CARDIAC REMODELING IN VHD

HEMODYNAMICS, VOLUMES,

CIRCULATING HORMONES

MYOCARDIAL SUBSTRATE FIBROSIS

PROTEINS, TRANSCRIPTIONAL FACTORS

GENOTYPE
Cardiac Remodeling in VHD

Critical points, Paradigm shifts, New perspectives

- Ventricular vs Valvular Remodeling
  (Dynamic essence of valvular disease)

- From ventricular volumes to myocardial substrate assessment

- From remodeling to reverse remodeling
  (TAVI and MitraClip as opportunities to study reverse remodeling)

- From ventricles to atria
Progression of Mitral Regurgitation
A Prospective Doppler Echocardiographic Study
Maurice Enriquez-Sarano, MD, FACC,* Arsene-Joseph Basmadjian, MD,* Andrea Rossi, MD,* Kent R. Bailey, PhD,† James B. Seward, MD, FACC,* A. Jamil Tajik, MD, FACC*
(J Am Coll Cardiol 1999;34:1137–44)
Recurrence of Mitral Regurgitation Parallels the Absence of Left Ventricular Reverse Remodeling After Mitral Repair in Advanced Dilated Cardiomyopathy

Michele De Bonis, MD, Elisabetta Lapenna, MD, Alessandro Verzini, MD, Giovanni La Canna, MD, Antonio Grimaldi, MD, Lucia Torracca, MD, Francesco Maisano, MD, and Ottavio Alfieri, MD

Department of Cardiac Surgery, San Raffaele University Hospital, Milan, Italy (Ann Thorac Surg 2008;85:932–9)
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LV reverse remodeling imparted by aortic valve replacement for severe aortic stenosis; is it durable? A cardiovascular MRI study sponsored by the American Heart Association

Robert WW Biederman¹*, James A Magovern³, Saundra B Grant¹, Ronald B Williams¹, June A Yamrozik¹, Diane A Vido¹, Vikas K Rathi¹, Geetha Rayarao¹, Ketheswaram Caruppannan¹,² and Mark Doyle¹

*Corresponding Author

Journal of Cardiothoracic Surgery 2011, 6:53

![Graph showing LV mass changes over time](image-url)
Impact of Myocardial Fibrosis in Patients With Symptomatic Severe Aortic Stenosis

Frank Weidemann, MD*; Sebastian Herrmann*; Stefan Störk, MD; Markus Niemann, MD; Stefan Frantz, MD; Volkmar Lange, MD; Meinrad Beer, MD; Stefan Gattenlöchner, MD; Wolfram Voelker, MD; Georg Ertl, MD; Jörg M. Strotmann, MD

Circulation 2009;120:577-84
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intact membrane

necrotic cell
disrupted membrane

post MI scar

interstitial fibrosis

Myocarditis

Amyloidosis
Prognosis of Cardiac Fibrosis in Patients with Myocardial Fibrosis: Histopathological and Imaging Correlations

Figure B: Scatter plot showing the correlation between myocardial fibrosis and EF difference. The equation of the line is given as $r = -0.47$, $p = 0.02$.

Figure D: Kaplan-Meier survival analysis with three groups: Group 1, n = 17; Group 2, n = 22; Group 3, n = 15. The survival probability for Group 1 is lower than for Groups 2 and 3. The survival probability for Group 3 is the lowest with $P = 0.02$. The groups are further divided based on myocardial fibrosis (MF) levels: MF ≤ 2.5%, MF > 2.5% and < 5.0%, and MF ≥ 5.0%.
Equilibrium-Contrast CMR

Key features:
- a bolus of Gadolinium followed by continuous infusion to achieve blood:myocardial contrast equilibrium
- a blood test to measure blood contrast volume of distribution (1-hematocrit)
- T1 measurement before and after contrast equilibrium to calculate changes in tissue signal

Precise estimation of myocardial contrast volume of distribution

Equilibrium-Contrast CMR

Histology in 3 biopsies from aortic stenosis patients. This demonstrates the range of fibrosis in aortic stenosis. Red is collagen (fibrosis), and the yellow counter stain is myocytes.

MRI-measured myocardial volume of distribution against histological CVF. Vd(m) correlates with CVF in aortic stenosis (left, n18), hypertrophic cardiomyopathy (middle, n8), and the combined population (right, n26).


Diffuse fibrosis could be not detected with standard LGE sequences. The contrast of the images relies on the signal difference between normal and fibrotic myocardium. In case of diffuse fibrosis this difference can be very tiny because of the widespread process of fibrosis and would result in images with homogeneous grey areas.
Myocardial remodeling with aortic stenosis and after aortic valve replacement: Mechanisms and future prognostic implications

William M. Yarbrough, MD, Rupak Mukherjee, PhD, John S. Ikonomidis, MD, PhD, Michael R. Zile, MD, and Francis G. Spinale, MD, PhD. J Thorac Cardiovasc Surg 2012;143:656-64
...other consequences of severe LVH with reduced cavity volumes
indexed AVA $< 0.6$ cm$^2$/m$^2$,
EF $>50\%$,
SVi $< 35$ mL/m$^2$

- a higher level of global LV haemodynamic load reflected by higher valvulo-arterial impedance (Zva);
- smaller and relatively thicker ventricles;
- lower values for LV mid-wall radius shortening
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LV systolic wall stress
arterial & LA impedance (hydraulic load)
Improvement Following Correction of Secondary Mitral Regurgitation in End-Stage Cardiomyopathy With Mitral Annuloplasty

David S. Bach, MD, and Steven F. Bolling, MD

Am J Cardiol 1996; 78: 966-969
Mitral valve surgery in heart failure: Insights from the Acorn Clinical Trial

Michael A. Acker, MD, Steven Bolling, MD, Richard Shemin, MD, James Kirklin, MD, Jae K. Oh, MD, Douglas L. Mann, MD, Mariell Jessup, MD, Hani N. Sabbah, PhD, Randall C. Starling, MD, and Spencer H. Kubo, MD, for the Acorn Trial Principal Investigators and Study Coordinators

J Thorac Cardiovasc Surg 2006; 132: 569-577

Basal Values: EDV 270 ± 12; EF 24 ± 9
Acute and 12-Month Results With Catheter-Based Mitral Valve Leaflet Repair

The EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study

Patrick L. Whitlow, MD,* Ted Feldman, MD,† Wes R. Pedersen, MD,‡ D. Scott Lim, MD,§ Robert Kipperman, MD,∥ Richard Smalling, MD, PhD,¶ Tanvir Bajwa, MD,# Howard C. Herrmann, MD,** John Lasala, MD, PhD,†† James T. Maddux, MD,‡‡ Murat Tuzcu, MD,* Samir Kapadia, MD,* Alfredo Trento, MD, §§ Robert J. Siegel, MD, §§ Elyse Foster, MD,|| Donald Glower, MD,¶¶ Laura Mauri, MD,## Saibal Kar, MD, §§ on behalf of the EVEREST II Investigators

(J Am Coll Cardiol 2012;59:130-9)
**EVEREST II HRR: Study Algorithm**

**KEY INCLUSION CRITERIA**
- Predicted procedural mortality risk
- $>12\%$ (STS calculated or Surgeon estimated based on pre-specified co-morbidities)
- Symptomatic 3+ or 4+ MR
- Degenerative or Functional

**KEY EXCLUSION CRITERIA**
- EF $\leq 20\%$ and/or LVESD $>60$mm
- MVA $<4cm^2$
- Leaflet anatomy unsuitable for MitraClip device

78 Enrolled

- FMR
  - $N=46$
  - (59%)

- DMR/Mixed
  - $N=32$
  - (41%)
HRR: Ejection Fraction/Forward Stroke Volume

MitraClip therapy results in Improved LV Efficiency

**FMR**
- EF Baseline: 47%
- EF 12 Months: 44%
- FSV Baseline: 51 ml/beat
- FSV 12 Months: 55 ml/beat

**DMR**
- EF Baseline: 67%
- EF 12 Months: 61%
- FSV Baseline: 48 ml/beat
- FSV 12 Months: 53 ml/beat

P-values:
- EF: P=0.06
- FSV: P=0.002
- FMR: P=0.05
MitraClip therapy results in reverse LV remodeling

**FMR, n=34**

- Diastolic: 192 (P<0.0001) vs. 153 (P=0.0002)
- Systolic: 103 vs. 87 (P=0.0002)

**DMR, n=20**

- Diastolic: 137 vs. 117 (P=0.0002)
- Systolic: 46 vs. 47

12 month Matched data
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Left Atrial Size Is a Potent Predictor of Mortality in Mitral Regurgitation Due to Flail Leaflets

Results From a Large International Multicenter Study

Dan Rusinaru, et al on behalf of the Mitral Regurgitation International DAtabase (MIDA) Investigators

(Circ Cardiovasc Imaging. 2011;4:473-481.)

N=788 patients
Left Atrial Size Is a Potent Predictor of Mortality in Mitral Regurgitation Due to Flail Leaflets

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![Graph showing overall survival with different left atrial sizes and their corresponding survival rates.](image-url)
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Medical Treatment

Medical + Surgical Treatment
Cardiac Remodeling and Therapeutical Decisions in VHD