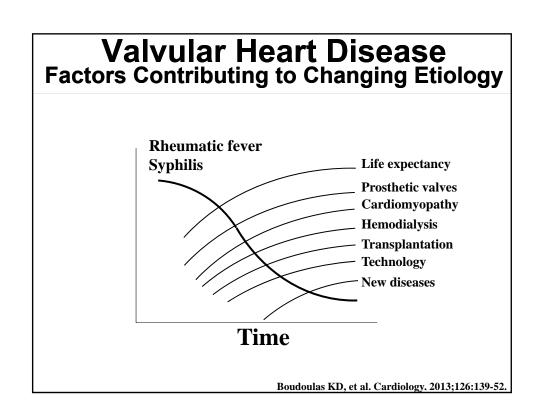
Mitral Regurgitation: Transcatheter Repair

Konstantinos Dean Boudoulas, MD
Associate Professor of Medicine
Division of Cardiovascular Medicine
Section of Interventional Cardilogy
The Ohio State University Wexner Medical Cente



Mitral Regurgitation Most Common Etiologies

Functional Mitral Regurgitation

- Dilated Cardiomyopathy
 - ischemic cardiomyopathy
 - non-ischemic cardiomyopathy

Organic (Degenerative) Mitral Regurgitation

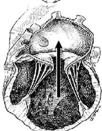
floppy mitral valve/mitral valve prolapse

Mechanisms of Functional Mitral Regurgitation in Dilated Cardiomyopathy

Normal left ventricle, left atrium and mitral valve

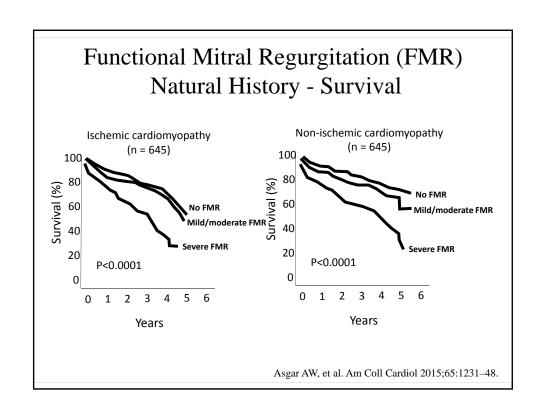


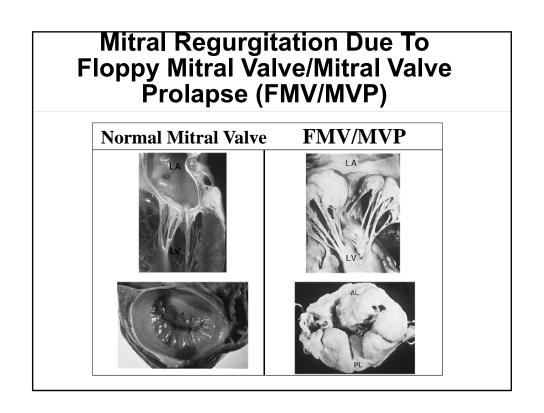
Cardiomyopathy: left ventricular and left atrial enlargement with mitral regurgitation



- Papillary muscle function, orientation
- Changes in LV geometry
- Annular dilation?

Boudoulas KD, et al. Cardiology. 2013;126:139-52.



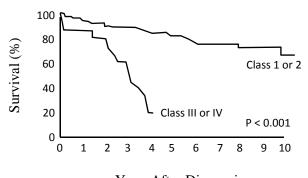


Floppy Mitral Valve/ Mitral Valve Prolapse (FMV/MVP)

- Prevalence is 2-3%.
- At least 2 forms of inheritance:
 - autosomal dominant with variable degree of penetration (most common)
 - chromosome X
- Collagen dissolution and pars fibrosa disruption of mitral valve leaflets.
- Leaflets replaced with loose myxomatous connective tissue.
- Similar histologic abnormalities may be seen in chordae tendineae.

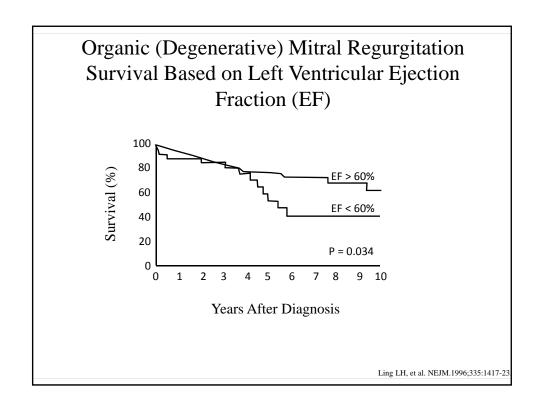
Boudoulas KD, et al. Cardiology 2013;126:69-80.

Organic (Degenerative) Mitral Regurgitation Survival Based on New York Heart Association Class



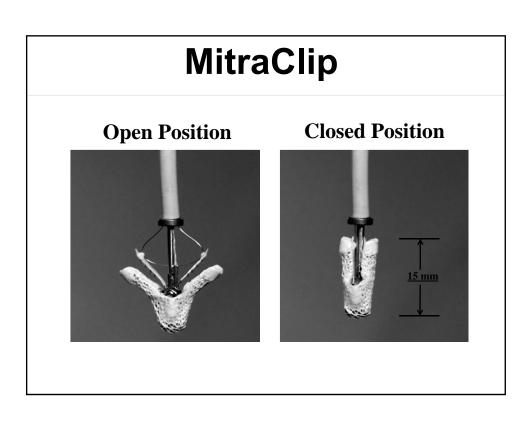
Years After Diagnosis

Ling LH, et al. NEJM.1996;335:1417-23



Anatomic Target	Device Name	Manufacturer	Development Status
Leaflets	MitraClip	Abbott	CE Mark/FDA Approved
	Mitra-Spacer	Cardiosolutions Inc	Clinical Trial
	Middle Peak Medical	Middle Peak Medical Inc	Preclinical
Chords	NeoChord	Neochord Inc	CE Mark
	V-Chordal	Valtech Cardio Inc	Clinical Trial
	MitraFlex	TransCardiac Therapeutics LLC	Preclinical
Annulus	Direct		
	Mitralign	Mitralign Inc	Clinical Trial
	Accucinch	Guided Delivery Systems	Clinical Trial
	Cardioband	Valtech Cardio	Clinical Trial
	Millipede System	Millipede LLC	Clinical Trial
	Boa RF Catheter	QuantumCor Inc	Preclinical
	TARSA	MitraSpan Inc	Clinical Trial
	Indirect		
	Carillion	Cardiac Dimensions Inc	CE Mark/Clinical Trial
	Kardium MR	Kardium Inc	Preclinical
	Mitral Loop Cerclage	National Heart, Lung, and Blood Institute	Clinical Trial
LV Remodeling	BACE	Mardil Medical	Clinical Trial
	Tendyne Repair	Tendyne Holdings Inc	Preclinical
	iCoapsys	Myocor Inc	Not active
Valve	CardiAQ	Edwards	Clinical Trial
	Fortis	Edwards	Clinical Trial
	Tiara	Neovasc Inc	Clinical Trial
	Twelve - Intrepid	Medtronic	Clinical Trial
	Tendyne	Abbott	Clinical Trial

Anatomic Target	Device Name	Manufacturer	Development Status
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	Middle Peak Medical	Middle Peak Medical Inc	Preclinical
Chords	NeoChord	Neochord Inc	CE Mark
	V-Chordal	Valtech Cardio Inc	Clinical Trial
	MitraFlex	TransCardiac Therapeutics LLC	Preclinical
Annulus	Direct		
	Mitralign	Mitralign Inc	Clinical Trial
	Accucinch	Guided Delivery Systems	Clinical Trial
	Cardioband	Valtech Cardio	Clinical Trial
	Millipede System	Millipede LLC	Clinical Trial
	Boa RF Catheter	QuantumCor Inc	Preclinical
	TARSA	MitraSpan Inc	Clinical Trial
	Indirect		
	Carillion	Cardiac Dimensions Inc	CE Mark/Clinical Trial
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	Tiara	Neovasc Inc	Clinical Trial
	Twelve - Intrepid	Medtronic	Clinical Trial



Mitral Regurgitation Mitral Leaflet Repair - MitraClip



Mitral Regurgitation Mitral Leaflet Repair - MitraClip

Chest radiograph showing two mitraclips projecting over the heart.

Author: Hellerhoff (CC BY-SA 3.0)

MitraClip Versus Surgery for Functional or Organic Mitral Regurgitation EVEREST II Randomized Trial

- Multicenter study that randomized patients with moderate-to- severe (3+) or severe (4+) mitral regurgitation to transcatheter MitraClip versus surgical repair/replacement of the mitral valve.
- 27% functional and 73% organic (degenerative) mitral regurgitation.

EVEREST II High Risk Study. J Am Coll Cardiol. 2012;59:130-9

MitraClip Versus Surgery for Functional or Organic Mitral Regurgitation EVEREST II Randomized Trial

Short Term Results

- 3+ or 4+ mitral regurgitation prior to hospital discharge:
 - 23% in MitraClip group (surgery within 6 months)
 - 0% in Surgical group
- Similar 30-day mortality (~1-2%)
- Small, but statistically significant decrease in LV size (systolic and diastolic) and LV ejection fraction (~2-6%) at 1 year in both groups compared to baseline.

EVEREST II. NEJM. 2011;364:1395-406.

MitraClip Versus Surgery for Functional or Organic Mitral Regurgitation EVEREST II Randomized Trial

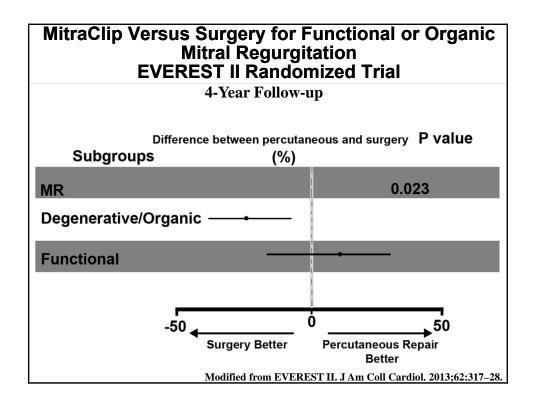
4-Year Follow-up

- Decrease in LV size (systolic and diastolic) sustained at 4 years in both groups.
- Decrease in LV ejection fraction < 5% in both groups.
- Improved NYHA functional class III-IV in both groups:
 - Baseline 46% and at 4 years ~ 6%

EVEREST II. J Am Coll Cardiol. 2013;62:317-28.

MitraClip Versus Surgery for Functional or Organic Mitral Regurgitation EVEREST II Randomized Trial 40 4-Year Follow-up □ MitraClip 30 Percent (%) NS n=279 p<0.001 24.7 NS 21.7 20 20.4 17.4 17.8 10 Surgery for Mitral

Data from EVEREST II. J Am Coll Cardiol. 2013;62:317–28 used to construct slide.



MitraClip for Organic (Degenerative) Mitral Regurgitation in High Risk Patients EVEREST II High Risk and REALISM Registries

Procedural Results

- 95% successful implantation
- Average hospital length-of-stay 2.9 days
- ~ 90% discharged to home
- No intra-procedural deaths
 - 30-day mortality 6.3% (STS predicted peri-operative mortality 13%)

Lim DS, et al. J Am Coll Cardiol. 2014;64:182-92.

MitraClip for Organic (Degenerative) Mitral Regurgitation in High Risk Patients EVEREST II High Risk and REALISM Registries

1 Year Follow-up

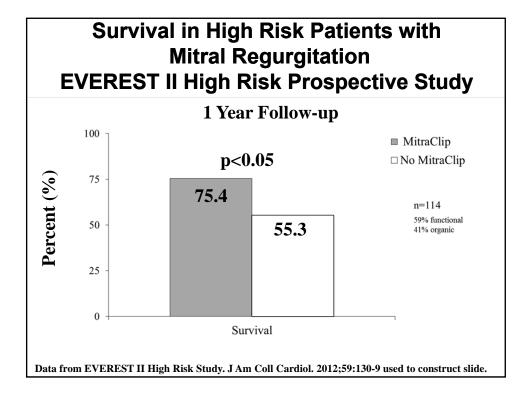
- Mortality 23.6%
- ~ 85% maintained ≤ 2+ mitral regurgitation
- Small, but statistically significant decrease LV size
- Improved NYHA functional class:
 - Baseline: 86% NYHA class III-IV
 - 1 year: 86% NYHA class I-II
- Significant reduction (73%) in hospitalizations (12 months pre- versus 12 months postprocedure)
- Improved quality-of-life

Lim DS, et al. J Am Coll Cardiol. 2014;64:182-92.

MitraClip for Organic (Degenerative) Mitral Regurgitation in High Risk Patients EVEREST II High Risk and REALISM Registries

- 1 year survival based on post-procedure residual mitral regurgitation:
 - 80% for ≤ 1+
 - 83% for 2+
 - 52% for 3-4+
- Patients with severe mitral regurgitation at discharge had no reduction in rate of hospitalizations related to heart failure.

Lim DS, et al. J Am Coll Cardiol. 2014;64:182-92.



FDA Approved MitraClip for Organic (Degenerative) Mitral Regurgitation

- Transcatheter reduction of significant symptomatic mitral regurgitation (≥ 3+) due to organic (degenerative) mitral regurgitation in patients determined to be at prohibitive risk for mitral valve surgery.
- Prohibitive risk includes ≥ 1 of the following:
 - STS ≥ 8% for mitral valve replacement or ≥ 6% for mitral valve repair
 - Porcelain aorta
 - Frailty
 - Hostile chest
 - Severe liver disease
 - Severe pulmonary hypertension
 - Other

MitraClip for Functional Mitral Regurgitation Non-Randomized Studies

- Inoperable or high-risk surgical patients with symptomatic heart failure and 3+ or 4+ functional mitral regurgitation.
- Mean LV ejection fraction ~ 30%.
- Follow-up 6 to 12 months post-MitraClip:
 - significant decrease mitral regurgitation
 - significant reduction LV size
 - significant increase LV ejection fraction
 - significant improvement NYHA functional class
 - 30 day mortality 1-6%

Franzen O, et al. Eur J Heart Fail. 2011;13:569–76. PERMIT-CARE. J Am Coll Cardiol. 2011;58:2183–9. Beigel, R, et al. J Am Coll Cardiol. 2014;64:2688–700. Taramasso M, et al. EuroIntervention. 2014;10:746–52.

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (The COAPT Trial)

- Randomized, multicenter study of the MitraClip device for the treatment of moderate/severe or severe functional mitral regurgitation in symptomatic heart failure patients not appropriate for mitral valve surgery.
- Randomized to MitraClip device or no device
- Primary end-point: safety and recurrent heart failure hospitalizations
- Secondary end-points: death, stroke, myocardial infarction, mitral regurgitation, LV size, symptoms.

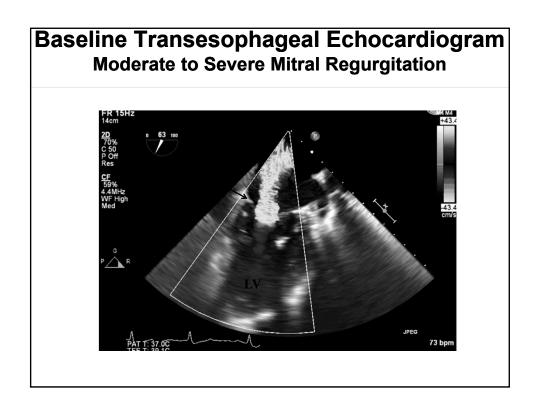
Factors Predicting Decrease Survival after MitraClip Implantation

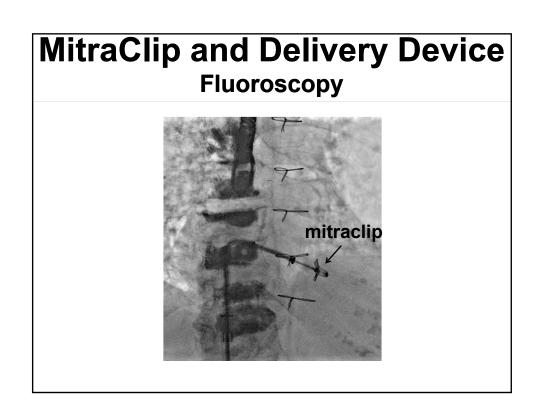
- End-stage heart failure with significant increase in NT-proBNP (≥ 5000 pg/ml)
- Severe renal impairment (GFR <30 ml/min)
- Chronic obstructive pulmonary disease
- Tricuspid regurgitation ≥ 3+
- Residual mitral regurgitation > 2+

Toggweiler S, et al. Open Heart 2014. TRAMI Registry. EuroIntervention. 2015. Neuss M, et al. Eur J Heart Fail. 2013 Jul;15(7):786-95. Boerlage-vanDijk K, et al. Int J Cardiol. 2015;189:238-43.

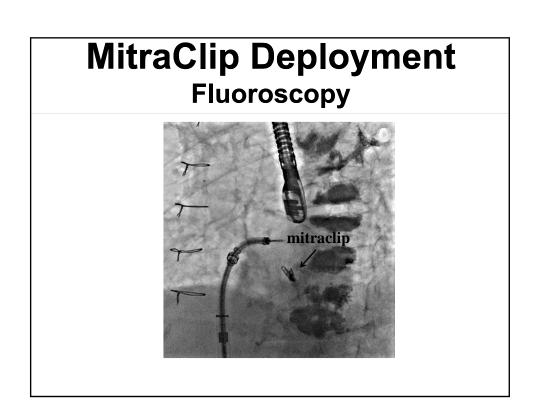
CASE

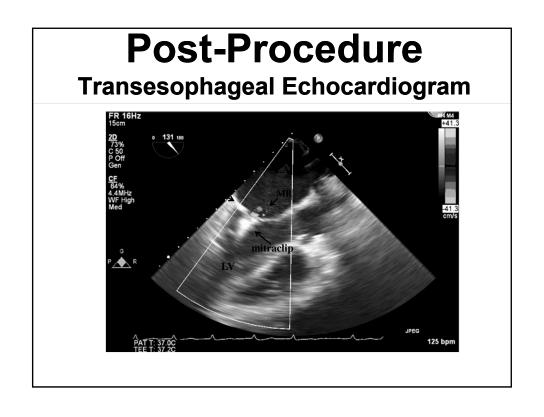
- 86 year old female with symptomatic NYHA class III heart failure.
- History of CABG.
- LVEF 30% and moderate-to-severe mitral regurgitation.
- Optimal medical therapy for heart failure (carvedilol, lisinopril, spironolactone, furosemide).
- QRS 94 ms on ECG.
- Coronary and bypass angiogram performed (did not require additional revascularization).
- Systolic pulmonary artery pressure (right heart catheterization) 55 mmHg.
- Assessed by Structural Heart Team for COAPT trial.

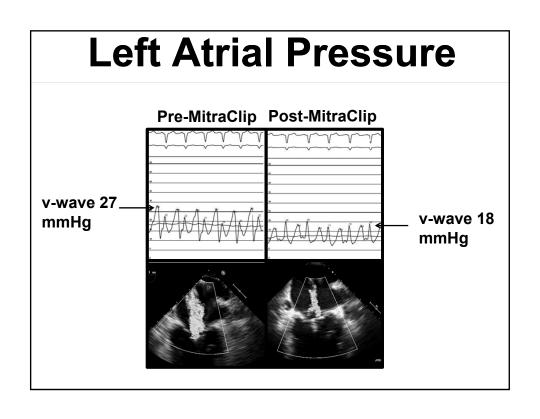




MitraClip Positioning Transesophageal Echocardiogram FR 37HZ 16cm 20 9 125 180 CLIP POSITIONING PATT 37.86C 70 bpr







Hemodynamics Changes Associated with MitraClip

- Pressure changes:
 - decrease left atrial pressure (v-wave by ~9 mmHg; mean by ~4 mmHg)
 - decrease PCWP (mean ~5 mmHg)
 - decrease pulmonary arterial pressure (systolic by ~9 mmHg; mean by ~5 mmHg)
- Increase cardiac output by 0.5 to 1.5 L/min

Gaemperli O, et al. Heart. 2012;98:126–32..
Biner S, et al. Eur J Heart Fail. 2012;14:939–45.
Grayburn PA, et al. Circulation. 2013;128:1667–74.
ACCESS-EU. J Am Coll Cardiol. 2013;62:1052–61.
Siegel RJ, et al. J Am Coll Cardiol. 2011;57:1658–65.
EVEREST II High Risk Study. J Am Coll Cardiol. 2012;59:130-9.

MitraClip for Significant Organic (Degenerative) Mitral Regurgitation (MR) Summary

- MitraClip is effective and can be used in patients at high risk for mitral valve surgery:
 - safe and effective in reducing severity of MR in majority of patients
 - improves symptoms
 - decreases hospitalizations
 - may have beneficial effect on survival if residual MR post-procedure was not severe
 - Mitraclip is FDA approved for use in patients with organic MR who are high surgical risk
- Low and intermediate risk patients do better with mitral valve surgery.

MitraClip for Significant Functional Mitral Regurgitation (MR) Summary

- MitraClip is safe and effective in reducing severity of MR in the majority of patients.
- Improves symptoms.
- May decrease LV size and improve LV function.
- May increase survival?
- These important questions will be further addressed in ongoing prospective, randomized studies (COAPT, other).

MitraClip for Significant Mitral Regurgitation (MR) Concluding Remarks and Future Considerations

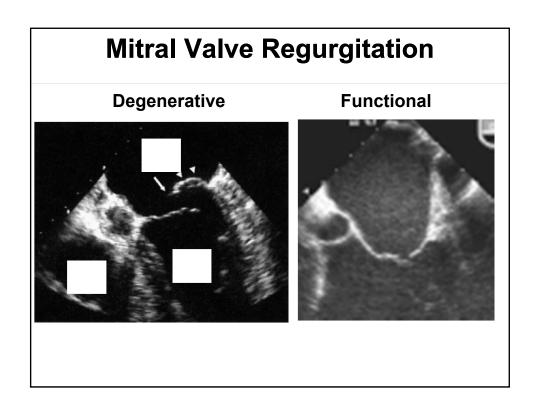
- MitraClip is a relatively new method still in evolution for the management of significant MR.
- MitraClip is beneficial in patients with severe organic (degenerative) MR who are at high risk for surgery;
 MitraClip may be considered in certain critically ill patients with severe organic MR who are high risk for surgery as a bridge to mitral valve surgery.
- MitraClip may be used in certain symptomatic patients due to heart failure with significant functional MR.
- MitraClip or other transcatheter devices may become a common procedure for functional MR in the near future.

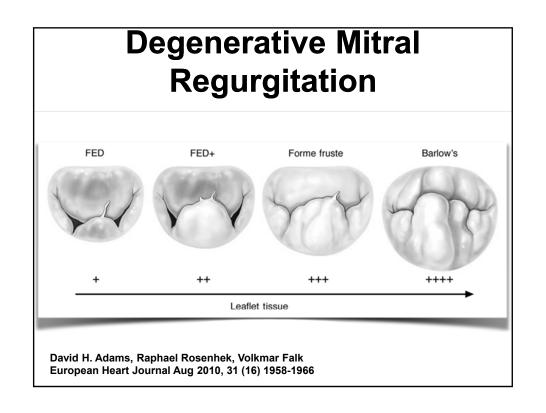
Mitral Valve Repair vs. Replacement for Degenerative Mitral Regurgitation

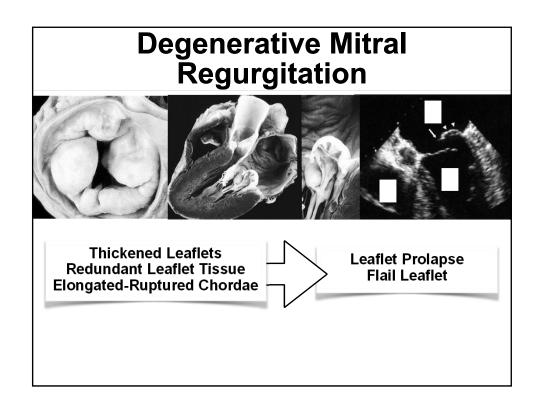
Juan Crestanello, MD
Professor of Surgery
Director, Division of Cardiac Surgery
The Ohio State University Wexner Medical Center

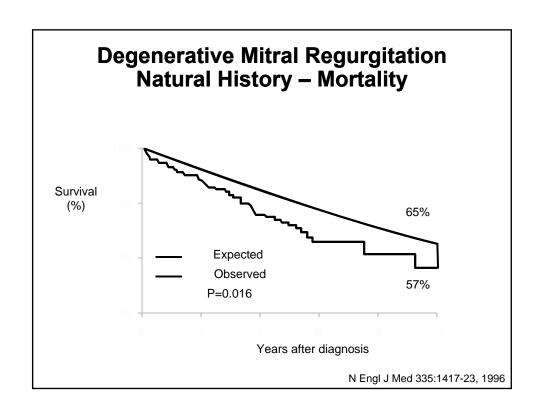
Disclosure

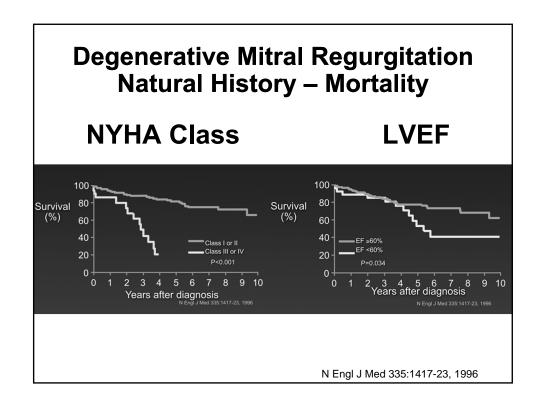
- Research Grants:
 - Medtronic Inc.
 - Abbot Vascular
 - Boston Scientific

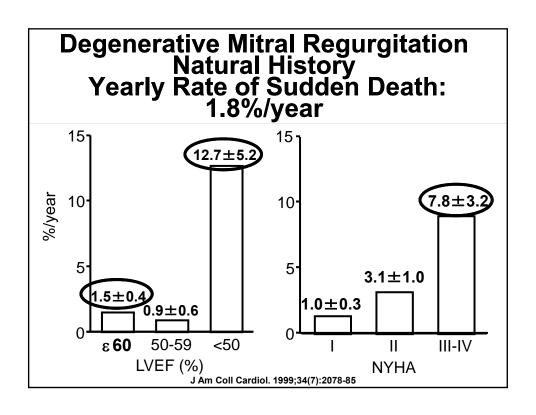


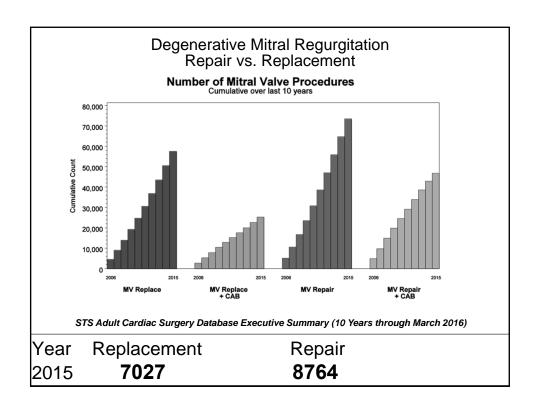




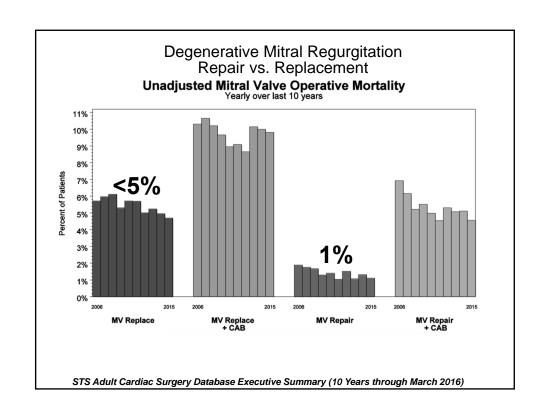


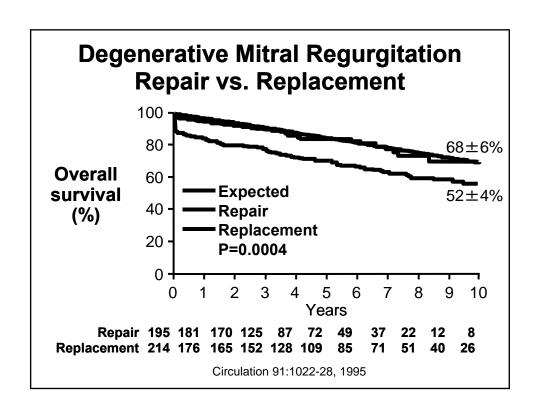






Degenerative Mitral Regurgitation Repair vs. Replacement Repair Replacement Survival Freedom from Reoperation Recurrence of Mitral Regurgitation Functional Status (symptoms) LV Function LV Volumes Freedom from: Bleeding Thromboembolism Endocarditis





Very Long-Term Survival and Durability of Mitral Valve Repair for Mitral Valve Prolapse

Dania Mohty, MD; Thomas A. Orszulak, MD; Hartzell V. Schaff, MD; Jean-Francois Avierinos, MD; Jamil A. Tajik, MD; Maurice Enriquez-Sarano, MD

917 patients (MVR in 238, MVRepair in 679) **Follow up: 20 years**

Re-Operation Rate: 23% vs 16% p=NS

Degenerative Mitral Regurgitation Surgical Results

Very Long-Term Survival and Durability of Mitral Valve Repair for Mitral Valve Prolapse

Dania Mohty, MD; Thomas A. Orszulak, MD; Hartzell V. Schaff, MD; Jean-Francois Avierinos, MD; Jamil A. Tajik, MD; Maurice Enriquez-Sarano, MD

Must do a Good Repair

Re-Operation Rate at 5, 10 and 15 years

No Residual MR: 5%, 9%, 14%

Residual MR: 14%, 18%, 21%

Valve repair versus valve replacement for degenerative mitral valve disease

A. Marc Gillinov, MD,^a Eugene H. Blackstone, MD,^{a,b} Edward R. Nowicki, MD,^a Worawong Slisatkorn, MD,^a Ghannam Al-Dossari, MD,^a Douglas R. Johnston, MD,^a Kristopher M. George, MD,^a Penny L. Houghtaling, MS,^b Brian Griffin, MD,^c Joseph F. Sabik, III, MD,^a and Lars G. Svensson, MD, PhD^a

3265 patients (MVR in 235, MVRepair in 3051) Follow up: 20 years

Long term survival was better for Repair than MVR

Propensity Matched Survival was the same

Degenerative Mitral Regurgitation Surgical Results

Mitral valve reconstruction in Barlow disease: Long-term echographic results and implications for surgical management

Jérôme Jouan, MD, ^{a,b} Alain Berrebi, MD, ^{a,b} Sylvain Chauvaud, MD, ^{a,b} Philippe Menasché, MD, PhD, ^{a,b,c} Alain Carpentier, MD, PhD, ^{a,b} and Jean-Noël Fabiani, MD, PhD^{a,b}

Objective: Owing to the complexity of the underlying lesions, Barlow disease remains a challenge for surgeons performing mitral valve repair. We aimed to assess whether our most recent results involving several surgeons were comparable with those of a previous experience in which mitral valve repair was performed by a more limited group of surgeons.

200 patients MVRepair **ECHOCARDIOGRAPHIC FOLLOW UP**

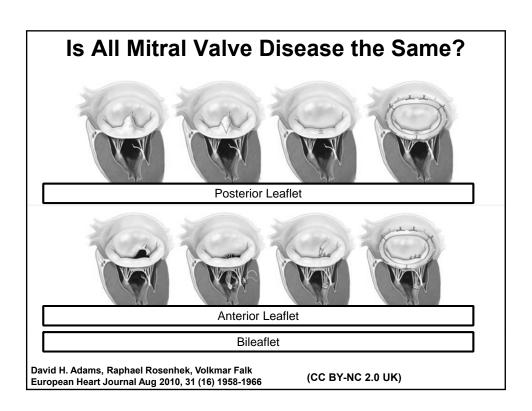
Freedom from MR>2+ 90% at 8 years

4-Year Results of a Randomized Controlled Trial of Percutaneous Repair Versus Surgery for Mitral Regurgitation

Laura Mauri, MD,*† Elyse Foster, MD,‡ Donald D. Glower, MD,§ Patricia Apruzzese, MS,† Joseph M. Massaro, PhD,†| Howard C. Herrmann, MD,¶ James Hermiller, MD,# William Gray, MD,** Andrew Wang, MD,‡ Wesley R. Pedersen, MD,†† Tanvir Bajwa, MD,‡‡ John Lasala, MD, PhD,§§ Reginald Low, MD,||| Paul Grayburn, MD,¶¶ Ted Feldman, MD,## for the EVEREST II Investigators

MVRepair (95 patients) vs. MitraClip (184 patients) Rigorous ECHO Follow up

MV Repair: MR 3+ or 4+: 9% at 4 years



Survival Advantage and Improved Durability of Mitral Repair for Leaflet Prolapse Subsets in the Current Era

Rakesh M. Suri, MD, DPhil, Hartzell V. Schaff, MD, Joseph A. Dearani, MD, Thoralf M. Su

Maurice Enric

Survival

Repair (1173 patients) or MVR(238 patients) for leaflet Prolapse **20 year follow-up**

Posterior Leaflet: Survival better for MV Repair (HR 0.49)

Bi Leaflet: Survival better for MV Repair (HR 0.59)

Anterior Leaflet: Survival MVR=Repair (HR 0.78)

Degenerative Mitral Regurgitation Surgical Results

Survival Advantage and Improved Durability of Mitral Repair for Leaflet Prolapse Subsets in the Current Era

Rakesh M. Suri, MD, DPhil, Hartzell V. Schaff, MD, Joseph A. Dearani, MD, Thoralf M. Sundt III, MD, Richard C. Dalv, MD, Charles I. Mullany, MB, MS, Maurice Enriquez

Re-Operation Rate

MD

Repair (1173 patients) or MVR(238 patients) for leaflet Prolapse **20 year follow-up**

MVRepair equal to MVR with Mechanical Valve

MVR with tissue valve much higher

Survival Advantage and Improved Durability of Mitral Repair for Leaflet Prolapse Subsets in the Current Era

Rakesh M. Suri, MD, DPhil, Hartzell V. Schaff, MD, Joseph A. Dearani, MD, Thoralf M. Sundt III, MD, Richard C. Dalv, MD, Charles I. Mullanv, MB, MS,

Re-Operation Rate and Risk of Reoperation

Repair (1173 patients) or MVR(238 patients) for leaflet Prolapse **20 year follow-up**

Lowest for Posterior Leaflet Prolapse (0.5%/yr)

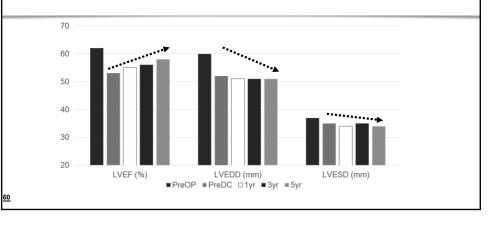
Highest for Anterior Leaflet Prolapse (1.6%/yr)

Bileaflet Prolapse=MVR with Mechanical valve (0.9%/yr)

Degenerative Mitral Regurgitation Surgical Results

Recovery of left ventricular function after surgical correction of mitral regurgitation caused by leaflet prolapse

Rakesh M. Suri, MD, DPhil, ^a Hartzell V. Schaff, MD, ^a Joseph A. Dearani, MD, ^a Thoralf M. Sundt, MD, ^a Richard C. Daly, MD, ^a Charles J. Mullany, MB, MS, ^a Maurice Enriquez-Sarano, MD, ^b and Thomas A. Orszulak, MD^a



Predictors of Left Ventricular Remodeling After Surgical Repair or Replacement for Pure Severe Mitral Regurgitation Caused by Leaflet Prolapse

Mario Sénéchal, MD^{a,*}, Jimmy MacHaalany, MD^a, Olivier F. Bertrand, MD, PhD^a, Kim O'Connor, MD^a, Julie Parenteau, MD^a, Isaïe-Nicolas Dubois-Sénéchal^a, Olivier Costerousse, PhD^a, Michelle Dubois, MSc^a, and Pierre Voisine, MD^b

Repair vs. Replacement

Repair (42 patients) or MVR(30 patients) for leaflet Prolapse **2 yr ECHO follow-up**

Similar Improvements in LVEF, LV dimensions and Volumes

Degenerative Mitral Regurgitation Surgical Results

4-Year Results of a Randomized Controlled Trial of Percutaneous Repair Versus Surgery for Mitral Regurgitation

Laura Mauri, MD,*† Elyse Foster, MD,‡ Donald D. Glower, MD,§ Patricia Apruzzese, MS,† Joseph M. Massaro, PhD,†|| Howard C. Herrmann, MD,¶ James Hermiller, MD,# William Gray, MD,** Andrew Wang, MD,‡ Wesley R. Pedersen, MD,†† Tanvir Bajwa, MD,†‡ John Lasala, MD, PhD,§§ Reginald Low, MD,||| Paul Grayburn, MD,¶¶ Ted Feldman, MD,## for the EVEREST II Investigators

MVRepair (**95 patients**) vs. MitraClip (184 patients) Rigorous Follow up

MV Repair: 93% NYHA class I or II 4 years

DURABILITY OF MITRAL VALVE REPAIR FOR DEGENERATIVE DISEASE

A. Marc Gillinov, MD^a Delos M. Cosgrove, MD^a Eugene H. Blackstone, MD^{a,b} Ramon Diaz, MD^a John H. Arnold, MD^a Bruce W. Lytle, MD^a Nicholas G. Smedira, MD^a Joseph F. Sabik, MD^a Patrick M. McCarthy, MD^a Floyd D. Loop, MD^a Background: Degenerative mitral valve disease is the most common cause of mitral regurgitation in the United States. Mitral valve repair is applicable in the majority of these patients and has become the procedure of choice. Objective: This study was undertaken to identify factors influencing the durability of mitral valve repair. Patients and methods: Between 1985 and 1997, 1072 patients underwent primary isolated mitral valve repair for valvular regurgitation caused by degenerative disease. Repair durability was assessed by multivariable risk factor analysis of reoperation. It was supplemented by a search for valve-related risk factors for death before reoperation. Three hospital deaths occurred (0.3%); complete fol-

Freedom From Thromboembolism, Bleeding, Endocarditis

1 yr (%)	5 yr (%)	10 yr (%)
98.8	96	88
99.7	99	99
100	99	98
	98.8 99.7	98.8 96 99.7 99

Degenerative Mitral Regurgitation Surgical Results

Outcomes 15 Years After Valve Replacement With a Mechanical Versus a Bioprosthetic Valve: Final

Report of the Veterans Affairs Randomized Trial

Karl Hammermeister, MD, FACC,* Gulshan K. Sethi, MD, FACC,† William G. Henderson, PhD,‡

Freedom From Thromboembolism, Bleeding, Endocarditis

15 years	Mechanical(%)	Bioprosthesis(%)
Thromboembolism	81	77
Bleeding	47	69
Endocarditis	89	83
Valve Failure	95	56

Degenerative Mitral Regurgitation Repair vs. Replacement

	Repair	Replacement
Survival	•	
Freedom from Reoperation	•	•
Recurrence of Mitral Regurgitation	•	•
Functional Status (symptoms)	•	•
LV Function	•	
LV Volumes	•	
Freedom from: • Bleeding • Thromboembolism • Endocarditis	v	