

**Percutaneous Mitral Repair with
the MitraClip[®] Device
for Functional Mitral Regurgitation:**

**Acute Success, One year Durability and Reverse
Remodeling in the Initial EVEREST Cohort**

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**On behalf of the
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EVEREST

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EVEREST II ONLY

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- All authors receive research support from Evalve
- Investigational Device:
 - Limited by Federal (or United States) Law to Investigational Use

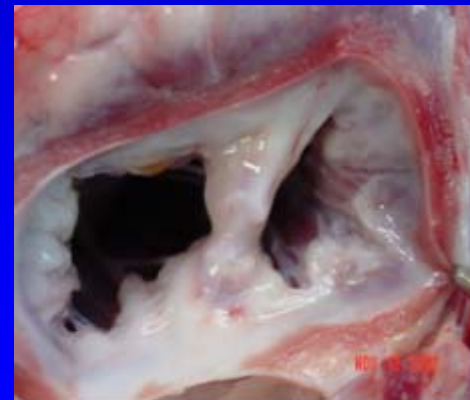
Background & Purpose

- Of the 250,000 patients in the United States developing significant mitral regurgitation (MR) each year, up to 60% have functional MR
- Isolated leaflet repair for functional mitral regurgitation (FMR) has not been well characterized
- The purpose of this study is to evaluate the safety and efficacy of isolated leaflet repair using the MitraClip device in patients with FMR

Edge to Edge & MitraClip Concepts



- Facilitates proper leaflet coaptation
 - Degenerative - Anchor flail and prolapsed leaflets
 - Functional - Coapt tethered leaflets
 - Reduces LV volume overload by reducing MR
- Creates tissue bridge
 - May limit dilatation of annulus
 - Septal-lateral (A-P) dimension
 - Supports durability of repair
- Restrains LV wall
 - Limits LV dilatation



Porcine model, 6M

Methods

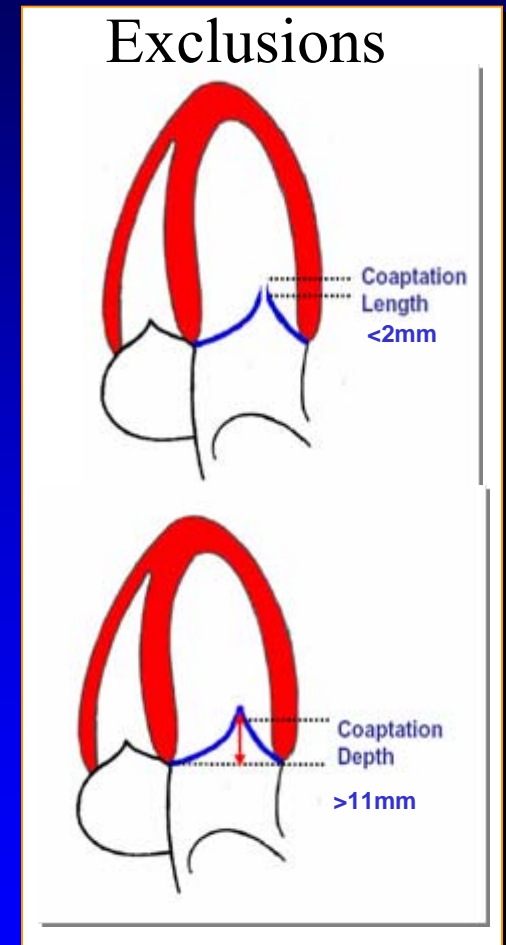
- Surgical candidates with FMR were treated with the MitraClip device as part of the EVEREST protocols.
- FMR was defined as the presence of MR without demonstrated echocardiographic structural valve defects as assessed by TEE.
- TTE performed to assess MR severity and LV function and dimensions at baseline and at 12 months.
- American Society of Echocardiography criteria were used for systematic Core Laboratory assessment of MR severity and LV function.

Methods: Key Eligibility Criteria

- Age 18 years or older
- Moderate to severe (3+) or severe (4+) MR
 - *Symptomatic*
 - *Asymptomatic with LVEF < 60% or LVESD > 40mm*
ACC/AHA Guidelines, Circ. 114;450,2006
- MR originates from A2-P2 mal-coaptation
- Candidate for mitral valve surgery
- Transseptal deemed feasible
- Key Exclusions
 - *EF < 25% or LVESD > 55 mm*
 - *Renal insufficiency*
 - *Endocarditis, rheumatic heart disease*

Methods: Anatomic Eligibility

- TEE evidence of FMR:
 - Absence of Degenerative valve disease
 - Presence of leaflet “tethering”
 - Not exceeding 10mm
- Sufficient leaflet tissue available for mechanical coaptation
 - $> 2\text{mm}$ “vertical” leaflet tissue available
- Absence of severe LV dysfunction
 - Excluding LVID-s $> 55\text{mm}$ or EF $< 25\%$
 - Ischemic or non-ischemic etiology



EVEREST Preliminary FMR Cohort

- Subset of patients with FMR treated in the EVEREST I Feasibility Study or as roll-ins in the EVEREST II Study.
 - Excludes EVEREST II Randomized patients or EVEREST II High Risk Registry patients.

Study	Population	n
EVEREST I (Feasibility)	FMR patients	8
EVEREST II (Pivotal)	Non-randomized FMR patients (excludes high risk patients)	15
Total		23

Analysis per EVEREST II definitions

EVEREST

MR Reduction Goals

- Eligibility requirement: 3+ or 4+ MR
- Protocol requirement: Reduce MR $\leq 2+$
- Procedural goal: Reduce MR $\leq 1+$
- Durability goal: Maintain MR reduction $\leq 2+$

EVEREST Initial FMR Cohort

Clinical Features

	FMR n = 23	EVEREST Overall N = 107
Median Age (range)	75 (50 – 88)	71 (26 – 88)
≥ age 65	74%	62%
Male gender	52%	62%
Diabetes mellitus	48%	21%
Hypertension	96%	69%
COPD	22%	12%
History CHF	87%	56%
Prior Cardiac Surgery	43%	19%
Atrial Fibrillation	26%	29%
Median EF	50%	62%
NYHA III or IV	83%	46%
LVID Systole (cm)	4.3 ± 0.7	3.5 ± 0.8

EVEREST Initial FMR Cohort

Patients with 30 Day Major Adverse Events (N = 23)

Freedom from Major Adverse Events 87%

Death – Unrelated to Clip 0

Stroke (>72 hours) 0

Myocardial Infarction 0

Re-operation for failed surgery 0

Non-elective Cardiac Surgery (Pericardial Effusion) 1

Renal failure 0

Deep wound infection 0

Ventilation > 48 hrs 0

GI complication requiring surgery 0

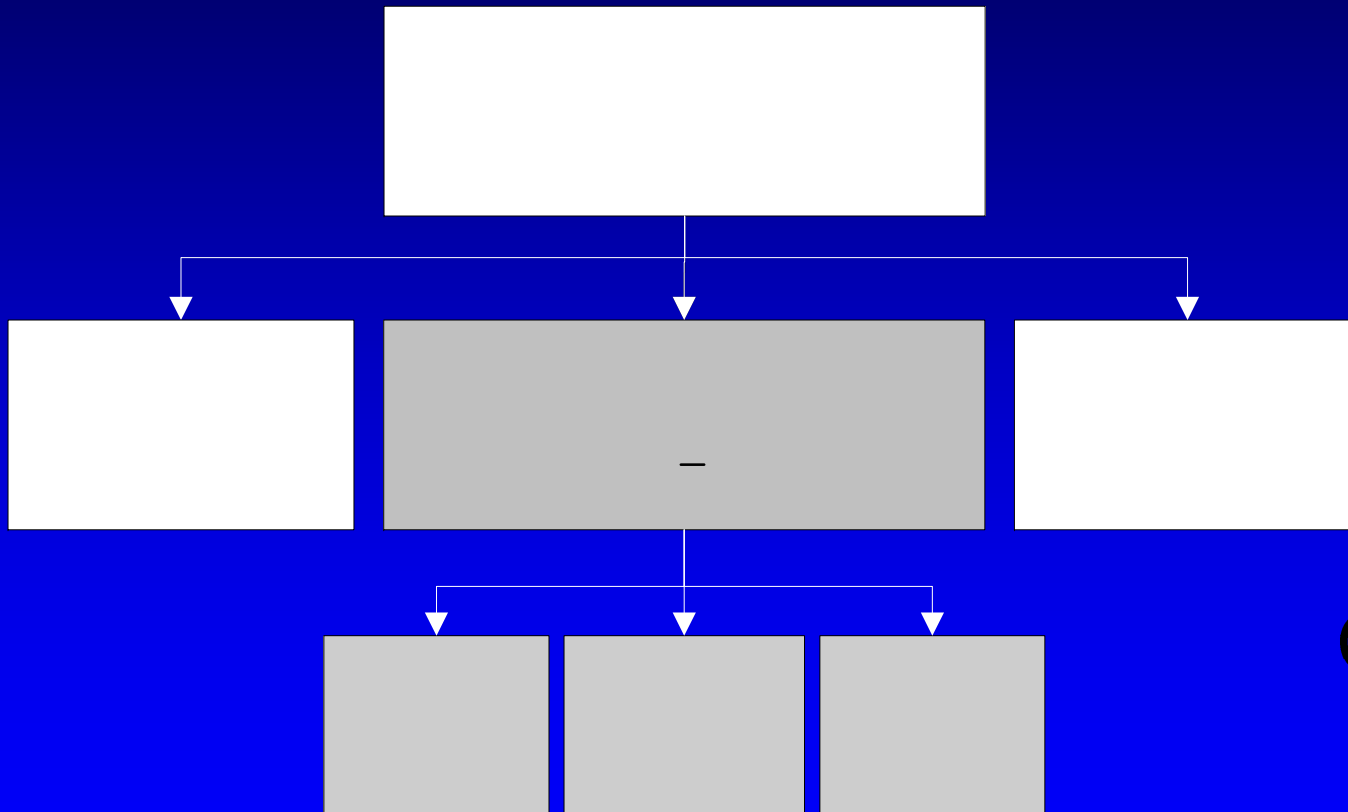
Septicemia 0

Bleeding requiring transfusion ≥ 2 units 2

EVEREST Initial FMR Cohort

Efficacy Results through Discharge

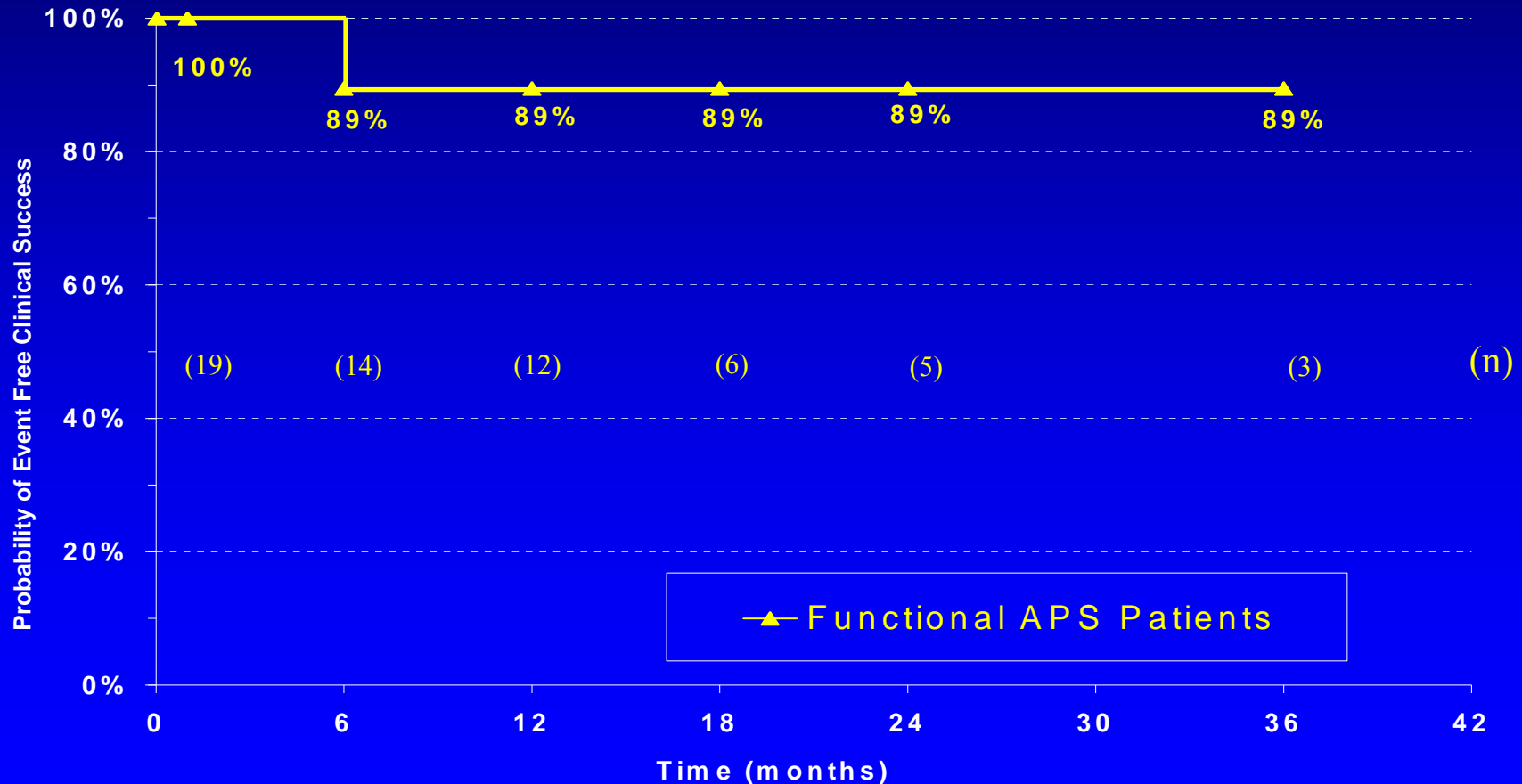
N = 23



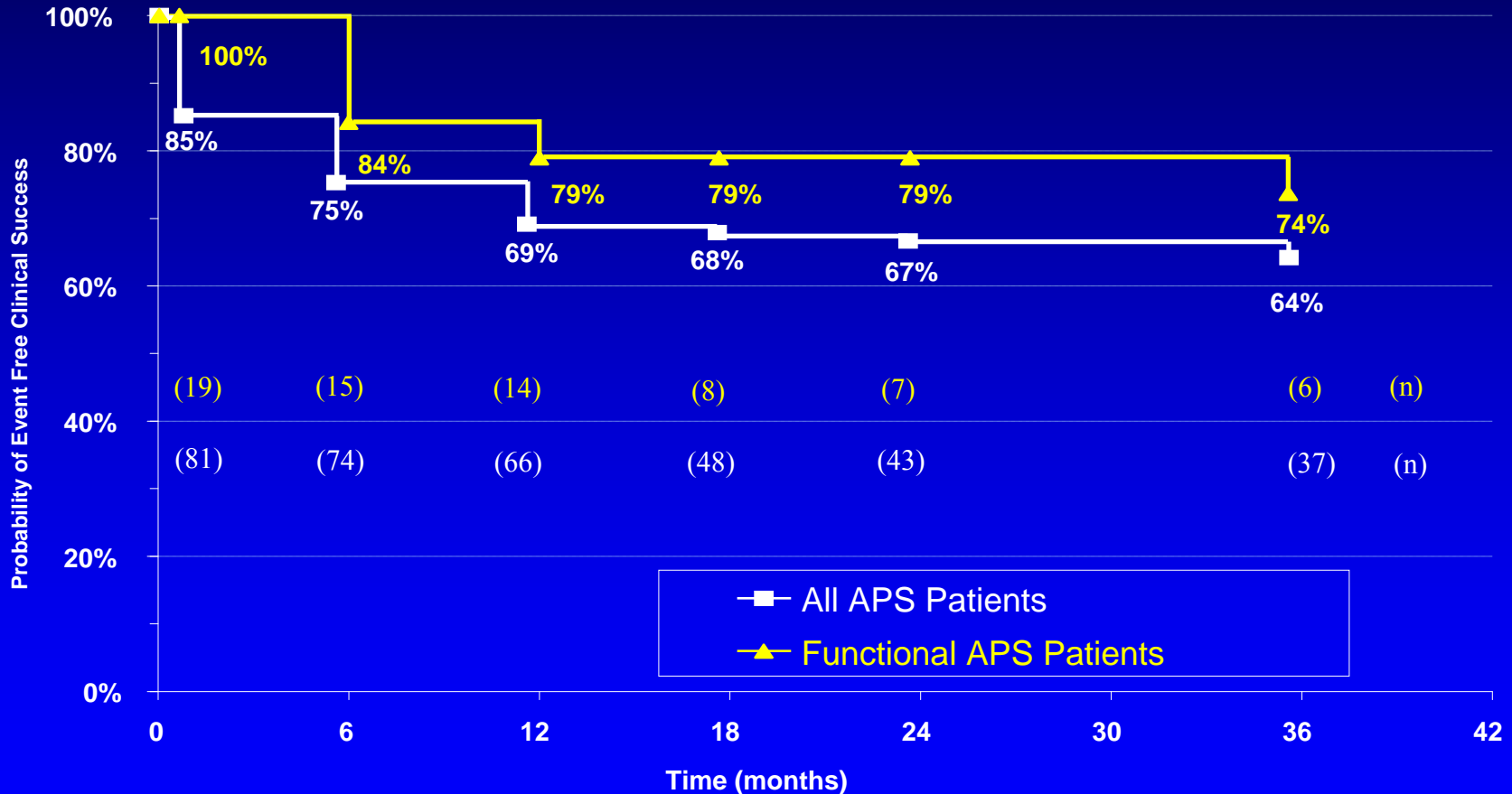
Clip Proc
N =

* Acute Procedural Success (APS): Defined as placement of one or more Clips resulting in discharge MR severity of 2+ or less, as determined by Core Lab.

EVEREST Initial FMR Cohort: Freedom From MR > 2+ Kaplan-Meier Acute Procedural Success (APS) Patients



EVEREST Initial FMR Cohort: Event Free Clinical Success Kaplan-Meier APS Patients

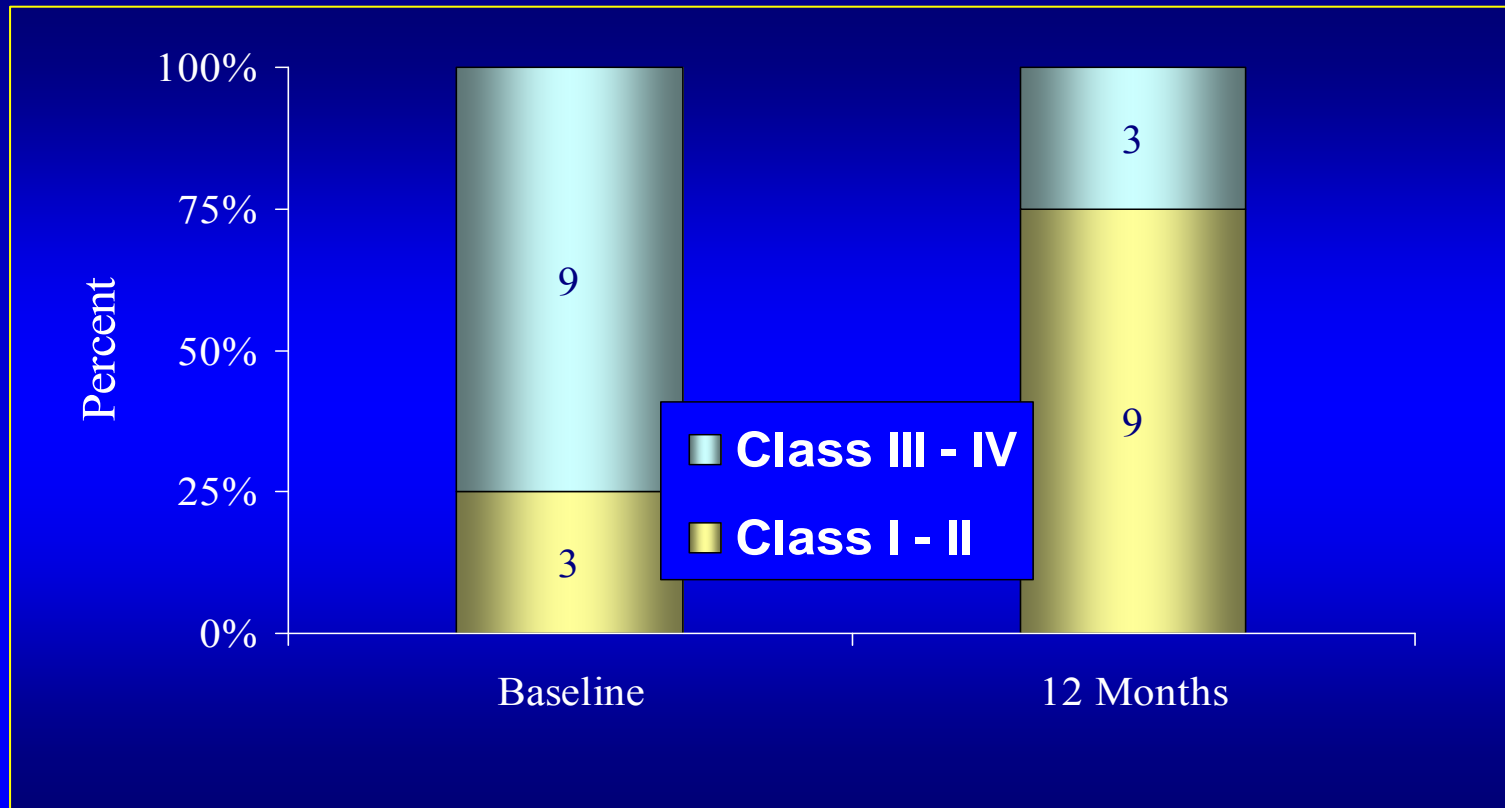


Freedom from death, mitral valve surgery, & MR > 2+

EVEREST Initial FMR Cohort

NYHA Class, APS Patients* (matched data, n = 12)

75% (9/12) Improved
17% (2/12) No Change
8% (1/12) Worsened w/o MR > 1+



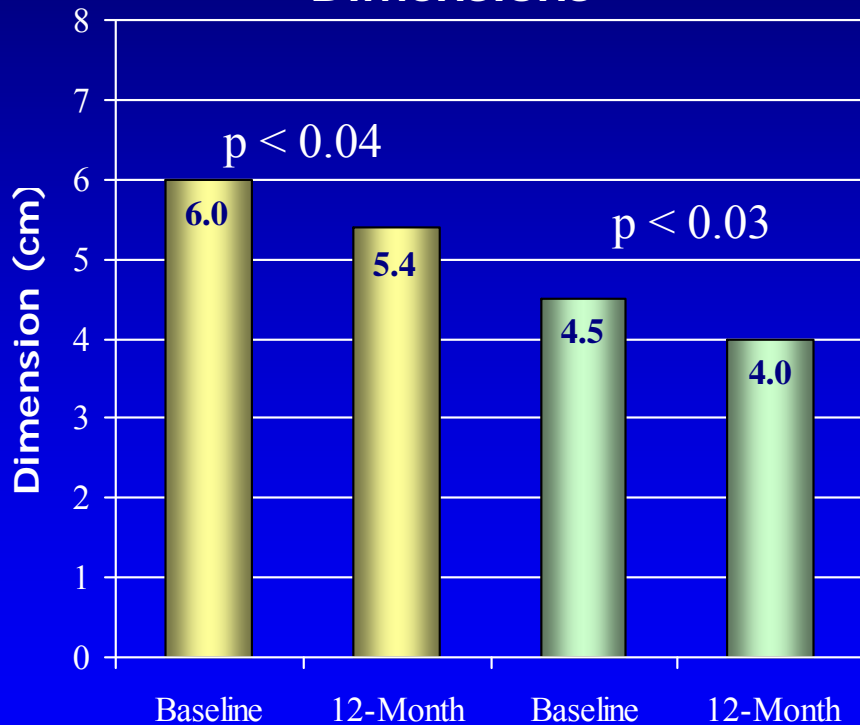
* Excludes patients that went to MV surgery post-Clip prior to 12-months or have not reached 12-month follow-up

EVEREST Initial FMR Cohort

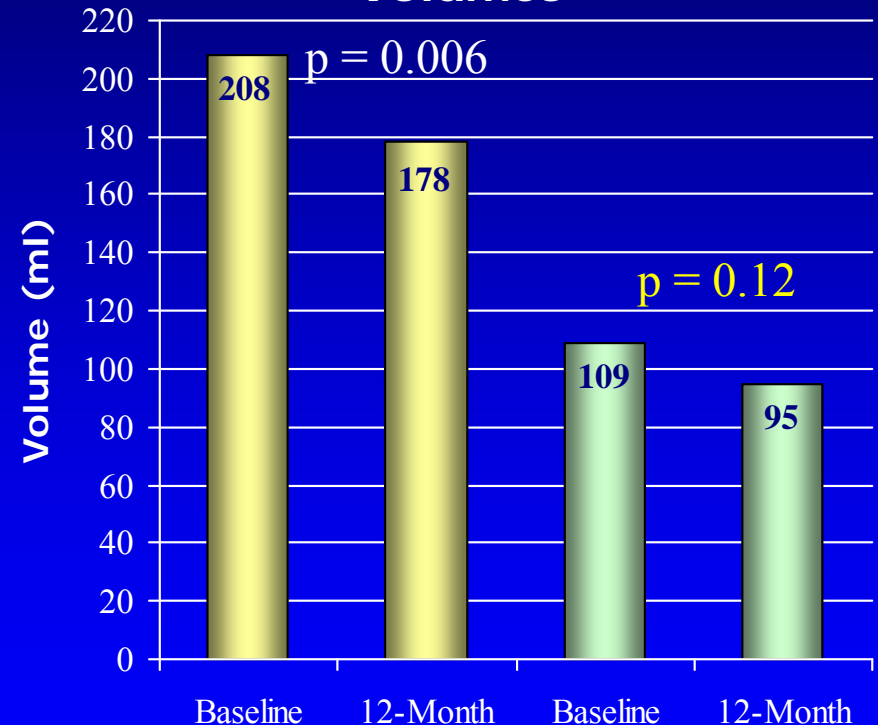
Reverse LV Remodeling

APS Patients* (matched data, n = 12)

LV End Diastolic & Systolic Dimensions



LV End Diastolic & Systolic Volumes

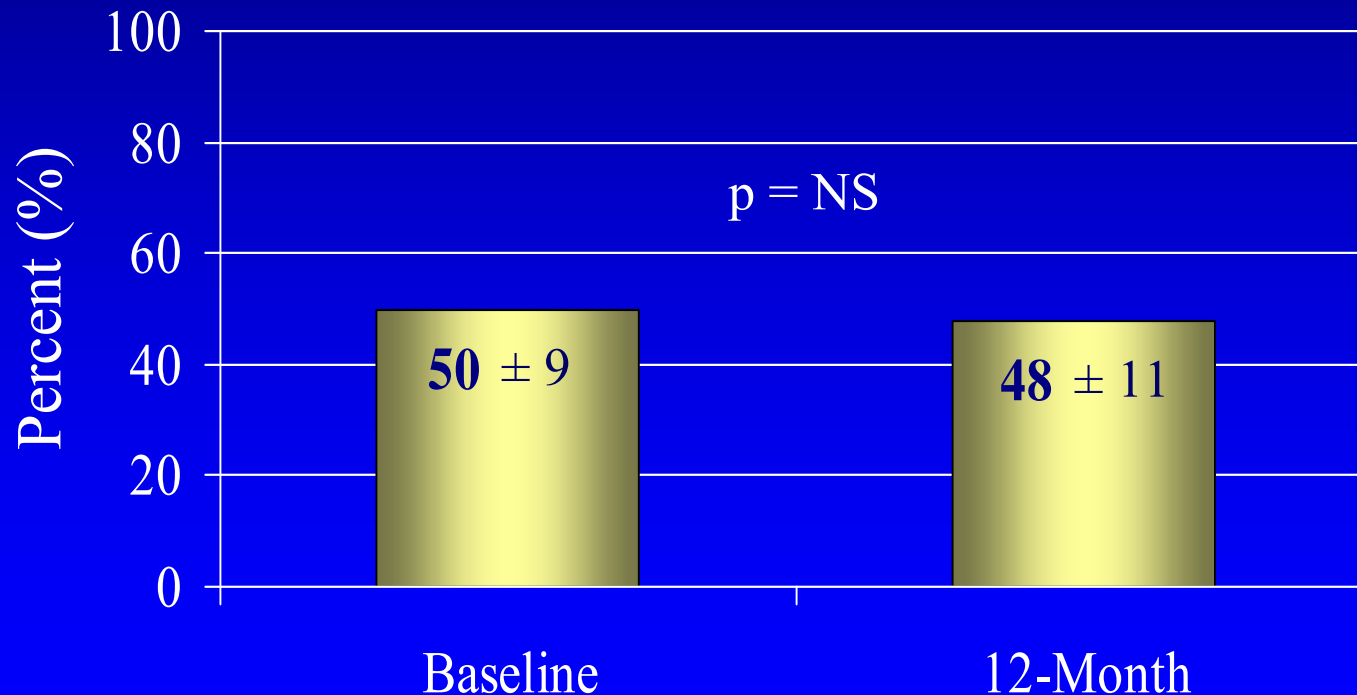


* Excludes patients that went to MV surgery post-Clip prior to 12-months or have not reached 12-month follow-up

EVEREST Initial FMR Cohort Ejection Fraction

APS Patients* (available matched data, n = 12)

Ejection Fraction



* Excludes patients that went to MV surgery post-Clip prior to 12-months or have not reached 12-months

EVEREST Initial FMR Cohort: Surgery Following Clip Procedure

N = 23

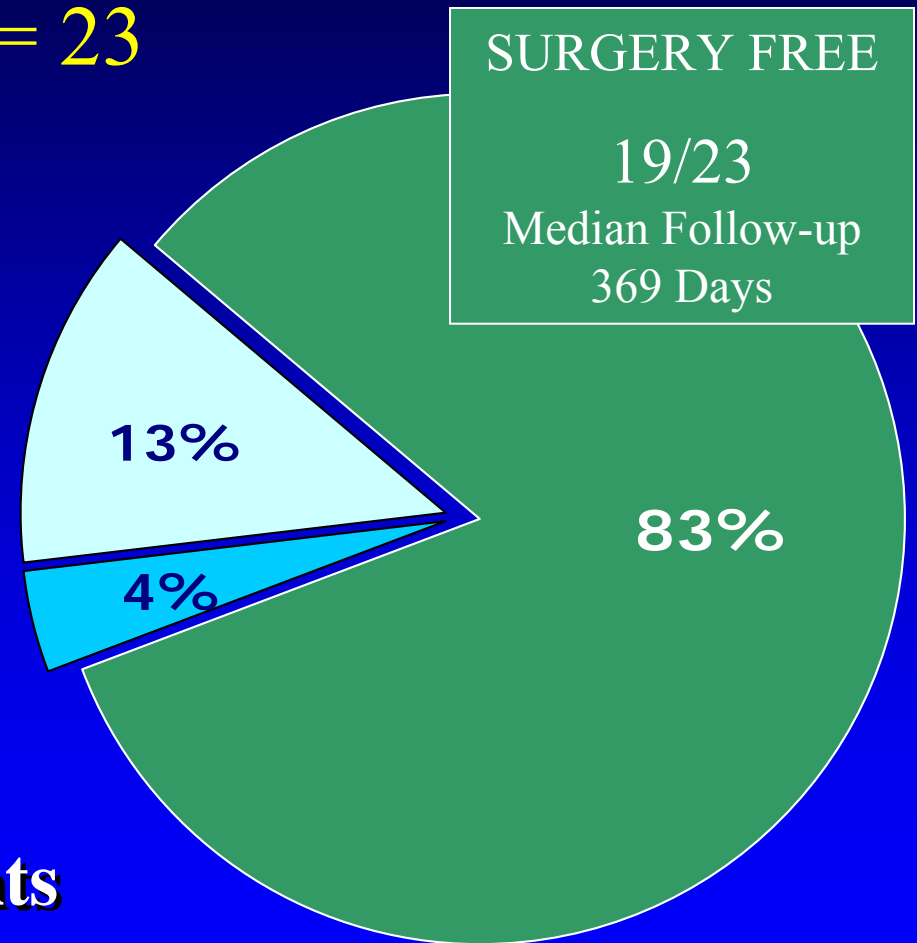
Surgery After Clip Implanted (n = 3)

- 2 Repairs
- 1 Replacement

Surgery After No Clip (n = 1)

- 1 Replacement

No Partial Clip Detachments
No Clip Embolizations



EVEREST Initial FMR Cohort Conclusions

Percutaneous mitral repair with the MitraClip:

- Effective in reducing MR with a low MAE rate
- Significant reverse LV remodeling at 1-year
- Clinical improvement with 58% of patients NYHA Class I at 1-year
- 79% freedom from death, surgery for valve dysfunction and MR $> 2+$ at 1-year
- MitraClip facilitates leaflet coaptation reducing MR in functional patients

Study Limitations

- Small number of patients
- Non randomized registry population
- Initial experience – early in learning curve
- Only 12/19 with acute procedural success have 1 year follow up (clinical and echo)

EVEREST II Randomized Trial

- Enrollment still open
 - Randomized sample size: ~280 patients
- Additional information available at:
 - www.mitralregurgitation.org

EVEREST Investigational Study Sites



- 01 - University of Pennsylvania
- 02 - Evanston Northwestern Healthcare
- 03 - Cleveland Clinic Foundation
- 04 - Emory University Hospital - Crawford Long
- 05 - Swedish Medical Center
- 06 - Washington Hospital Center
- 07 - Columbia University Medical Center
- 08 - Univ. of Texas Health Science Center
- 09 - Shawnee Mission Medical Center
- 10 - Carolinas Medical Center (Sanger Clinic)

- 11 - Brigham & Women's Hospital
- 12 - Memorial Hermann Hospital
- 13 - University of Colorado Hospital
- 14 - Nebraska Heart Institute
- 15 - St. Francis Hospital
- 16 - Duke University Medical Center
- 17 - Terrebonne General Medical Center
- 18 - The Care Group
- 19 - UCD Medical Center
- 20 - Cedars-Sinai Medical Center

- 21 - Washington Univ. Medical Center
- 22 - University of Virginia
- 23 - Toronto General Hospital
- 24 - Banner Good Samaritan Medical Center
- 25 - St. Luke's Medical Center
- 26 - Ochsner Clinic Foundation
- 27 - NYU Medical Center
- 28 - Baylor University Medical Center
- 29 - St. Joseph Mercy Hospital (Michigan Heart PC)
- 30 - Victoria Heart Institute Foundation

- 31 - NY Presbyterian Hospital
- 32 - The University of Kansas Medical Center
- 33 - Minneapolis Heart Institute
- 34 - St. Patrick Hospital
- 35 - Oklahoma Heart Hospital
- 36 - University of Alabama at Birmingham
- 37 - LDS Hospital
- 38 - William Beaumont Hospital
- 39 - Royal Alexandra Hospital