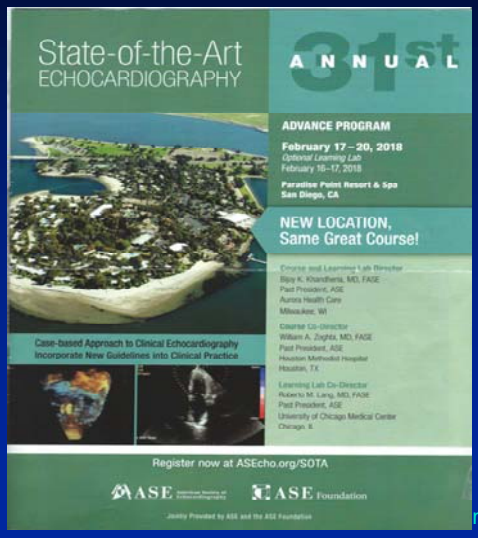
MITRAL STENOSIS: MANY FLAVORS
Rheumatic and Calcification

- David S Rubenson MD FACC FASE
- Founding Director, Cardiac Non-Invasive Laboratory
- Scripps Clinic Medical Group



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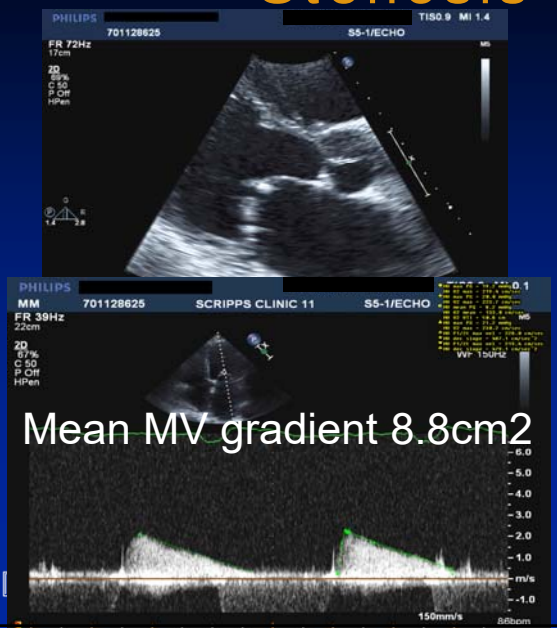
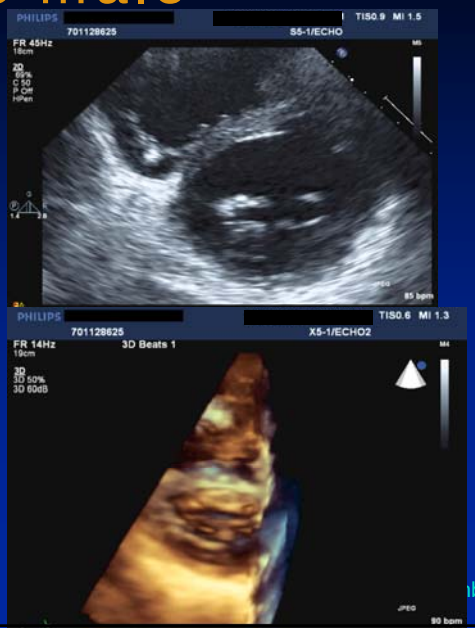
Rheumatic Mitral Stenosis 76yo male





ıber 2

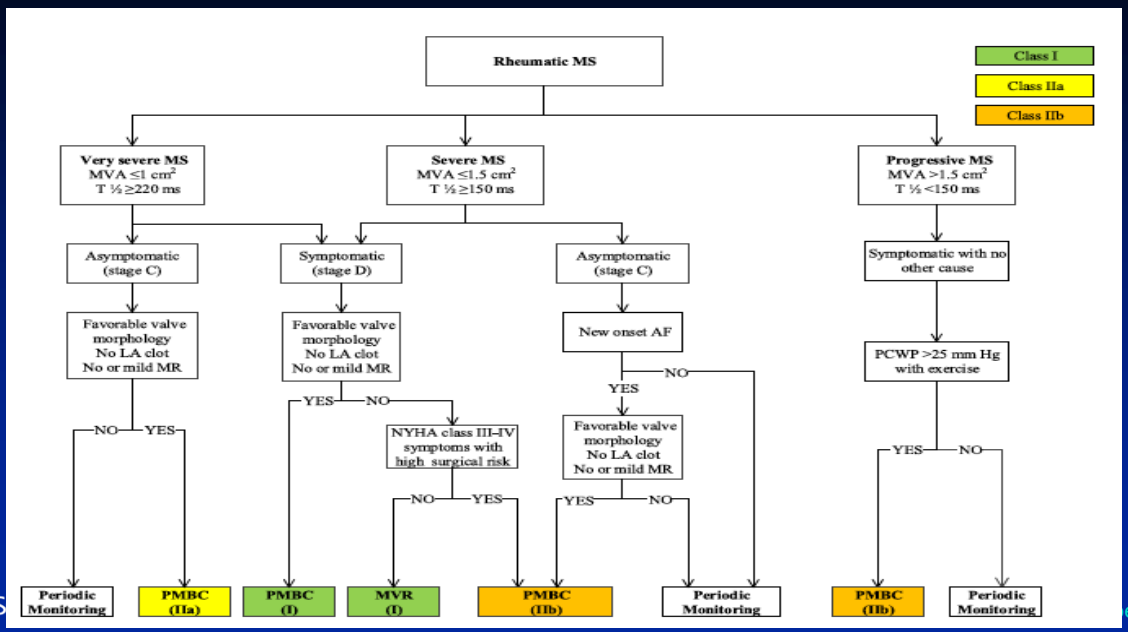
Etiologies of MS

- Rheumatic Heart Disease
- Mitral Annular calcification
- Radiation-associated valve disease
- Rare causes
  - Fabrys, mucopolysacaridosis
  - Methysergide therapy
  - Carcinoid heart disease
  - Post MV repair

SCRIPPS CLINIC

number 3

Guideline Algorithm: Treatment of MS



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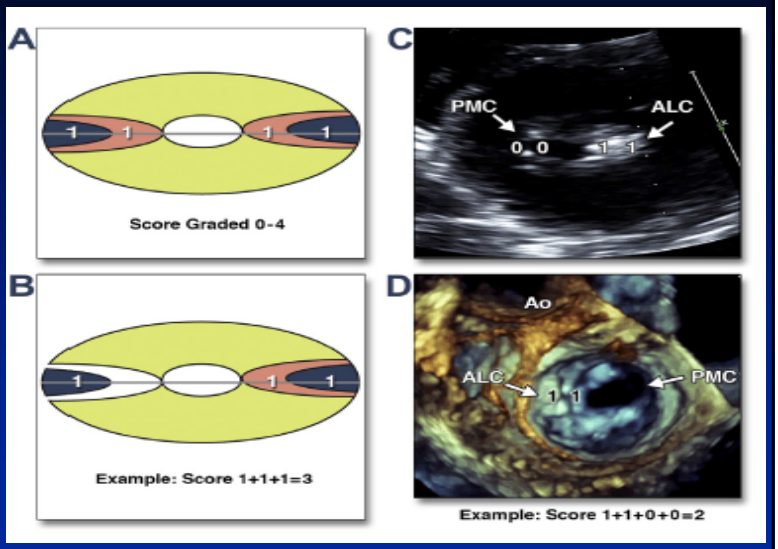
Scoring Systems

- Wilkins
  - Mobility, calcification, thickening and subvalvular
- Anwar
  - 3D assessment of Ca++ and subvalvular



SCRIPPS CLINIC

JACC CV Imag 2013;6:1191

number 5

45 y/o male with symptomatic Rheumatic Mitral Stenosis

SCRIPPS CLINIC

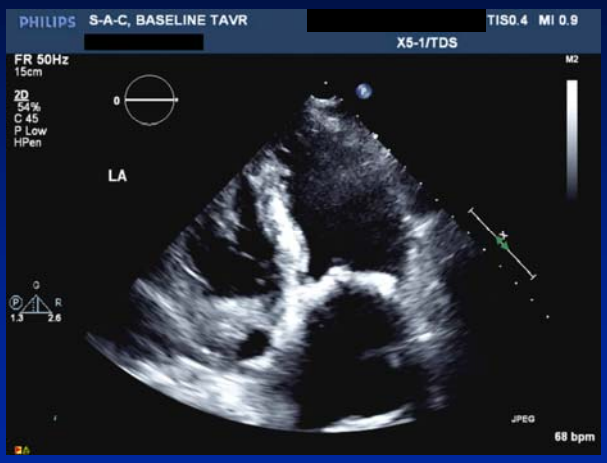
number 6

CALCIFICATION

SCRIPPS CLINIC

number 7

A 79 yo male presents for a TAVR evaluation. The echo image shown is associated with a 10mmHg mitral valve gradient at a HR of 68 bt/min. Survival in such patients with degenerative calcific mitral stenosis is:

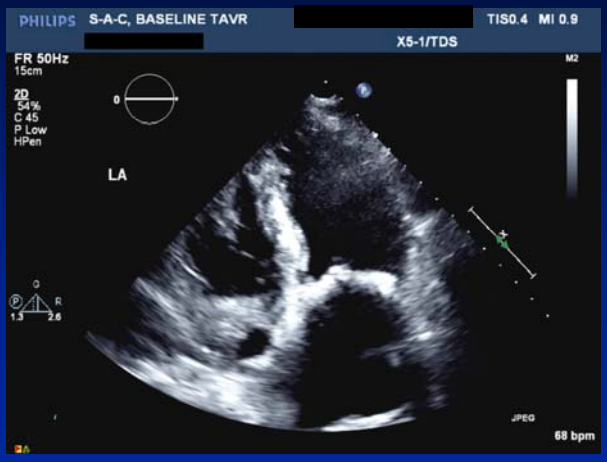


1. Same as the "expected" survival in the general population
2. Moderately reduced compared with "expected"
3. Determined entirely by the patient's aortic stenosis and unaffected by the MAC
4. Unknown – this has not been studied in such patients

SCRIPPS CLINIC

number 8

A 79 yo male presents for a TAVR evaluation. The echo image shown is associated with a 10mmHg mitral valve gradient at a HR of 68 bt/min. Survival in such patients with degenerative calcific mitral stenosis is:

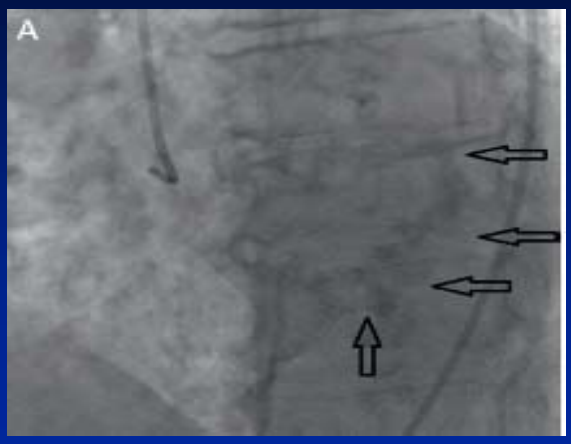


1. Same as the "expected" survival in the general population
2. Moderately reduced compared with "expected"
3. Determined entirely by the patient's aortic stenosis and unaffected by the MAC
4. Unknown – this has not been studied in such patients

SCRIPPS CLINIC

number 9

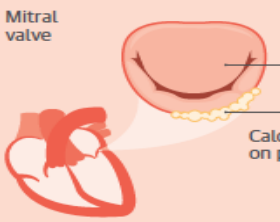
MAC may result in important MITRAL STENOSIS



SCRIPPS CLINIC

number 10

CENTRAL ILLUSTRATION Mitral Annulus Calcification Overview: Diagnosis, Risk Factors, and Clinical Implications

MITRAL VALVE CALCIFICATION	DIAGNOSTIC IMAGING	RISK FACTORS FOR MAC	CLINICAL IMPLICATIONS
 **Definition:** chronic degenerative process in the fibrous base of the MV, more commonly in the posterior annulus than the anterior annulus	• **Echocardiography:** MAC is visualized as an echodense structure with an irregular, lumpy appearance and an associated acoustic shadowing. • **Computed tomography:** Highly effective for cardiac, coronary, and aortic calcification imaging. A useful tool to evaluate the extent and location of MAC.	• Increased age • Female • Chronic kidney disease • Multiple cardiovascular risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking) • Increased MV stress (hypertension, aortic stenosis, hypertrophic cardiomyopathy, MV prolapse) • Metabolic disorders (Marfan syndrome, Hurler syndrome) • Osteoporosis	• Increase in cardiovascular disease and mortality • Increase in MV disease (mitral regurgitation, mitral stenosis, endocarditis) • Increase in arrhythmias (conduction system disease, atrial fibrillation) • Increase in MV surgery complications and mortality

Abramowitz, Y. et al. J Am Coll Cardiol. 2015; 66(17):1934–41.

Histological, clinicopathological, and contemporary imaging studies that examined the association between mitral annulus calcification and other disease entities enhanced our knowledge of the pathogenesis of MAC and enabled a better understanding of this process and its clinical importance. MAC = mitral annulus calcification; MV = mitral valve.

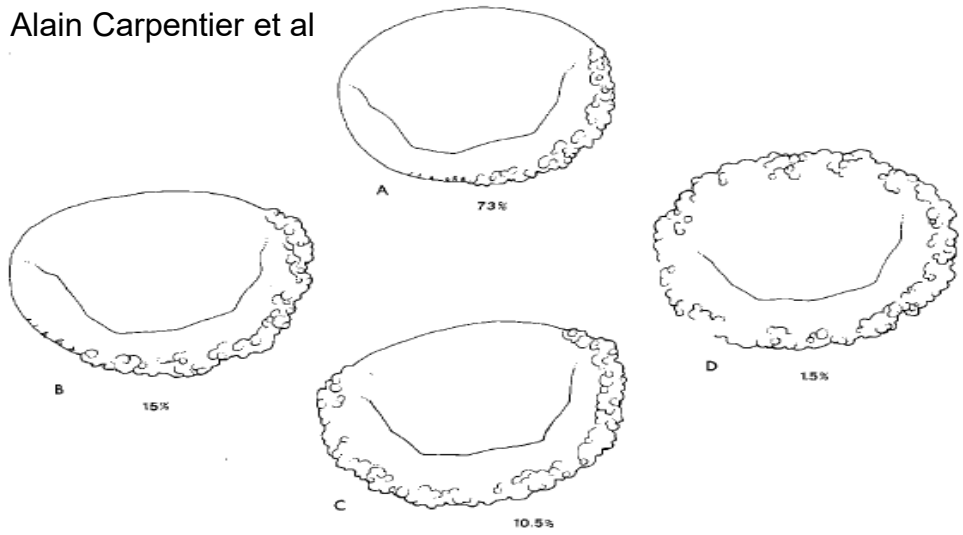
SCRIPPS CLINIC

JACC 2015:66:1934

number 11

MITRAL VALVE CALCIUM DISTRIBUTION

Alain Carpentier et al

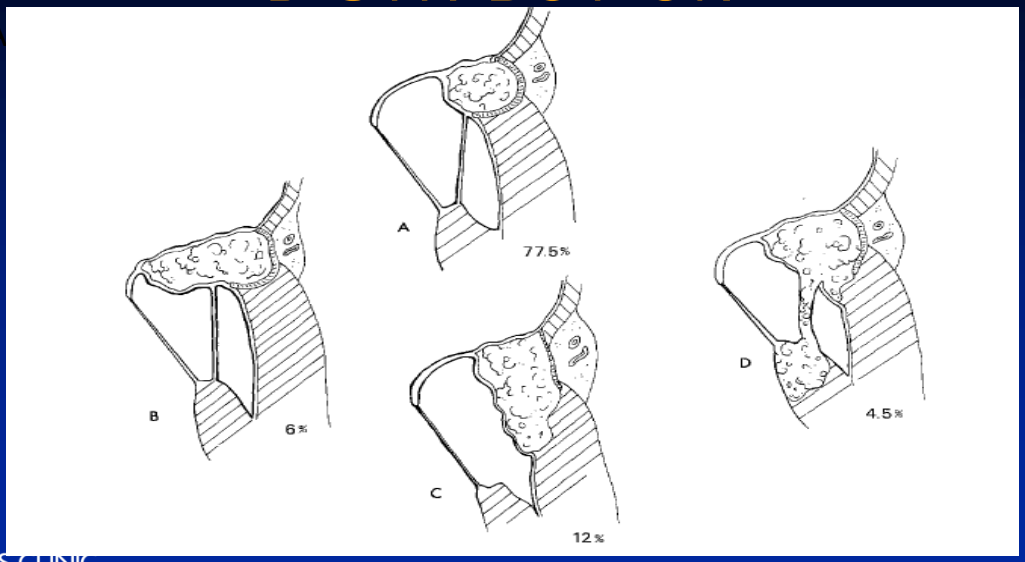


SCRIPPS CLINIC

J Thor and CV Surg 1996;111:718

number 12

MITRAL VALVE CALCIUM DISTRIBUTION



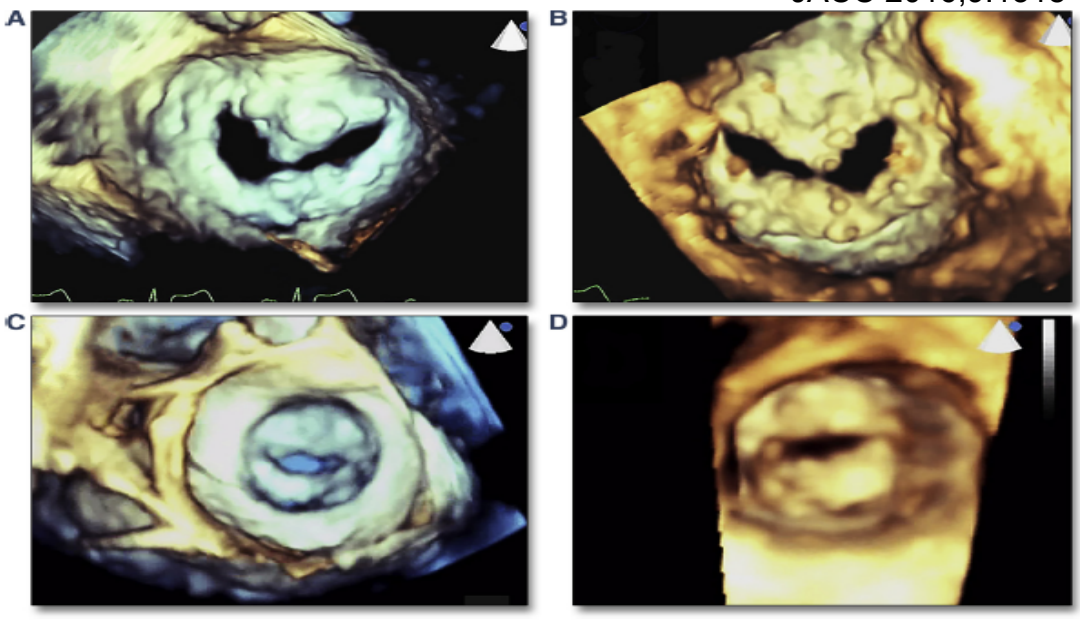
SCRIPPS CLINIC

J Thor and CV Surg 1996;111:718

number 13

FIGURE 2 Unique Features of Calcific Mitral Stenosis

JACC 2016;9:1318



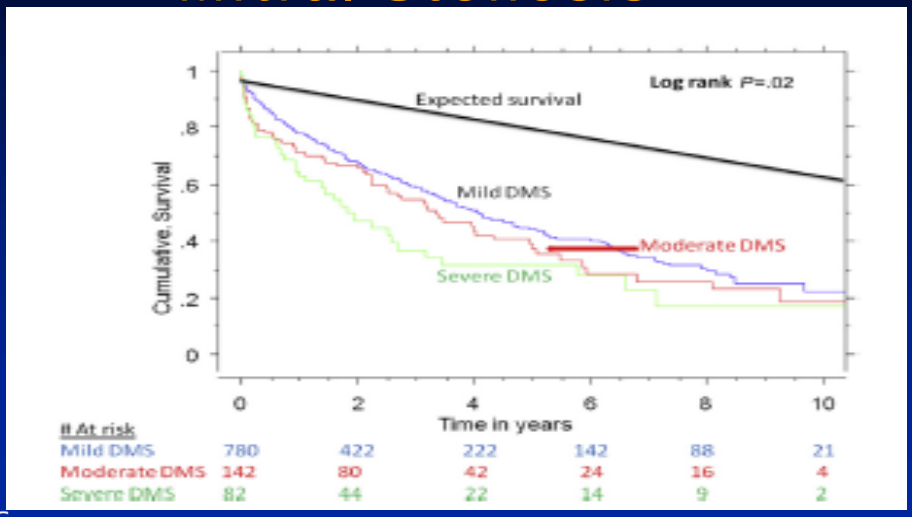
MAC Epidemiology

- MAC prevalence 8-15%
  - Increased with adv age and in pts with multiple CV risk factors or chronic kidney disease
  - Increasing prevalence due to growing population of elderly pts in developed world
- Associated with stenosis and regurgitation
  - (? Prevalence 0.2% of significant gradient)
- BAV not suitable for mitral stenosis due to MAC
- Mitral valve surgery - excess morbidity and mortality
- Transcatheter devices – unique challenges

SCRIPPS CLINIC

number 15

Survival with Degenerative Mitral Stenosis

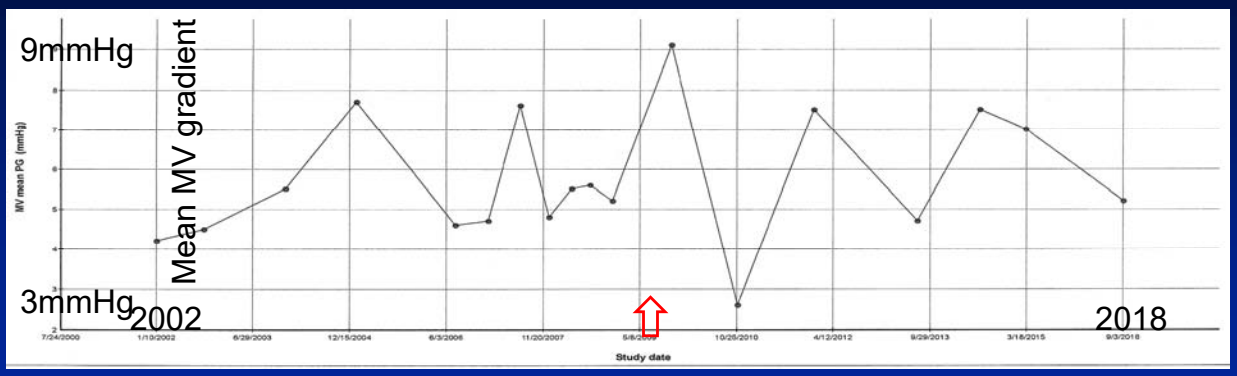


SCRIPPS CLINIC

JASE 2016;29:461

number 16

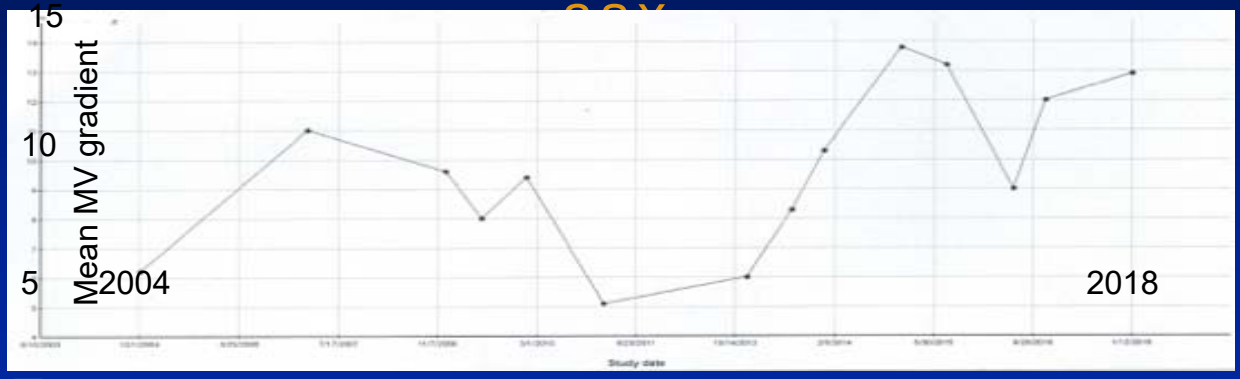
84 yo female post SAVR 2008
HTN, CKD III, HLD, PAF
Sedentary and asymptomatic



SCRIPPS CLINIC

number 17

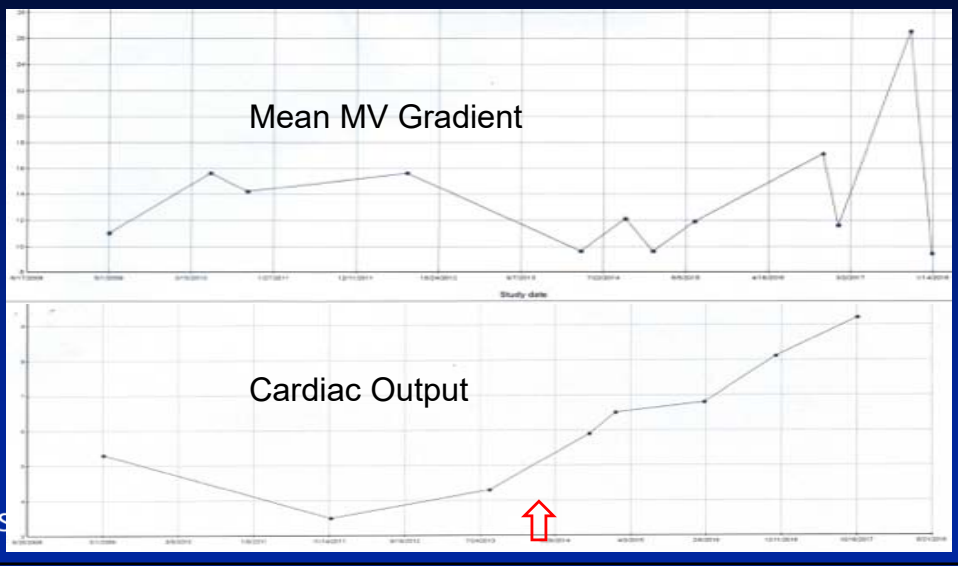
69 yo female with alcoholic liver disease
Initial transplant eval 2004 PHT
Slowly rising MV gradient, new AF



SCRIPPS CLINIC

number 18

75 yo male SAVR 2008. Moderate calcific MS not approached



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number 19

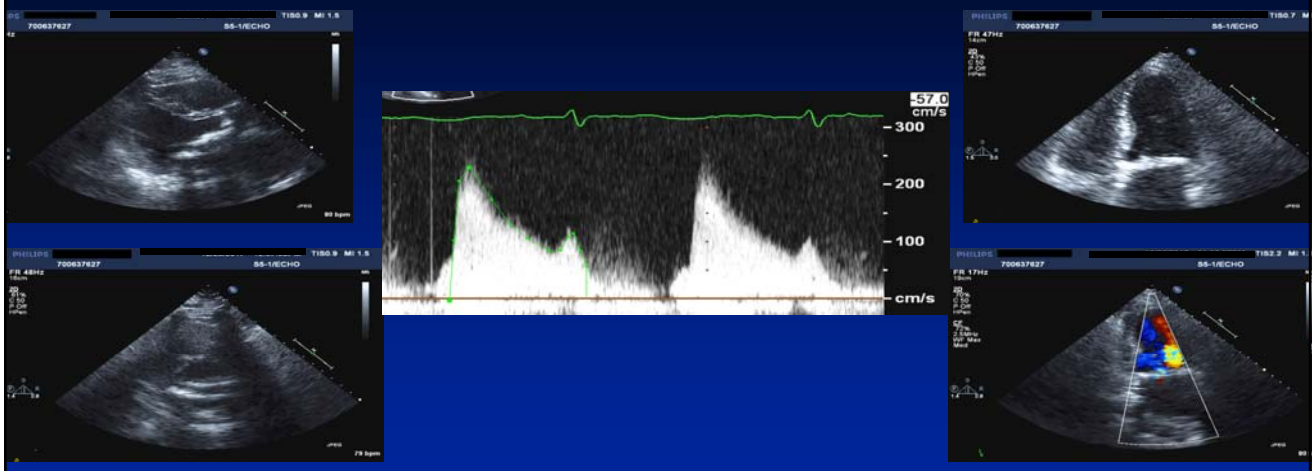
Progression in MAC

- Paucity of serial data
- SCMG
  - Retrospective review of echo database 2001-2009
  - "moderate/severe MAC" = >4mm annulus/leaflet
  - > 2mmHg mean MV gradient
- 30 patients who met inclusion criteria
  - Mean F/U 47.1±20 months
  - Initial Mean MV gradient 4.8±1.8mmHg
  - Average gradient progression 1.4±2.1mmHg

SCRIPPS CLINIC

number 20

Elderly female post transfemoral TAVR



Mean MV gradient 9mmHg

SCRIPPS CLINIC

number 21

IMAGING MAC
Qualitative and Quantitative

- VISUAL EXTENT OF CALCIFICATION
  - Annulus : ant post annulus and commissures
  - Leaflet involvement
  - En Face view – 3D key
- SEVERITY ASSESSMENT OF MS
  - Gradients – note HR and flow dependence
  - MV Area: continuity, planimetry or PISA
  - Exercise via PA pressure and gradients
  - Invasive hemodynamics-may alter loading and flow
  - ? CT-based MAC score

SCRIPPS CLINIC

number 22

Grading MAC

Mild:

- Maximal thickness <4mm
- Focal, limited increase in echodensity of the mitral annulus

Moderate:

- Maximal thickness is usually <4mm
- Marked echodensity involving 1/3 to 1/2 of the annular ring circumference

Severe:

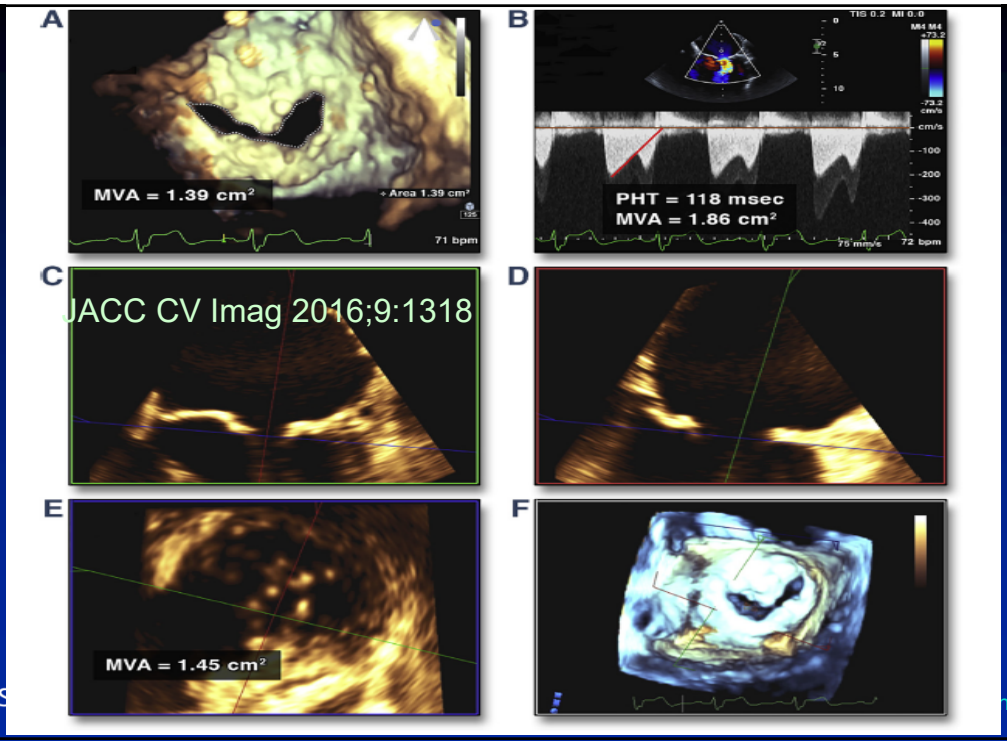
- Maximal thickness >4mm
- Marked echodensity involving > 1/2 of the annular ring circumference
- May be accompanied by an increased mean mitral pressure gradient when restricted anterior leaflet mobility is present

-or-

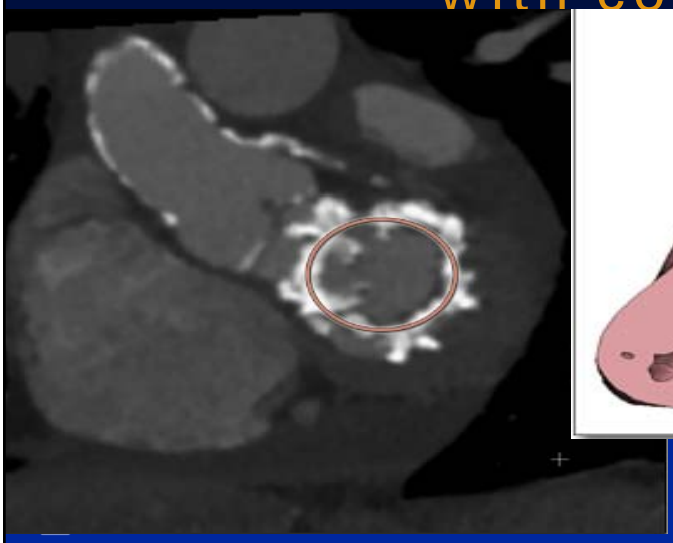
- Intrusion of the calcification into the LVOT

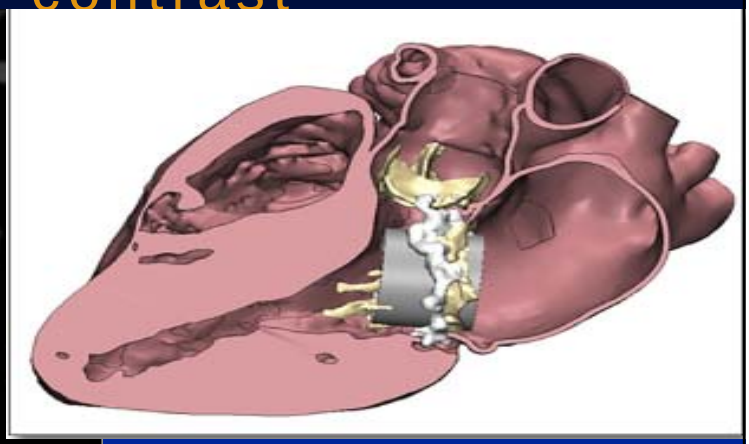
-or-

- Calcification extending on a continuous bar from the annulus to > 1/2 of the anterior or posterior leaflet length



CARDIAC CT
Retrospectively EKG gated with contrast





JACC CV Imag 2016;9:1318 number 25

Mitral Annular Calcium and Mitral Stenosis Determined by Multidetector Computed Tomography in Patients Referred for Aortic Stenosis

Am J Card 2016;118:1251

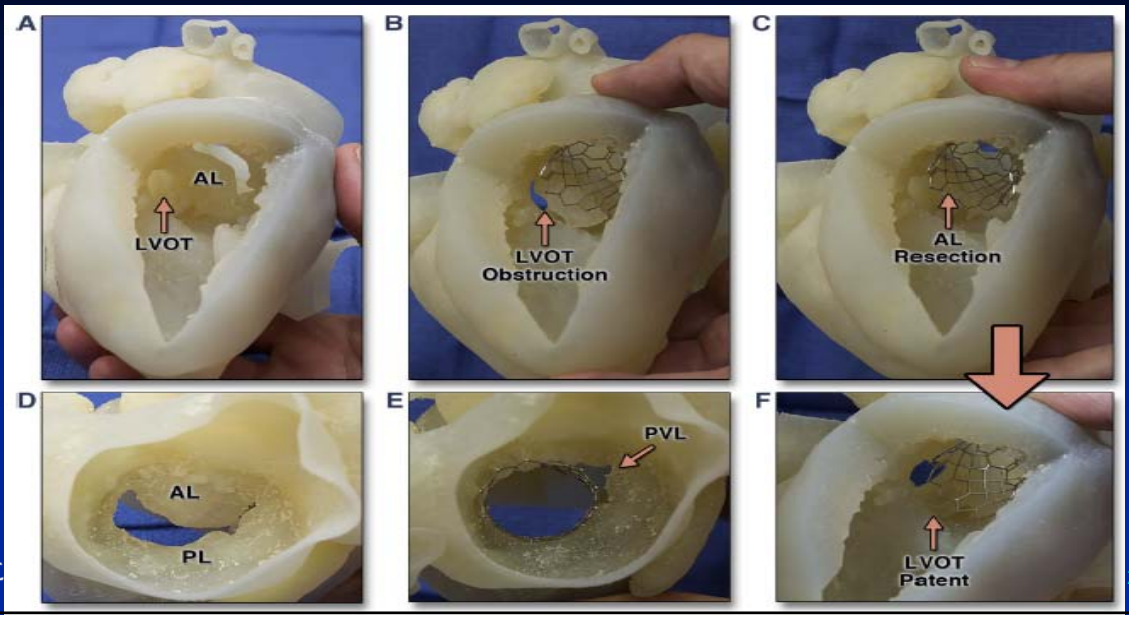
Simon Mejean, MD[a,b], Erik Bouvier, MD[a,*], Vincent Bataille, MPH[b], Patrick Seknadji, MD[a], Dominique Fourchy, MD[a], Jean-Yves Tabet, MD[a], Olivier Lairez, MD, PhD[b], and Bertrand Cormier, MD[a]

- High prevalence of MAC in pts referred for TAVR
  - 34% patients with mitral calcific deposits
  - 12% severe to very severe mitral stenosis (CT planimetry)
- Agatston score correlates with severity of MS
  - Weaker relationship than for AS
  - Severity is highly dependent on topography
  - Anterior leaflet extension (A2) important role in stenosis
- Questions remain about thresholds of severity by CT, functional impact, prognosis and therapeutic strategy implications

SCRIPPS CLINIC number 26

3D Printing for Procedural Simulation

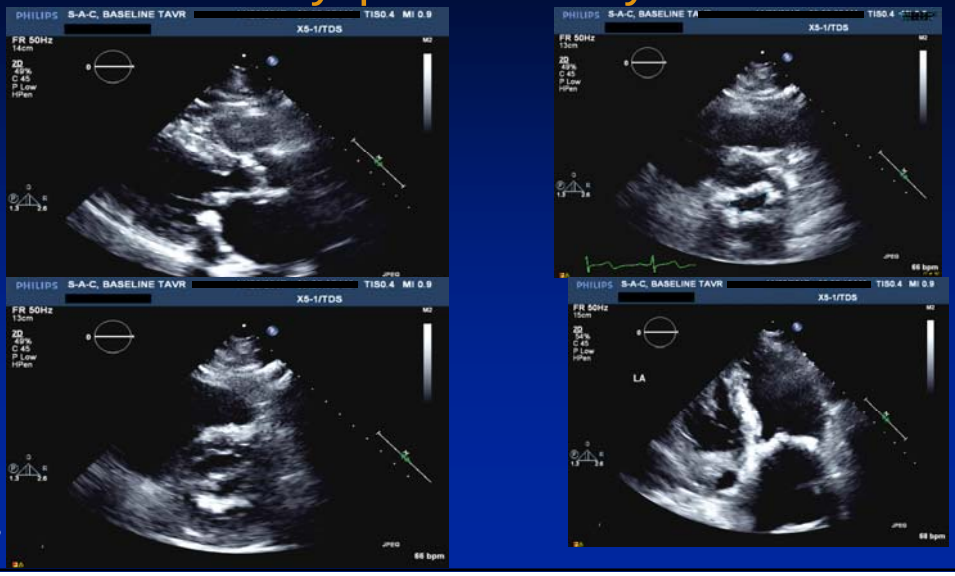
JACC CV Imag 2016;9:1318



IMPORTANT CLINICAL ISSUES related to MAC

- Associated with gradient complicating valve surgical planning-possibly symptomatic
- Symptomatic mitral stenosis, regurgitation or both
- Associated with increased intra-procedural surgical risk during MV repair or replacement
- Percutaneous MV interventions
  - MitraClip – feasibility
  - TMVR - risk factor for rupture , embolization or a potential useful anchor

79 yo pre TAVR patient
Mean MV gradient 10mmHg
MVA by planimetry 1.7cm2



SCRIPPS

number 29

Scripps Clinic Echo Lab 2017

CY17 Aortic Stenosis Analysis with MV Pressure Grad >= 4

	MV Press Grad >= 4		
Aortic Stenosis Text	**Yes**	**No**	**Grand Total**
Mild to moderate valvular aortic stenosis.	6	311	317
Mild valvular aortic stenosis.	26	1052	1078
Moderate to severe valvular aortic stenosis.	13	269	282
Moderate valvular aortic stenosis.	20	637	657
Severe valvular aortic stenosis.	53	858	911
Grand Total	**118**	**3127**	**3245**

	MV Press Grad >= 4	
	Yes	**No**
Severe valvular aortic stenosis.	5.8%	94.2%

SCRIPPS CLINIC

number 30

Mitral valve annular calcium

Risk factors for posterior ventricular rupture after mitral valve replacement: results of 2560 patients☆

Hayati Deniz, Onur Sokullu *, Soner Sanioglu, Murat Sargin, Batuhan Ozay, Umut Ayoglu, Serap Aykut Aka, Fuat Bilgen

Department of Cardiovascular Surgery, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

- 1996 through 2007, 2560 patients
- 23 ruptures (0.8%) with 20 mortalities (86%)
- "… aggressive decalcification should be avoided during mitral valve resection …"

Deniz et al. Eur J Cardiothorac Surg. 2008.

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Mitral valve annular calcium

Risk factors for posterior ventricular rupture after mitral valve replacement: results of 2560 patients☆

Risk factors for posterior ventricular rupture:
- Age ≥ 60 years
- Female sex
- Posterior leaflet resection
- Repeat mitral valve replacement

- "… aggressive decalcification should be avoided during mitral valve resection …"

Deniz et al. Eur J Cardiothorac Surg. 2008.

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MITRAL ANNULAR CALCIFICATION AND INCREASED SURGICAL RISK

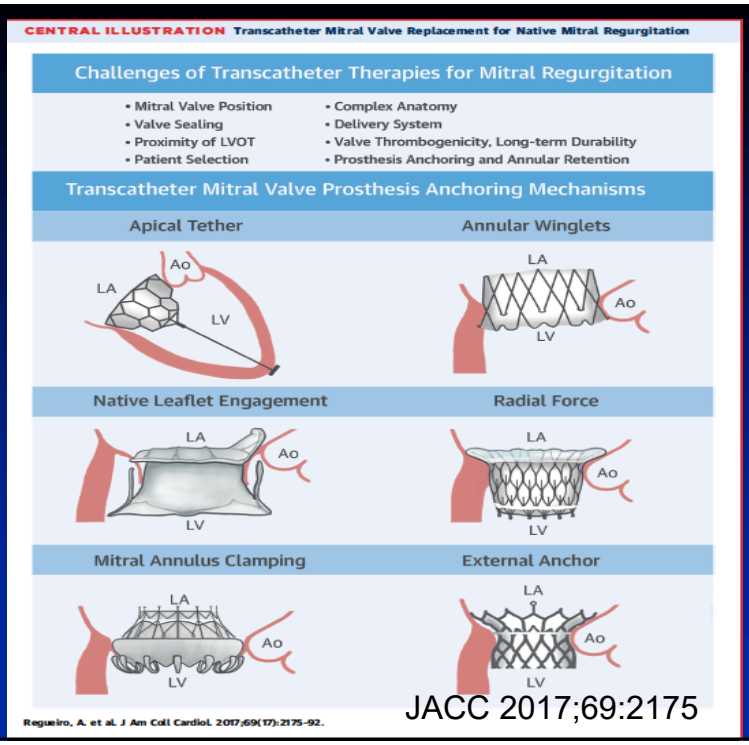
- PLACEMENT OF SMALLER VALVE SIZE
- DEBRIDMENT CAN INCREASE STROKE
- RISK LONGER PUMP RUN AND OP TIME
- RISK OF AV GROOVE DISRUPTION
- INCREASED RATE PARAVALVULAR LEAK

- ALL MORE TRUE IN THE ELDERLY WITH COMORBID CONDITIONS

TMVR : Is it applicable in patients with MAC ?

- PERCUTANEOUS MITRAL INTERVENTIONS
  - MITRACLIP – feasibility of grasp and adequate repair
  - TMVR - risk factor for rupture , embolization and LVOT obstruction
- MIGHT MAC BE A USEFUL ANCHOR ?

CENTRAL ILLUSTRATION Transcatheter Mitral Valve Replacement for Native Mitral Regurgitation



Regueiro, A. et al. J Am Coll Cardiol. 2017;69(17):2175-92.

JACC 2017;69:2175

SCRIPPS CLINIC

number 35

Transcatheter Mitral Valve Replacement for Patients With Symptomatic Mitral Regurgitation

A Global Feasibility Trial

Abbott Tendyne System

David W.M. Muller, MBBS, MD,[a] Robert Saeid Farivar, MD,[b] Paul Jansz, MBBS, PhD,[a] Richard Bae, MD,[b] Darren Walters, MBBS, MPhil.,[c] Andrew Clarke, MBBS,[c] Paul A. Grayburn, MD,[d] Robert C. Stoler, MD,[d] Gry Dahle, MD,[e] Kjell A. Rein, MD,[e] Marty Shaw, MBBS,[a] Gregory M. Scalia, MBBS,[c] Mayra Guerrero, MD,[f] Paul Pearson, MD,[f] Samir Kapadia, MD,[g] Marc Gillinov, MD,[g] Augusto Pichard, MD,[h] Paul Corso, MD,[h] Jeffrey Popma, MD,[i] Michael Chuang, MD,[j] Philipp Blanke, MD,[j] Jonathon Leipsic, MD,[j] Paul Sorajja, MD,[b] on behalf of the Tendyne Global Feasibility Trial Investigators

JACC 2017;69:381

Early Experience With New Transcatheter Mitral Valve Replacement

Medtronic Intrepid

Vinayak Bapat, MBBS, MS, MCh,[a,b] Vivek Rajagopal, MD,[c] Christopher Meduri, MD, MPH,[c] R. Saeid Farivar, MD,[d] Antony Walton, MD,[e] Stephen J. Duffy, MBBS, PhD,[e] Robert Gooley, MBBS, PhD,[f] Aubrey Almeida, MD,[f] Michael J. Reardon, MD,[g] Neal S. Kleiman, MD,[g] Konstantinos Spargias, MD,[h] Stratis Pattakos, MD,[h] Martin K. Ng, MBBS, PhD,[i] Michael Wilson, MD,[i] David H. Adams, MD,[j] Martin Leon, MD,[b] Michael J. Mack, MD,[k] Sharla Chenoweth, MS,[l] Paul Sorajja, MD,[d] for the Intrepid Global Pilot Study Investigators[e]

JACC 2018;71:12

EXCLUDE MORE THAN "MINIMAL" MAC

SCRIPPS CLINIC

number 36

IMAGES IN INTERVENTION

Transseptal Transcatheter Mitral Valve Implantation for Severely Calcified Mitral Stenosis

SCRIPPS CLINIC

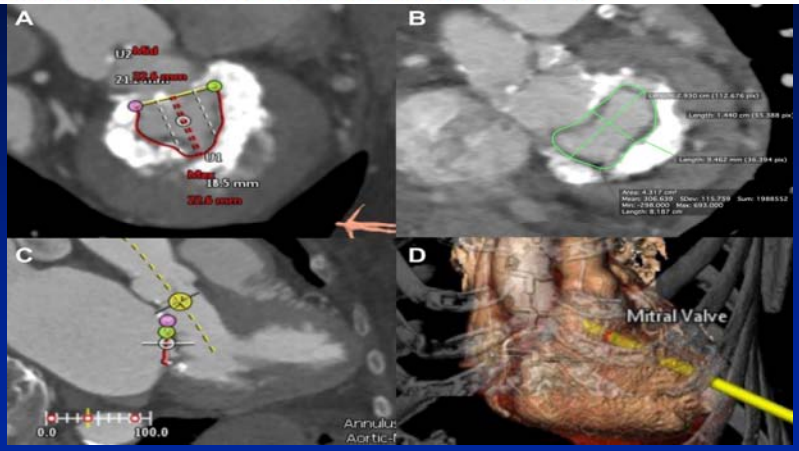
JACC CV Intervent 2014;7:696

number 37

STRUCTURAL

Transcatheter Mitral Valve Replacement in Native Mitral Valve Disease With Severe Mitral Annular Calcification

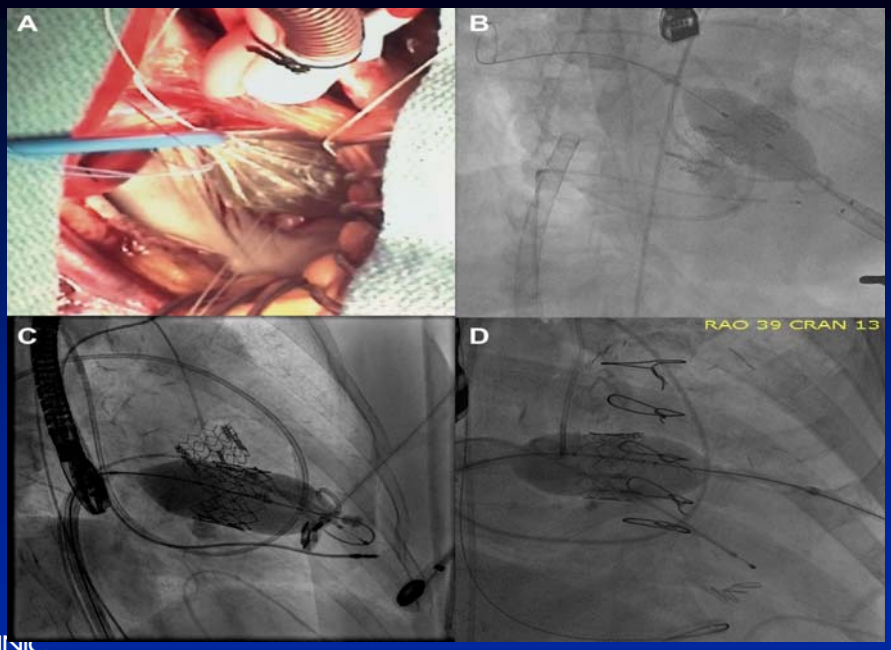
Results From the First Multicenter Global Registry



SCRIPPS CLINIC

JACC CV Interv 2016;9:1361

number 38



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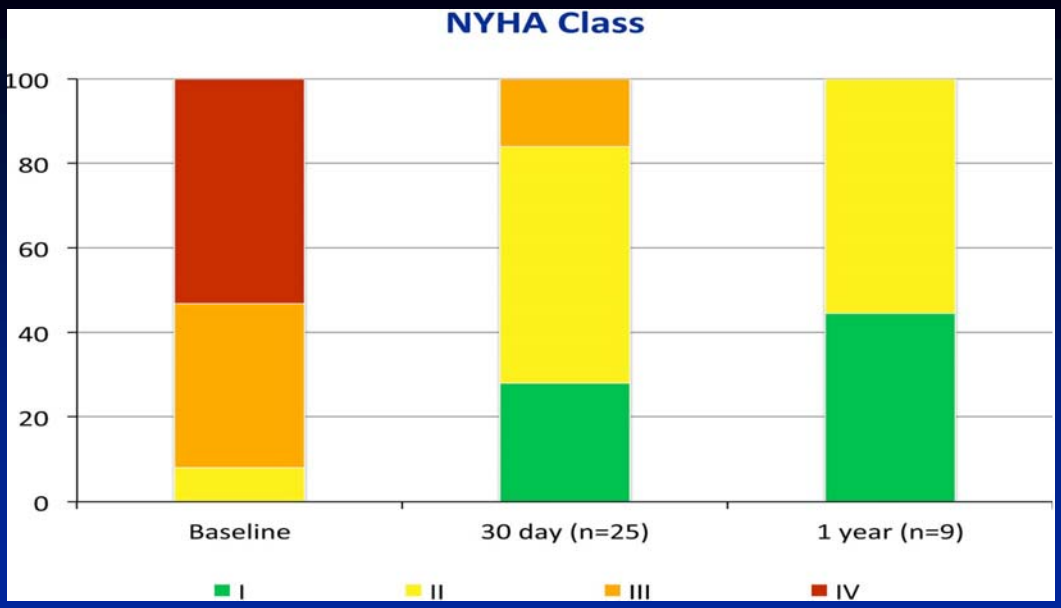
JACC CV Interv 2016;9:1361

number 39



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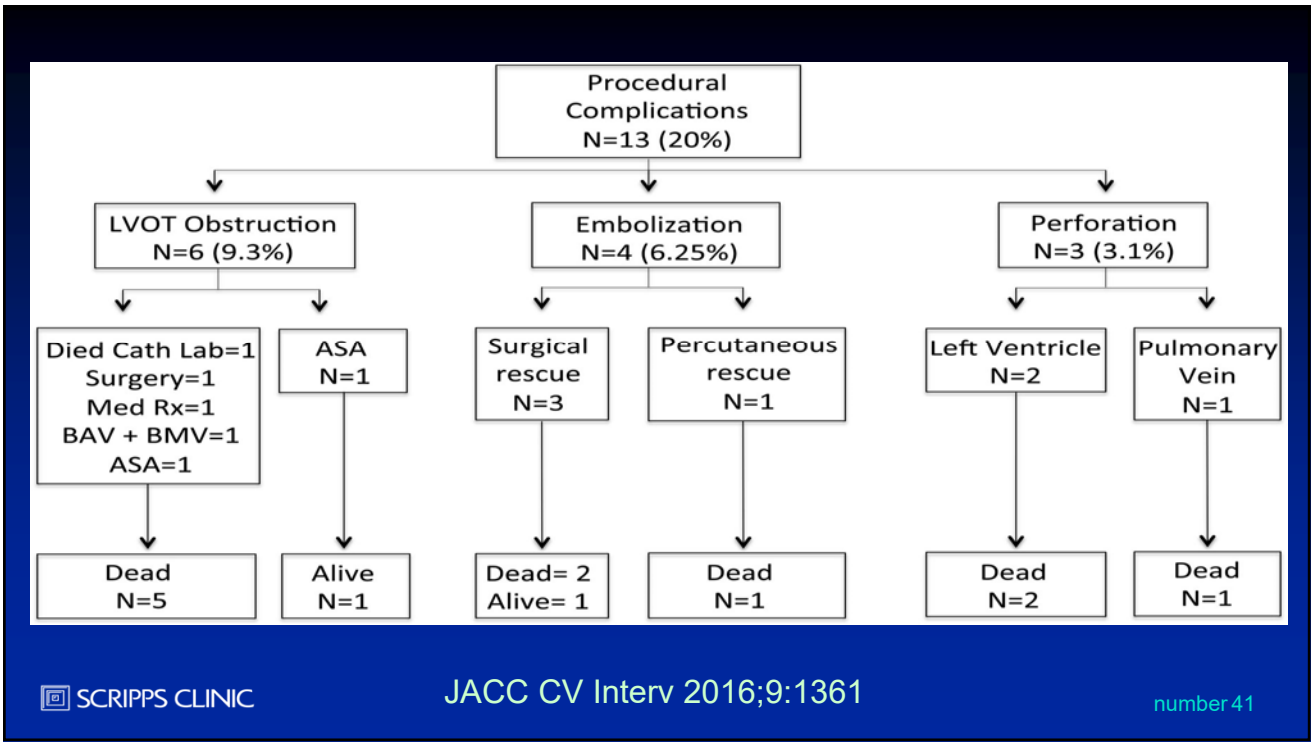
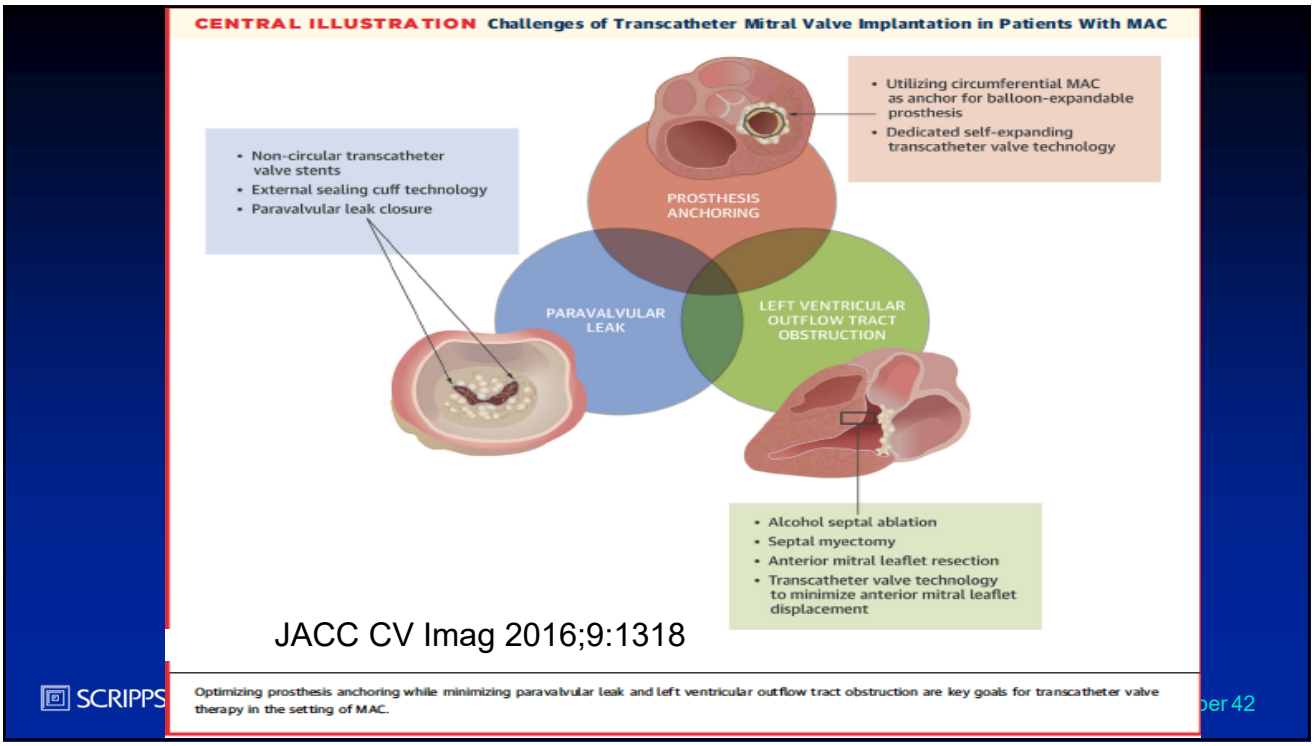
JACC CV Interv 2016;9:1361

number 40


Procedural Complications N=13 (20%)
LVOT Obstruction N=6 (9.3%)
Embolization N=4 (6.25%)
Perforation N=3 (3.1%)
Died Cath Lab=1 Surgery=1 Med Rx=1 BAV + BMV=1 ASA=1
ASA N=1
Surgical rescue N=3
Percutaneous rescue N=1
Left Ventricle N=2
Pulmonary Vein N=1
Dead N=5
Alive N=1
Dead= 2 Alive= 1
Dead N=1
Dead N=2
Dead N=1
SCRIPPS CLINIC
JACC CV Interv 2016;9:1361
number 41


CENTRAL ILLUSTRATION Challenges of Transcatheter Mitral Valve Implantation in Patients With MAC
• Utilizing circumferential MAC as anchor for balloon-expandable prosthesis
• Dedicated self-expanding transcatheter valve technology
• Non-circular transcatheter valve stents
• External sealing cuff technology
• Paravalvular leak closure
PROSTHESIS ANCHORING
PARAVALVULAR LEAK
LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION
• Alcohol septal ablation
• Septal myectomy
• Anterior mitral leaflet resection
• Transcatheter valve technology to minimize anterior mitral leaflet displacement
JACC CV Imag 2016;9:1318
Optimizing prosthesis anchoring while minimizing paravalvular leak and left ventricular outflow tract obstruction are key goals for transcatheter valve therapy in the setting of MAC.
SCRIPPS
ber 42

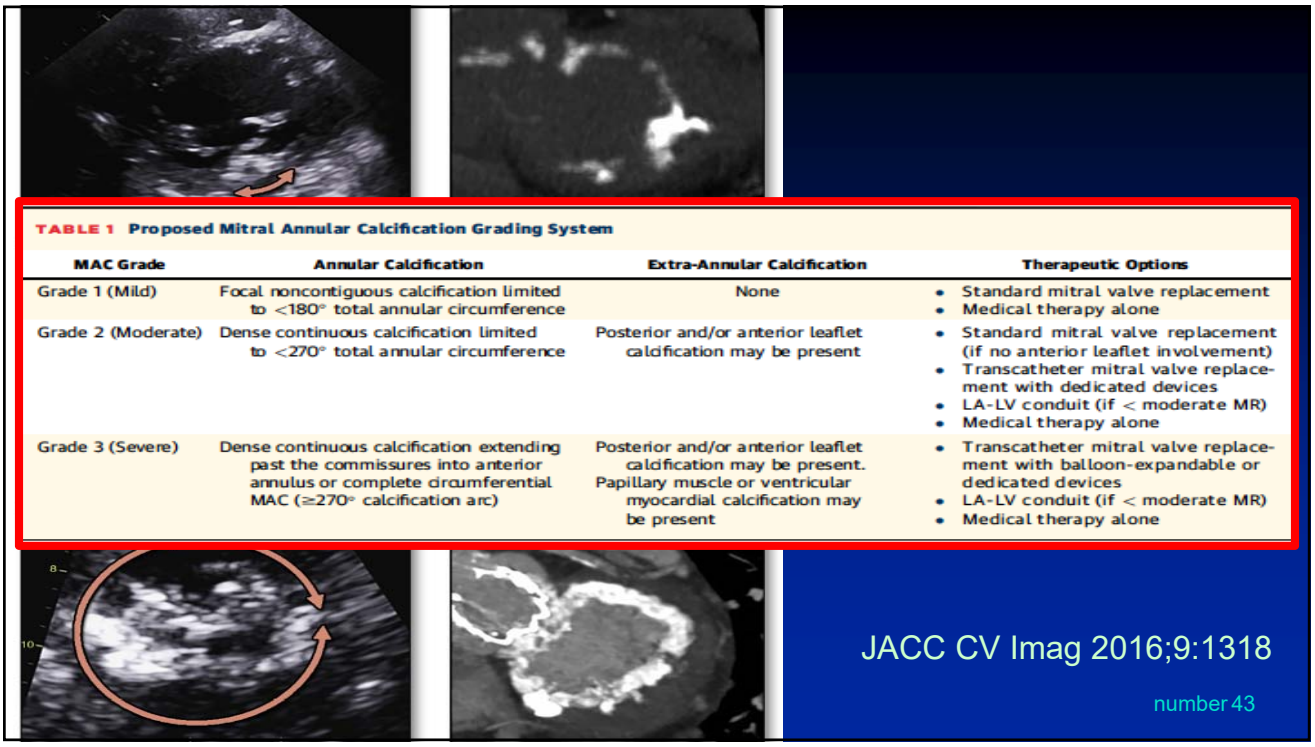
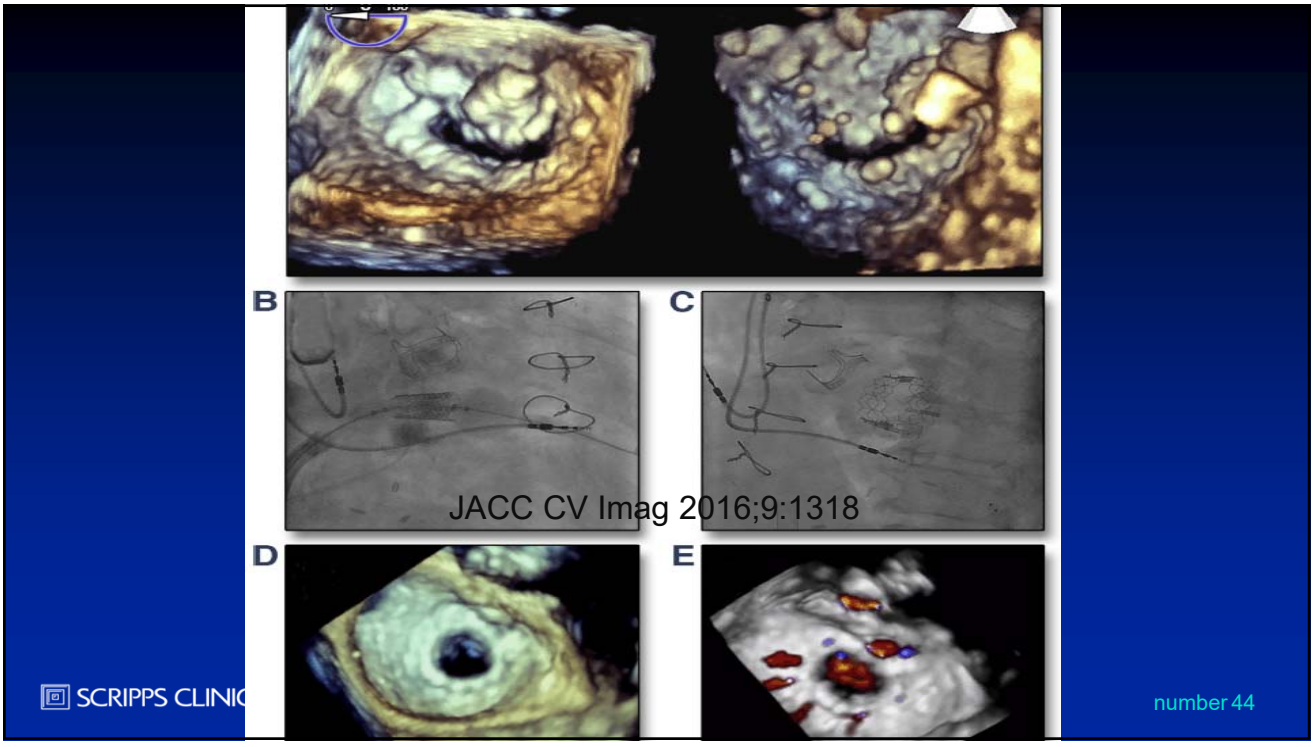


TABLE 1 Proposed Mitral Annular Calcification Grading System

MAC Grade	Annular Calcification	Extra-Annular Calcification	Therapeutic Options
Grade 1 (Mild)	Focal noncontiguous calcification limited to <180° total annular circumference	None	• Standard mitral valve replacement • Medical therapy alone
Grade 2 (Moderate)	Dense continuous calcification limited to <270° total annular circumference	Posterior and/or anterior leaflet calcification may be present	• Standard mitral valve replacement (if no anterior leaflet involvement) • Transcatheter mitral valve replacement with dedicated devices • LA-LV conduit (if < moderate MR) • Medical therapy alone
Grade 3 (Severe)	Dense continuous calcification extending past the commissures into anterior annulus or complete circumferential MAC (≥270° calcification arc)	Posterior and/or anterior leaflet calcification may be present. Papillary muscle or ventricular myocardial calcification may be present	• Transcatheter mitral valve replacement with balloon-expandable or dedicated devices • LA-LV conduit (if < moderate MR) • Medical therapy alone

JACC CV Imag 2016;9:1318

number 43



JACC CV Imag 2016;9:1318

SCRIPPS CLINIC

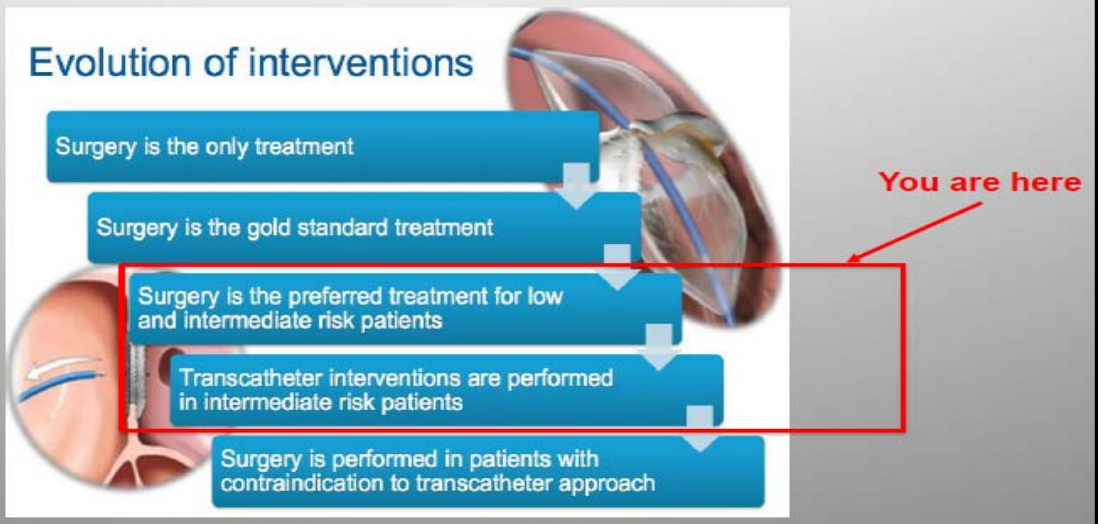
number 44

MITRAL ANNULAR CALCIFICATION
Transcatheter Therapies

- May be an option in carefully selected patients
  - Clinically significant MS or combined MS/MR
- Learning curve
- More studies needed
  - Define best method to quantitate MAC and its significance in individual patients
  - Device development
  - Delivery systems development
  - Strategies to prevent LVOT obstruction
- Current Need: focus attention on MAC in all new areas of MV intervention

SCRIPPS CLINIC

number 45



Professor Attavio Alfieri 2017