MitraClip and TMVR Challenges and Failures

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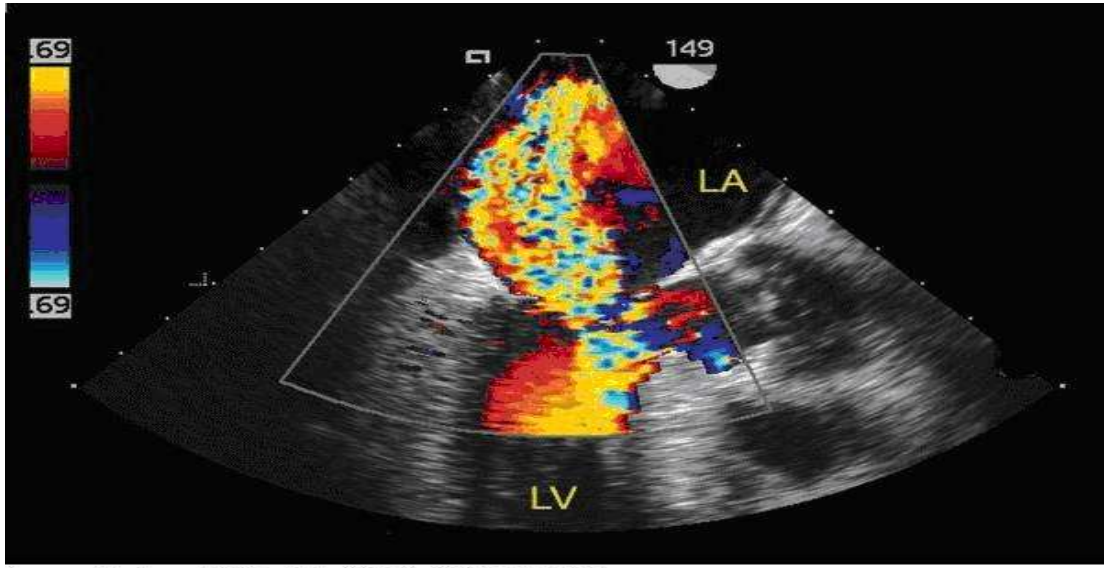
MitraClip and TMVR

Challenges and Failures



Hammerl H Journal für Kardiologie 2004; 11 (4): 176-177 ©

TAVI vs TMVR
Anatomy und Management

Aortic Valve

Mitral Valve

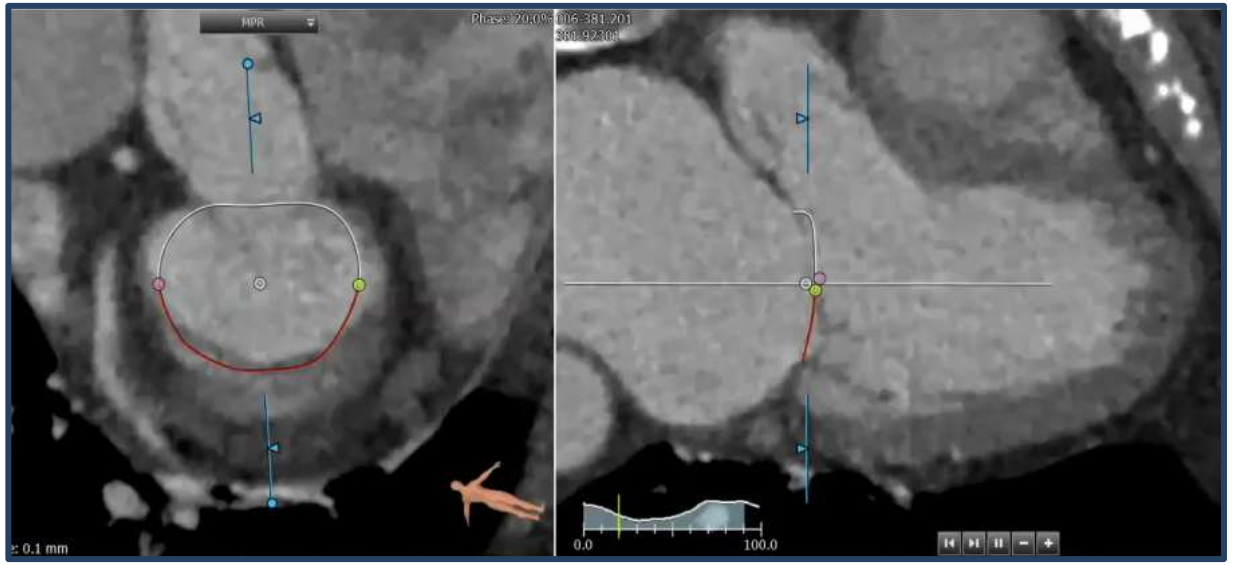
Simple

Complex

What are the anatomical and technical Challenges in percutaneous Mitral Valve Replacement (TMVR)?

Mitral Valve
Anatomical Challenges

Anatomically and physiologically, the mitral valve is clearly more challenging than the aortic valve

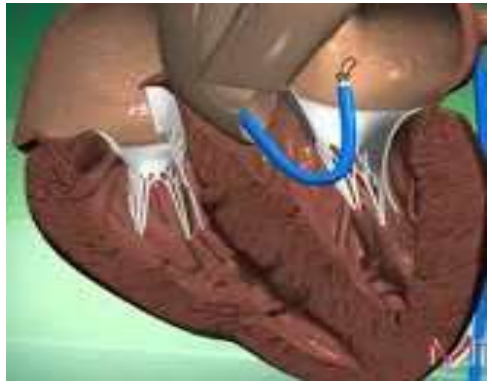


Native mitral annulus is large & asymmetric

Highly mobile over cardiac cycle
Very little to “hold on to”
LVOT is sensitive to obstruction

The Technical Challenge

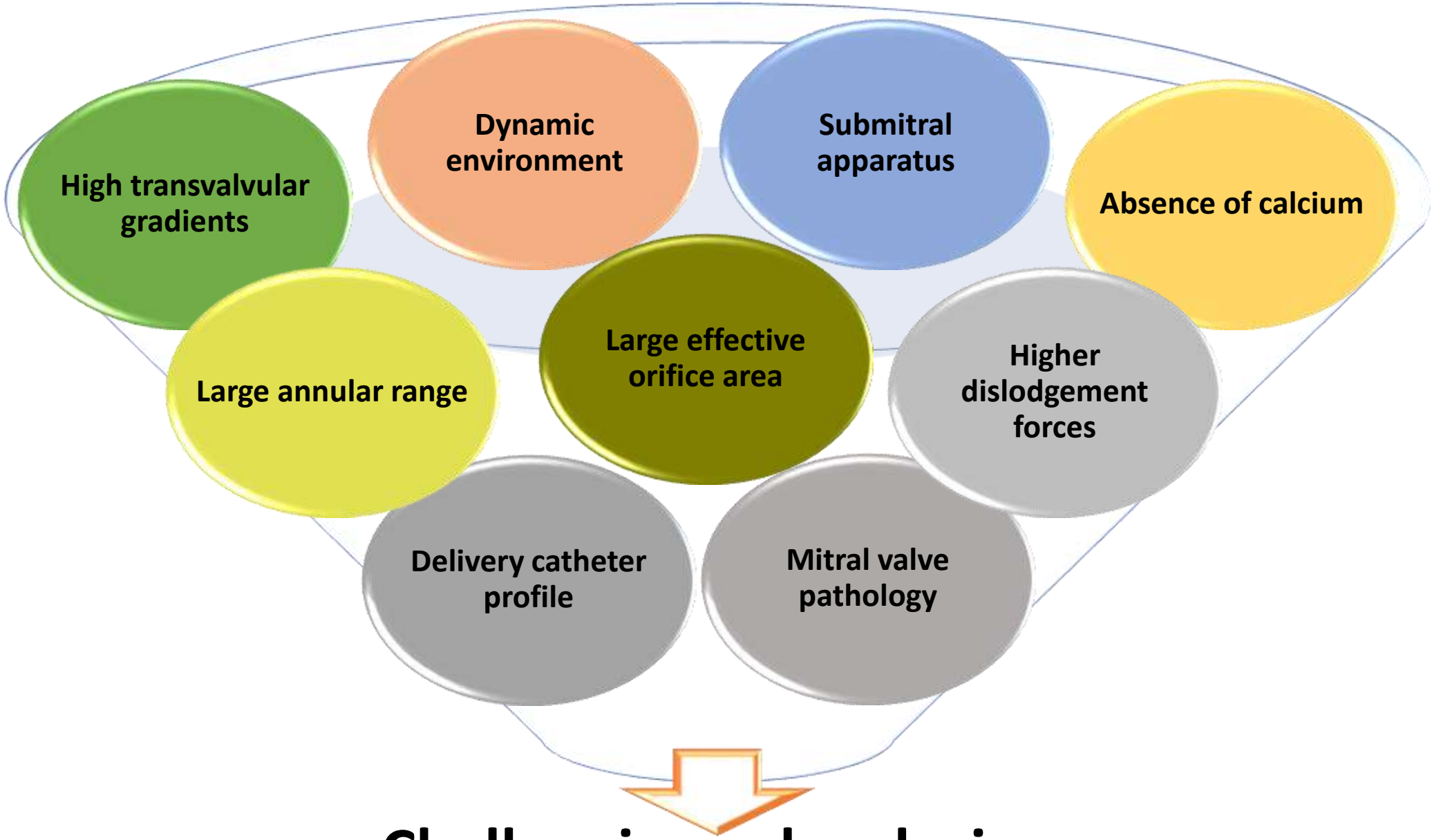
- *High variability and instability of the anatomy*
  - No defined structure for anchoring (like calcified annulus in TAVI)
  - Dilatation of the annulus creates big range of sizes
- *Complex apparatus with multi intra-dependencies:*
  - LVOT, SAM, Tethering, Continuous dilatation, complex flow and motion patterns through the cardiac cycle.
- *Delivery challenges:*
  - Trans-apical - thin and dilated ventricles
  - Retrograde – size, navigation, LV interaction
  - Trans septal – size, navigation
- *Two pathologies:*
  - Primary and secondary Mitral Regurgitation



„R²“ War

Competitive or Complementary?

What are the additional Challenges for TMVR?


High transvalvular gradients
Dynamic environment
Submitral apparatus
Absence of calcium
Large annular range
Large effective orifice area
Higher dislodgement forces
Delivery catheter profile
Mitral valve pathology
Challenging valve design

Potential concerns with TCMV replacement

Stent fatigue

Leaflet durability

Valve dislodgment

PVL and hemolysis

Left ventricular outflow obstruction

Available valve sizes

Repair vs. Replacement? Access Route ?

TCMV replacement devices

Braile Biomedica

Braile Biomedica

CardiAQ 1st G

CardiAQ Edwards

Cephea

Direct Flow Medical

Twelve Medtronic

M-Valve

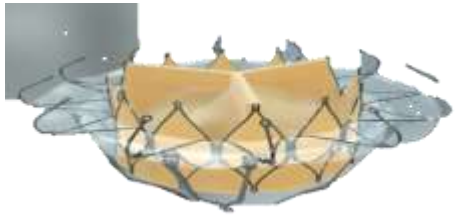
Edwards Fortis

HighLife

Navigate

Neovasc Tiara

PermaValve MID



Sinomed

Tendyne Abbott

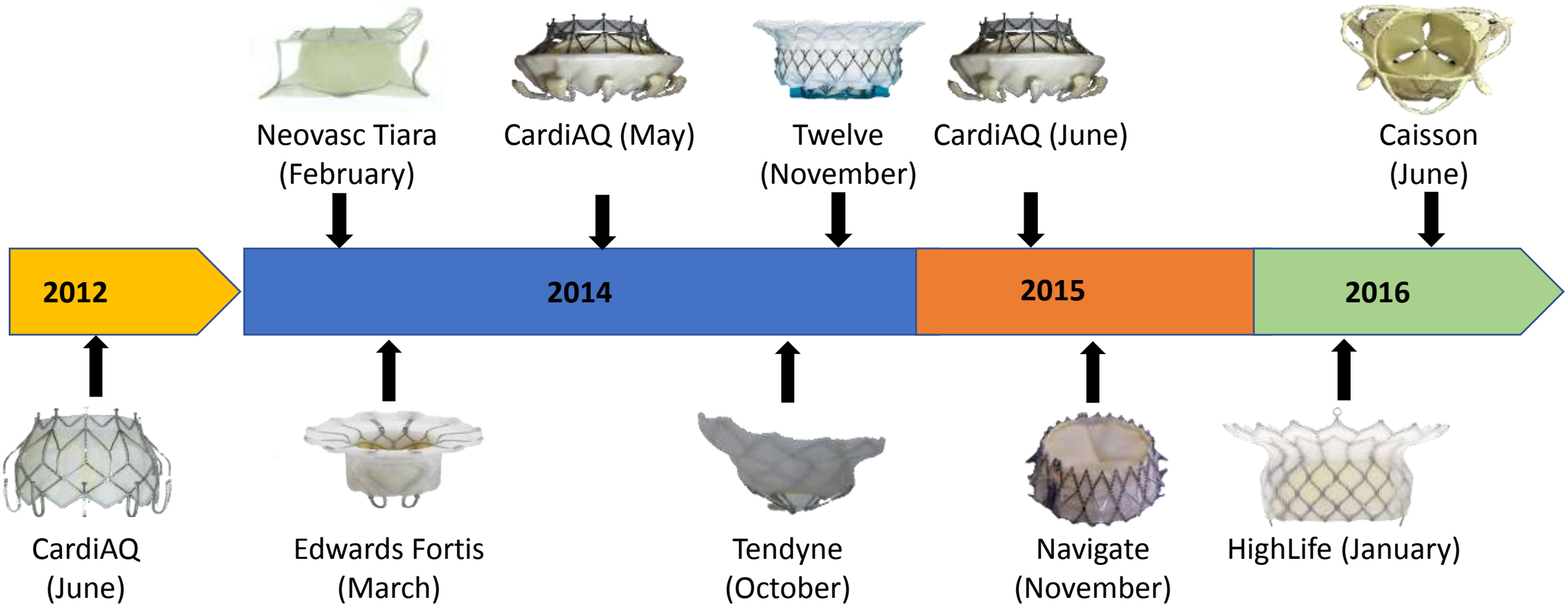
SATURN TMVR

Valtech CardioValve

Caisson

Others: MitraHeal, Mitrassist, Mitraltech, Mehr Medical, Mitracath, Mitralix MAESTRO, Nakostech, St. George ATLAS, Transcatheter Technologies Tresillo

Transcatheter mitral valve replacement:
First-in-Human timeline

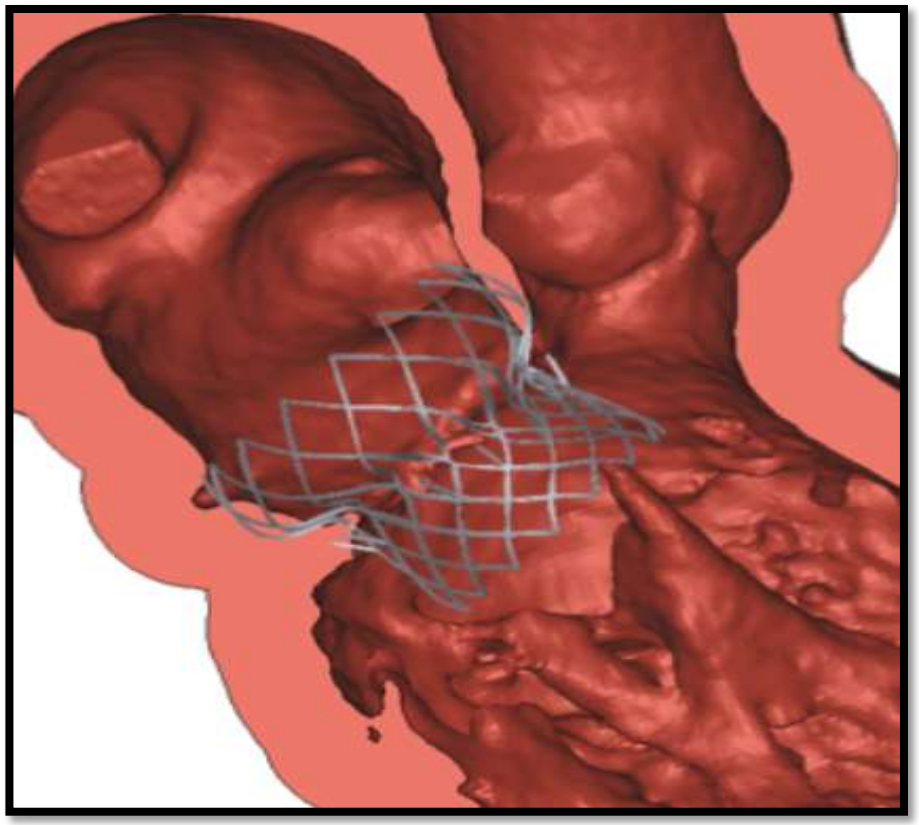


Design Targets

Anchor

Seal

Avoid interference



Adaptable

Recapture

Durable

User friendly

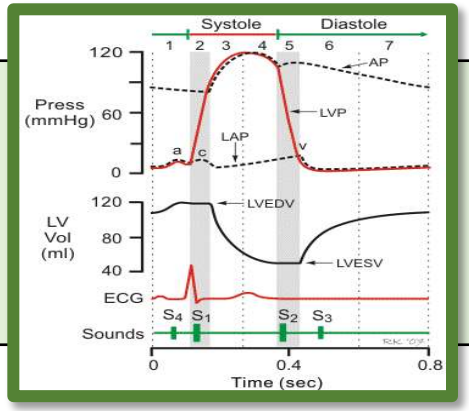
Technically, How Does This Boil Down?

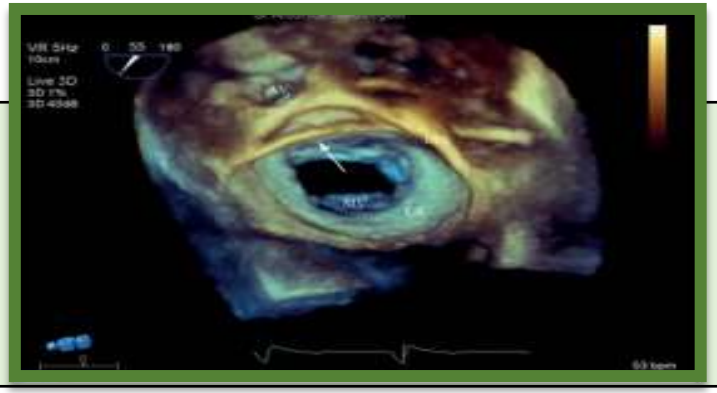
- Mitral Valve Pathology
- Absence of Calcium
- Variable Calcification (MAC)
- Sub-valvular apparatus
- Large Effective Orifice Area
- Large Annular Range

Anatomy & Pathology

Dynamic Environment

- Ventricular & Annular Motion
- High Transvalvular Gradients
- High Dislodgement Forces

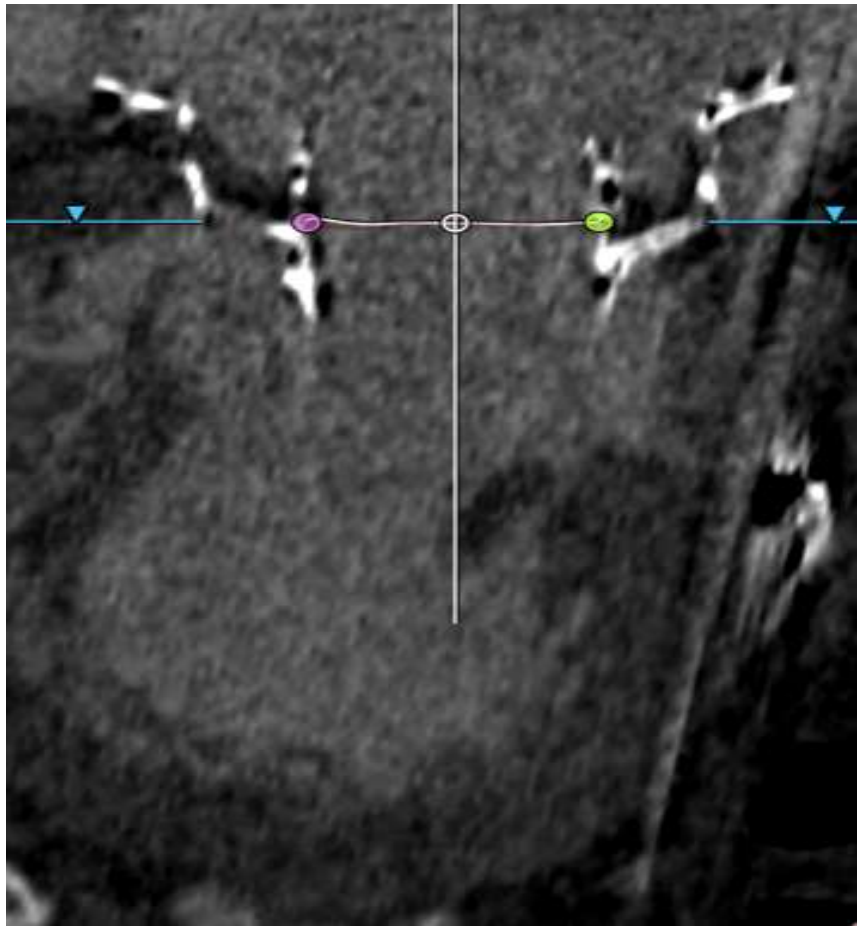




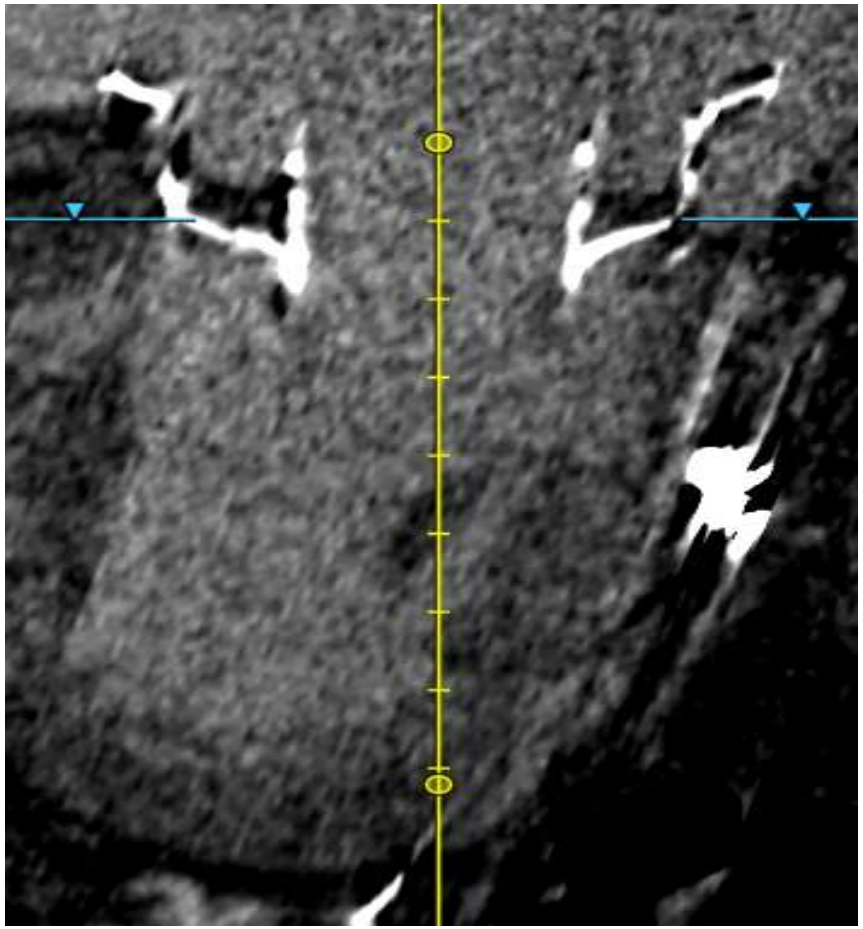
- Poor Ventricular Function
- Thin Ventricular Walls
- Steering
- Delivery System Profile

Access & Positioning

Good Sealing and Positionig with minimal “Low-Flow Areas”

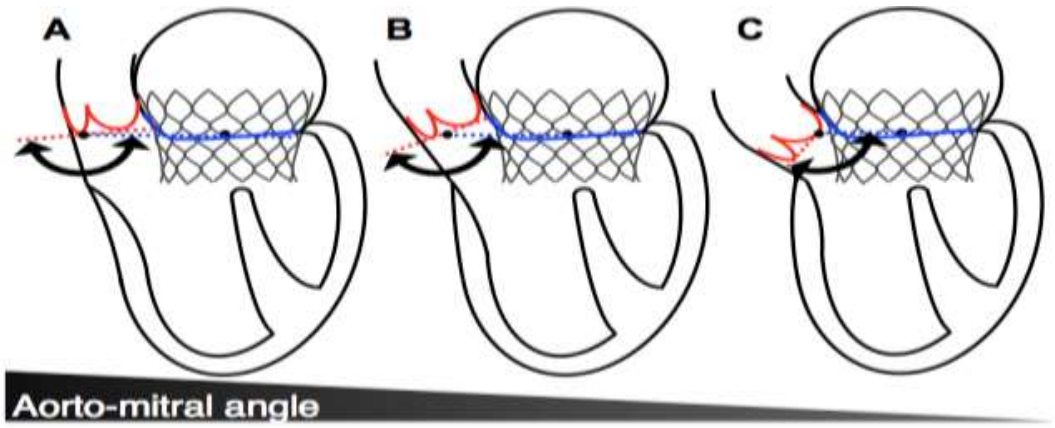


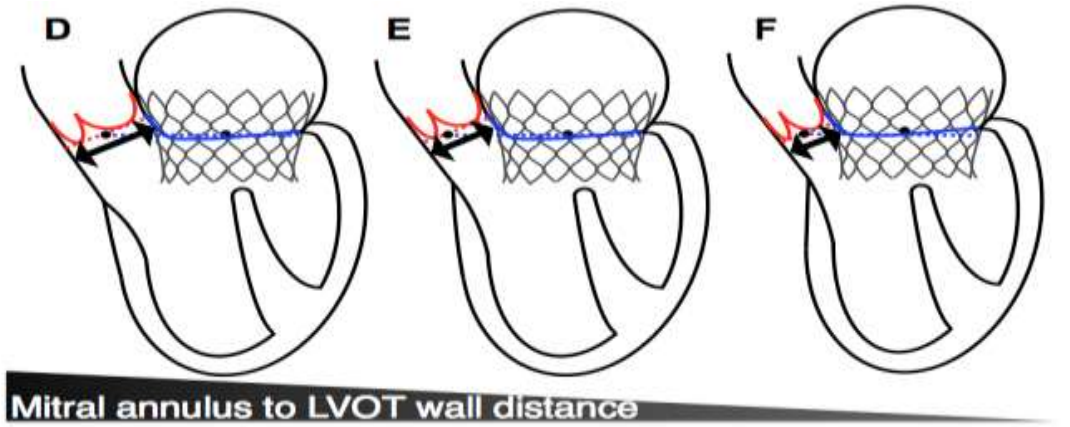
6 months

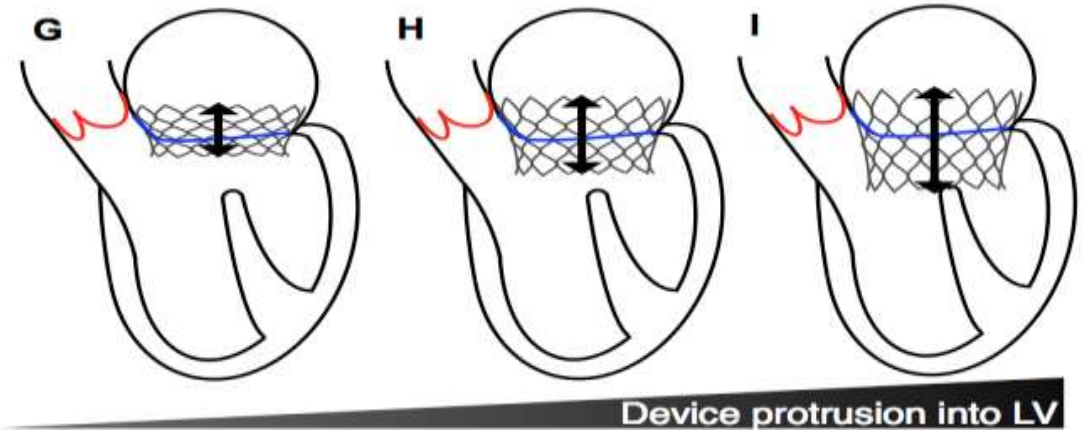


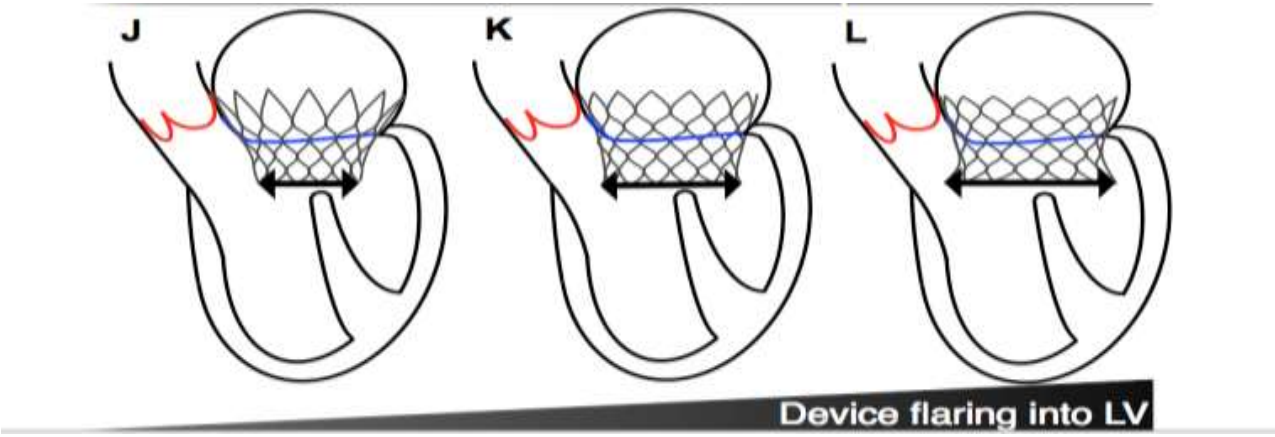
12 months

Sensitive to LVOT obstruction









Lauzier P, Piazza N et al.

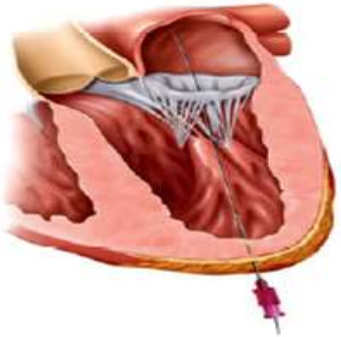
Approaches

Pros

- Straight shot
- TAVR experience
- Apical closure devices

Cons

- LV dysfunction / large catheter OD
- Subvalvular apparatus entanglement
- More invasive



Pros

- Direct antegrade approach
- Avoids submitral apparatus
- Avoids LV puncture
- Minimally invasive MV surgery
- Less sensitive to catheter OD

Cons

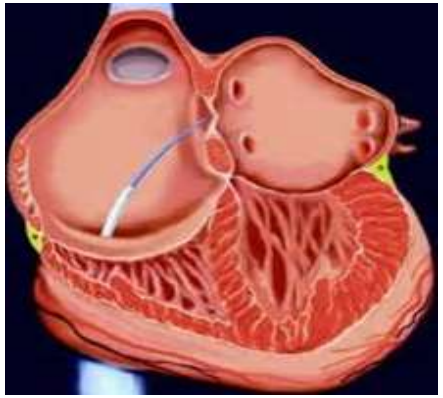
- More invasive than transfemoral
- Steering and navigation

Pros

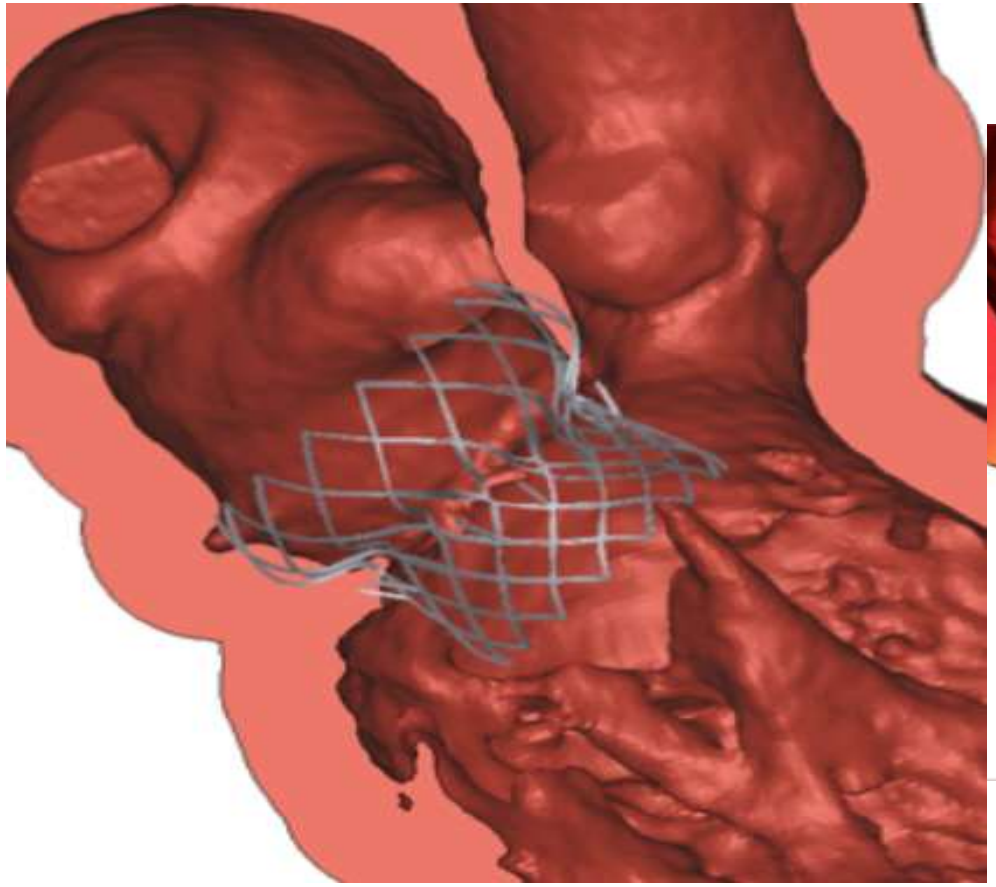
- Direct antegrade approach
- Avoids LV puncture
- Transseptal puncture
- Less sensitive to catheter OD

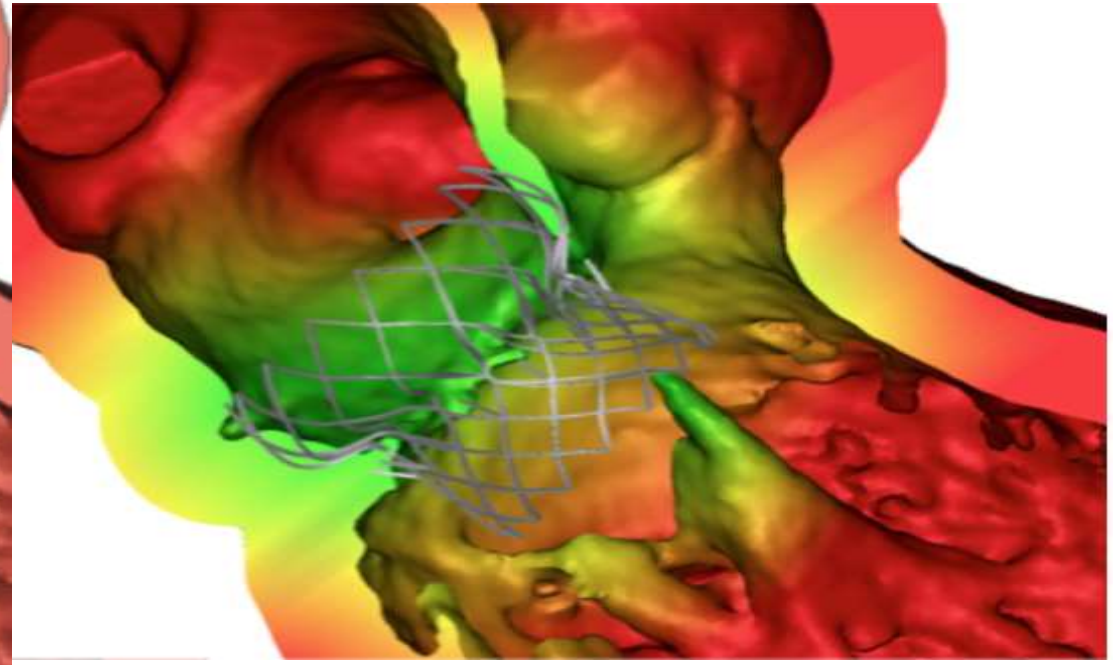
Cons

- Navigation and steering
- Veno-arterial access (submitral apparatus)
- Atrial septal defect / large catheter OD



Virtual implantations





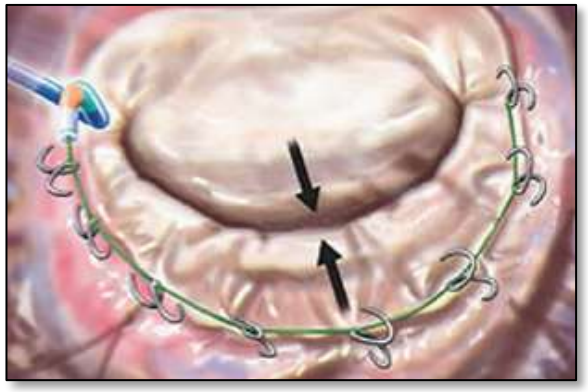
How to overcome the challenges?

- Know and respect the mitral anatomy!
- Know the existing solutions and their limitations
- Remember the “real user” – (ease of use is critical!)
- Look for a good risk/benefit ratio:
  - Safe procedure
  - Keep options open
  - Durability

Mitral Interventions

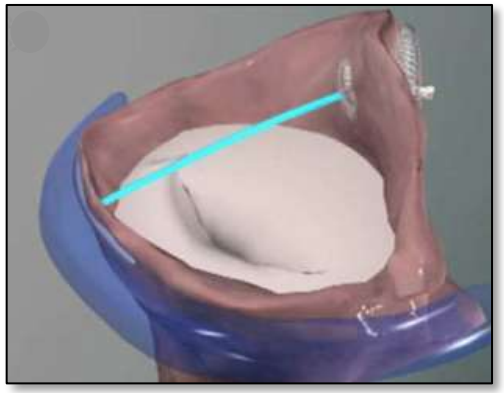
Transcatheter MV Repair Systems

Accucinch (Ancora Heart)

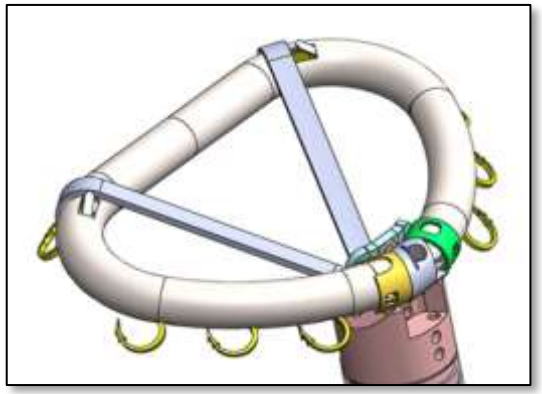


NeoChord

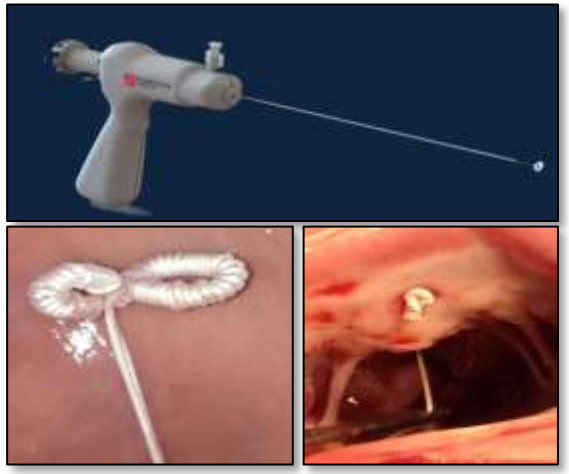
Arto (MVRx, Inc.)



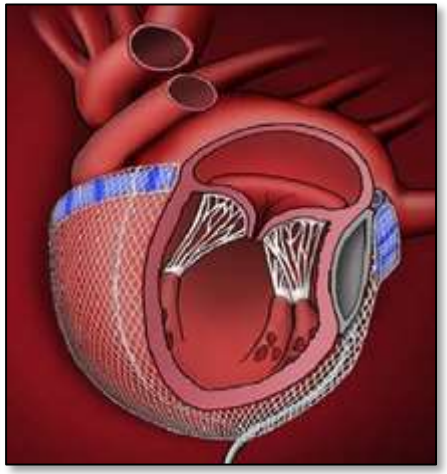
Valcare AMEND



Millipede IRIS



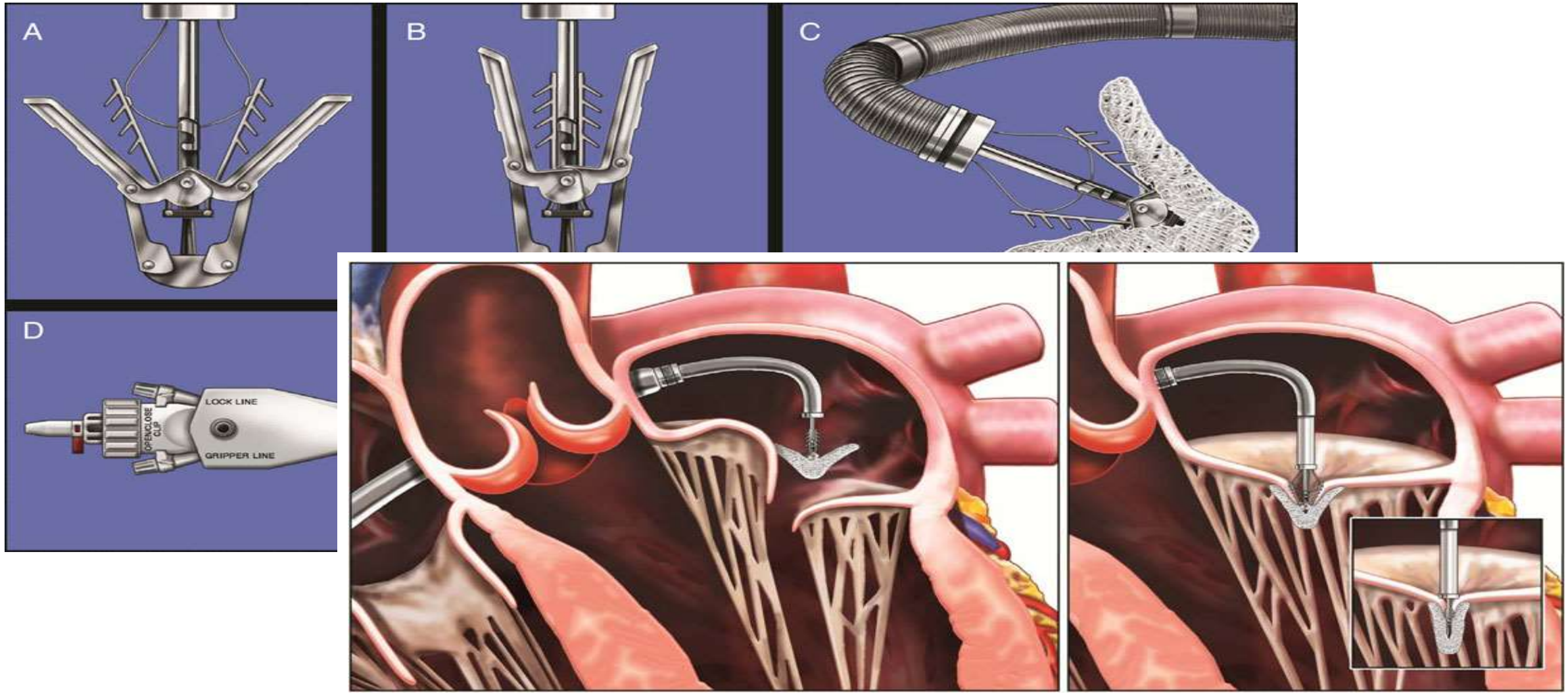
Harpoon



VenTouch

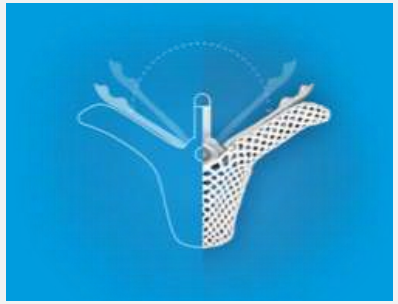
Middle Peak

MitraClip System – „Edge-to-edge“-Reconstruction



TODAY

MitraClip® NT

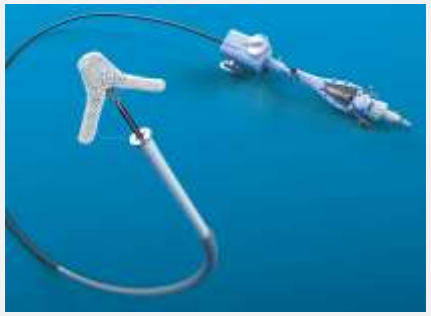


DESIGN FOCUS:
Improved leaflet grasping
Enhanced steering

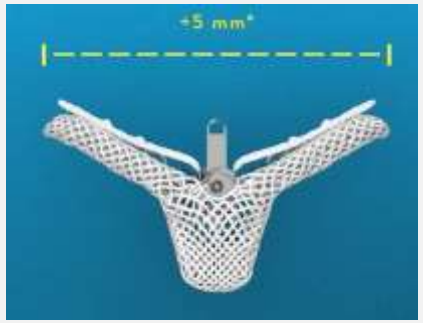
LAUNCHED:
2016

NEW

MitraClip® NTR* | MitraClip® XTR*



DESIGN FOCUS:
Enhanced steering accuracy
Improved ease-of-use



DESIGN FOCUS:
Improved leaflet grasping
Greater MR reduction
Complex cases

LAUNCHING:
2018

FUTURE

MitraClip® †
Generation 4

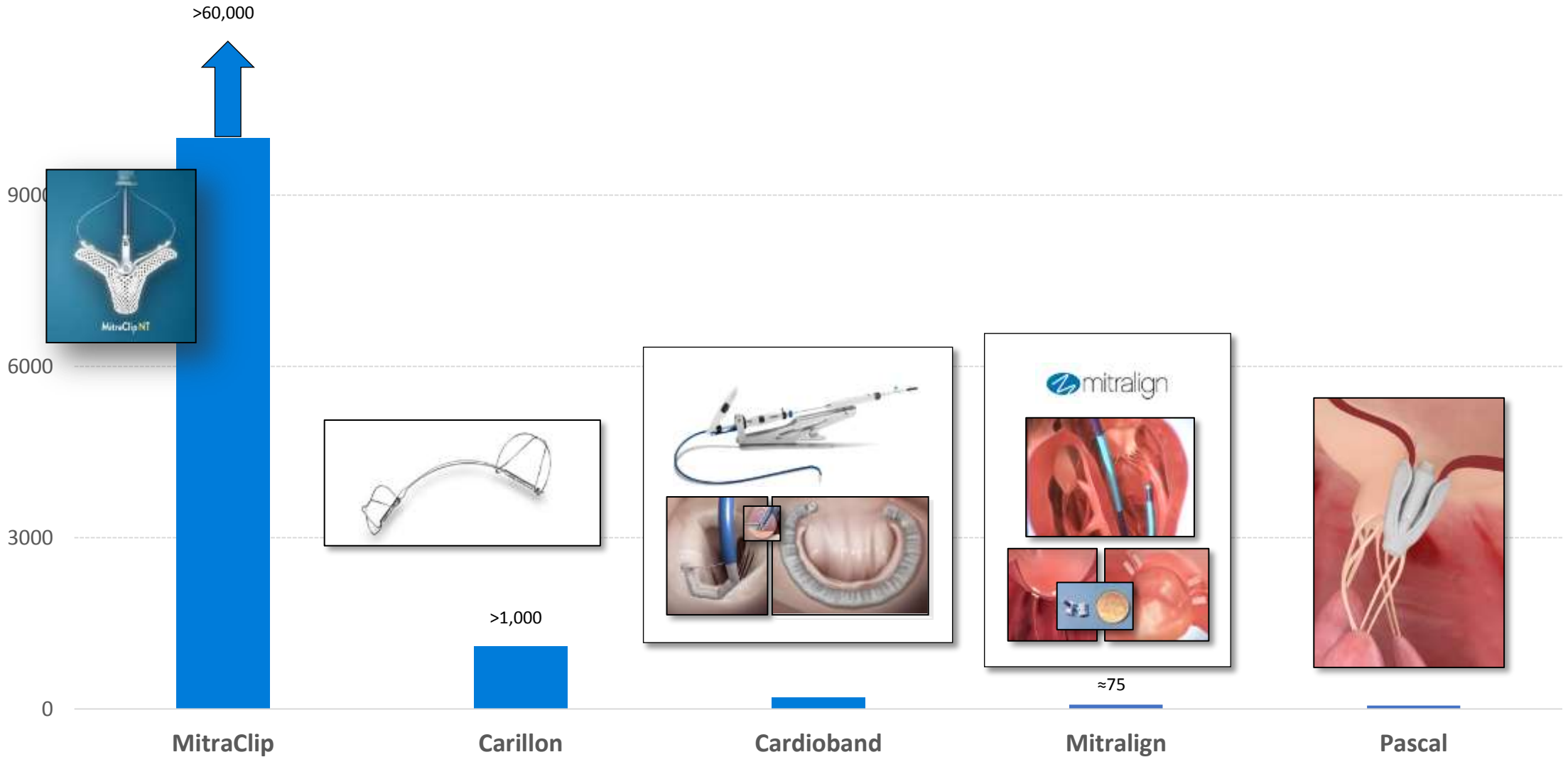
DESIGN FOCUS:
Improved ease-of-use
Improved leaflet grasping
Greater MR reduction
Complex cases

MitraClip® †
Generation 5

DESIGN FOCUS:
Enhanced Steering accuracy
Improved ease-of-use

*CE Marked. Not for sale in U.S.
†Currently in development at Abbott. Not currently for sale. Image for illustration purposes only.

Mitral Repair Devices in Use



PROBLEMS - DEVICE

- Clip catheter too unflexible, length of catheter to0 static, therefore localization of transseptal puncture (too) is crucial
- Clip arms too small
- Clip arms do not work independently
- Once the clip is placed, no other options than surgery remains

With TMVR at the horizon, in patients suitable for TMVR, only clips with perfect results should be left (applies also for the first clip of a procedure!)

Mechanisms of Clip Failure

- Patient selection
- Mitral regurgitation
  - persistent
  - recurrent
- Intra-procedural complications
  - SLDA
  - Stuck in chords
- Creating mitral stenosis

Negative Predictors 1
Anatomic

- Coaptation length <2.7 mm
- Coaptation depth >6.3 mm
- Distance between papillary muscles >32 mm
- Thickening and calcification of the subvalvular apparatus
- Cleft
- Effective regurgitant orifice area (EROA)
- Mitral valve orifice area (MVOA) <4cm^2

Negative Predictors 2
Clinical

- Mean transmitral pressure gradient (TMPG)
- TAPSE <15mm
- TR>2+
- EF<25%
- PASP
- RV function
- Ischemic etiology
- NTPro BNP >10000
- NYHA Class 4
- CKD, Diabetes, Age >80

STS/ACC TVT Registry

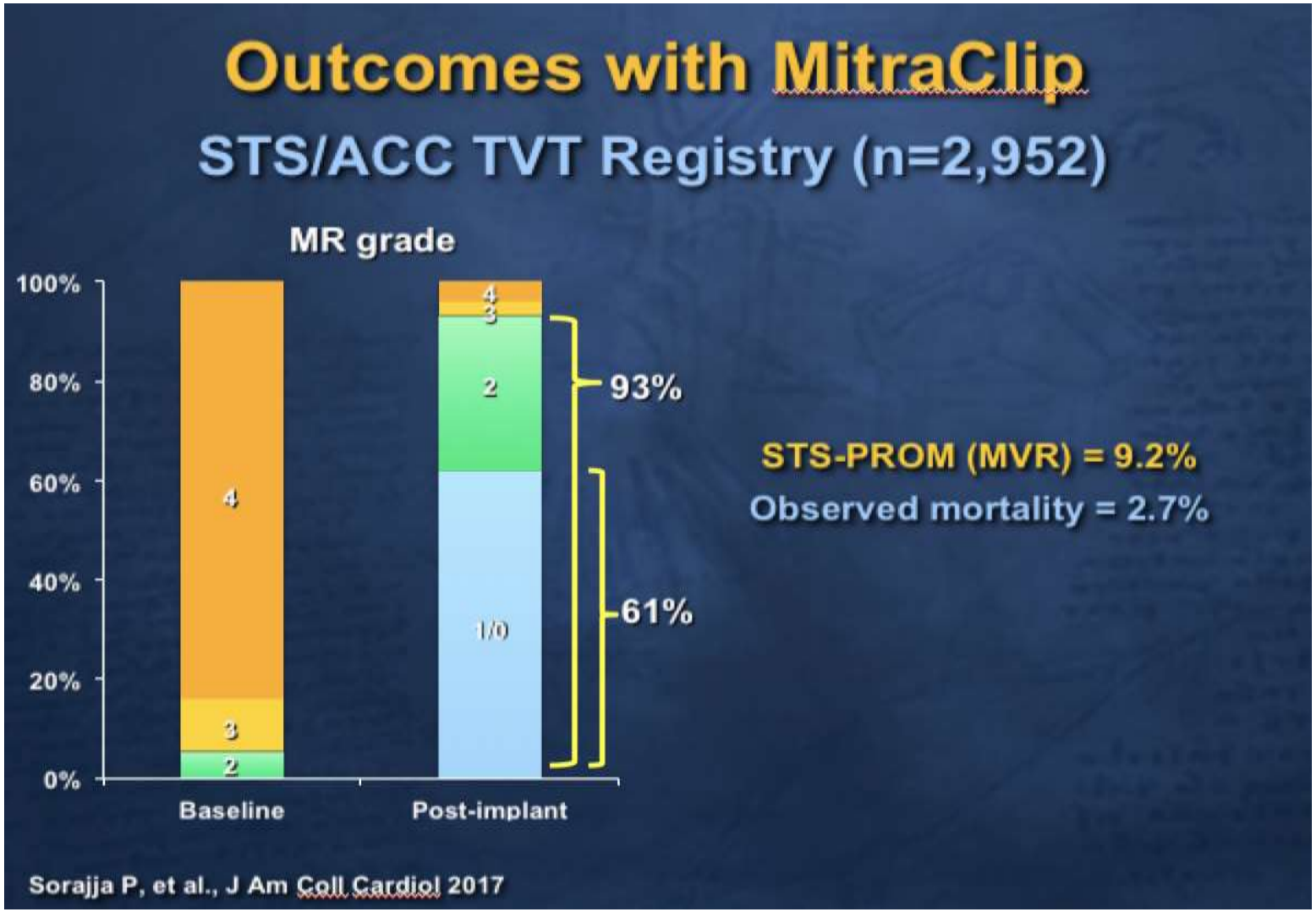
Transcatheter Mitral Valve Repair

- **Collaboration of STS, ACC, CMS, hospitals, medical industry**
- **Patient-level data with DCRI as analytic center**
- **Participation satisfies NCD***

**patients may not reflect all procedures during this study period*

Change in Mitral Regurgitation

Clip implanted in 94%



Adverse Events

In-hospital mortality……	2.3%
30-day mortality……	5.8%
Cardiac surgery……	0.5%
Stroke……	1.8%
Myocardial infarction……	0%
Major bleeding……	3.9%
Cardiac perforation……	0.7%
Device-related events……	2.7%
Single leaflet device detachment....	1.1%
Device embolization……	0.4%
Other……	1.2%

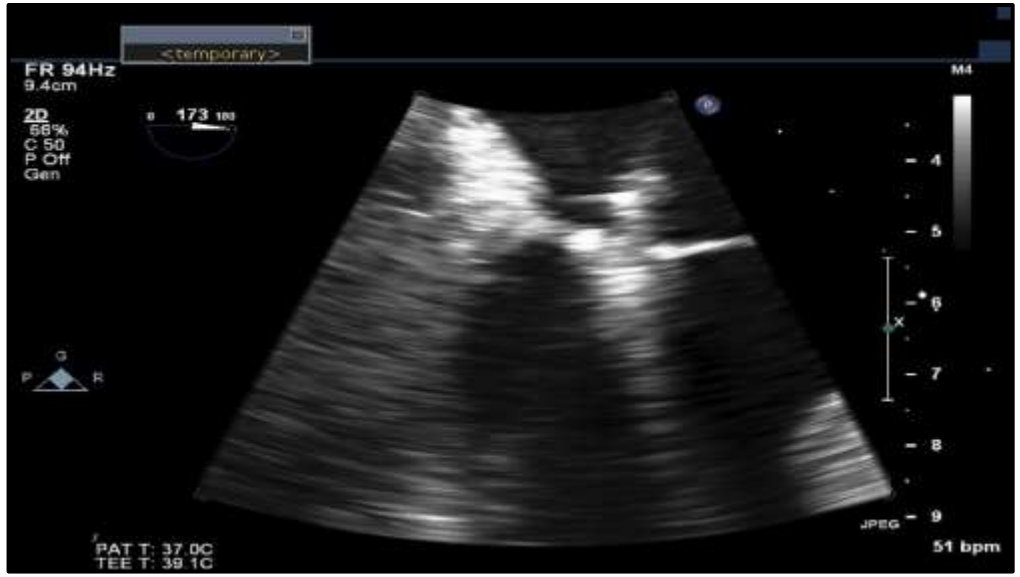
Sorajja P: J Am Coll Cardiol 2016;67:1129–40

Anatomical Challenges

MitraClip in STS/ACC TVT Registry

Prior Surgical Repair……	1.5%
FMR……	17.5%
MVA < 4.0cm^2……	20.5%
Gradient > 5mmHg……	17.7%
Leaflet Ca +2……	18.8%

Sorajja P: J Am Coll Cardiol 2017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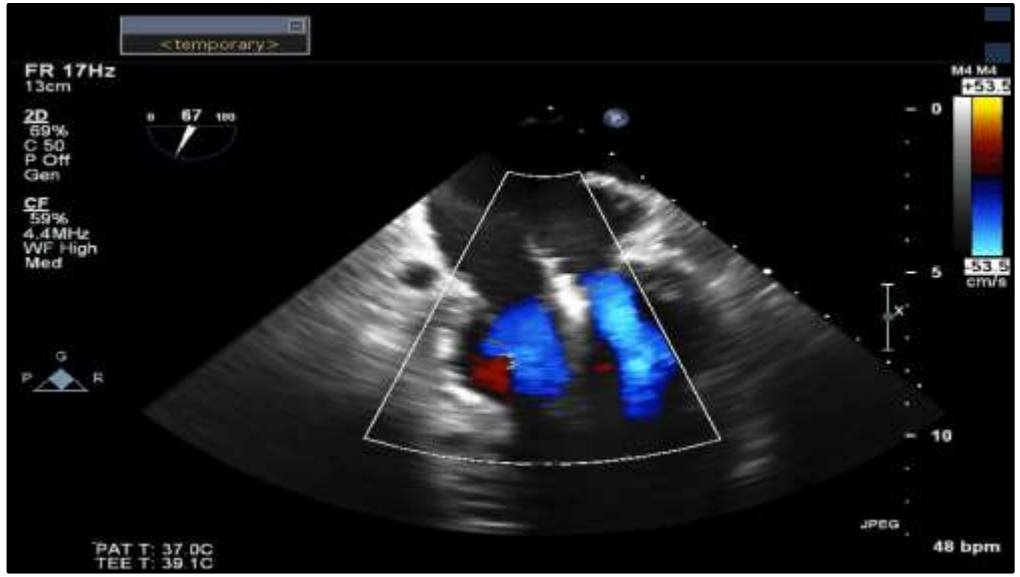
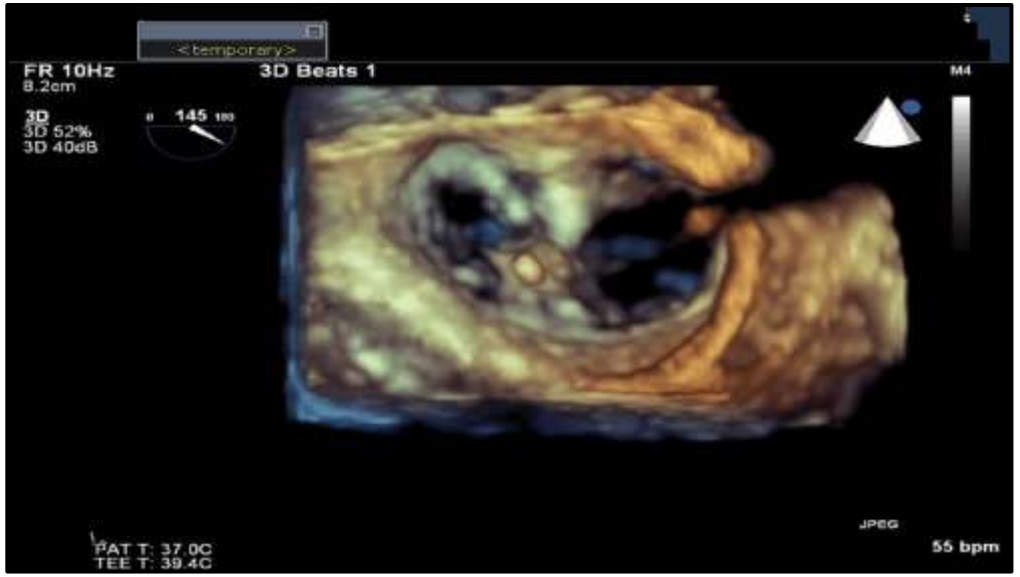
FR 94Hz
9.4cm
2D
68%
C 50
P Off
Gen
M4
PAT T: 37.0C
TEE T: 39.1C
JPEG
51 bpm

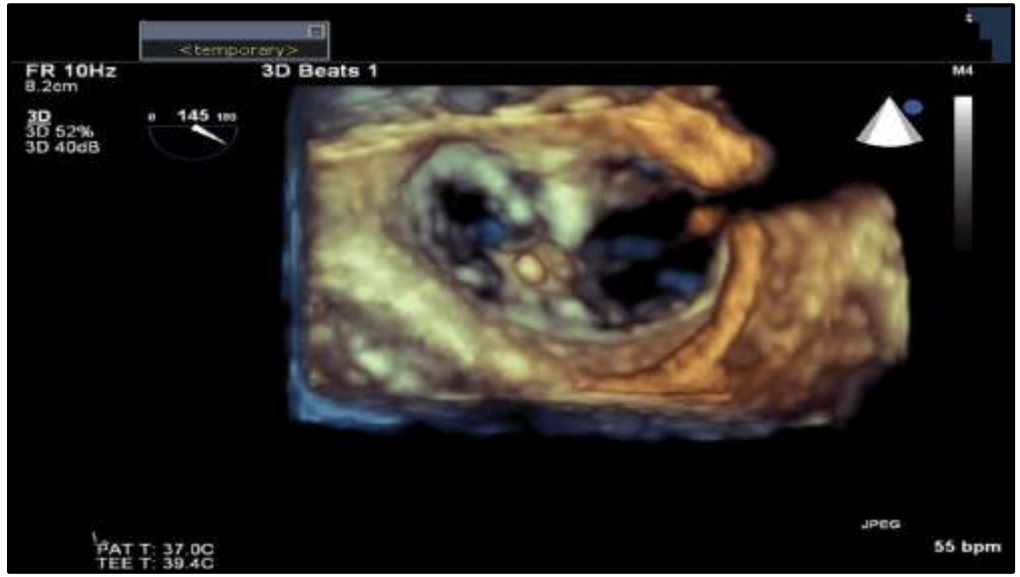

<temporary>
FR 50Hz
13cm
2D
68%
C 50
P Off
Gen
M4
PAT T: 37.0C
TEE T: 39.1C
JPEG
76 bpm


<temporary>
FR 17Hz
13cm
2D
69%
C 50
P Off
Gen
CF
59%
4.4MHz
WF High
Med
M4 M4
53.9
cm/s
PAT T: 37.0C
TEE T: 39.1C
JPEG
48 bpm


<temporary>
FR 10Hz
8.2cm
3D Beats 1
3D
3D 52%
3D 40dB
M4
PAT T: 37.0C
TEE T: 39.4C
JPEG
55 bpm

What next?

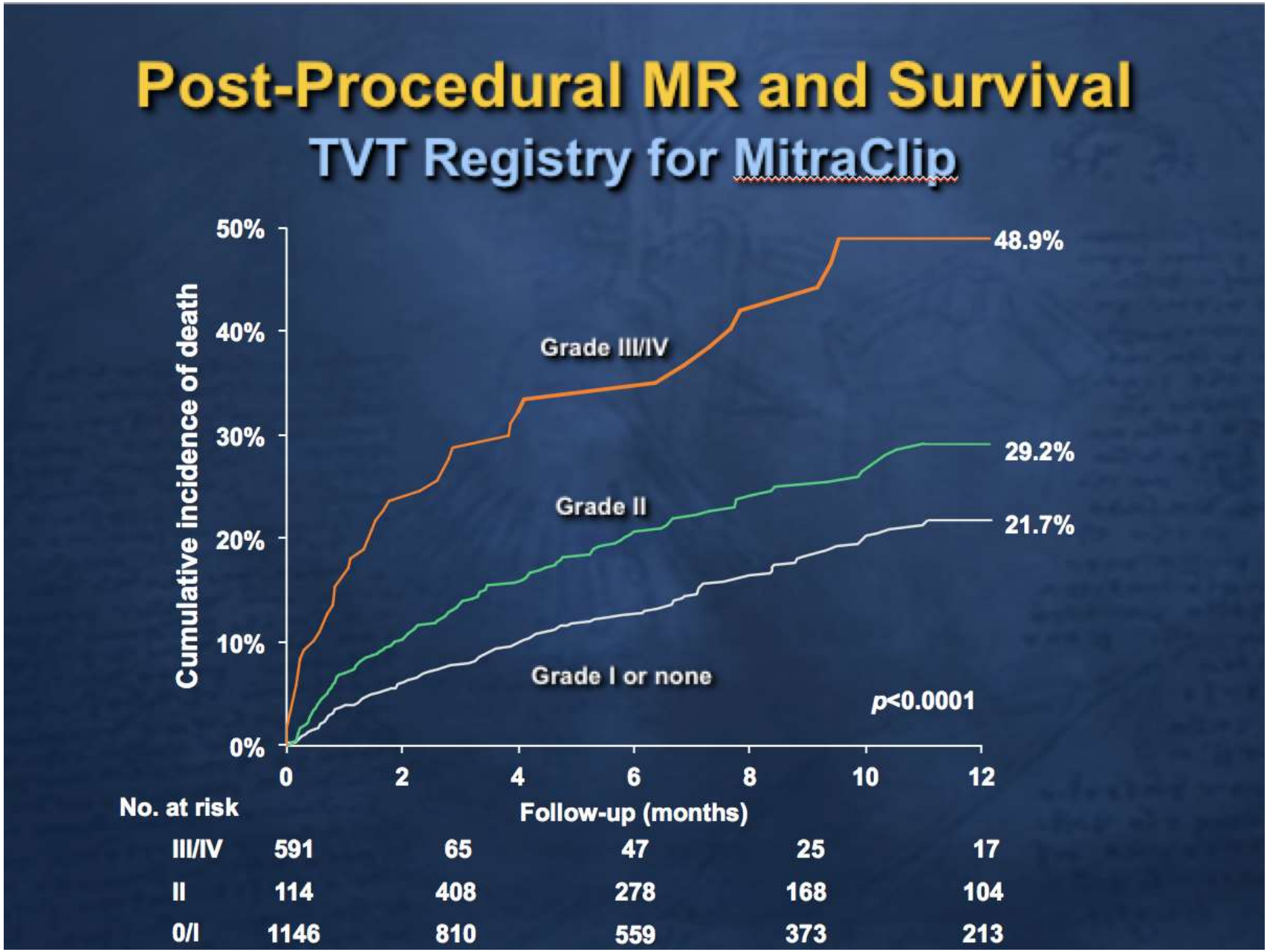
Getting surgical-like



Lateral move

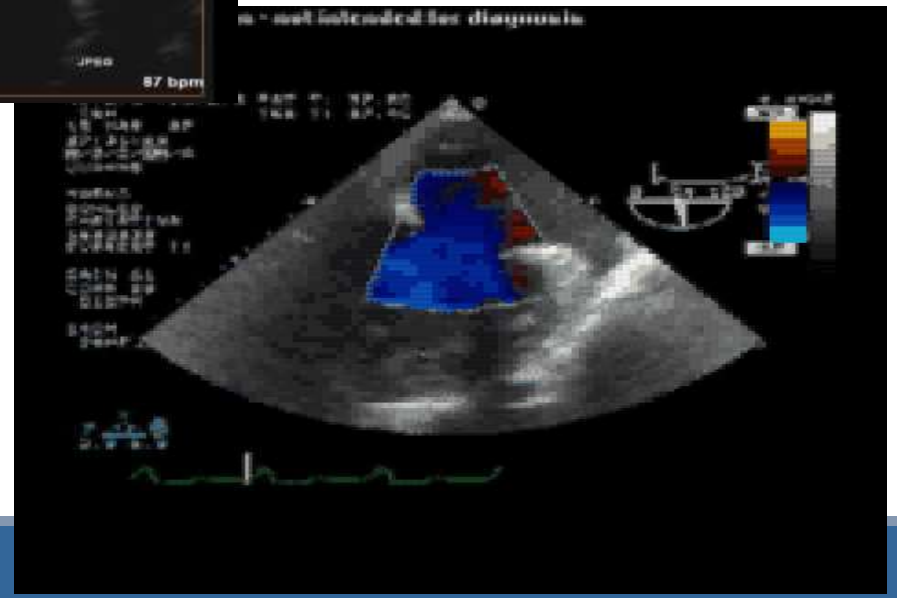
Post-Procedural MR and Survival

TVT Registry for MitraClip

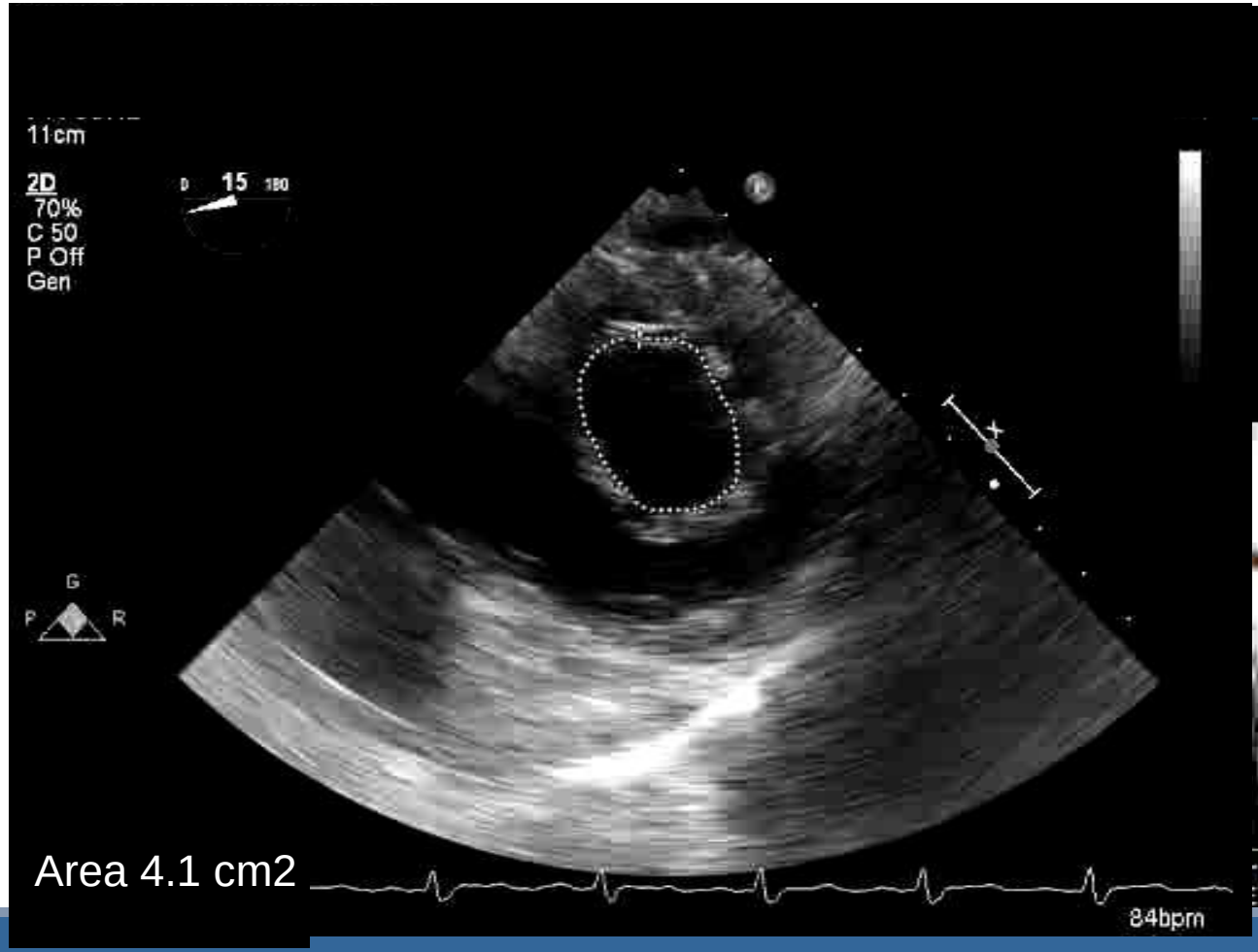


What other factors have to be considered?

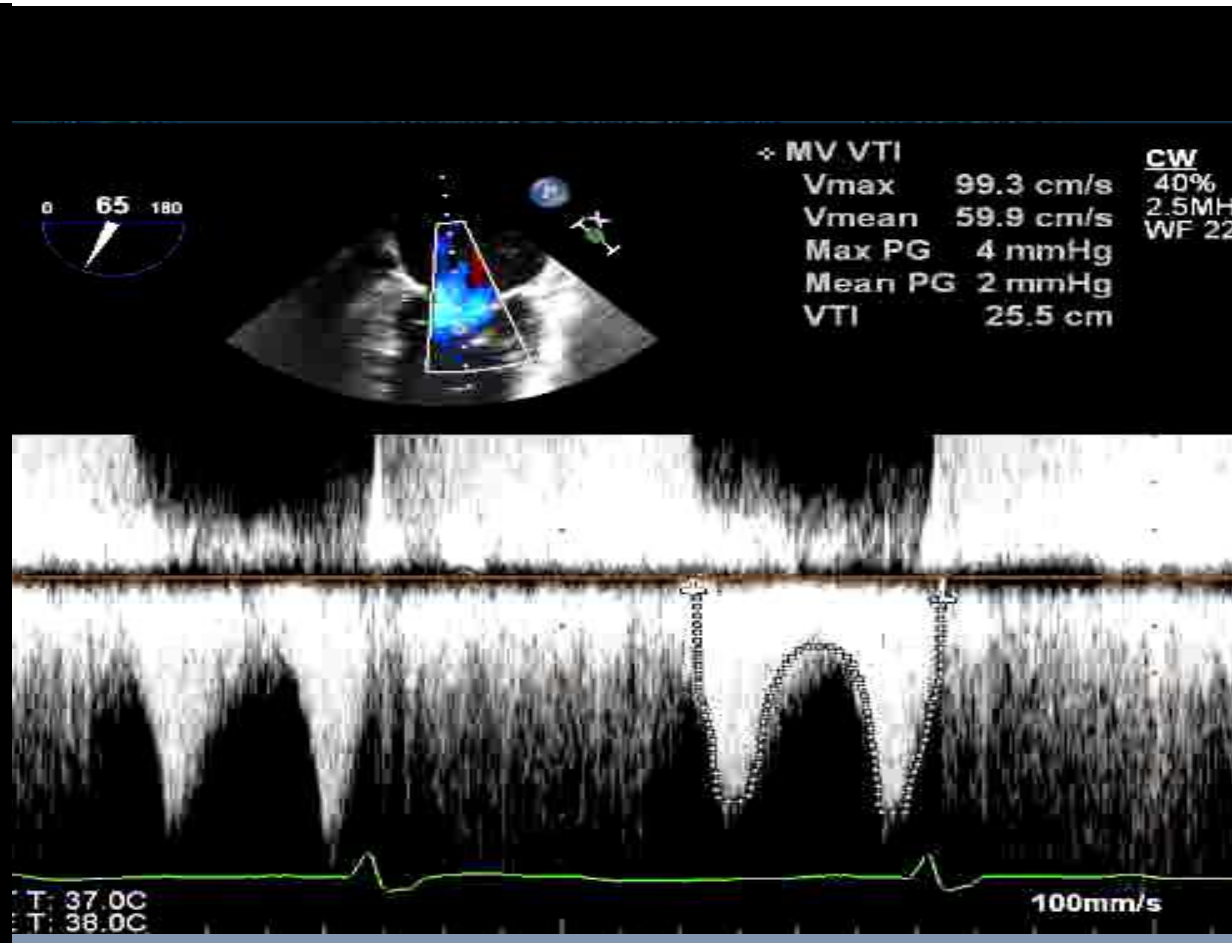
Degree of Posterior Leaflet Restriction



Mitral Orifice Area



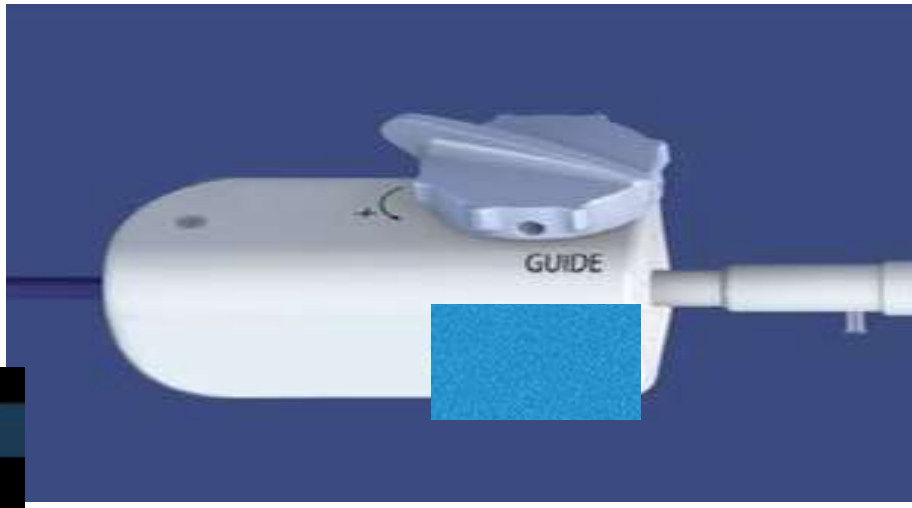
Area 4.1 cm2

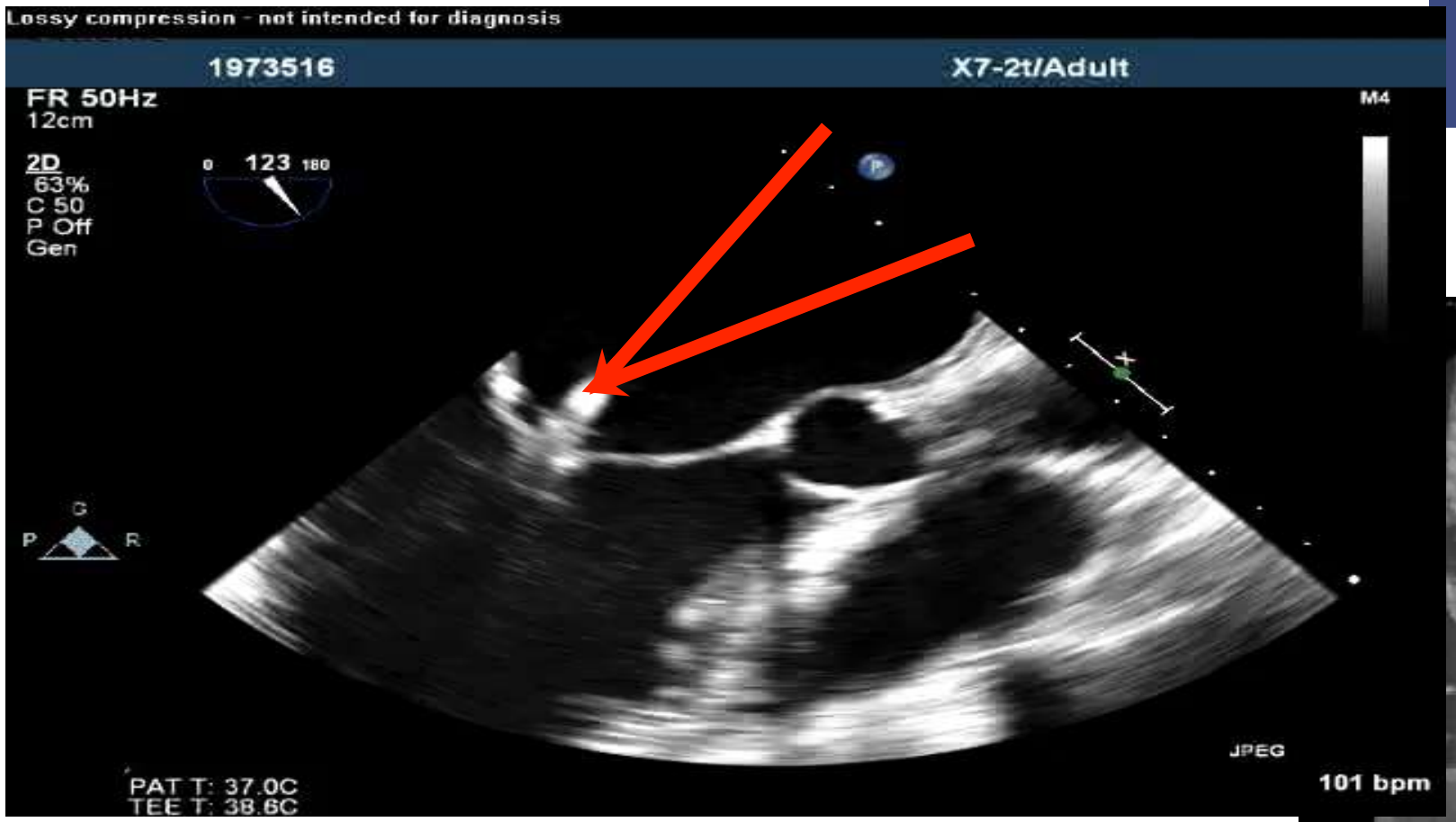


Transseptal Issues

Trajectory Issues

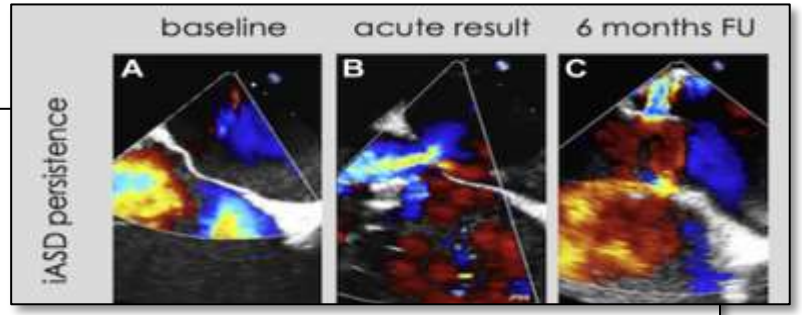
- Angle of Attack





Persistence of Iatrogenic ASD After MitraClip

A Note of Caution



- 66 patients
- persistent iASD in 50% of cases
- patients with iASD not different vs without ASD baseline characteristics
- procedures took longer for iASD (82±39.7min vs. 68.9±45.5 min; p<0.05)
- less decrease of PASP for iASD (1.6±14.1 mmHg vs. 9.3±17.4 mmHg; p 0.02)
- Patients with iASD
  - more often NYHA Class >II after FU (57% vs. 30%; p 0.04)
  - higher levels of N-terminal pro-BNP(6,667.3±7,363.9 ng/dl vs. 4,835.9±6,681.7 ng/dl; p<0.05)
  - less improvement in 6-min walking distances (20.8±107.4 m vs. 114.6±116.4 m; p<0.001).
- **Patients with iASD showed higher death rates during 6 months** (16.6% vs. 3.3%; p<0.05).
  - Cox regression found that only persistence of iASD (p<0.04) associated with 6-month survival.

Schueler R, Öztürk C, Wedekind JA, Werner N, Stöckigt F, Mellert F, Nickenig G, Hammerstingl C. JACC Cardiovasc Interv. 2015 Mar;8(3):450-9

5 Rules for ideal MitraClip Patient Selection

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1. OMT Pretreatment.

Symptoms are related to MR.

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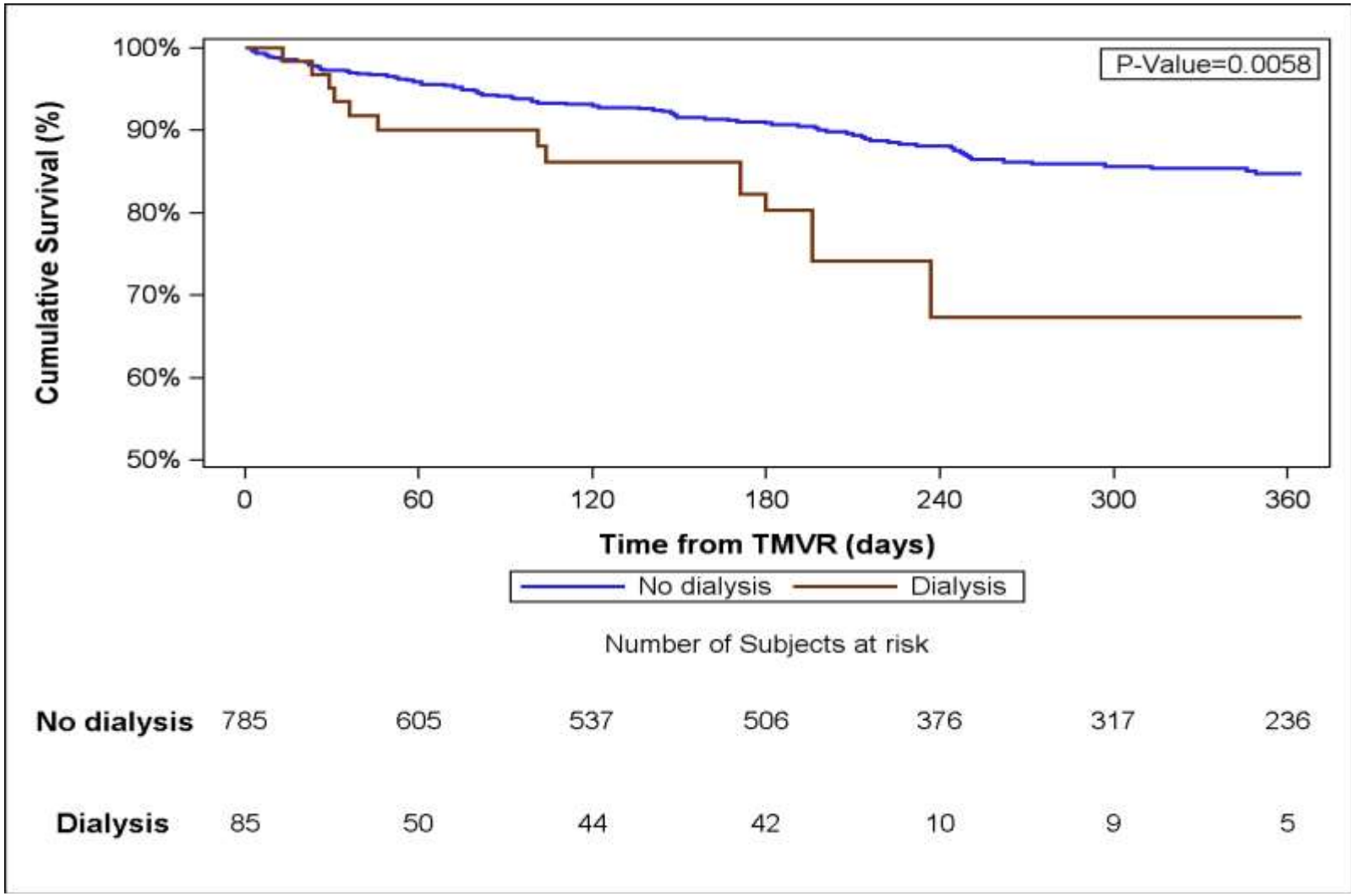
2. Patients with severe CHF, dialysis, or/and life expectancy < 12mo may be less suitable candidates. Futility?

Predictors of mortality after Mitraclip. The EU-Registry



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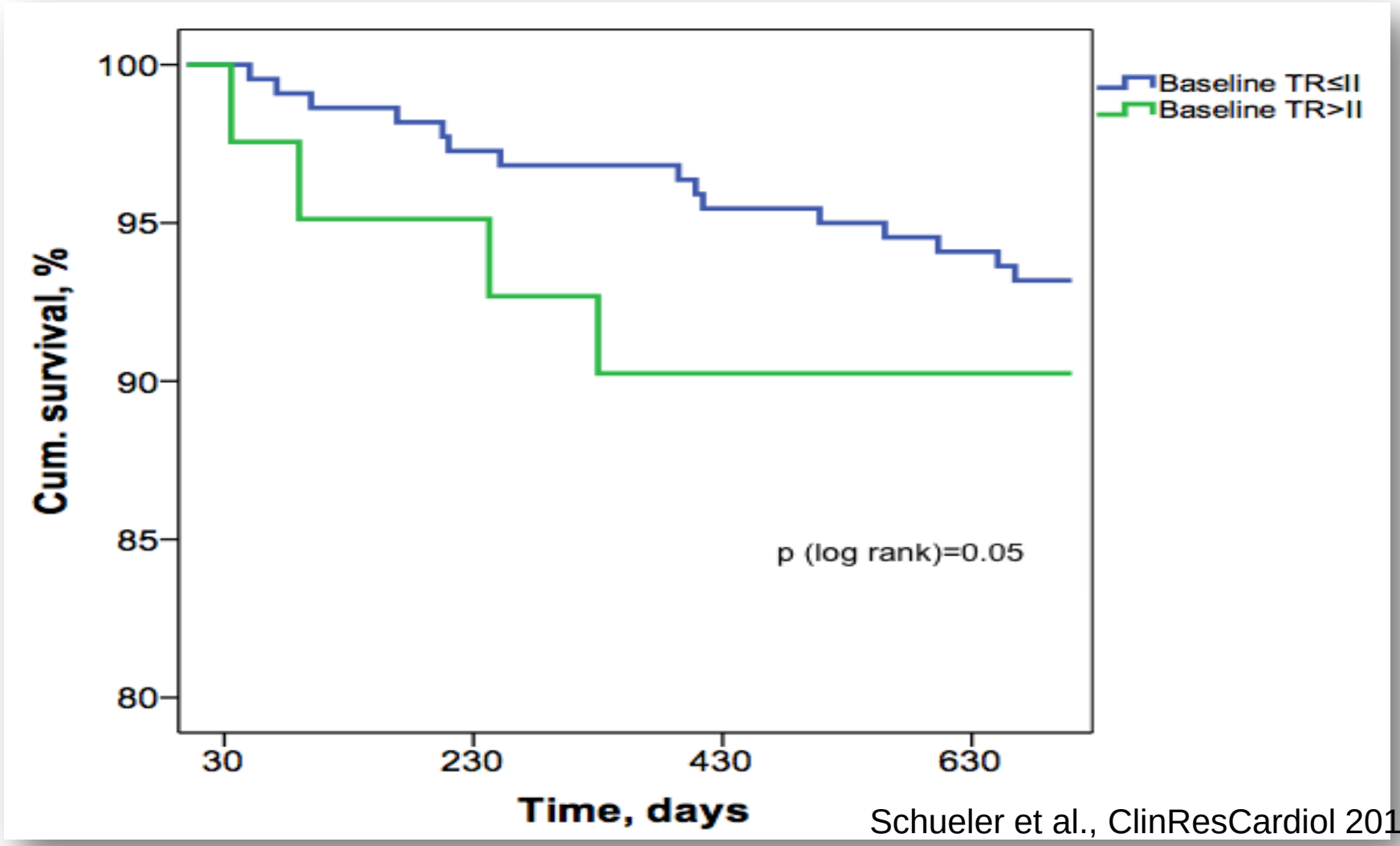
Predictors of mortality after MitraClip therapy : German transcatheter mitral valve interventions registry

	Multivariable analysis (Cox regression model)	
	HR (95% CI)	*P*
Age >75 years	1.29 (0.90–1.87)	0.16
Female gender	1.13 (0.78–1.64)	0.53
NYHA IV	1.62 (1.10–2.40)	0.02
Anaemia	2.44 (1.16–5.12)	0.02
Previous aortic valve intervention	2.12(1.32–3.41)	0.002
Creatinine ≥1.5 mg/dL	1.77 (1.24–2.54)	0.002
Peripheral artery disease	2.12 (1.41–3.20)	0.0003
LVEF <30%	1.58 (1.10–2.31)	0.01
Severe tricuspid regurgitation	1.84 (1.23–2.77)	0.003
Procedural failure[a]	4.36 (2.37–8.02)	<0.0001

European Heart Journal doi:10.1093/eurheartj/ehv627, 2015

Tricuspid regurgitation - Outcome after Mitral repair



Schueler et al., ClinResCardiol 2016

5 rules for ideal MitraClip patient selection

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3. Patients with severe TR or RV dysfunction may be less suitable candidates.

4. Avoid patients with severe MV calcification or MV stenosis.

MitraClip Suitability

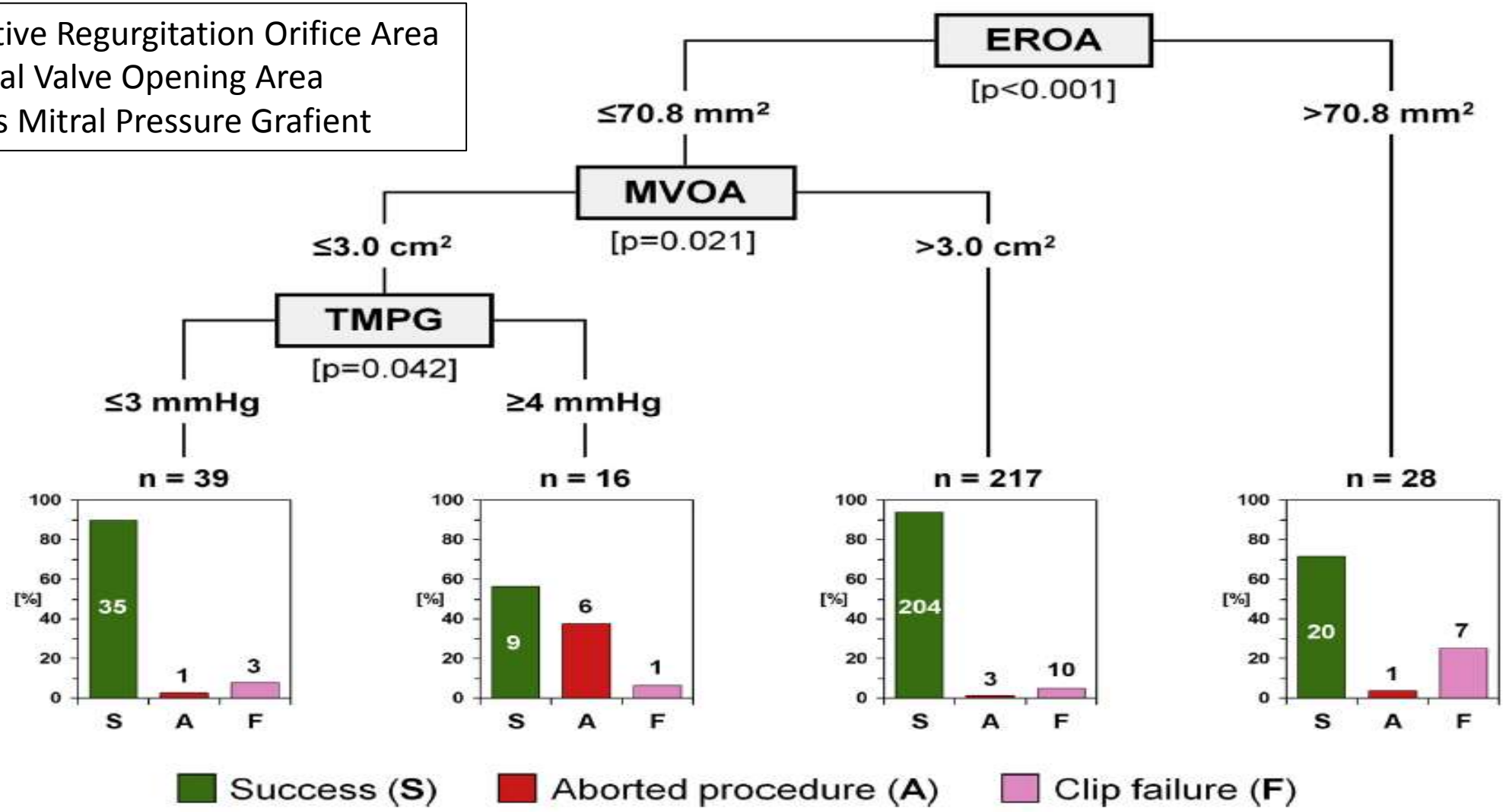
German Society Cardiology Manual and Guidelines 2013

Optimal	Limited suitable	Inappropriate
Pathology in segment 2	Pathology in segment 1 or 3	Leaflet perforation or cleft
No calcification	- Slight calcification outside the grasping area - Ring calcification - Anuloplasty with ring	Severe calcification
Valve area >4cm^2	Valve area >3 cm^2 & good leaflet mobility	Mitral stenosis (< 3cm^2, gradient >5mmHg)
Length of the posterior leaflet > 10mm	Length of the posterior leaflet 7-10mm	Length of the posterior leaflet < 7mm
Coaptation depth < 11mm	Coaptation depth >11mm	
Normal thickness and mobility of the leaflets	Restriction (Carpentier IIIB)	Rheumatic thickening and restriction (Carpentier IIIA)
MR with prolaps Flail size < 15mm Flail gap < 10mm	Flail size > 15mm only with large mitral aulus and option for more than 1 clip	Barlows desease

Boekstegers,-P; Hausleiter,-J, Baldus S,[50]von Bardeleben RS, et al . Clin Res Cardiol 2013

Predictors of failure:
Small valve orifice and excessive MR

EROA= Effective Regurgitation Orifice Area
MVOA= Mitral Valve Opening Area
TMPG= Trans Mitral Pressure Grafient



5 rules for ideal MitraClip patient selection

1. GCP Pretreatment.
   Symptoms are related to MR.

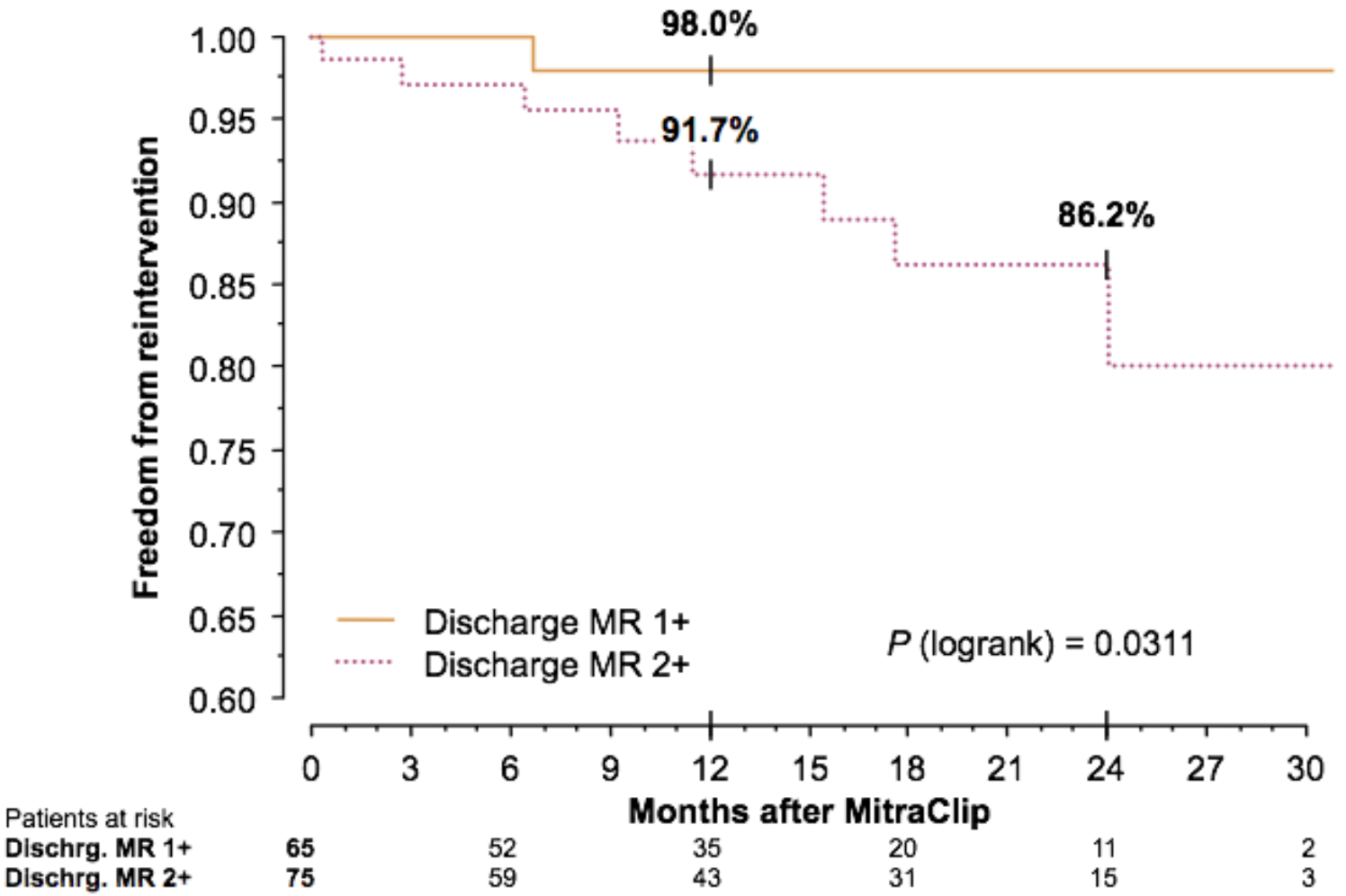
2. Patients with severe CHF, dialysis, or/and life expectancy < 12mo may be less suitable candidates. Futility?

3. Patients with severe TR or RV dysfunction may be less suitable candidates.

4. Avoid patients with severe MV calcification or MV stenosis.

5. Avoid relevant residual MR predicted by lack of coaptation, massive annular dilation, restriction, tenting, or Barlow.

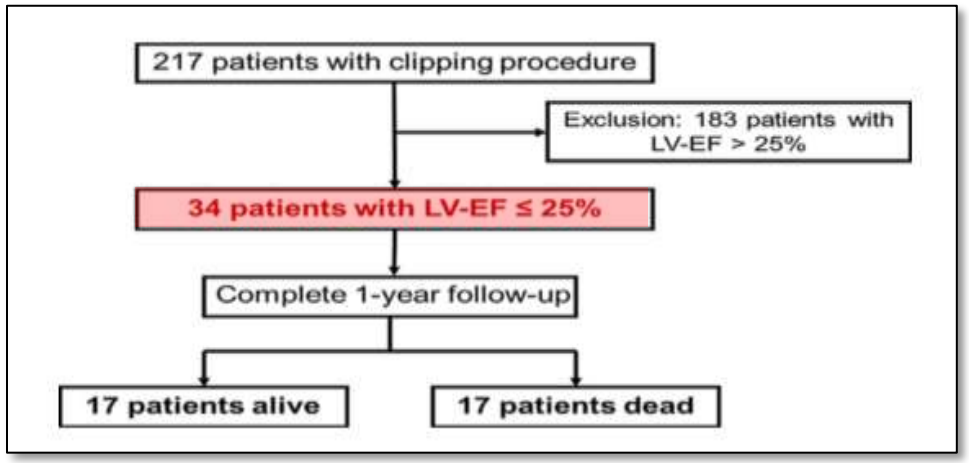
Predictor of Failure: Residual MR



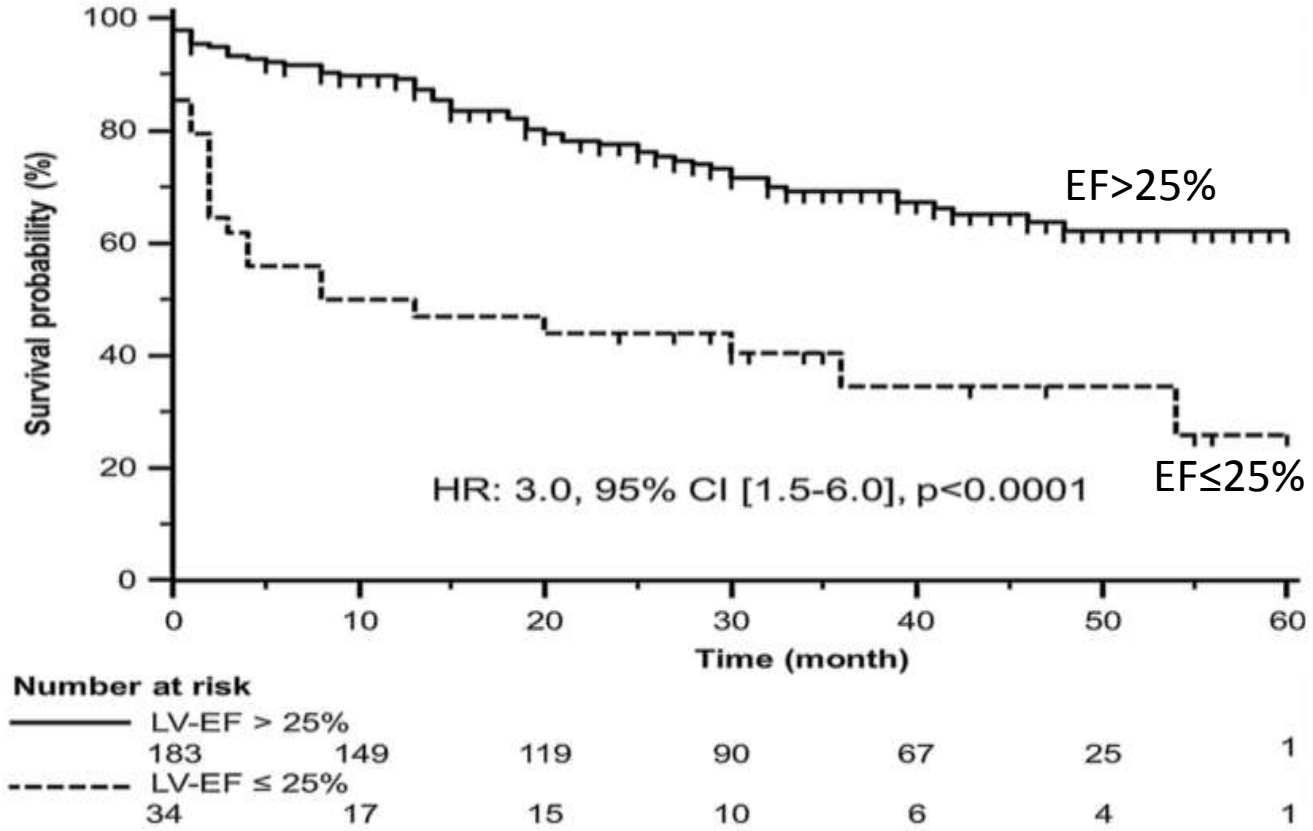
Rudolph et al, Eur J Heart Failure 2013

Long-Term Outcome of Patients with Severe Biventricular Heart Failure after MitraClip

Predictive valve of LVEF

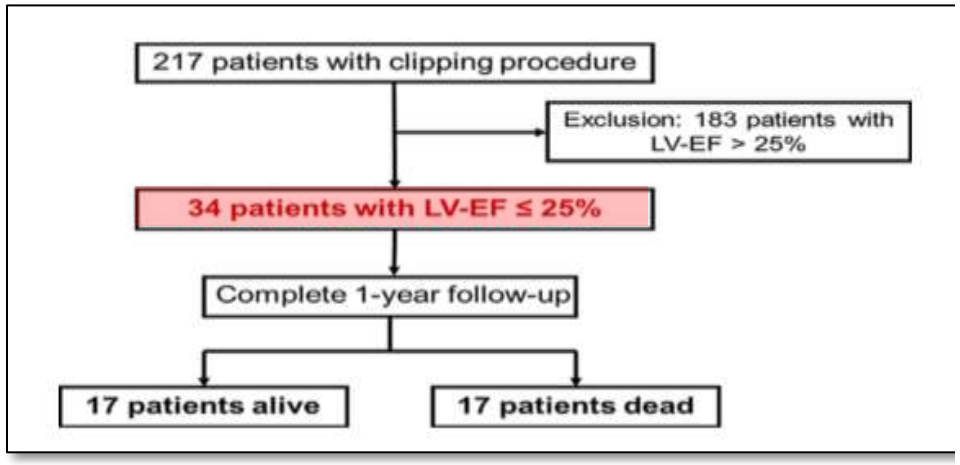


None of the patients met the inclusion criteria of EVEREST II



Long-Term Outcome of Patients with Severe Biventricular Heart Failure after MitraClip

Predictive valve of PASP + RV function



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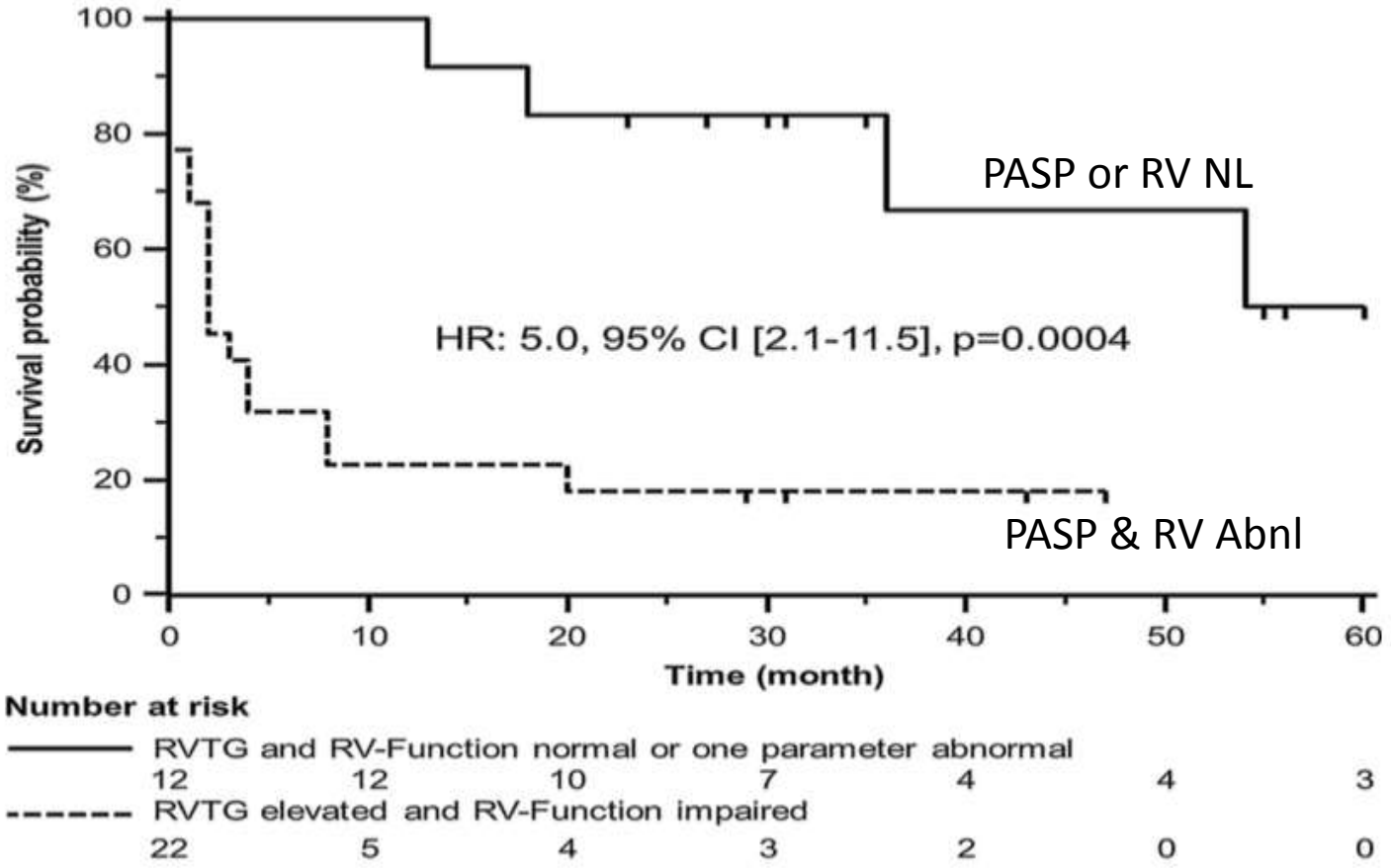

Thank you for your kind Attention!