Mitraclip - How Do We Best Measure Residual MR Post Procedure?

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Disclosure

- Consultant and proctor to Edwards, Boston, St Jude.
- Clinical trial arrangements with Edwards, Boston, St Jude, Abbott, Symentis, Medtronic.

EVEREST II Randomized Clinical Trial:

Clinical Benefit by MR Grade in Patients One Year Following Successful MitraClip Therapy

On behalf of the EVEREST II Investigators

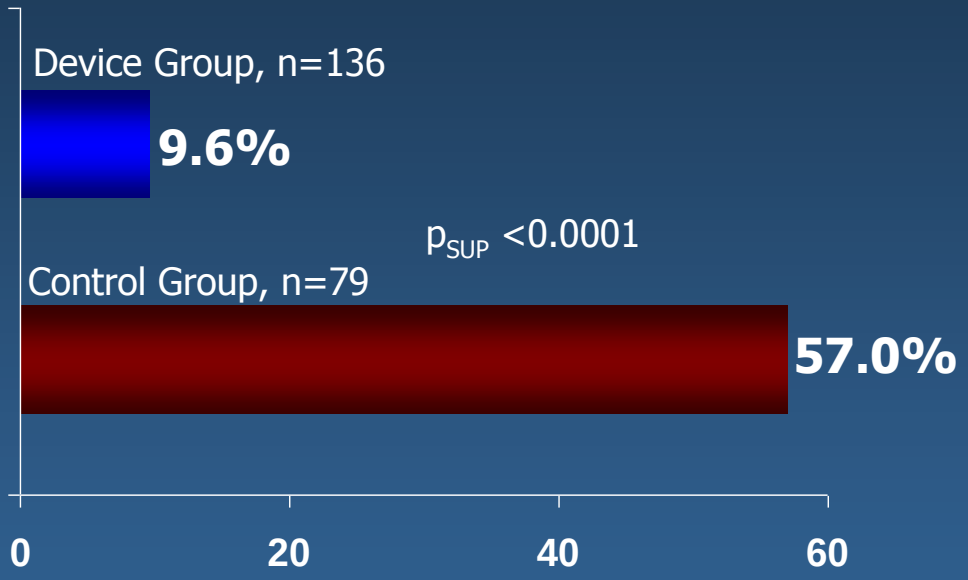
EVEREST II RCT: Primary Endpoints

Per Protocol Cohort

Safety

Major Adverse Events

30 days



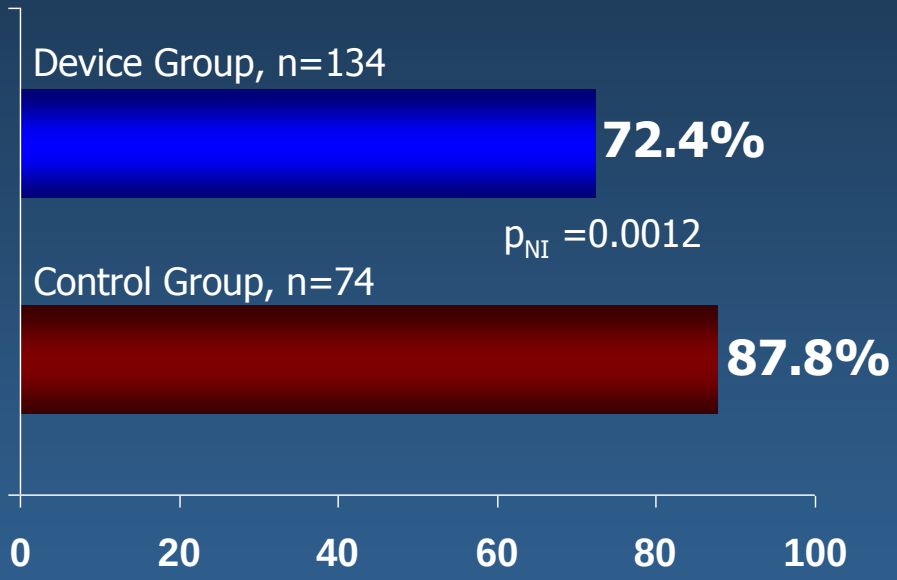
Met superiority hypothesis

- Pre-specified margin = 6%
- Observed difference = **47.4%**
- 97.5% LCB = 34.4%

Effectiveness

Clinical Success Rate*

12 months



Met non-inferiority hypothesis

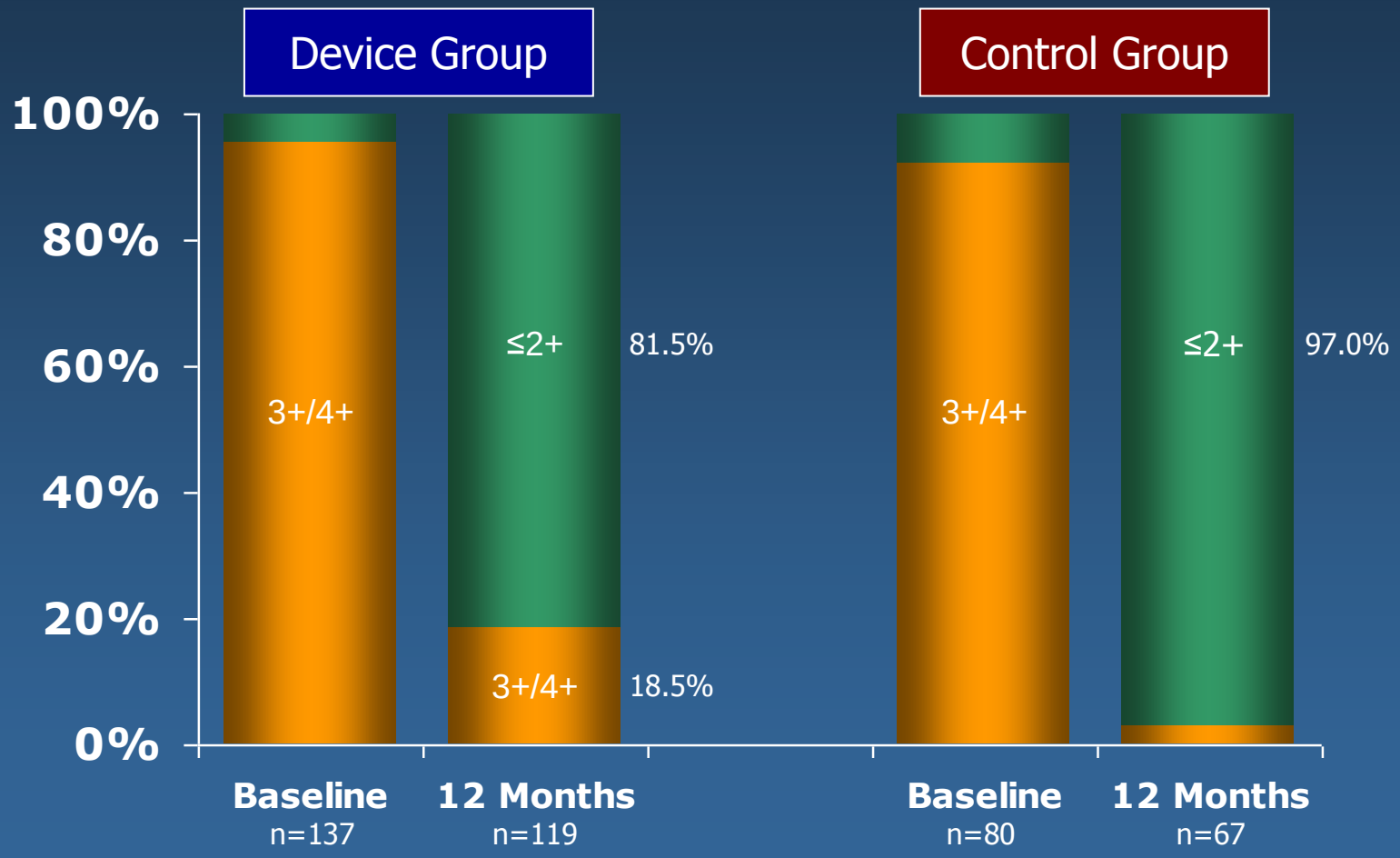
- Pre-specified margin = 31%
- Observed difference = **15.4%**
- 95% UCB = 25.4%

LCB = lower confidence bound
UCB = upper confidence bound

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

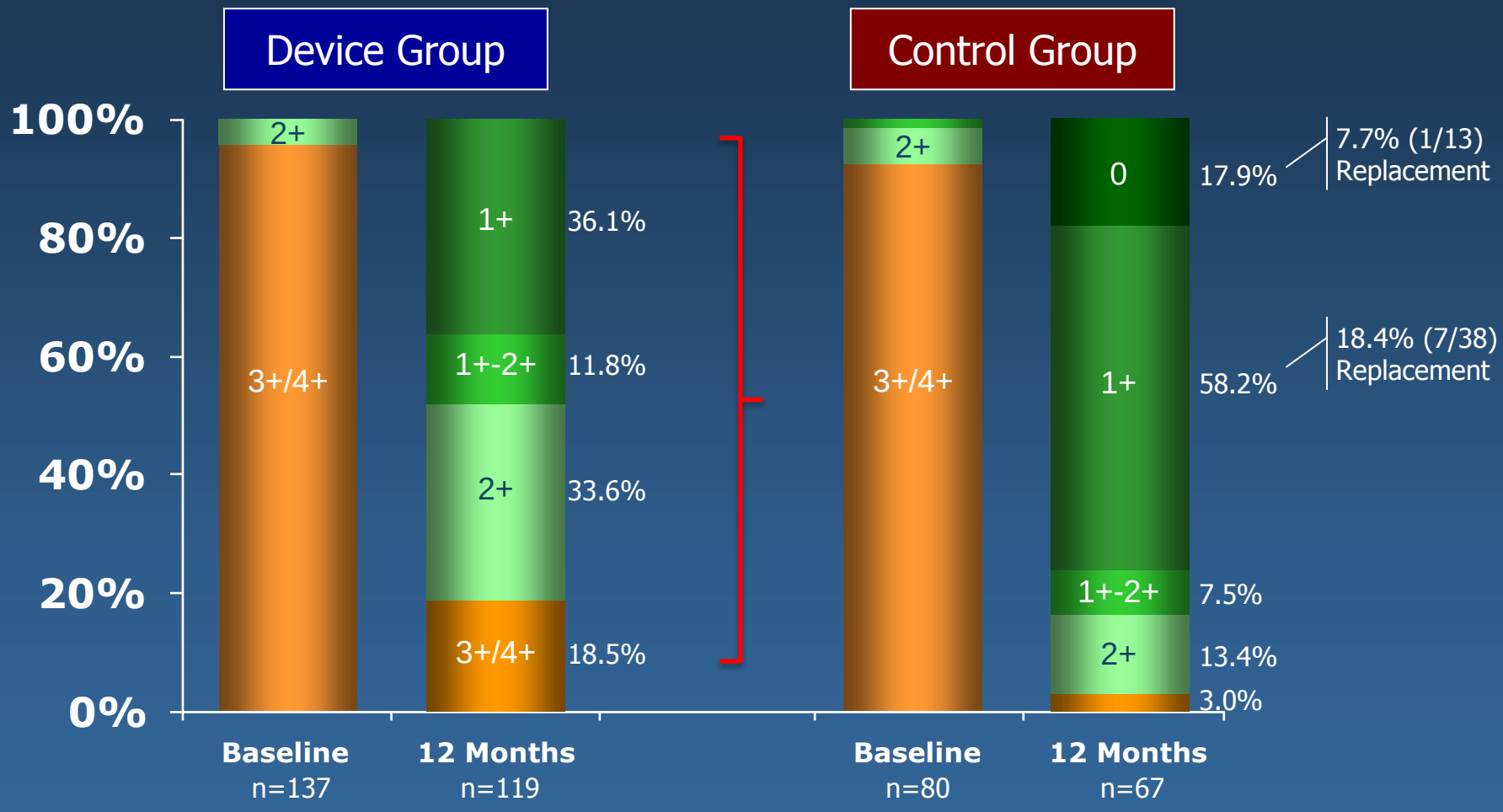
EVEREST II RCT: MR Reduction

Per Protocol Cohort



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

EVEREST II RCT: MR Reduction
Per Protocol Cohort



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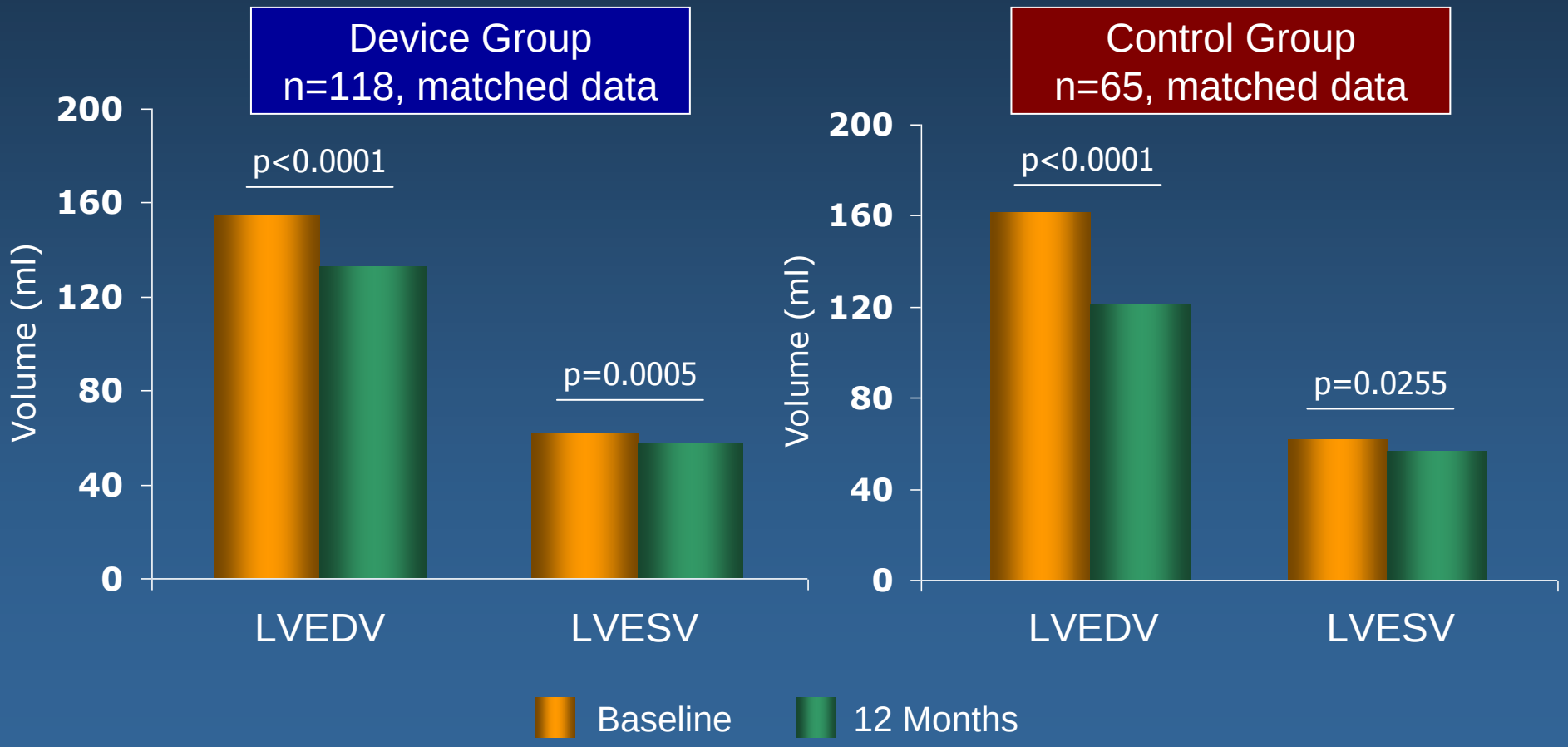
EVEREST II RCT: Left Ventricular Volume

Per Protocol Cohort



LVEDV = left ventricular end diastolic volume
LVESV = left ventricular end systolic volume

Pre-specified hypothesis for statistical analysis

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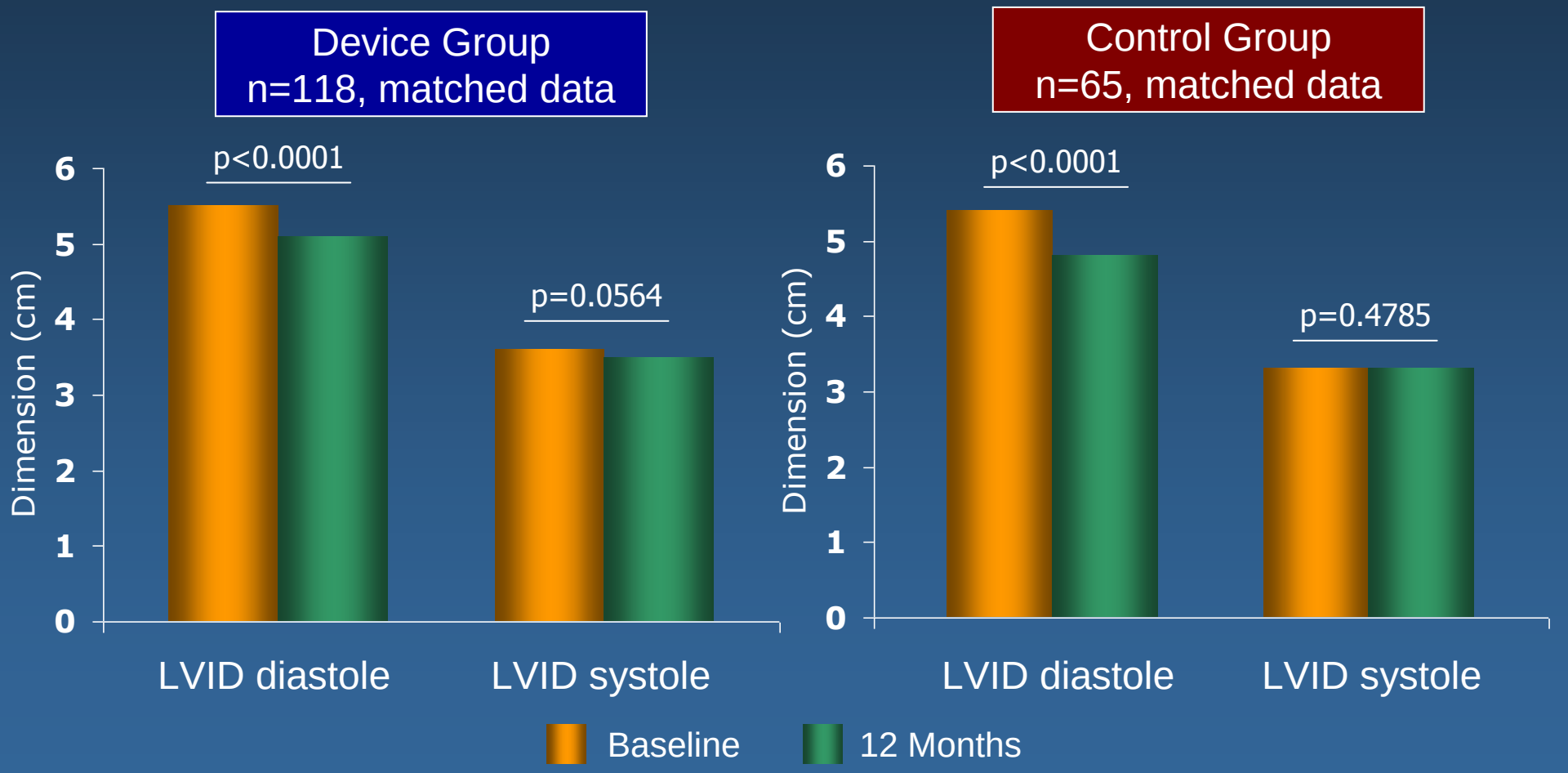
EVEREST II RCT: Left Ventricular Dimension

Per Protocol Cohort



LVIDd = left ventricular internal diameter, diastole
LVIDs = left ventricular internal diameter, systole

Pre-specified hypothesis for statistical analysis

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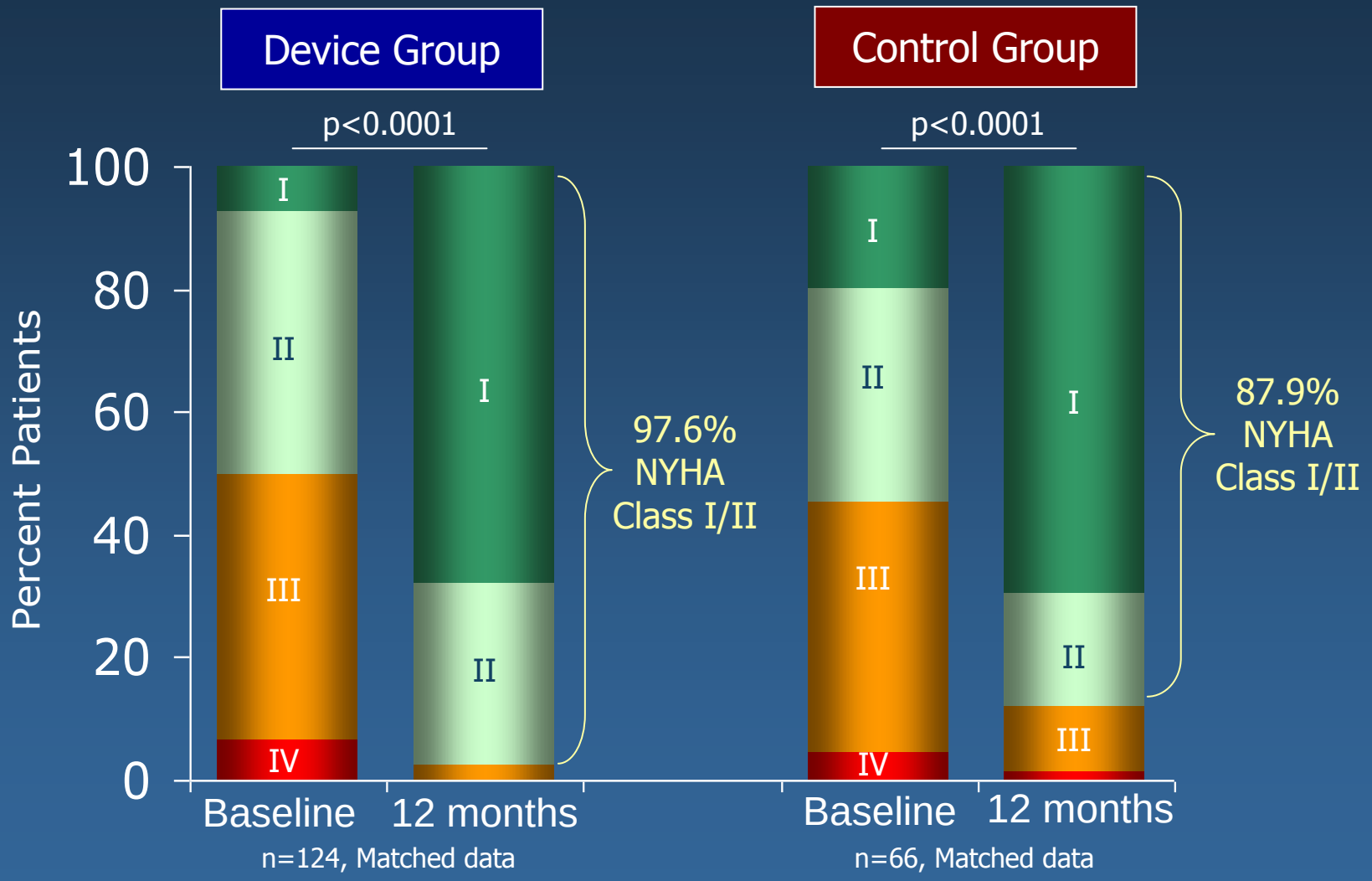
EVEREST II RCT: NYHA Functional Class

Per Protocol Cohort



Hypothesis not pre-specified for statistical analysis

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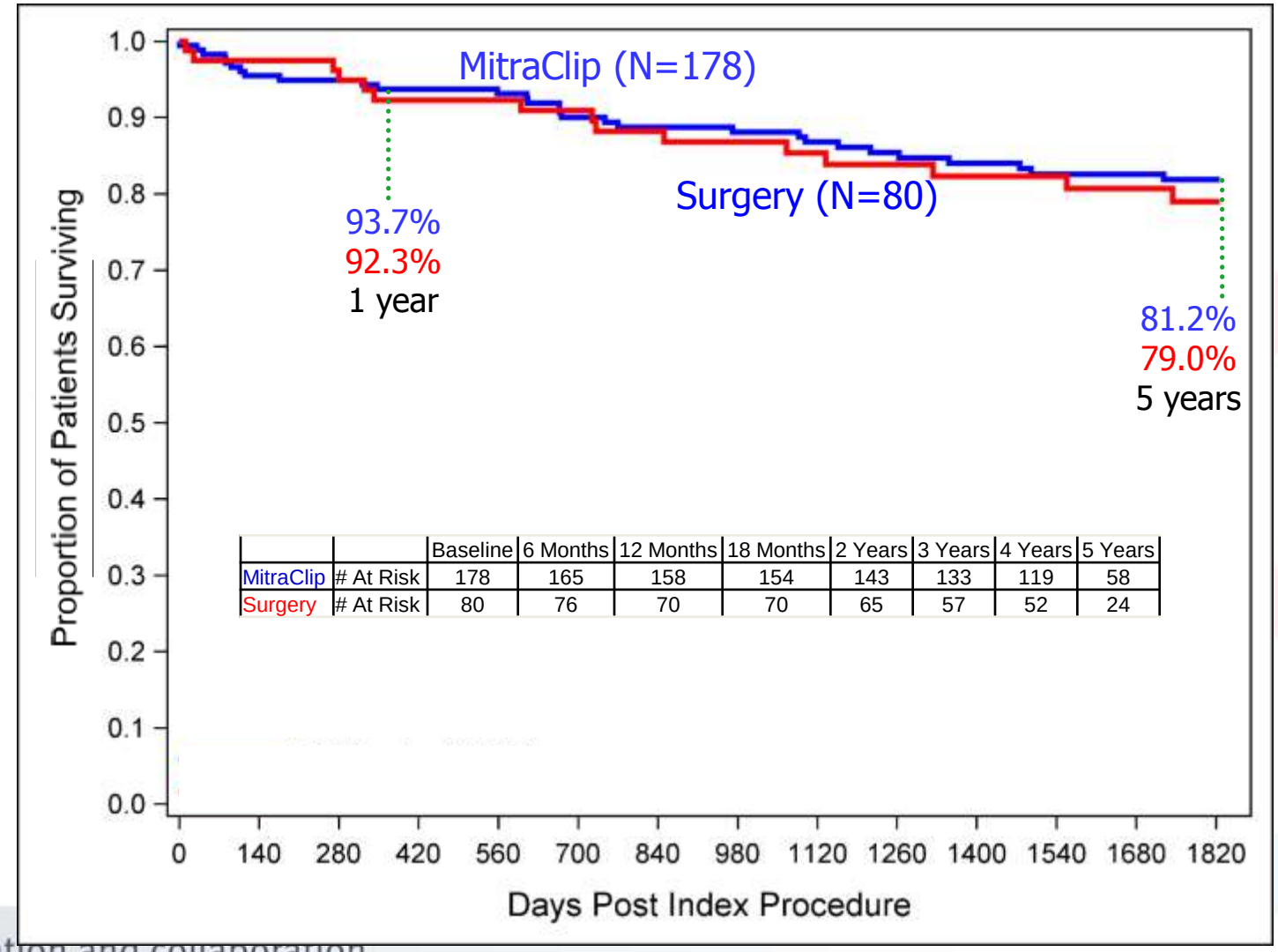
Kaplan-Meier Freedom From Mortality

EVEREST II RCT



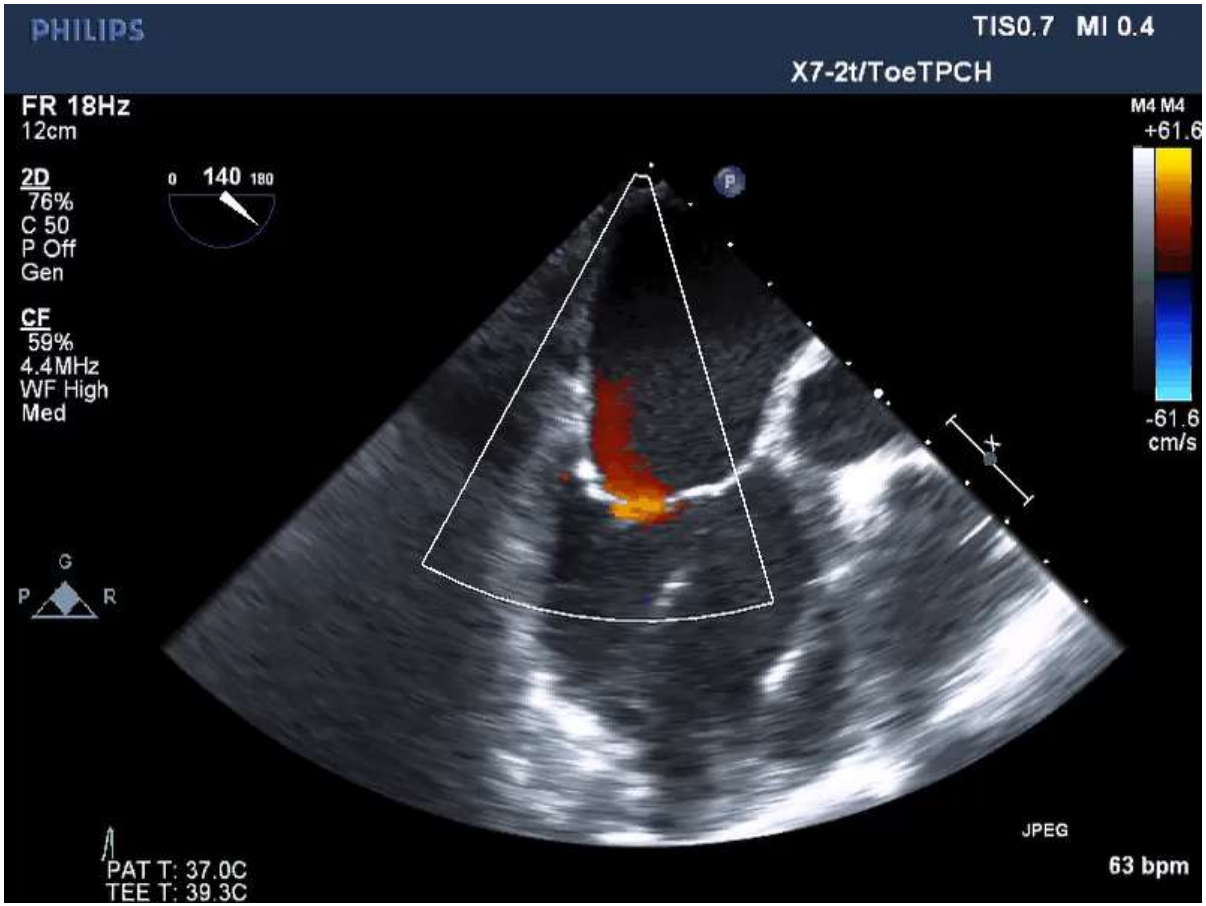
		Baseline	6 Months	12 Months	18 Months	2 Years	3 Years	4 Years	5 Years
MitraClip	# At Risk	178	165	158	154	143	133	119	58
Surgery	# At Risk	80	76	70	70	65	57	52	24

Mitraclip

- Assessment of residual mitral regurgitation is a key outcome measure for mitral valve repair
- Clinical parameters are more favourable than the residual mitral regurgitation would suggest

Are we confident in the quantification residual Mitral regurgitation post intervention?

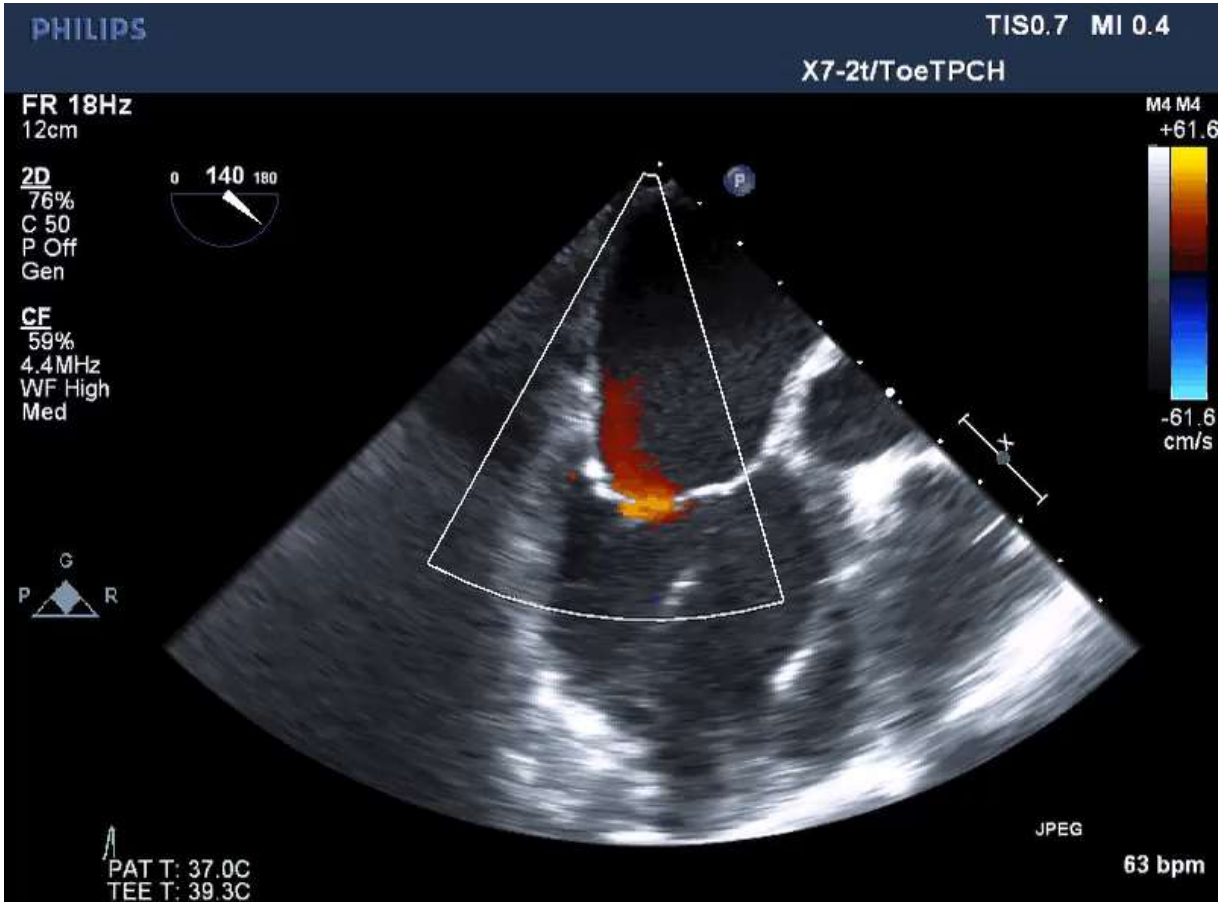
How do we assess mitral regurgitation?



American Society Echo assessment of Mitral Regurgitation

Parameter	Mild	Mod	Mod-Sev	Severe
JetArea / LA (%)	<15	15-35	35-55	≥ 55
ROA (cm2)	<0.20	0.20-0.29	0.30-0.39	≥ 0.40
PW-PulmVeinRevers	S>D	S<D	S<<D,noS	SystRev
CW density	faint	<anteg.	<anteg.	=anteg.
Reg Volume (cc)	<30	30-44	45-59	≥60
Vena Contracta (cm)	<0.3	0.3-0.4	0.5-0.6	≥0.7

Frequently combination of visual assessment and ≥ 1 quantified measures



Edge-to-Edge & MitraClip Concepts

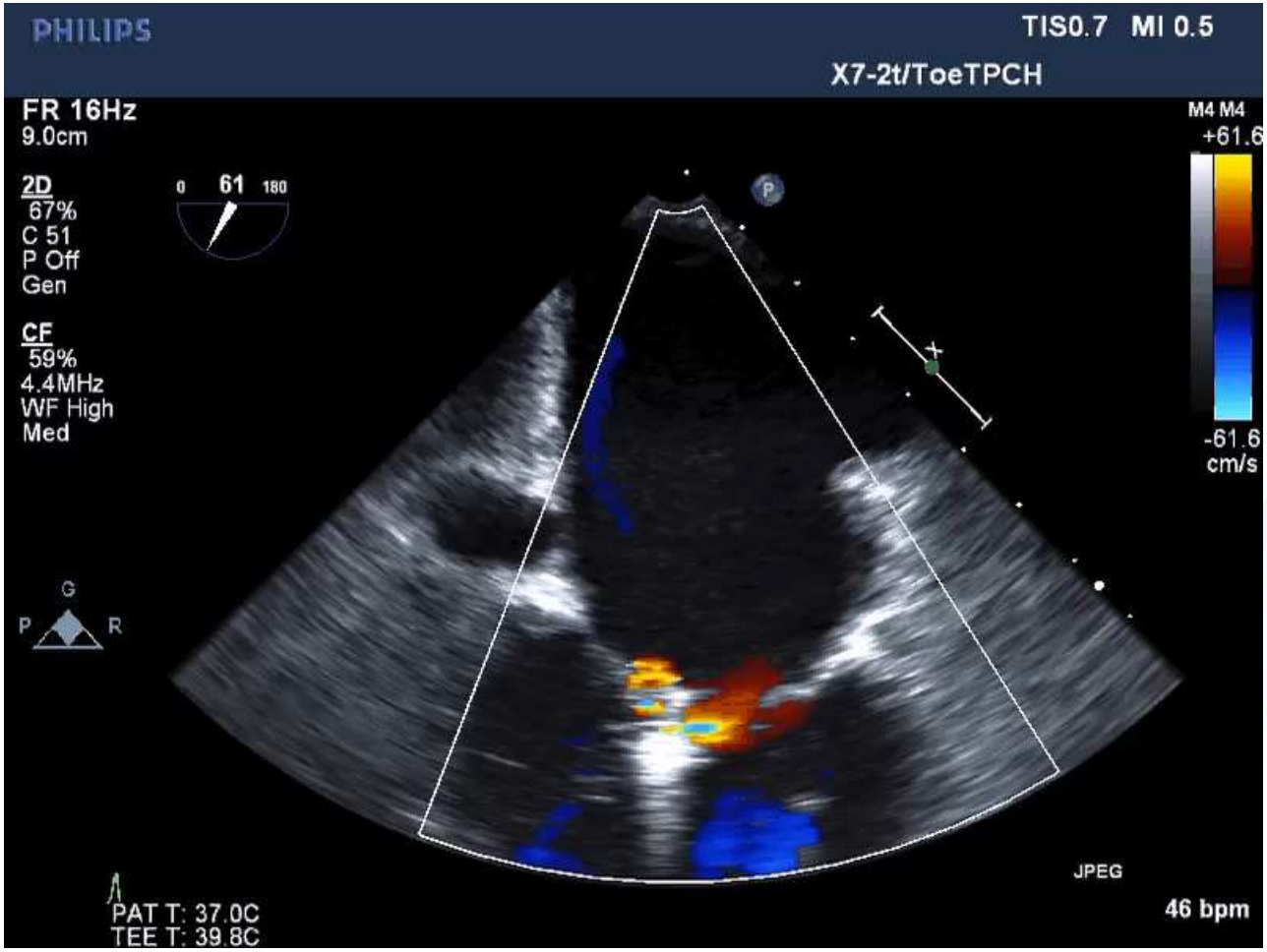
- Facilitates proper leaflet coaptation
  - Mechanical solution to a mechanical problem
  - Degenerative - Anchor flail and prolapsed leaflets (similar to chordal transfer/replacement)
  - Functional - Coapt tethered leaflets to reduce time and force required to close valve
  - Reduces LV volume overload by reducing MR

- Creates tissue bridge
  - Limits dilatation of annulus
    - Septal-lateral (anterior-posterior) dimension
  - Supports durability of repair

- Restrains LV wall
  - Limits LV dilatation

Produce two orifice- how do you measure residual MR

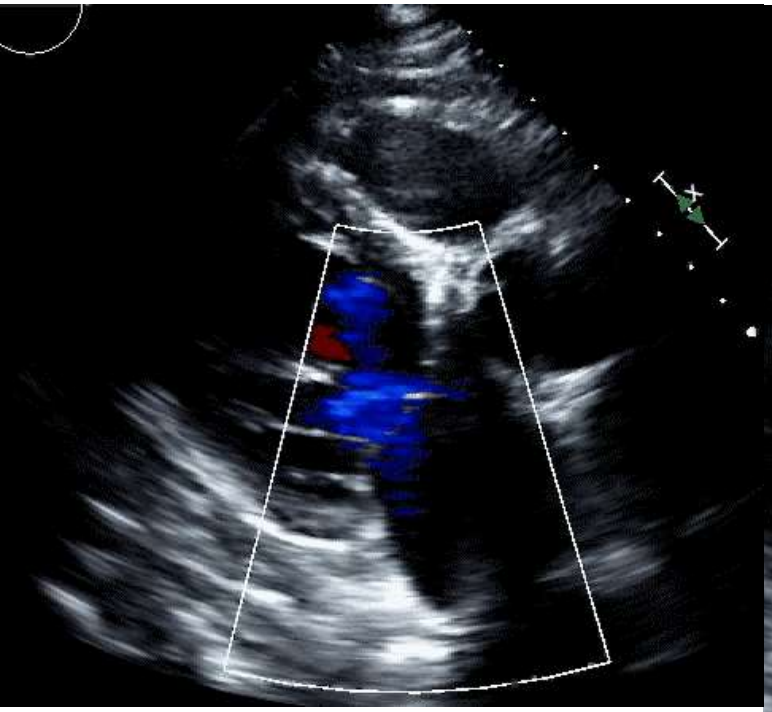
How do you assess and quantify after Mitraclip?

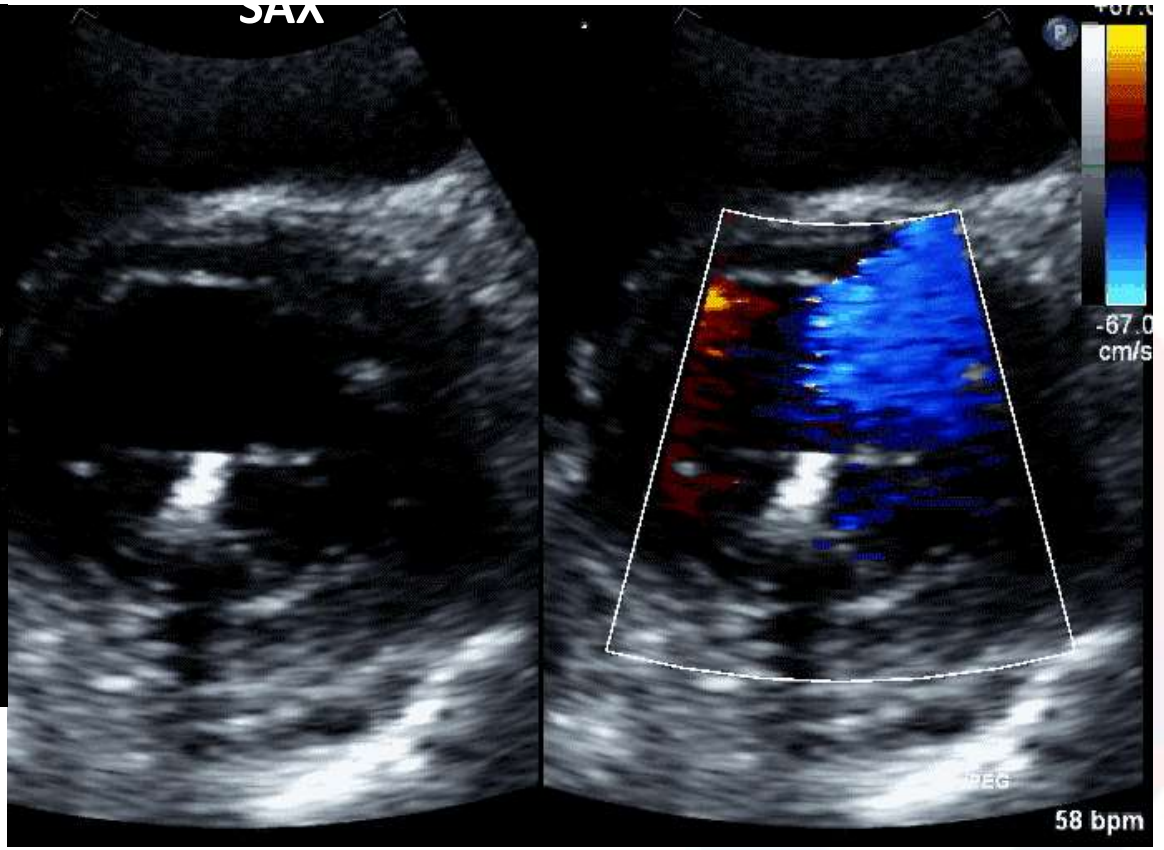


Quantification of residual MR following a MitraClip is challenging due to several reasons

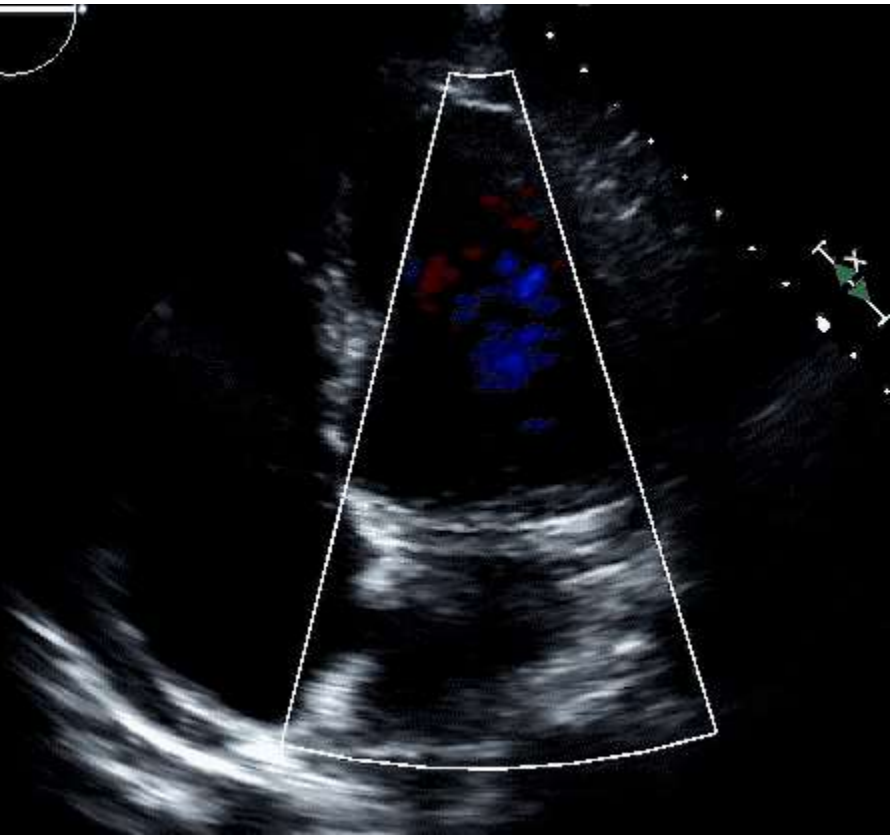
- the presence of the clip limits visualization of the jet origin,
- eccentricity of the MR jets,
- potential multiple sites of regurgitation,
- the dynamic nature
- altered anatomy of the MR orifice secondary to the presence of a clip after the edge-to-edge “Alfieri”-type repair

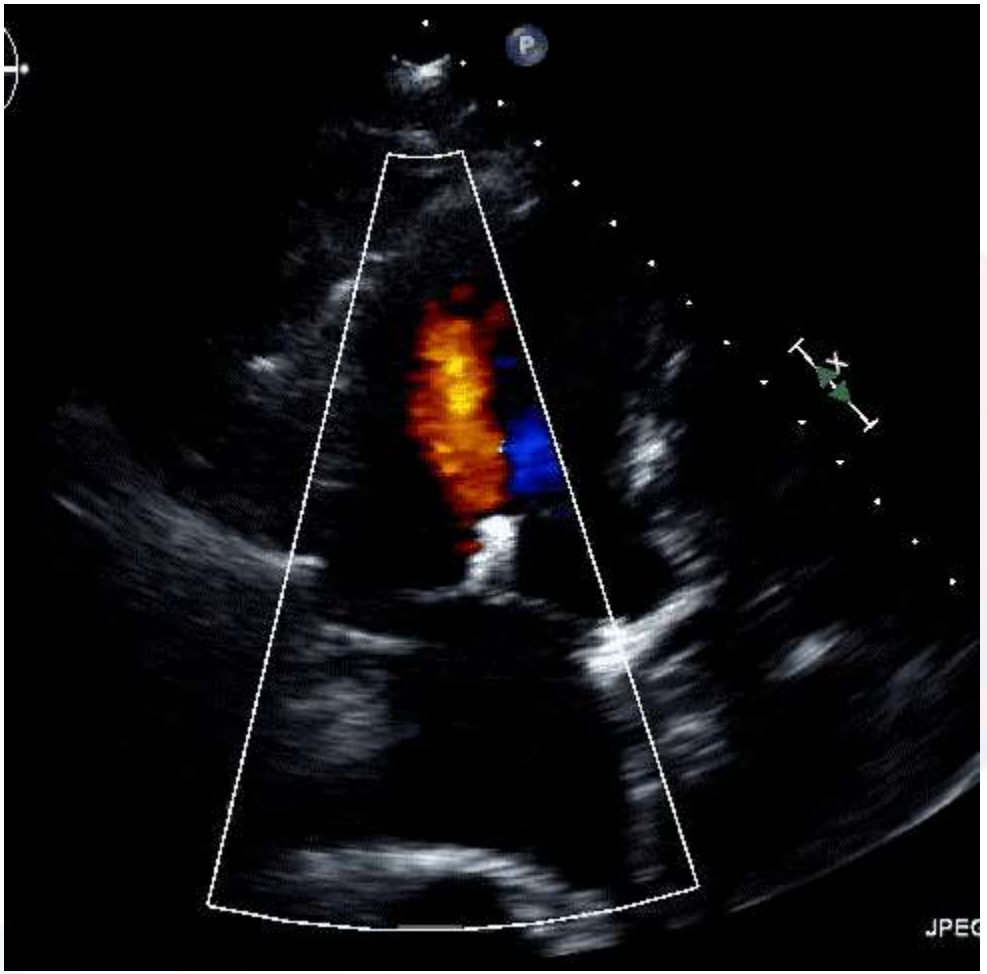
Case residual MR post Mitraclip 1





Case residual MR post Mitraclip 1



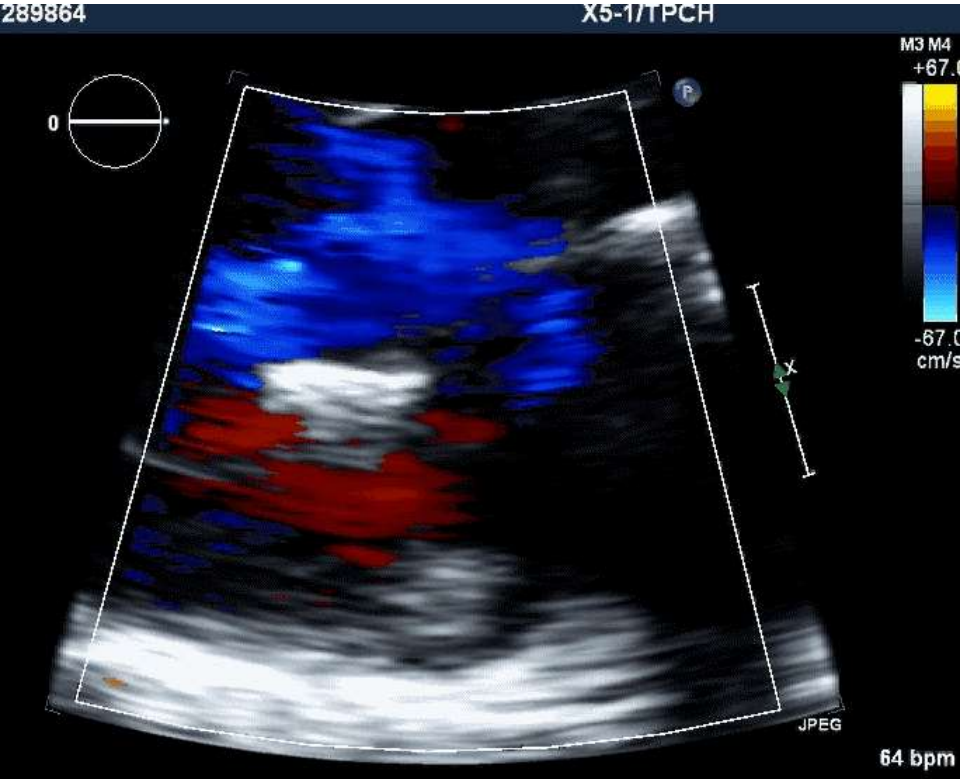


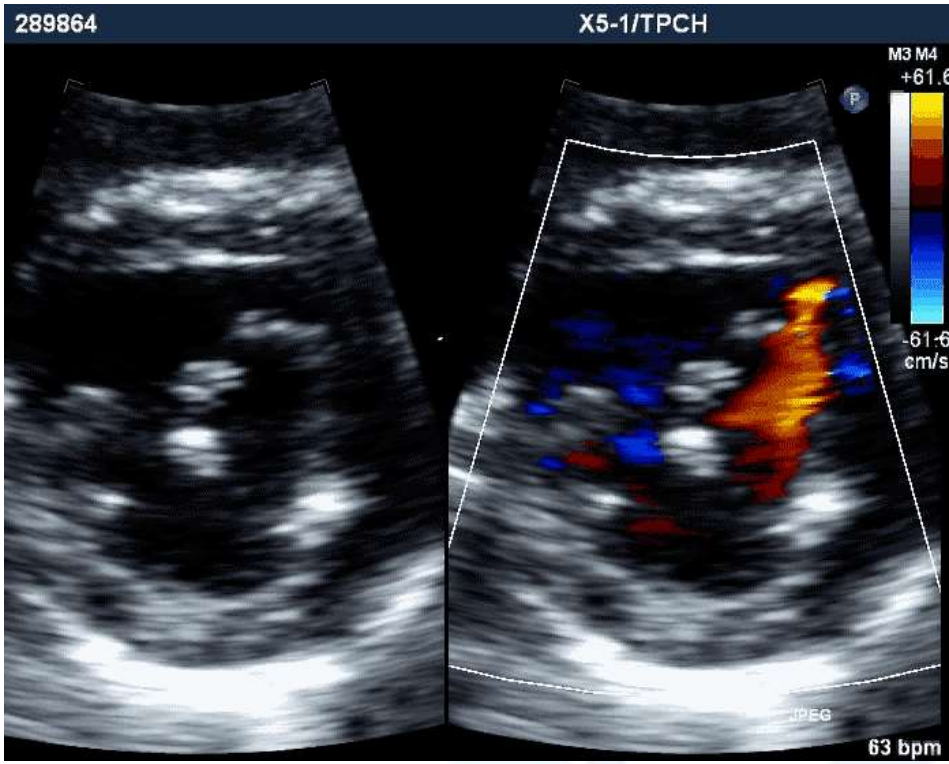
Case residual MR post Mitraclip 1 Compare to

- Expert Consensus
  - Reader 1 = 0.5
  - Reader 2 = 1
  - Reader 3 = 0.5
  - Average = 0.66

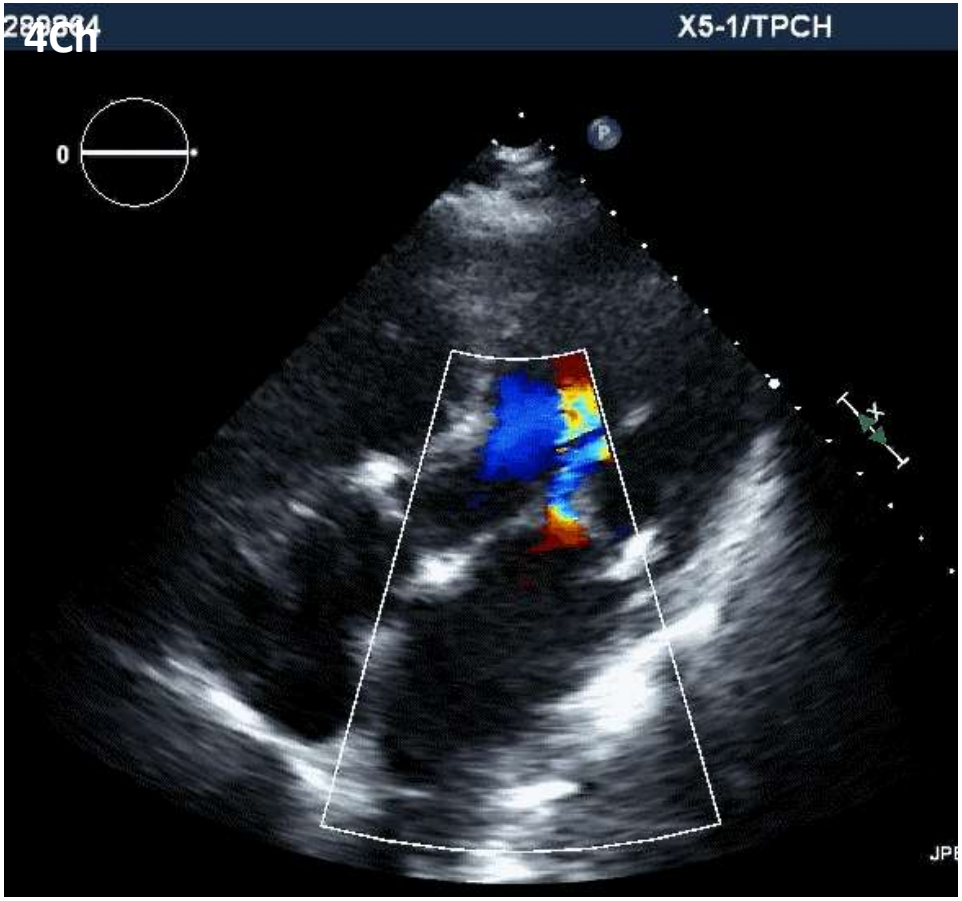
- Cardiac MRI
  - Regurgitant fraction 19%
  - MRI grade = 2

Case residual MR post Mitraclip 2





Case residual MR post Mitraclip 2



Case residual MR post Mitraclip 2 Compare to

- Expert Consensus – *controversial*!
  - Reader 1 = 1
  - Reader 2 = 3
  - Reader 3 = 2
  - Average = 2

- Cardiac MRI
  - Regurgitant fraction 4 % !

How to assess residual MR post Mitraclip

Featured Article

Quantitation of mitral regurgitation after percutaneous MitraClip repair: comparison of Doppler echocardiography and cardiac magnetic resonance imaging

Christian Hamilton-Craig[1,2,3], Wendy Strugnell[1], Niranjan Gaikwad[1], Matthew Ischenko[1], Vicki Speranza[1], Jonathan Chan[4], Johanne Neill[1], David Platts[1,2], Gregory M. Scalia[1,2], Darryl J. Burstow[1,2], Darren L. Walters[1,2]

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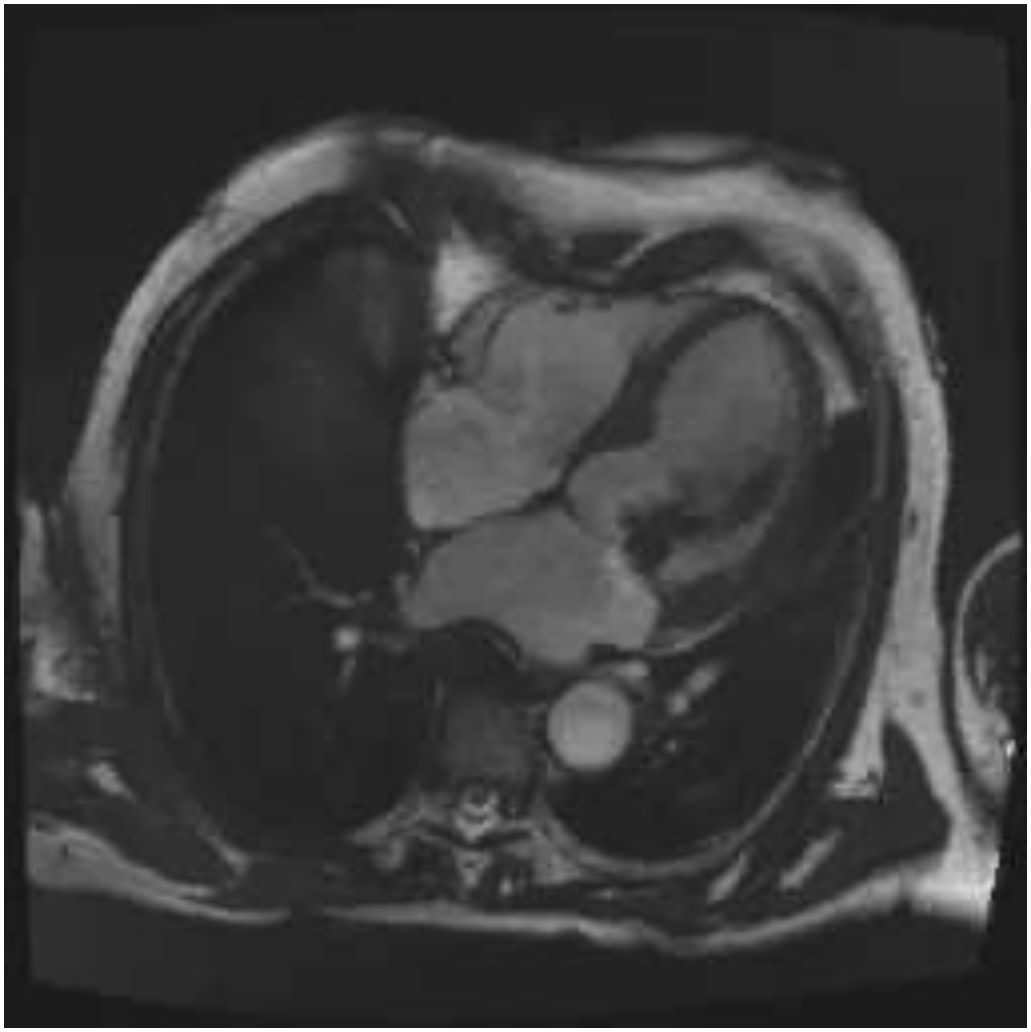
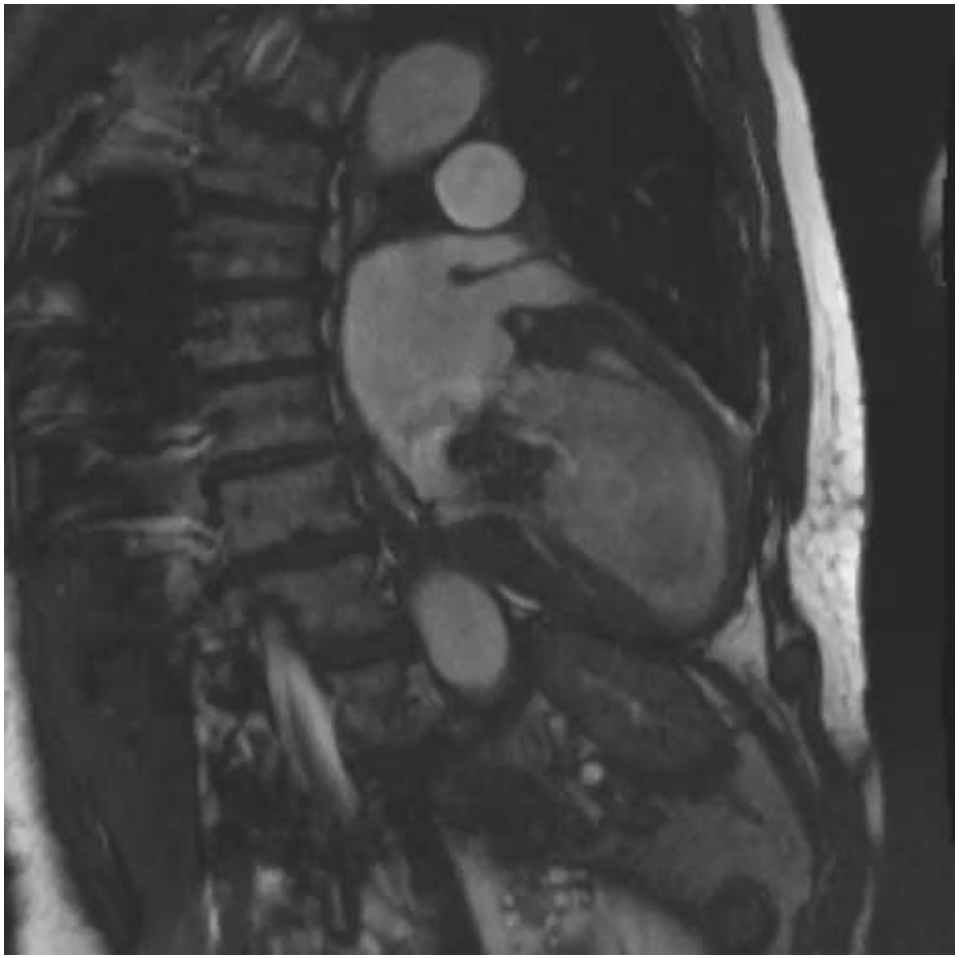
How to assess residual MR post Mitraclip Aim:

- Quantitative assessment of residual MR by transthoracic echocardiography (TTE) is challenging, with multiple eccentric jets and artifact from the clips.
- Cardiovascular magnetic resonance (CMR) is the reference standard for left and right ventricular volumetric assessment.
- CMR phase-contrast flow imaging has superior reproducibility for quantitation of MR compared to echocardiography.
- The objective of this study was to establish the feasibility and reproducibility of CMR in quantitating residual MR after MitraClip insertion in a prospective study.

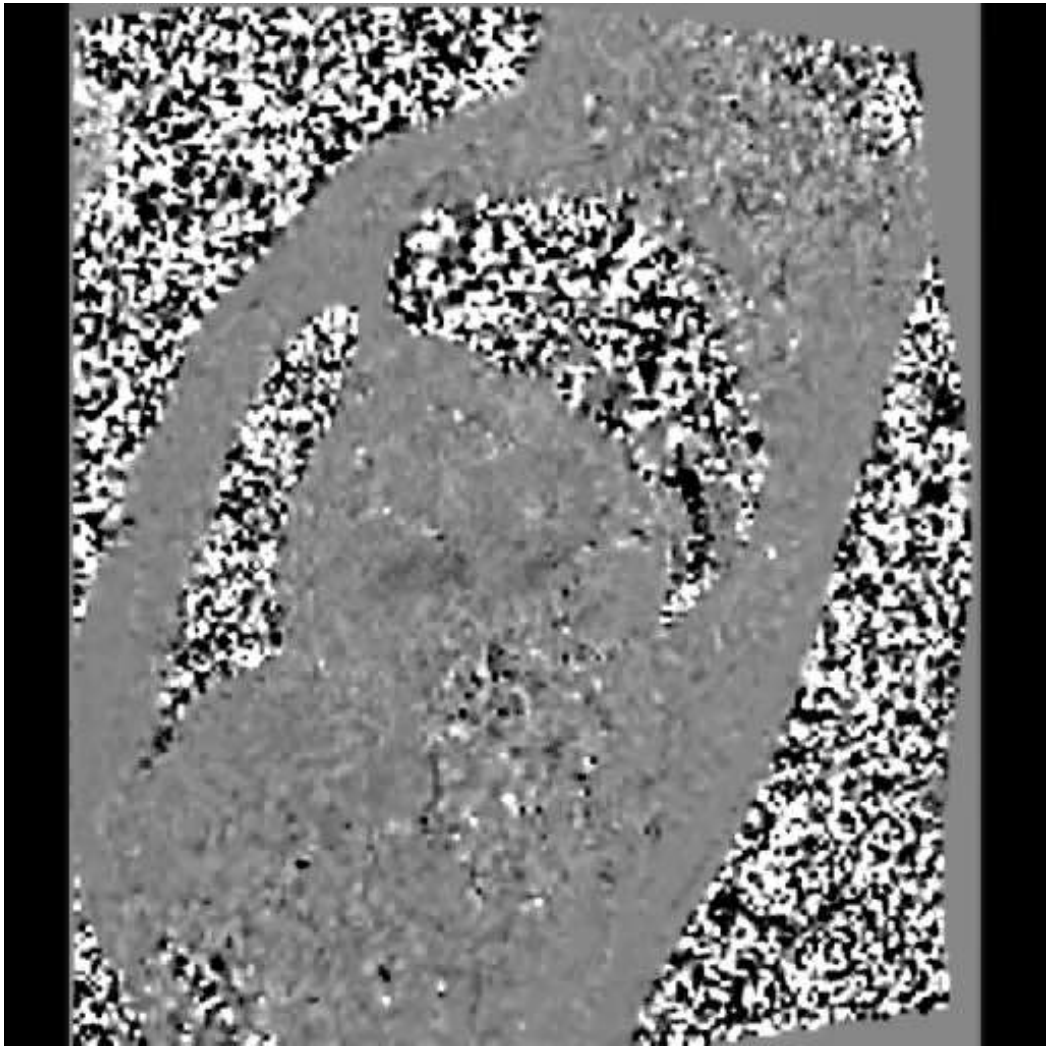
Post-MitraClip



Post-MitraClip



Flow quantiatation image

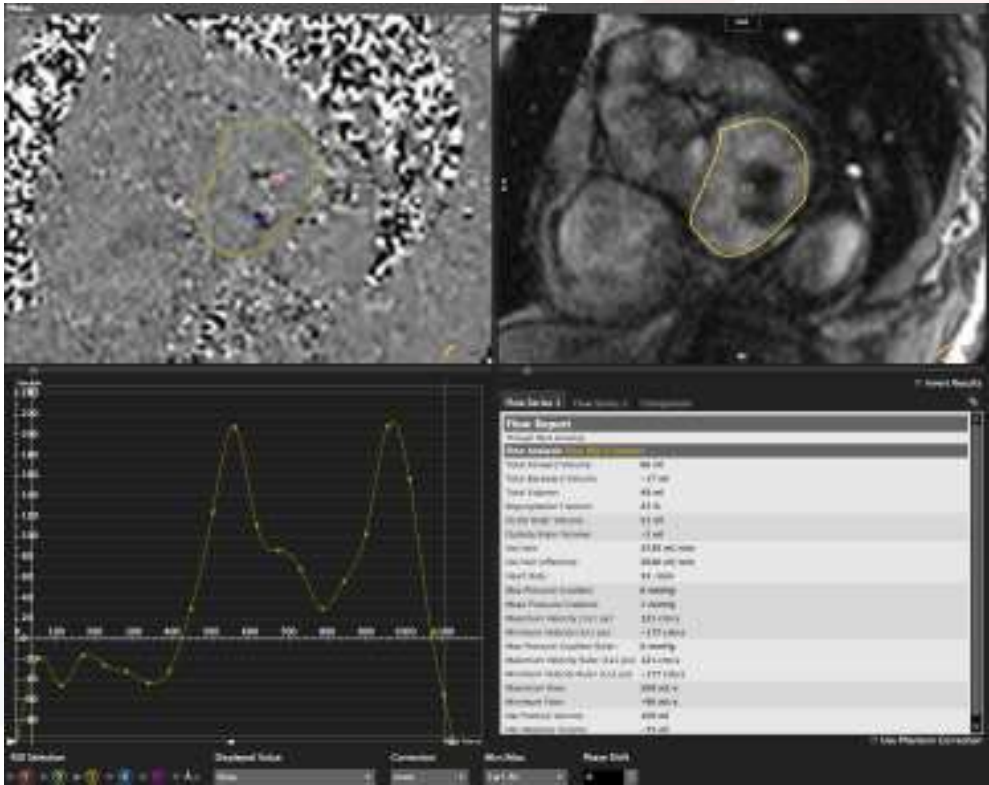


How to assess residual MR post Mitraclip Method:

- Mitral phase contrast flow image analysis, using dedicated software.
- Phase velocity image on the top left, magnitude image on the top right, with manual tracing of atrial contour.
- A flow-velocity curve is generated on the bottom left, showing diastolic ‘early’ (E) and ‘atrial’ (A) waveforms, with regurgitant flow seen in systole.
- Automated quantitative analysis (bottom right) shows forward flow 66 mL, reverse flow -17 mL and

  regurgitant fraction 25%

  (moderate).

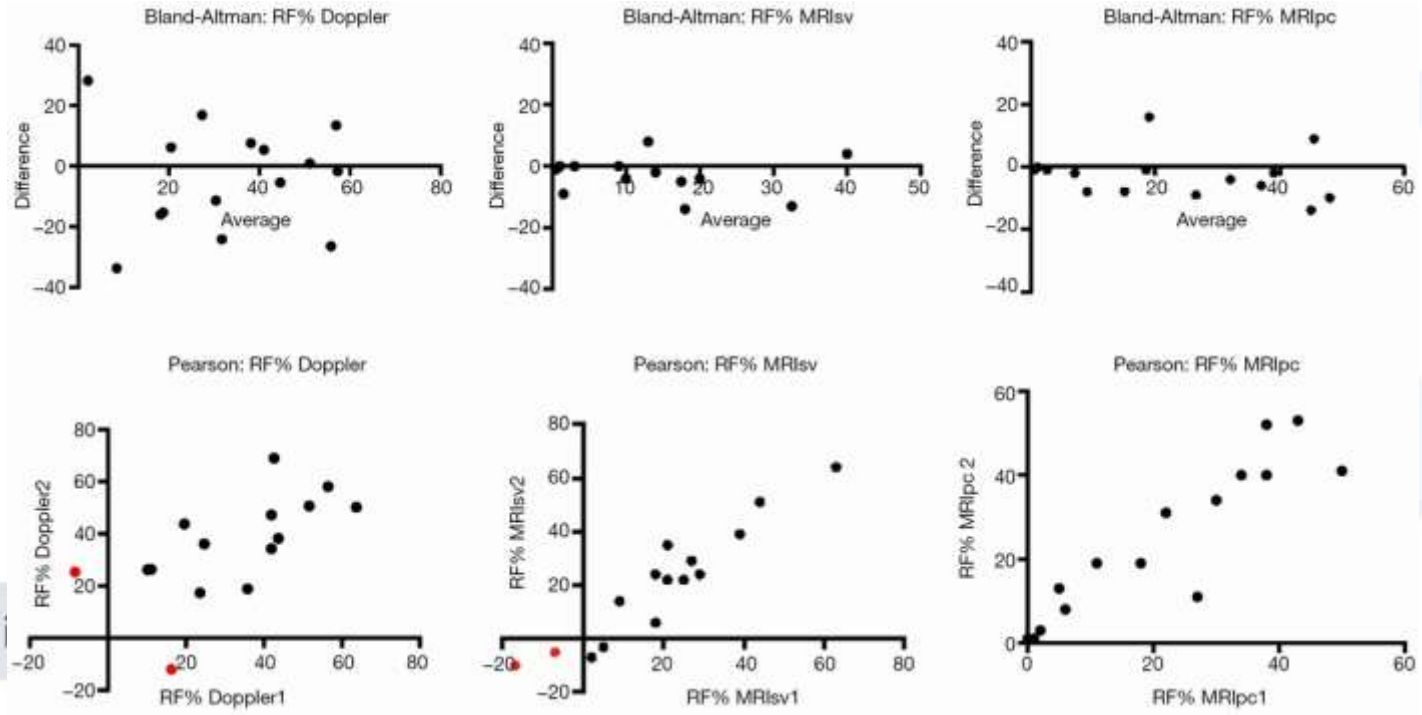


How to assess residual MR post Mitraclip Method:

- 16 who underwent a comprehensive CMR examination at 1.5 T (Siemens Aera) with multiplanar steady state free precession (SSFP) cine imaging (cine CMR), and phase-contrast flow acquisitions (flow CMR) at the mitral annulus atrial to the MitraClip, and the proximal aorta.
- Same-day echocardiography was performed with two-dimensional (2D) visualization and Doppler.
- CMR and echocardiographic data were independently and blindly analyzed by expert readers.
- Inter-rater comparison was made by concordance correlation coefficient (CCC) with 95% confidence intervals (CIs), and Bland-Altman (BA) methods.

How to assess residual MR post Mitraclip Results:

- Echocardiographic Doppler regurgitant fraction reproducibility was modest (CCC 0.59, 0.15-0.84; BA mean difference −3.7%, −38% to 31%).
- CMR regurgitant fraction reproducibility was excellent (CCC 0.95, 0.86-0.98; BA mean difference −2.4%, −11.9 to 7.0), with a lower mean difference and narrower limits of agreement compared to echocardiography.
- Categorical severity grading by CMR using published ranges had good inter-observer agreement (CCC 0.86, 0.62-0.95).



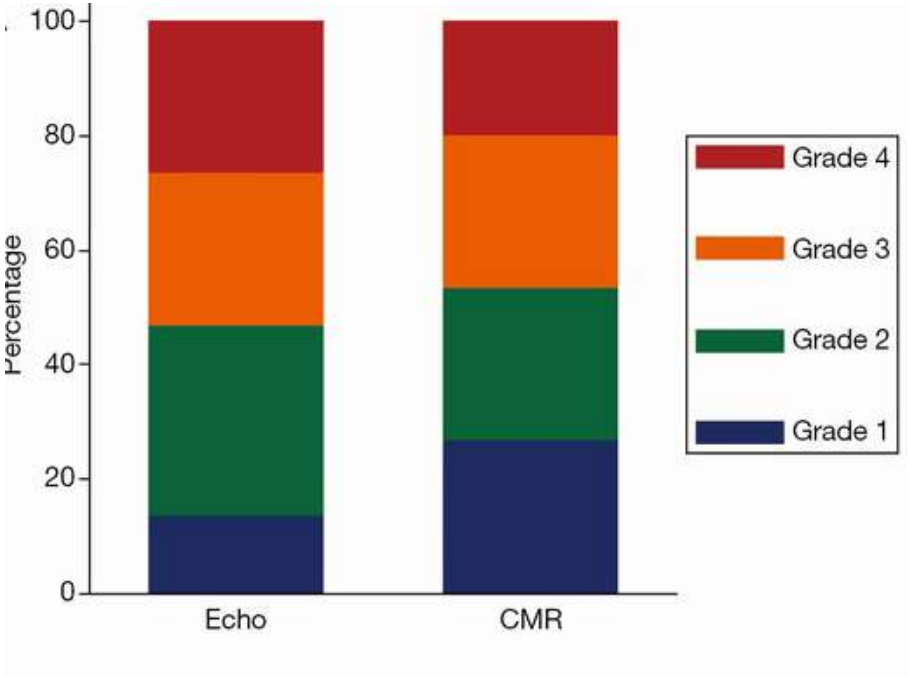
How to assess residual MR post Mitraclip Results:

Table 2 Inter-observer reproducibility of expert reader, echo Doppler and CMR metrics of regurgitant volume (Rvol) and regurgitant fraction (RF%)

Variables	Bland-Altman		Concordance correlation coefficient (CCC)	95% CI (low, high)	Pearson's P (precision)	Bias correction factor *Cb* (accuracy)
	Limits of agreement	Bias				
Doppler echo						
Multiparametric grading	−0.7 to 2.3	−0.8	0.475	0.0713-0.744	0.669	0.709
$RVol_{Doppler}$ (mL)	−61.3 to 52.84	−4.2	0.633	0.205-0.856	0.6338	0.991
$RF\%_{Doppler}$ (%)	−37.9 to 0.5	−3.7	0.599	0.155-0.841	0.610	0.982
CMR						
$RVol_{MRI-SV}$ (mL)	−14.7 to 12.45	−1.1	0.949	0.874-0.980	0.958	0.990
$RF\%_{MRI-SV}$ (%)	−14.1 to 12.6	−0.75	0.947	0.859-0.980	0.950	0.997
$RVol_{MRI-PC}$ (mL)	−14.9 to 8.2	−3.1	0.828	0.588-0.934	0.853	0.971
$RF\%_{MRI-PC}$ (%)	−11.9 to 7.0	−2.4	0.950	0.867-0.982	0.960	0.989

CMR, cardiovascular magnetic resonance; CI, confidence interval; $RVol_{Doppler}$, regurgitant volume by Doppler echocardiography method; $RF\%_{Doppler}$, regurgitant fraction by Doppler echocardiography method; $RVol_{MRI-SV}$, regurgitant volume by stroke volume method; $RF\%_{MRI-SV}$, regurgitant fraction by stroke volume method; $RVol_{MRI-PC}$, regurgitant volume by phase contrast method; $RF\%_{MRI-PC}$, regurgitant fraction by phase contrast method.

How to assess residual MR post Mitraclip Results:



Echo increased levels of residual MR compared to MRI quantification
Echo less reproducible and greater variability

Conclusion

- TTE assessment of residual mitral regurgitation post Mitraclip is difficult even in expert hands
- TTE tends to overestimate residual mitral regurgitation compared to MR quantification
- Consider MRI to assess residual MR post Mitraclip in select if not all cases
- If MRI is not available consider a dedicated readers who include careful review of all indirect measures of MR post mitraclip in conjunction with quantified measures
- Implication for the evaluation of future intervention/device