Mitral Valve Interventions:
What's Next?

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Disclosures

Grant Support/Drugs

- MyoKardia/BMS

Grant Support/Devices

- Edwards Lifesciences
- Boston Scientific
- Corvia
- I-Rhythm

- Abbott Vascular
- CathWorks
- Phillips
- Zoll/Therox

Consulting/Advisory Boards

- Medtronic
- Boston Scientific
- Corvia

- Edwards Lifesciences
- Abbott Vascular
- Impulse Dynamics

What's Next in Mitral Valve Interventions?

- Current guidelines– where do things stand?
- Expanding indications for TEER
- Where will transcatheter mitral valve replacement fit in?

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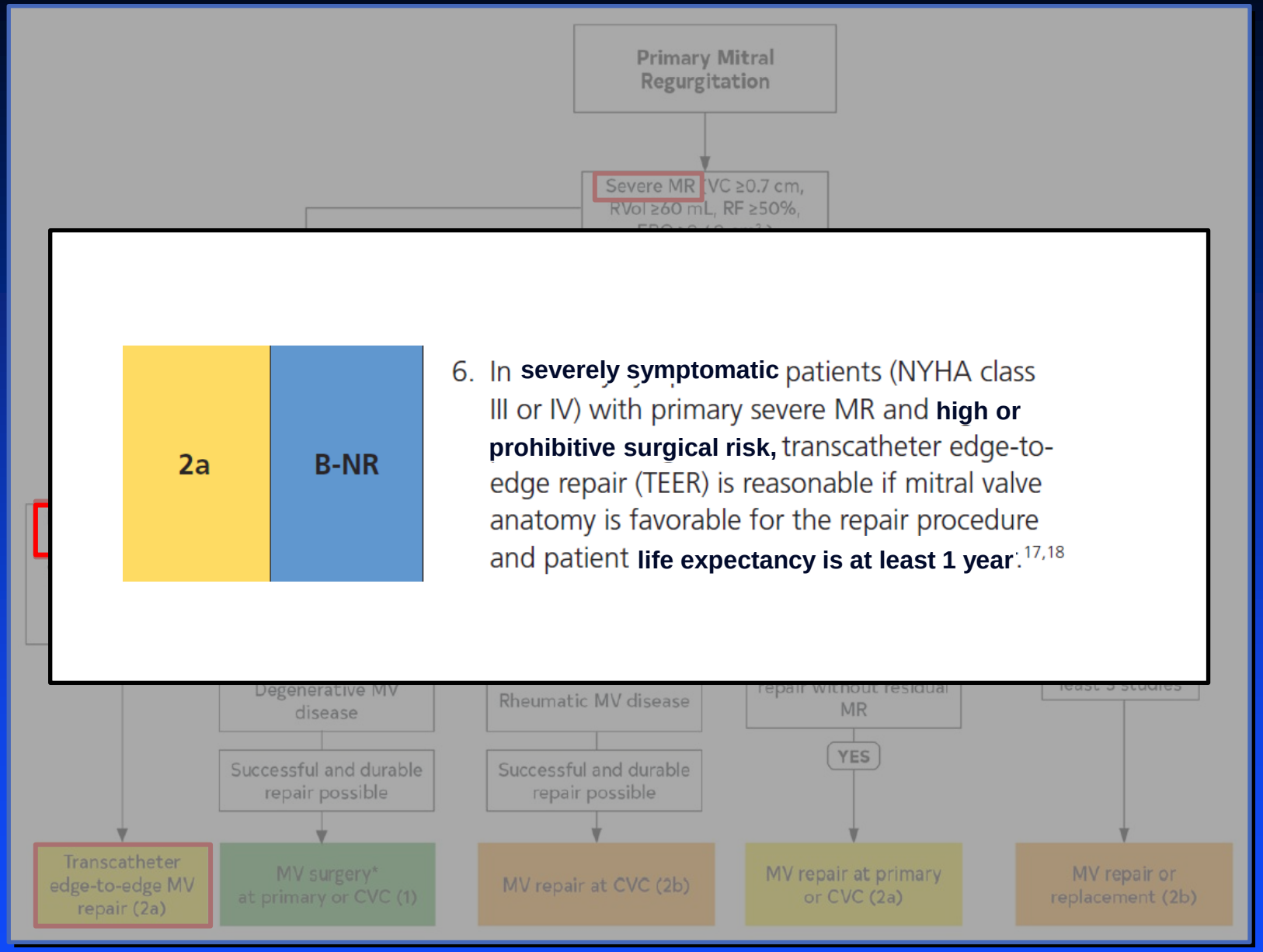
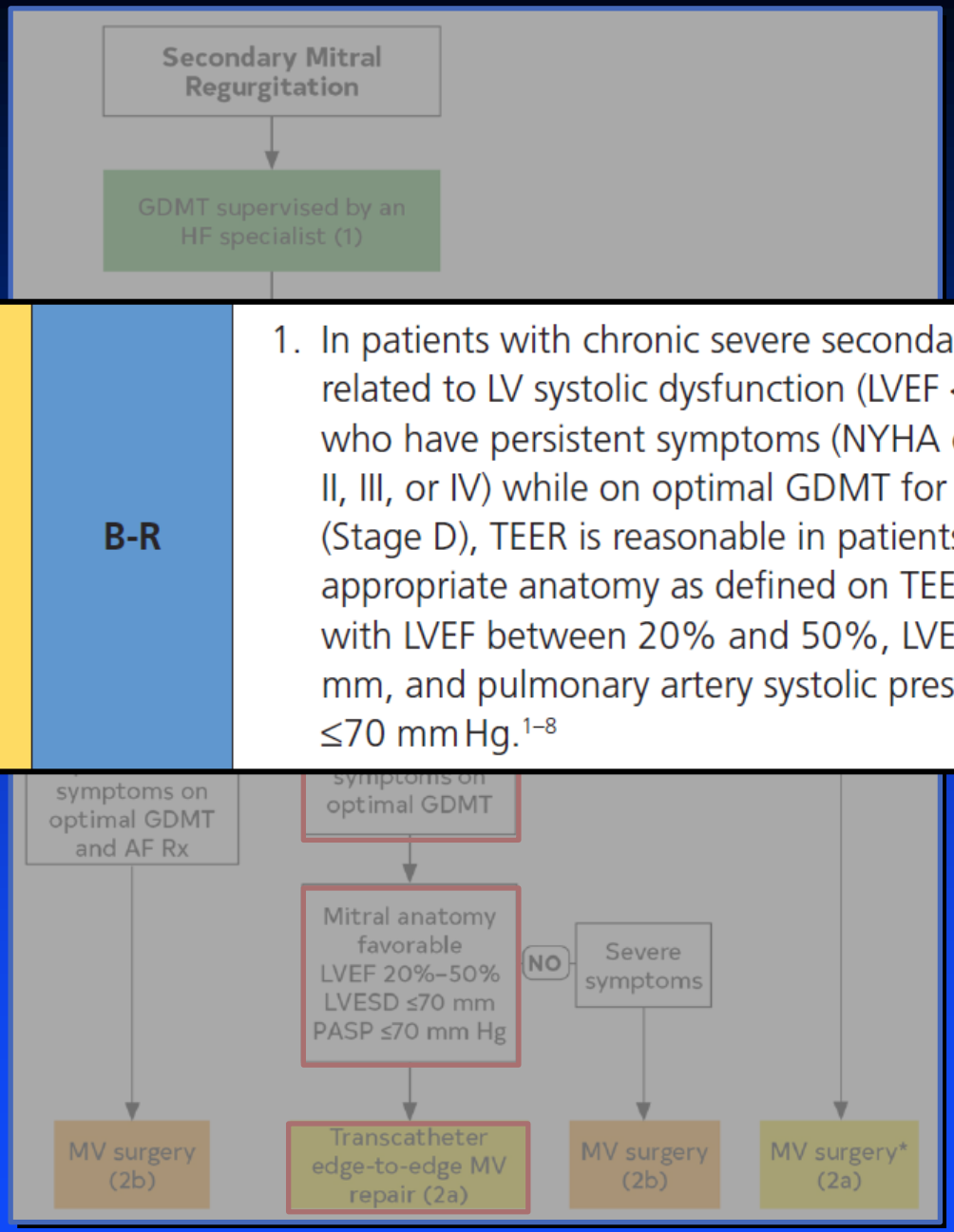
AHA/ACC Guidelines: Primary MR



AHA/ACC Guidelines: Secondary MR



2a	B-R	1. In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal GDMT for HF (Stage D), TEER is reasonable in patients with appropriate anatomy as defined on TEE and with LVEF between 20% and 50%, LVESD ≤70 mm, and pulmonary artery systolic pressure ≤70 mm Hg.[1–8]

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Repair MR Trial: Design

Patient Population

- Patients with **severe primary MR** who are either **age > 75 OR at moderate surgical risk** (defined as STS-PROM >2% or presence of specific comorbidities that increase risk)
- All patients suitable for surgical MV repair (local Heart Team) and M-TEER (Eligibility Committee) with high likelihood of achieving 1+ MR

Study Design

- 500 pts randomized 1:1 to M-TEER with MitraClip or surgical repair
- Approximately 60 study sites in U.S., Canada, and Europe
- Sponsor = Abbott

Slide Courtesy: Dr. Patrick McCarthy

Endpoints and Follow-Up

Primary Endpoints	• Co-Primary Endpoint #1: All-cause mortality, stroke, cardiac rehospitalization, or AKI at 2 years (cardiac hospitalizations in first 30 days excluded) • Co-Primary Endpoint #2: >2+ MR or need for recurrent MV intervention within 2 years
Secondary Endpoints	• Discharge to home • Hospital LOS • QOL (KCQQ) at 2 years
Follow-up	• Through 10 years

Adapted from Patrick McCarthy, MD

PRIMARY Trial

PRIMARY: **P**ercutaneous versus Surgical **R**epair **I**n **M**itral Prolapse **A**nd **R**egurgitation for Patients ≥65 **Y**ears

Jo Chikwe MD, Marty Leon MD, Patrick O'Gara MD, Michael Mack MD, Michael Acker MD, Michael Borger MD, Marissa Miller DVM MPH, Kathleen Fenton MD, Gorav Ailawadi MD MBA, James Gammie MD, Alexander Iribarne MD, Stephen Fremes MD, Marc Gillinov MD, Isaac George MD, Nicholas Freemantle PhD, Judy Hung MD, Bart Ferket MD, Natalia Egorova PhD, Anu Lala MD, Donna Mancini MD, Jessica Overbey MD, Alan Moskowitz MD, Emilia Bagiella PhD, Annetine Gelijns PhD

27th January 2021

National Institutes of Health
National Heart, Lung, and Blood Institute
National Institute of Neurological Disorders and Stroke

Slide Courtesy: Dr Joanne Chikwe

PRIMARY Trial: Design

- ≥ 65 years of age with 3+ or 4+ primary MR
- Accepted clinical indication for valve repair and both surgical and TEER strategies are feasible (Heart Team evaluation)
- Low, intermediate or high surgical risk
- Randomized to surgical mitral valve repair or TEER

PRIMARY Trial: Endpoints

Primary Endpoint

- All-cause mortality, valve re-intervention, hospitalizations/urgent visits for heart failure, or development of ≥ 3+ MR with a minimum follow-up of 3 years post randomization

Secondary Endpoints

- Adequacy of MR correction at 1-year post randomization
- Disease-specific quality of life as measured by the KCCQ through 5 years
- All-cause mortality, and valve re-interventions through 5, 8 and 10 years since randomization

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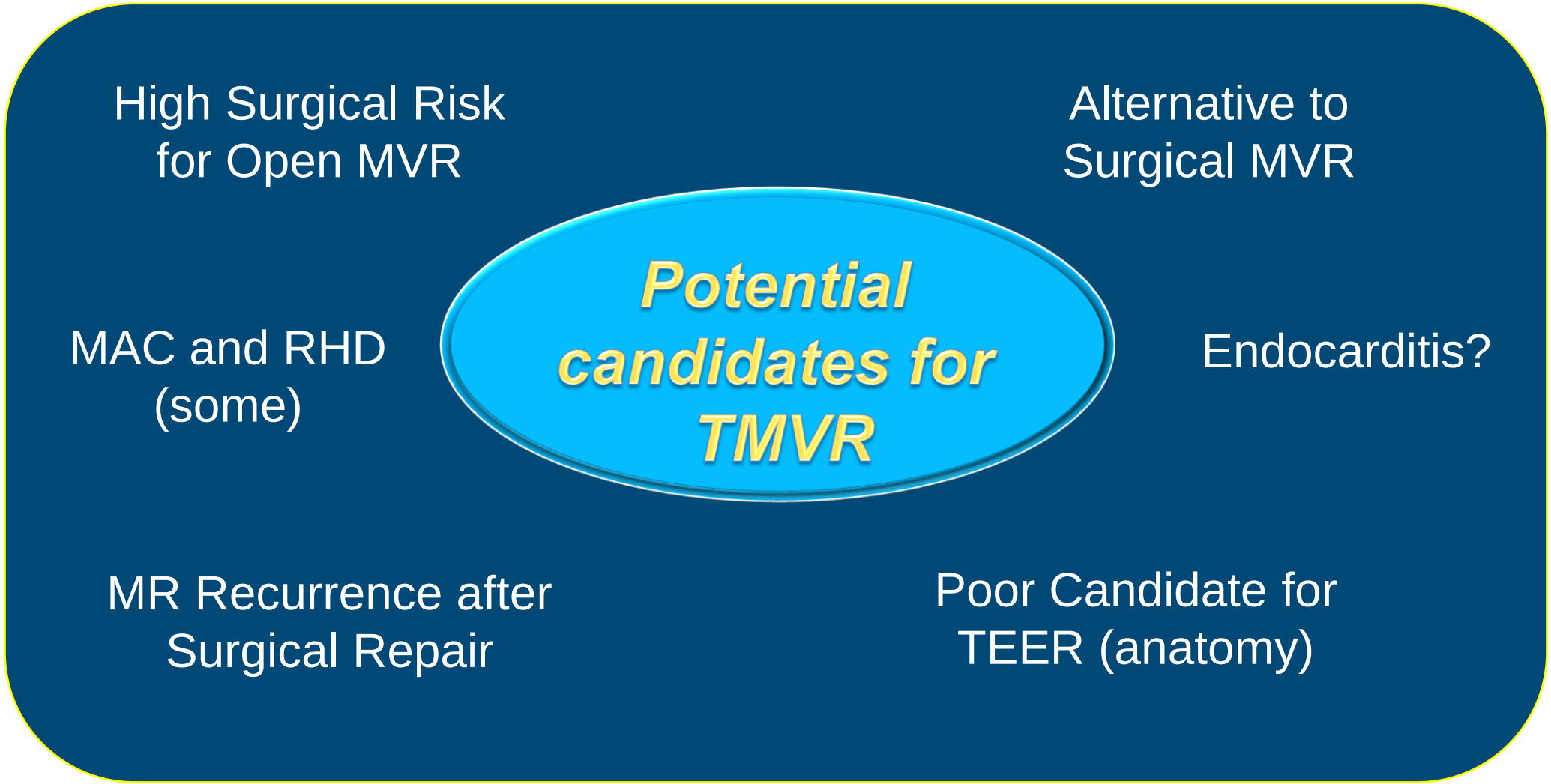
Do We Really Need TMVR?



Why is TMVR Developing More Slowly than Predicted? Technical and Clinical Root Causes

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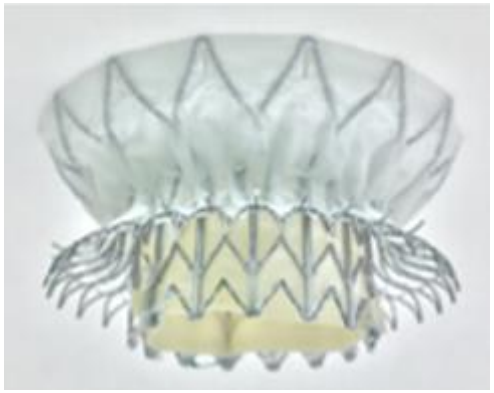
Clinical/Anatomical Market Targets	Resulting Technological + Design Attributes
Large Ventricles	Large Catheter Sizes = TA Route
Large Annular Sizes	High Valve Profiles (Depth into LV)
Non-Calcific Annuli	“Low” Radial Force
Low EF (<30%)	Diverse Methods of Anchoring

Why is TMVR Developing More Slowly than Predicted? Technical and Clinical Root Causes

Clinical/Anatomical Market Targets	Resulting Technological + Design Attributes	TODAY's Challenges (Technical and Clinical)
Large Ventricles	Large Catheter Sizes = TA Route	Large Bore Transseptal
Large Annular Sizes	High Valve Profiles (Depth into LV)	LVOT Obstruction
Non-Calcific Annuli	"Low" Radial Force	Mitral Annular Calcification
Low EF (<30%)	Diverse Methods of Anchoring	Myocardial Interaction in HF patients

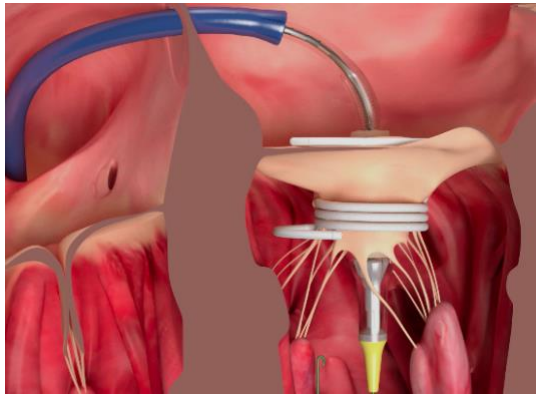
Potential Valve-Related Solutions

Low-profile valves
Minimize footprint in LVOT



Cephea

Leaflet-Dependent Fixation
Retract Anterior Mitral Leaflet



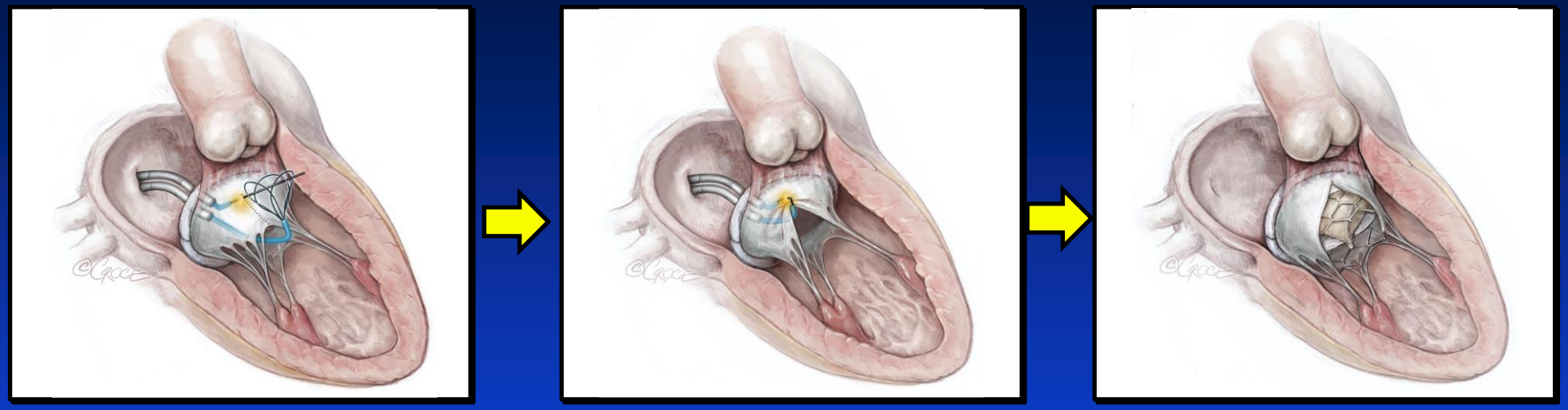
M3 Platform

Atrial Valve
No protrusion into LVOT

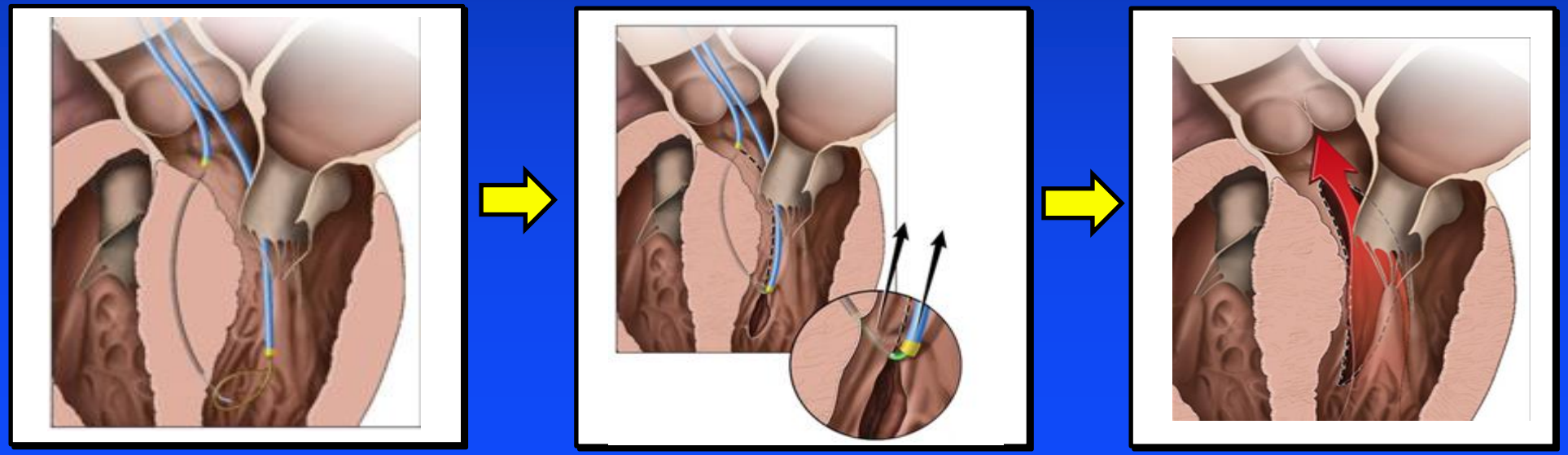
4C AltaValve

LVOT Obstruction: Potential Procedure-Related Solutions

LAMPOON
Splitting Anterior
Mitral Leaflet



SESAME:
Catheter-Based
Septal Myotomy



Figures courtesy of Jaffar Khan, MD

Mitral Valve Therapies: Predictions for the Field

- Given the complexity of the mitral valve complex and the multiple mechanisms of MR, catheter-based approaches to mitral valve therapies will continue to lag behind approaches to the aortic (and tricuspid) valves
- Based on its unparalleled safety and widespread adoption, TEER will remain the mainstay of therapy for the foreseeable future → may extend to intermediate-risk patients with specific anatomic features
- TMVR will initially be approved (and used) almost exclusively for MAC, where surgical outcomes are poor
- True catheter-based “solutions” to MR will require a multi-pronged approach including technology, technique, and combination approaches (“toolbox” approach)