# Mid-term Outcomes Following Mitral Valve Repair with The MitraClip System


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# Disclosure statement of financial interest

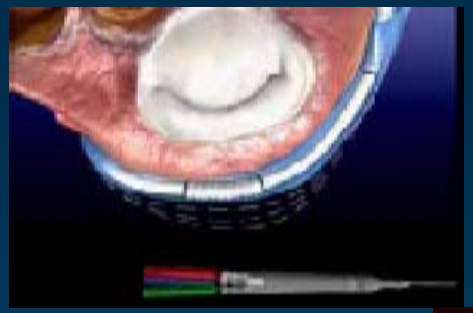
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

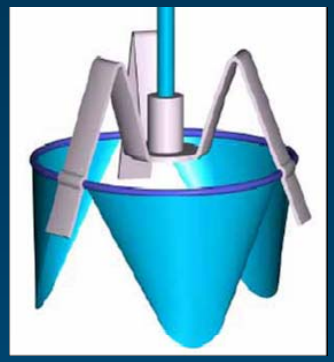
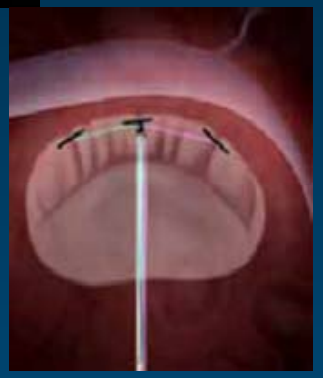
**Consulting fees/honoraria**: Medtronic, Abbott Vascular, Boston Scientific, Stentys, Celonova

# Percutaneous MV Repair

- **Edge-to-Edge (2)**
  - Evalve *Pivotal Completed, RCT, Registries*
  - Edwards Mobius
- **Coronary sinus annuloplasty (3)**
  - Cardiac Dimensions Carillon
  - Edwards Monarc
  - Viacor PTMA
- **Indirect annuloplasty (3)**
  - Ample PS3
  - St. Jude AAR
  - Mycor i-Coapsys
- **Direct annuloplasty (3)**
  - Mitralign, Guided Delivery Systems
  - QuantumCor, Cordis DPA
  - MiCardia
- **Mitral valve replacement (1)**
  - Endovalve





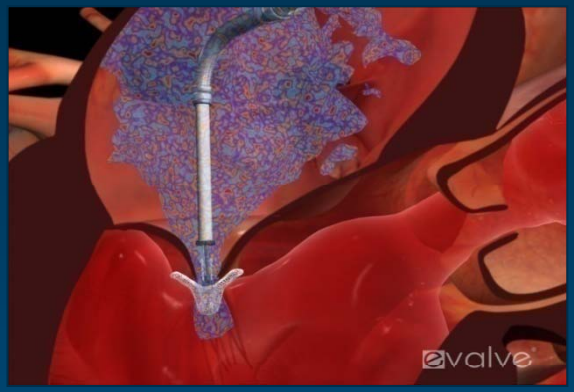



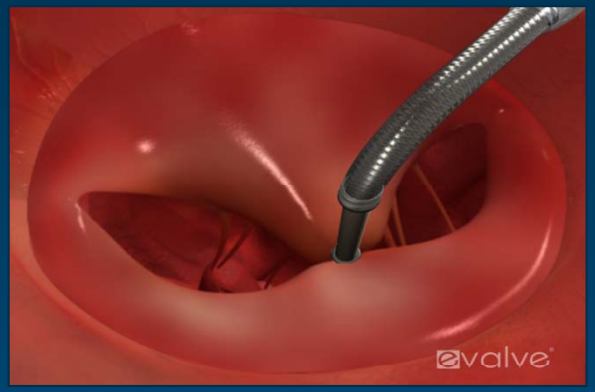
CE 0050

# MitraClip™

- ✓ Edge-to-Edge Technique
- ✓ Permanent leaflet approximation using a sutures + clip
- ✓ Trans-septal approach
- ✓ Echocardiographic and fluoroscopy guidance on a beating heart

**Catheter Delivery System**





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*Alfieri, J Thorac Cardiovasc Surg. 2001*
*Herrmann, EuroInterv. 2006*

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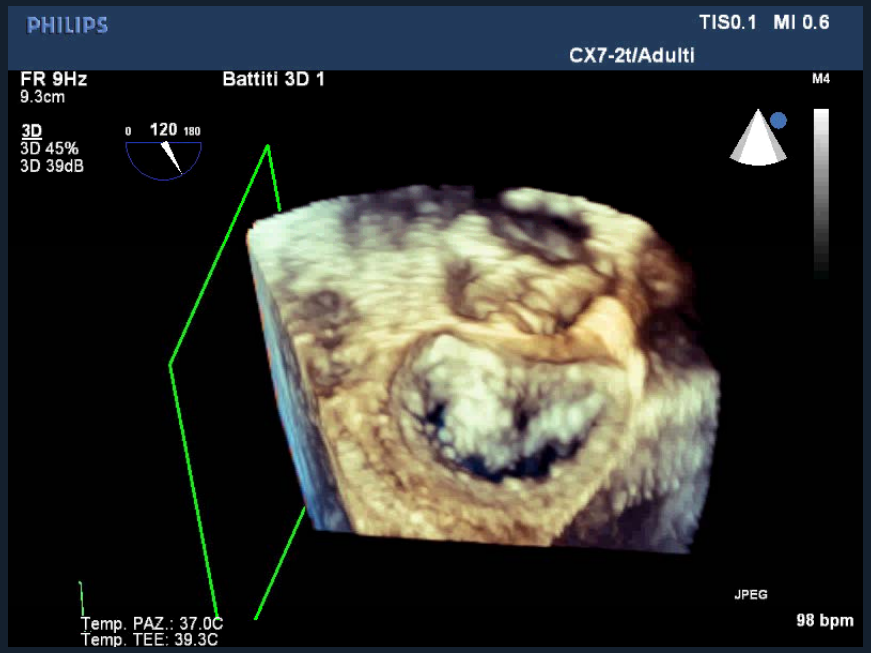
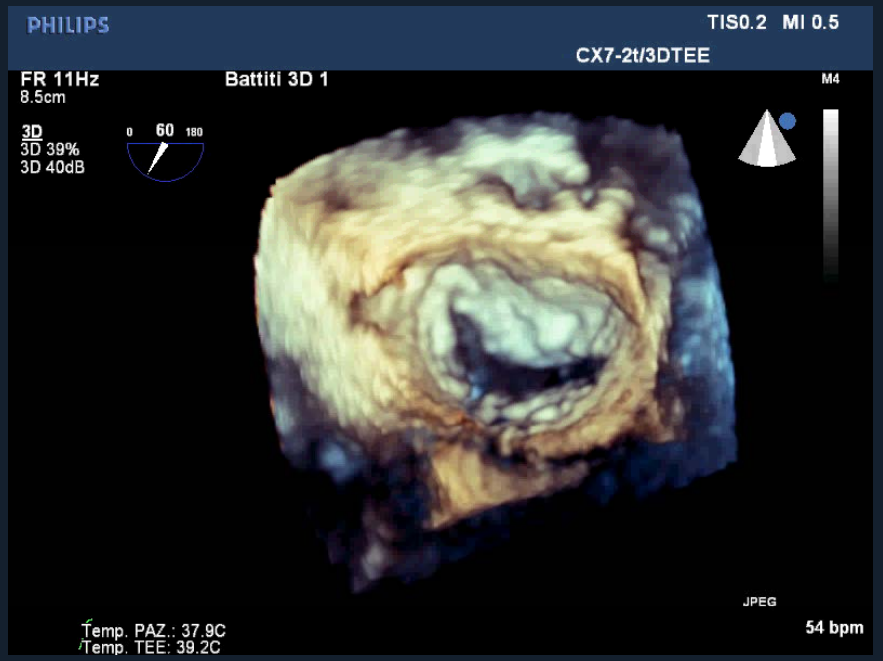
# Percutaneous MV repair

## Degenerative MR




## Functional MR



# Percutaneous MV repair

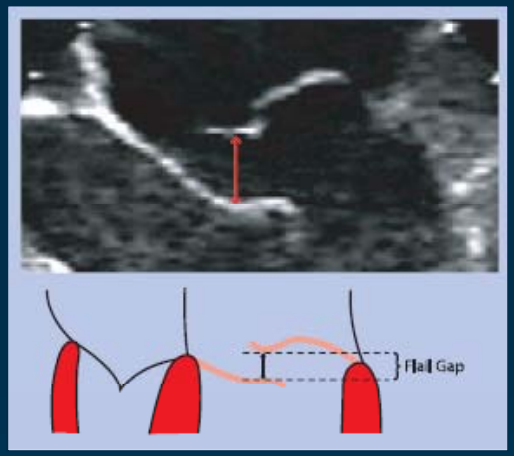
## *Anatomic Eligibility*

**Sufficient leaflet tissue for mechanical coaptation**

**Non-rheumatic/endocarditic valve morphology**

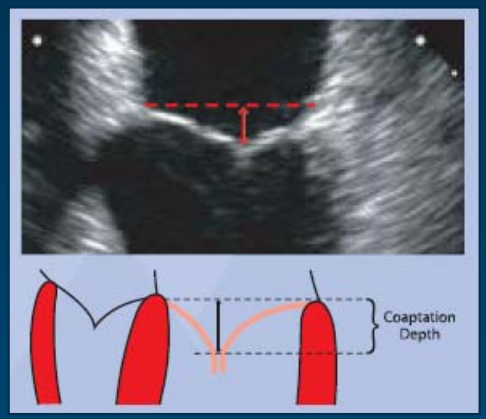
**Absence of severe LV dysfunction**

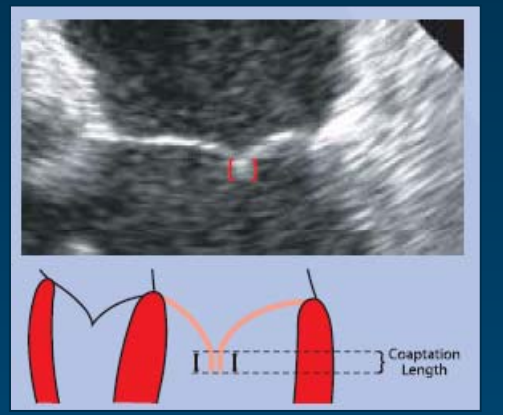
**Absence of severe calcification**



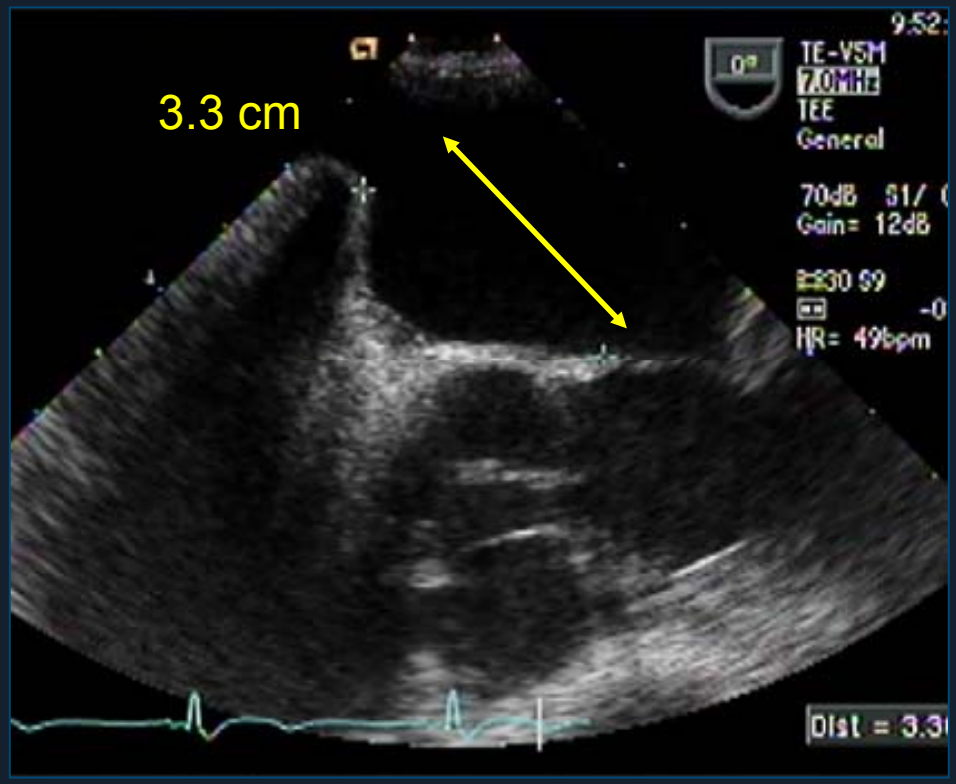

### Protocol anatomic exclusions

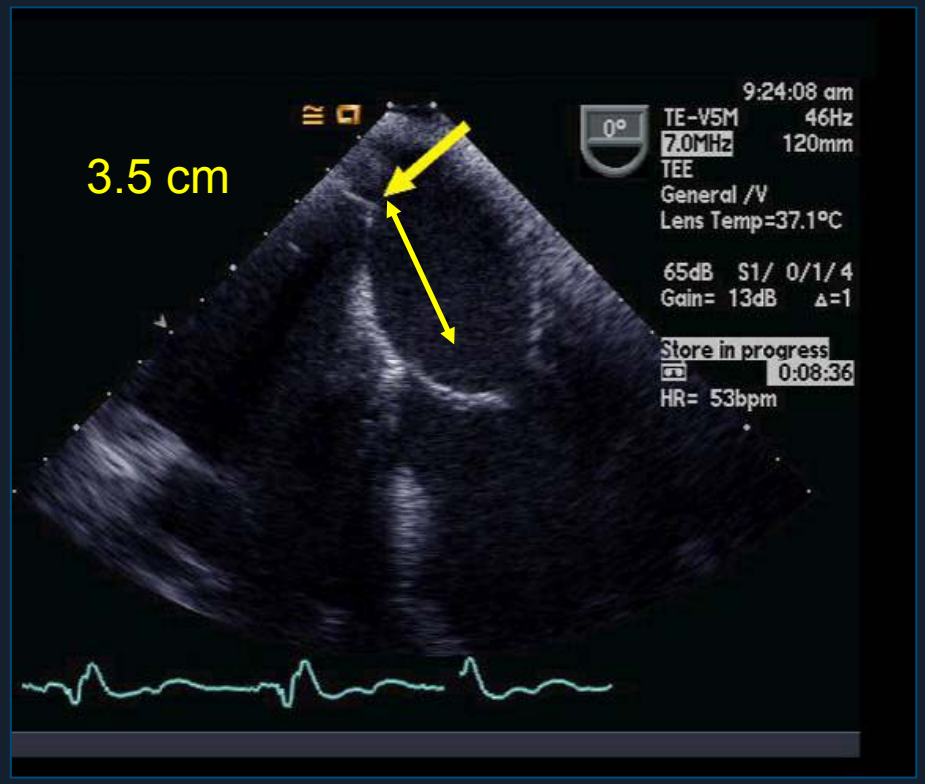
- ✓ Flail gap >10mm
- ✓ Flail width >15mm
- ✓ LVISD > 55mm
- ✓ Coaptation depth >11mm
- ✓ Coaptation length < 2mm



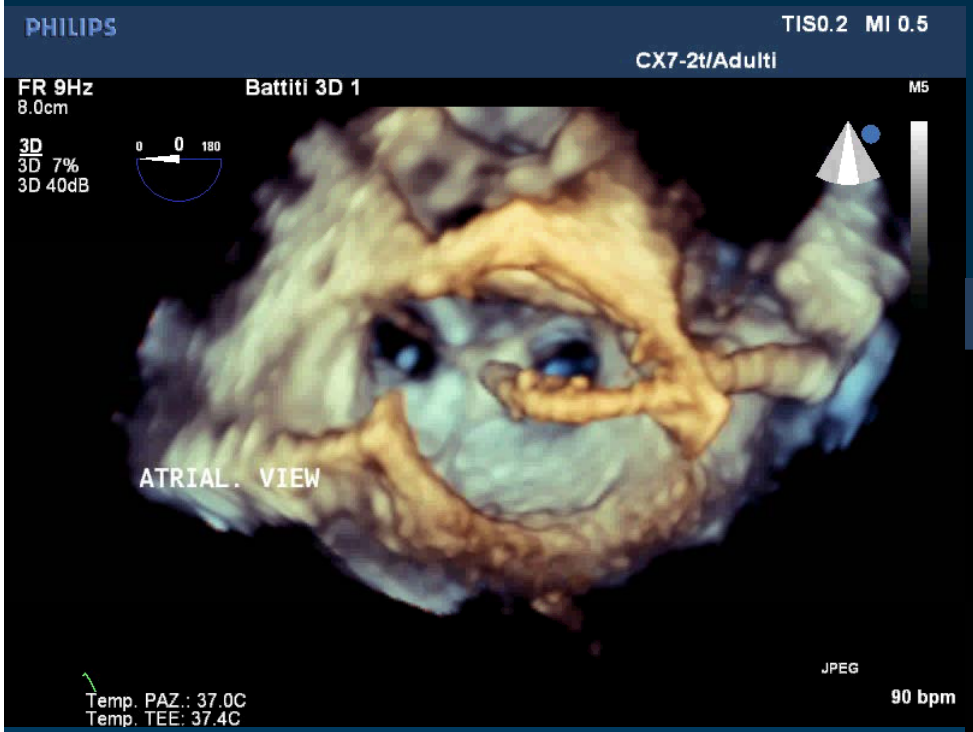
# Tenting (Height) above the MV annulus

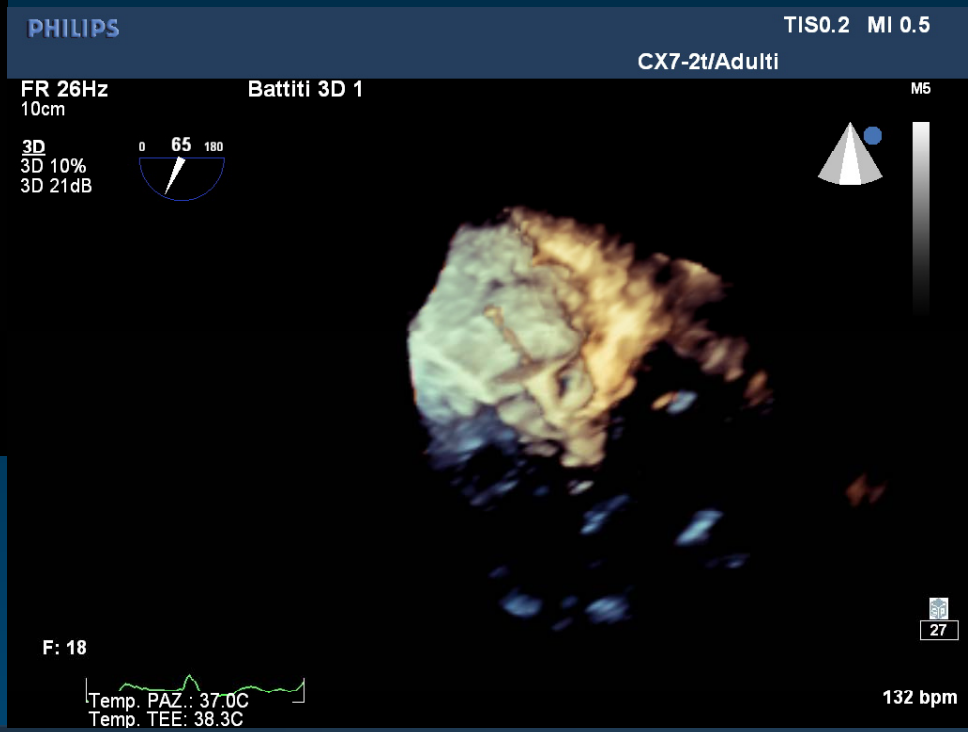


# Procedure

## *Clip orientation*

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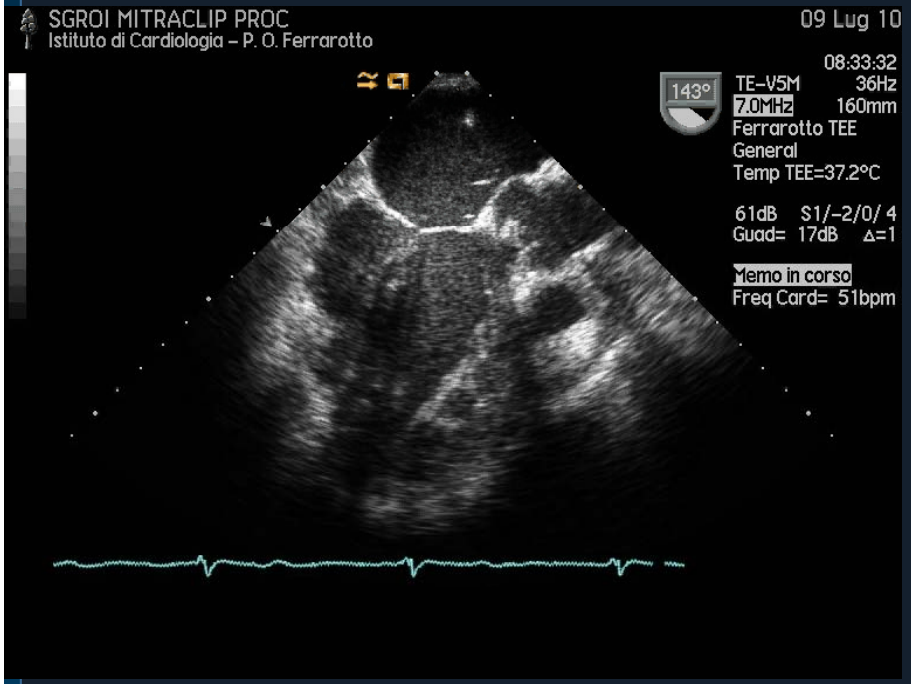
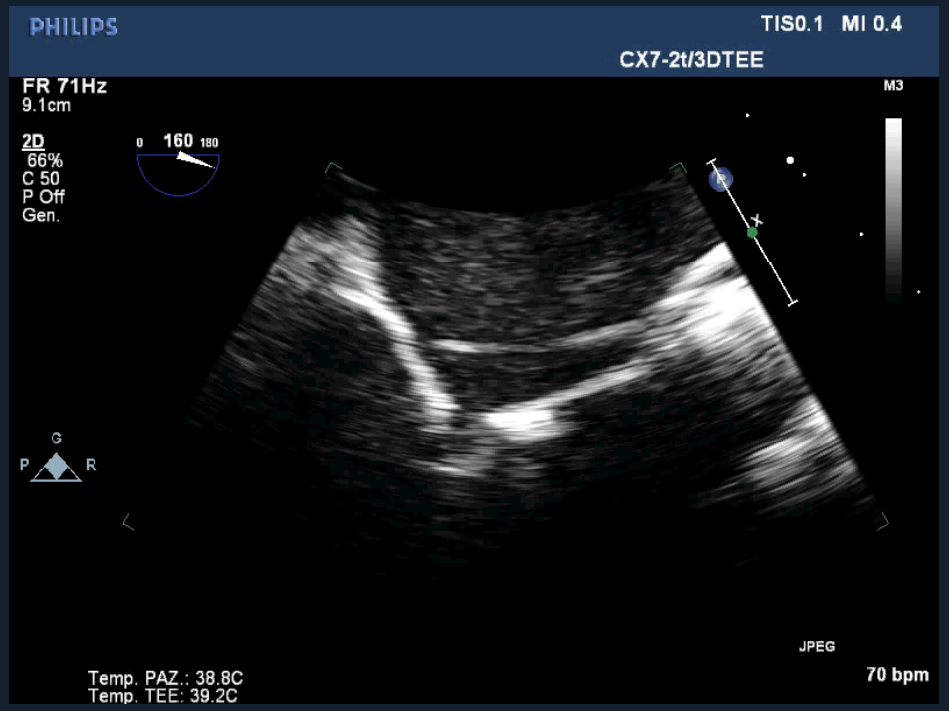
# Procedure

## *Grasping Check*

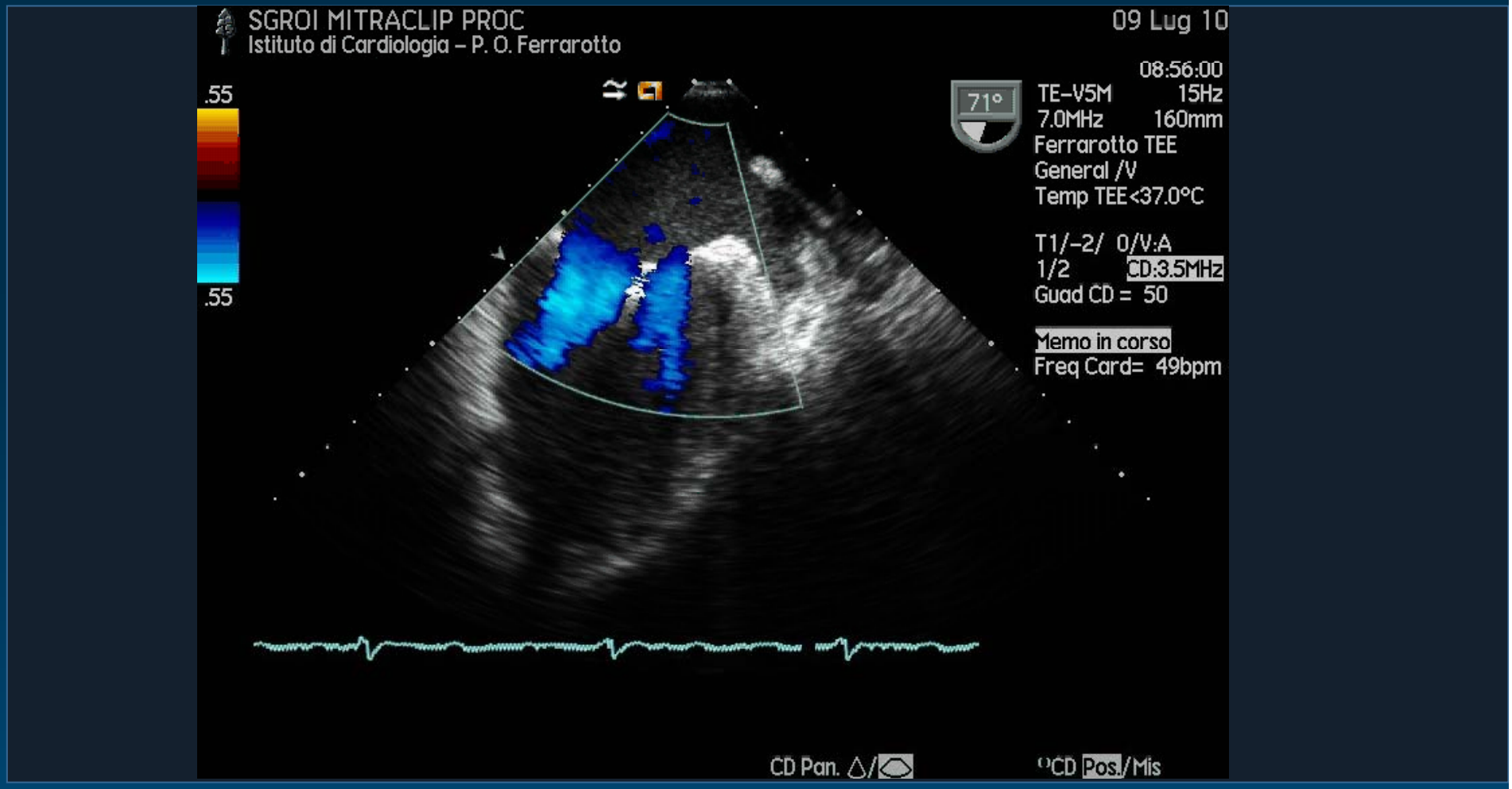



***Zoom on three views: 4C, 2 C, LVOT***

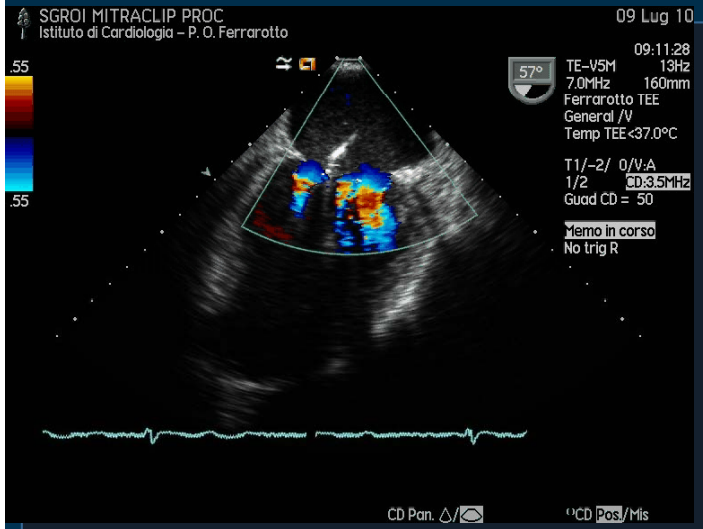
# Procedure

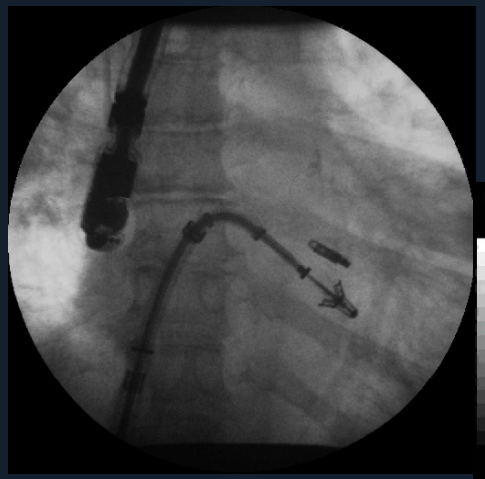
## *One Clip Deployment*

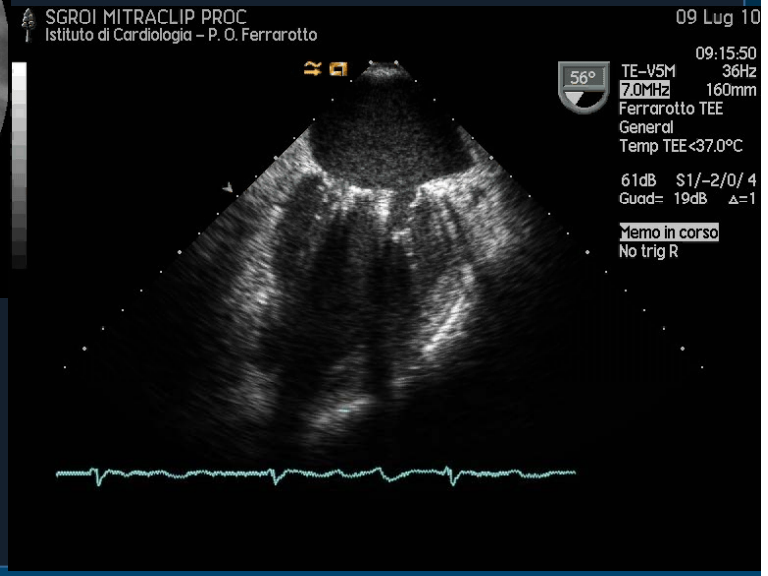


# Procedure

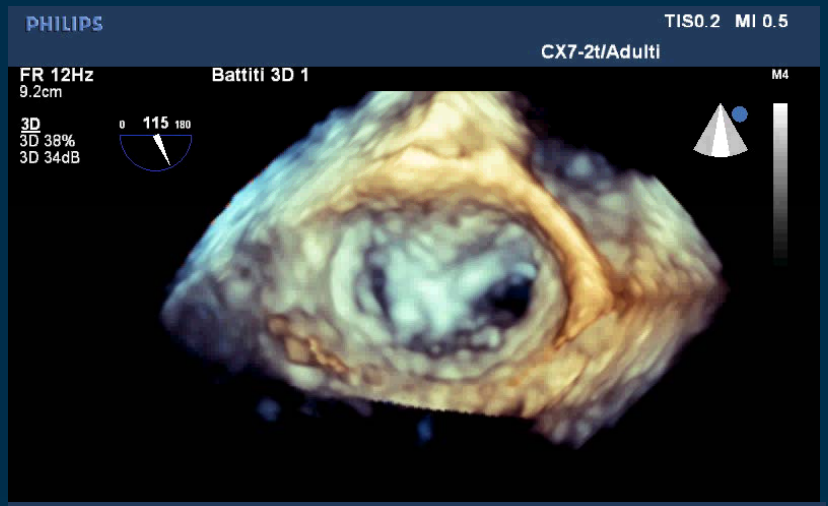
## *2nd Clip Deployment*

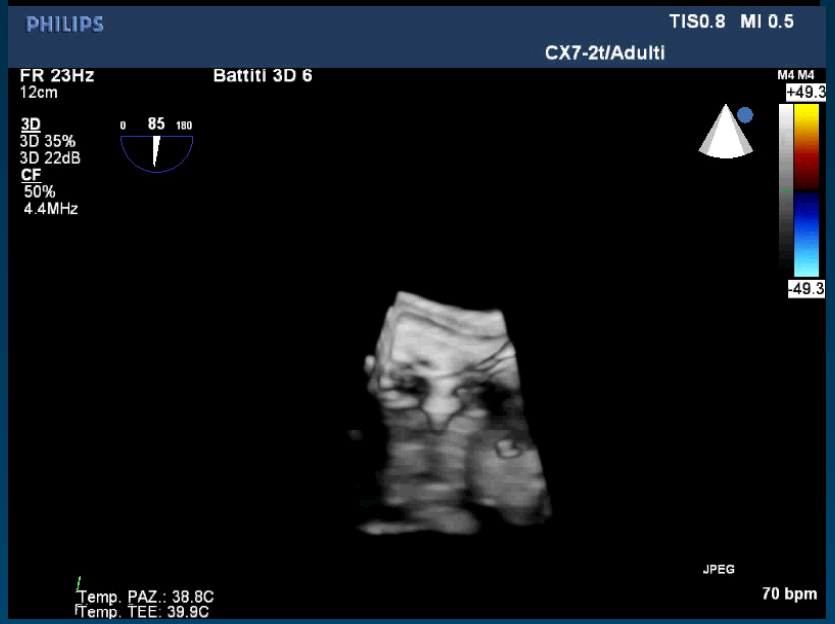


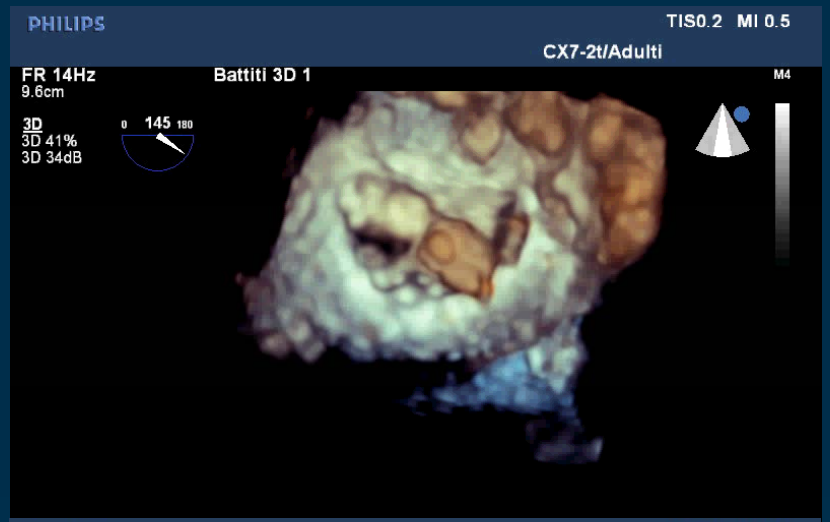



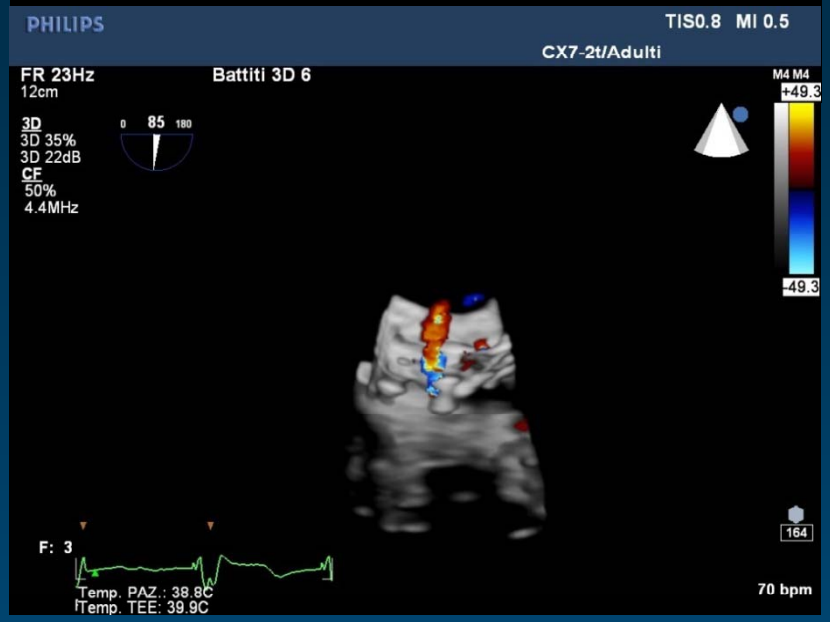


# *Final Result 3D-RT*

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The NEW ENGLAND JOURNAL of MEDICINE

# Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald G. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators*

# EVEREST II Randomized Clinical Trial

## *Study Design*

279 Patients enrolled at 37 sites

Significant MR (3+-4+)

Specific Anatomical Criteria

↓

Randomized 2:1

**Device Group**
***MitraClip System***
***N=184***

**Control Group**
***Surgical Repair or Replacement***
***N=95***

**Echocardiography Core Lab and Clinical Follow-Up**
***Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years***

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# EVEREST II Randomized Clinical Trial

## *Primary Endpoints*

### Safety (30 days)

- Major Adverse Event Rate at 30 days
- Per protocol cohort
- Superiority hypothesis

### Effectiveness (12 mos)

- Clinical Success Rate

***Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 months***

- Per protocol cohort
- Non-inferiority hypothesis

**Pre-specified MAEs**

Death
Major Stroke
Re-operation of Mitral Valve
Urgent / Emergent CV Surgery
Myocardial Infarction
Renal Failure
Deep Wound Infection
Ventilation >48 hrs
New Onset Permanent Atrial Fib
Septicemia
GI Complication Requiring Surg
All Transfusions ≥2 units (≥4)

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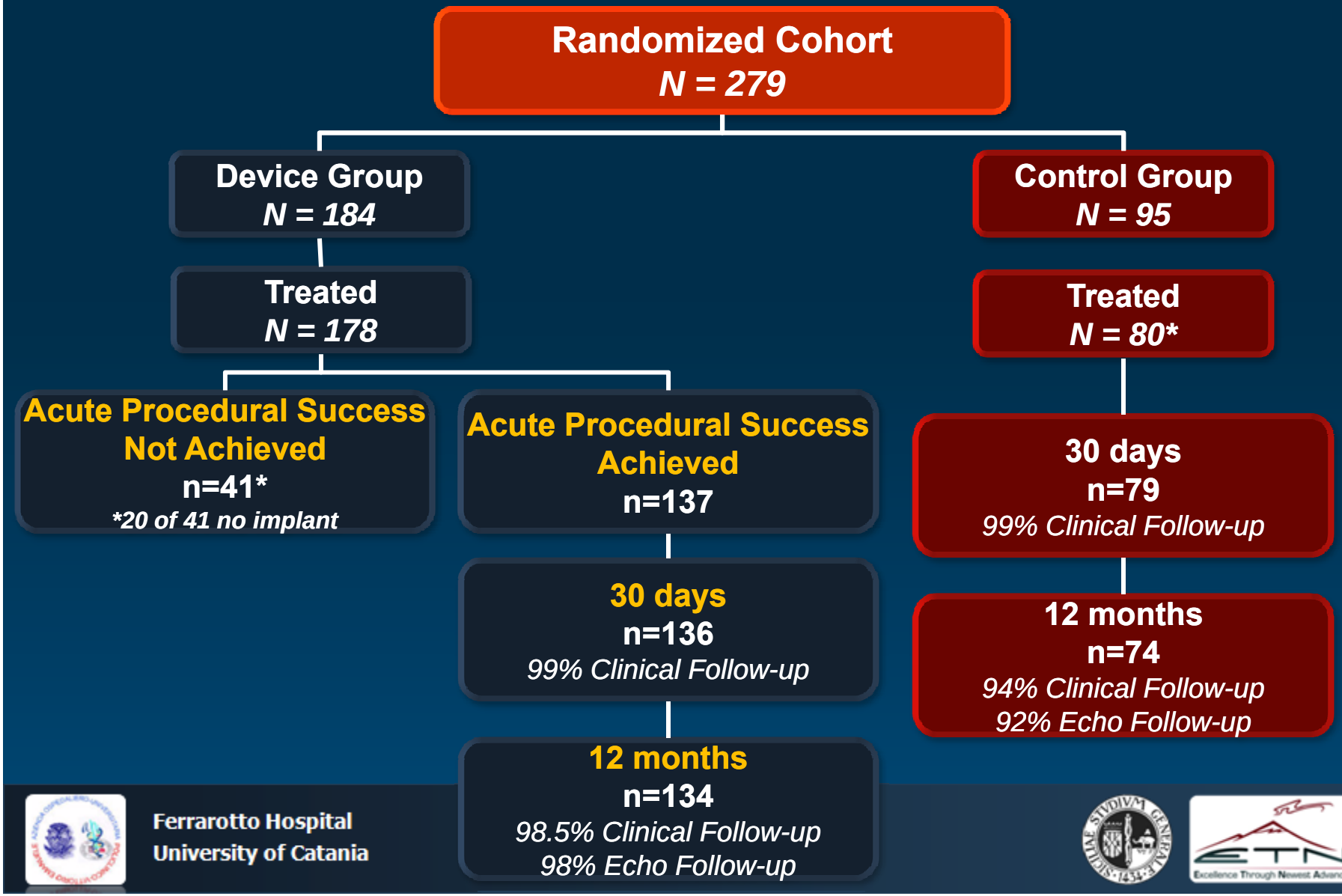
EVEREST II PP definition: Pts assigned to the MitraClip in whom acute procedural success was achieved, and those assigned to surgery in whom surgery was performed

# EVEREST II Randomized Clinical Trial

## *Patient flow*

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# EVEREST II RCT: Primary Safety Endpoint

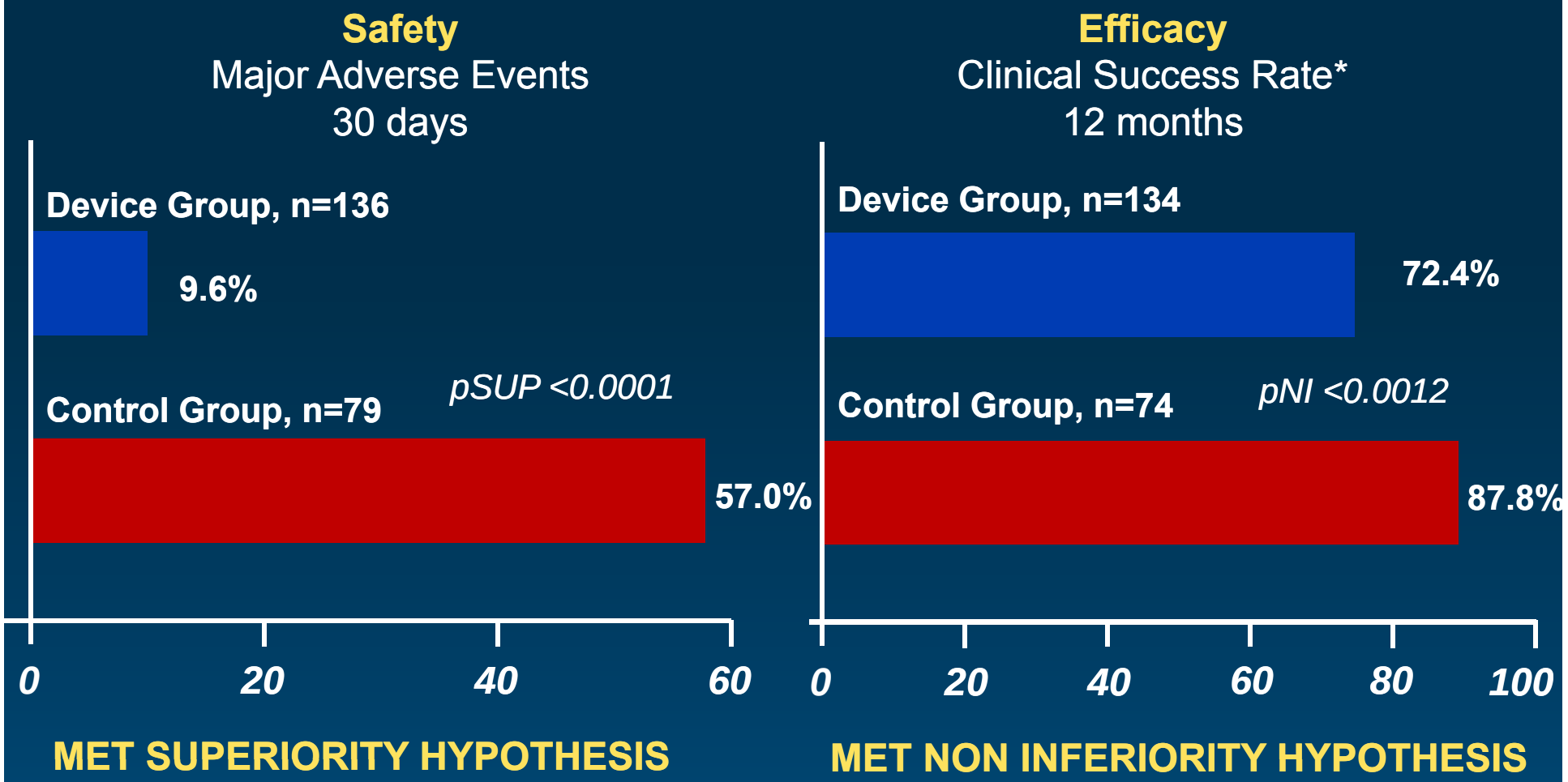
## Per Protocol Cohort

| 30 Day MAE, non-hierarchical | # Patients experiencing event<br>Device Group (n=136) | <br>Control Group (n=95) |
|---|---|---|
| Death | 0 | 2 (2.1%) |
| Major Stroke | 0 | 2 (2.1%) |
| Re-operation of Mitral Valve | 0 | 1 (1.1%) |
| Urgent / Emergent CV Surgery | 0 | 4 (4.3%) |
| Myocardial Infarction | 0 | 0 |
| Renal Failure | 0 | 0 |
| Deep Wound Infection | 0 | 0 |
| Ventilation >48 hrs | 0 | 4 (4.3%) |
| New Onset Permanent Atrial Fib | 0 | 0 |
| Septicemia | 0 | 0 |
| GI Complication Requiring Surgery | 1 (0.7%) | 0 |
| All Transfusions ≥2 units* | 12 (8.8%) | 37(39.4%) |
| **TOTAL % of Patients with MAE** | **9.6%** | **42.6%** |
| | pSUP<0.0001* | |
| | (95% CI 34.4%, 60.4%) | |

*p<0.0001 if include Major Bleeding only

# EVEREST II Randomized Clinical Trial

## *Per Protocol Cohort*

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**Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 months*

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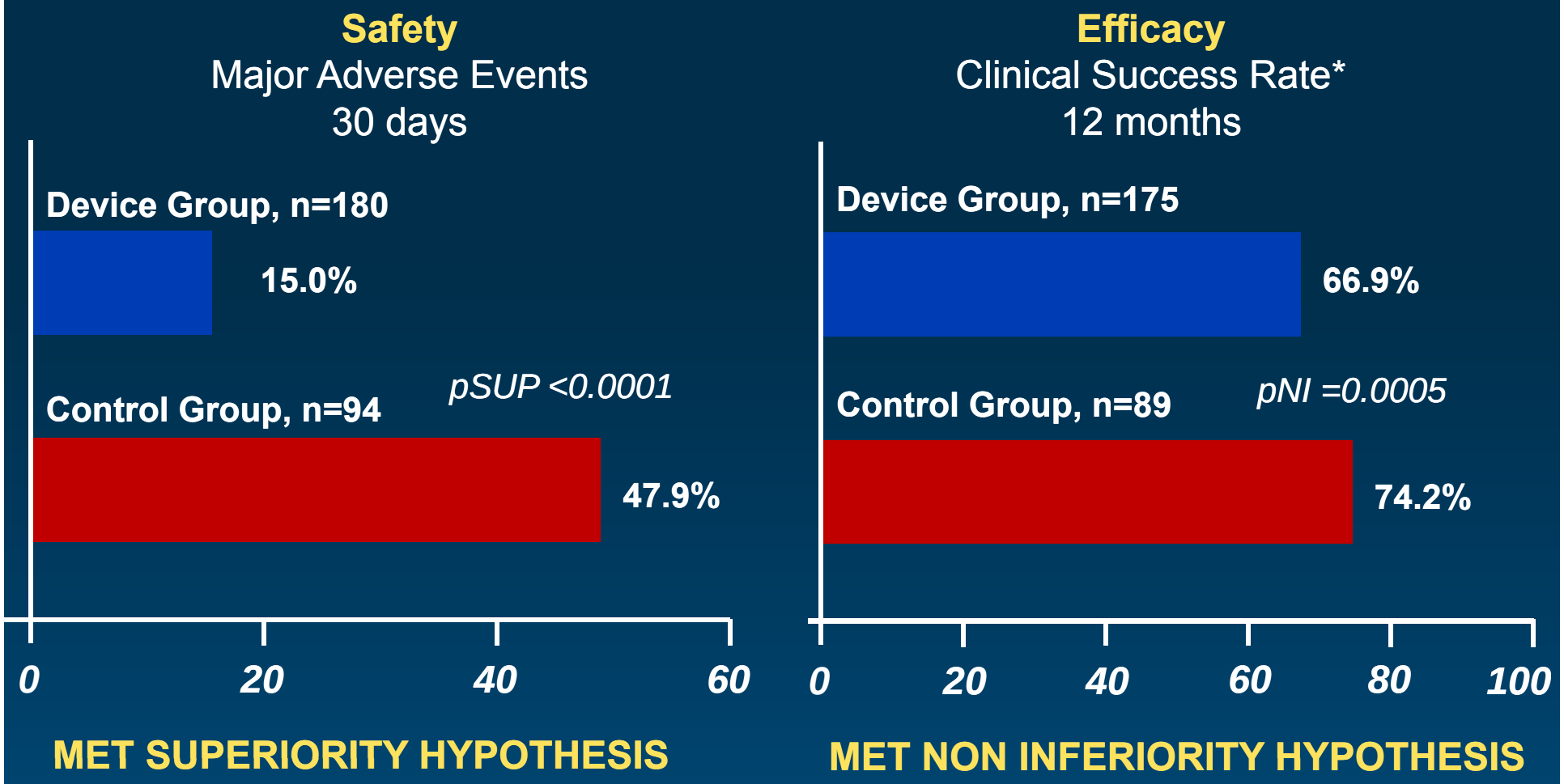
# EVEREST II Randomized Clinical Trial

## *Intention to Treat Cohort*

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**Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 months*

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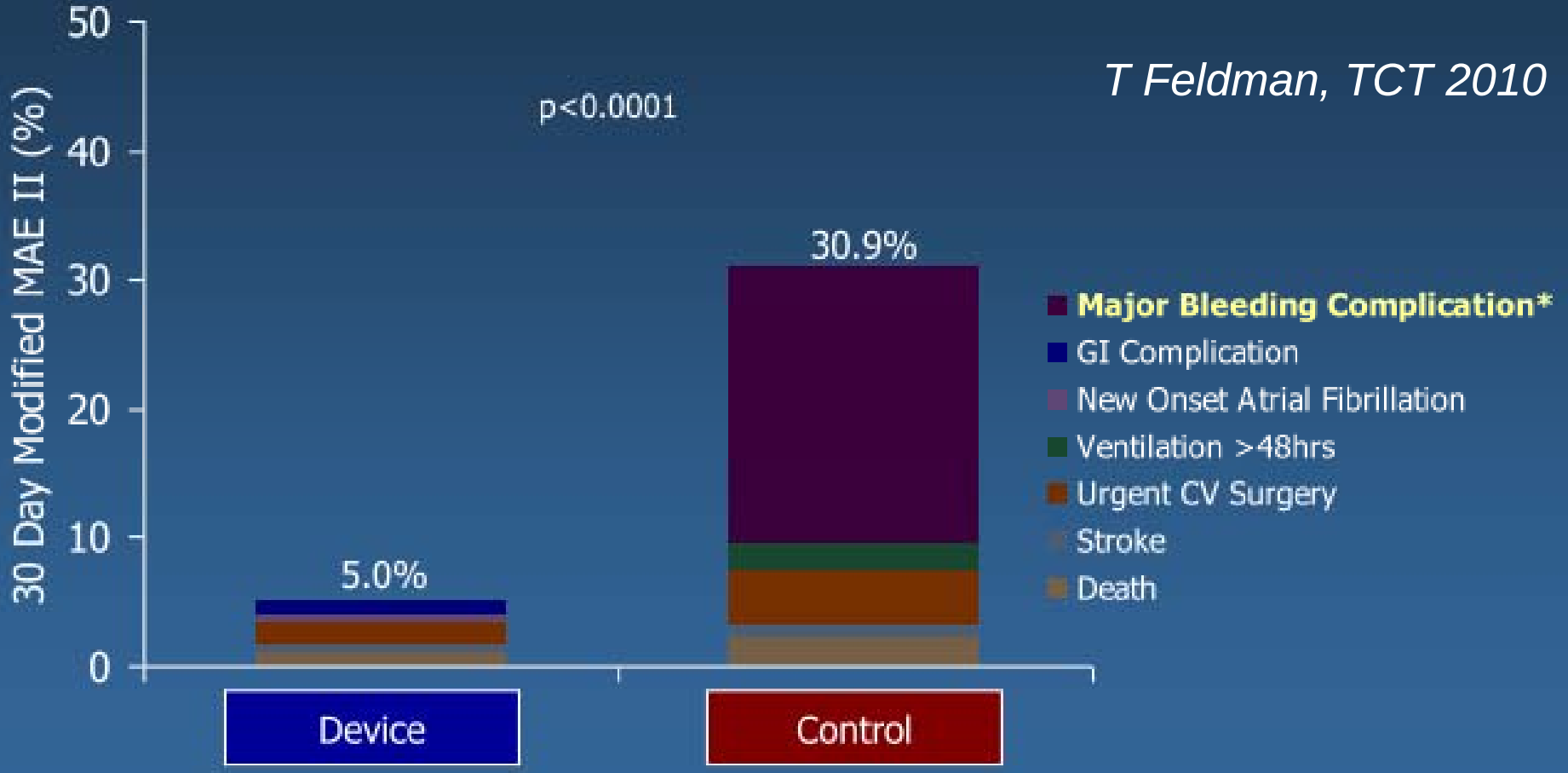
# 30 Day Modified MAE II*

## Intent to Treat, Hierarchical Events

*Safety endpoint met with a wide margin*

*T Feldman, TCT 2010*




*Major bleeding requiring transfusion ≥ **4U** or surgical intervention
Based on STS reporting of RBC transfusions

NorthShore University HealthSystem
Evanston Hospital

Investigational Device only in the US; Not available for sale in the US

# EVEREST II RCT: Primary Efficacy Endpoint

## Intention to Treat Cohort

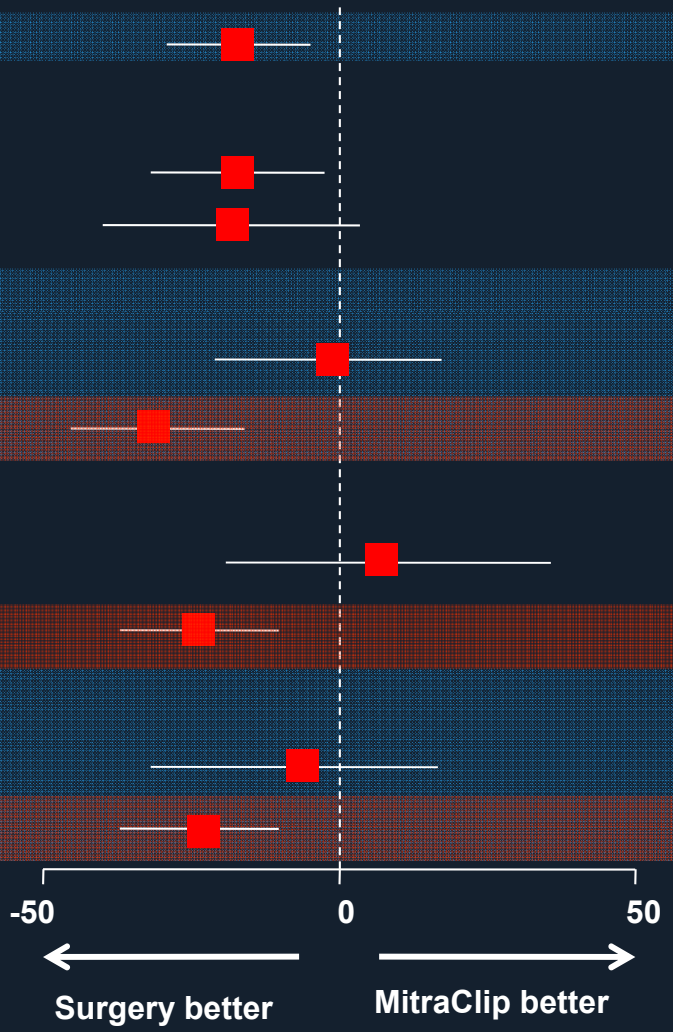
| 12-months MAEs | Device Group (n=180) | Control Group (n=94) | P value |
|---|---|---|---|
| Freedom from death, from surgery for mitral-valve dysfunction, and from grade 3+ or 4+ MR | 100 (55) | 65 (73) | 0.007 |
| Death | 11 (6) | 5 (6) | 1.00 |
| Surgery for mitral-valve dysfunction‡ | 37 (20) | 2 (2) | <0.001 |
| Grade 3+ or 4+ mitral regurgitation | 38 (21) | 18 (20) | 1.00 |

‡*This component is the rate of the first mitral-valve surgery in the percutaneous-repair group and the rate of reoperation for mitral-valve dysfunction in the surgery group.*



*Feldman et al. NEJM 2011*

| Subgroup | MitraClip | Surgery | P value for Interaction |
|---|---|---|---|
| | *no. of events/total no. (%)* | | |
| All patients | 100/181 (55) | 65/89 (73) | |
| Sex | | | 0.97 |
| Male | 63/114 (55) | 43/59 (73) | |
| Female | 37/67 (55) | 22/30 (73) | |
| Age | | | 0.009 |
| ≥70 yr | 52/86 (60) | 23/38 (61) | |
| <70 yr | 48/95 (51) | 42/51 (82) | |
| MR | | | 0.02 |
| Functional | 26/48 (54) | 12/24 (50) | |
| Degenerative | 74/133 (56) | 53/65 (82) | |
| LVEF | | | 0.06 |
| <60% | 35/68 (51) | 15/28 (54) | |
| ≥60% | 64/111 (58) | 50/61 (82) | |

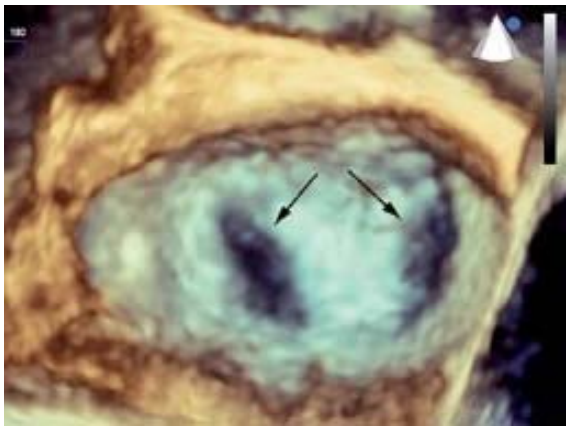



*Adapted from Feldman et al. NEJM 2011*

European Heart Journal
doi:10.1093/eurheartj/ehq051

CLINICAL RESEARCH

# Percutaneous mitral valve repair with the MitraClip system: acute results from a real world setting



**Corrado Tamburino[1,2]*, Gian Paolo Ussia[1], Francesco Maisano[3], Davide Capodanno[1,2], Giovanni La Canna[3], Salvatore Scandura[1], Antonio Colombo[3], Andrea Giacomini[3], Iassen Michev[3], Sarah Mangiafico[1], Valeria Cammalleri[1], Marco Barbanti[1], and Ottavio Alfieri[3]**

[1]Cardiology Department, Ferrarotto Hospital, University of Catania, Via Citelli 6, 95124 Catania, Italy; [2]ETNA Foundation, Catania, Italy; and [3]San Raffaele Hospital, Milan, Italy

***Italian Experience***

***Catania, Ferrarotto***

***Milano, S. Raffaele***

***n. 31 patients***

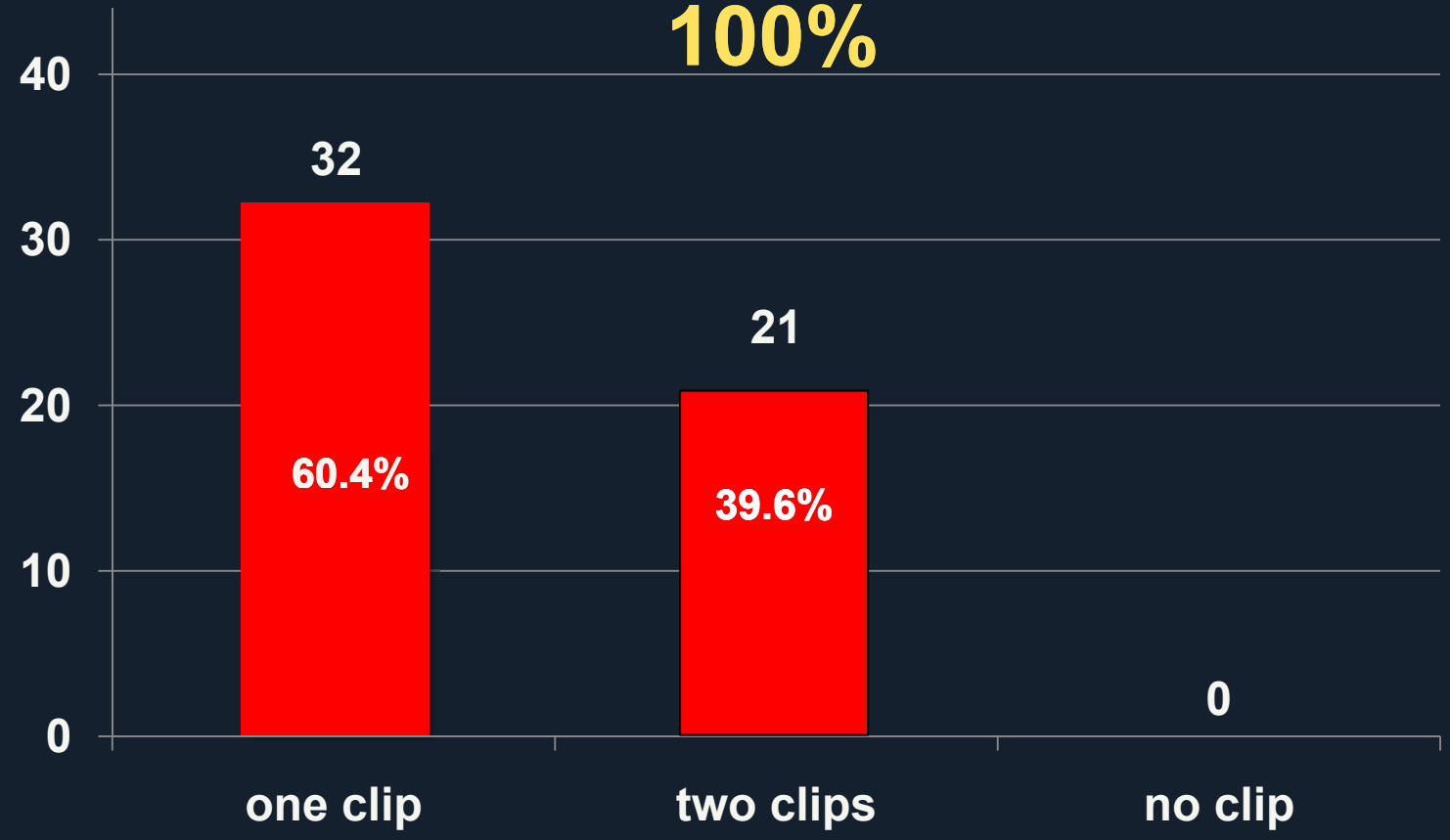
# Catania Experience
## *Clinical Characteristics*

| Patients (n=53) | N (%) |
|---|---|
| Male, n (%) | 41 (77) |
| Age, (mean±SD) | 72 ±11 |
| EuroSCORE (%) | 27 ± 6 |
| Chronic Renal Insufficiency, n (%) | 17 (32) |
| Chronic Pulmonary Disease, n (%) | 19 (36) |
| History of coronary artery disease, n (%) | 26 (46) |
| Solid cancer, n(%) | 6 (11) |
| Multiple sclerosis, n (%) | 1 (2) |
| Systemic lupus erythematosus, n (%) | 1 (2) |
| Liver cirrhosis, n (%) | 2 (4) |
| Previous cardiac surgery, n (%) | 13 (24) |
| Previous TAVI, n (%) | 4 (7) |
| CRT, n (%) | 5 (9) |

# Catania Experience

*Procedural Data*

## Procedural Success 100%

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# Catania Experience

## *Hemodynamic Assessment*

| | Baseline | Post procedure | p value |
|---|---|---|---|
| sPAP (mmHg) | 42 ± 15 | 34 ± 9 | 0.003 |
| mPAP (mmHg) | 24 ±10 | 20 ± 4 | 0.010 |
| WP (mmHg) | 17± 8 | 12 ± 4 | 0.003 |
| CO (l/min) | 4,3 ±2 | 5,4 ± 2 | 0.010 |
| SAPs (mmHg) | 106 ± 19 | 113 ±13 | 0.040 |
| SatO2 PA (%) | 71 ±10 | 77± 9 | 0.003 |

# Catania Experience

## *In hospital Adverse Events at FU*

| | |
|---|---|
| **Death - Unrelated to Clip Device, n (%)** | **1 (1.8)*** |
| **Mechanical ventilation > 48 hours, n (%)** | **1 (1.8)** |
| **Bleeding requiring transfusion ≥ 2 units (procedural) , n (%)** | **0** |
| **Bleeding requiring transfusion ≥ 2 units (in hospital) , n (%)** | **2 (3.7)** |
| **Conversion to surgery, n (%)** | **0** |
| **Transseptal complications, n (%)** | **0** |
| **Renal failure or dialysis (new onset), n (%)** | **0** |
| **Length of hospital stay (mean days ± 2) , n (%)** | **5.6 ± 2.8** |
| **Myocardial infartion, n (%)** | **0** |
| **Stroke, n (%)** | **0** |
| **Clip detachment,/embolization, n(%)** | **0** |

*One patient, a 76-year-old man with thrombocytopenia and renal failure on haemodialysis, died 2 weeks after the procedure from gastrointestinal bleeding

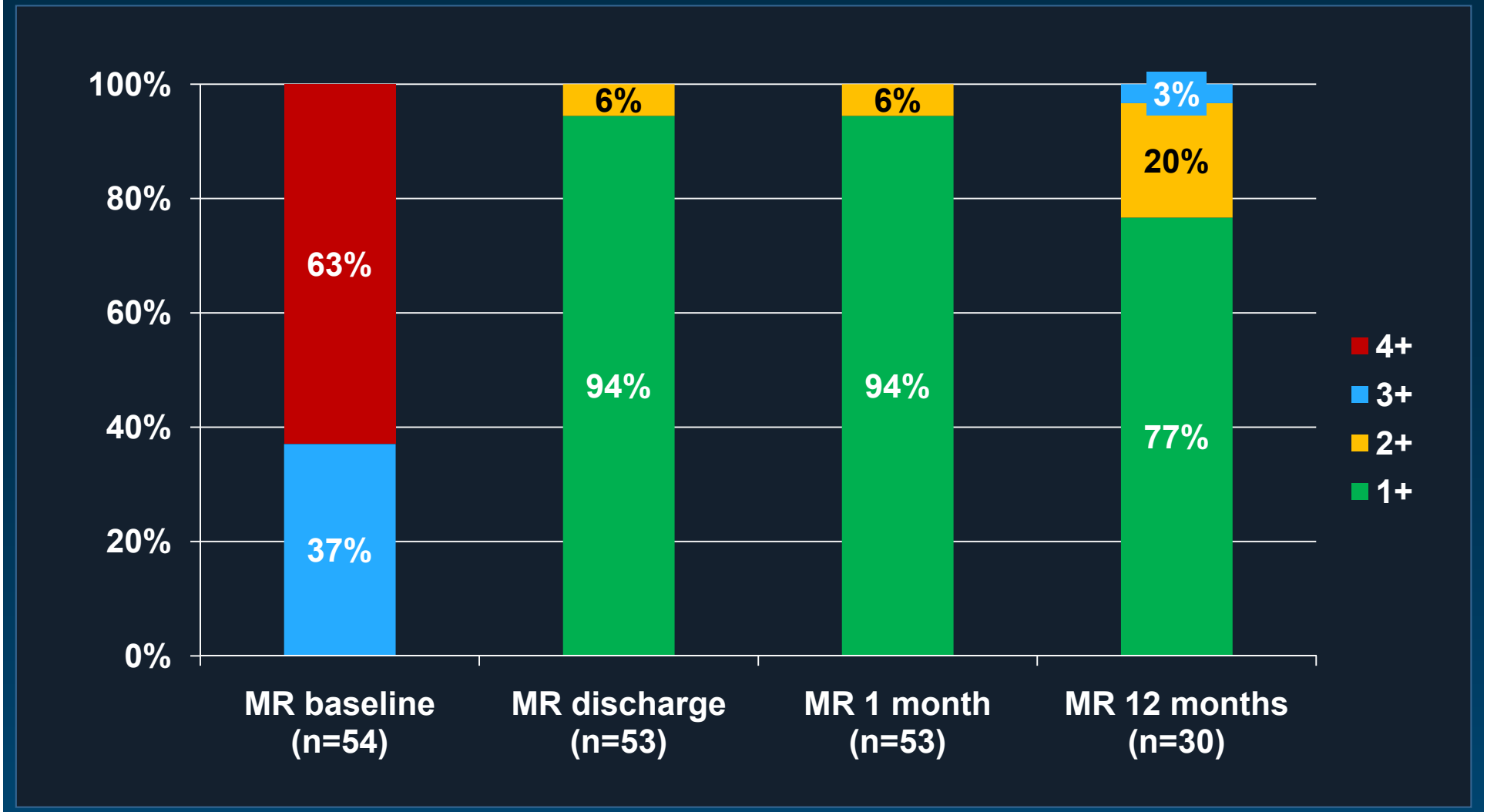
# Catania Experience

## *Causes of death at FU*

| Pt | Gender | Age | Log EuroSCORE | Other risk factors | MR etiology | Basal LVEF (%) | Cause | Month FU |
|---|---|---|---|---|---|---|---|---|
| # 1 | Female | 67 | 3,5 | hepatic cirrhosis child C; thrombocytopenia | DMR | 58 | Liver failure | 3 |
| # 2 | Male | 76 | 31,9 | renal failure on haemodialysis; thrombocytopenia | FMR | 30 | GI bleeding | 1 |
| # 3 | Male | 79 | 8,7 | // | DMR | 60 | Acute Leukemia | 3 |
| # 4 | Male | 58 | 6,9 | Colon Cancer; severe impairment | FMR | 18 | Heart Failure | 4 |
| # 5 | Male | 85 | 11,6 | // | FMR | 50 | Broncho-pneumonia complicated by septicemia | 3 |
| #6 | Male | 83 | 16.5 | Prior Colon Cancer | FMR | 35 | GI bleeding | 18 |

# Catania Experience

## *MR Reduction at FU*

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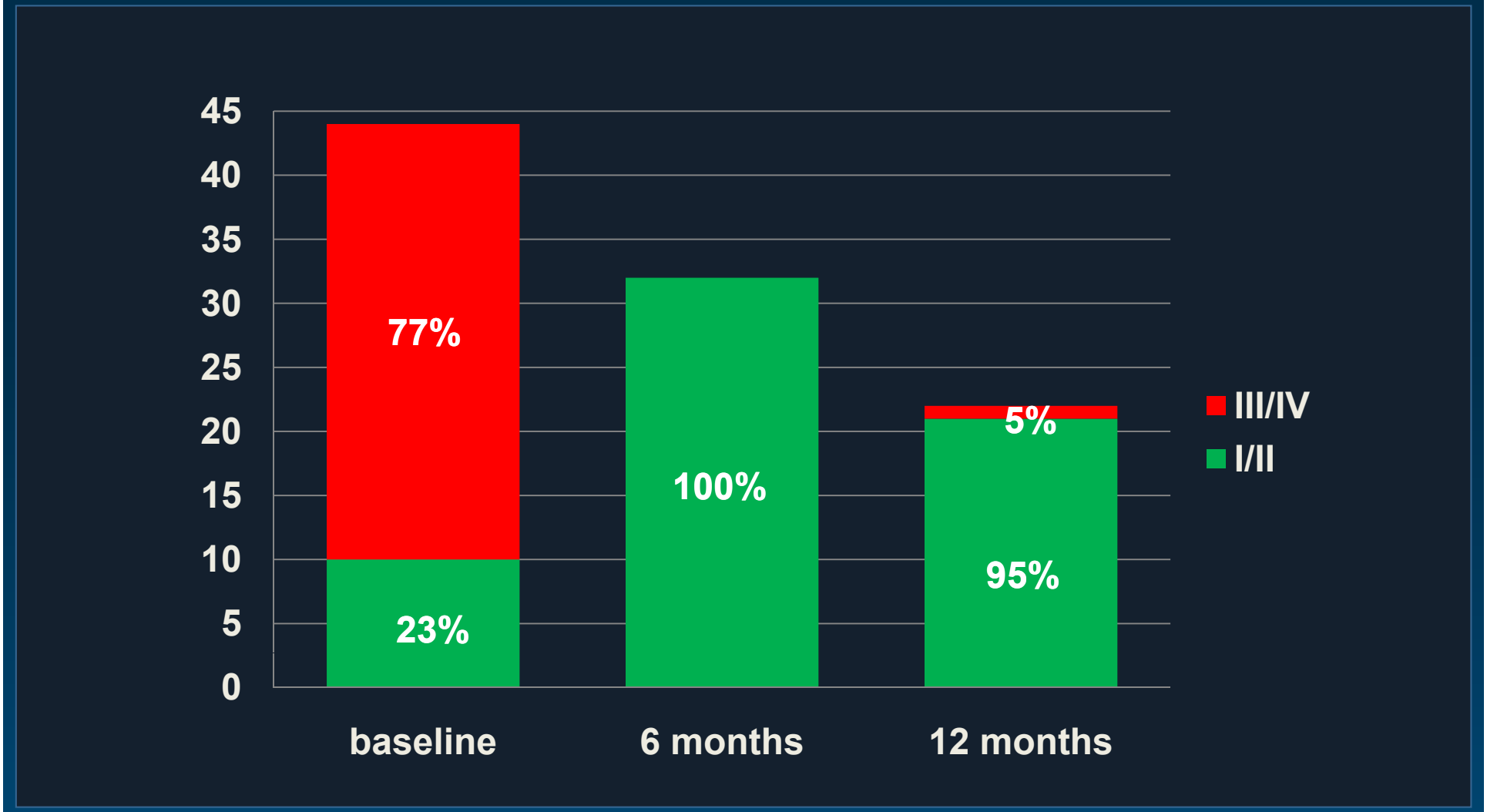
# Catania Experience

## *NYHA Functional Class at FU*

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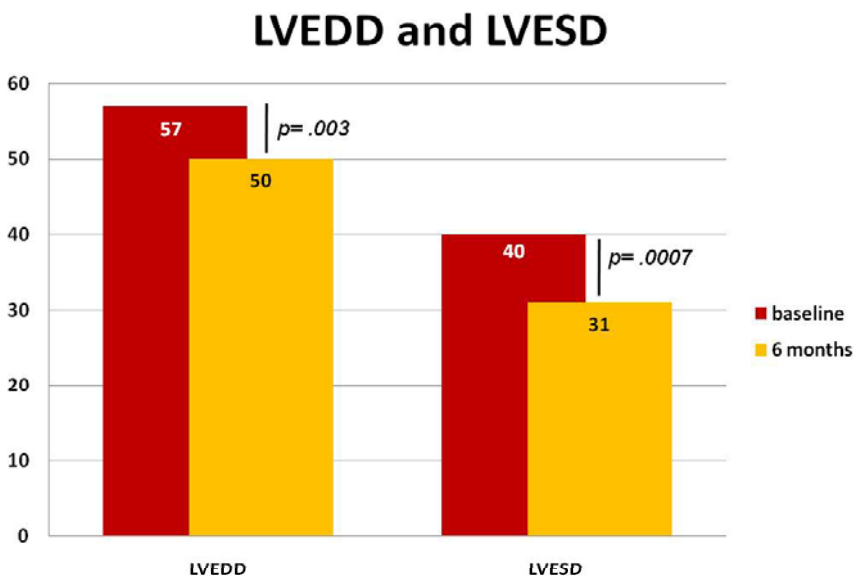
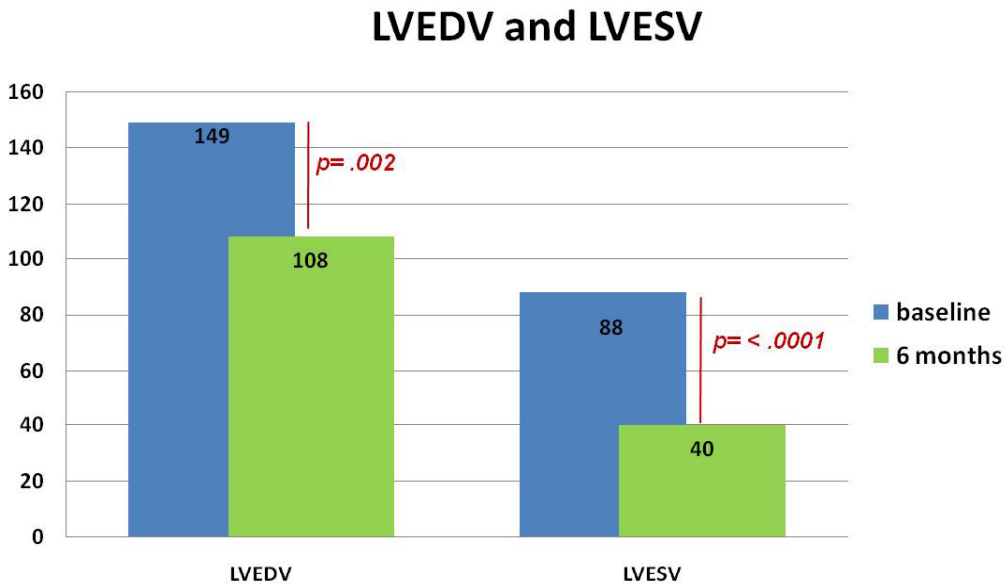
# Catania Experience

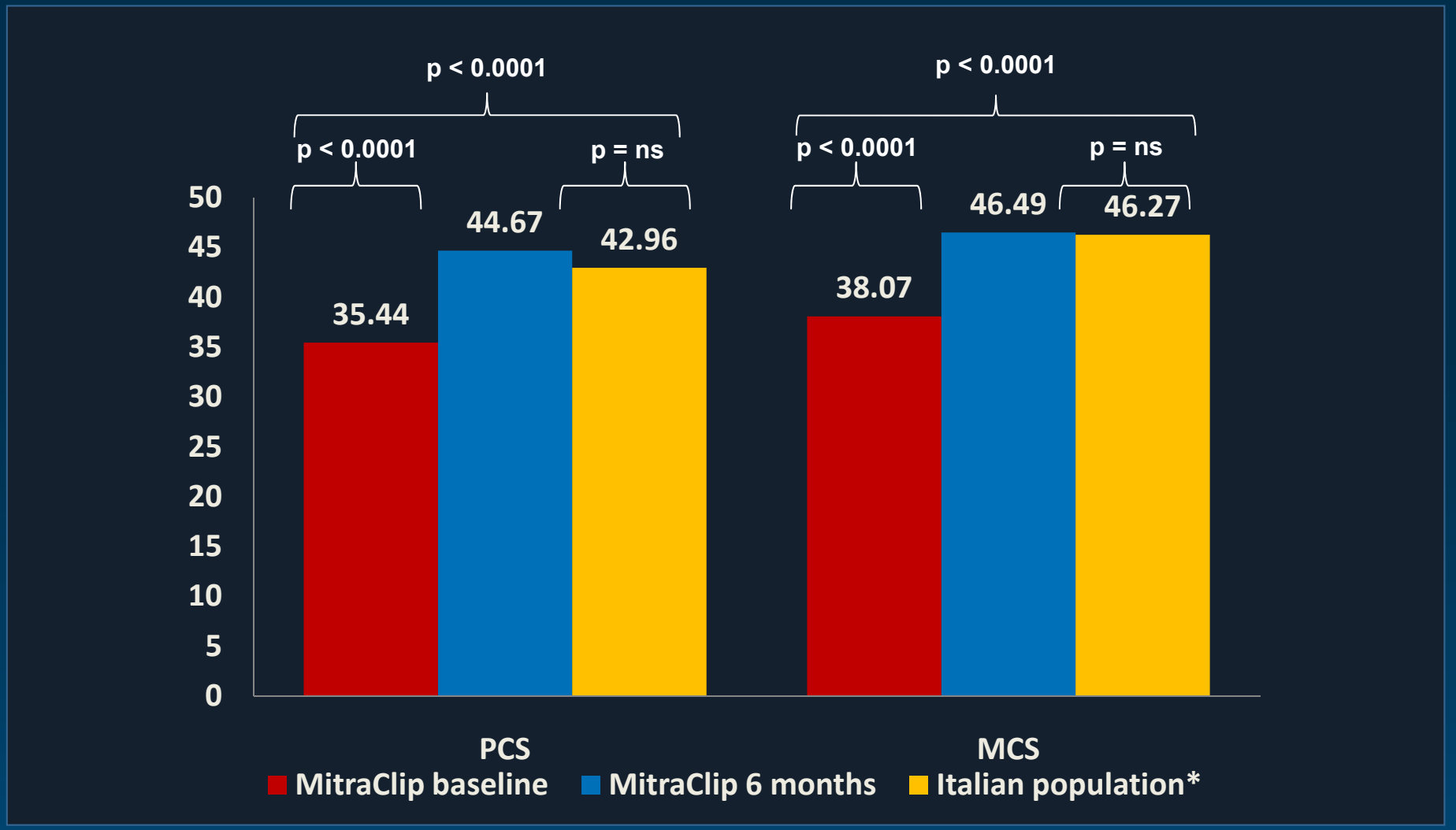
## *Left Ventricle Remodeling*



# Catania Experience

## *QoL assessment*




Ferrarotto Hospital
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# Conclusions

*Limitations of Registry data…*

- **Selection bias – treatment centers, patients, access sites, and devices**
- **Reporting bias – largely site/physician reported**
- **Lack of consistency in endpoint definitions**
- **No core laboratories (esp. echo)**
- **No clinical events committees for outcome adjudication**

# Conclusions

*Limitations of EVEREST II Trial…*

- **Sample size, powered for DMR and FMR?**
- **Degenerative and functional MR are 2 different diseases, with different pathophysiologies and control treatments. Ideally the trial would have included only one MR etiology, or have been powered for each.**
- **Much more…**

# Conclusions

- ***MitraClip System has good procedural and short term results***
- ***The learning curve is steep***
- ***The "real world" is expanding the use in FMR***
- ***The procedure is safe also in HR pts and with low LVEF***
- ***Indication for MVR by percutaneous clip implantation is currently undefined and needs to be proven by further specifically designed randomized trials***