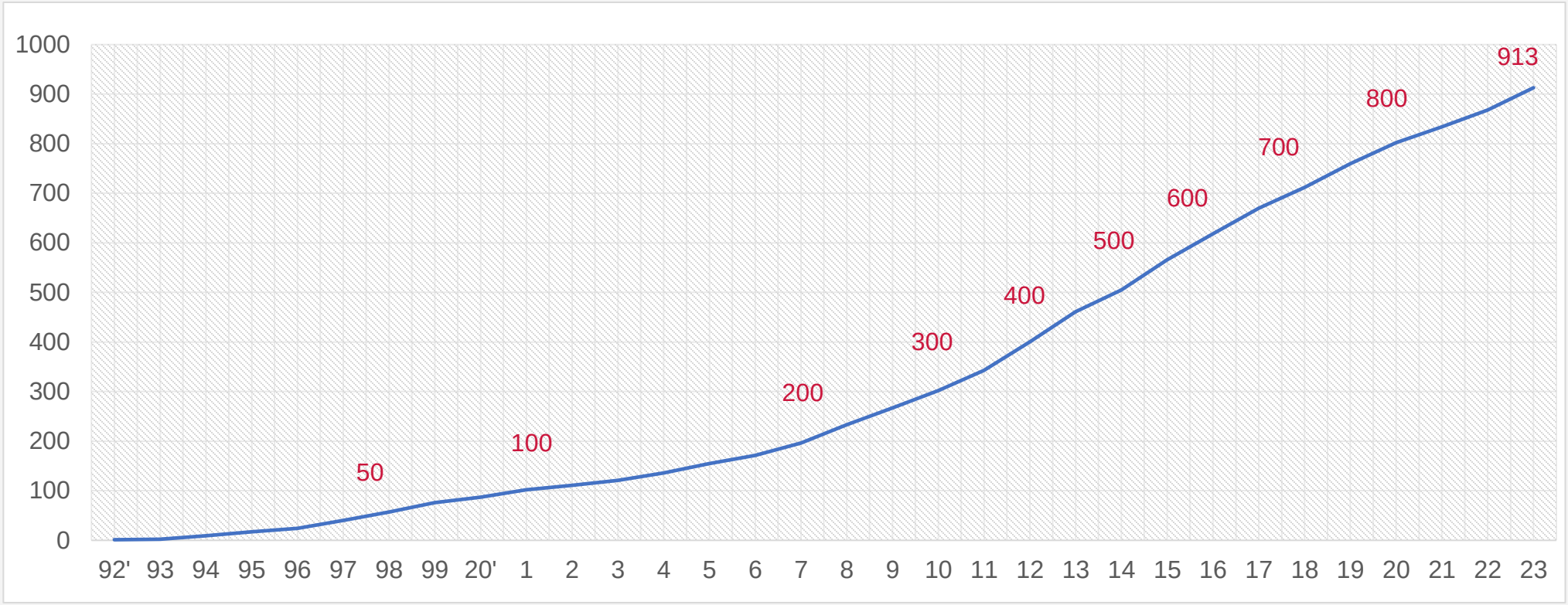
By Types of Mechanical Circulatory Support (year 2015-2020)





Journey of Heart Transplants in AMC

Immunosuppression, EMBx



Immunosuppression

Endomyocardial Bx

Immunosuppression Protocol

~ 1999. 6

- Preoperative
  - Cyclosporin: 5 mg/kg po (if SCr >1.5mg%, no CsA)
  - Azathioprine: 4mg/kg po
- Intraoperative
  - Methyl PD 500mg intravenous
- Postoperative
  - intravenous cyclosporine at ICU
  - Cyclosporine ; 300- 400 ng/ml during the 1st year
    then 150 -250ng/ml
  - Azathioprine ; 1–2mg/kg/day (WBC>4,000/mm3)
  - Steroid
    - Methyl PD 125 mg IV every 8 hrs 3 times
    - then 1mg/kg/day tapering to 0.25mg/kg/day at 1 month and less than 0.1mg/kg/day at 1 year

1999.7~

Induction with anti-IL_2 R mAb

Preoperative

Mycophenolate mofetil; 1-1.5 gm po

Intraoperative

Methyl PD 500mg intravenous

- Postoperative

No intravenous CNI

Cyclosporine

or
- 200 - 300 ng/ml during the 1st year
  then 80 - 150ng/ml

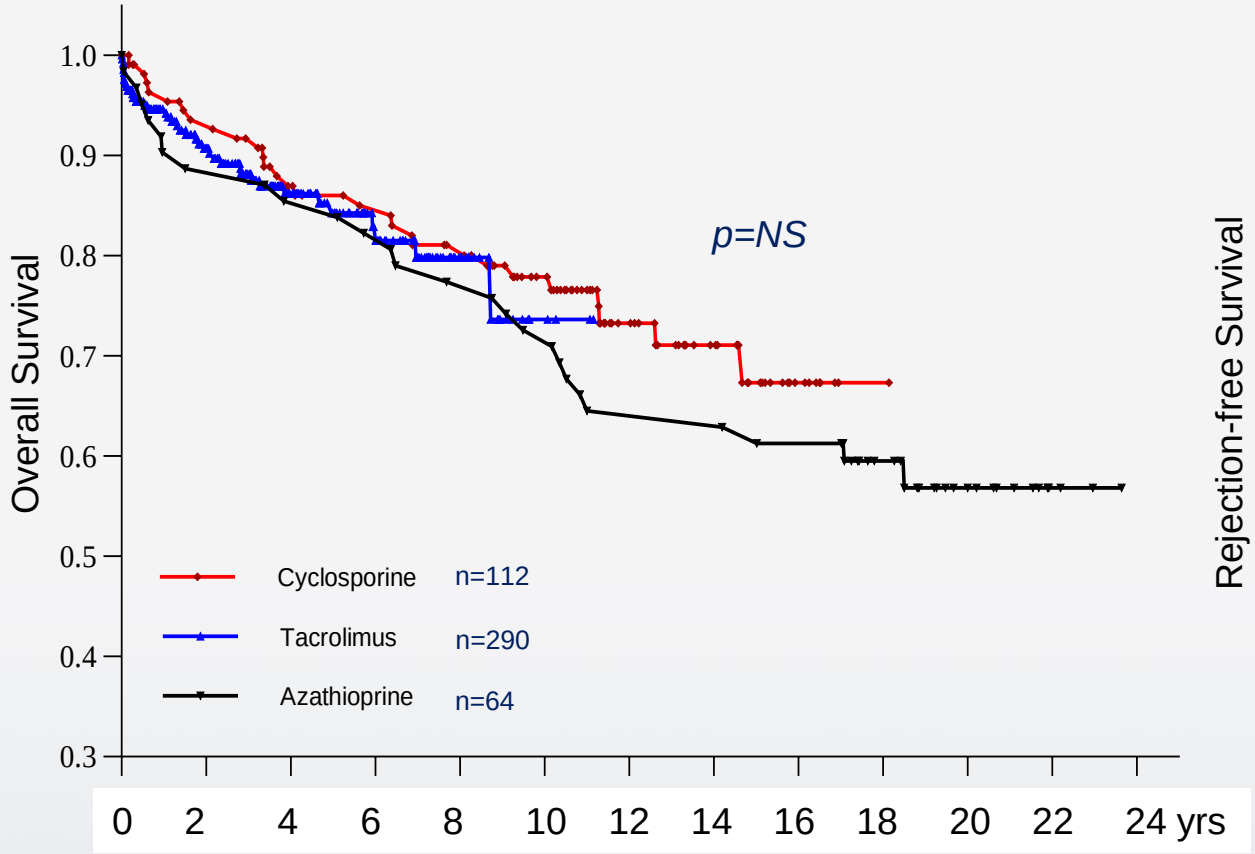
- Tacrolimus
  - 8-12ng/mL then 4-6ng/mL
- Mycophenolate mofetil
  - 1 – 2 gm/day to keep WBC> 4000/mm3

Steroid; Tapering out within 1st year in low risk patients

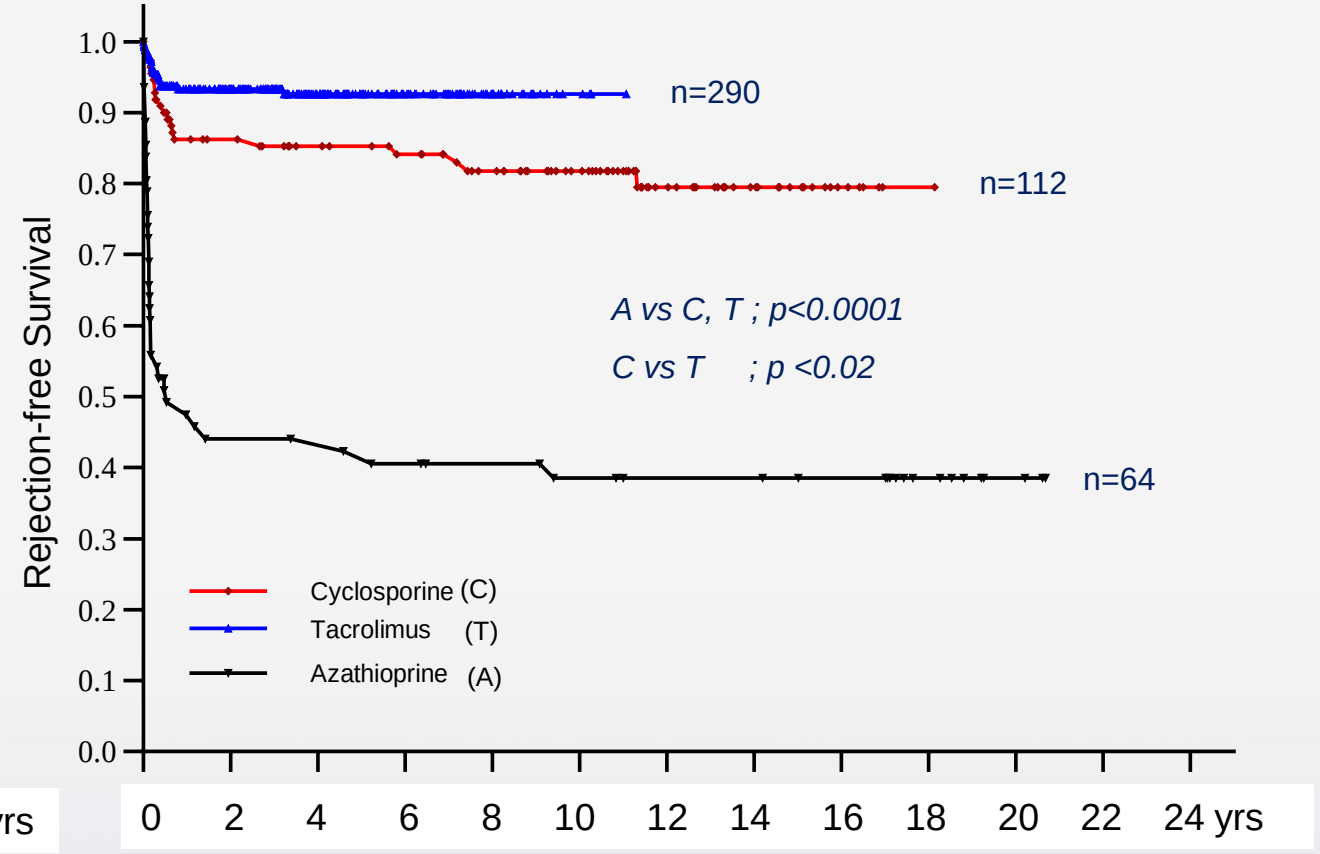
Comparison of Immunosuppression

CsA + Azathioprine vs CsA + MMF + IL2mAb vs Tac + MMF + IL2mAb

(1992.11 – 2016.3)

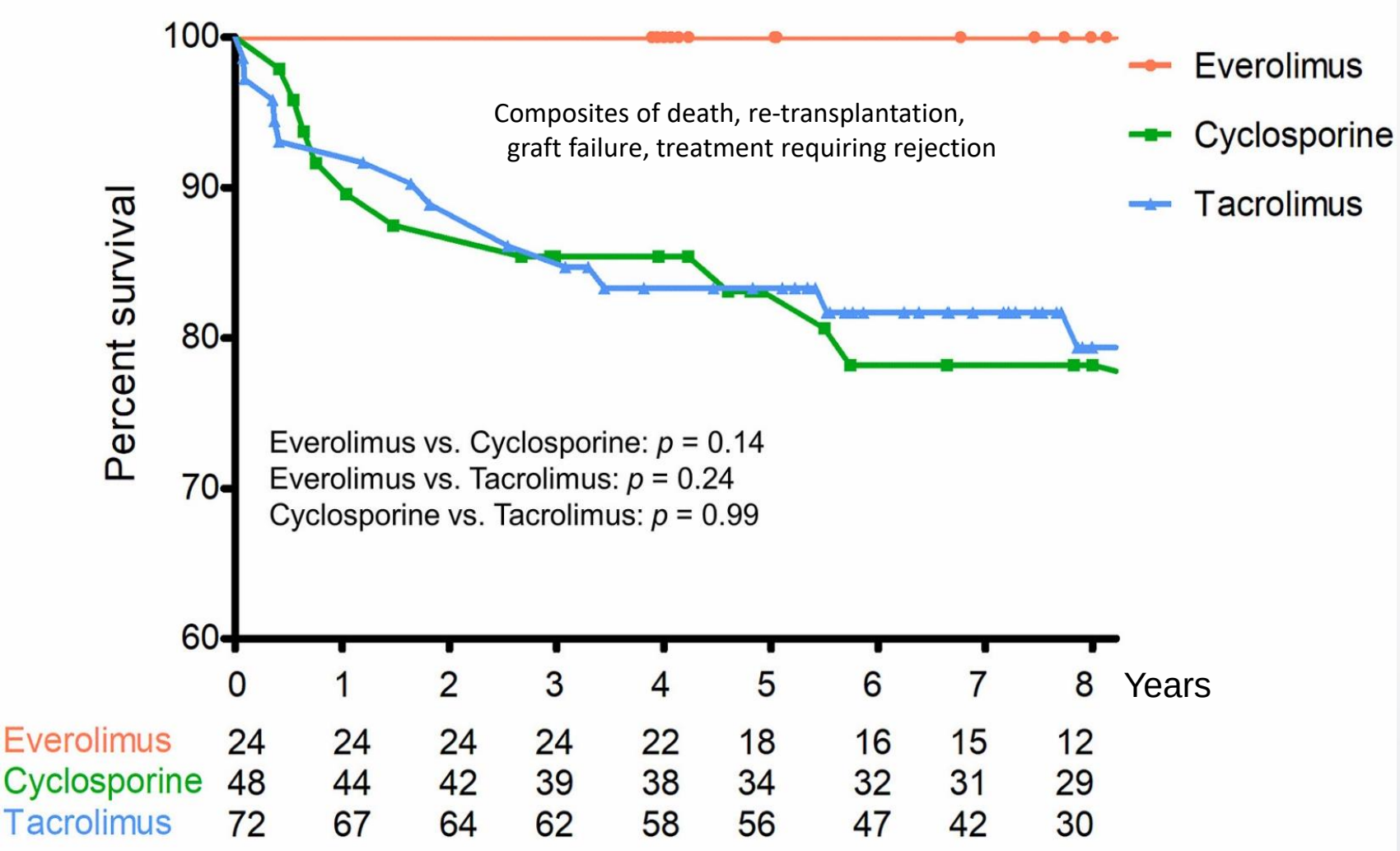


(1992.11 – 2016.3)



Comparison of Immunosuppression

CsA + MMF vs Tac + MMF vs CsA + EVL



Choi HI, Kim JJ et al. Atherosclerosis 2021;357:1-8

Immunosuppression Protocol

Current protocol

Induction

- Anti-IL_2 R mAb

Intraoperative

Methyl PD 500mg intravenous

- Maintenance

Calcineurin inhibitor; usually Tacrolimus

- Mycophenolic acid derivatives
- mTOR inhibitor; replace MPA at 3-12 weeks
- Steroid
  - Tapering out within 1st year in low risk patients
  - No DSA, no episodes of AMR, no episodes of recurrent ACR

For immunologically high risk recipients

(preformed DSA, high PRA, (+) flow matching, retransplantation, GFR<45ml/min)

Induction

ATG

- ATG 1.5mg/kg for 5-7 days up to total 7.5mg/kg

Intraoperative

Methyl PD 500mg intravenous

- Maintenance

Calcineurin inhibitor; usually Tacrolimus

- Mycophenolic acid derivatives
- mTOR inhibitor; replace MPA at 3-12 weeks
- Steroid
  - Tapering out within 1st year for low risk patients
  - No DSA, no episodes of AMR, no episodes of recurrent ACR

Endomyocardial Biopsy Protocol

Toward Rejection Diagnosis without EMB

- **Surveillance EMB (15 times)**
  - Every week x4
  - Every 2 weeks x2
  - Every 4 weeks x2
  - Every 2 months x2
  - At 1 year
  - Every year usually up to 5 years
- **Not scheduled biopsy**
  - Sxs of HF and/or Graft dysfunction
  - After treatment of acute rejection

→

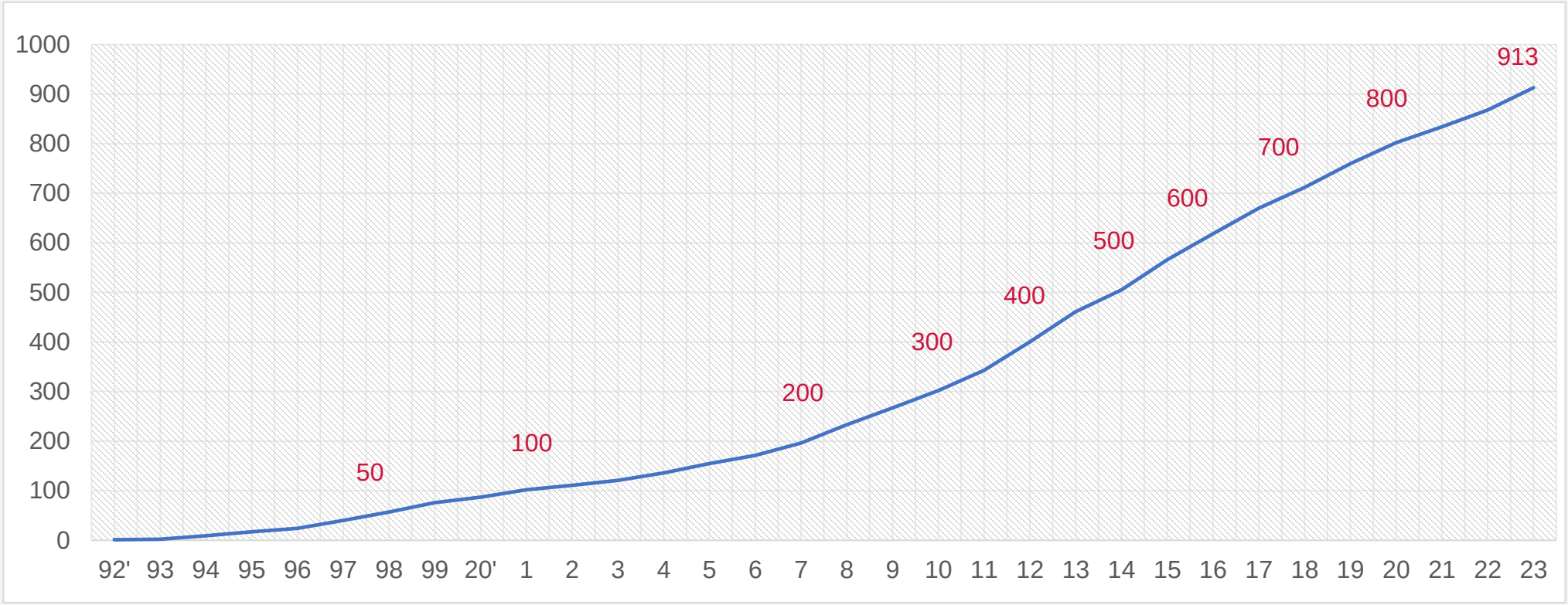
- **Surveillance EMB (8 times)**
  - Every 2 weeks x2
  - Every 4 weeks x2
  - Every 2 months x3
  - At 1 year
  - No annual surveillance biopsy
- **Not scheduled biopsy**
  - Sxs of HF and/or Graft dysfunction
  - After treatment of acute rejection

→

- **Surveillance EMB (6 times)**
  - At 4 weeks
  - Every 3-4 weeks x2
  - After 2 months
  - After 3 months
  - At 1 year
  - No annual surveillance biopsy
- **Not scheduled biopsy**
  - Sxs of HF and/or Graft dysfunction
  - After treatment of acute rejection

Journey of Heart Transplants in AMC

CMV prophylaxis



CMV prophylaxis

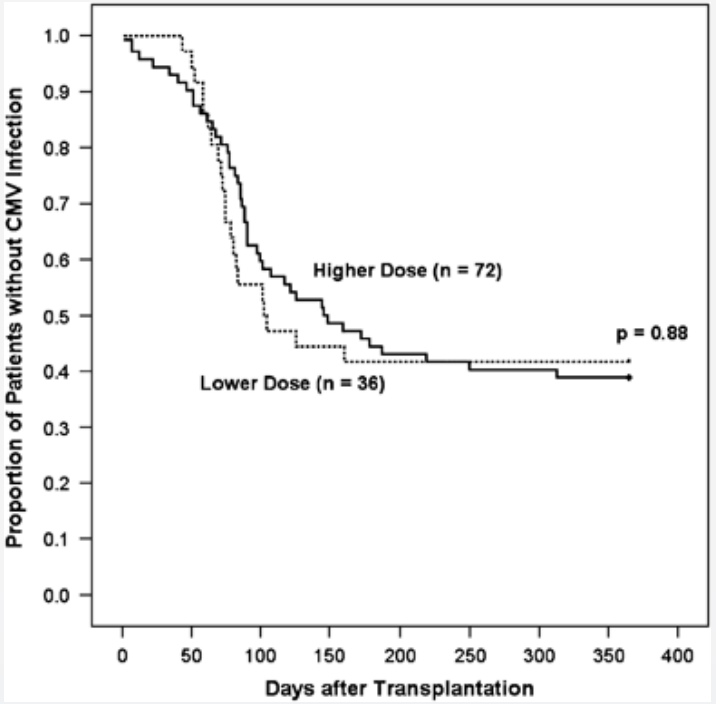
Ganciclovir 5mg/kg bid for 2 wks then qd for 2 wks

Ganciclovir 5mg/kg qd for 4 wks

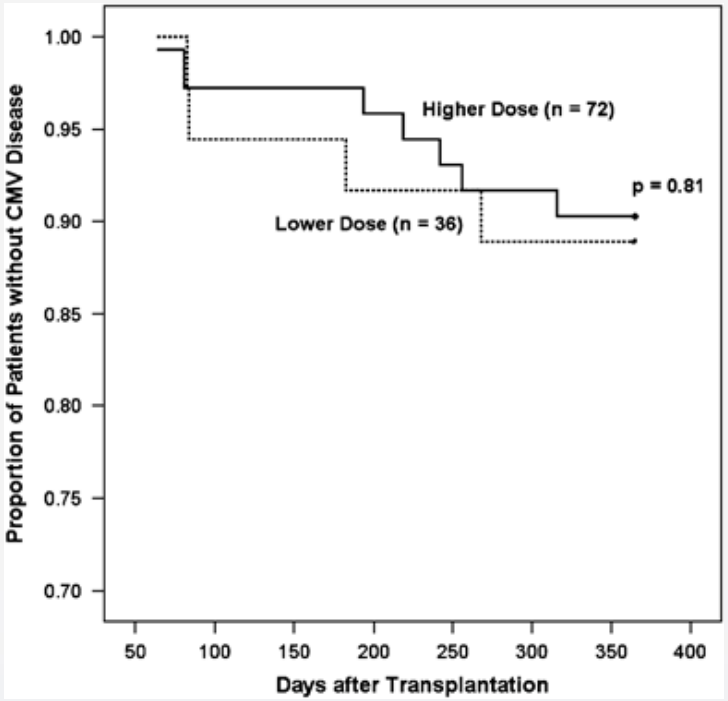
CMV Prevention Protocol

- Single center(AMC) analysis
  - Same protocols for the diagnosis and management of CMV infection
  - Same protocol for immunosuppressive therapy
    - ✓ Induction with basiliximab
    - ✓ Maintenance with cyclosporine and mycophenolate deriv.
- Total 108 patients during 1999.6 ~ 2007.12
- CMV prophylaxis
  - HD (high dose); iv GCV 5mg/kg bid for 2 weeks then qd for another 2 weeks
  - LD (low dose); iv GCV 5mg/kg qd for 4 weeks
- CMV infection; any CMV antigenemia(+) or CMV disease
- Analysis of the CMV infection during the 1st year

CMV infection



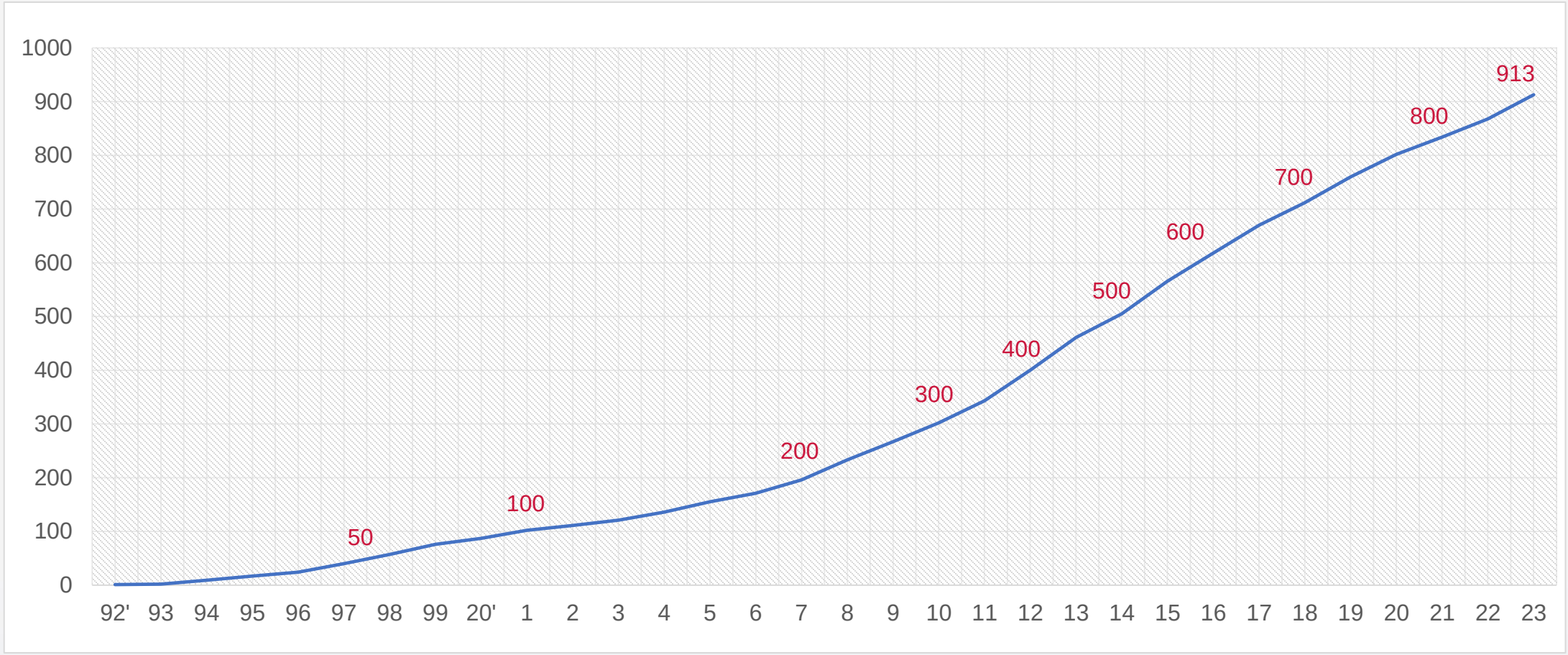
CMV disease only



Lee SO, Kim JJ et al. Transplant Infectious Disease 2010;12(1):31-37

Journey of Heart Transplants in AMC

Cardiac Allograft Vasculopathy



CAV

Diagnosis ⇧ *IVUS*

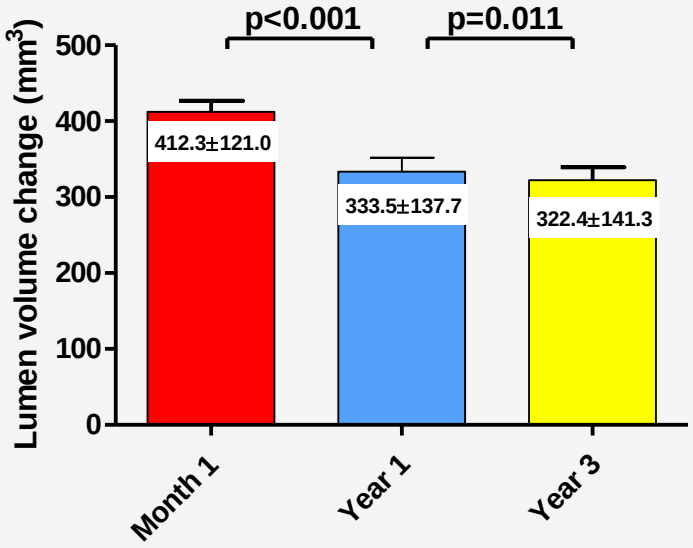
Prevention/Treatment

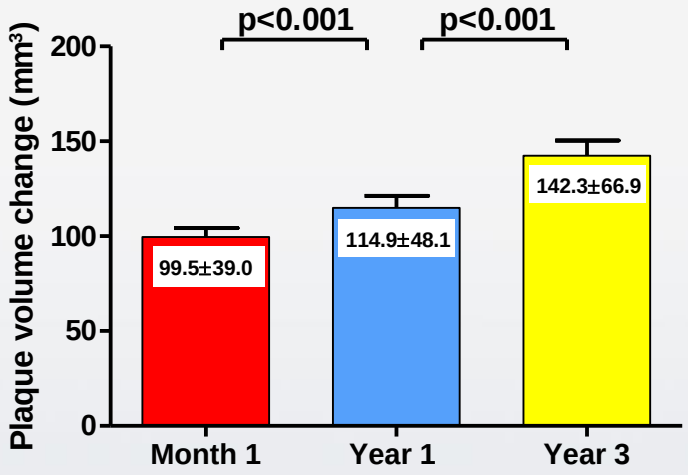
⇧ *EVL*

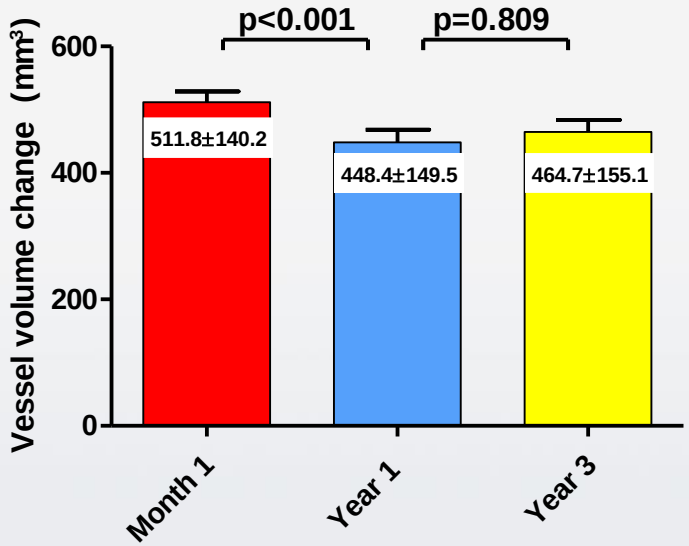
IMR, FFR ⇧ ⇧ *CT-MPI* ⇧ *CMR-MPI*

Vascular Remodeling after Heart TPL

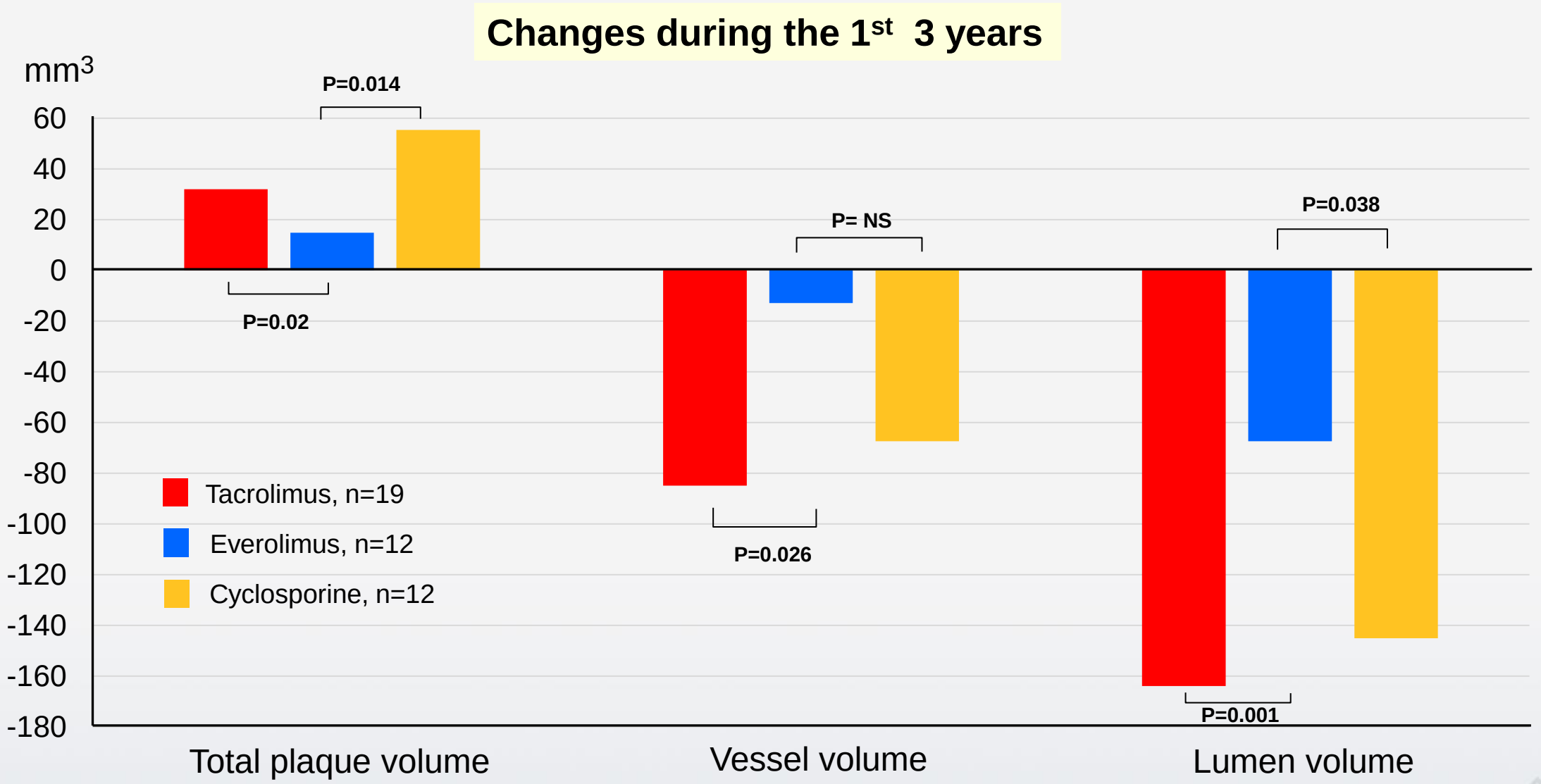
Serial volume changes
by serial IVUS
AMC data, CAST 2011





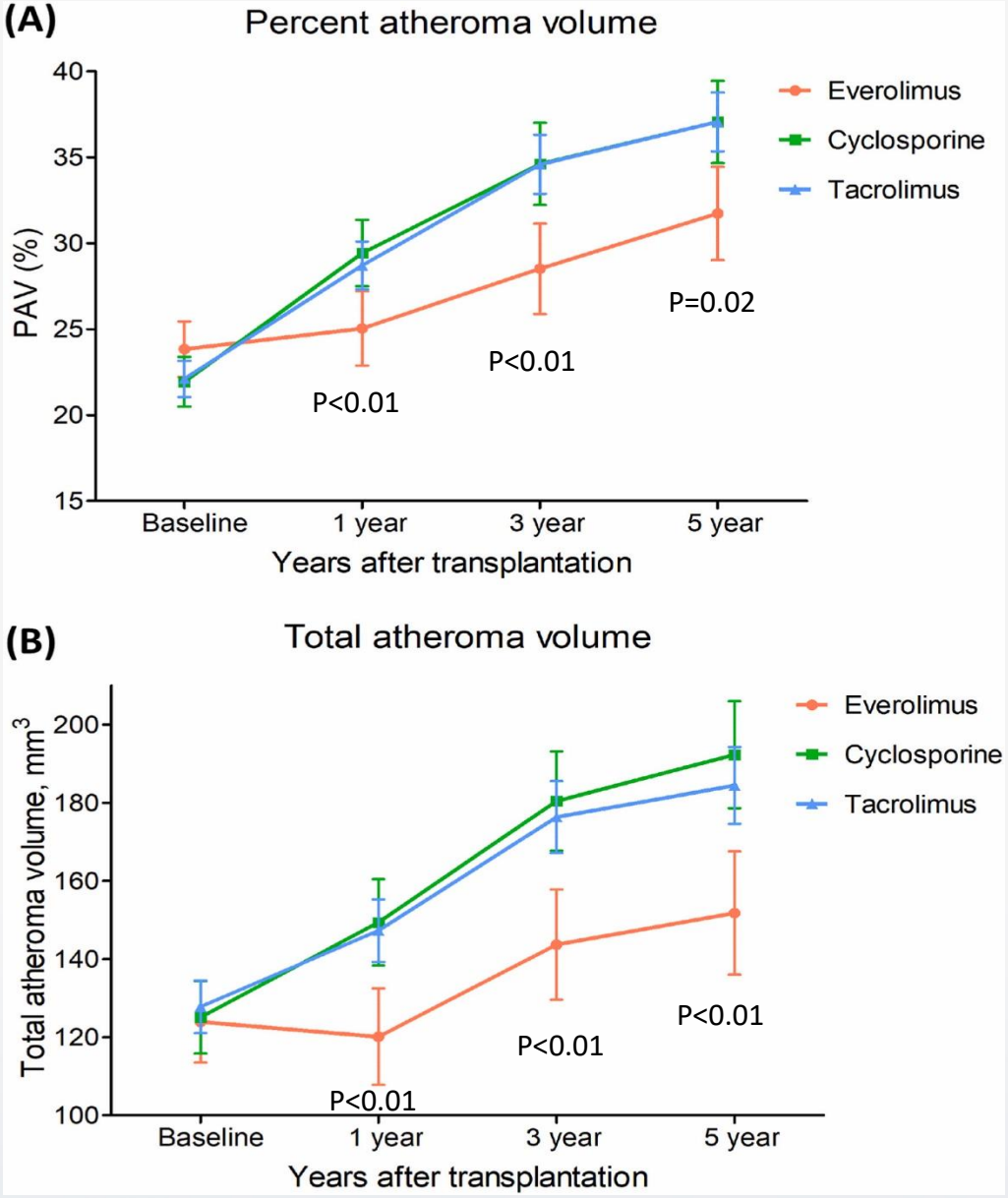


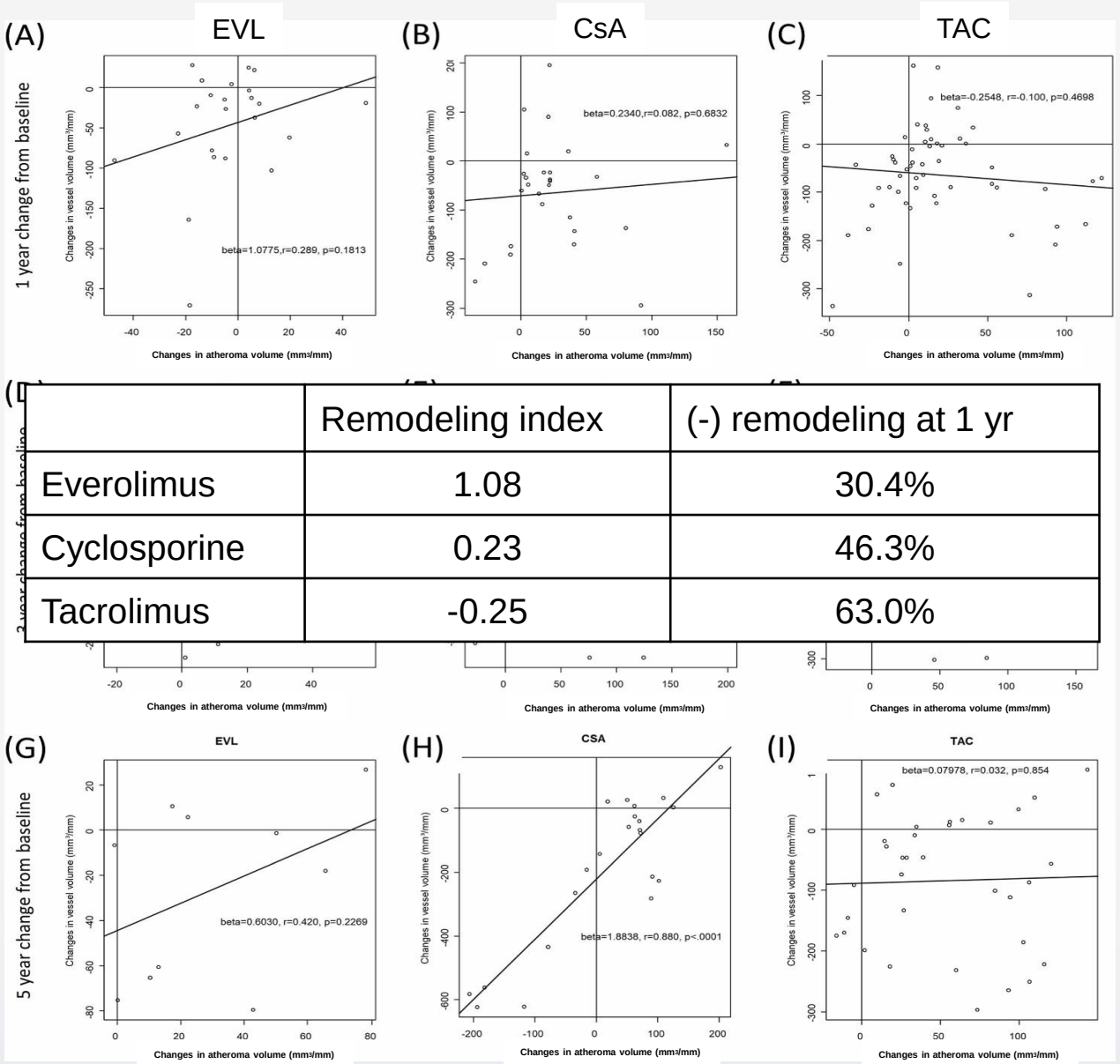
Changes of Coronary Plaques



AMC data, CAST 2011

Effect of Everolimus on CAV

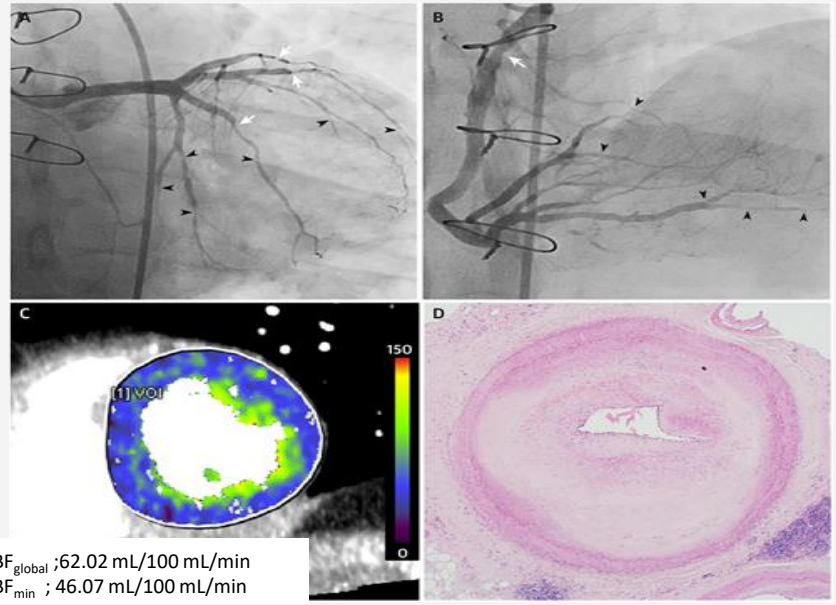




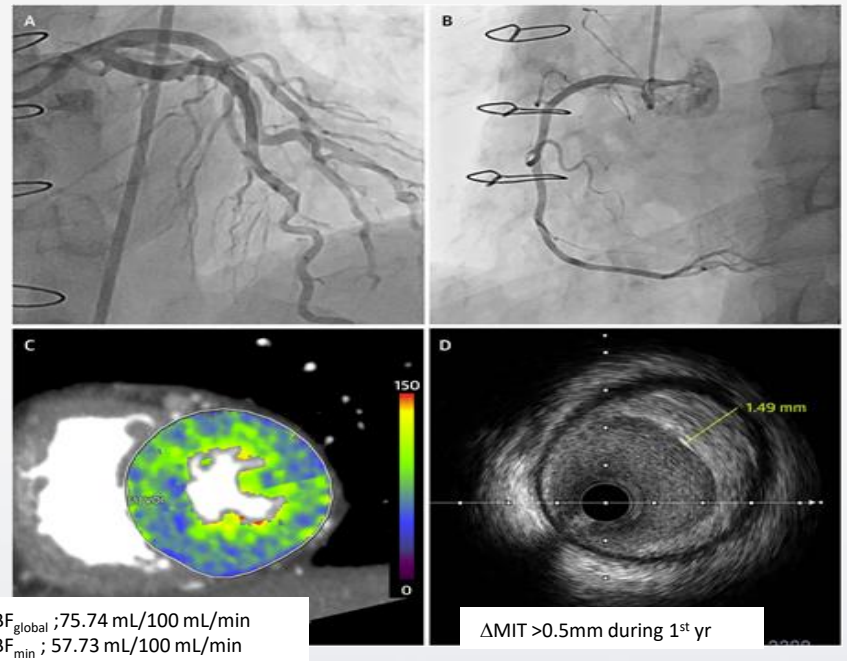
	Remodeling index	(-) remodeling at 1 yr
Everolimus	1.08	30.4%
Cyclosporine	0.23	46.3%
Tacrolimus	-0.25	63.0%

Choi HI, Kim JJ et al. Atherosclerosis 2021;357:1-8

CCTA and CT-MPI for CAV

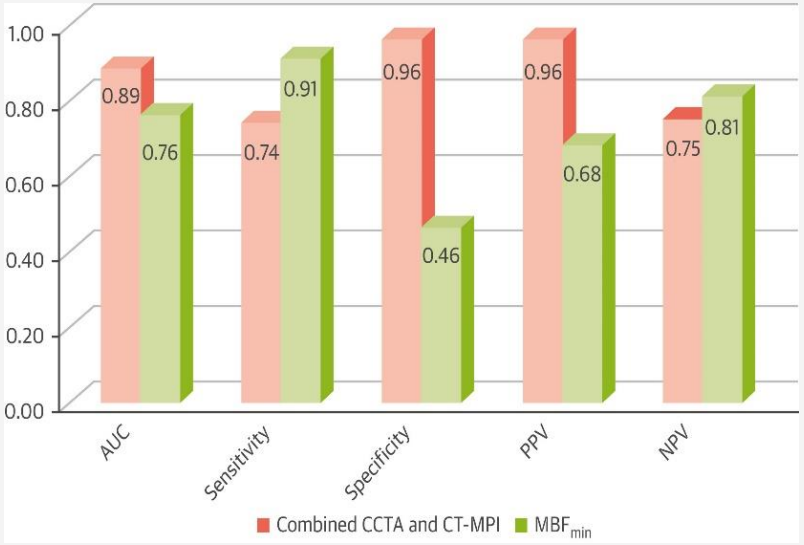


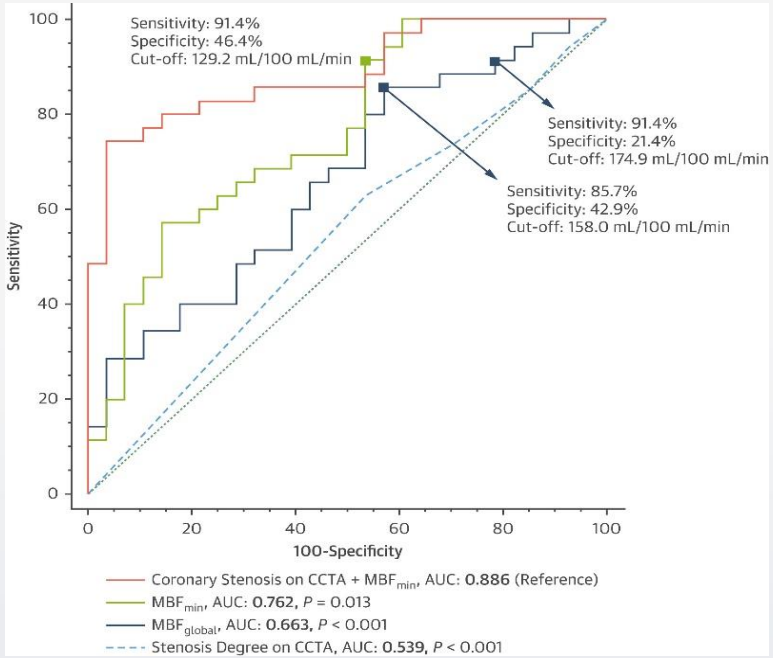
MBF_{global} ;62.02 mL/100 mL/min
MBF_{min} ; 46.07 mL/100 mL/min



MBF_{global} ;75.74 mL/100 mL/min
MBF_{min} ; 57.73 mL/100 mL/min

ΔMIT >0.5mm during 1st yr





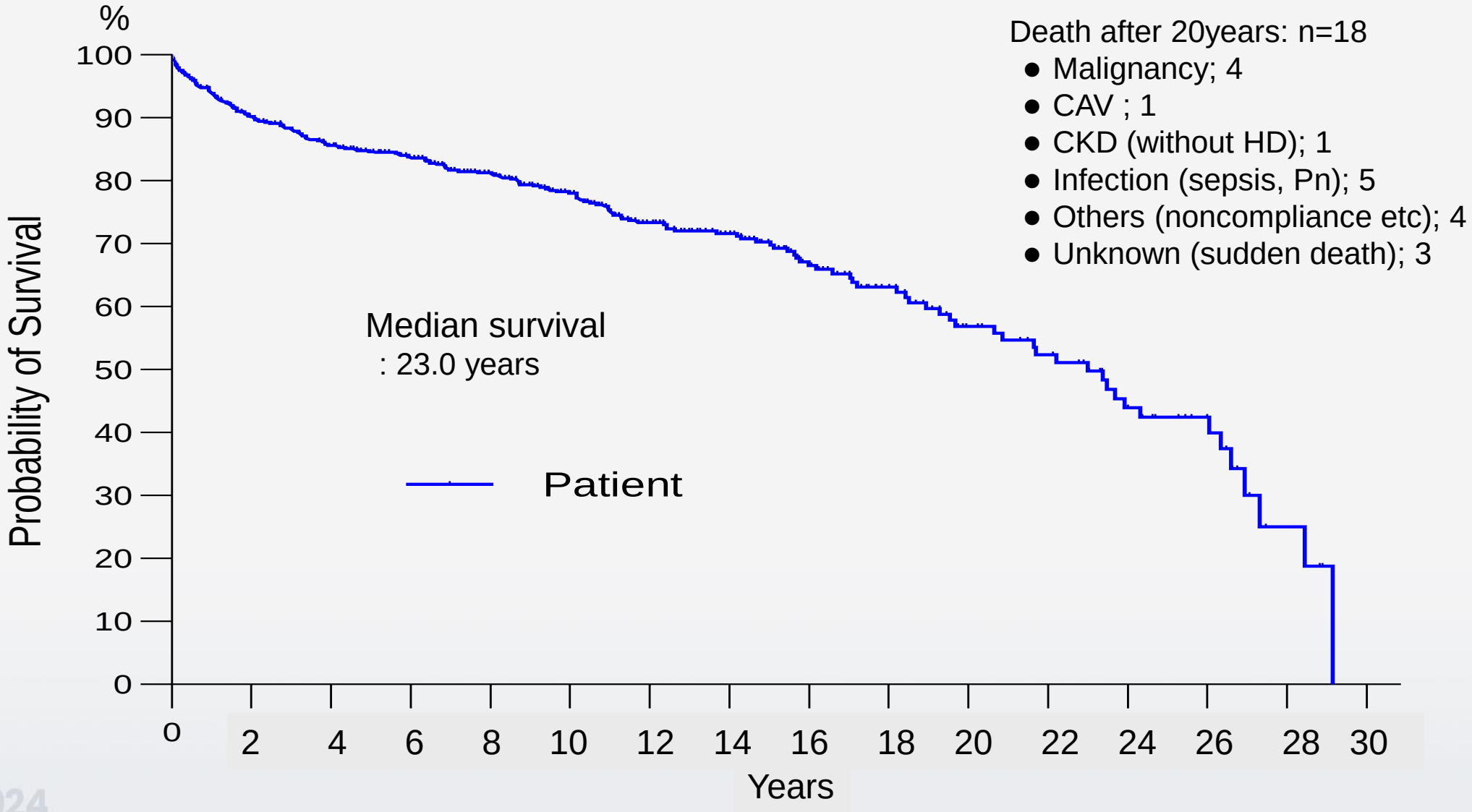
N=63
Median 4.3 yrs after TPL

Median 79 days
between ICA and CT-MPI

Yura Ahn et al. J Am Coll Cardiol Imaging 2023;16:934-947

Survival of Heart Transplants in AMC

Toward to Better Survival

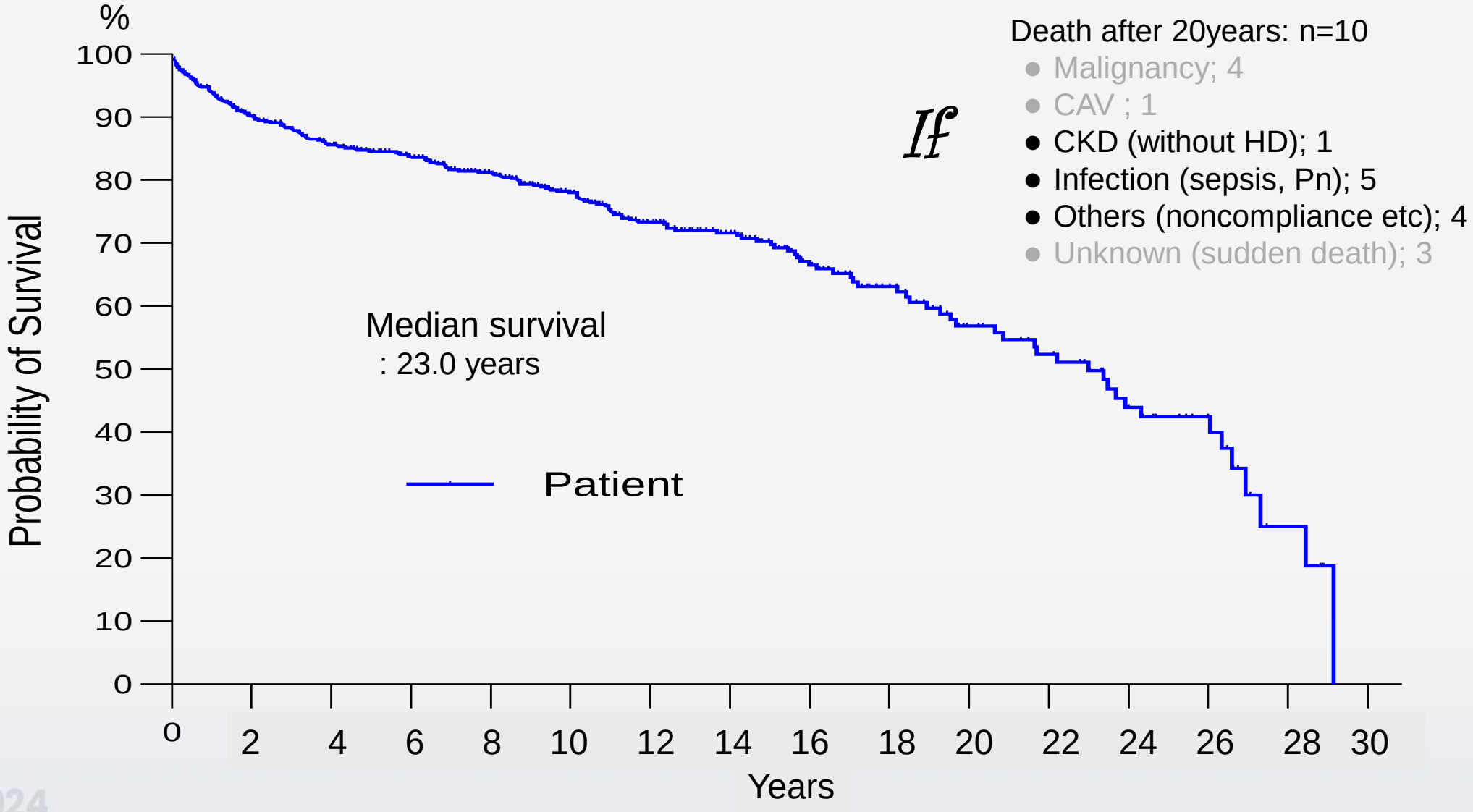


Death after 20years: n=18

- Malignancy; 4
- CAV ; 1
- CKD (without HD); 1
- Infection (sepsis, Pn); 5
- Others (noncompliance etc); 4
- Unknown (sudden death); 3

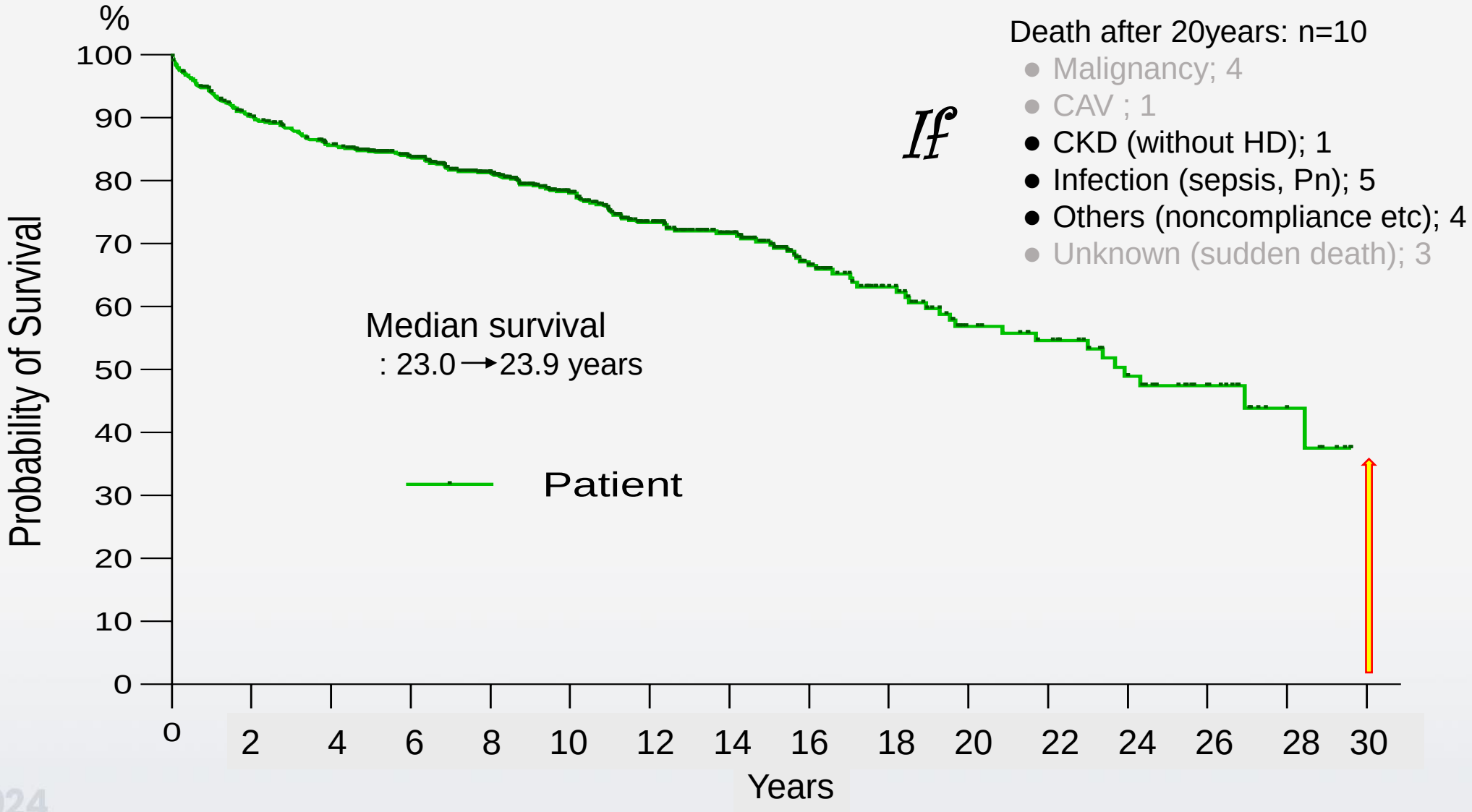
Survival of Heart Transplants in AMC

Toward to Better Survival

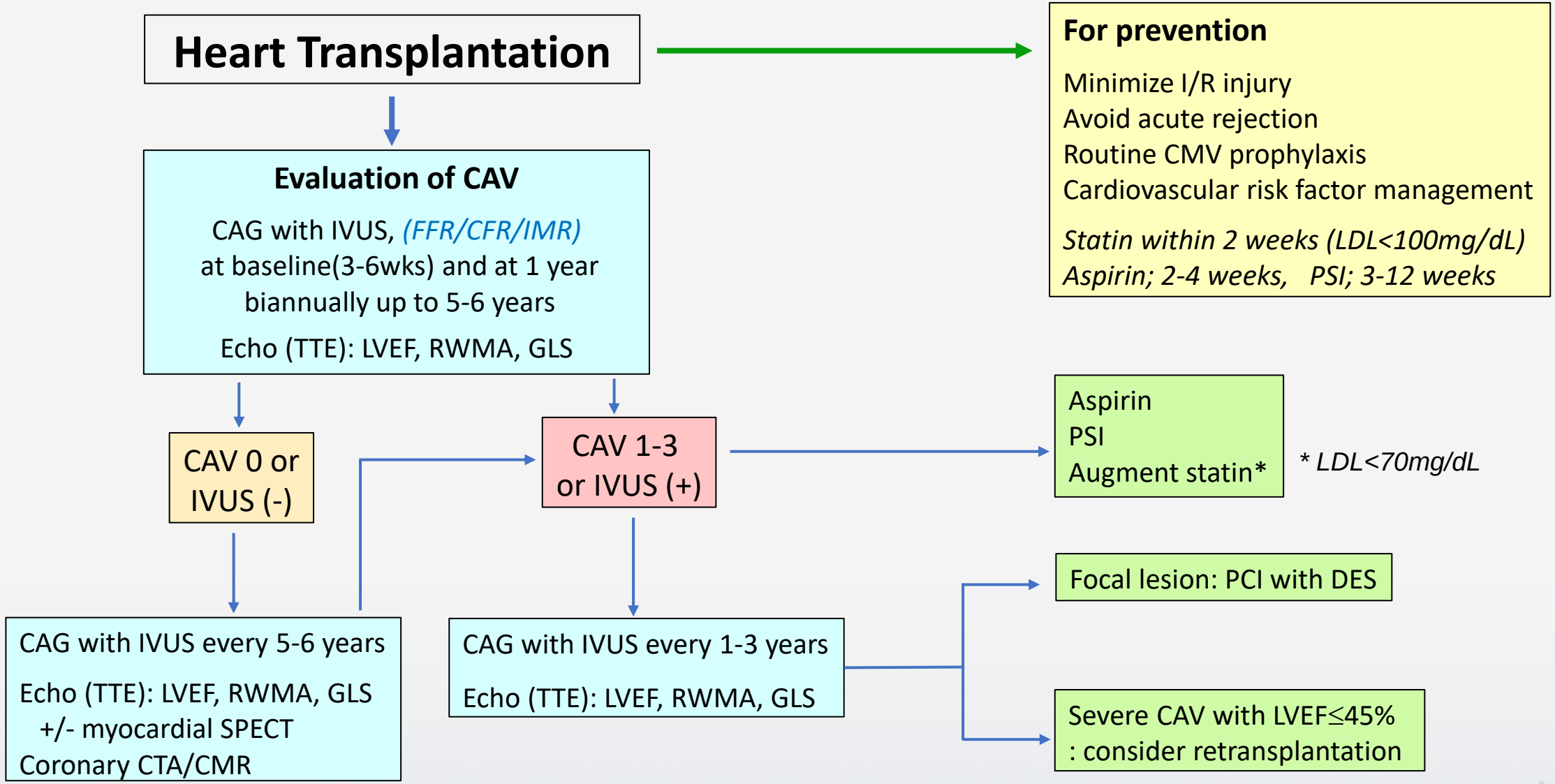


Survival of Heart Transplants in AMC

Toward to Better Survival



AMC Strategy for CAV



Thank for Your Attention !