Aortic & Mitral Valve Disease – Surgical Treatments and Future Directions

American Council of Life Insurers, Medical Section Scientific Program 2018

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Department of Cardiovascular Sciences

February 19, 2018

MORSANI
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UNIVERSITY OF SOUTH FLORIDA

USF
HEALTH

Disclosures

None

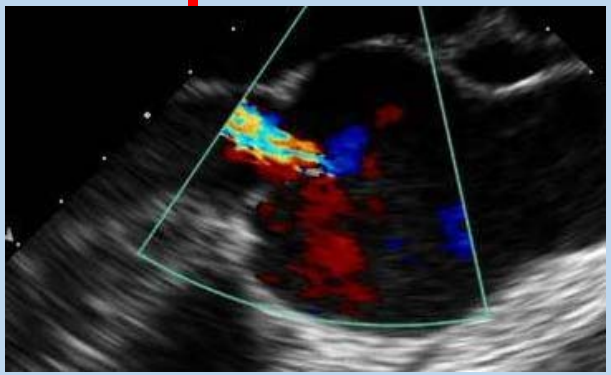
Objectives

- Provide an update on current surgical interventions being done to correct and/or improve common aortic and mitral valve disorders
  - including the rationale behind timing of these interventions.
- Provide an update on minimally invasive valve surgery
  - morbidity and mortality outcomes
  - best suited patient populations
- Discuss postoperative surveillance of patients undergoing heart valve surgery.
- Discuss the morbidity and mortality implications of operative *vs.* non-operative treatment of common aortic and mitral valve disorders

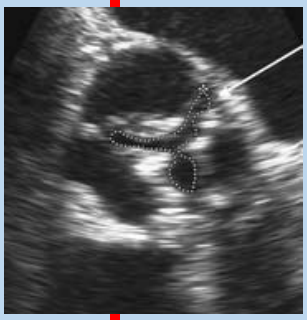
The Aortic Valve

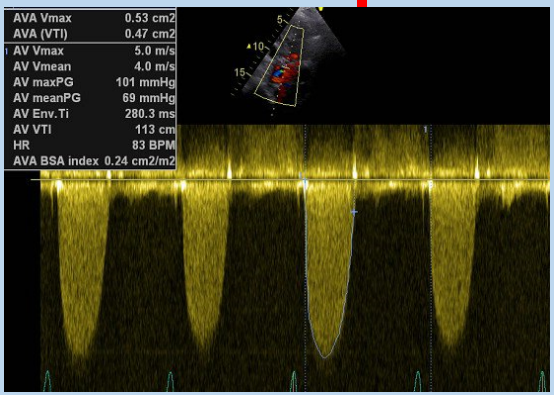
The Mitral Valve

REGURGITATION

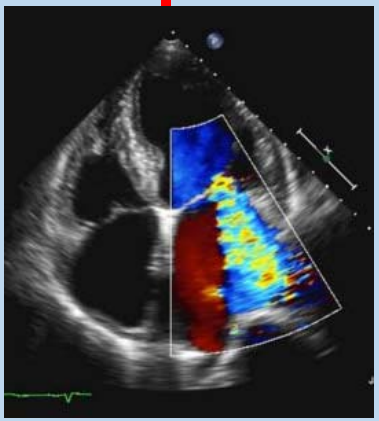


STENOSIS

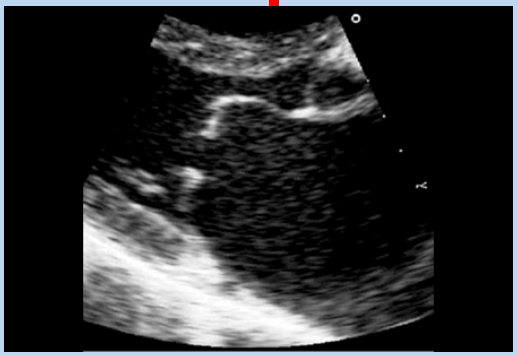




REGURGITATION

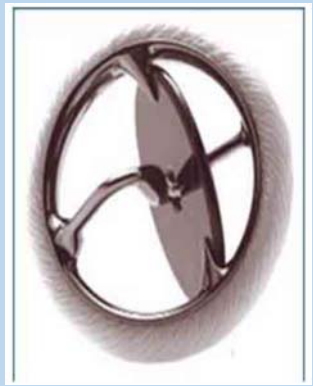


STENOSIS



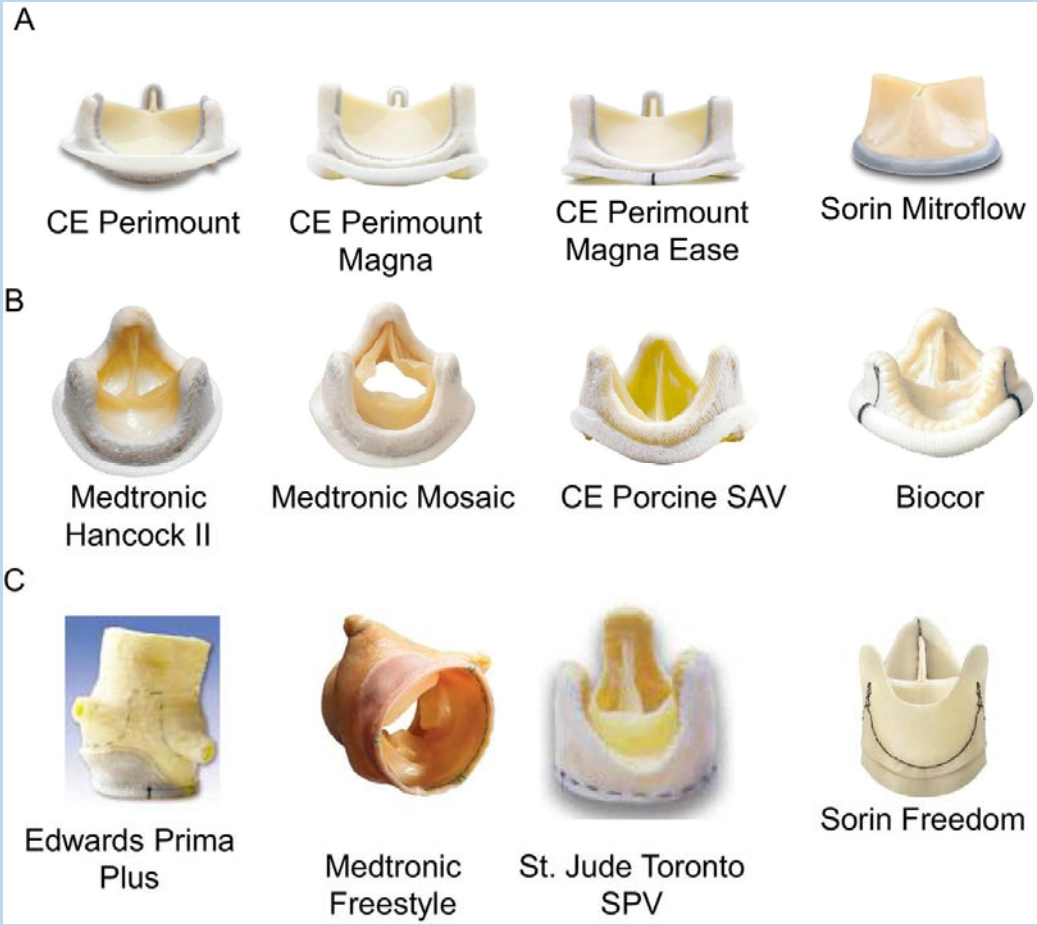
Clevelandclinicmeded.com, Cardiophile.org, epocrates.com, Stanford Echocardiography

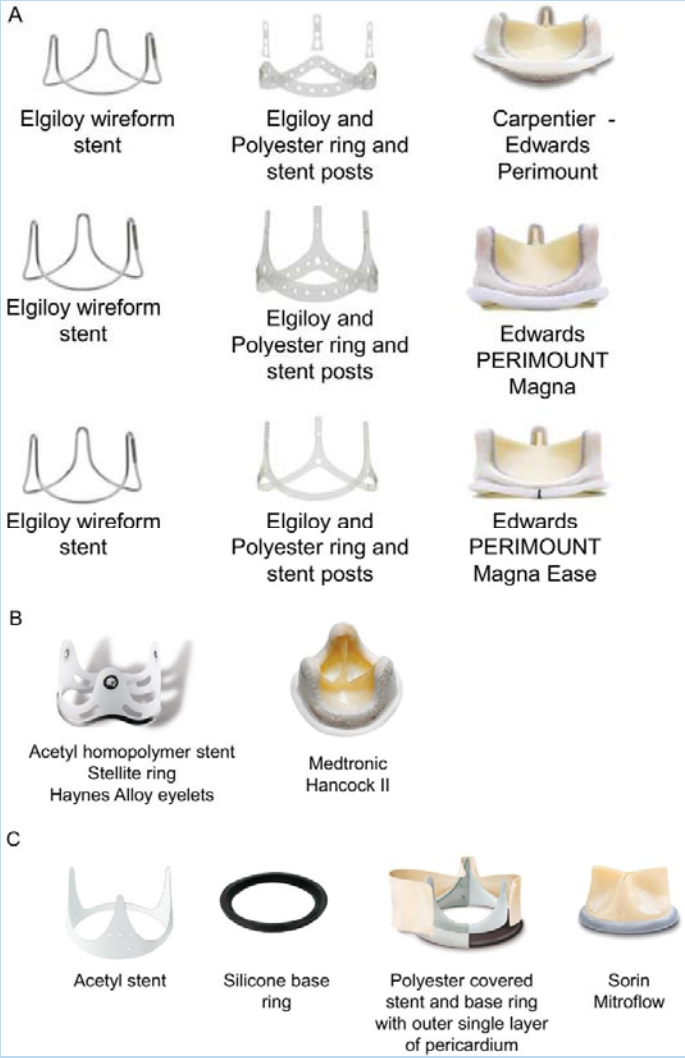
Mechanical Heart Valves



themitralvalve.org

Bio-prosthetic Heart Valves





Piazza et al., JACC Card Intv, 2011

Mechanical problems require a mechanical fix.

. . . . When?

The Aortic Valve

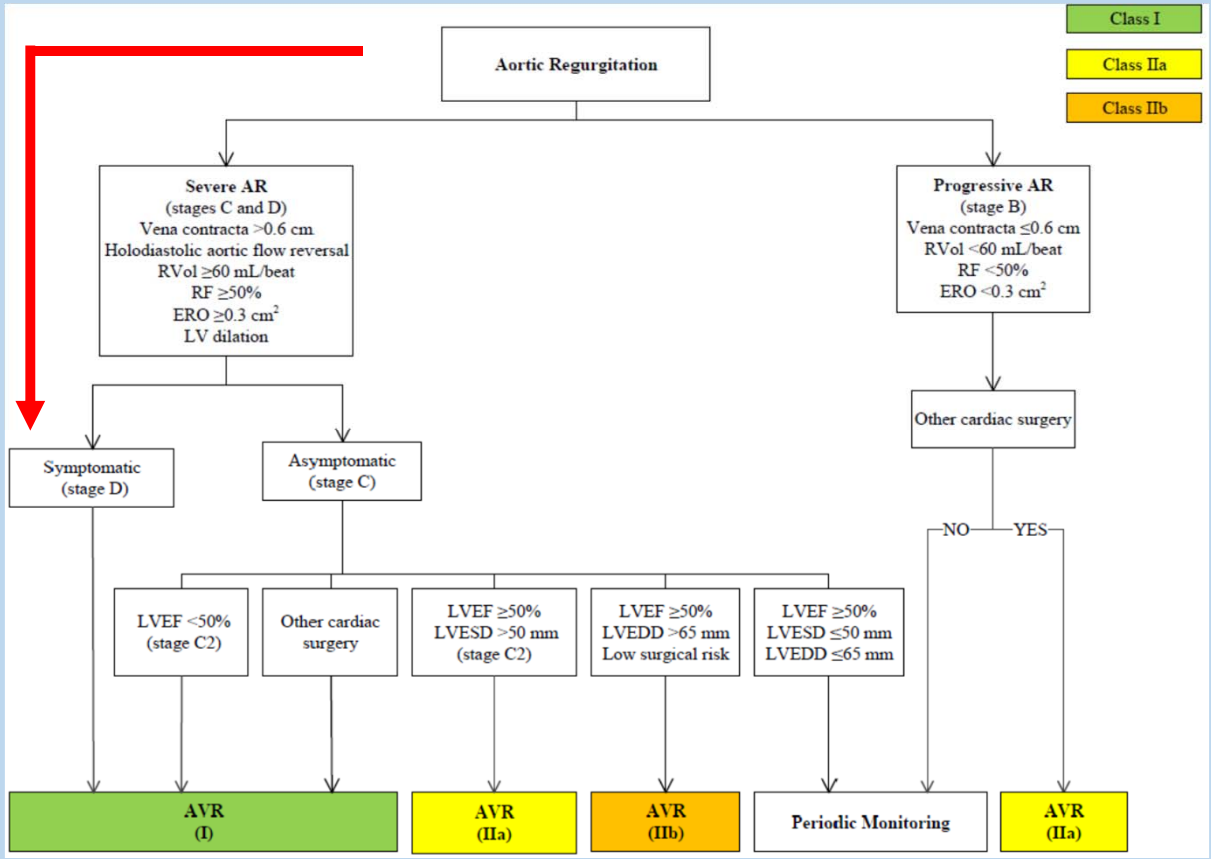
Healthwise, Inc.

The Aortic Valve - Regurgitation

Recommendations	COR	LOE
AVR is indicated for symptomatic patients with severe AR regardless of LV systolic function (stage D)	I	B
AVR is indicated for asymptomatic patients with chronic severe AR and LV systolic dysfunction (LVEF <50%) (stage C2)	I	B
AVR is indicated for patients with severe AR (stage C or D) while undergoing cardiac surgery for other indications	I	C
AVR is reasonable for asymptomatic patients with severe AR with normal LV systolic function (LVEF ≥50%) but with severe LV dilation (LVESD >50 mm, stage C2)	IIa	B
AVR is reasonable in patients with moderate AR (stage B) who are undergoing other cardiac surgery	IIa	C
AVR may be considered for asymptomatic patients with severe AR and normal LV systolic function (LVEF ≥50%, stage C1) but with progressive severe LV dilation (LVEDD >65 mm) if surgical risk is low*	IIb	C

Nishimura et al. Circulation, 2014

The Aortic Valve - Regurgitation

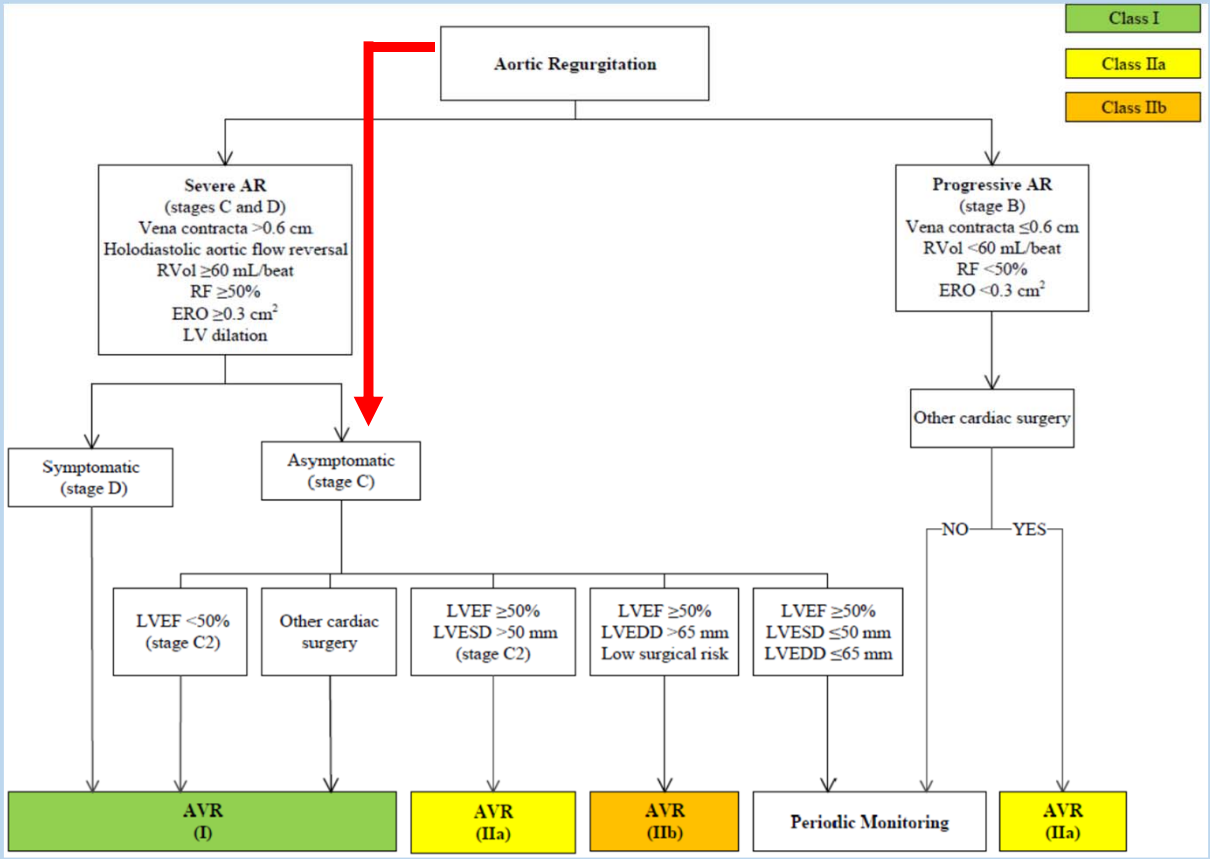


Symptomatic, severe

AVR
(I)

Nishimura et al. Circulation, 2014

The Aortic Valve - Regurgitation



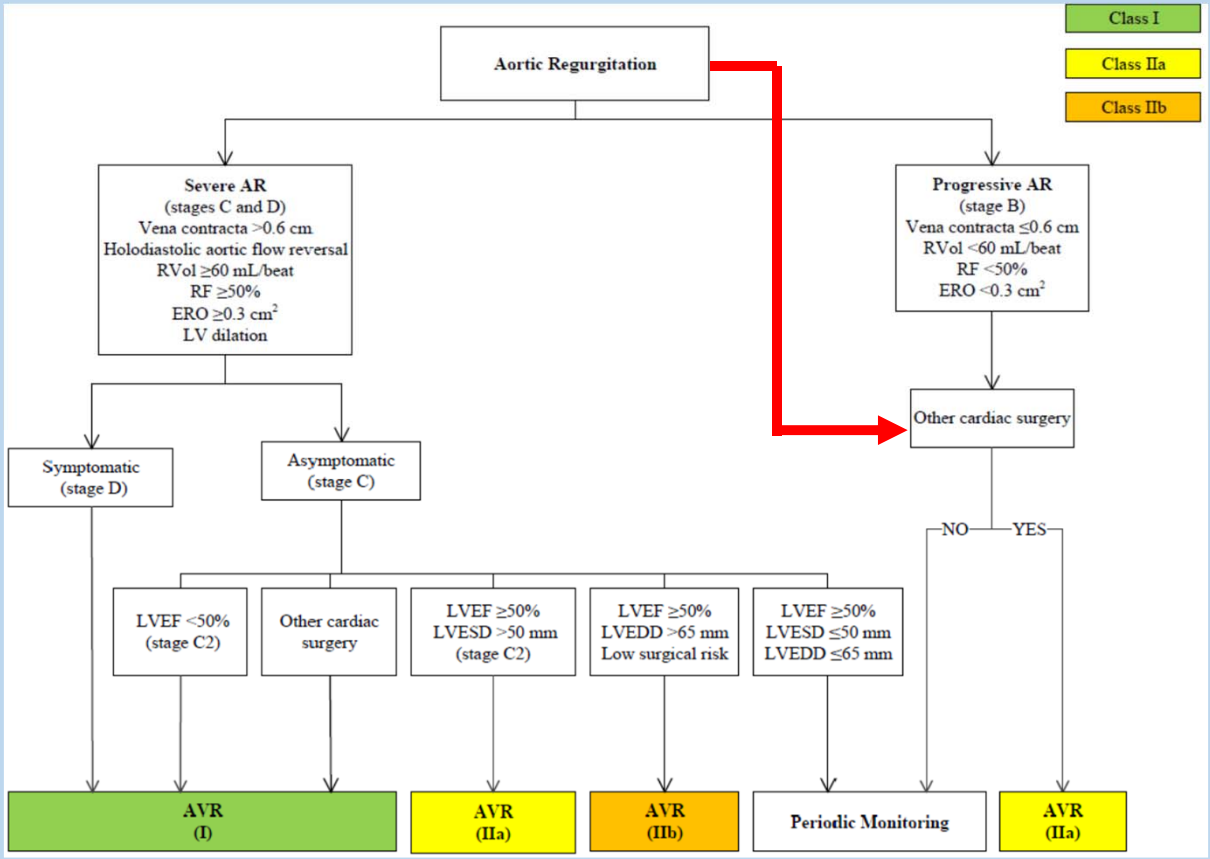
Symptomatic, severe

Asymptomatic, severe with signs of LV dysfunction

AVR (I) | AVR (IIa) | AVR (IIb)

Nishimura et al. Circulation, 2014

The Aortic Valve - Regurgitation



Symptomatic, severe

Asymptomatic, severe with signs of LV dysfunction

Asymptomatic, progressive, with other cardiac surgery

AVR (IIa)

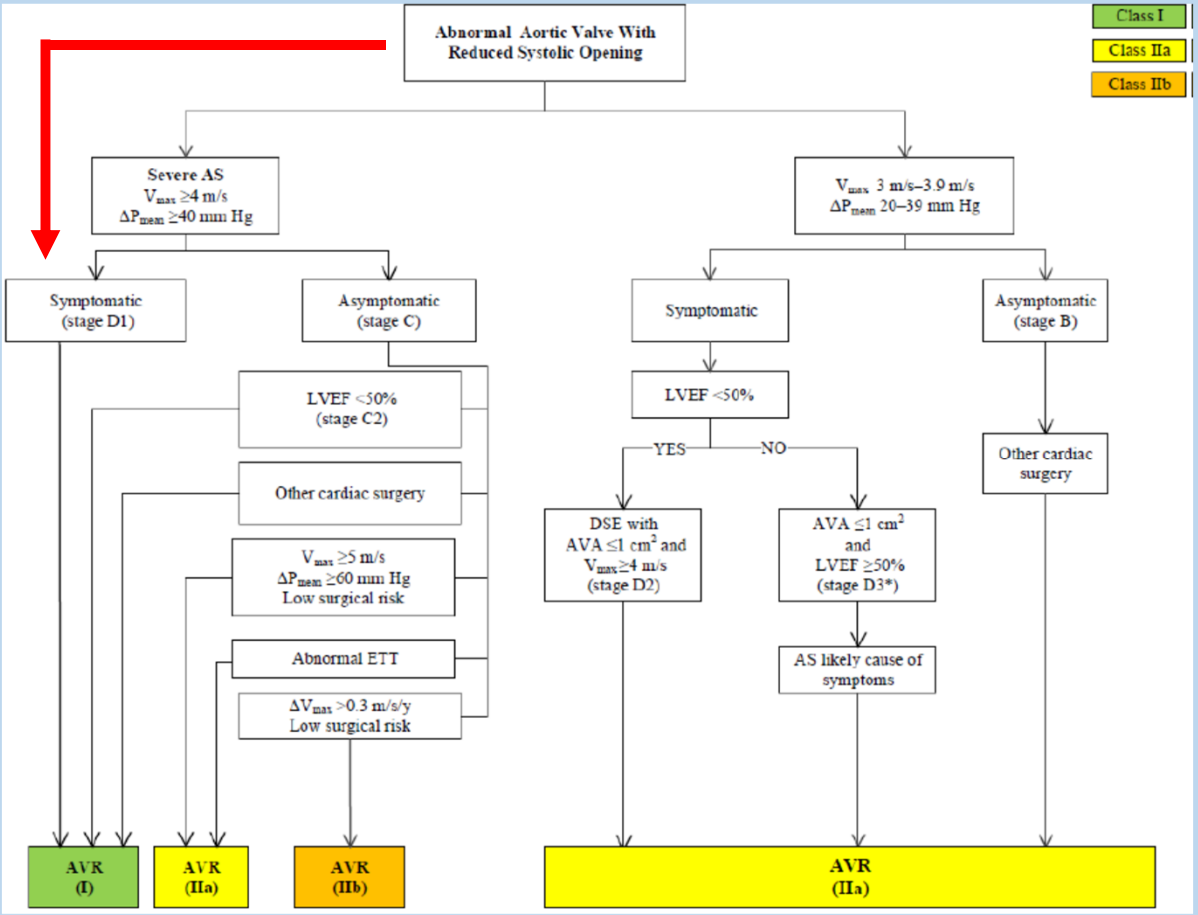
Nishimura et al. Circulation, 2014

The Aortic Valve – Stenosis - timing

Recommendations	COR	LOE
AVR is recommended with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥5.0 m/s) and low surgical risk	IIa	B
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	IIa	B
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm^2 at any dobutamine dose	IIa	B
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa	C
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	IIa	C
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C

Nishimura et al. Circulation, 2014

The Aortic Valve - Stenosis

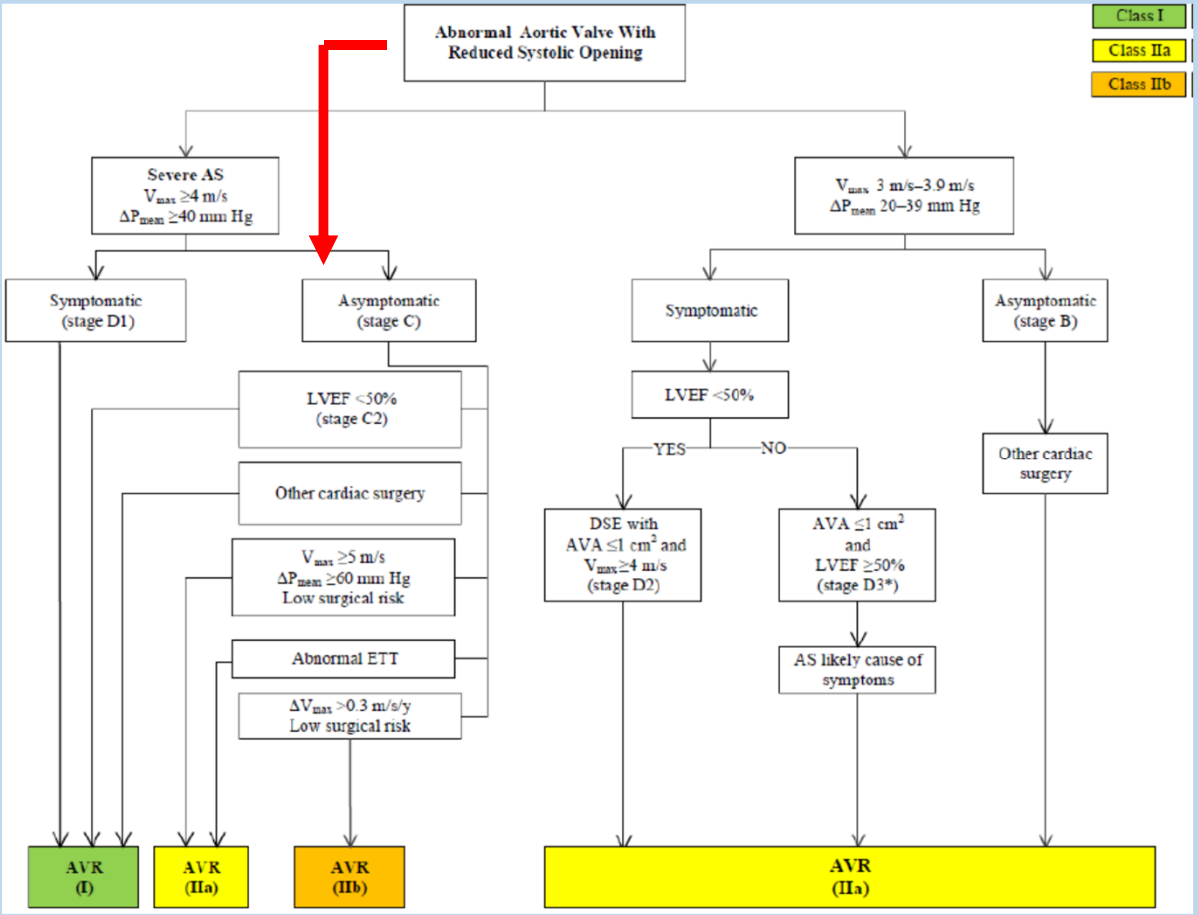


Symptomatic, severe

AVR (I)

Nishimura et al. Circulation, 2014

The Aortic Valve - Stenosis



Symptomatic, severe

Asymptomatic, severe with signs of LV dysfunction or Abnl ETT

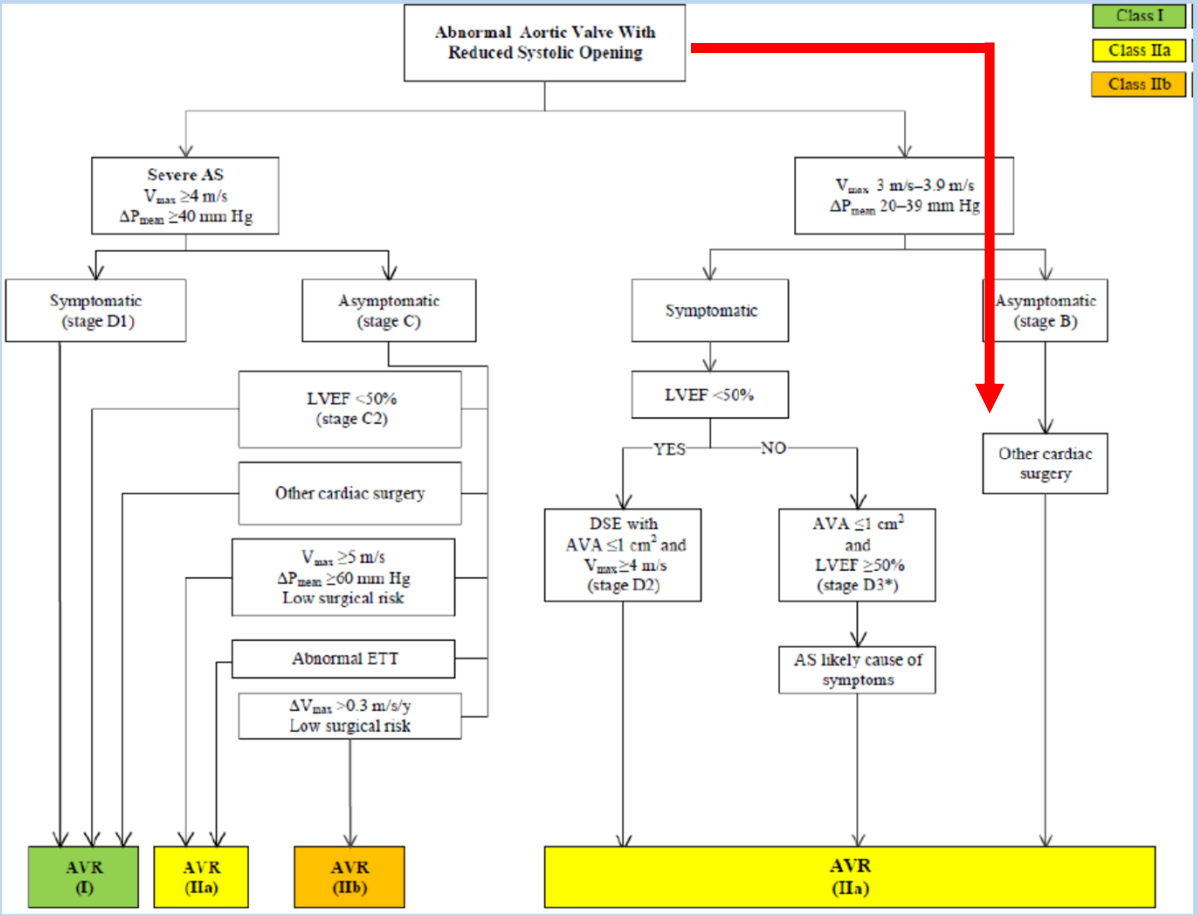
AVR (I)

AVR (IIa)

AVR (IIb)

Nishimura et al. Circulation, 2014

The Aortic Valve - Stenosis



Symptomatic, severe

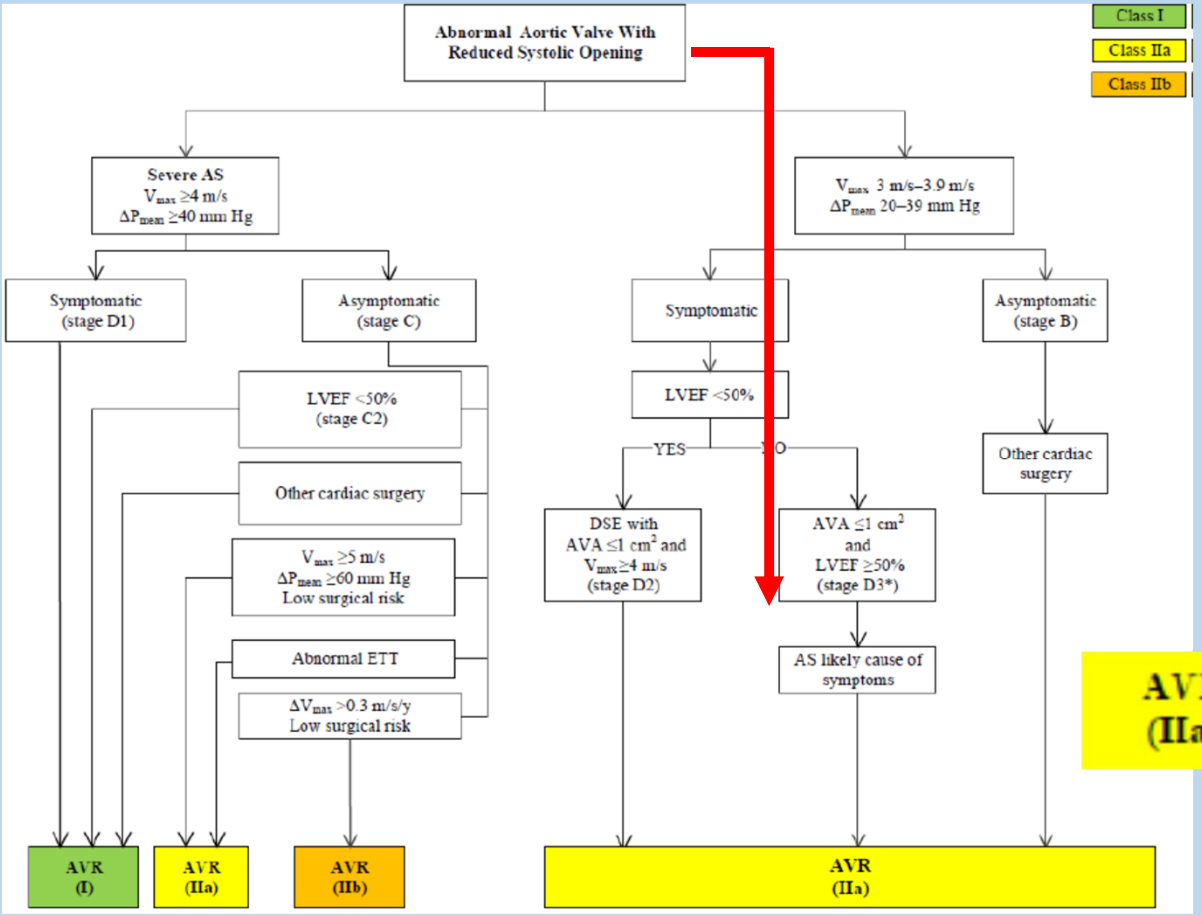
Asymptomatic, severe with signs of LV dysfunction or Abnl ETT

Other cardiac surgery

AVR (IIa)

Nishimura et al. Circulation, 2014

The Aortic Valve - Stenosis



AVR (IIa)

Symptomatic, severe

Asymptomatic, severe with signs of LV dysfunction or Abnl ETT

Other cardiac surgery

Moderate parameters with attributable symptoms or severe findings on DSE

Nishimura et al. Circulation, 2014

The Aortic Valve – Stenosis: tx choice

Recommendations	COR	LOE
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.4) with low or intermediate surgical risk (Section 2.5 in the full-text guideline)	I	A
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo	I	B
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.4) and who have high surgical risk (Section 2.5 in the full-text guideline)	IIa	B
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B

Nishimura et al. Circulation, 2017

Valve selection: bioprosthetic vs. mechanical

I	C-LD	The choice of type of prosthetic heart valve should be a shared decision-making process that accounts for the patient's values and preferences and includes discussion of the indications for and risks of anticoagulant therapy and the potential need for and risk associated with reintervention (141-146).

I	C	A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired.

Nishimura et al. Circulation, 2017

Valve selection: bioprosthetic vs. mechanical

IIa	B-NR	An aortic or mitral mechanical prosthesis is reasonable for patients less than 50 years of age who do not have a contraindication to anticoagulation (141,149,151,155-157).

IIb	C	Replacement of the aortic valve by a pulmonary autograft (the Ross procedure), when performed by an experienced surgeon, may be considered for young patients when VKA anticoagulation is contraindicated or undesirable (167-169).

Younger

IIa	B-NR	For patients between 50 and 70 years of age, it is reasonable to individualize the choice of either a mechanical or bioprosthetic valve prosthesis on the basis of individual patient factors and preferences, after full discussion of the trade-offs involved (141-145,157-160).

Older

IIa	B	A bioprosthesis is reasonable for patients more than 70 years of age (163-166).

Nishimura et al. Circulation, 2017

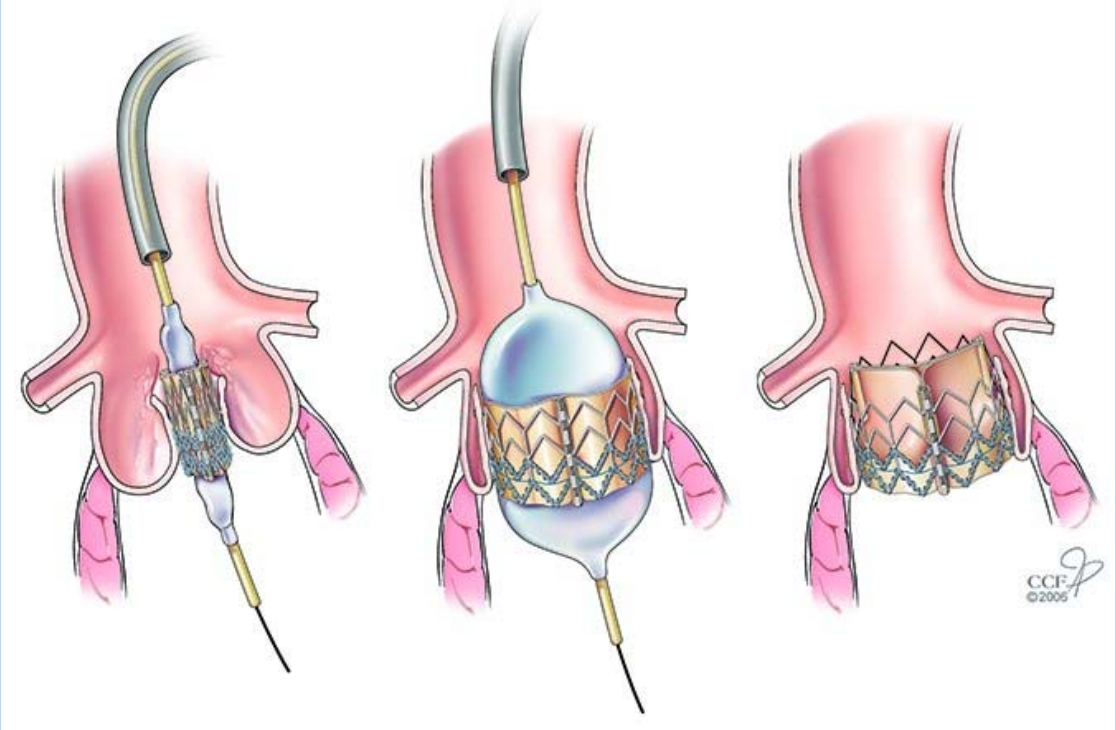
Valve selection: bioprosthetic vs. mechanical

Favor Mechanical Prosthesis	Favor Bioprosthesis
Age <50 y • Increased incidence of structural deterioration with bioprosthesis (15-y risk: 30% for age 40 y, 50% for age 20 y) • Lower risk of anticoagulation complications	Age >70 y • Low incidence of structural deterioration (15-y risk: <10% for age >70 y) • Higher risk of anticoagulation complications
Patient preference (avoid risk of reintervention)	Patient preference (avoid risk and inconvenience of anticoagulation and absence of valve sounds)
Low risk of long-term anticoagulation	High risk of long-term anticoagulation
Compliant patient with either home monitoring or close access to INR monitoring	Limited access to medical care or inability to regulate VKA
Other indication for long-term anticoagulation (e.g., AF)	Access to surgical centers with low reoperation mortality rate

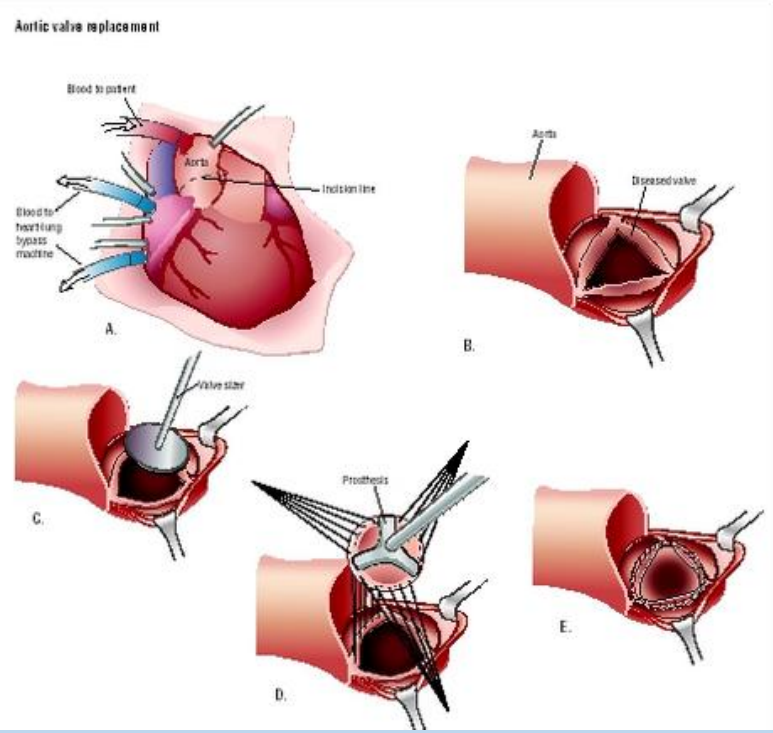
Nishimura et al. Circulation, 2017

Aortic Valve Replacement in 2018

Trans-catheter Approach



Surgical Approach

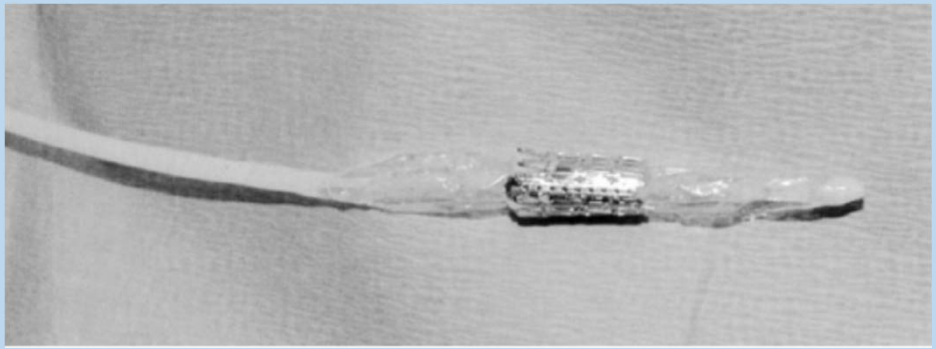


Cleveland clinic foundation, 2006 Surgeryencyclopedia.com

Trans-catheter Aortic Valve Replacement

How far we've come . . .

April 16, 2002



Special Report

Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis

First Human Case Description

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD

Cribier et al. Circulation, 2002

US Landmark Clinical trials:

October, 2010

Inoperable Patients

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery

Jeffrey J. Popma, MD,* David H. Adams, MD,† Michael J. Reardon, MD,‡ Steven J. Yakubov, MD,§ Neal S. Kleiman, MD,‡ David Heimansohn, MD,‖ James Hermiller, Jr, MD,‖ G. Chad Hughes, MD,¶ J. Kevin Harrison, MD,¶ Joseph Coselli, MD,# Jose Diez, MD,# Ali Kafi, MD,** Theodore Schreiber, MD,** Thomas G. Gleason, MD,†† John Conte, MD,‡‡ Maurice Buchbinder, MD,§§ G. Michael Deeb, MD,‖‖ Blasé Carabello, MD,¶¶ Patrick W. Serruys, MD, PhD,## Sharla Chenoweth, MS,*** Jae K. Oh, MD,††† for the CoreValve United States Clinical Investigators

May, 2014

Leon et al. NEJM, 2010; Popma et al. JACC, 2014

US Landmark Clinical trials:

June, 2011

Inoperable
↓
High Risk

Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D., Steven J. Yakubov, M.D., Joseph S. Coselli, M.D., G. Michael Deeb, M.D., Thomas G. Gleason, M.D., Maurice Buchbinder, M.D., James Hermiller, Jr., M.D., Neal S. Kleiman, M.D., Stan Chetcuti, M.D., John Heiser, M.D., William Merhi, D.O., George Zorn, M.D., Peter Tadros, M.D., Newell Robinson, M.D., George Petrossian, M.D., G. Chad Hughes, M.D., J. Kevin Harrison, M.D., John Conte, M.D., Brijeshwar Maini, M.D., Mubashir Mumtaz, M.D., Sharla Chenoweth, M.S., and Jae K. Oh, M.D., for the U.S. CoreValve Clinical Investigators*

May, 2014

Smith et al. NEJM, 2011; Adams et al. NEJM, 2014

US Landmark Clinical trials:

June, 2015

Inoperable
↓
High Risk
↓
Long term data

5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial

Michael J Mack, Martin B Leon, Craig R Smith, D Craig Miller, Jeffrey W Moses, E Murat Tuzcu, John G Webb, Pamela S Douglas, William N Anderson, Eugene H Blackstone, Susheel K Kodali, Raj R Makkar, Gregory P Fontana, Samir Kapadia, Joseph Bavaria, Rebecca T Hahn, Vinod H Thourani, Vasilis Babaliaros, Augusto Pichard, Howard C Herrmann, David L Brown, Mathew Williams, Jodi Akin, Michael J Davidson†, Lars G Svensson, for the PARTNER 1 trial investigators*

3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement

G. Michael Deeb, MD,[a] Michael J. Reardon, MD,[b] Stan Chetcuti, MD,[a] Himanshu J. Patel, MD,[a] P. Michael Grossman, MD,[a] Steven J. Yakubov, MD,[c] Neal S. Kleiman, MD,[b] Joseph S. Coselli, MD,[d] Thomas G. Gleason, MD,[e] Joon Sup Lee, MD,[e] James B. Hermiller, Jr, MD,[f] John Heiser, MD,[g] William Merhi, MD,[g] George L. Zorn III, MD,[h] Peter Tadros, MD,[h] Newell Robinson, MD,[i] George Petrossian, MD,[i] G. Chad Hughes, MD,[j] J. Kevin Harrison, MD,[j] Brijeshwar Maini, MD,[k] Mubashir Mumtaz, MD,[k] John Conte, MD,[l] Jon Resar, MD,[l] Vicken Aharonian, MD,[m] Thomas Pfeffer, MD,[m] Jae K. Oh, MD,[n] Hongyan Qiao, PhD,[o] David H. Adams, MD,[p] Jeffrey J. Popma, MD,[q] for the CoreValve US Clinical Investigators

June, 2016

Mack et al. Lancet, 2015; Deeb et al. JACC, 2016

US Landmark Clinical trials:

April, 2016

Inoperable
↓
High Risk
↓
Long term data
↓
Intermediate Risk

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

M.J. Reardon, N.M. Van Mieghem, J.J. Popma, N.S. Kleiman, L. Søndergaard, M. Mumtaz, D.H. Adams, G.M. Deeb, B. Maini, H. Gada, S. Chetcuti, T. Gleason, J. Heiser, R. Lange, W. Merhi, J.K. Oh, P.S. Olsen, N. Piazza, M. Williams, S. Windecker, S.J. Yakubov, E. Grube, R. Makkar, J.S. Lee, J. Conte, E. Vang, H. Nguyen, Y. Chang, A.S. Mugglin, P.W.J.C. Serruys, and A.P. Kappetein, for the SURTAVI Investigators*

March, 2017

Leon et al. NEJM, 2016; Reardon et al. NEJM 2017

US Landmark Clinical trials:

Inoperable
↓
High Risk
↓
Long term data
↓
Intermediate Risk
↓
Low Risk

The Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low Risk Patients With Aortic Stenosis (PARTNER 3)

This study is currently recruiting participants. (see Contacts and Locations)

Verified May 2016 by Edwards Lifesciences

Sponsor:
Edwards Lifesciences

Information provided by (Responsible Party):
Edwards Lifesciences

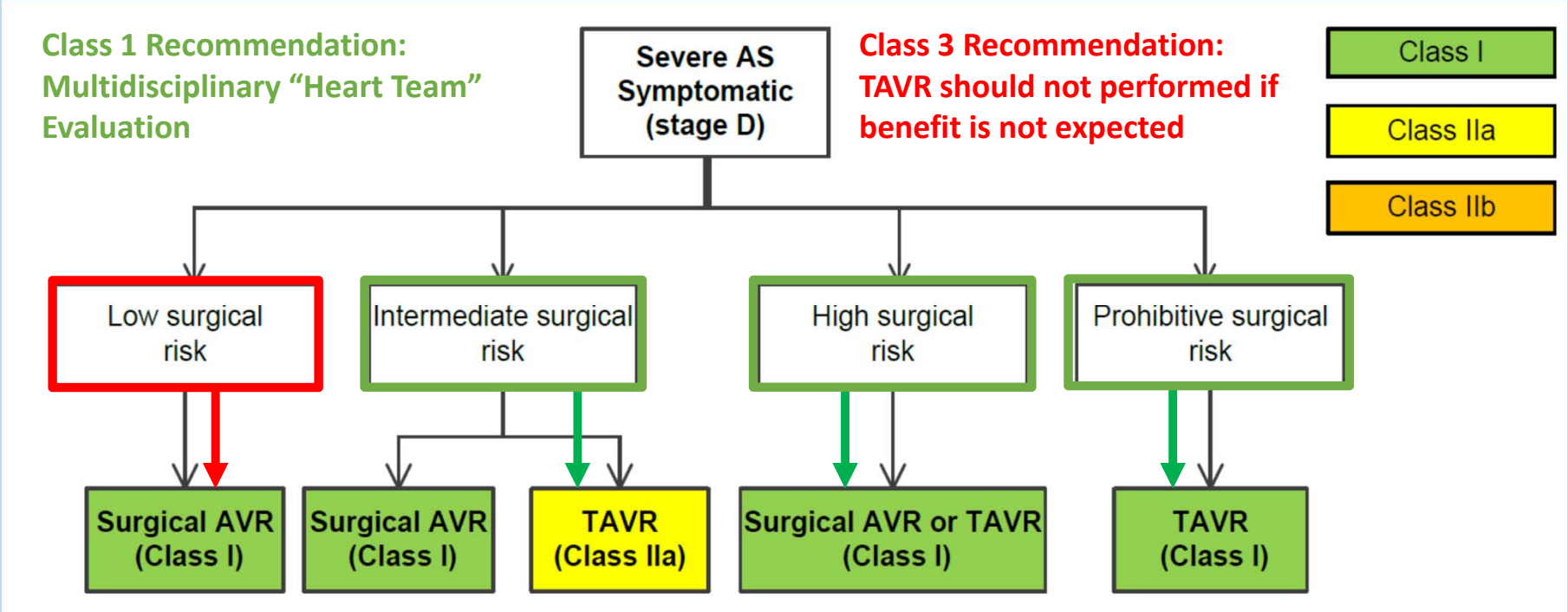
ClinicalTrials.gov Identifier:
NCT02675114

First received: January 22, 2016
Last updated: May 26, 2016
Last verified: May 2016
History of Changes

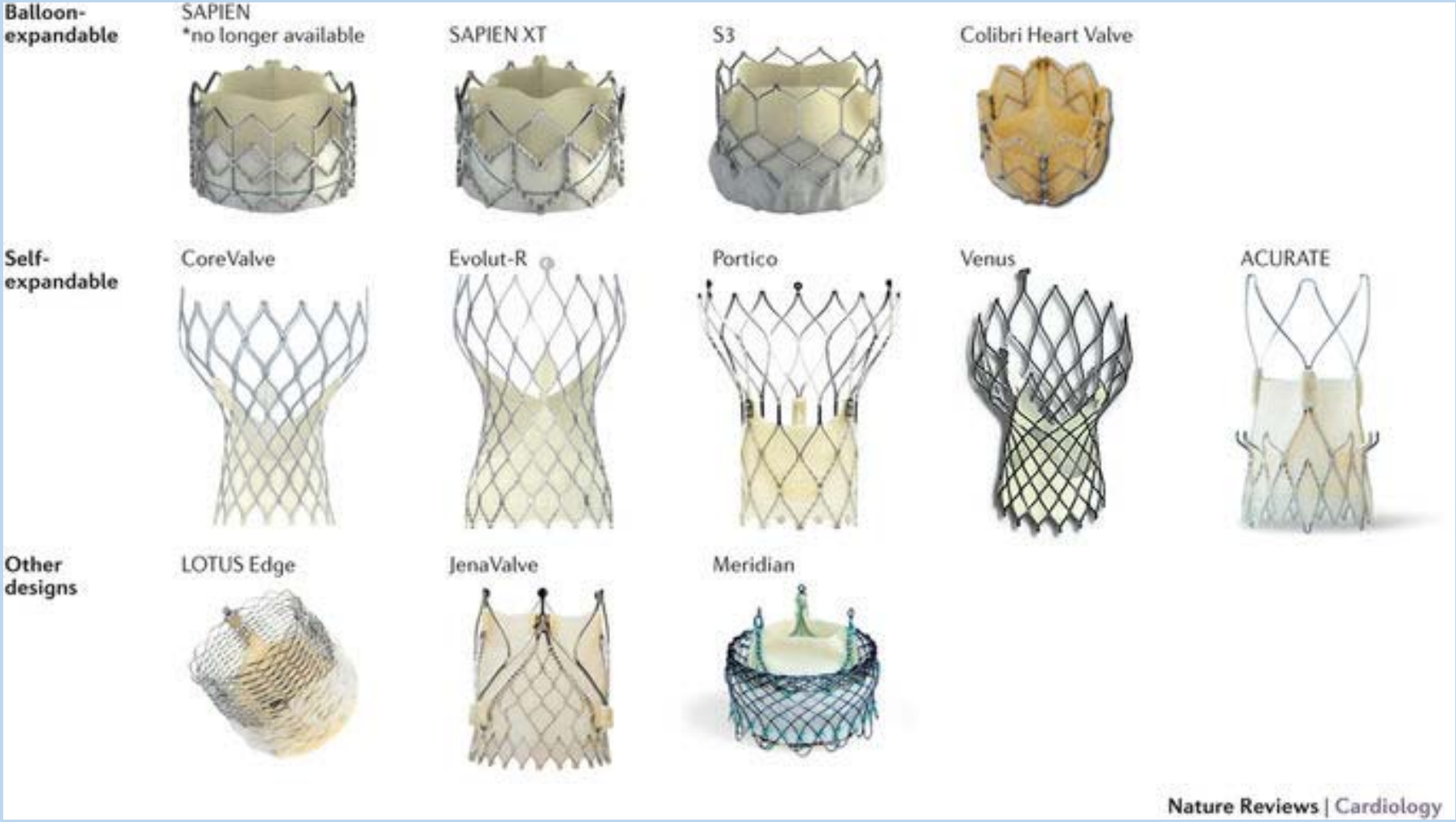
clinicaltrials.gov

Trans-catheter Aortic Valve Replacement

Current Indications:



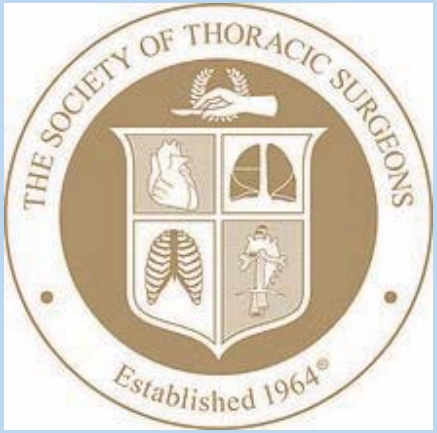
Mack et al. Lancet, 2016



Jones et al. Nat. Rev Cardiol 2017

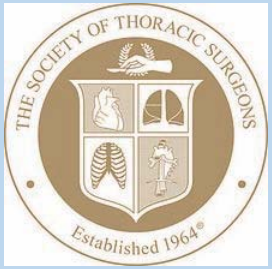
How do we assess Risk in the United States?

The STS Score



The STS Score

Surgery type	**Clinical Heart Failure**	**CVA**	**IABP**
Age	**Ejection Fraction**	**Arrhythmia/Afib**	**Prev Cardiac Intv**
Sex	**Dialysis**	**PAD**	**Valve disease (S/R)**
Height	**Creatinine**	**Diabetes**	**Mitral Insuff.**
Weight	**Symptoms at admission**	**Hypertension**	**Aortic Insuff.**
Race	**Symptoms at surgery**	**Endocarditis**	**Tricuspid Insuff.**
Heart Re-op #	**Immunocompromised**	**Lung disease/severity**	
Op Status	**CAD**	**Cardiogenic Shock**	
Resuscitation?	**Prior MI**	**Ionotropes**	



Home Calculate Support

Procedure Type

- CAB Only
- **AV Replacement**
- MV Replacement Only
- MV Repair
- AV Replacement + CAB
- MV Replacement + CAB
- MV Repair + CAB

Patient Age

85

Sex

Male | **Female**

Risk Model and Variables - STS Adult Cardiac Surgery Database Version 2.81

RISK SCORES

About the STS Risk Calculator

Procedure: AV Replacement

Risk of Mortality: 2.683%

Morbidity or Mortality: 15.759%

Long Length of Stay: 7.992%

Short Length of Stay: 26.606%

Permanent Stroke: 1.885%

Prolonged Ventilation: 9.695%

DSW Infection: 0.187%

Renal Failure: 2.827%

Reoperation: 8.195%

The STS Score – What's Missing?

Frailty: The "Eyeball Test" or Functional limitation

- Pulmonary hypertension
- Hematologic abnormalities: anemia, thrombocytopenia
- Rehab potential (orthopedic or rheumatologic impediments)
- Liver disease
- Oncologic disease
- Infection (non-IE)
- Anatomic factors (Hostile Chest)

Frailty

Frailty Index
ADLS
Grip Strength
5MWT
Albumin

5/6 or 6/6 is normal

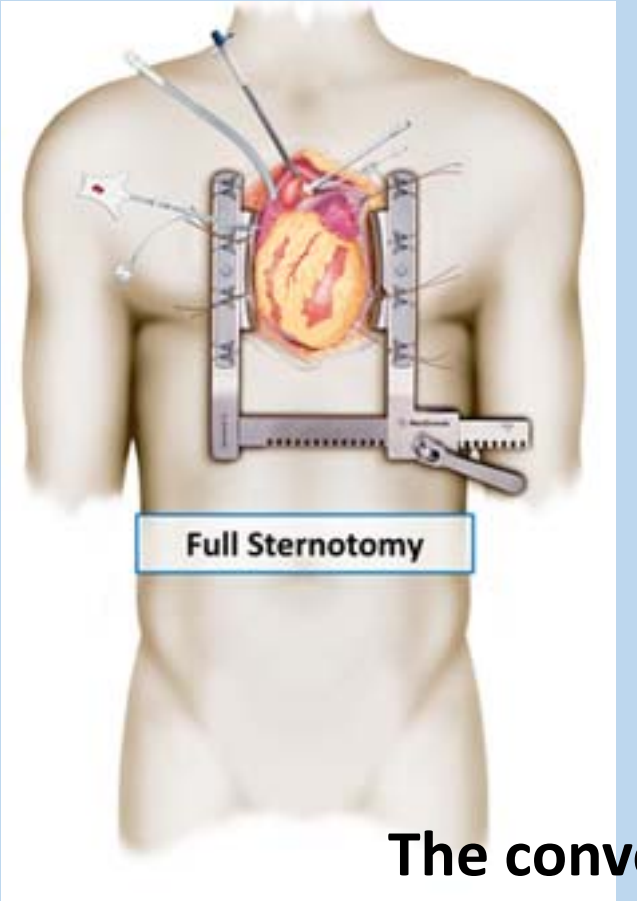
3.5-5.0 g/dL is normal

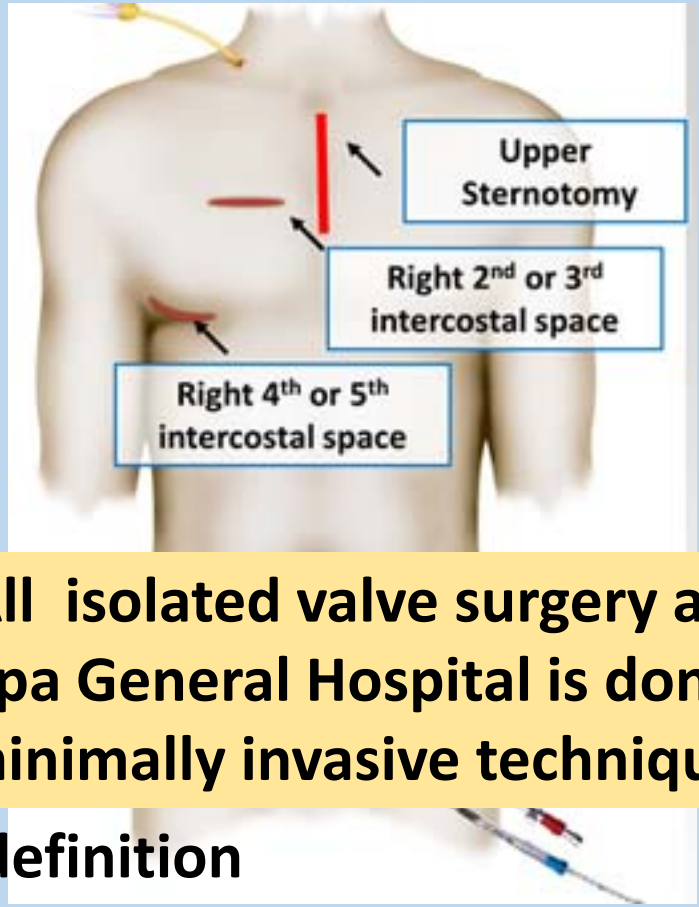
Men	*Cutoff for grip strength (Kg)*
BMI ≤ 24	≤ 29
BMI 24.1-26	≤ 30
BMI 26.1-28	≤ 30
BMI > 28	≤ 32
Women	*Cutoff for grip strength (Kg)*
BMI ≤ 23	≤ 17
BMI 23.1-26	≤ 17.3
BMI 26.1-29	≤ 18
BMI > 29	≤ 21

Men	*Cutoff Time to walk 15 feet*
Height ≤ 173 cm	≥ 7 seconds
Height > 173 cm	≥ 6 seconds
Women	
Height ≤ 159 cm	≥ 7 seconds
Height > 159 cm	≥ 6 seconds

With this in mind . . .

What is “minimally invasive surgery?”





All isolated valve surgery at Tampa General Hospital is done by minimally invasive technique

The conventional definition

Lemalas, J. Medscape Education, 2013;

A Word on "Off-pump" Surgery

On-Pump versus Off-Pump Coronary-Artery Bypass Surgery

A. Laurie Shroyer, Ph.D., Frederick L. Grover, M.D., Brack Hattler, M.D., Joseph F. Collins, Sc.D., Gerald O. McDonald, M.D., Elizabeth Kozora, Ph.D., John C. Lucke, M.D., Janet H. Baltz, R.N., and Dimitri Novitzky, M.D., Ph.D., for the Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group

Off-Pump or On-Pump Coronary-Artery Bypass Grafting at 30 Days

André Lamy, M.D., P.J. Devereaux, M.D., Ph.D., Dorairaj Prabhakaran, M.D., David P. Taggart, Ph.D., Shengshou Hu, M.D., Ernesto Paolasso, M.D., Zbynek Straka, M.D., Leopoldo S. Piegas, M.D., Ahmet Ruchan Akar, M.D., Anil R. Jain, M.D., Nicolas Noiseux, M.D., Chandrasekar Padmanabhan, M.D., Juan-Carlos Bahamondes, M.D., Richard J. Novick, M.D., Prashant Vaijyanath, M.D., Sukesh Reddy, M.D., Liang Tao, M.D., Pablo A. Olavegogeascoechea, M.D., Balram Airan, M.D., Toomas-Andres Sulling, M.D., Richard P. Whitlock, M.D., Yongning Ou, M.Sc., Jennifer Ng, M.Sc., Susan Chrolavicius, B.A., and Salim Yusuf, D.Phil., for the CORONARY Investigators*

On-Pump Versus Off-Pump Coronary Artery Bypass Surgery in Elderly Patients

Results From the Danish On-Pump Versus Off-Pump Randomization Study

Kim Houlind, MD, PhD; Bo Juul Kjeldsen, MD, PhD; Susanne Nørgaard Madsen, MD; Bodil Steen Rasmussen, MD, PhD; Susanne Juel Holme, MD; Per Hostrup Nielsen, MD; Poul Erik Mortensen, MD; for the DOORS Study Group

Off-Pump versus On-Pump Coronary-Artery Bypass Grafting in Elderly Patients

Anno Diegeler, M.D., Ph.D., Jochen Börgermann, M.D., Ph.D., Utz Kappert, M.D., Ph.D., Martin Breuer, M.D., Andreas Böning, M.D., Ph.D., Adrian Ursulescu, M.D., Ardawan Rastan, M.D., Ph.D., David Holzhey, M.D., Ph.D., Hendrik Treede, M.D., Ph.D., Friedrich-Christian Rieß, M.D., Ph.D., Philippe Veeckmann, M.D., Amjad Asfoor, M.D., Wilko Reents, M.D., Michael Zacher, M.D., and Michael Hilker, M.D., Ph.D., for the GOPCABE Study Group*

Houlind K et al. *Circulation*, 2012; Diegeler A et al. *NEJM*, 2013; Lamy A et al. *NEJM*, 2012; Shroyer AL et al. *NEJM*, 2009

A Word on “Off-pump” Surgery

Death, Stroke, Myocardial Infarction
No Difference at 30 days

Signal towards higher repeat revascularization in the Off-pump group

Houlind K et al. *Circulation*, 2012; Diegeler A et al. *NEJM*, 2013; Lamy A et al. *NEJM*, 2012; Shroyer AL et al. *NEJM*, 2009

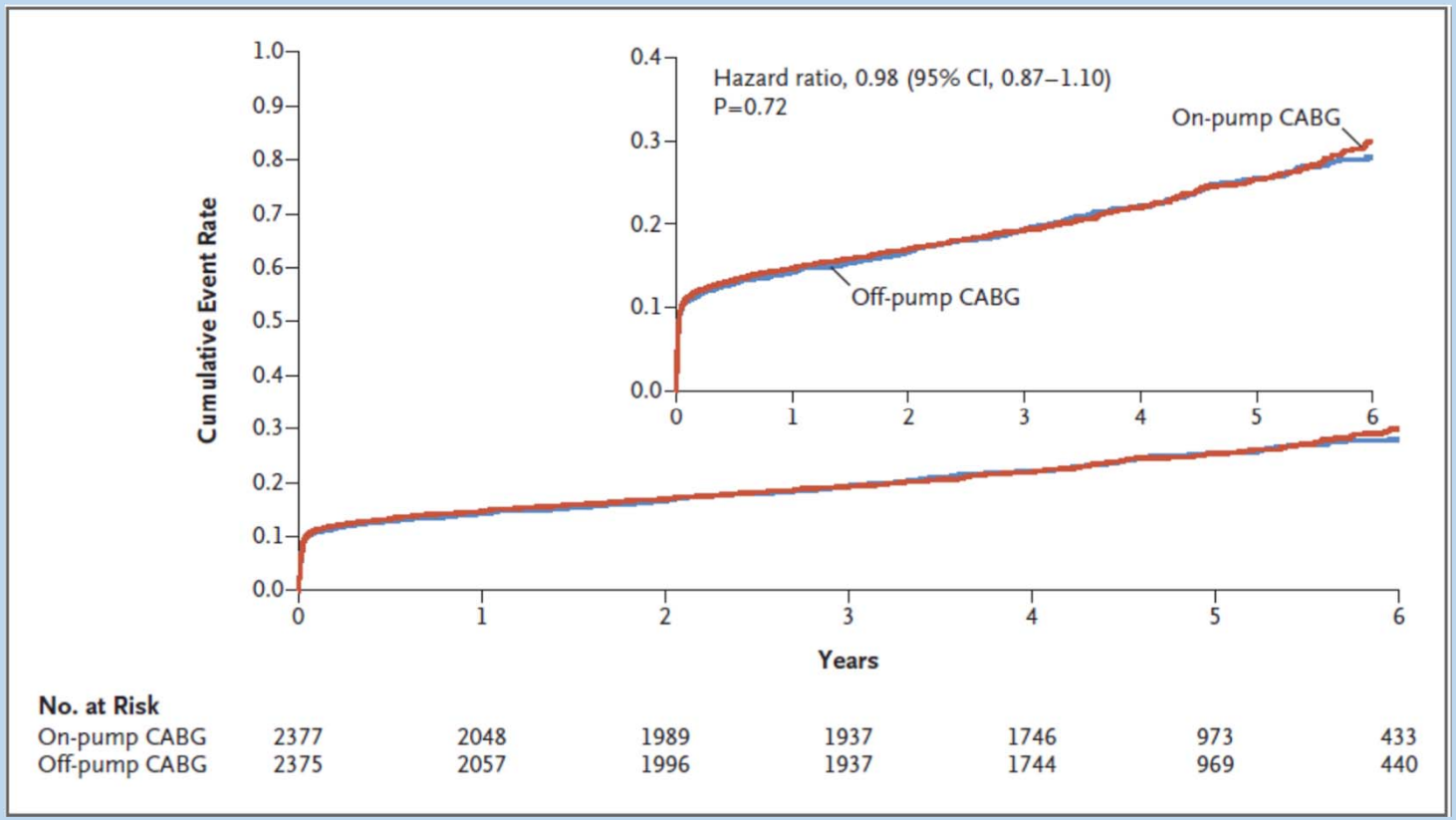
5- Year Outcomes from CORONARY

Five-Year Outcomes after Off-Pump or On-Pump Coronary-Artery Bypass Grafting

André Lamy, M.D., P.J. Devereaux, M.D., Ph.D., Dorairaj Prabhakaran, M.D., David P. Taggart, Ph.D., Shengshou Hu, M.D., Zbynek Straka, M.D., Leopoldo S. Piegas, M.D., Alvaro Avezum, M.D., Ahmet R. Akar, M.D., Fernando Lanas Zanetti, M.D., Anil R. Jain, M.D., Nicolas Noiseux, M.D., Chandrasekar Padmanabhan, M.D., Juan-Carlos Bahamondes, M.D., Richard J. Novick, M.D., Liang Tao, M.D., Pablo A. Olavegogeascoechea, M.D., Balram Airan, M.D., Toomas-Andres Sulling, M.D., Richard P. Whitlock, M.D., Yongning Ou, M.Sc., Peggy Gao, M.Sc., Shirley Pettit, R.N., and Salim Yusuf, D.Phil., for the CORONARY Investigators*

Lamy A et al. *NEJM*, 2016

5- Year Outcomes from CORONARY



Lamy A et al. *NEJM*, 2016

5- Year Outcomes from CORONARY

Table 1. Outcomes at 5 Years.

Outcome	Off-Pump Group (N=2375)	On-Pump Group (N=2377)	Hazard Ratio (95% CI)	P Value
Second coprimary outcome — no. (%)*	548 (23.1)	560 (23.6)	0.98 (0.87–1.10)	0.72
Death	346 (14.6)	322 (13.5)	1.08 (0.93–1.26)	0.30
Myocardial infarction	178 (7.5)	194 (8.2)	0.92 (0.75–1.13)	0.41
Stroke	55 (2.3)	66 (2.8)	0.83 (0.58–1.19)	0.32
New renal failure requiring dialysis	40 (1.7)	45 (1.9)	0.89 (0.58–1.37)	0.60
Repeat revascularization†	66 (2.8)	55 (2.3)	1.21 (0.85–1.73)	0.29
PCI	59 (2.5)	52 (2.2)	1.15 (0.79–1.66)	0.48
CABG	9 (0.4)	4 (0.2)	2.27 (0.70–7.38)	0.17
Nonprespecified outcomes — no. (%)				
Cardiovascular death‡	237 (10.0)	230 (9.7)	1.04 (0.87–1.24)	0.69
Repeat coronary angiography	125 (5.3)	114 (4.8)	1.11 (0.86–1.43)	0.43
Recurrent angina	41 (1.7)	39 (1.6)	1.05 (0.68–1.63)	0.81
Primary outcome in per-protocol population — no./total no. (%)§	487/2148 (22.7)	499/2182 (22.9)	0.99 (0.87–1.12)	0.86

Lamy A et al. *NEJM*, 2016

Valve surgery – even if minimally invasive – cannot be performed without cardio-pulmonary bypass.

“Minimally invasive surgery” in 2018

Trans-catheter Approach

Catheter based vascular access
- Preferably Trans-femoral access
- Alternatives include
  - Subclavian (by cut down)
  - Trans-apical (by cut down)
  - Direct Aortic (by cut down)
  - Carotid
  - Trans caval

No sternotomy or thoracic incision
- Faster functional recovery
- Potential to avoid general anesthesia
- Possible next day discharge if by femoral approach

Minimally invasive Surgical Approach

Reduce operative time
- Experienced program / surgeon

Select populations
- Re-do valve surgery
- Reduced morbidity
- Obese patient at risk

Minimize incision trauma
- Mini-sternotomy (multiple variations)
- Left anterior thoracotomy
- Faster recovery (less 1-2 days)
- Reduced pain/blood loss

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Minimally invasive surgery Aortic: Short term

Minimally Invasive Aortic Valve Replacement Via Right Anterior Mini-Thoracotomy: Propensity Matched Initial Experience

Michael Seitz, BMedSc, MBBS [a*], Joshua Goldblatt, MBBS [a], Eldho Paul, MSc [b], Thomas Marcus, MBBS [c], Marco Larobina, MBBS, FRACS, FCSAN [d], Cheng-Hon Yap, MBBS, MS, FRACS [c]

	RAMT (p = 53)	Sternotomy (p = 53)	p value
30-Day Mortality	1 (1.9%)	3 (5.7%)	0.34
4hr ICC Output (ml)	102.5 (52.5–161)	141 (100–220.5)	0.072
Mechanical Ventilation (hrs)	7 (5–12)	8 (5–13)	0.61
Red Cell Transfusion	14 (26.4%)	14 (26.4%)	1.0
Non-Red Cell Transfusion	9 (17.0%)	15 (28.3%)	0.10
ICU LOS (hrs)	46.5 (23–59.5)	20 (14–23)	<0.001
Hospital LOS (days)	8 (6–12)	6 (5.5–9.5)	0.04
New Onset AF	22 (41.5%)	15 (28.3%)	0.17
CVA	0 (0%)	1 (1.9%)	1.0
Re-Intubation	2 (3.8%)	1 (1.9%)	1.0
Pneumonia	1 (1.9%)	2 (3.8%)	1.0
Return to Theatre for Bleeding	3 (5.7%)	4 (7.6%)	0.66
Wound Infection	0 (0%)	0 (0%)	1.0

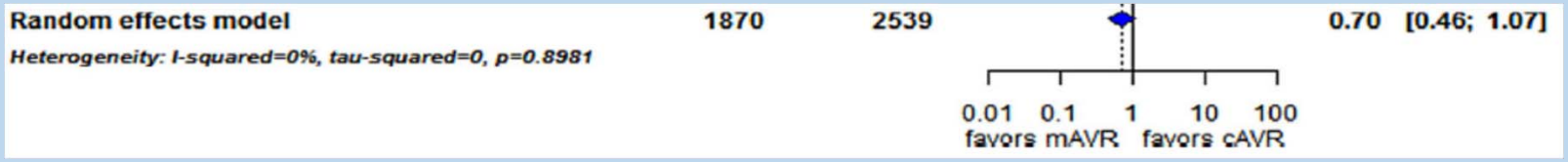
Seitz et al. Heart Lung and Circ, 2017

Minimally invasive surgery Aortic: Short term

Conventional Versus Minimally Invasive Aortic Valve Replacement: Pooled Analysis of Propensity-Matched Data

Ju Y. Lim, M.D.,* Salil V. Deo, M.S., M.Ch.,† Salah E. Altarabsheh, M.D.,‡ Sung H. Jung, M.D.,* Patricia J. Erwin, M.L.S.,§ Alan H. Markowitz, M.D.,† and Soon J. Park, M.D.†

Mortality



Cross-Clamp Time

Lim et al. J Card Surg, 2015

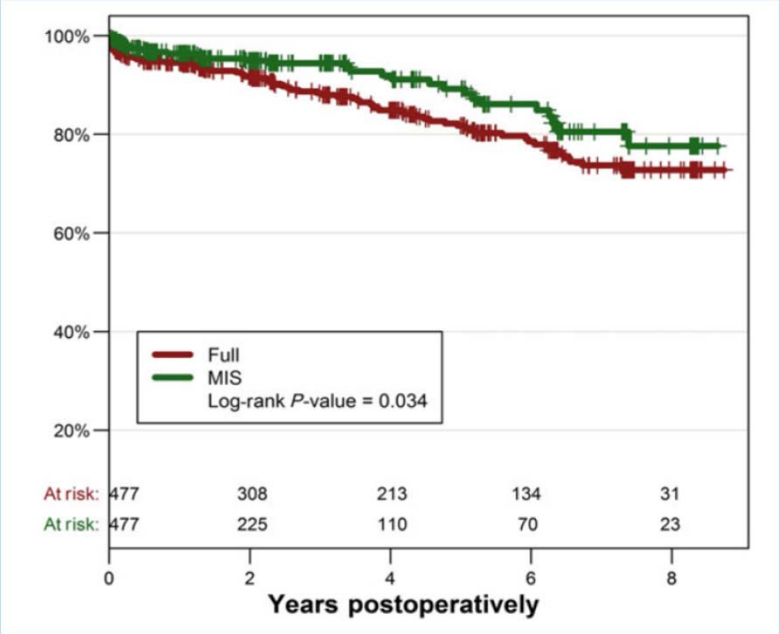
Minimally invasive surgery Aortic: Long term

Minimal invasive aortic valve replacement surgery is associated with improved survival: a propensity-matched comparison†

Denis R. Merk[a,*], Sven Lehmann[a,*], David M. Holzhey[a], Pascal Dohmen[a], Pascal Candolfi[b], Martin Misfeld[a], Friedrich W. Mohr[a] and Michael A. Borger[a,*]

5 years Survival:
89.3 ± 2.4% vs 81.8 ± 2.2% in

8 years Survival:
77.7 ± 4.7 vs 72.8 ± 3.1%



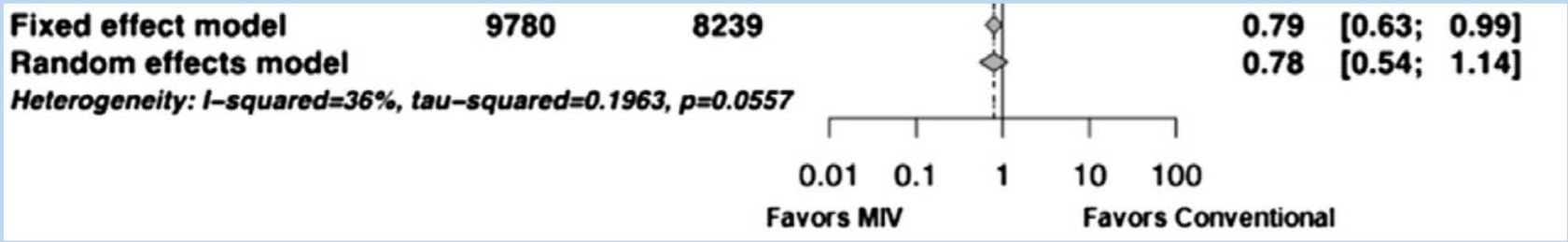
Merk et al.Eur J Cardthorac Surg, 2015

Minimally invasive surgery Mitral: Short term

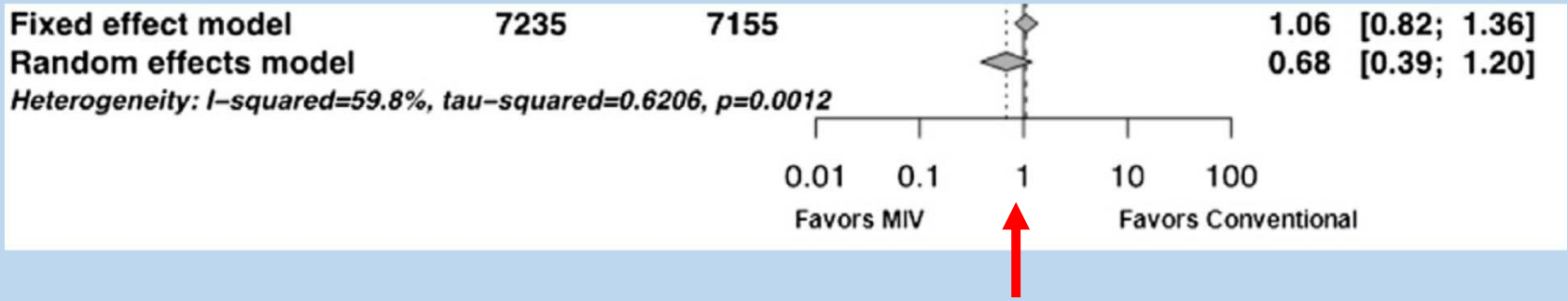
Mitral valve surgery: Right lateral minithoracotomy or sternotomy? A systematic review and meta-analysis

Simon H. Sündermann, MD,[a] Juri Sromicki, MD,[a] Héctor Rodriguez Cetina Biefer, MD,[a,b] Burkhardt Seifert, MD, PhD,[c] Tomas Holubec, MD,[a] Volkmar Falk, MD, PhD,[a] and Stephan Jacobs, MD[a]

Mortality



Stroke



Sundermann et al. J Thorac CardioVasc Surg, 2014

Minimally invasive surgery Mitral: Long term

Right Minithoracotomy Versus Full Sternotomy for Mitral Valve Repair: A Propensity Matched Comparison

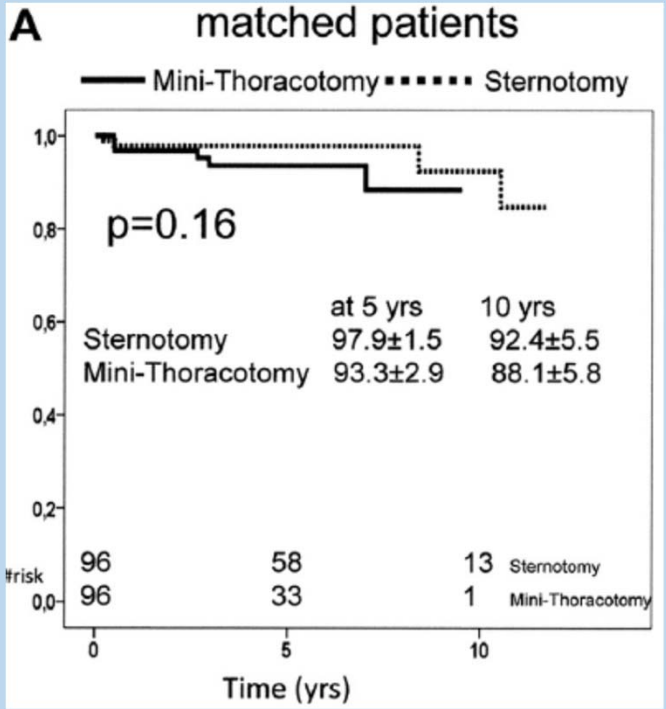
Rüdiger Lange, MD, PhD, Bernhard Voss, MD, Victoria Kehl, DrRerNat, Domenico Mazzitelli, MD, Peter Tassani-Prell, MD, PhD, and Thomas Günther, MD

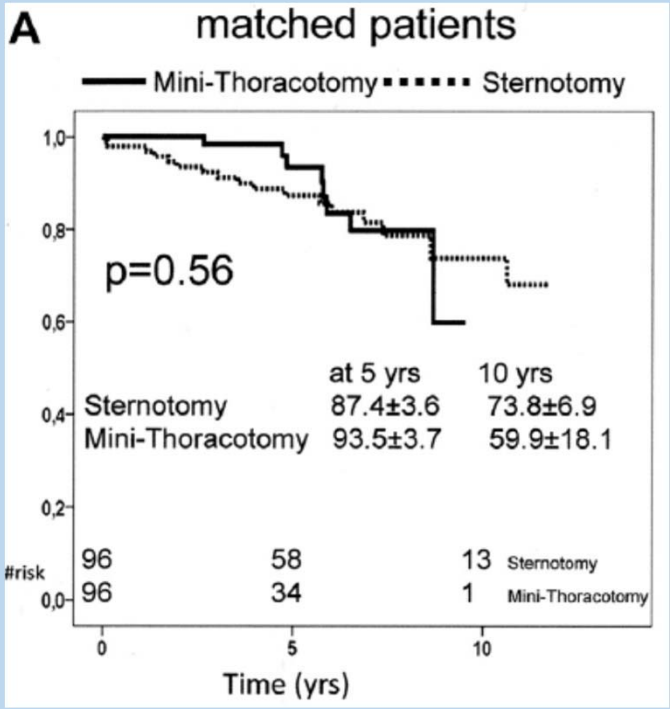
	Unmatched Patients			Matched Patients		
Variable	Group RT	Group MS	*p* Value	Group RT	Group MS	*p* Value
Cardiopulmonary bypass time, minutes	121 ± 33	97 ± 29	<0.001	120 ± 28	99 ± 30	<0.001
Cross-clamp time, minutes	87 ± 25	70 ± 24	<0.001	86 ± 23.5	74 ± 25	<0.001
Ventilatory support, hours	24 (4–256)	34 (5–480)	<0.001	30 (8–256)	30 (5–235)	0.39
Intensive care unit stay, days	3.6 ± 3.2	5.0 ± 4.8	<0.001	4.5 ± 4.6	4.5 ± 2.0	0.99
Hospital stay, days	7.9 ± 5.4	9.4 ± 5.1	<0.001	8.6 ± 4.6	8.4 ± 2.4	0.75
Red blood cells transfusion, mL	167 ± 429	345 ± 753	0.002	258 ± 472	228 ± 449	0.67
30-day mortality, %	0	2	<0.001	0	1	0.13
5-year survival, %	96.9 ± 1.1	82.6 ± 2.6	<0.001	93.5 ± 3.7	87.4 ± 3.6	0.56
5-year freedom from MV reoperation, %	94.7 ± 1.2	92.6 ± 1.8	0.24	93.3 ± 2.9	97.9 ± 1.5	0.16
5-year freedom from stroke, %	95 ± 1.1	95 ± 1.5	0.94	98 ± 1.9	96 ± 2.2	0.15
5-year freedom from bleeding, %	99 ± 0.4	99 ± 0.7	0.69	99 ± 1.0	98 ± 1.6	0.60
SF-36 physical score	49.3 ± 9.1	45.5 ± 10.7	<0.001	47.7 ± 7.7	46.3 ± 10.6	0.45
SF-36 psychological score	48.9 ± 10.2	49.2 ± 10.7	0.79	50.2 ± 9.2	49.5 ± 11.0	0.69

Lange et al. Ann Thorac Surg, 2017

Minimally invasive surgery Mitral: Long term

Reoperation





Mortality

Lange et al. Ann Thorac Surg, 2017

"Minimally invasive surgery" Aortic Valve

Table 1. Summary of the relative merit of minimally invasive aortic valve replacement

Outcomes	Relative merit	Quality of evidence
Early mortality	MIAVR results in equivalent 30-d mortality when compared with CS	Moderate
Respiratory complications	MIAVR is associated with a 1- to 2-h reduction in ventilation time	Poor
	Reintubation rates are similar between MIAVR and CS	Moderate
Bleeding and transfusions	MIAVR may reduce postoperative bleeding and transfusion	Very poor
	The rate of reintervention for bleeding is similar between MIAVR and CS	Moderate
Strokes	The incidence of postoperative stroke is similar between MIAVR and CS	Moderate
Wound complications	RAT may reduce postoperative wound complications	Very poor
	PS is associated with infection rates that are similar to those of complete sternotomy	Moderate
Length of stay	The ICU length of stay is similar between MIAVR and CS	Moderate
	MIAVR is associated with a reduction in overall hospital length of stay (average reduction of 1-2 d).	Moderate

Bouhout et al. Can J Cardiol, 2017

"Minimally invasive surgery" Aortic Valve

Respiratory complications	MIAVR is associated with a 1- to 2-h reduction in ventilation time	Poor
Wound complications	RAT may reduce postoperative wound complications	Very poor
Bleeding and transfusions	MIAVR may reduce postoperative bleeding and transfusion	Very poor
Length of stay	MIAVR is associated with a reduction in overall hospital length of stay (average reduction of 1-2 d).	Moderate

Bouhout et al. Can J Cardiol, 2017

"Minimally invasive surgery" Mitral Valve

Table 2. Summary of the relative merit of minimally invasive mitral valve surgery

Outcomes	Relative merit	Quality of evidence
Early mortality	MIMVS results in an equivalent 30-d mortality compared with CS	Moderate
Bleeding and transfusion	MIMVS may reduce postoperative transfusions	Very poor
	The rate of reintervention for bleeding is similar between MIMVS and CS	Moderate
Stroke	The incidence of postoperative stroke is similar between MIMVS and CS	Moderate
Durability	MIMVS is associated with a similar initial successful repair rate when compared with CS	Moderate
	The durability of repair by MIMVS is equivalent to that of CS	Moderate

Bouhout et al. Can J Cardiol, 2017

“Minimally invasive surgery” Mitral Valve

Bleeding and transfusion	MIMVS may reduce postoperative transfusions	Very poor

Bouhout et al. Can J Cardiol, 2017

“Minimally invasive surgery” in 2018

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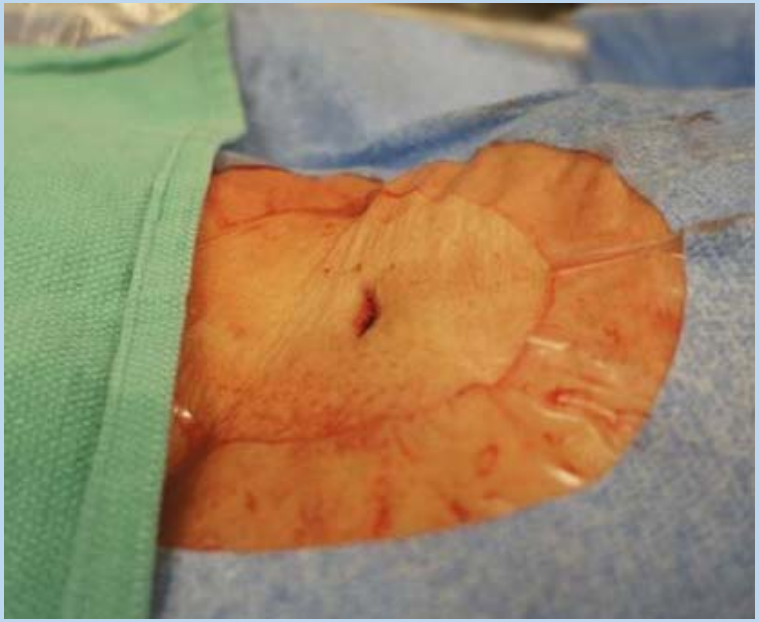
“Minimally invasive surgery” in 2018



Webb and Wood, JACC 2012; heartsurgeryinfo.com, triadctsurgeons.com

Appears better than this . . .But, hold on . . .

Ongoing respective concerns . . .

Trans-catheter Appro

Lack of Experience

Lack of Data
- Comparative effic
- Randomized data

Limited candidacy crit
- Leads to diagnost
- Limited to anator

ve - Surgical Approach

als vs clinical success

ndent
sis rates; improves with
erience

o standard sternotomy
ypass / cross clamp time
Bleeding, repeat surgery
de-airing and Chest tube

www.surgeryencyclopedia.com; Bouhout et al. Can J Cardiol, 2017

“Minimally invasive?”. . . the right question?

The Low Risk TAVR Example

Transcatheter versus surgical aortic valve replacement in patients at low surgical risk: A meta-analysis of randomized trials and propensity score matched observational studies

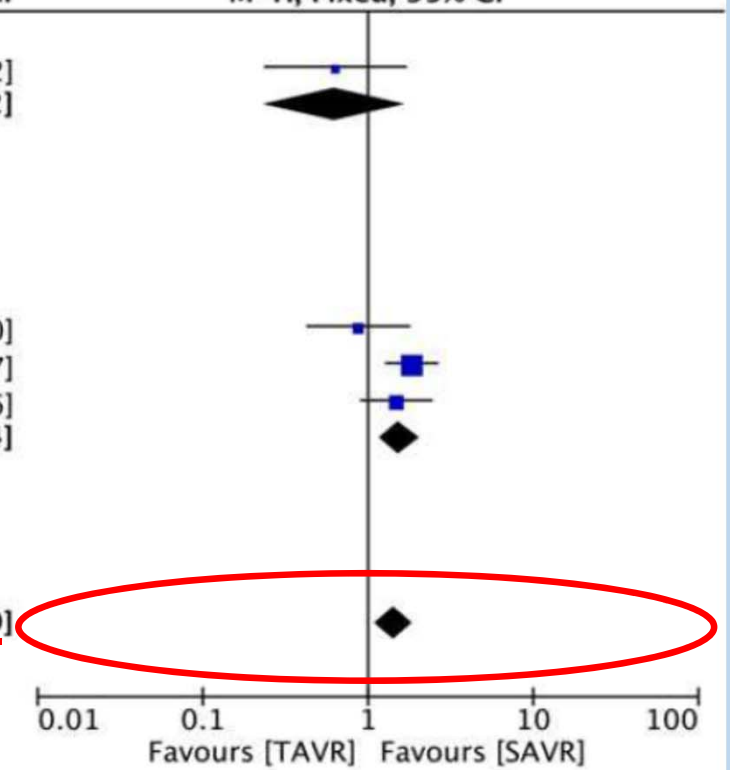
Guy Witberg, MD[1,2*] | Adi Lador, MD[1,2*] | Dafna Yahav, MD[2,3] | Ran Kornowski, MD[1,2]

Witberg et al. CCI, 2018

“Minimally invasive?”. . . the right question?

B

Study or Subgroup	TAVR Events	TAVR Total	SAVR Events	SAVR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2.1.1 RCT						
Thyregoed 2015	7	145	10	135	10.7%	0.63 [0.23, 1.72]
Subtotal (95% CI)		**145**		**135**	**10.7%**	**0.63 [0.23, 1.72]**
Total events	7		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.90 (P = 0.37)						
2.1.2 PSM						
Piazza 2013	15	191	17	191	17.0%	0.87 [0.42, 1.80]
Rosato 2016	91	355	56	355	45.3%	1.84 [1.27, 2.67]
Schymik 2015	43	216	31	216	27.0%	1.48 [0.89, 2.46]
Subtotal (95% CI)		**762**		**762**	**89.3%**	**1.55 [1.18, 2.04]**
Total events	149		104			
Heterogeneity: $Chi^2 = 3.26$, df = 2 (P = 0.20); $I^2 = 39\%$						
Test for overall effect: Z = 3.11 (P = 0.002)						
Total (95% CI)		**907**		**897**	**100.0%**	**1.45 [1.11, 1.89]**
Total events	156		114			
Heterogeneity: $Chi^2 = 6.12$, df = 3 (P = 0.11); $I^2 = 51\%$						
Test for overall effect: Z = 2.76 (P = 0.006)						
Test for subgroup differences: $Chi^2 = 2.87$, df = 1 (P = 0.09), $I^2 = 65.1\%$						



Witberg et al. CCI, 2018

Is “minimally invasive” the right question?

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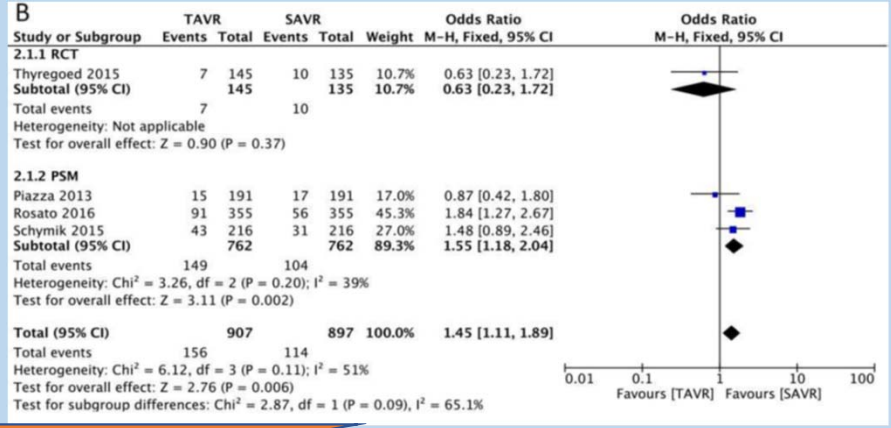
Transcatheter versus surgical aortic valve replacement in patients at low surgical risk: A meta-analysis of randomized trials and propensity score matched observational studies

Guy Witberg, MD[1,2*] | Adi Lador, MD[1,2*] | Dafna Yahav, MD[2,3] | Ran Kornowski, MD[1,2]



The Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low Risk Patients With Aortic Stenosis (PARTNER 3)

This study is currently recruiting participants. (see Contacts and Locations)

Verified May 2016 by Edwards Lifesciences

Sponsor:
Edwards Lifesciences

Information provided by (Responsible Party):
Edwards Lifesciences

ClinicalTrials.gov Identifier:
NCT02675114

First received: January 22, 2016
Last updated: May 26, 2016
Last verified: May 2016
History of Changes

Witberg et al. CCI, 2018; clinicaltrials.gov

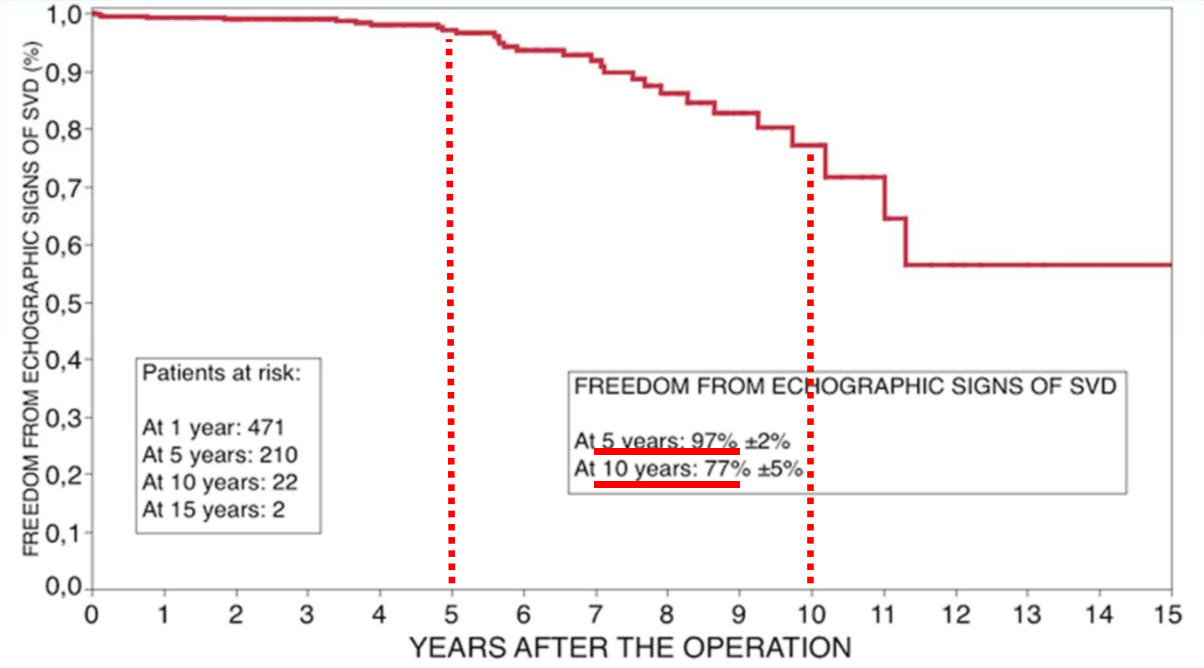
What are we truly interested in?

Clinical durability.

Witberg et al. CCI, 2018; clinicaltrials.gov

Durability of Surgical Bioprostheses

18 year observational data SAVR: Mitroflow aortic bioprosthesis

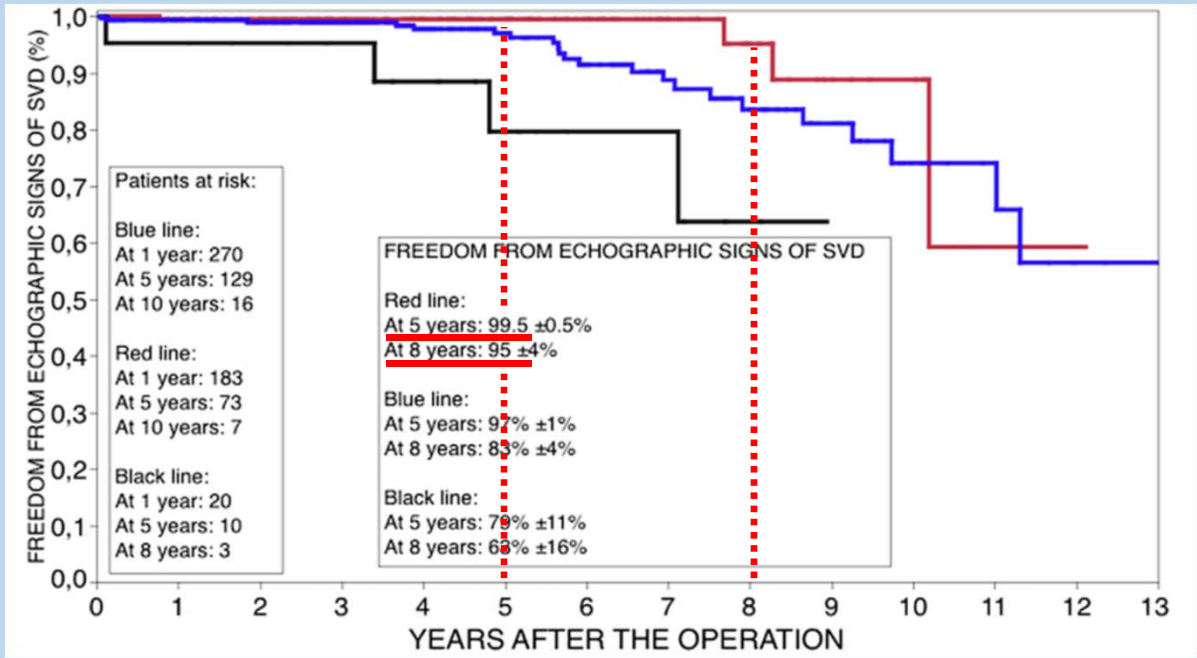


Echocardiographic signs of SVD
- Greater than mild AR
- Mean trans-prosthetic gradient > 40 mmHg

Piccardo et al. J Thorac Cardiovasc Surg, 2016

Durability of Surgical Bioprostheses

18 year observational data SAVR: Mitroflow aortic bioprosthesis



Freedom from Echocardiographic signs of SVD

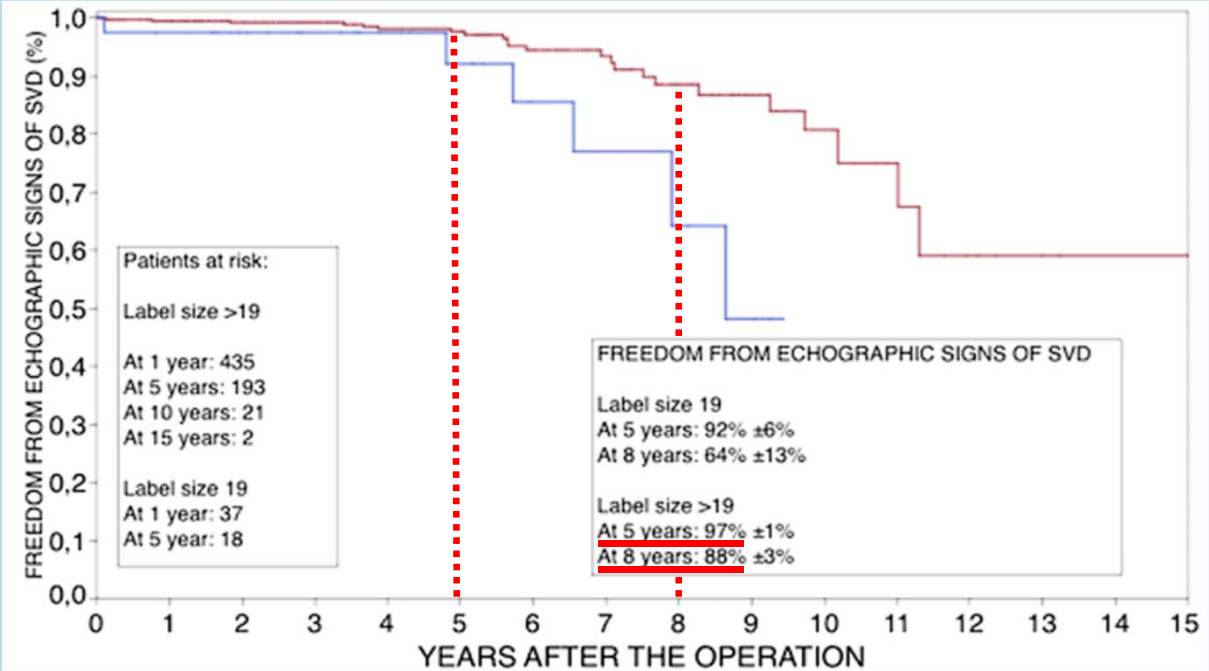
Patient-prosthesis mismatch

- Black: severe
- Blue: moderate
- **Red: None**

Piccardo et al. J Thorac Cardiovasc Surg, 2016

Durability of Surgical Bioprostheses

18 year observational data SAVR: Mitroflow aortic bioprosthesis



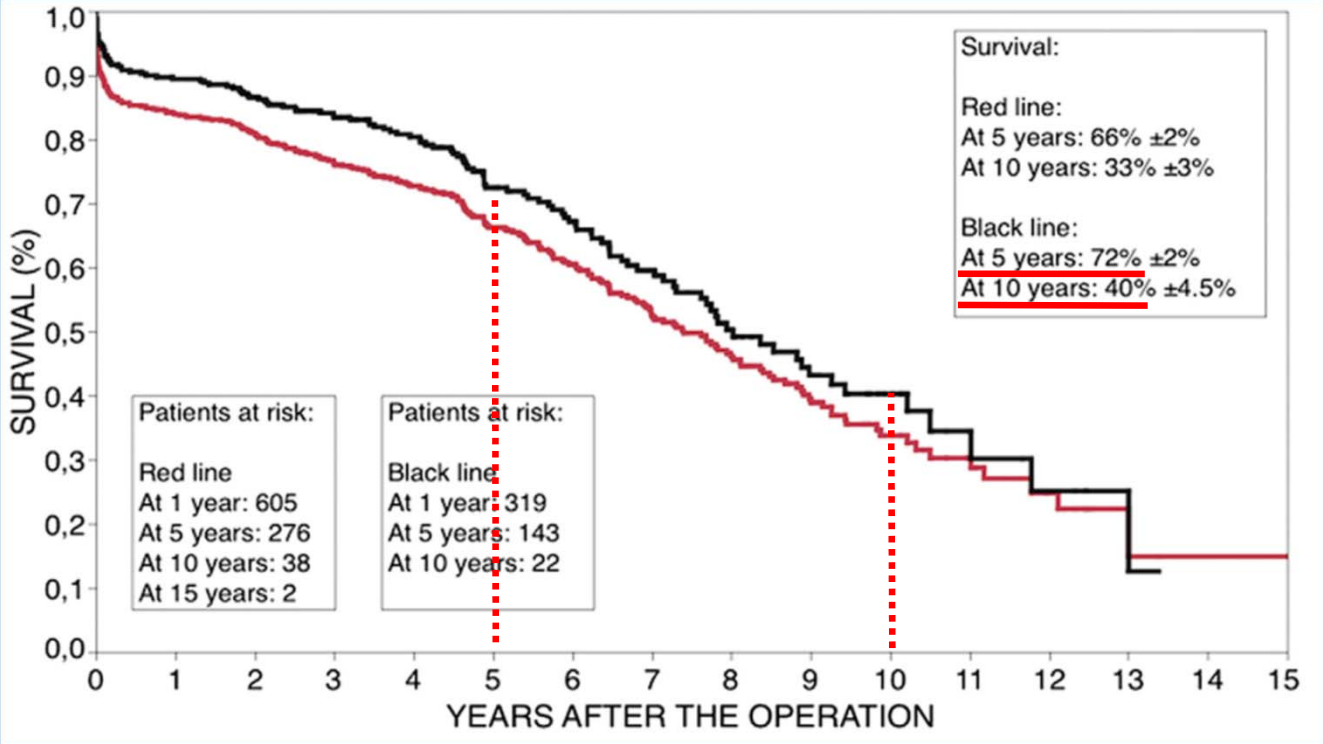
Freedom from Echocardiographic signs of SVD

- Blue: 19 mm prosthesis
- Red: >19 mm

Piccardo et al. J Thorac Cardiovasc Surg, 2016

Durability of Surgical Bioprostheses

18 year observational data SAVR: Mitroflow aortic bioprosthesis



Overall Survival
Black:
Non-emergent isolated aortic valve replacement
Red:
Overall AVR population

Piccardo et al. J Thorac Cardiovasc Surg, 2016

The Question of Durability

Long term clinical trial data: 5 year outcomes from PARTNER

	At 1 year		At 5 years		
	TAVR group (n=348)	SAVR group (n=351)	TAVR group (n=348)	SAVR group (n=351)	Log-rank p value
Death					
From any cause	84 (24·2%)	89 (26·8%)	229 (67·8%)	198 (62·4%)	0·76
From cardiovascular causes	46 (14·0%)	40 (13·0%)	147 (53·1%)	123 (47·6%)	0·67
Repeat hospital admission	59 (18·5%)	51 (17·7%)	108 (42·3%)	81 (34·2%)	0·17
Death from any cause or repeat hospital admission	121 (34·9%)	125 (37·7%)	265 (77·8%)	228 (71·3%)	0·49
Stroke or transient ischaemic attack					
All	28 (8·6%)	13 (4·3%)	42 (15·9%)	33 (14·7%)	0·35
Stroke	20 (6·0%)	10 (3·2%)	29 (10·4%)	26 (11·3%)	0·61
Transient ischaemic attack	8 (2·6%)	4 (1·5%)	14 (6·3%)	8 (3·8%)	0·30
Stroke or death from any cause	95 (27·4%)	95 (28·6%)	236 (69·8%)	200 (62·9%)	0·39
Stroke or transient ischaemic attack, or death from any cause	102 (29·4%)	98 (29·5%)	242 (71·6%)	205 (64·4%)	0·35
Myocardial infarction	0 (0·0%)	2 (0·6%)	5 (2·9%)	11 (5·9%)	0·15
Major vascular complication	40 (11·6%)	13 (3·8%)	41 (11·9%)	14 (4·7%)	0·0002
Major bleeding	52 (15·7%)	88 (26·7%)	75 (26·6%)	103 (34·4%)	0·003
Endocarditis	2 (0·6%)	3 (1·0%)	5 (2·0%)	6 (2·5%)	0·65
Renal failure	18 (5·4%)	20 (6·5%)	24 (8·6%)	24 (8·5%)	0·69
New pacemaker	21 (6·4%)	17 (5·3%)	28 (9·7%)	23 (9·1%)	0·64

Data are number of patients (Kaplan-Meier probability [%]). TAVR=transcatheter aortic valve replacement. SAVR=surgical aortic valve replacement.

Table 1: **Clinical outcomes at 1 year and 5 years for the intention-to-treat population**

Mack et al. Lancet, 2016

The Question of Durability

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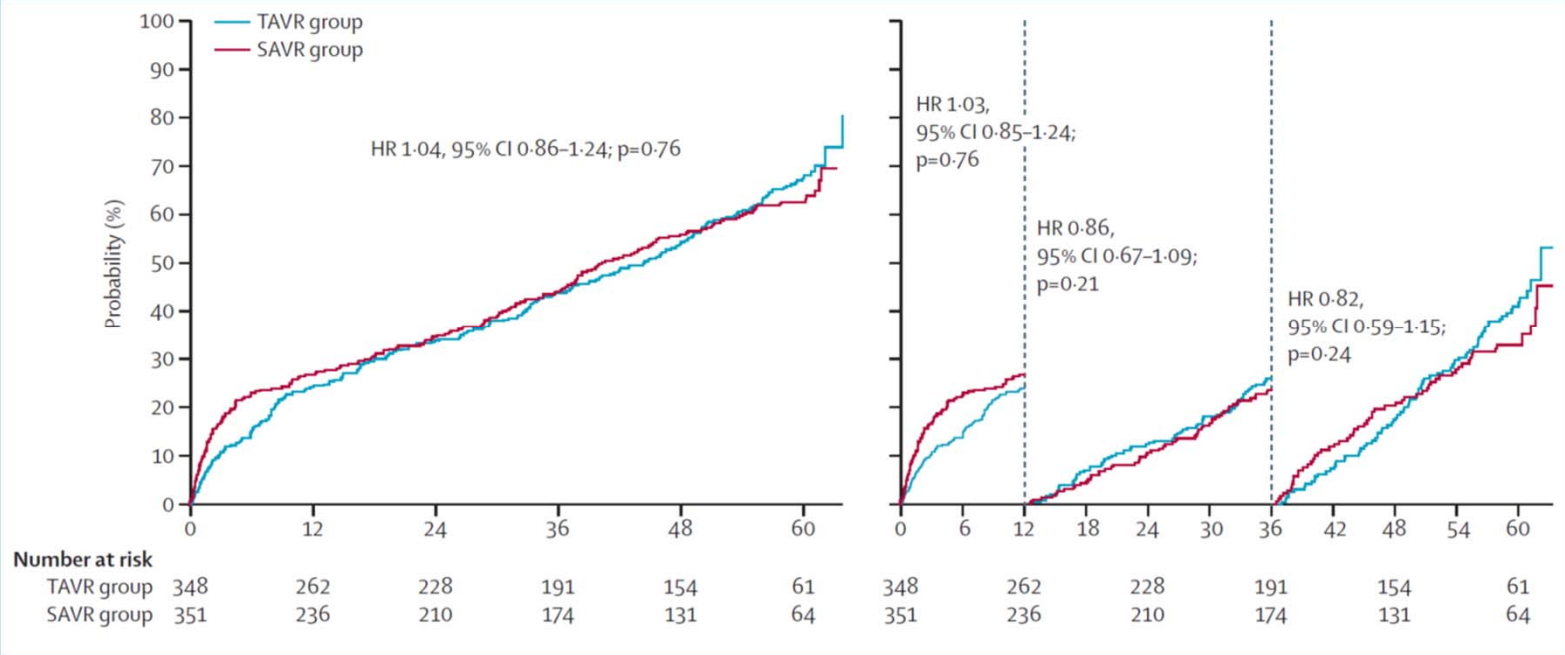
Mack et al. Lancet, 2016

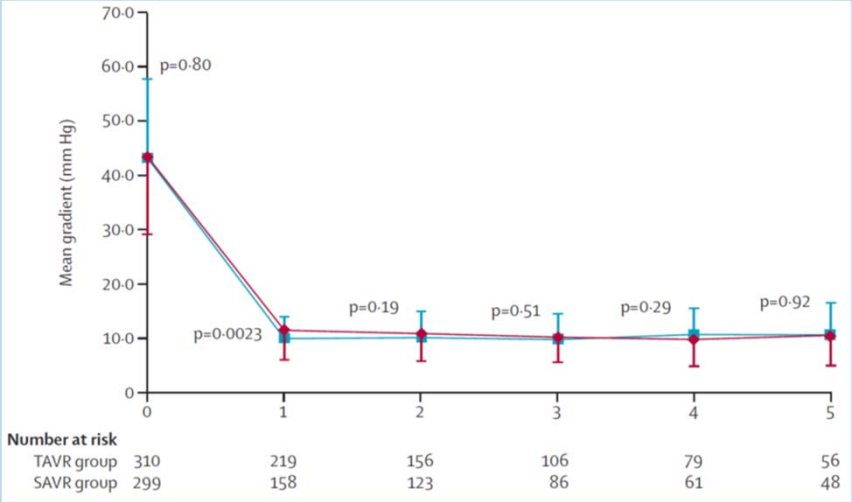
The Question of Durability

Long term clinical trial data: 5 year outcomes from PARTNER

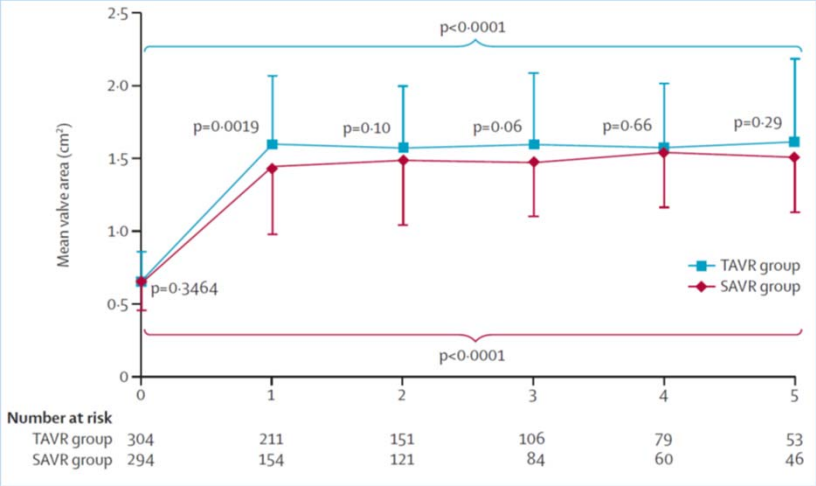


Mack et al. Lancet, 2016

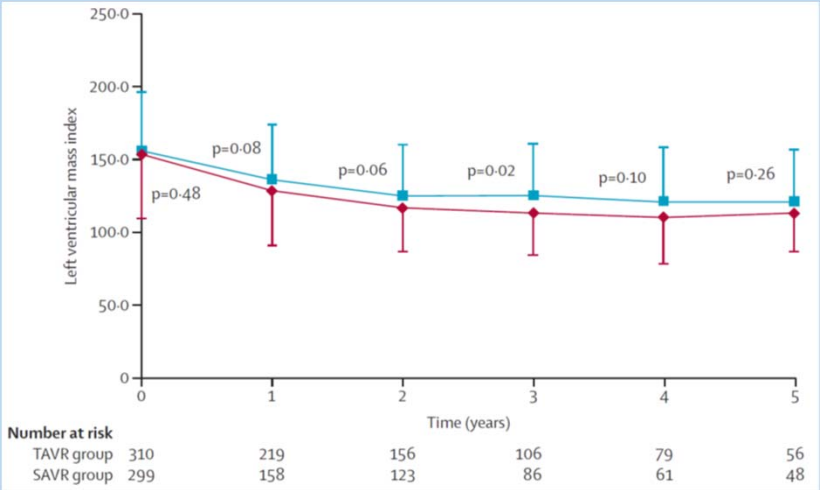
Hemodynamic data



Mean gradient



Mean valve area



LV mass index

Mack et al. Lancet, 2016

PARTNER 5 year outcomes: Notable factors:

- Trans-femoral approach (ONLY):

  Risk of all-cause mortality: 63% (TAVR) vs 64% (SAVR), $p = 0.41$

  - Trans-apical approach ONLY: 79% vs 60% ($p = 0.067$)

- Central vs paravalvular regurgitation

  Mod- severe AR at 30 days post implant: 14% (TAVR) vs 1% (SAVR), $p < 0.0001$), **mostly paravalvular**

  Central regurgitation no different in both groups (2/280 TAVR, 1/228 SAVR)

  *Total AR: increased 5 year mortality in TAVR group: 72.4% (mod-sev) vs 56.6% (mild or less), $p = 0.003$

- **Valve deterioration: none recorded in either group at the 5 year time point.**

Mack et al. Lancet, 2016

Expanding indications:

Valve-in-Valve IIa

TMVR

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease

Valve-in-Valve International Data
VIVID

Original Investigation

Transcatheter Aortic Valve Implantation in Failed Bioprosthetic Surgical Valves

Danny Dvir, MD; John G. Webb, MD; Sabine Bleiziffer, MD; Miralem Pasic, MD, PhD; Ron Waksman, MD; Susheel Kodali, MD; Marco Barbanti, MD; Azeem Latib, MD; Ulrich Schaefer, MD; Josep Rodés-Cabau, MD; Hendrik Treede, MD; Nicolo Piazza, MD, PhD; David Hildick-Smith, MD; Dominique Himbert, MD; Thomas Walther, MD; Christian Hengstenberg, MD; Henrik Nissen, MD, PhD; Raffi Bekeredjian, MD; Patrizia Presbitero, MD; Enrico Ferrari, MD; Amit Segev, MD; Arend de Weger, MD; Stephan Windecker, MD; Neil E. Moat, FRCS; Massimo Napodano, MD; Manuel Wilbring, MD; Alfredo G. Cerillo, MD; Stephen Brecker, MD; Didier Tchetche, MD; Thierry Lefèvre, MD; Federico De Marco, MD; Claudia Fiorina, MD; Anna Sonia Petronio, MD; Rui C. Teles, MD; Luca Testa, MD; Jean-Claude Laborde, MD; Martin B. Leon, MD; Ran Kornowski, MD; for the Valve-in-Valve International Data Registry Investigators

PARTNER II Valve-in-Valve registry suggests alternative to reoperation in failed aortic bioprostheses

November 30, 2015

Dvir et al. JAMA, 2014; Dvir et al. TCT, 2015

Expanded indications:

Valve-in-Valve IIa

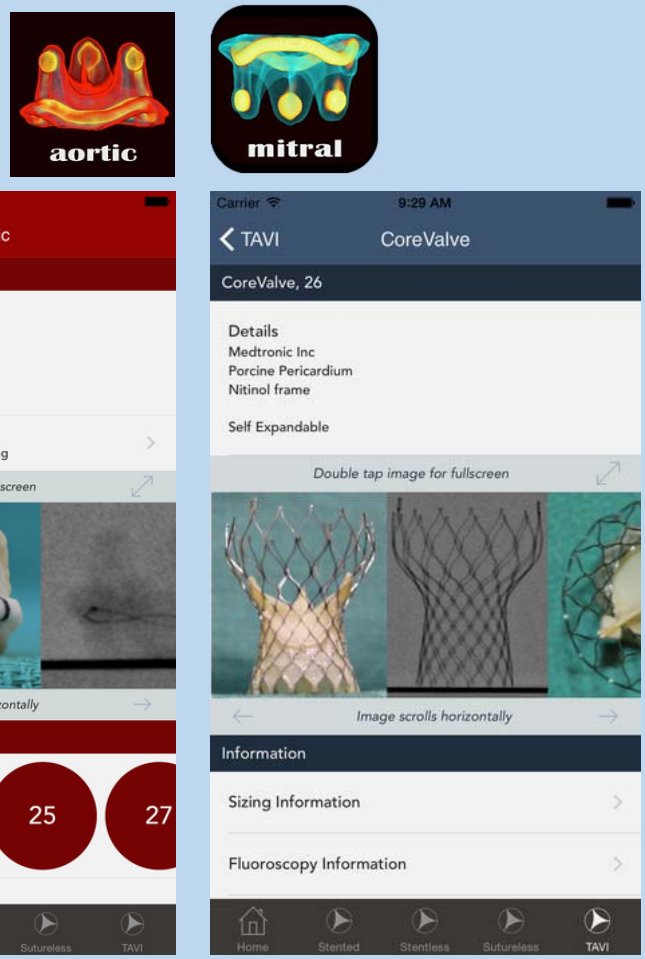
TMVR

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease



Bapat, V./UBQO, ViV App.

Expanded indications:

Valve-in-Valve

TMVR

2017. No guideline Comment

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease

Mitral Implantation of TRAnscatheter vaLves (MITRAL)

This study is currently recruiting participants. (see Contacts and Locations)

Verified May 2016 by NorthShore University HealthSystem

Sponsor:
Mayra Guerrero

Collaborator:
Henry Ford Hospital

Information provided by (Responsible Party):
Mayra Guerrero, NorthShore University HealthSystem

ClinicalTrials.gov Identifier:
NCT02370511

First received: February 18, 2015
Last updated: May 16, 2016
Last verified: May 2016
History of Changes

The purpose of this trial is to establish the safety and efficacy of the Edwards SAPIEN XT™ and SAPIEN 3™ device and delivery systems in patients with severe symptomatic calcific mitral valve disease with severe mitral annular calcification who are not candidates for surgery.

clinicaltrials.gov

Expanded indications:

Valve-in-Valve

TMVR

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease

The Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low Risk Patients With Aortic Stenosis (PARTNER 3)

This study is currently recruiting participants. (see Contacts and Locations)

Verified May 2016 by Edwards Lifesciences

Sponsor:
Edwards Lifesciences

Information provided by (Responsible Party):
Edwards Lifesciences

ClinicalTrials.gov Identifier:
NCT02675114

First received: January 22, 2016
Last updated: May 26, 2016
Last verified: May 2016
History of Changes

To establish the safety and effectiveness of the Edwards SAPIEN 3 Transcatheter Heart Valve in patients with severe, symptomatic aortic stenosis who are at low operative risk for standard aortic valve replacement (AVR).

clinicaltrials.gov

Expanded indications:

Valve-in-Valve

TMVR

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease

Transcatheter Aortic Valve Replacement to UNload the Left Ventricle in Patients With ADvanced Heart Failure (TAVR UNLOAD)

This study is currently recruiting participants. (see Contacts and Locations)

Verified September 2016 by Cardiovascular Research Foundation, New York

Sponsor:
Cardiovascular Research Foundation, New York

Collaborators:
Cardialysis BV
Boston Biomedical Associates LLC

Information provided by (Responsible Party):
Cardiovascular Research Foundation, New York

ClinicalTrials.gov Identifier:
NCT02661451

First received: January 15, 2016
Last updated: September 15, 2016
Last verified: September 2016
History of Changes

The objective of this study is to determine the safety and efficacy of transcatheter aortic valve replacement (TAVR) via the trans-femoral approach in HF patients with moderate AS as compared with OHFT.

clinicaltrials.gov

Expanded indications:

Valve-in-Valve

TMVR

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease

Transcatheter Aortic Valve Replacement for the Treatment of Pure Native Aortic Valve Regurgitation

A Systematic Review

Anna Franzone, MD,[a] Raffaele Piccolo, MD,[a] George C.M. Siontis, MD,[a] Jonas Lanz, MD,[a] Stefan Stortecky, MD,[a] Fabien Praz, MD,[a] Eva Roost, MD,[b] René Vollenbroich, MD, MPP,[a] Stephan Windecker, MD,[a] Thomas Pilgrim, MD[a]

Drawing from 13 small studies, totaling 237 patients, and using predominantly self expanding prostheses,
- 7% (17) of patients required implantation of a second valve
- 2.5% (6) of patients required conversion to SAVR
- There were no cerebrovascular events.
- 7% 30-day mortality

Franzone et al. JACC Cv Intv, 2016

Expanded indications:

Valve-in-Valve

TMVR

Low Risk Aortic stenosis

Heart Failure with AS

Aortic Regurgitation

Mixed AoV Disease

ORIGINAL INVESTIGATIONS

Outcomes in Moderate Mixed Aortic Valve Disease

Is it Time for a Paradigm Shift?

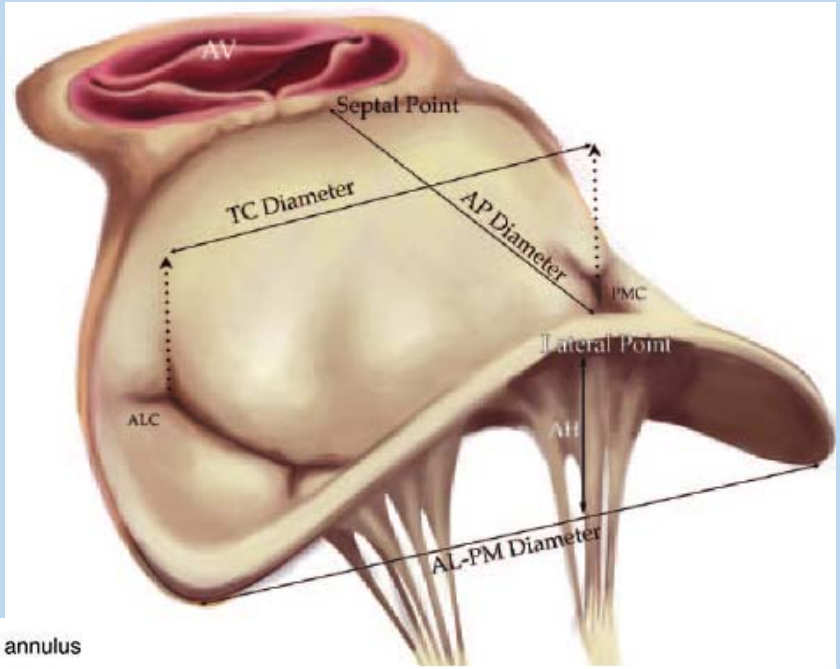
Alexander C. Egbe, MD, MPH, Sushil A. Luis, MBBS, Ratnasari Padang, MBBS, PhD, Carole A. Warnes, MD

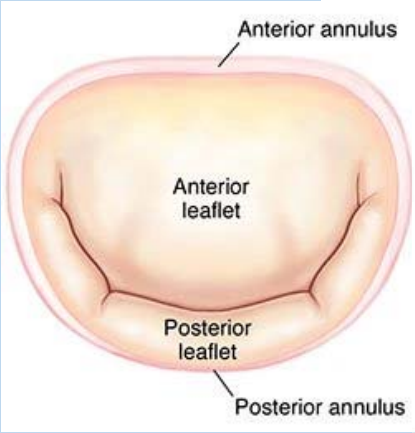
251 Mixed Moderate AS/AR patients with normal EF over a 20 year period
Compared to isolated-: moderate AR, moderate AS, and severe AS (117 each).
Mixed group: Mean 9.1 ± 4.2 year follow up.

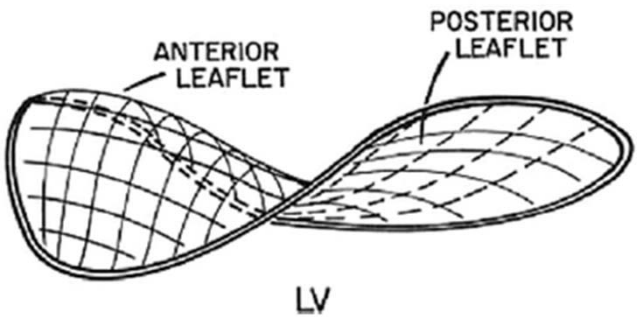
Adverse events in this group (symptom development, aortic valve replacement, cardiac death) at 5 years:
- similar to severe AS group **(71 vs 68%, p =0.49)**
- much higher than **mod AS (31%)**
- much higher than **mod AR (22%)**

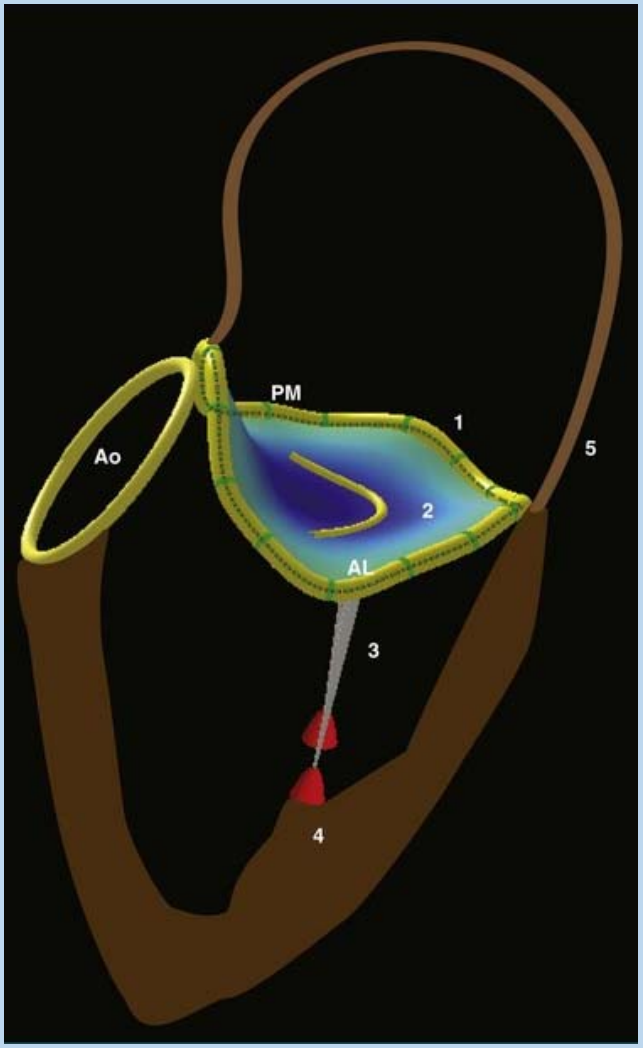
Egbe et al. JACC 2016

The Mitral Valve









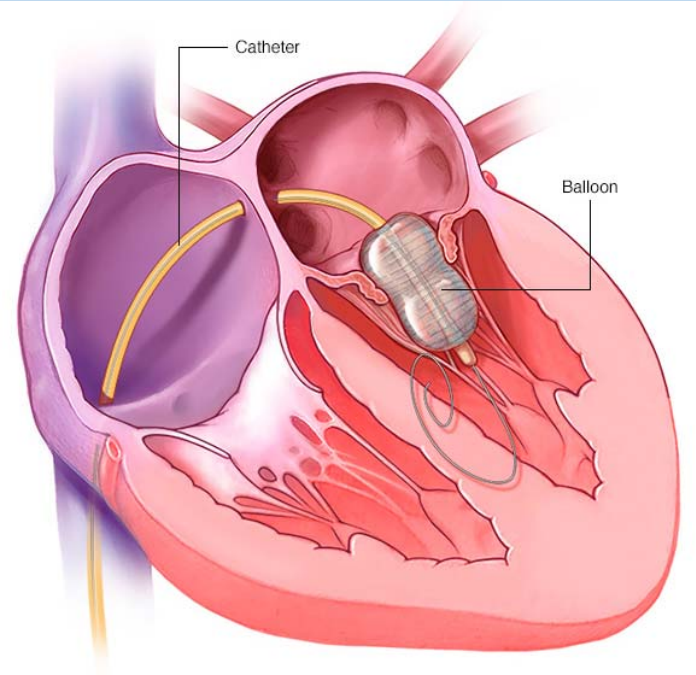
Mahmood and Matyal, Anesth Analg, 2015; Dorosz and Salcedo, RadiologyKey.com, 2016; Mitralvalverepair.org

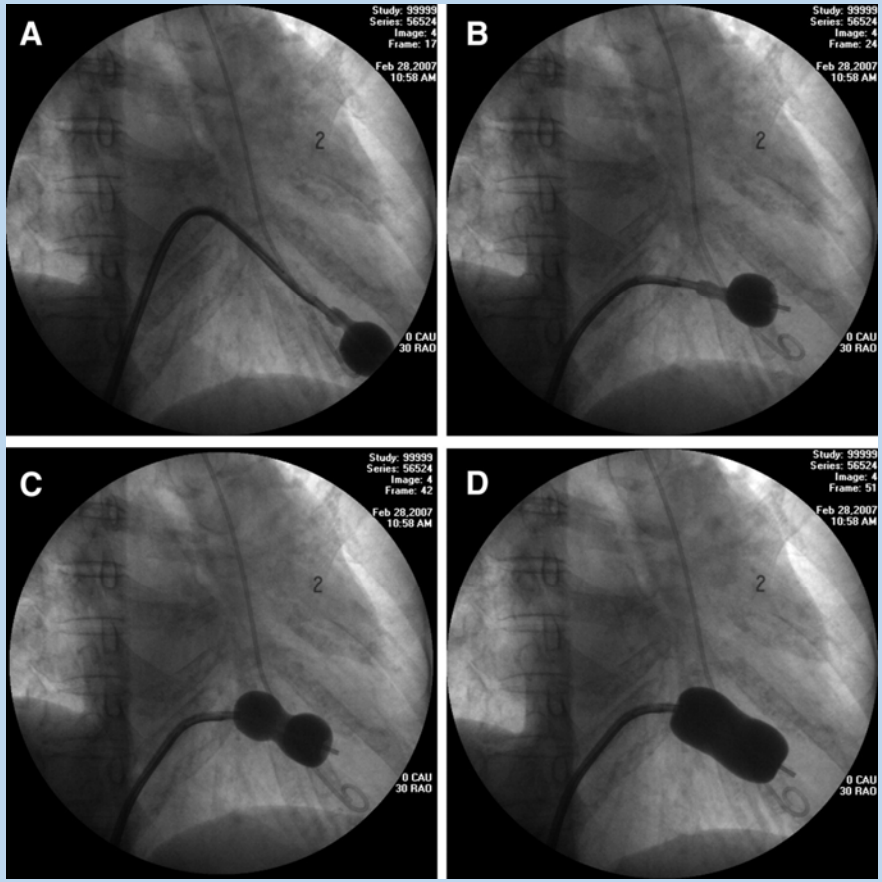
The Mitral Valve - Stenosis

Recommendations	COR	LOE
PMBC is recommended for symptomatic patients with severe MS (MVA ≤1.5 cm^2, stage D) and favorable valve morphology in the absence of contraindications	I	A
Mitral valve surgery is indicated in severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤1.5 cm^2, stage D) who are not high risk for surgery and who are not candidates for or failed previous PMBC	I	B
Concomitant mitral valve surgery is indicated for patients with severe MS (MVA ≤1.5 cm^2, stage C or D) undergoing other cardiac surgery	I	C
PMBC is reasonable for asymptomatic patients with very severe MS (MVA ≤1.0 cm^2, stage C) and favorable valve morphology in the absence of contraindications	IIa	C
Mitral valve surgery is reasonable for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤1.5 cm^2, stage D), provided there are other operative indications	IIa	C
PMBC may be considered for asymptomatic patients with severe MS (MVA ≤1.5 cm^2, stage C) and favorable valve morphology who have new onset of AF in the absence of contraindications	IIb	C
PMBC may be considered for symptomatic patients with MVA >1.5 cm^2 if there is evidence of hemodynamically significant MS during exercise	IIb	C
PMBC may be considered for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤1.5 cm^2, stage D) who have suboptimal valve anatomy and are not candidates for surgery or at high risk for surgery	IIb	C
Concomitant mitral valve surgery may be considered for patients with moderate MS (MVA 1.6–2.0 cm^2) undergoing other cardiac surgery	IIb	C
Mitral valve surgery and excision of the left atrial appendage may be	IIb	C

Nishimura et al. Circulation, 2014

Percutaneous Mitral Balloon Commissurotomy

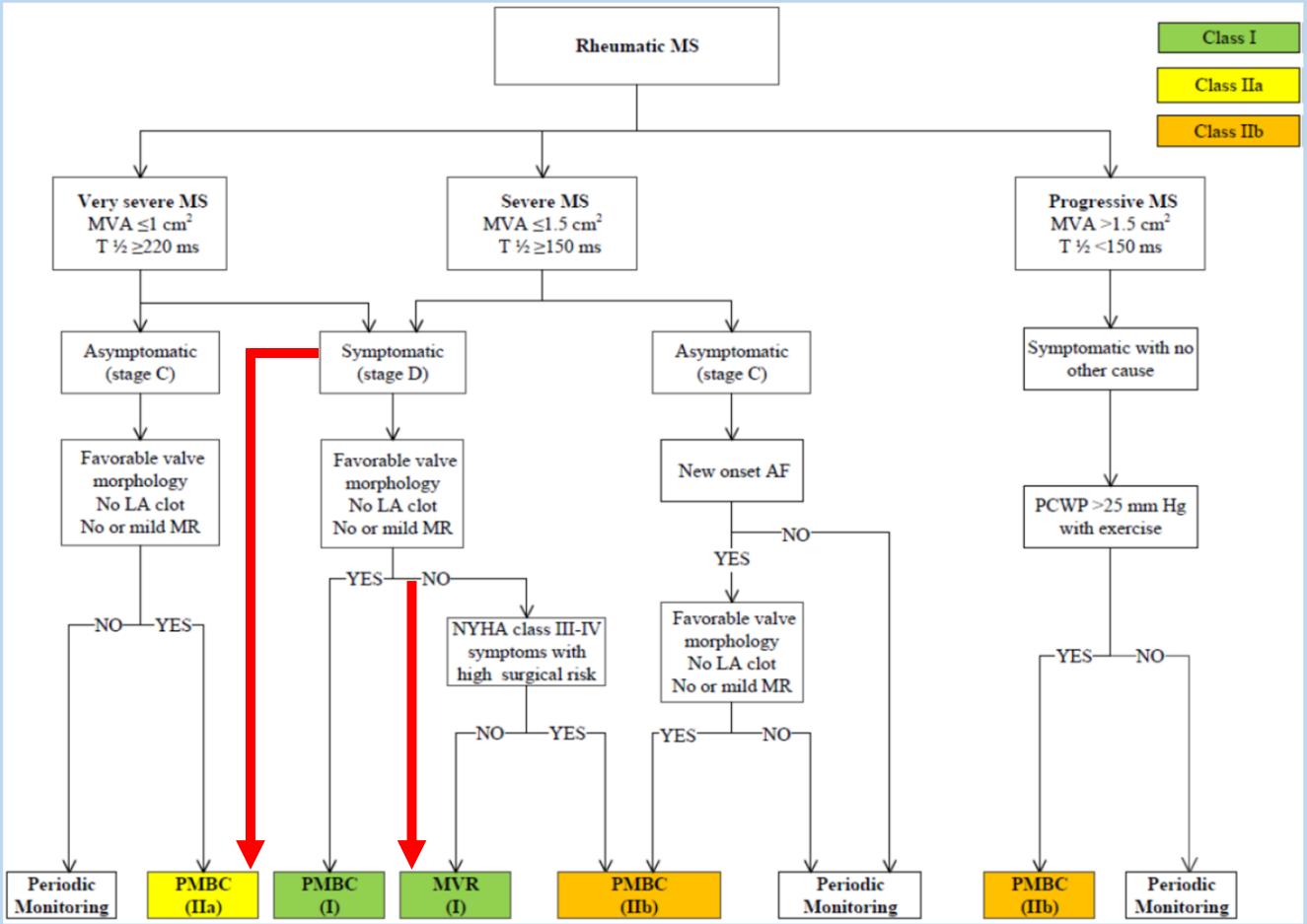




If valve anatomy is favorable based on Wilkins-Abascal Score

Mayoclinic.com, Nobuyoshi et al., Circulation 2009

The Mitral Valve - Stenosis



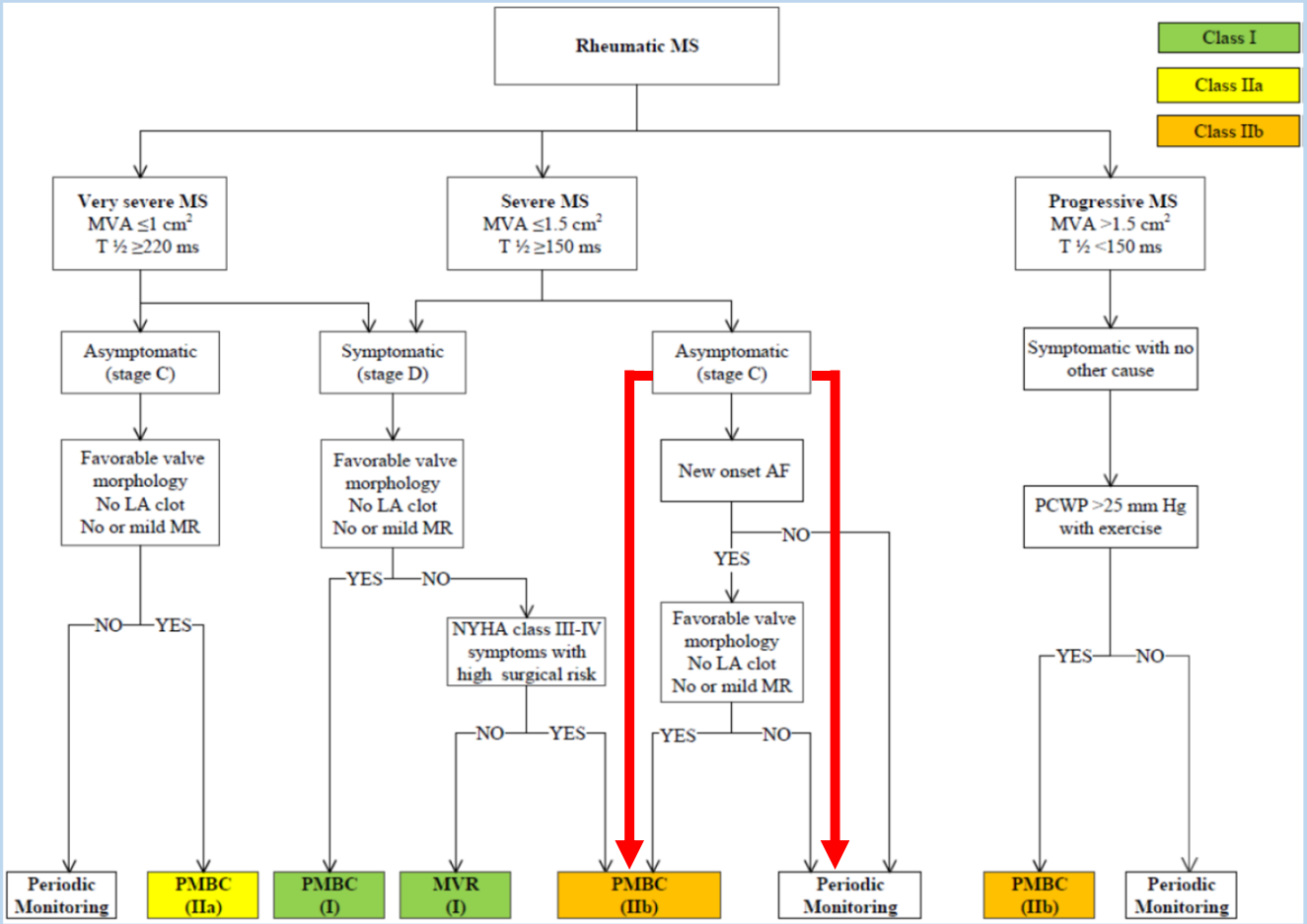
(Very) Severe
Symptomatic

MVR (I)

PMBC (IIa)

Nishimura et al. Circulation, 2014

The Mitral Valve - Stenosis



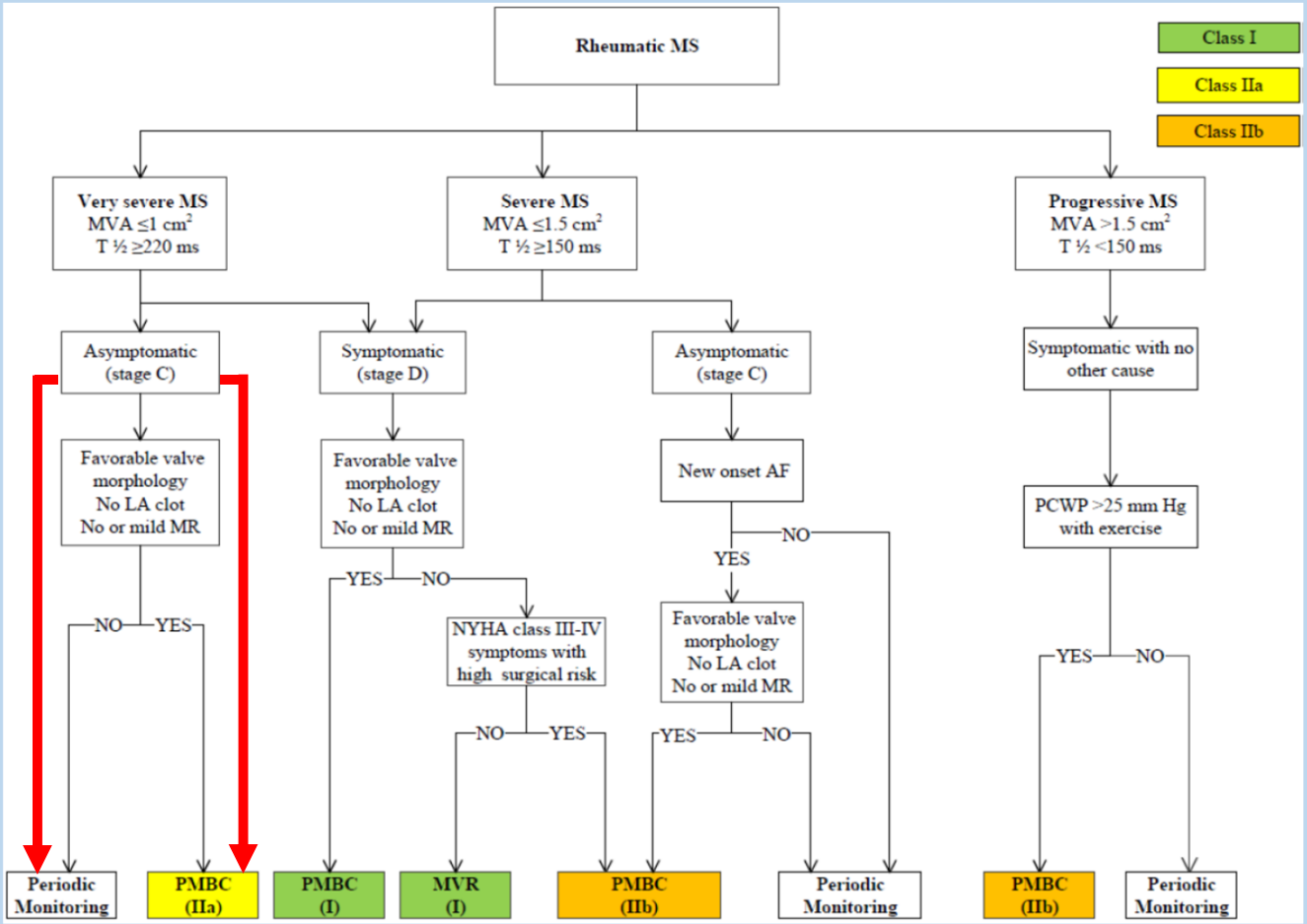
(Very) Severe **Symptomatic**

Severe **Asymptomatic,** with new Afib

PMBC (IIb)

Nishimura et al. Circulation, 2014

The Mitral Valve - Stenosis



(Very) Severe **Symptomatic**

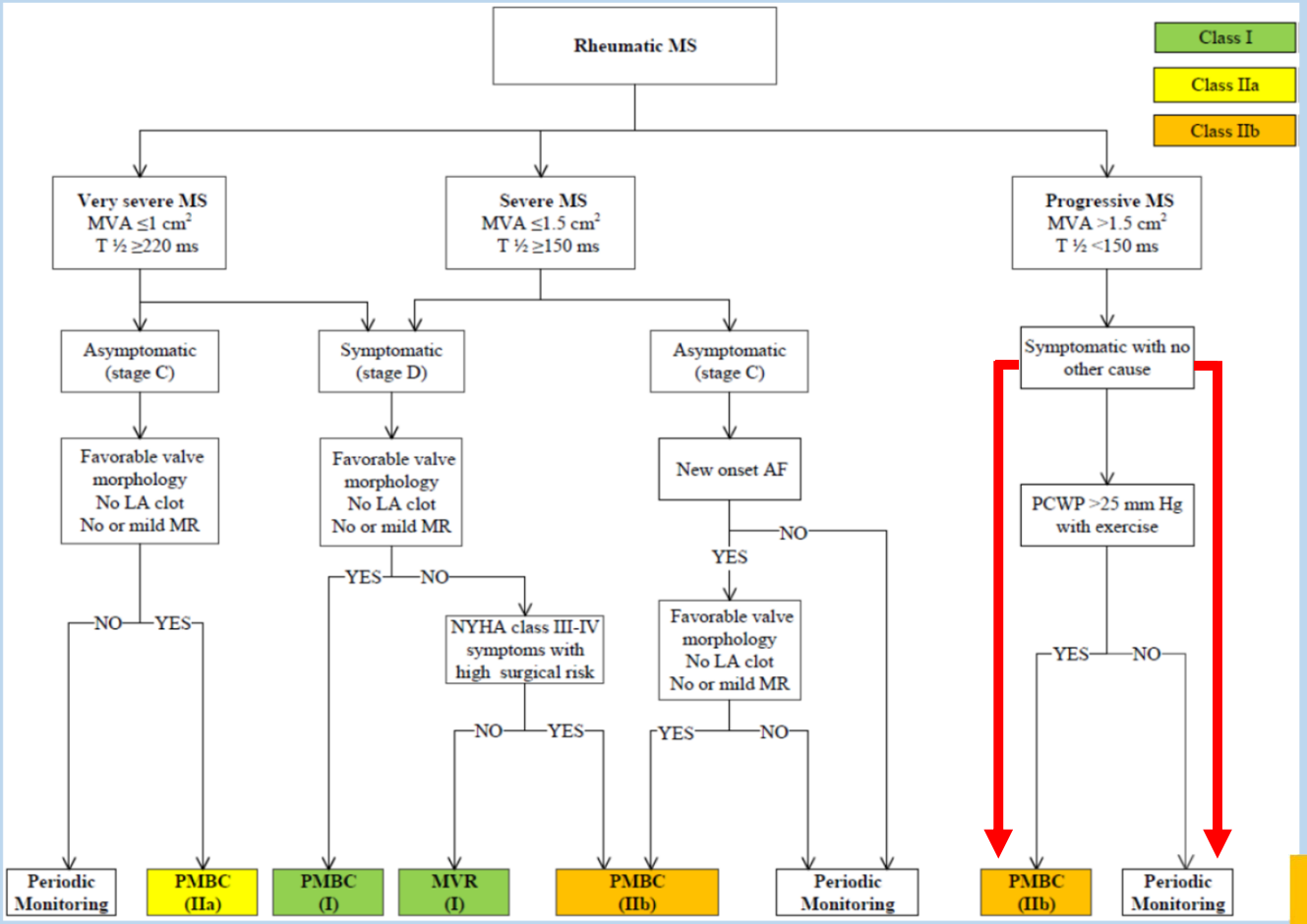
Severe **Asymptomatic**, with new Afib

Very Severe **Asymptomatic**

PMBC (IIa)

Nishimura et al. Circulation, 2014

The Mitral Valve - Stenosis



(Very) Severe **Symptomatic**

Severe **Asymptomatic**, with new Afib

Very Severe **Asymptomatic**

Progressive **Symptomatic**, elevated PCWP w/ exercise

PMBC (IIb)

Nishimura et al. Circulation, 2014

The Mitral Valve – Primary Regurgitation

Recommendations	COR	LOE
MV surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF >30%	I	B
MV surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30%–60% and/or LVESD ≥40 mm, stage C2)	I	B
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet	I	B
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished	I	B
Concomitant MV repair or replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications	I	B
MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1% when performed at a Heart Valve Center of Excellence	IIa	B
MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure >50 mm Hg)	IIa	B
Concomitant MV repair is reasonable in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications	IIa	C
MV surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF ≤30% (stage D)	IIb	C
MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation management is questionable	IIb	B
Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B
MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful	III: Harm	B

Mack et al. Lancet, 2016

The Mitral Valve – secondary Regurgitation

Recommendations	COR	LOE
MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR	IIa	C
MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)	IIb	B
MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery	IIb	C

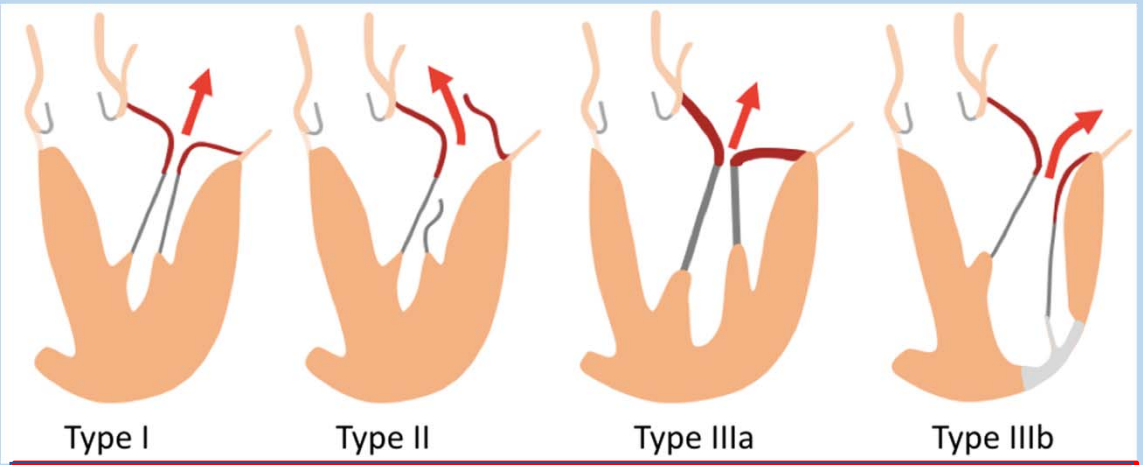
Mack et al. Lancet, 2016

The Mitral Valve - Regurgitation

Degenerative (Primary)
The valve itself is the primary site of pathology

Functional (Secondary)
The valve is structurally normal, but is functioning abnormally due to other cardiac pathology
- Most commonly, myocardial dysfunction.

Mixed
There are components of both myocardial dysfunction and degeneration of the valvular apparatus.



Carpentier Classification

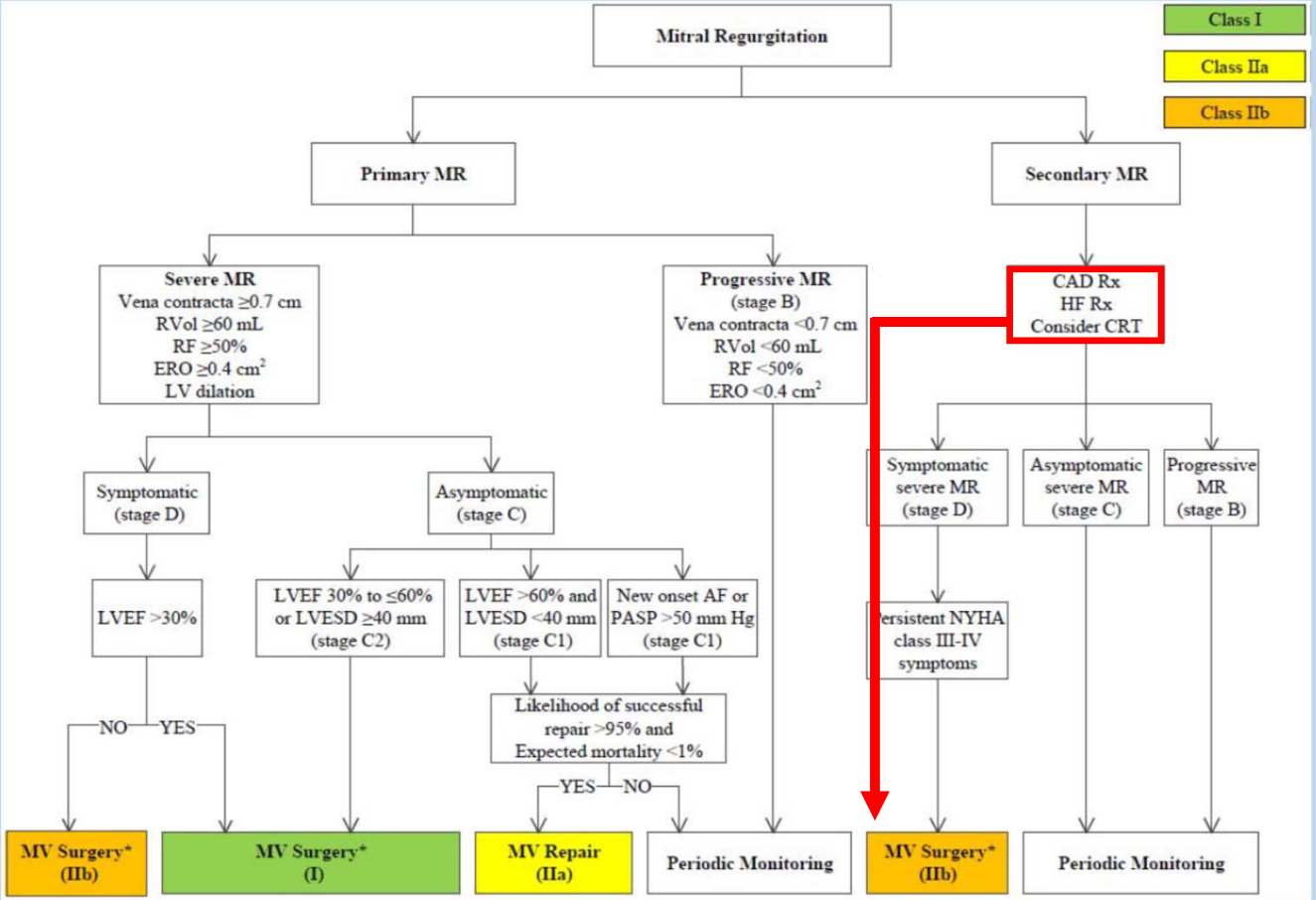
Type 1: normal leaflet motion, mitral annulus is dilated

Type 2: Leaflet prolapse or flail (Approval for Mitraclip)

Type 3a: restricted leaflet motion in both systole and diastole (Rheumatic disease)

Type 3b: restricted motion in systole (Functional/Ischemic)

The Mitral Valve - Regurgitation

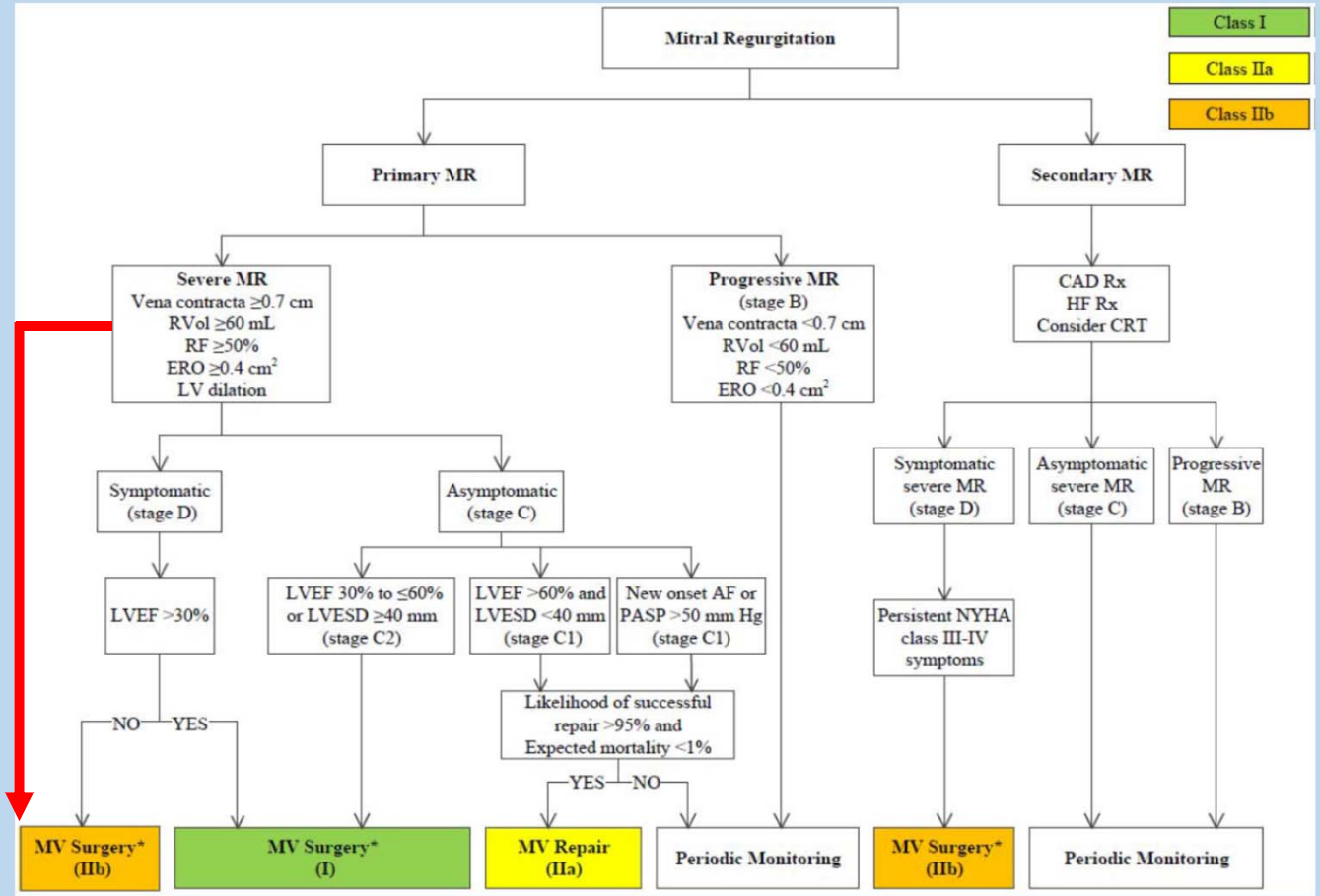


Secondary, Severe
Symptomatic

MV Surgery*
(IIb)

Nishimura et al. Circulation, 2014

The Mitral Valve - Regurgitation



Secondary, Severe
Symptomatic

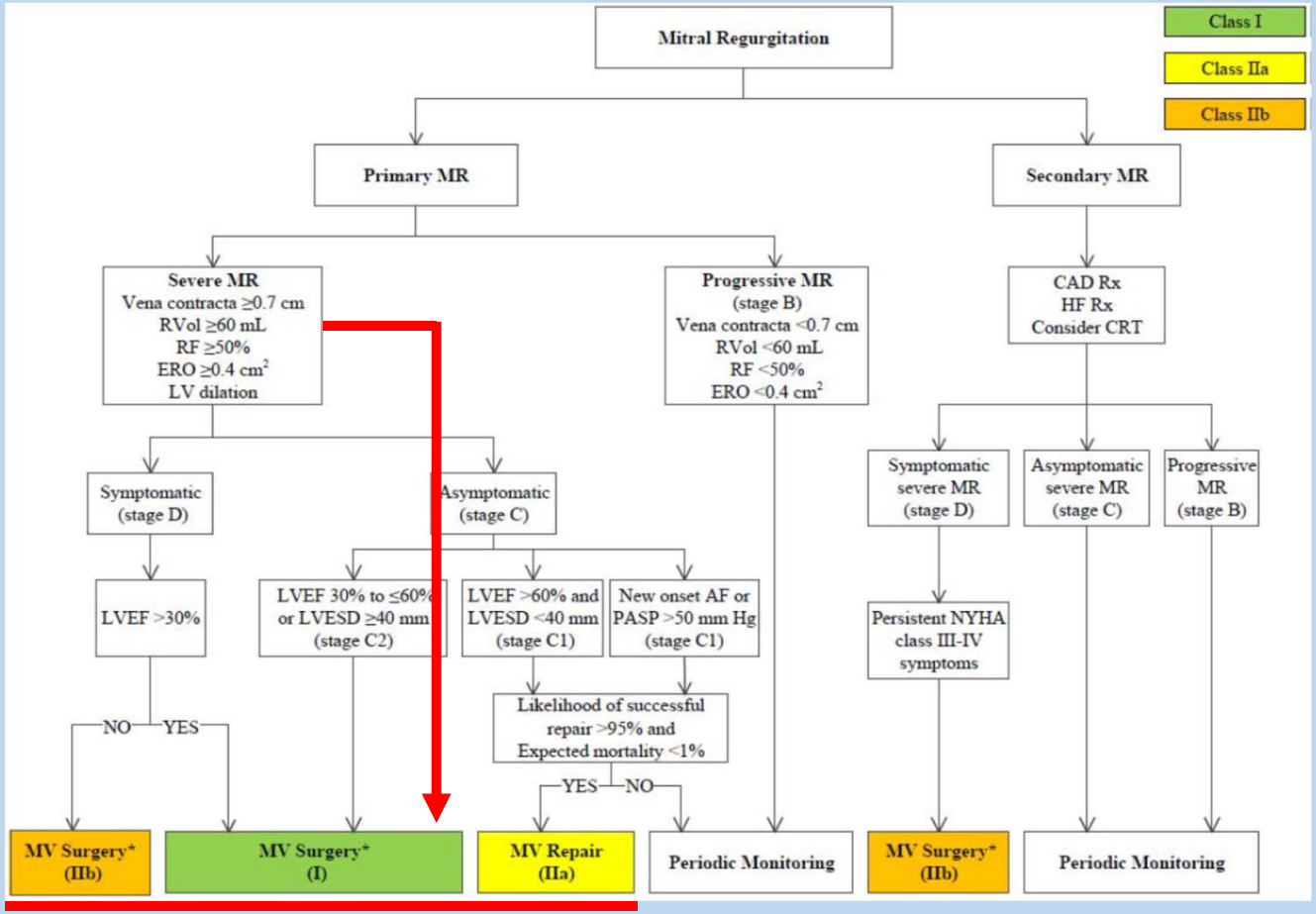
Primary, Severe
Symptomatic

MV Surgery*
(IIb)

MV Surgery*
(I)

Nishimura et al. Circulation, 2014

The Mitral Valve - Regurgitation



Secondary, Severe
Symptomatic

Primary, Severe
Symptomatic

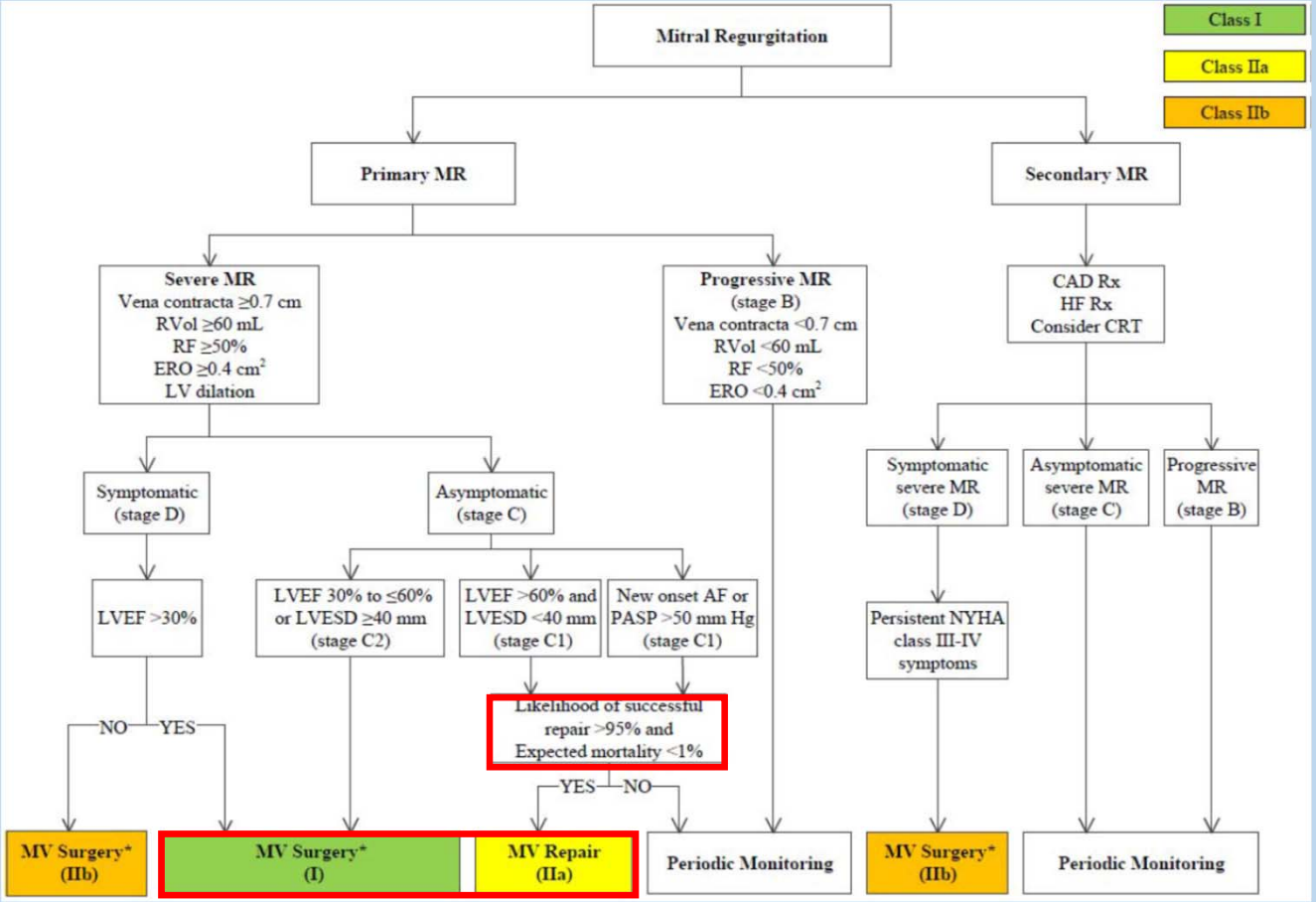
Primary, Severe
Asymptomatic

MV Surgery*
(I)

MV Repair
(IIa)

Nishimura et al. Circulation, 2014

The Mitral Valve - Regurgitation



Secondary, Severe
Symptomatic

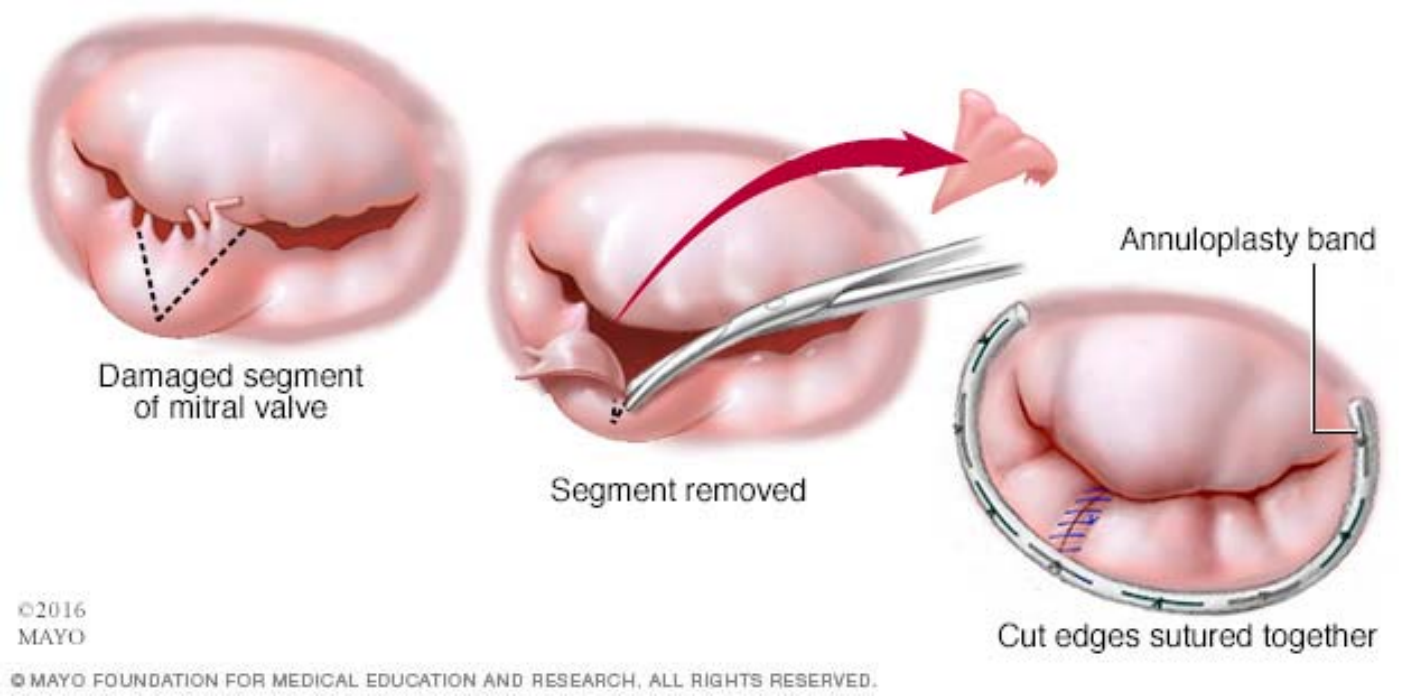
Primary, Severe
Symptomatic

Primary, Severe
Asymptomatic

Repair over Replace, if feasible

Mack et al. Lancet, 2016

Surgical Mitral Valve Repair vs Replacement



Mayoclinic.org

Robotic Surgery: Mitral Valve

Impediments

Inadequate training / retraining ops

Inadequate visualization

Insufficient outcomes data

Installation/maintenance cost

Limited application

Longer by-pass / clamp times

Investment in trans-catheter technology

Benefits

Smaller incisions

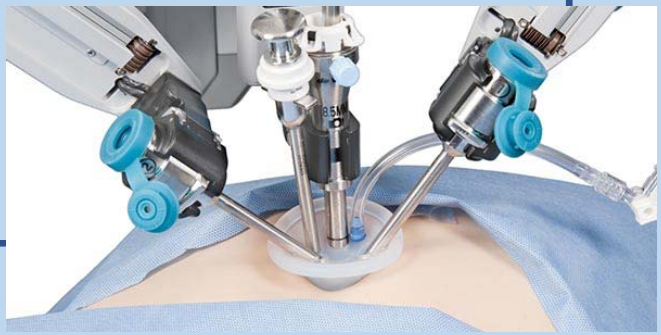
Faster recovery

3D maneuverability

3D visualization

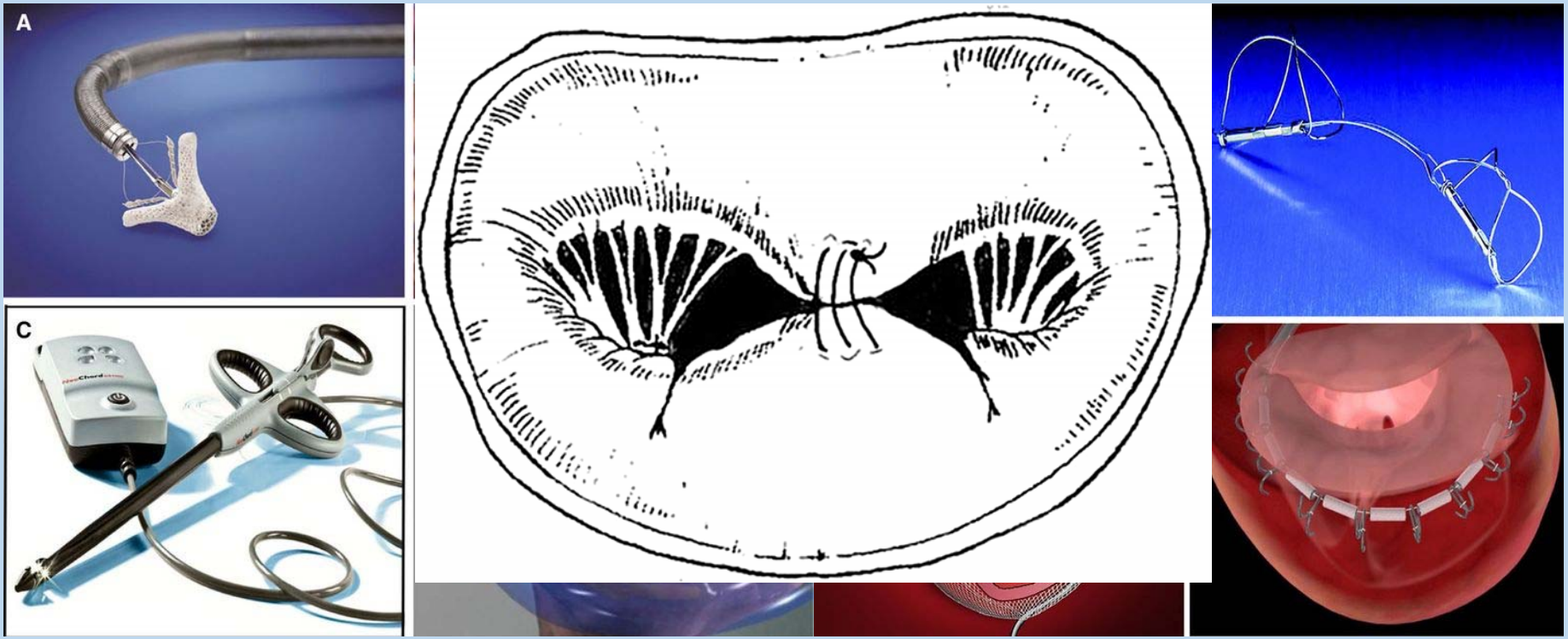
Potential for more complete repair

Lower Transfusion/ A-fib reqs



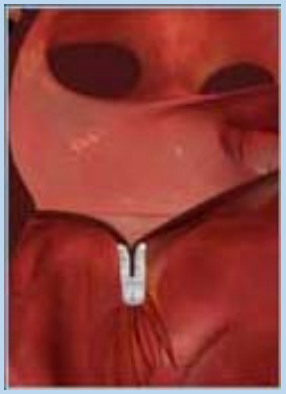
Kcmedcenter.com, heart-valve-surgery.com

Investigational Transcatheter Mitral Repair



Sarojja et al, Circulation 2017; , Fedak et al. Circulation, 2008

Edge-to-Edge Repair



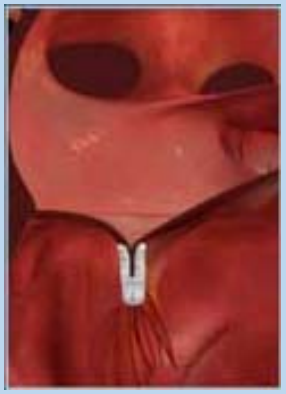
<u>Mitraclip</u>: The only approved device in the US for Trans-catheter repair:
Indicated for

Degenerative Disease only.

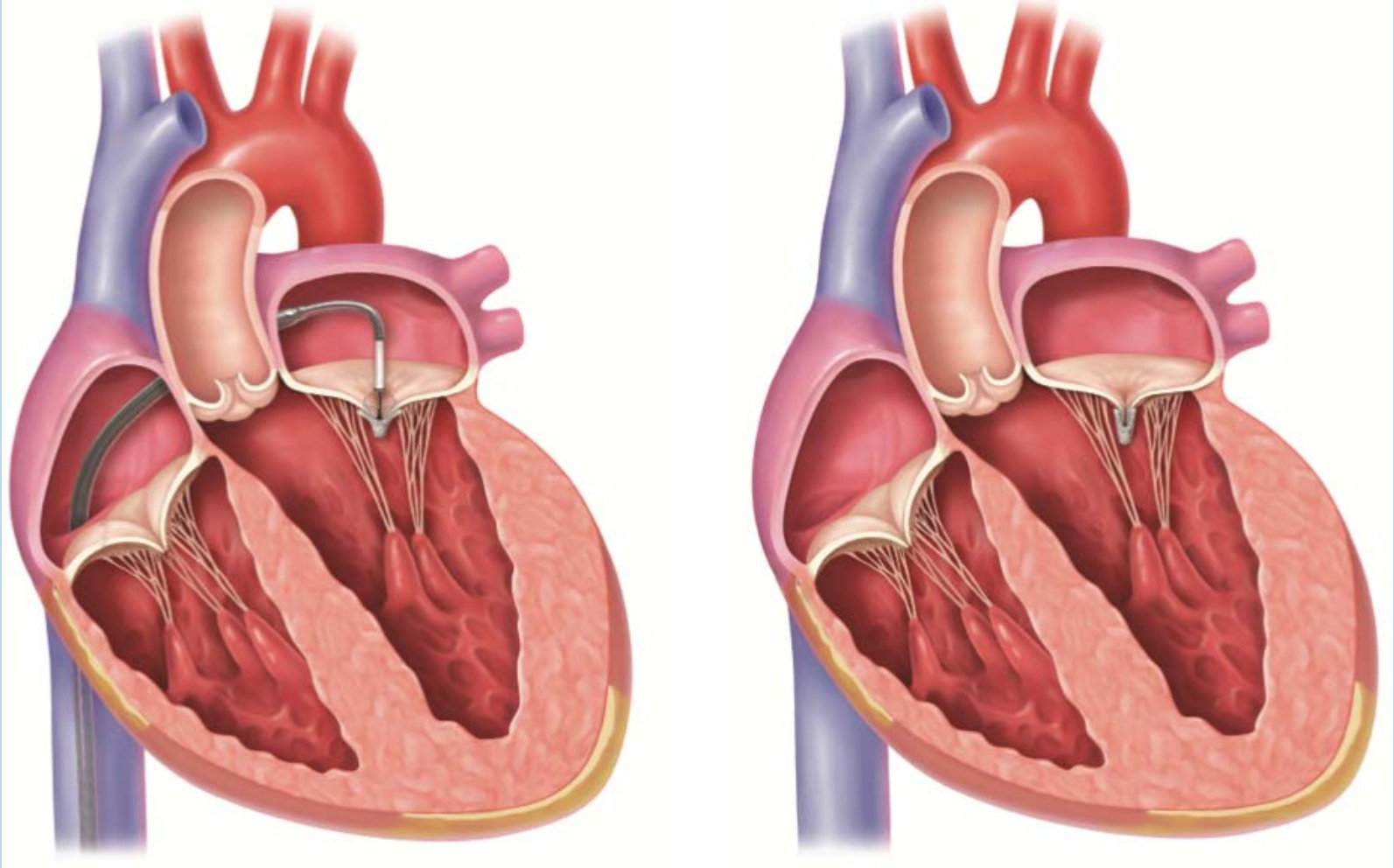
Dicardiology.com, AbbottVascular, Carminati et al. Expert Rev Cardiovasc, 2013

MitraClip TMVr

IIb	B	Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for heart failure (HF) (124).



Dicardiology.com, AbbottVascular, Carminati et al. Expert Rev Cardiovasc, 2013; Nishimura et al. Circulation, 2017



Mayoclinic.org

Mitraclip- EVEREST Trials

Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

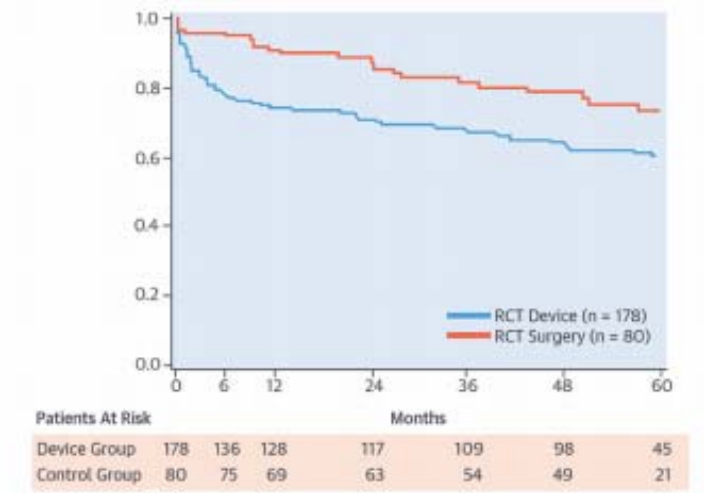
5-Year Results of EVEREST II

Ted Feldman, MD,* Saibal Kar, MD,† Sammy Elmariah, MD, MPH,‡§ Steven C. Smart, MD,* Alfredo Trento, MD,‖ Robert J. Siegel, MD,† Patricia Apruzzese, MS,§ Peter Fail, MD,¶ Michael J. Rinaldi, MD,# Richard W. Smalling, MD, PHD,** James B. Hermiller, MD,†† David Heimansohn, MD,‡‡ William A. Gray, MD,§§ Paul A. Grayburn, MD,‖‖ Michael J. Mack, MD,¶¶ D. Scott Lim, MD,## Gorav Ailawadi, MD,*** Howard C. Herrmann, MD,††† Michael A. Acker, MD,‡‡‡ Frank E. Silvestry, MD,††† Elyse Foster, MD,§§§ Andrew Wang, MD,‖‖‖ Donald D. Glower, MD,¶¶¶ Laura Mauri, MD,§### for the EVEREST II Investigators

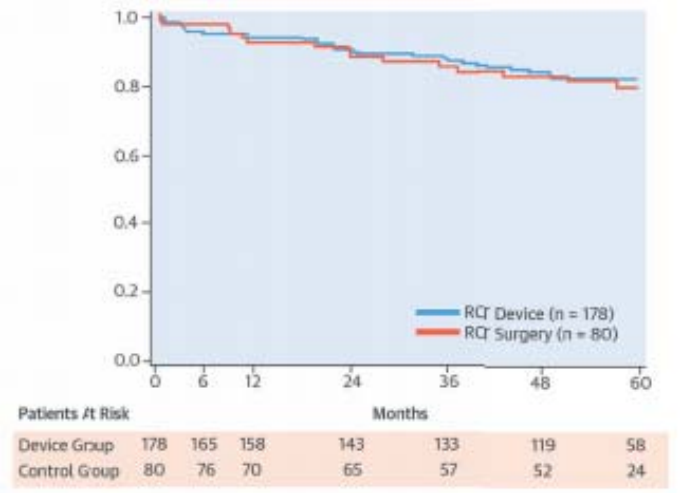
TABLE 2 All-Treated Cohort: Efficacy Endpoint and Components at 5 Years*

	5 Years			5 Years if Event-Free at 1 Year		
	Percutaneous Repair (n = 154)	Surgery (n = 56)	p Value	Percutaneous Repair (n = 87)	Surgery (n = 48)	p Value
Freedom from death, MV surgery, or reoperation, and 3+ or 4+ MR	44.2 (68)	64.3 (36)	0.01	69.0 (60)	75.0 (36)	0.55
Death	20.8 (32)	26.8 (15)	0.36	16.1 (14)	16.7 (8)	>0.99
MV surgery or reoperation	27.9 (43)	8.9 (5)	0.003	5.7 (5)	6.3 (3)	>0.99
3+ or 4+ MR	12.3 (19)	1.8 (1)	0.02	11.5 (10)	2.1 (1)	0.10

Feldman et al. JACC, 2015

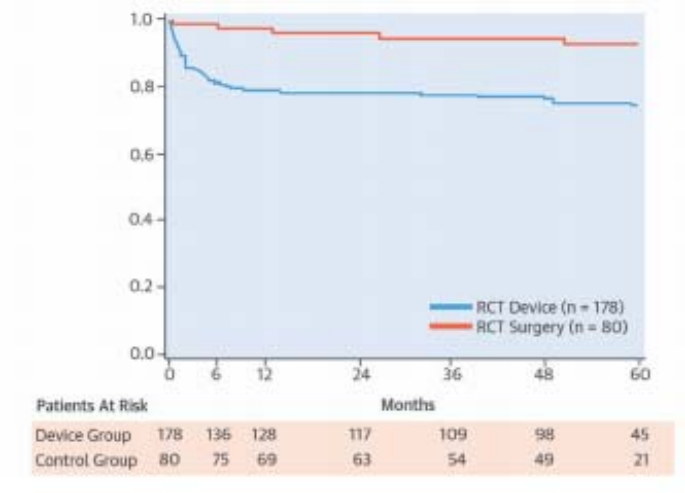


Freedom from Death, MV Surgery or Reoperation

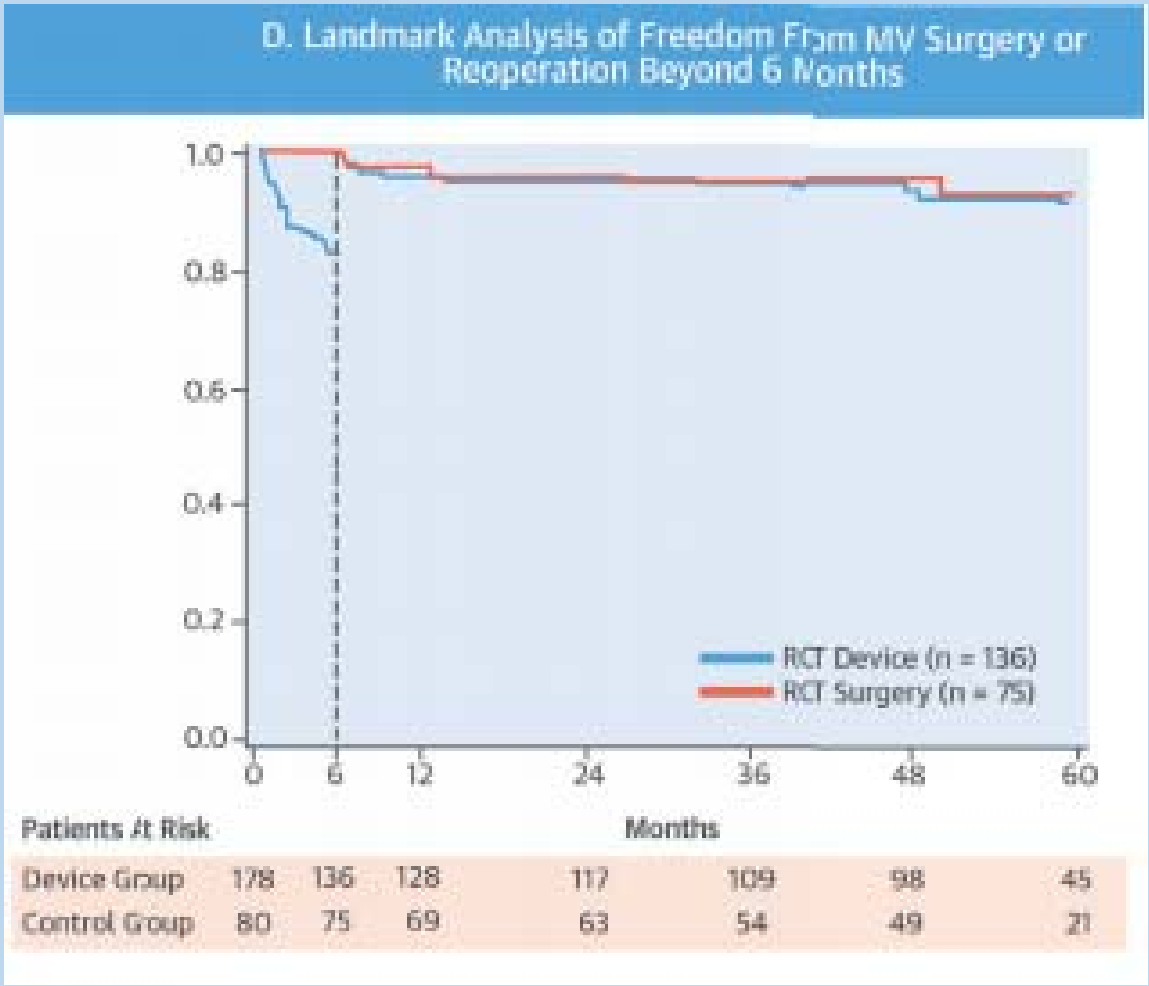


Freedom from Death

Freedom from MV Surgery or Reoperation

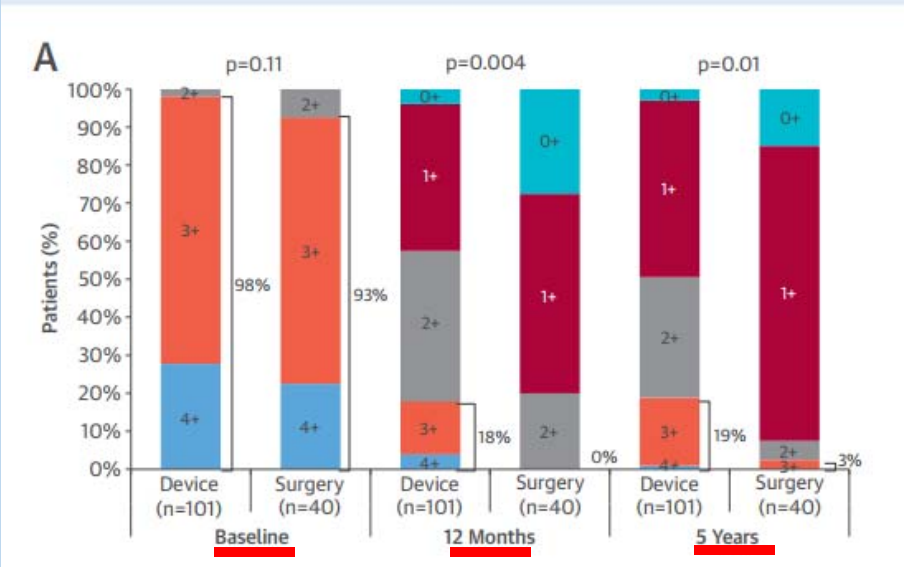


Feldman et al. JACC, 2015

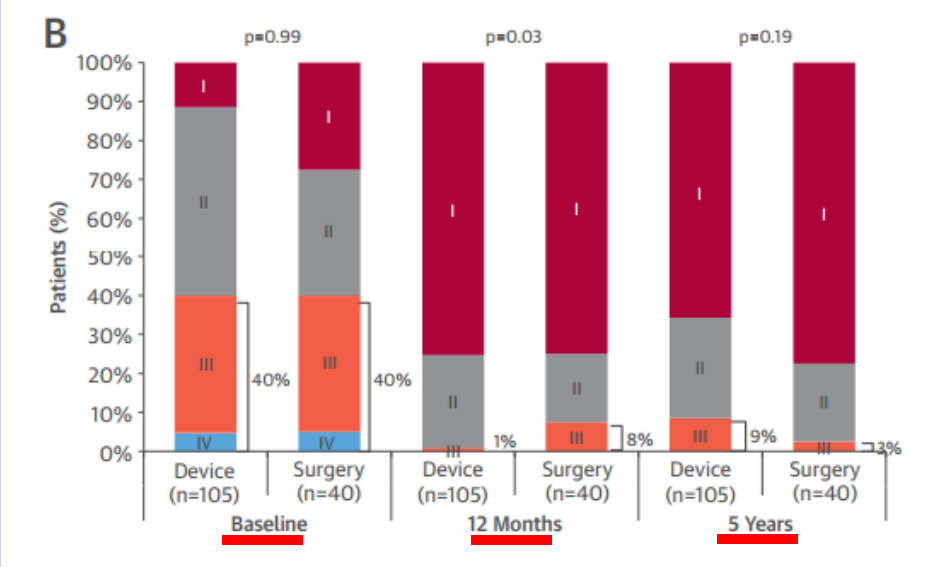


Feldman et al. JACC, 2015

Echocardiographic vs Clinical Response



Echocardiographic Grade



NYHA Class Category

Feldman et al. JACC, 2015

Mitraclip- Meta-analysis

STRUCTURAL HEART DISEASE

(Meta)-Analysis of Safety and Efficacy Following Edge-to-Edge Mitral Valve Repair Using the MitraClip System

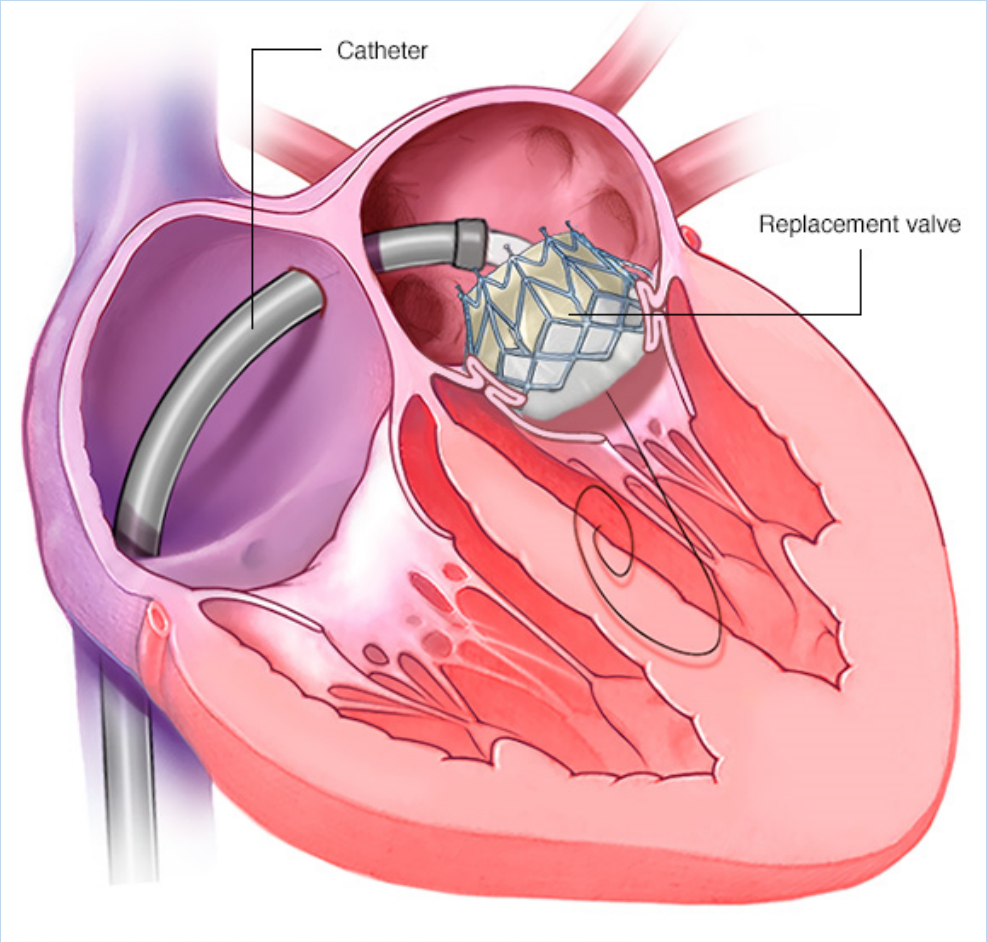
DOROTHEE H.L. BAIL, M.D., PH.D.

	12-month outcome		
	Numbers (n)	Weighted mean (%)	95% CI
MR<2+		80.6	77.7; 83.0
Death (Survival)		17.4 (82.6)	15.1; 19.9
NYHA class 1–2		66.1	62.9; 69.2
MAE all (death excluded)			
oMVS		11.4	9.6; 13.5

	30-day outcome			6-month outcome			12-month outcome		
	Numbers (n)	Weighted mean (%)	95% CI	Numbers (n)	Weighted mean (%)	95% CI	Numbers (n)	Weighted mean (%)	95% CI
MR<2+	2862/2473	86.4	85.1; 87.6	575 (717)	80.2	77.1; 83.1	676 (839)	80.6	77.7; 83.0
Death (Survival)	3586/102	2.8 (97.2)	2.3; 3.4	129 (1061)	11.9 (88.0)	10.2; 14.3	245 (1405)	17.4 (82.6)	15.1; 19.9
NYHA class 1–2	350/232	66.3	61.1; 71.2	703 (894)	78.6	75.8; 81.3	605 (915)	66.1	62.9; 69.2
MAE all (death excluded)	3551/649	18.3	17.0; 19.6	61 (316)	18.9	15.1; 24.1			
oMVS	3206/112	3.5	2.9; 4.2	27 (607)	4.5	2.9; 6.4	124 (1084)	11.4	9.6; 13.5

Bail DH, J Interven Cardiol, 2014

The Holy Grail: TMV- Replacement



MayoClinic.com

The Holy Grail: TMVR

Carrel, Ann Trans Med, 2017

Post-procedure care – In Hospital

Trans-catheter

Day of – extubate (if necessary)
wean vasoactive agents
remove all vascular access sites
same day ambulation

Day 1 – follow up imaging and labs
removal of remain tubes/lines
med titration
physical therapy

Day 2 – possible discharge

Average: 2-3 days (Min 1)

Surgery

Day of – extubate, wean vasoactive agents

Day 1 – wean meds, lines, up to chair

Day 2 – wound care, remove lines, remove chest tube

Day 3 – progressive ambulation, med titration, advance diet

Day 4 – physical therapy, med titration

Day 5 – possible discharge.

Average: 4-8 days (Min 3-4)

www.surgeryencyclopedia.com

Post-procedure care – Long term

Trans-catheter

Wk 1 – monitor access sites, restful activity at home

Wk 3 – start formal physical therapy

Wk 4-6 – shift from recovery to benefit

Surgery

Wk 1-2 – monitor incision, pain management, restful activity at home.

Wk 2 – removal stitches, adjust medications, echocardiogram

Wk 3-4 – initiate physical therapy
Cardiology follow up

Wk 8-12 – shift from recovery to benefit.

Thank you

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COLLEGE OF MEDICINE
UNIVERSITY OF SOUTH FLORIDA

USF HEALTH