

Current and Future Trials on Transcatheter Mitral Valve Repair/Replacement

Saibal Kar, MD, FACC, FSCAI

Professor of Medicine, UCLA School of Medicine

Los Robles Regional Medical Center,

Los Angeles, CA

Disclosure Statement of Financial Interest

Saibal Kar, MD, FACC

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria
- Other Financial Benefit

Company

- Abbott Vascular, Boston Scientific, Gore, Edwards Lifesciences
- Abbott Vascular, Boston Scientific, Gore

Treatment of Mitral Regurgitation

- Treatment of MR will require a tool box
 - There is role for both replacement and repair
- Repair where possible is preferable
- Replacement is required
 - Non repairable valve
 - Combined MR/MS
 - Functional MR ??

Percutaneous therapy for mitral regurgitation

- Percutaneous MV repair is considered as standard therapy for selected patients with severe MR
 - Excellent safety
 - Compatible efficacy
 - Durability up to 4 years
- There are several percutaneous MV replacement devices, but they are still in FIM or preclinical studies

Commercial TMVR/r Devices Landscape

- MitraClip:
 - PMR or DMR (10/24/2013): prohibitive surgical risk
 - SMR or FMR (03/14/2019): all surgical risk
- SAPIEN 3:
 - Mitral valve-in-valve (06/05/2017): high or greater surgical risk

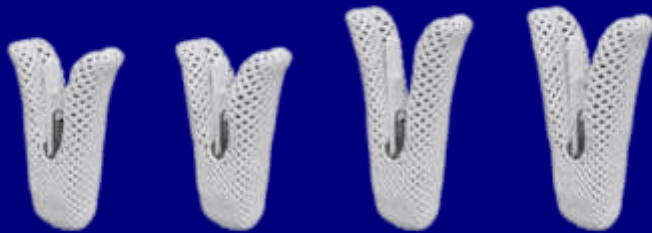
Investigational TMVR/r Devices Landscape

- Pivotal:
 - Intrepid; Tendyne; Carillon; Cardioband; Neochord; MitraClip; PASCAL
- Early feasibility study
 - Neovasc; EVOQUE; CardioValve; Highlife; AltaValve; Transcatheter Mitral Cerclage Annuloplasty (TMCA); M3; MVRx; Caisson; Accucinch



The 4th Generation MitraClip: MitraClip G4

Finally



WIDER CLIP ARMS, 4 CLIP SIZES

Provide increased coaptation area with wider Clip options

CONTROLLED GRASPING ACTUATION

Ability to simultaneously as well as optimize individual leaflet grasping

CONTINUOUS LAP MONITORING

Integrated left atrial pressure monitoring capability in the SGC

DELIVERY SYSTEM DESIGNED FOR THE MITRAL VALVE

Precise and predictable steering specifically for the mitral valve

MitraClip G4 commercial available in US, CE Mark approval pending

Baseline TEE : X plane

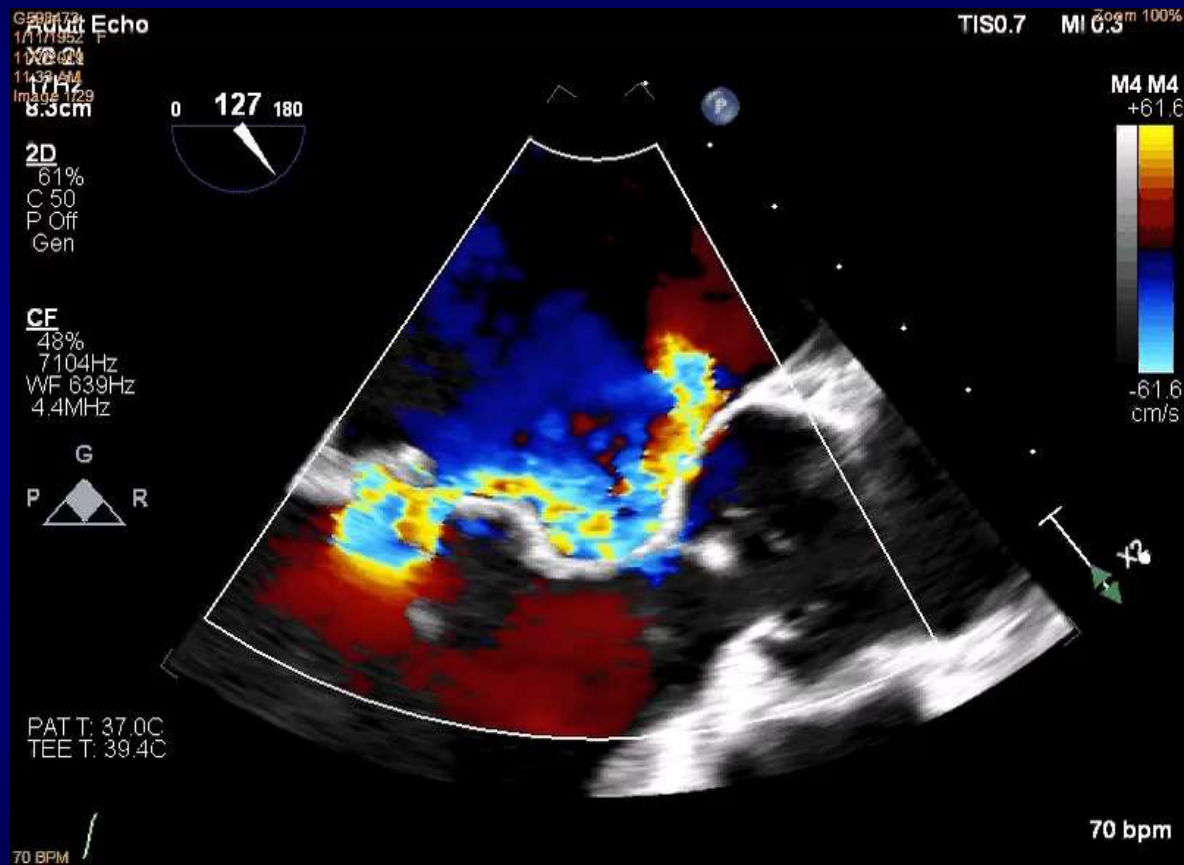


Bicommissural view

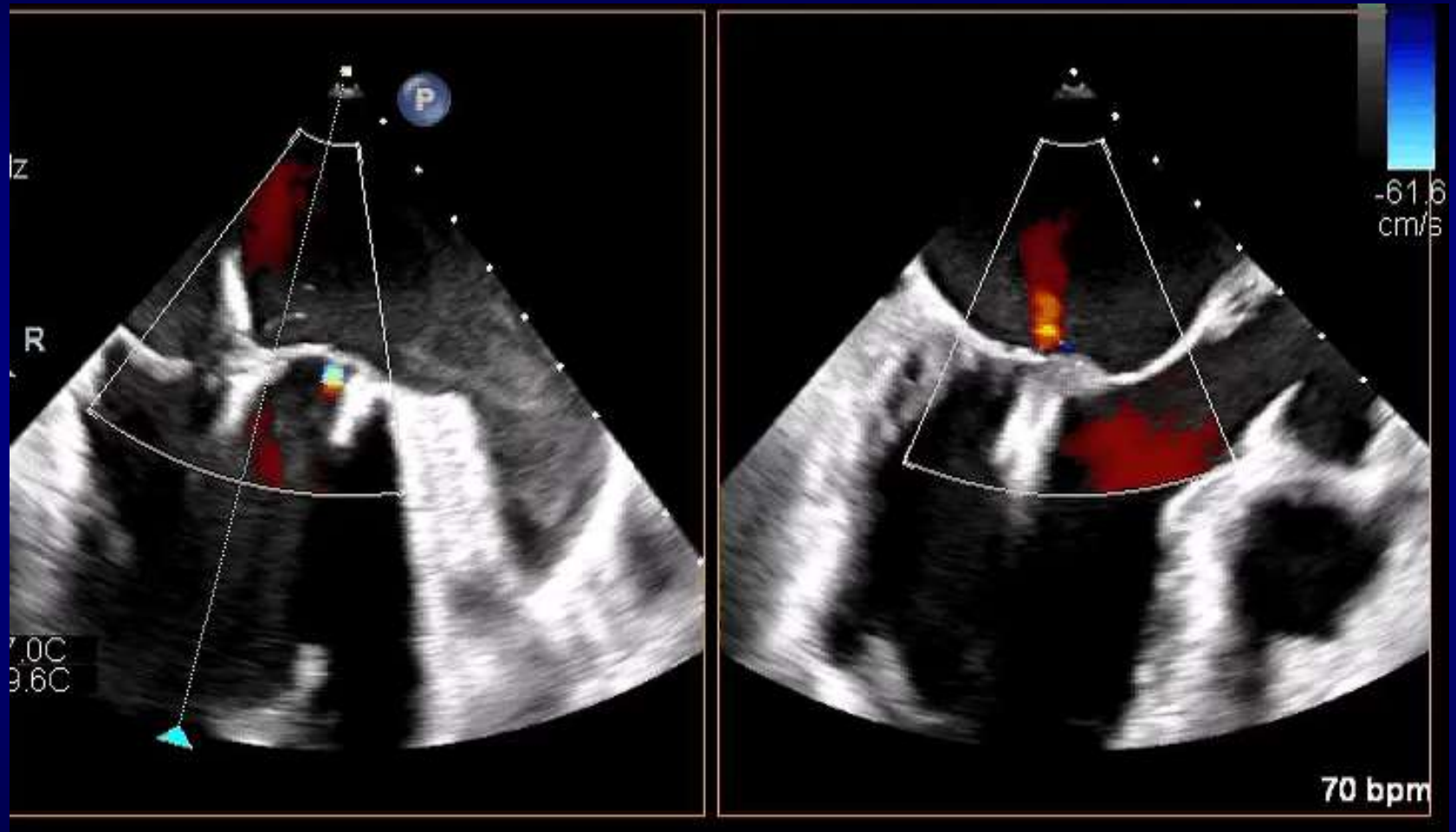


Left ventricular outflow tract view

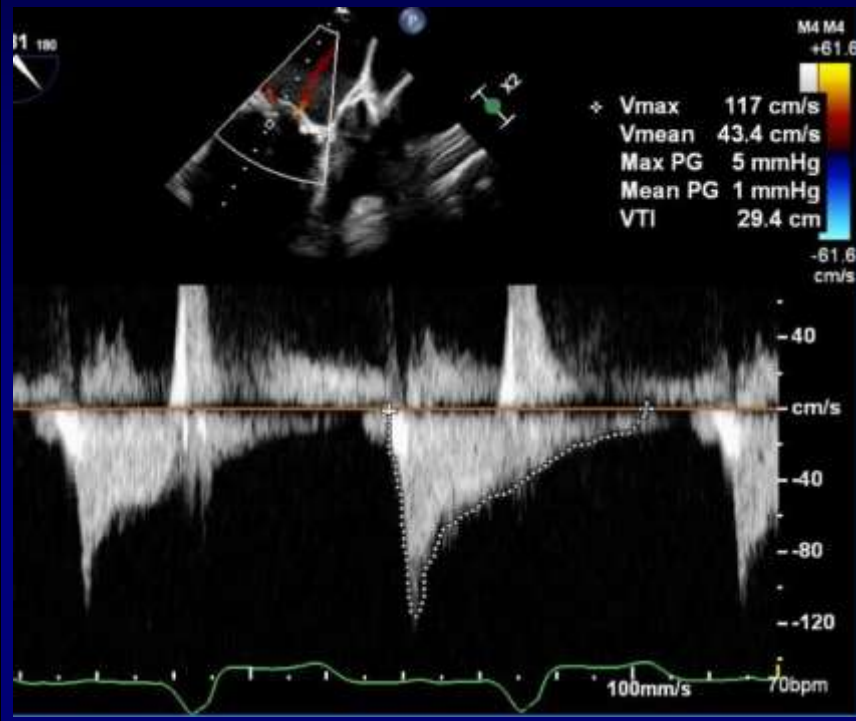
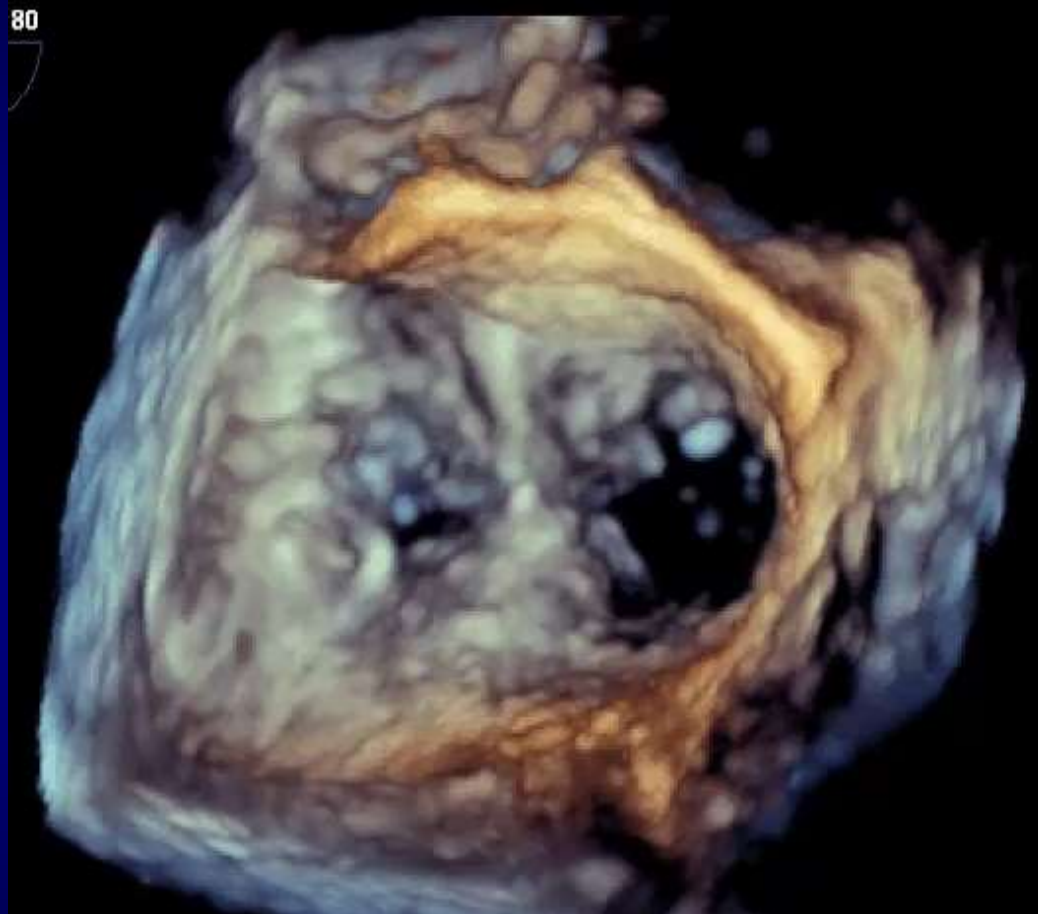
Baseline TEE : LVOT view with color



Disappearance of MR



Creation of bridge with no significant gradient

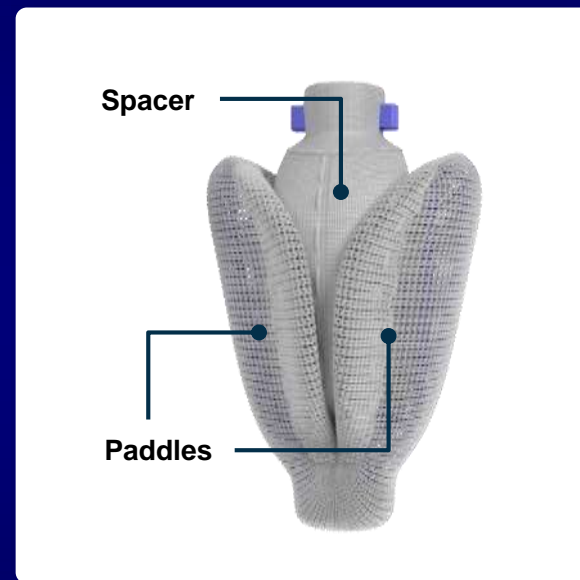


The PASCAL Implant Contains Three Differentiated Features for Efficacy and Safety

Central spacer

Broad, contoured paddles

Independent leaflet capture



CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.

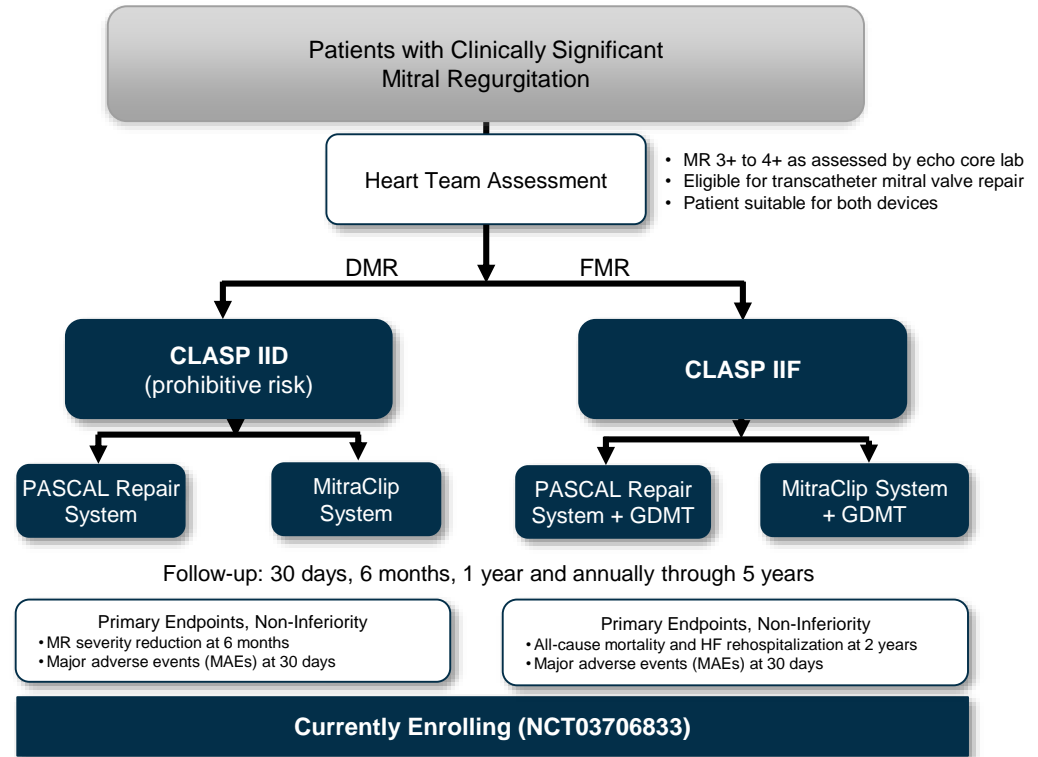
Clinical summary: PASCAL

- The CLASP I study is completed
 - Safe
 - Effective uptill one year
- CE Mark approved in Feb 2019
- Investigtional in US
- Randomized study vs MitraClip is ongoing in the US

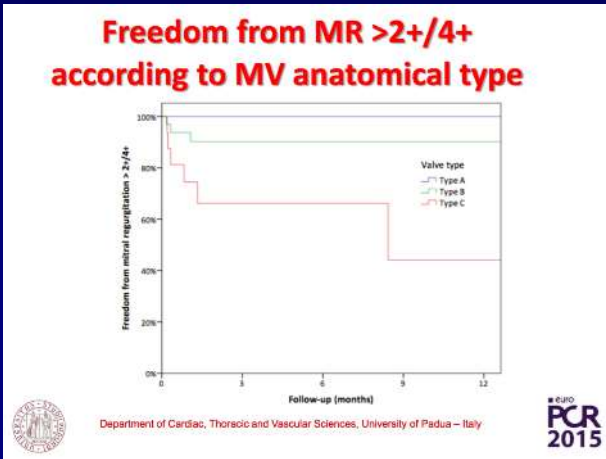
THE CLASP IID/IIF TRIAL

The Edwards PASCAL TrAnScatheter Mitral Valve RePair System Pivotal Clinical Trial (CLASP IID/IIF Trial)

- Prospective, multicenter, randomized, controlled pivotal trial
- Purpose | Evaluate the safety and effectiveness of the PASCAL Repair System compared to the MitraClip System in patients with degenerative and functional mitral regurgitation
- IID Principal Investigators
 Scott Lim, MD
 Robert Smith, MD
 Linda Gillam, MD
- IIF Principal Investigators
 Jeff Popma, MD
 Vinod Thourani, MD
 Paul Grayburn, MD



NEOCHORD



Type A: Isolated P2 prolapse/flail

Type B: Multisegment prolapse/flail (P1-P2, P2-P3 or P1-P2-P3)

Type C: Anterior Prolapse/flail, Paracommissural, Annular and Leaflet Calcifications

Courtesy of R. Colli, Padova

Clinical Summary: Neochord

- CE Mark approved
- >1000 cases
- Ideal for simple prolapse of P2, with non dilated annulus
- Has been tried with transcatheter annuloplasty techniques
- Ongoing clinical trial in US: Neochord vs open surgical repair
- Transseptal approach is being developed

Carillon and Cardioband devices

- Carillon indirect annuloplasty Device
 - Randomized sham controlled study
 - Carillon vs GDMT
 - Grade 2 to 4 MR functional MR
- Cardioband device
 - Following COAPT change of design of study

Transcatheter Mitral Valve Replacement studies

Tendyne and Intrepid valves have most largest clinical experience

Pivotal Phase

Transapical



Tendyne TMV



Medtronic Intrepid™ TMVI

Comparison of SUMMIT and APOLLO

	SUMMIT	APOLLO
Investigational Device	Tendyne™ TMVI	Intrepid™ TMVI
Valve Securement	Tether and apical pad	Cleats
Retrievability	Fully-retrievable after deployment until final tether cut	Retrievable until deployed
No. Valve Sizes	23 total (15 SP, 8 LP)	3
Delivery Catheter	36 Fr	35 Fr
Control Treatment	MitraClip	Mitral Valve Surgery
No. Randomized Subjects	382	450-650
No. Non-randomized Subjects	313	250-550
No. MAC Subjects	103	N/A
Anatomic Screen Pass Rate	48% (57/118)	42% (154/364)

Transseptal TMVR

Early Feasibility Trial phase

- EVOQUE
- M3 Edwards TMV
- Cardiovalve
- Highlife

Edwards SAPIEN M3 System

Dock Delivery

SAPIEN M3 Dock



SAPIEN M3 Dock Delivery System



Valve Delivery

SAPIEN M3 Valve



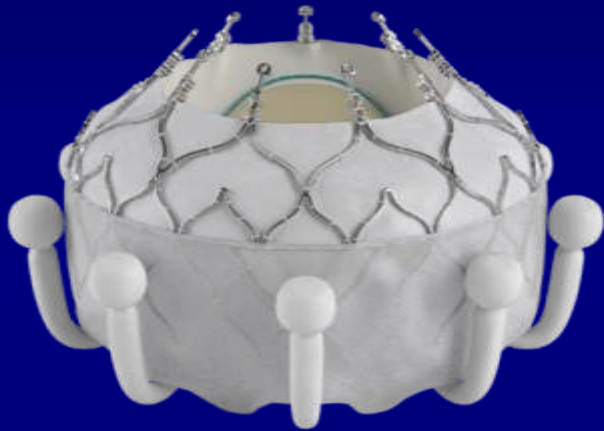
Commander Delivery System



Final Implant



EVOQUE Mitral Valve Replacement System



- **Unique anchoring mechanism utilizes annulus, leaflets, and chords, respecting the native mitral anatomy**

- **Intra-annular sealing skirt and frame to minimize PV leak**

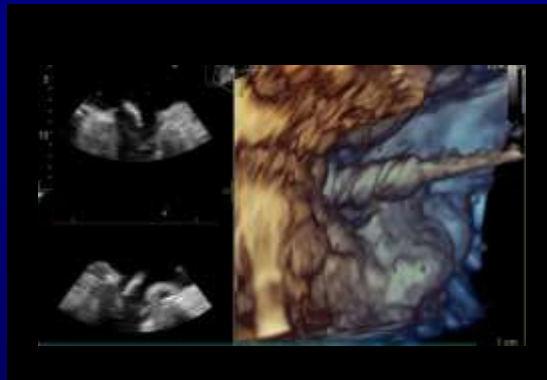
- **Low atrial and ventricular profile to reduce procedural complications**

- **Integrates Edwards bovine pericardial leaflet design and tissue treatment**

- **Both valve sizes (44 and 48 mm) compatible with one size delivery system**

EVOQUE Delivery System

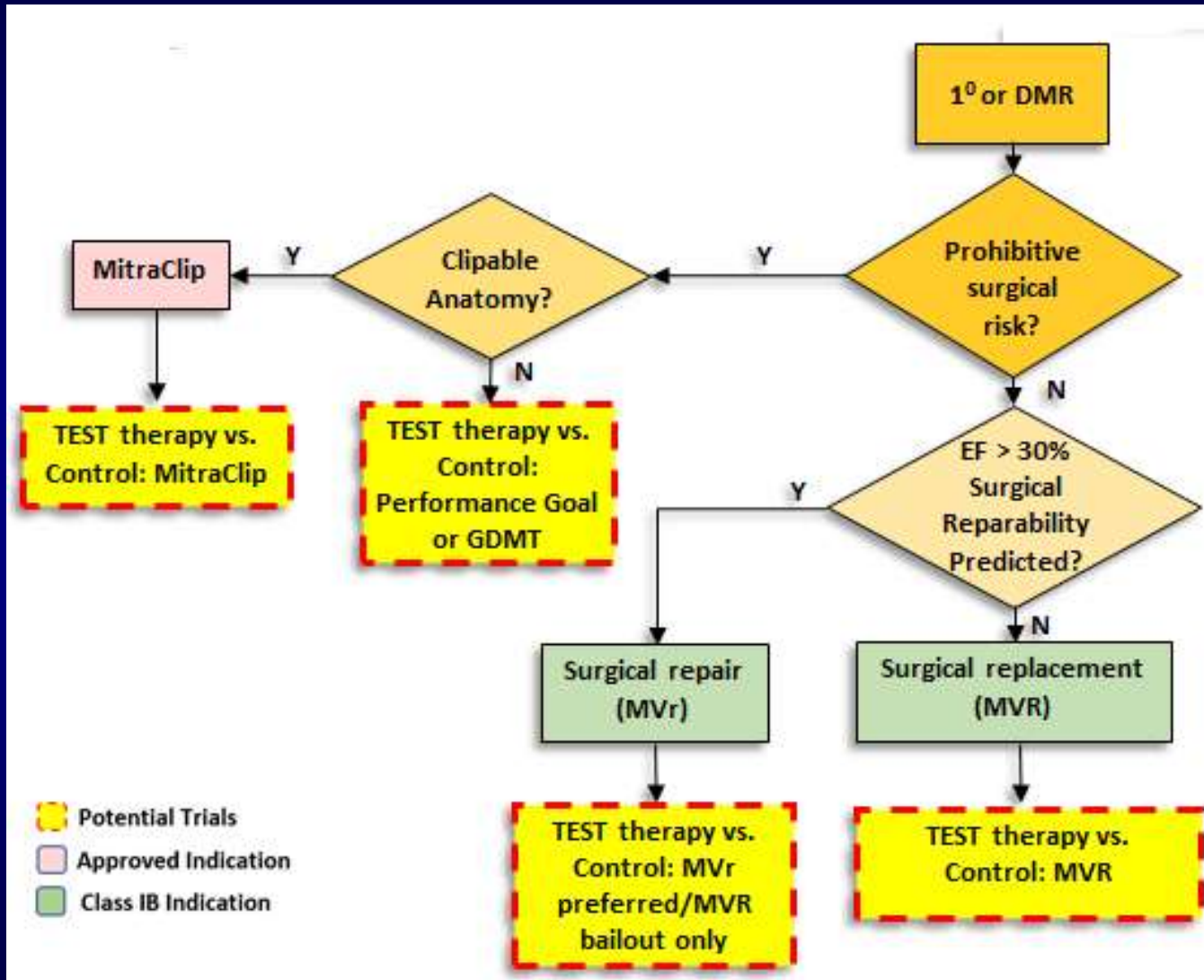
- **Low profile 28Fr transseptal steerable delivery system (for both valve sizes) increases maneuverability and may reduce the need for septal closure**
- **Stabilizer system allows for increased ease of control during procedure**
- **Multiple planes of flexion enable coaxiality**
- **Independent depth control allows for precise positioning**



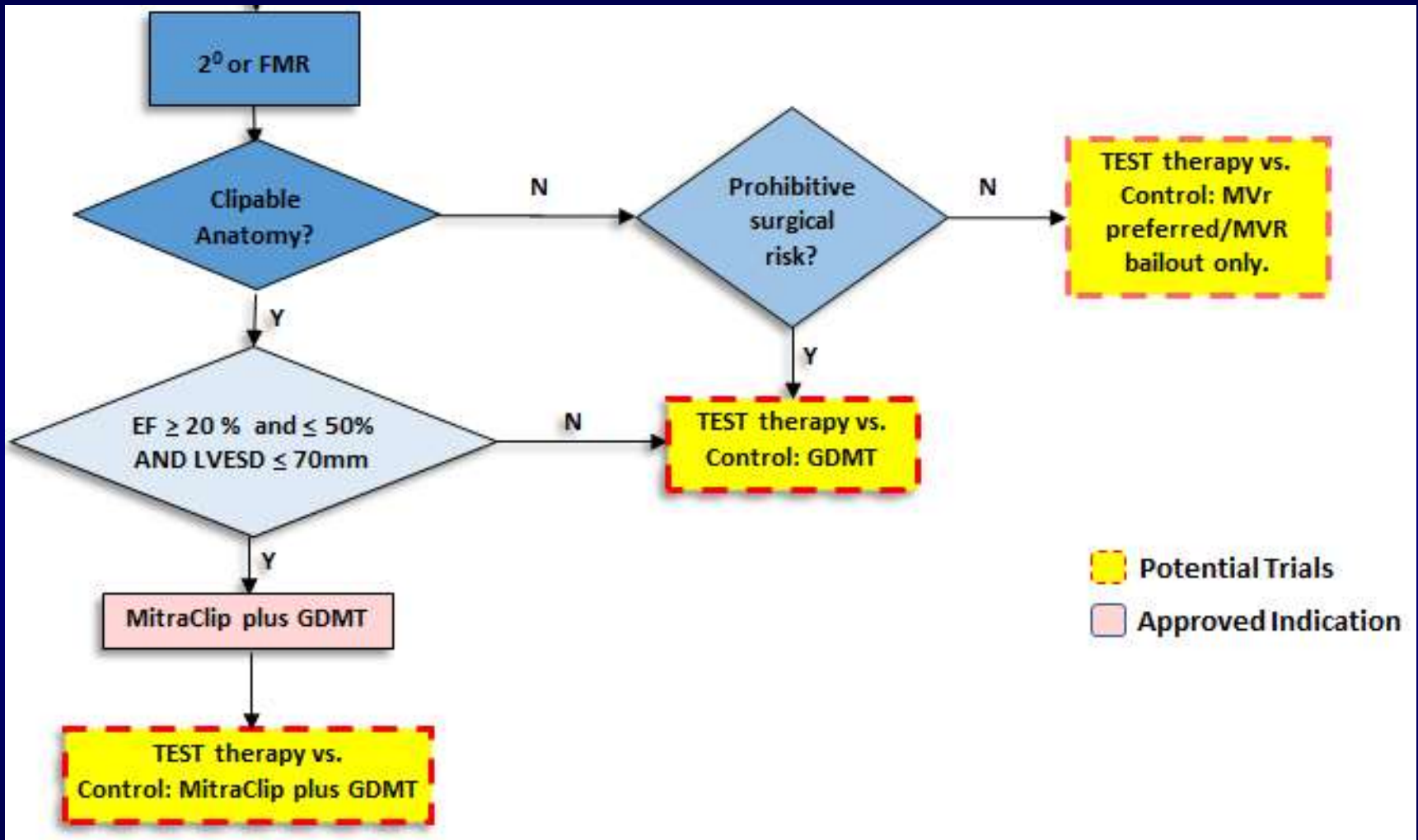
Courtesy of Howard G. Herrmann, MD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

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Potential Trials for DMR



Potential Trials for FMR



Tiara TMVI



- Early transapical experience
- Most cases were compassionate cases done in Canada and Europe
- Early feasibility study in US is not enrolling patients

Repair vs. Replacement

- Percutaneous MV replacement seems technically more complex than percutaneous MV repair
- In most patient cohorts, surgical MV repair results in superior outcomes to replacement
- Percutaneous MV replacement may need to be applied in patients who would also get a surgical replacement in operating room

Conclusions

- Transcatheter Mitral Valve implantation is much more challenging than TAVR
- Unique challenges,
- Several devices are in very early phases of clinical trial
- In the light of Mitraclip, there will be challenges in case selection of transcatheter TMVI