# TMVR

## INDICATIONS, DEVICES & DATA

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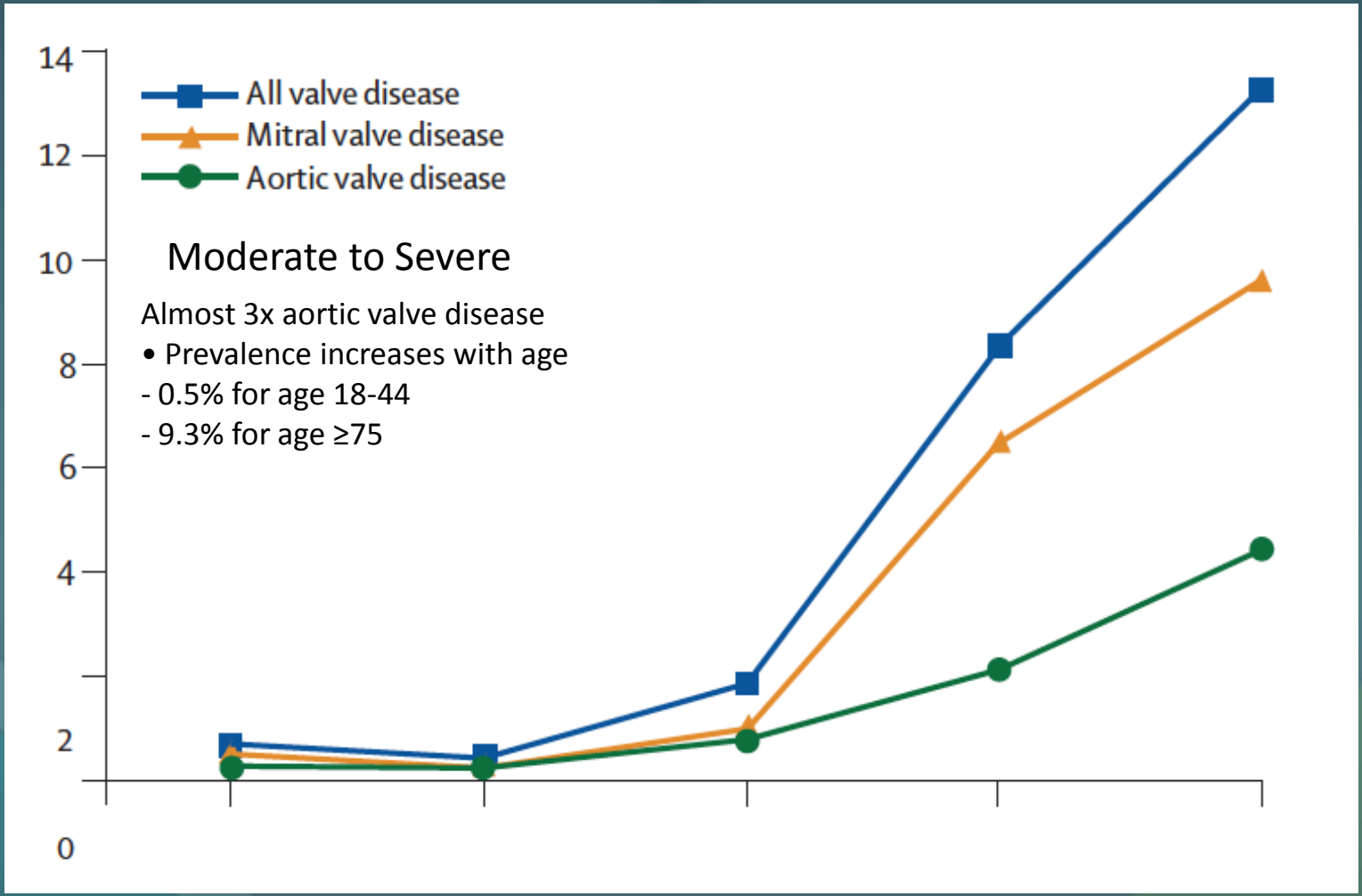
# INDICATIONS

# TMVR – UNMET NEED

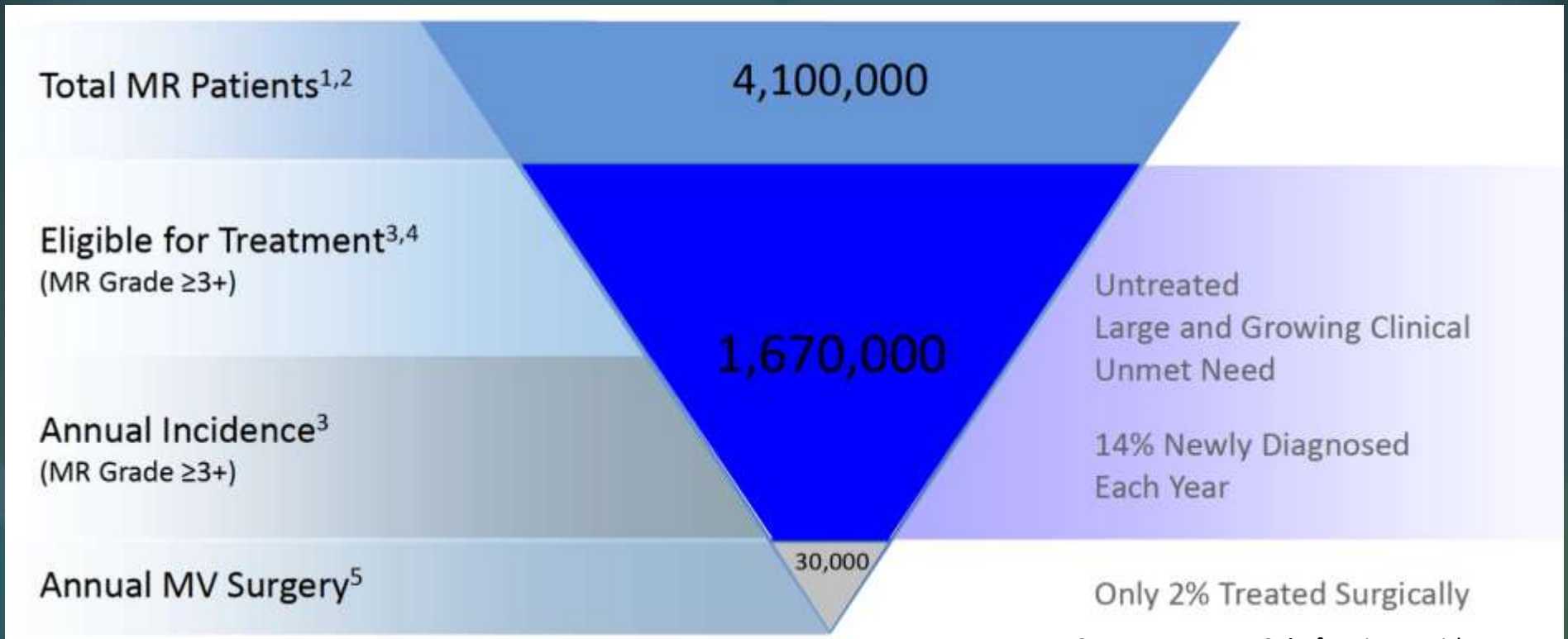
- High Prevalence – Disease Burden
- Under Treatment
- Treatment beneficial
- Current Therapies not meeting needs of all patients

# MITRAL VALVE DISEASE PREVELANCE




Nkomo et al. Burden of valvular heart diseases: a population-based study. Lancet. 2006; 368: 1005-1011

# A LARGELY UNTREATED POPULATION




Euro Heart Survey on VHD: **49%** of patients with severe MR are denied surgery
– Impaired LVEF
– Older age
– Comorbidities


1. US Census Bureau. Statistical Abstract of the US: 2006, Table 12.
2. Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study, Lancet, 2006; 368: 1005-11.
3. Patel et al. Mitral Regurgitation in Patients with Advanced Systolic Heart Failure, J of Cardiac Failure, 2004.
4. ACC/AHA 2008 Guidelines for the Management of Patients with Valvular Heart Disease, Circulation: 2008
5. Gammie, J et al, Trends in Mitral Valve Surgery in the United States: Results from the STS Adult Cardiac Database, Annals of Thoracic Surgery 2010.

# TMVR – different patient populations

- Primary Degenerative MR (DMR)
- Functional (Secondary) MR - Ischemic or Non- Ischemic Cardiomyopathy (FMR)
- Calcific Mitral valve disease (CMR)

# DMR

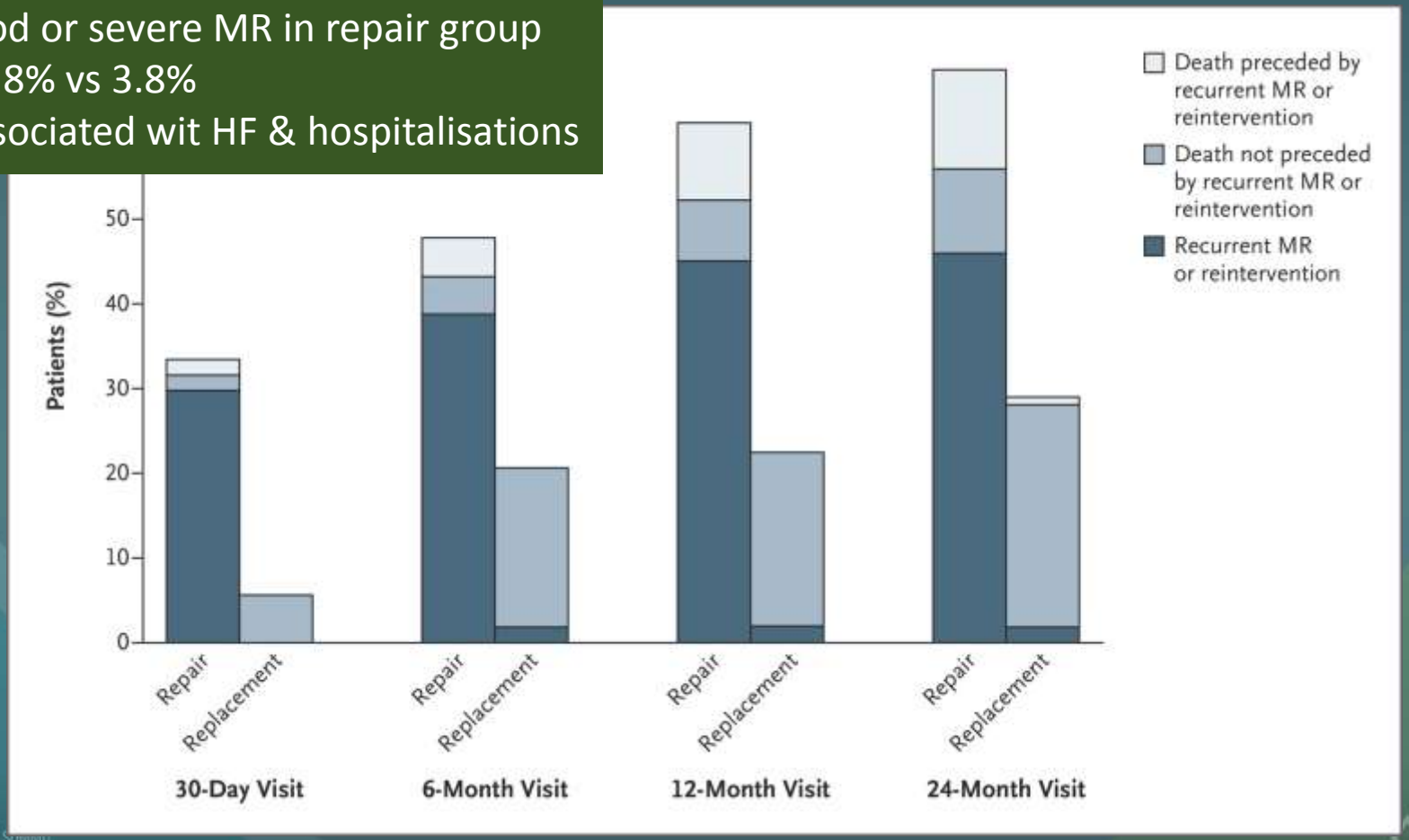
- Excellent surgical repair results *
- Low mortality - <1%
- Good clinical benefit & durability
- Surgical treatment rates ~ 53%
- Low Rx rates due to
  - Asymptomatic
  - Normal LVEF
  - Patient preference
  - Co-morbidities with high surgical risk

# FMR

- Medical +/- CRT device therapy primary Rx
- Surgical results of repair/replacement variable & uncertain
- Generally high risk group of patients – clinical benefit of reducing MR maybe attenuated by surgical risk
- Surgical Rx rates for Mod-severe MR ~ 16%
- Low Rx rates due to
  - High surgical risk
  - Low LVEF
  - Co-morbidities
  - Lack of clear benefit/guidelines
- Repair compared to Replacement not durable with recurrence of MR

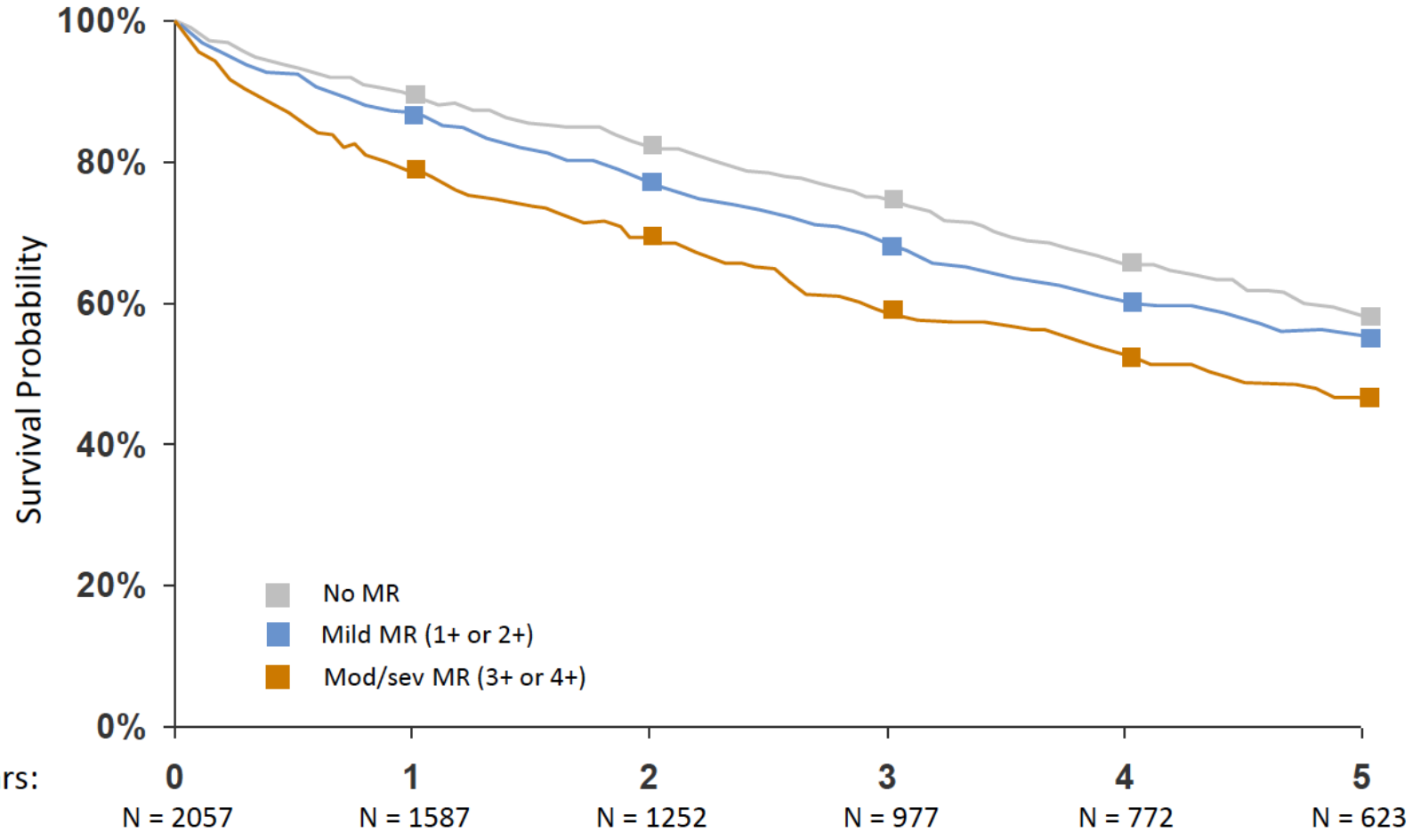
# FMR – 2-yr outcomes following surgical Rx

- 251 patients !:! MVR vs repair
- No survivial difference
- Mod or severe MR in repair group 58.8% vs 3.8%
- Associated wit HF & hospitalisations




Goldstein et al NEJM 2016;374(4):344-

# FMR - Survival stratified to severity of FMR



# TMVR – INDICATIONS

## DMR

- Symptomatic
- High risk for surgical MVR
- TAVR creep……!

## FMR

- Symptomatic
- On full medical & device therapy
- Not requiring CABG

# NEXT QUESTION: TMVR vs TMV Repair

| TMVR | TMV Repair |
| --- | --- |
| “Simpler” | More complex |
| Durability unknown | Appears durable if initial reduction in MR is good (MitraClip) |
| Still FIM and early clinical trials | Established therapy (MitraClip) |

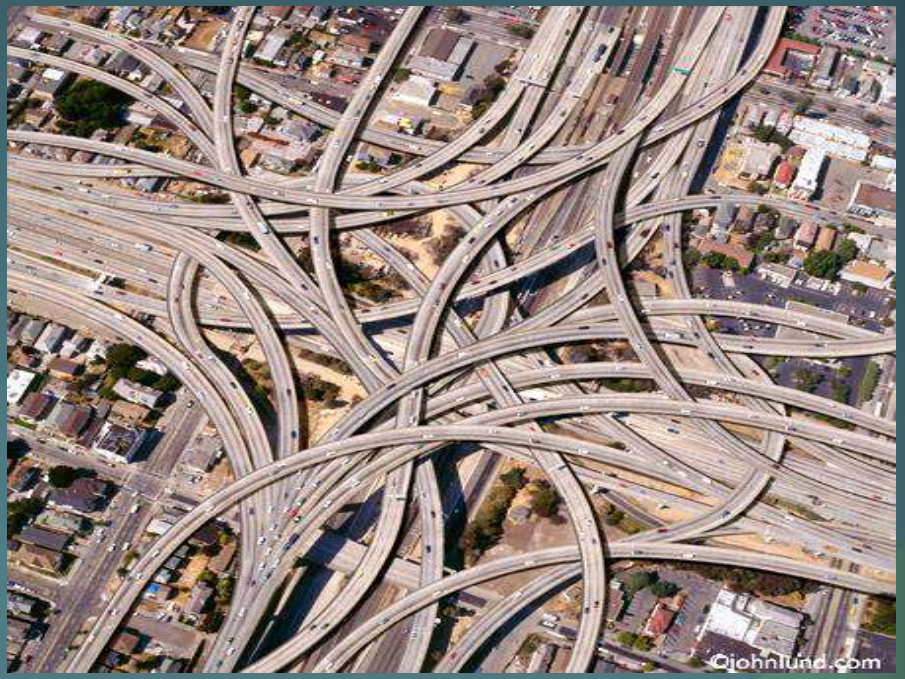
INDICATIONS WILL EVOLVE WITH DEVICE DEVELOPMENT AND EXPERIENCE

# DEVICES

# TMVR – DEVICES (not a TAVR!)

AORTIC STENOSIS

MITRAL REGURGITATION




Francesco Maisano

# TMVR - THE PERFECT DEVICE!

Large Valve Size

Longevity/ Durability

Stable Anchoring

Retrievable Reposition

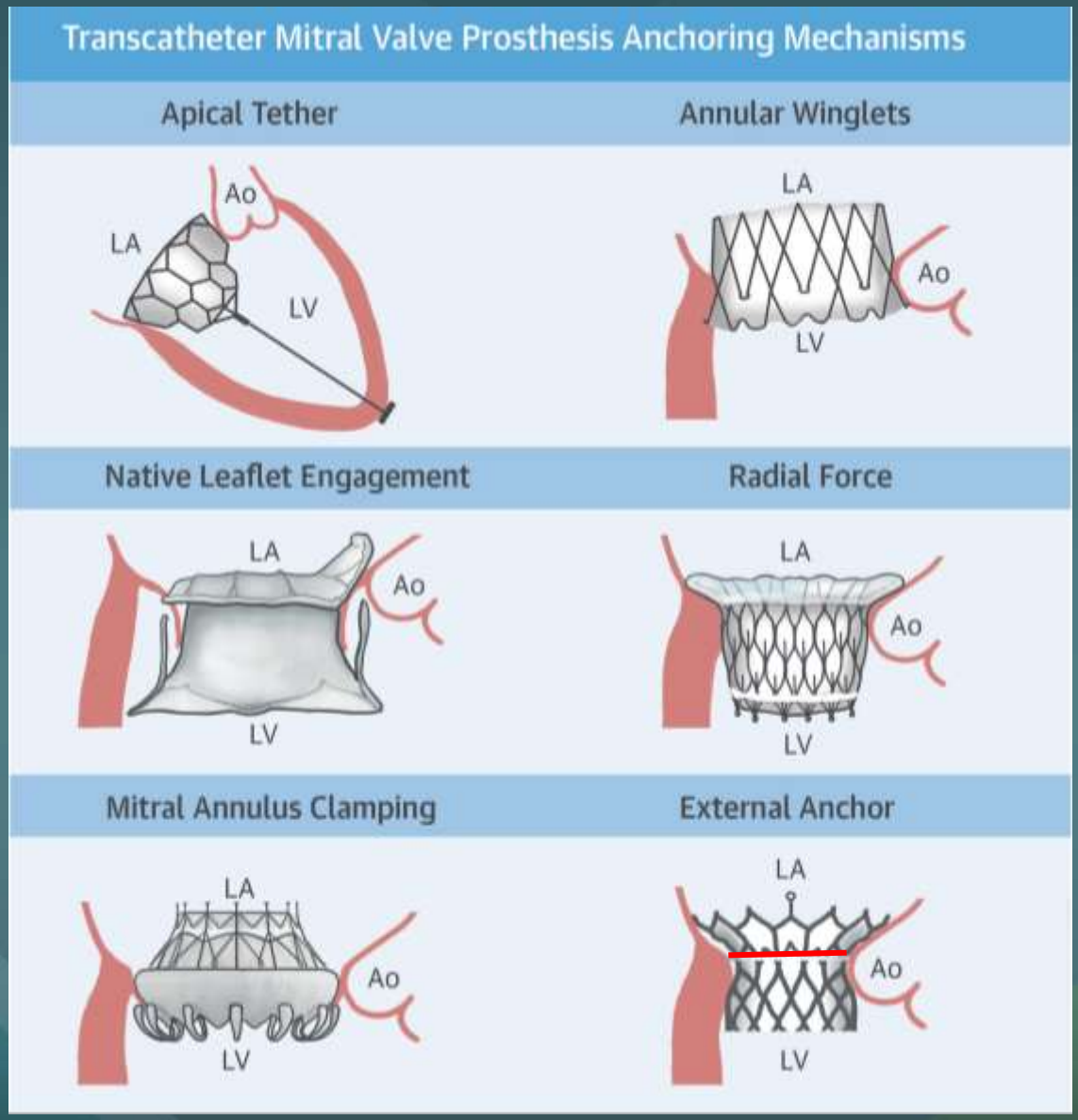
Large Neo-LVOT

Low Thrombo-genecity

Easily Deployable Access

Sealing No PVL

# CHALLENGES OF TMVR – ANCHORING SOLUTIONS




Regueiro et al. JACC2017 May 2;69(17):2175-2192

# TMVR – A SLOW BOAT TO SOME WHERE…..? >30 DEVICES

MitraClip

2003

Tendyne

Feb 2013

Fortis

Feb 2014

Navi VS

Jan 2015

Caisson

June 2016

June 2012

CardiAQ

Jan 2014

Tiara

Nov 2014

Intrepid

Feb 2016

Highlife

# TMVR – CURRENT CLINICAL EXPERIENCE

| TMV Device | Number |
|---|---|
| Abbott TENDYNE TMV | >110 |
| INTREPID | 50 |
| TIARA | 47* |
| Edwards CardiAQ | 16+ |
| CAISSON | 15 |
| HIGHLIFE | 11 |
| FORTIS | 11 |
| NAVI | 2 |

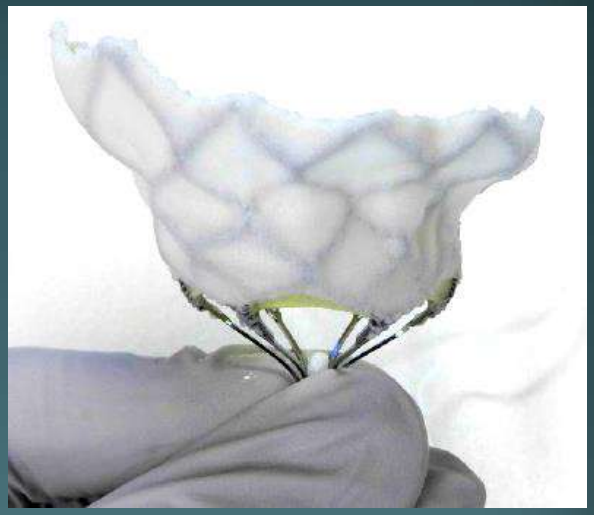
Q4 2017

* As of Jan 2018

# TMVR PATIENT DEMOGRAPHICS (Q4 2017)

| Valve | N= | Age | M Sex% | FMR% | NYHA II/III/IV | EF% | STS |
|---|---|---|---|---|---|---|---|
| Tendyne | 75 | 74.7 | 67 | 73 | 35/61/4 | 48 | 7.1 |
| Intrepid | 44 | 73 | 66 | 80 | 14/68/18 | 42 | 6.6 |
| Tiara | 37 | 72 | 80 | 68 | 2/84/18 | 36 | 9.9 |
| CardiAQ | 11 | - | - | 64 | - | - | - |
| Caisson | 15 | | 29 | 57 | 78.6(III,IV) | - | - |
| Highlife | 11 | 69 | 73 | 72 | - | 35 | - |
| Navi | 2 | - | - | - | - | - | - |
| TOTAL | 225 | | | | | | |

# TENDYNE



Construction & Shape:

- Self-Expanding Nitinol double frame.
- D-Shaped Outer Frame with anterior cuff
- Designed to conform with native MV anatomy

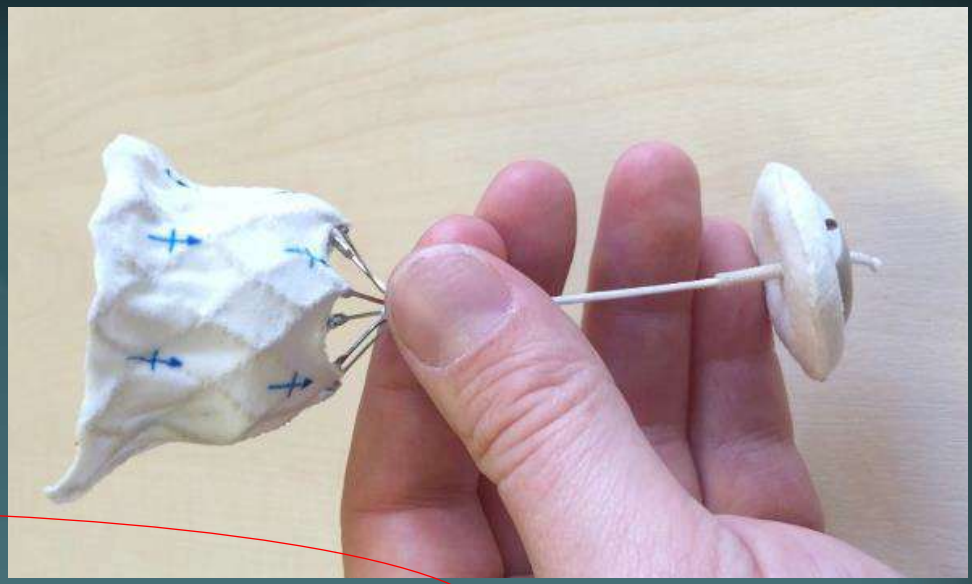
Leaflets:

- Trileaflet, porcine pericardial valve.

Valve sizes:

Large Valve Size Matrix to Treat Varying Anatomie

# TENDYNE



Anchoring:

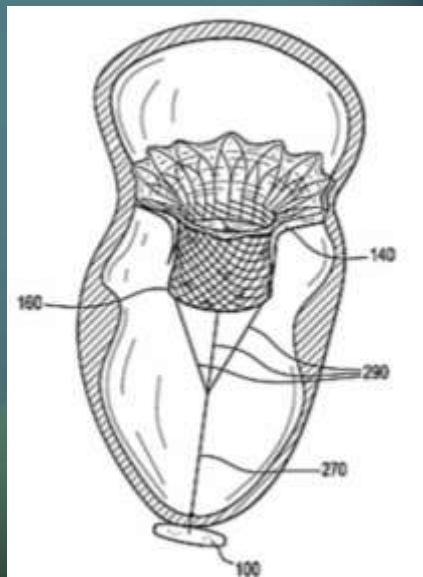
- Atrial flange
- left ventricular apical tethered system with apical pad

Effects on LVOT

- Some limitations especially with v 1.0, excluding small LVOT's and wide AM angles.

Deployment:

- Fully retrievable and repositionable.
- Controlled deployment but not "simple"
- Usually no need for pacing.



# TMVR – TENDYNE

Access

- Transapical

Delivery system size:

- 36 F

# TENDYNE

Strengths

- Fully retrievable, repositionable, controlled deployment\
- Well tolerated hemodynamically, no need for pacing
- Excellent valve performance -effective control of MR
- Low 30day mortality and adverse outcomes

Weaknesses/limitations

- Small observational experience, short-term follow-up
- Currently 36F transapical system – complex deployment
- Longer term consequence of TA + apical tether.

# INTREPID (Medtronic)

Construction & Shape:

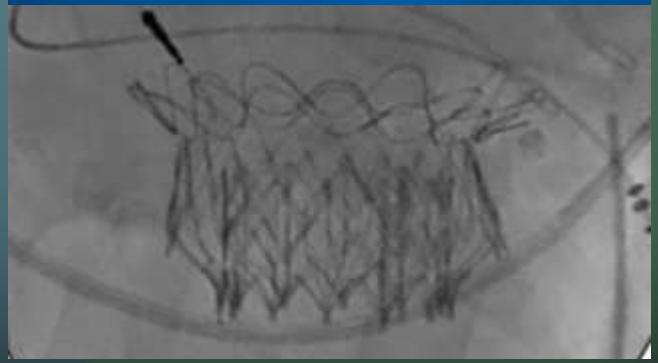
- Self-Expanding Nitinol frame.
- Dual – stent design with conformable Outer Stent engages the annulus & circular inner stent to house the valve
- Design isolates the inner stent from the dynamic MV anatomy

Leaflets:

- Trileaflet, bovine pericardial valve.

Valve sizes:

- 43 mm, 46 mm, and 50 mm outer diameters
- Circular inner stent: 27mm valve



# INTREPID


Anchoring:

- "Cork effect" produced at the level of the annulus due to the variable stiffness of the conformable stent frame is the primary mechanism for fixation. Flexible Brim aids imaging during delivery & subsequent healing
- Small cleats on the outer stent also help by engaging with the mitral leaflets and promoting tissue ingrowth

Effects on LVOT

- Minimal as stent is short

Deployment:

- Current design not retrievable

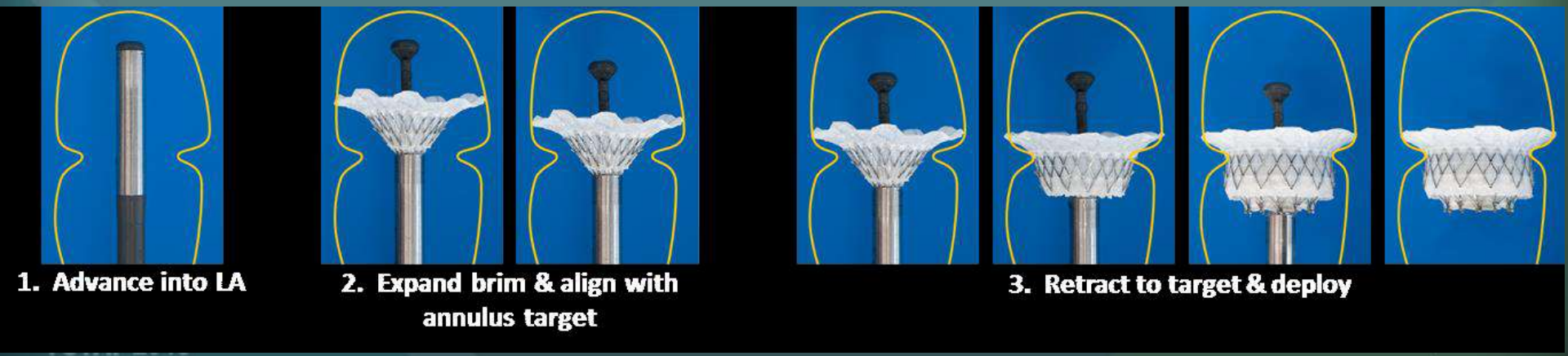
# INTREPID

Access

- Transapical (TS & retrievable versions in design)

Delivery system size:

- 35 F


Images Vinnie Bapat TCT 2017

# INTREPID: Current status

FIM

Krakov, Poland. Late 2014

Global Pilot Study n =50

US Feasibility trial

- Ongoing

# INTREPID

Strengths

- TAVR like: ‘Position and Deploy’
- Simple procedure –echo guided
- Lower profile device
- Stability is excellent

Weaknesses/limitations

- Transapical, non-retrievable
- Anticoagulation
- LVOTO risk?

# TIARA

Construction & Shape:

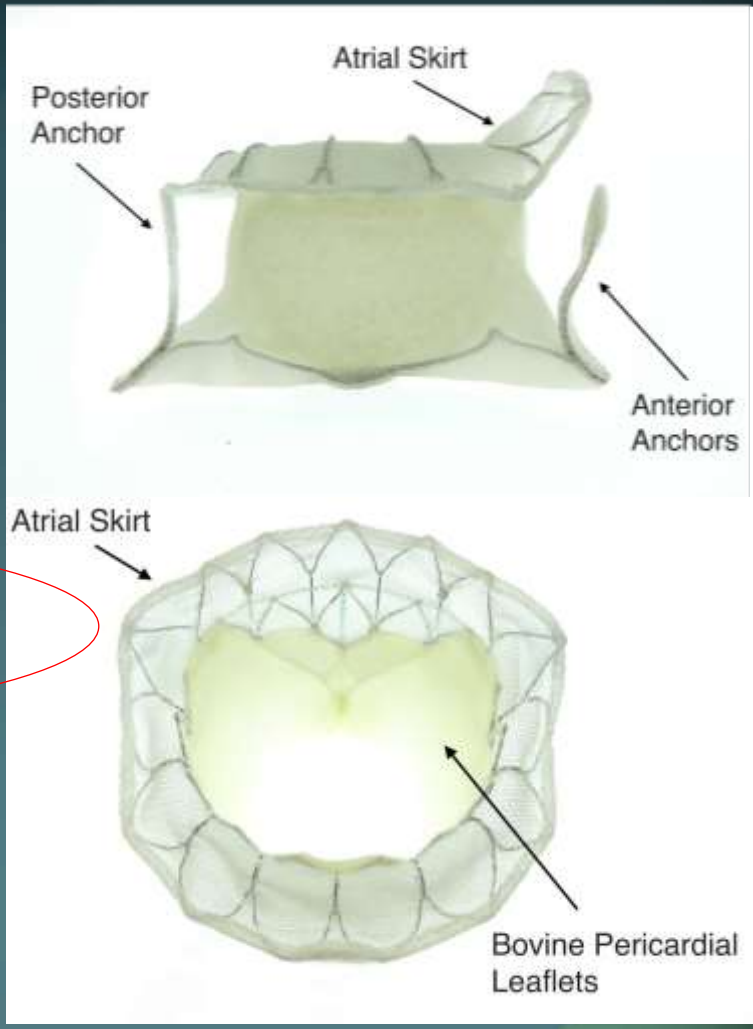
- Self-Expanding Nitinol frame.
- D-Shaped for MV anatomy
- Designed to conform with native MV anatomy

Leaflets:

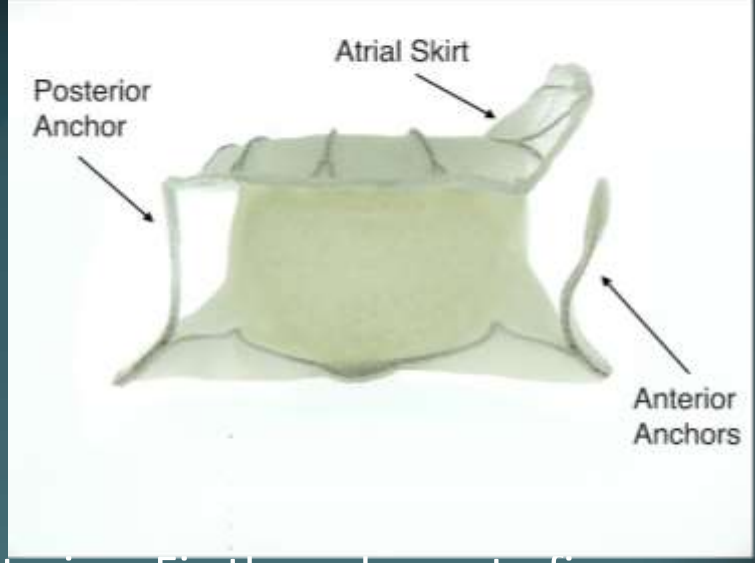
- Trileaflet, bovine pericardial valve.

Valve sizes:

- 35 and 40 mm devices



# TIARA




Anchoring:

- Ventricular anchors, two anterior and one posterior. Fix the valve onto fi brous trigone and posterior annulus – captures AMVL & PMVL
- Atrial skirt/flange

Effects on LVOT

- Minimal. D –shaped, no flaring, short.

Deployment:

- Not retrievable But simple implant procedure
- Usually no need for pacing.
- Not contraindicated in patients with AVR or previous MV surgery

# TIARA

Access

- Transapical

Delivery system size:

- 32 and 36 F
- Sheathless
- Self dilating

# TIARA: Current status

FIM implant

- St Paul's, Vancouver, Canada Jan 2014

Special Access/Compassionate Use (n=21)

- Canada, Italy, Germany, Switzerland, Israel

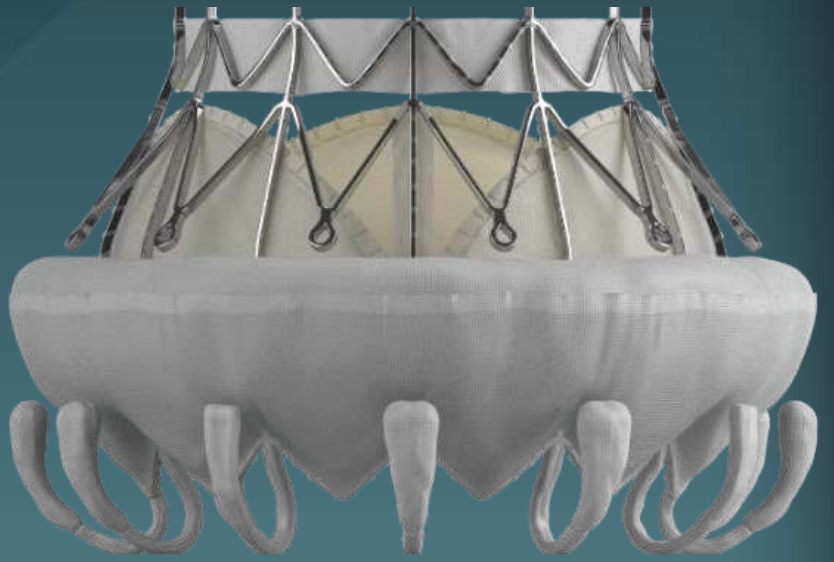
TIARA-I Early Feasibility Clinical Study (n=13)

- Belgium, Canada, USA

TIARA-II European CE Mark Clinical Study (n=3)

- Italy, Germany, UK

# CardiAQ



Construction & Shape:

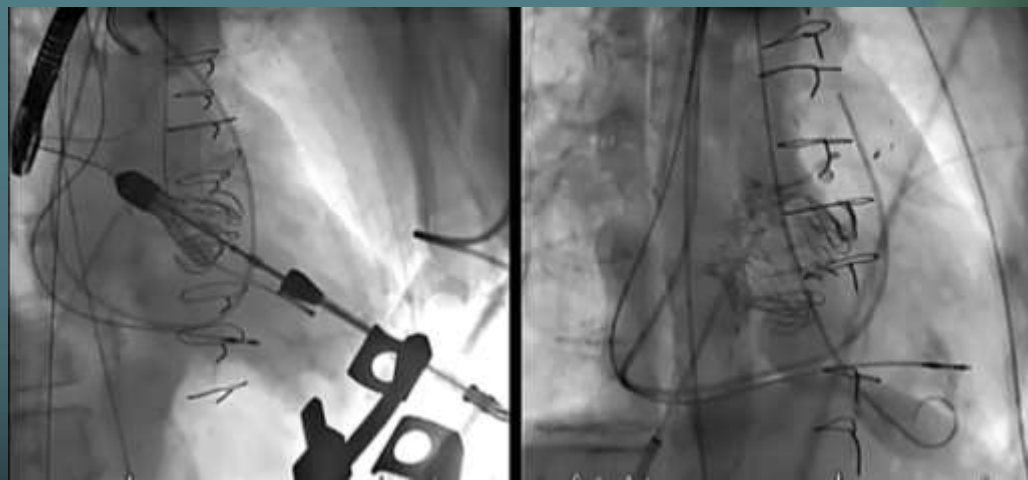
- Self-Expanding Nitinol frame.
- Circular
- Fabric skirt

Leaflets:

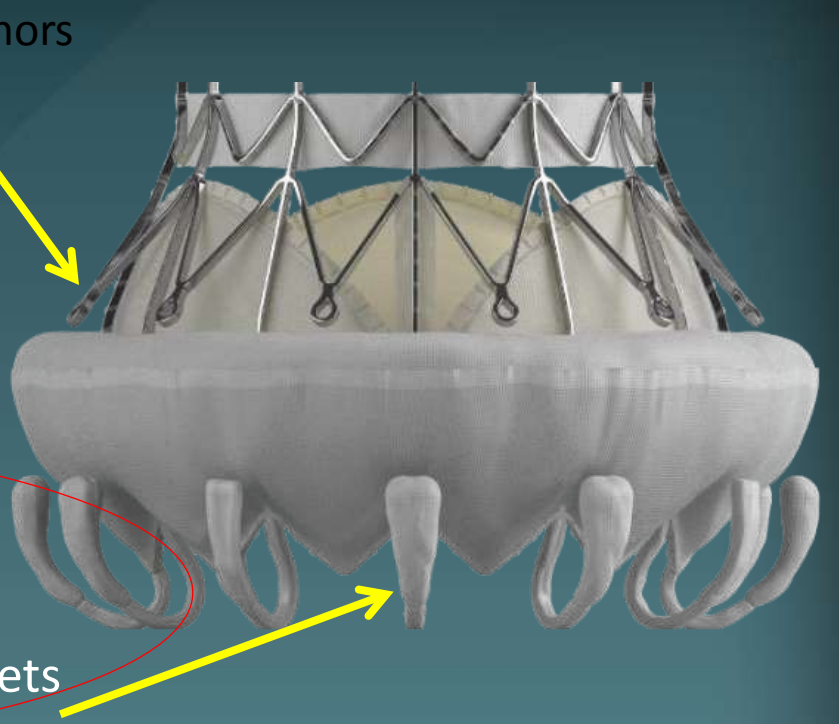
- Trileaflet, bovine pericardial valve.

Valve sizes:

- Suitable for native annulus size: 36 to 39.5 mm
- Single valve size: 30 mm at the inflow and 40 mm at the annulus



# CardiAQ




Anchoring:

- Two sets of opposing anchors, atrial and ventricular. Preserves MVL/chordae
- Ventricular anchors hook around the leaflets

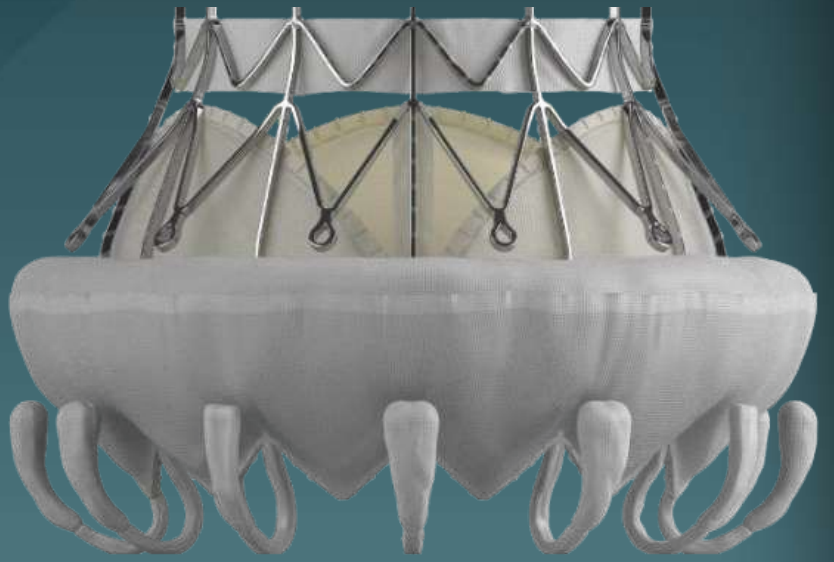
Effects on LVOT

- Device sits relatively high in atrium – minimal LVOT obstruction.

Deployment:

- Controlled (multi stage) deployment
- Accurate positioning
- Self-positioning within native valve annulus, no rotation required.

# CardiAQ



Access

- Transeptal & Transapical

Delivery system size:

- 33 F


# CardiAQ: CURRENT STATUS

- Focused on TF – TS access
- 3rd generation: Includes lower profile valve for TS
- Durabilty appears good - >3years with good va lve function

# HIGHLIFE

Construction & Shape:

- Self-Expanding Nitinol frame. Circular. Grooved.
- Retrograde transarotic sub-valvular ring (SAI)
- Valve – in –ring 2 component concept. Atrial flange and SAI hold valve in place.

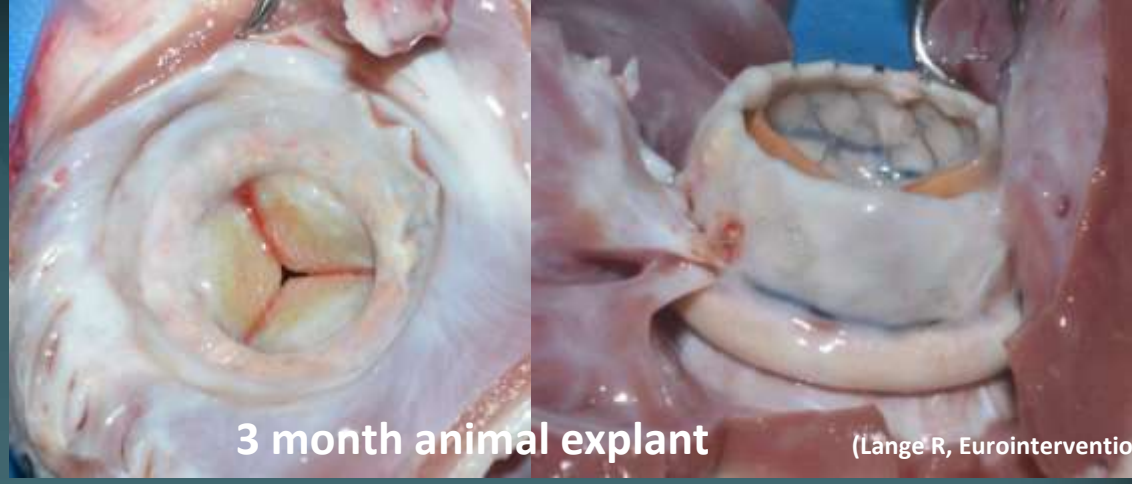
Leaflets:

- Glutaraldehyde cross-linked bovine pericardium.

Valve sizes:

- 31mm valve
- TA access accommodates wide MV annular size - 32mm to 48mm

# HIGHLIFE




Anchoring:

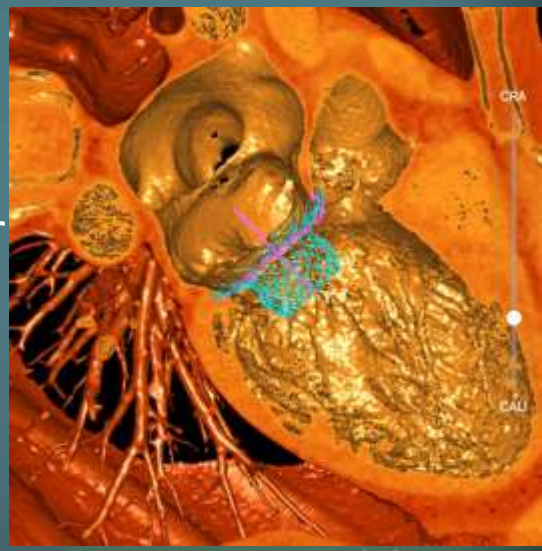
- Subannular implant [SAI]) around the native leaflets holds the grooved v alve stent
- Together with the native leaflets provide complete paravalvular sealing

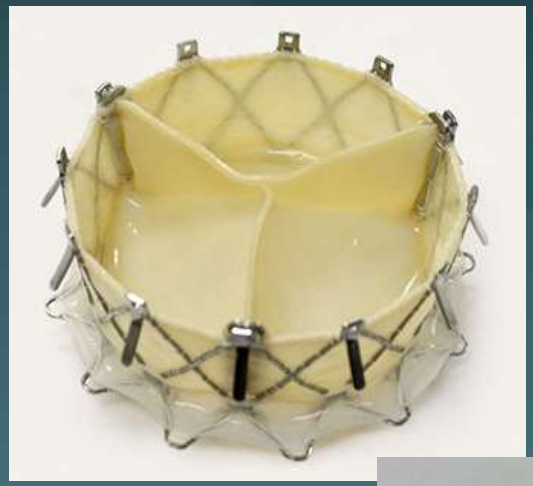
Effects on LVOT

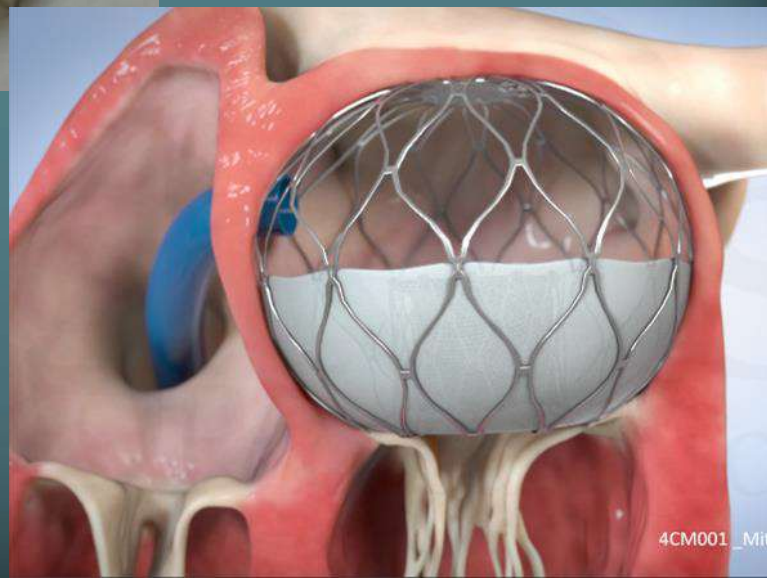
- Minimal. LV extension small and  no flaring.

Deployment:

- Self centering. Not dependant on radial force for anchor
- No rotation required.
- Not retrievable.
- SAI via FA, Valved stent into ring via TA, Tatrial or TS.





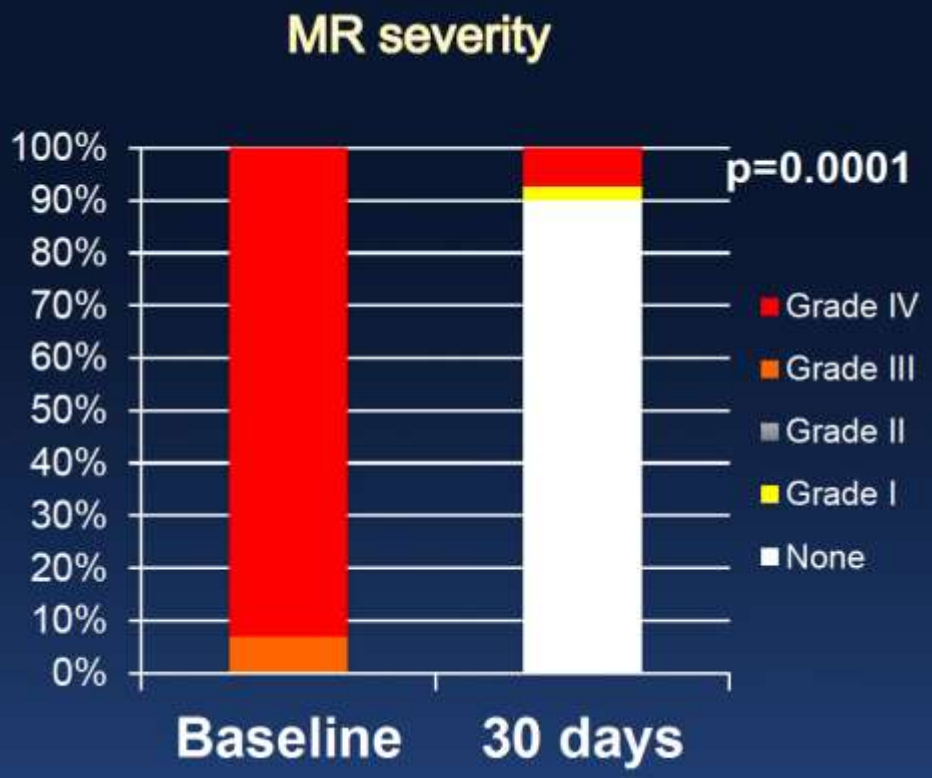


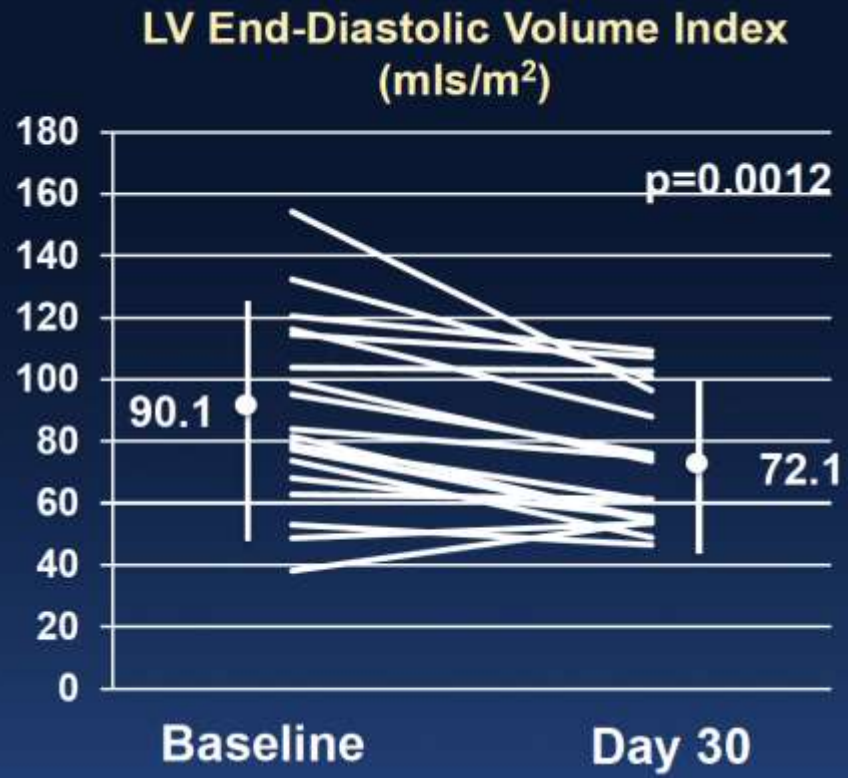


4CM001_Mi

# DATA

# TENDYNE: Global Feasibility Study @ 30d (n=30)




Mortality 3.3%
Stroke/MI 0.0%

| NYHA functional class | |
|---|---|
| I | 25.0 (7/28) |
| II | 50.0 (14/28) |
| III | 17.9 (5/28) |
| IV | 7.1 (2/28) |



Muller DW et al JACC 2017;69:381-391

# TENDYNE: GF Study (n=75)

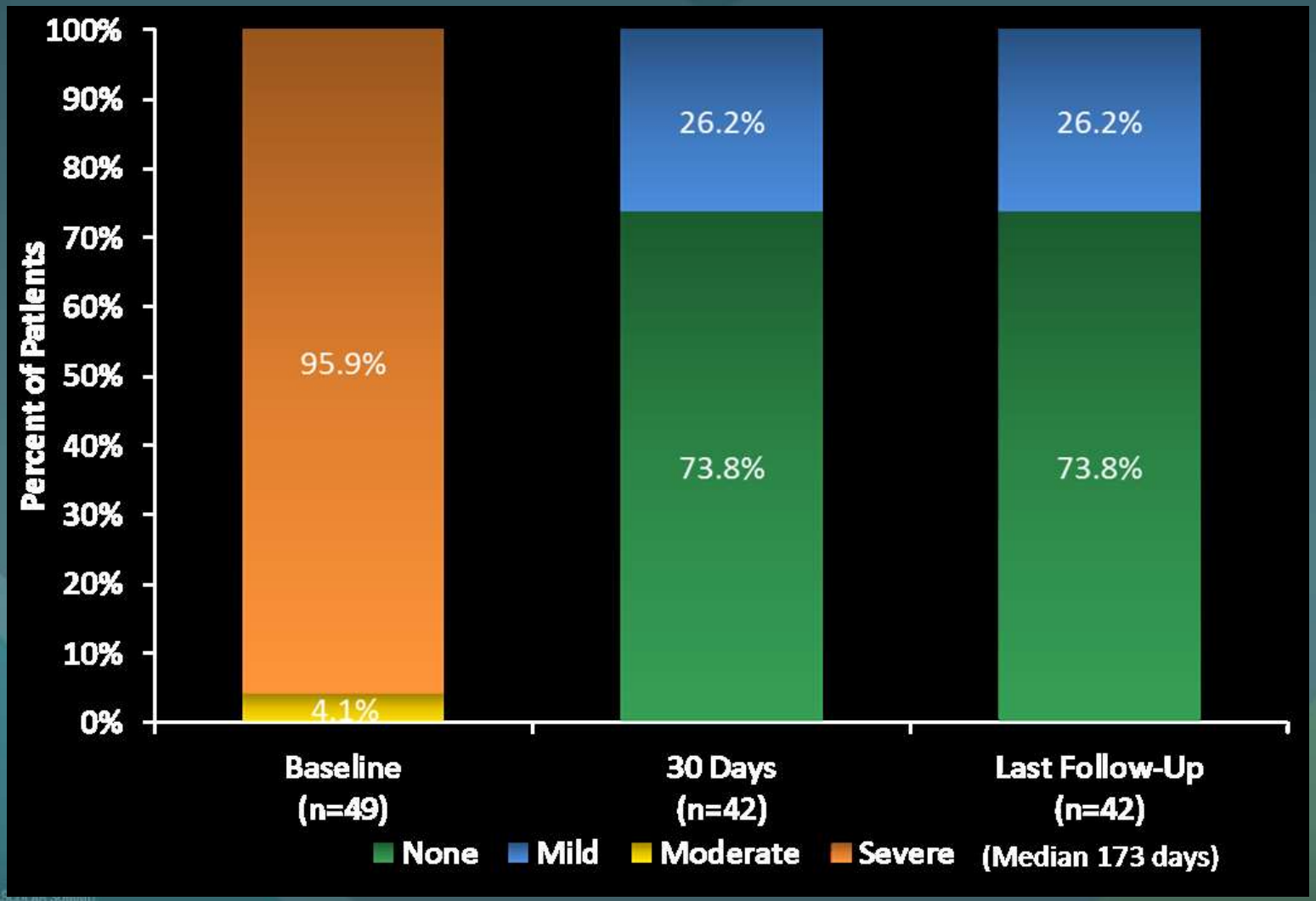
| | |
|---|---|
| Success | 80% (60/75) |
| Non-success | 20% (15/75) |
| Mortality | 6.7% (5/75) |
| Implant not Successful | 4.0% (3/75) |
| LVOT obstruction | 1.3% (1/75) |
| Valve not seated properly | 1.3% (1/75) |
| Patient unstable, procedure not completed, unplanned circulatory support | 1.3% (1/75) |
| Re-intervention | 2.6% (2/75) |
| Reposition device -resolve PVL | 1.3% (1/75) |
| Bleeding with re-operation | 1.3% (1/75) |
| Valve performance | 6.7% (5/75) |
| Mitral valve gradient > 6 mmHg | 5.3% (4/75) |
| Malpositioning/paravalvularleak | 1.3% (1/75) |

David Muller, TCT 2017

100% MR 0-1

# INTREPID GPS: MR SEVERITY

Paravalvular: 3 (7.1%)
Transvalvular: 8 (19.0%)



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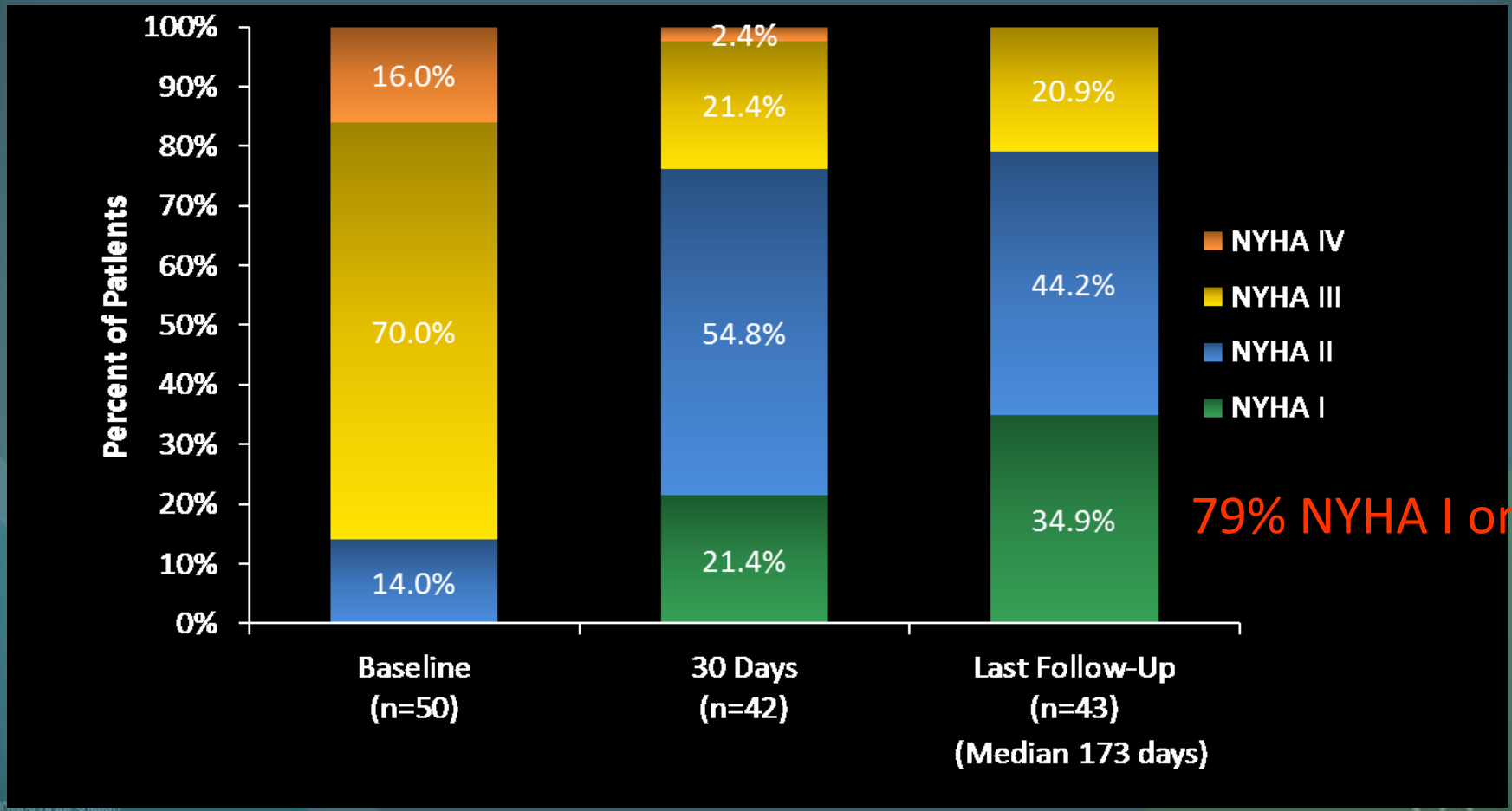
# INTREPID GPS: NYHA CLASS




79% NYHA I or II



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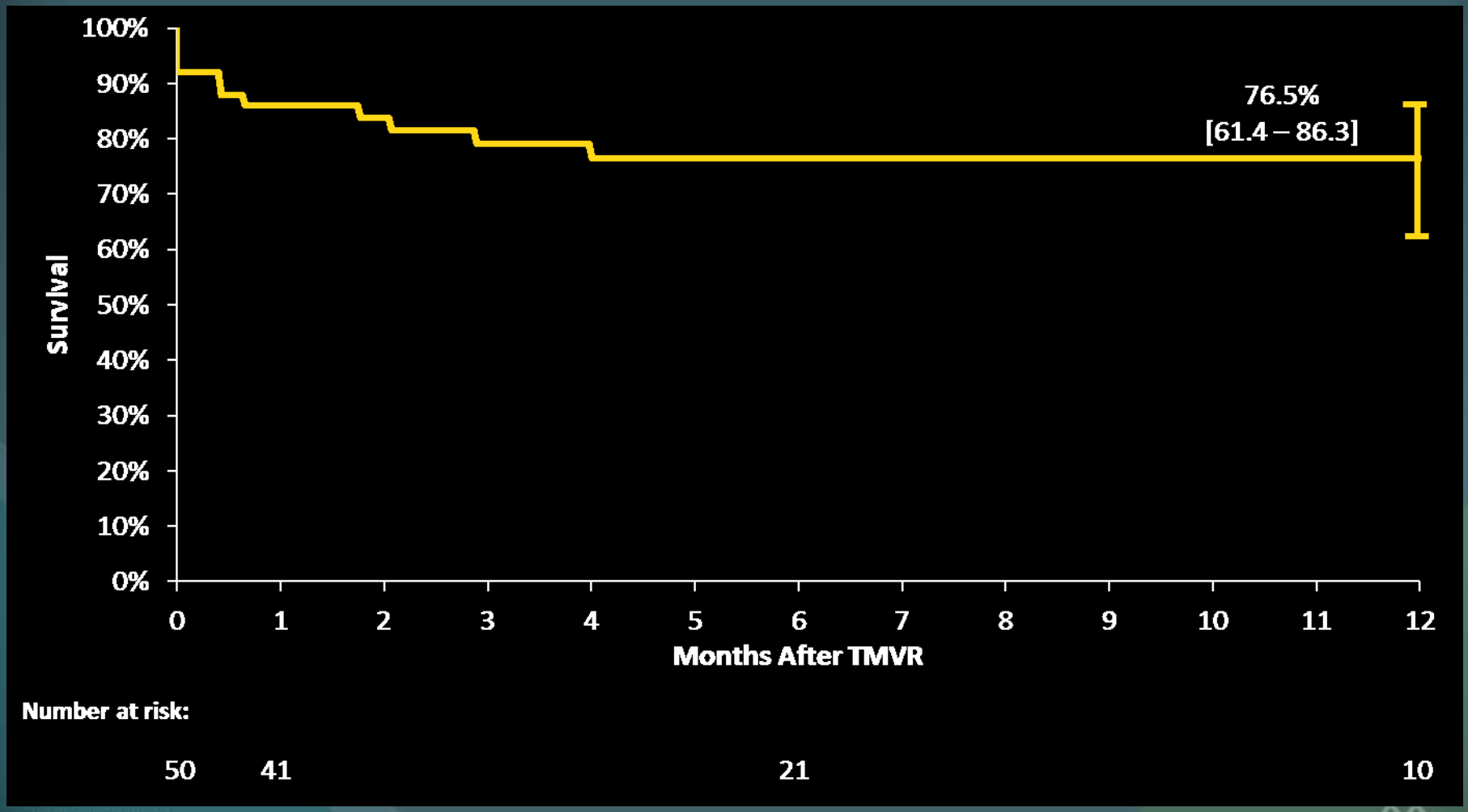
# INTREPID GPS: 1 YEAR SURVIVAL



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# TIARA: DATA ON CURRENT IMPLANTS

| Clinical Outcomes | N=37 |
|---|---|
| Peri-procedural Death | 0 |
| Peri-procedural CVA | 0 |
| Peri-procedural MI | 0 |
| Access Site Complication | |
| Minor | 0 |
| Major | 1 (3%) |
| > Mild Paravalvular Leakage | 0 |
| LVOT Obstruction | 0 |
| Acute Kidney Injury | 4(12%) |
| Device Success | 34 (92%) |
| U.Surgery or Repeat Intervention | 3 (8%) |
| All-cause 30-Day Mortality | 4 (12%)* |
| Cardiac 30-Day Mortality | 2 (5%)* |

Longest f/u >3.8yrs



Anson Cheung, TCT 2017

# CONCLUSIONS

- An unmet need for DMR and FMR
- Indications for TMVR will evolve as the devices evolve - "TAVR creep"
- There may not be a single device for all MR – device based on mechanism, anatomy.
- Results to date promising – when implant is successful – MR reduction is very good.
- Still not ready for prime time – headed in the right direction.

# THANK YOU