

# Mitral Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

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For the CTSN Investigators  
AHA November 2013

# Acknowledgements



- Supported by U01 HL088942 Cardiothoracic Surgical Trials Network (CTSN)
- Funding Agencies:
  - National Heart Lung and Blood Institute
  - National Institutes for Neurological Diseases and Stroke
  - Canadian Institutes for Health Research

ORIGINAL ARTICLE

## Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

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### ABSTRACT

#### BACKGROUND

Ischemic mitral regurgitation is associated with a substantial risk of death. Practice guidelines recommend surgery for patients with a severe form of this condition but acknowledge that the supporting evidence for repair or replacement is limited.

#### METHODS

We randomly assigned 251 patients with severe ischemic mitral regurgitation to undergo either mitral-valve repair or chordal-sparing replacement in order to evaluate efficacy and safety. The primary end point was the left ventricular end-systolic volume index (LVESVI) at 12 months, as assessed with the use of a Wilcoxon rank-sum test in which deaths were categorized below the lowest LVESVI rank.

#### RESULTS

At 12 months, the mean LVESVI among surviving patients was  $54.6 \pm 25.0$  ml per square meter of body-surface area in the repair group and  $60.7 \pm 31.5$  ml per square meter in the replacement group (mean change from baseline,  $-6.6$  and  $-6.8$  ml per square meter, respectively). The rate of death was 14.3% in the repair group and 17.6% in the replacement group (hazard ratio with repair, 0.79; 95% confidence interval, 0.42 to 1.47;  $P=0.45$  by the log-rank test). There was no significant between-group difference in LVESVI after adjustment for death ( $z$  score, 1.33;  $P=0.18$ ). The rate of moderate or severe recurrence of mitral regurgitation at 12 months was higher in the repair group than in the replacement group (32.6% vs. 2.3%,  $P<0.001$ ). There were no significant between-group differences in the rate of a composite of major adverse cardiac or cerebrovascular events, in functional status, or in quality of life at 12 months.

#### CONCLUSIONS

We observed no significant difference in left ventricular reverse remodeling or survival at 12 months between patients who underwent mitral-valve repair and those who underwent mitral-valve replacement. Replacement provided a more durable correction of mitral regurgitation, but there was no significant between-group difference in clinical outcomes. (Funded by the National Institutes of Health and the Canadian Institutes of Health; ClinicalTrials.gov number, NCT00807040.)

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\* A list of members of the Cardiothoracic Surgical Trials Network (CTSN) is provided in the Supplementary Appendix, available at [NEJM.org](http://NEJM.org).

This article was published on November 18, 2013, at [NEJM.org](http://NEJM.org).

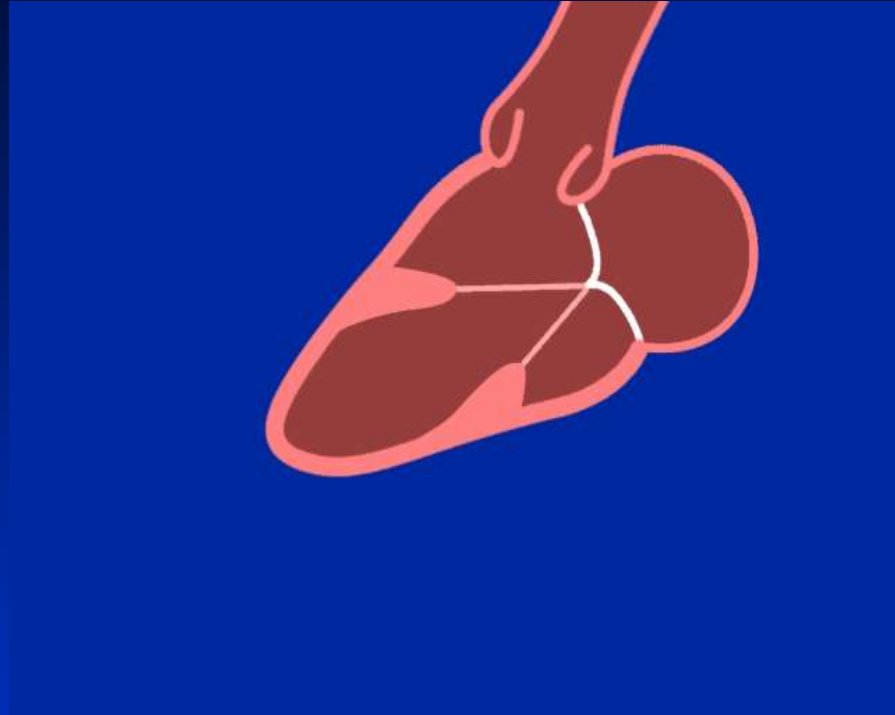
*N Engl J Med* 2014.

DOI: 10.1056/NEJMoa1312808

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# Ischemic MR is not Degenerative MV Disease



- LV enlarges-loss of elliptical shape; more spherical
  - Mitral annulus dilates
  - Papillary muscles displace
  - Chordae tether leaflets
  - Valve leaflets are not in coaptation...

**= Functional Mitral Regurgitation**



Annular Dilatation  
Type I



Restricted Leaflets  
Type IIIb

# AHA/ACC and ESC Guidelines



**Circulation**



2008 Focused Update Incorporated Into the ACC/AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease). Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons  
 2008 WRITING COMMITTEE MEMBERS: Robert O. Bonow, Blase A. Carabello, Kenneth Chatterjee, Antonio C. de Leon, Jr., David P. Faxon, Michael D. Freed, William H. Gansch, Bruce W. Lytle, Rick A. Nishimura, Patrick T. O'Gara, Robert A. O'Rourke, Catherine M. Otto, Pravin M. Shah and Jack S. Shanewise

Circulation. 2008;118:e523-e661; originally published online September 26, 2008; doi:10.1161/CIRCULATIONAHA.108.190748  
 Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75221  
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 Print ISSN: 0009-7322; Online ISSN: 1524-4539

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- Class IIb Level C evidence for severe secondary MR

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No conclusive evidence for superiority of repair or replacement

European Heart Journal (2012) 33, 3401–3406  
 doi:10.1093/eurheartj/ehs327

ESC/EACTS GUIDELINES

## Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France)\*, Ottavio Alfieri (Chairperson)† (Italy), Felicitas Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michela De Bonis (Italy), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Bernard Jung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Jan-Joachim Schöfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

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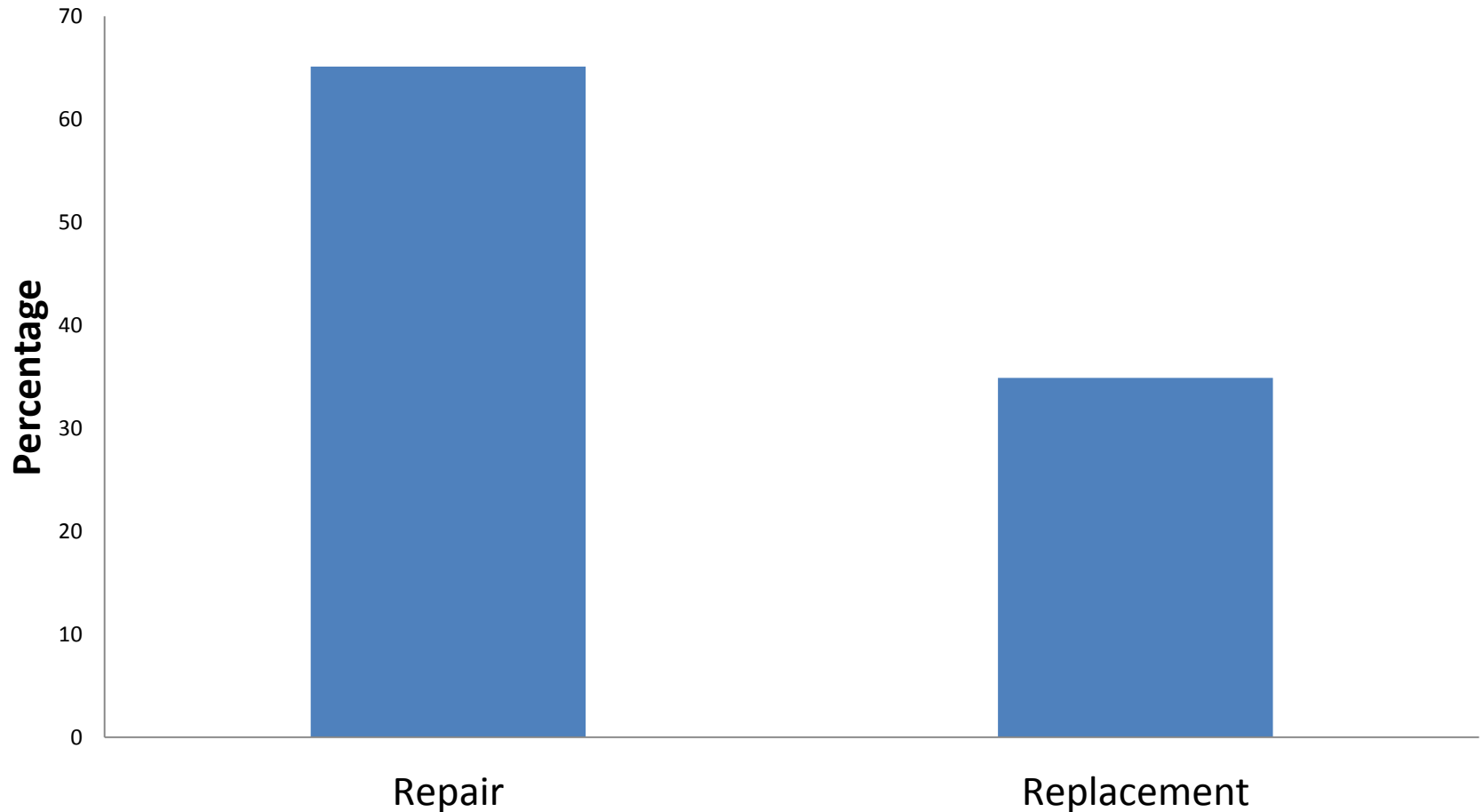
Document Reviewers: Bogdan A. Popescu (ESC CPG Review Coordinator) (Romania), Ludwig Von Segesser (EACTS Review Coordinator) (Switzerland), Luigi P. Badier (Italy), Marjan Bunc (Slovenia), Mort J. Ceylan (Belgium), Niklas Eriksson (Sweden), Gerasimos Filippatos (Greece), Gilbert Habib (France), A. Pieter Kappetein (The Netherlands), Roland Kozlik-Fischer (Germany), Gregory Y.H. Lip (UK), Neil Moor (UK), Georg Nickeny (Germany), Catherine M. Otto (USA), John Page (UK), Nicola Piazza (Germany), Francesco G. Pece (The Netherlands), Rainer Rosthalski (Austria)

- Class I Level C evidence for IMR patients undergoing CAB w/ EF > 30%
- Class IIa Level C evidence for IMR patients undergoing CAB w/ EF < 30%
- Class IIb Level C evidence for IMR patients not undergoing CAB

# Preference for Repair Over Replacement



**Mitral Repair and Replacement with CABG**



Years 2008-2012, The Adult Cardiac Surgery Database, The Society of Thoracic Surgeons

# Treatment Choice is Controversial



- Lower periop morbidity and mortality with repair
  - Vasileva et al, Eur J Cardiothoracic Surg 2011;39:295-303
- Better long-term correction with replacement
  - Di Salvo et al, J Am Coll Cardiol. 2010; 55:271-82
  - Grossi et al, J Thorac Cardiovasc Surg 2001;122:1107-24
  - Gillinov et al, J Thorac Cardiovasc Surg 2001;122:1125-41
- Based on retrospective observational studies
- Need randomized evidence

# SMR Trial Design



Enrollment

Assessed for Eligibility  
(n=3458)

**Excluded (n = 3207)**

- Did not meet inclusion criteria (n=3011)
- Refused to participate (n=131)
- Other (n=65)

Randomized  
(n = 251)

Allocation

**Allocated to Mitral Valve Repair  
(n=126)**

- Received MV Repair (n=115)
- Received MV Replacement (n=11)

**Allocated to Mitral Valve Replacement  
(n=125)**

- Received MV Replacement (n=124)
- Received MV Repair (n=1)

Follow-Up

- Withdrawal before month 12 (n=3)
- Death before month 12 (n=18)

- Withdrawal before month 12 (n=1)
- Death before month 12 (n=22)

Analysis

**Primary Endpoint Analysis (n=126)**  
Excluded from Analysis (n=0)

**Primary Endpoint Analysis (n=125)**  
Excluded from Analysis (n=0)



# Primary Endpoint

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- Degree of left ventricular reverse remodeling
  - Assessed by left ventricular end systolic volume index (LVESVI) using TTE at 12 months
  - Group difference based on Wilcoxon Rank-Sum test with deaths categorized as lowest LVESVI rank
- Powered (90%) to detect an improvement of 15mL/m<sup>2</sup> from repair or replacement in LVESVI at 12 months

# Secondary Endpoints

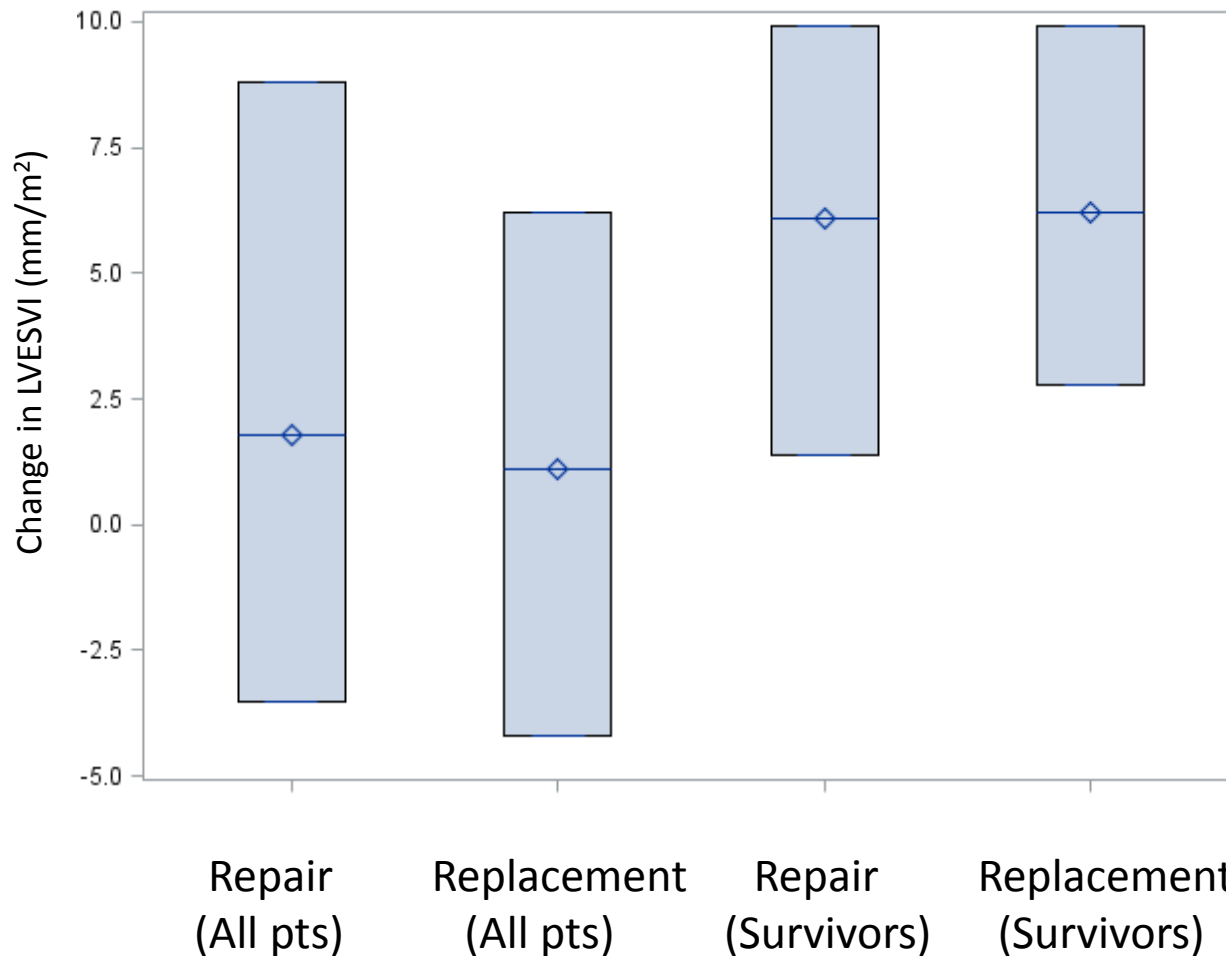


- Mortality
- Recurrent MR
- MACCE
  - Mortality
  - Stroke
  - Subsequent MV surgery
  - HF hospitalization
  - Increase in NYHA class  $\geq 1$
- Serious adverse events
- Quality of life

# Median change in LVESVI



Median with 95% CI for change in LVESVI from baseline to 1 yr

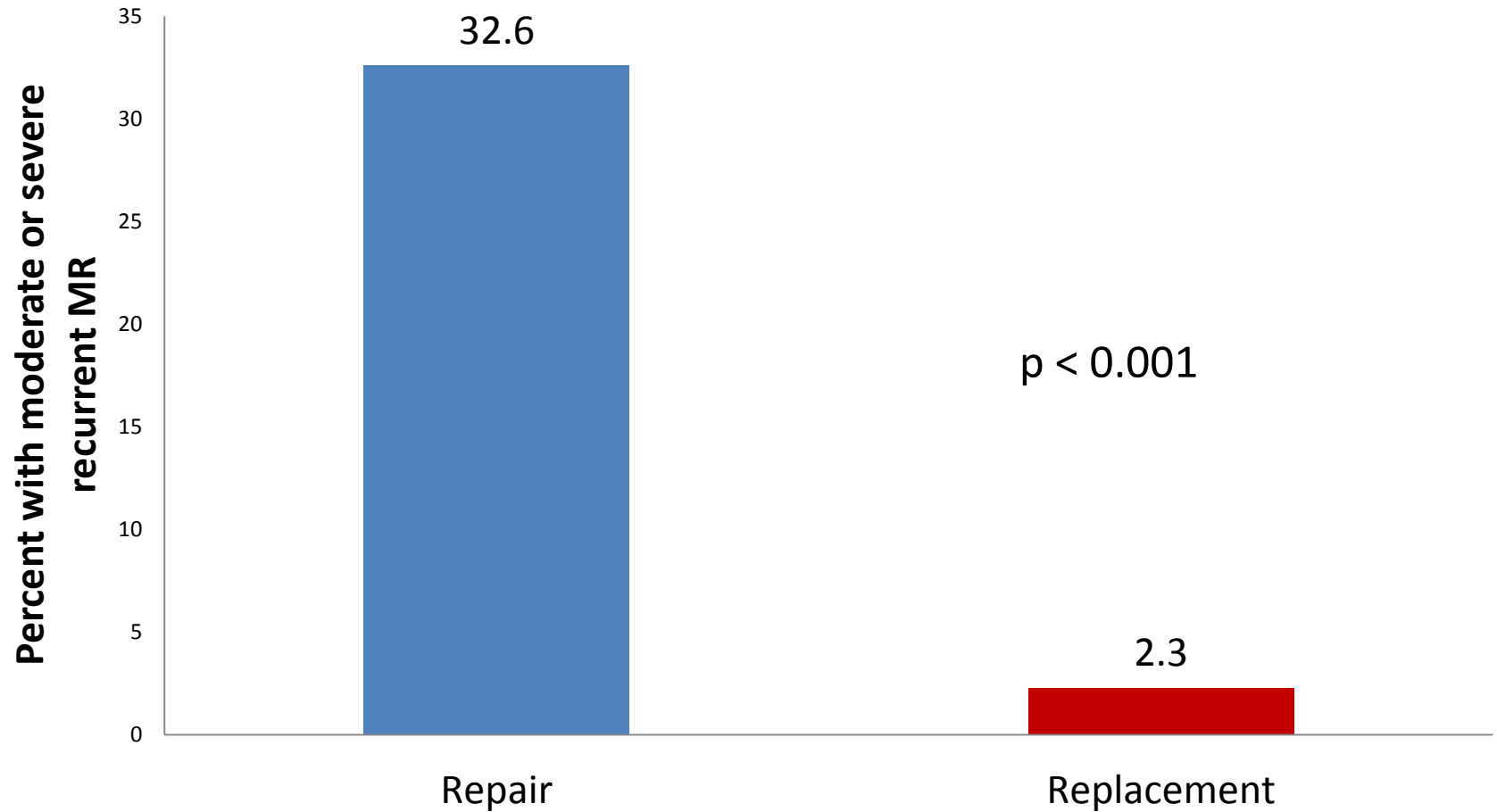


Z=1.33, p=0.18  
(All pts)

# Recurrent MR at 1 year

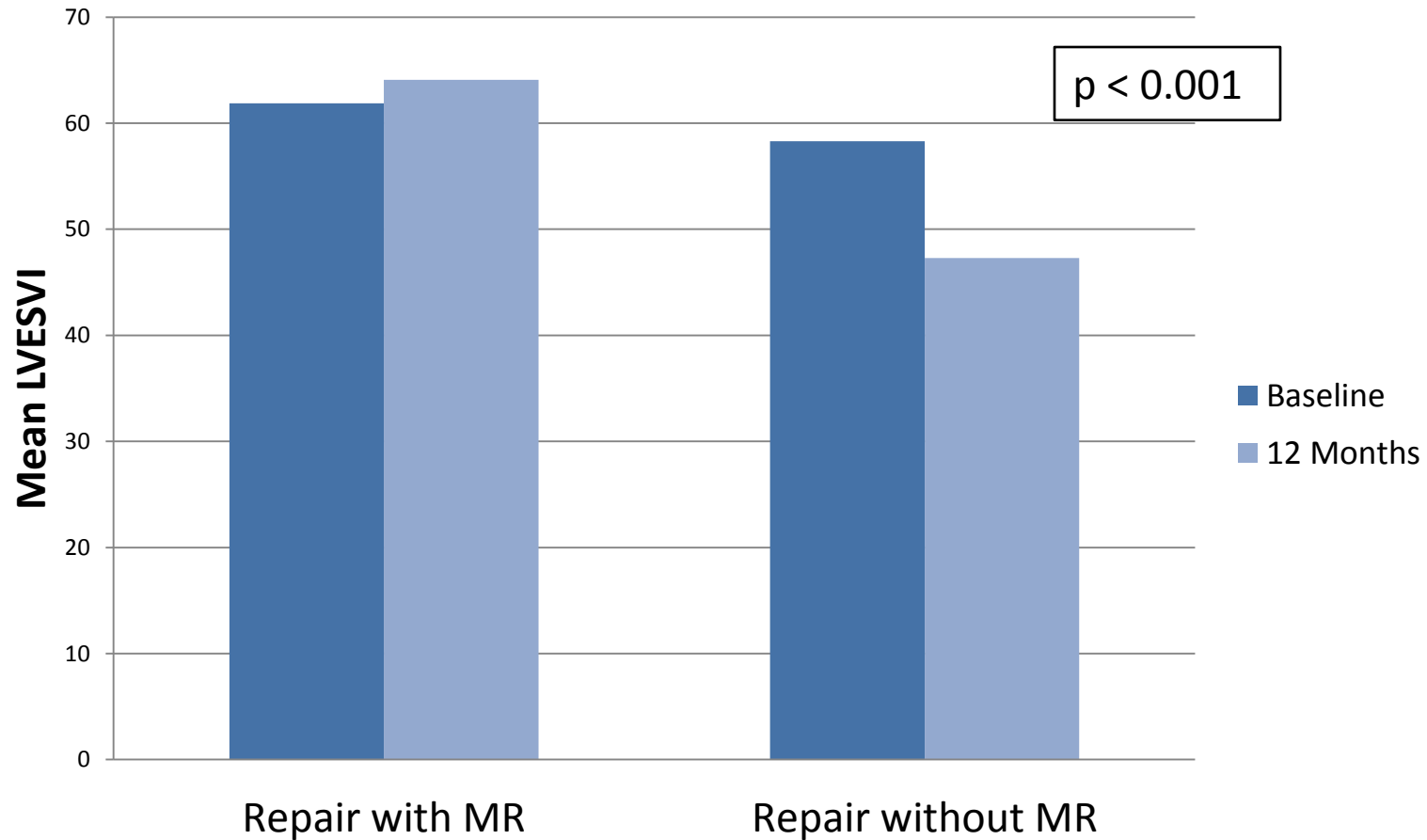


## Moderate or Severe Recurrent MR

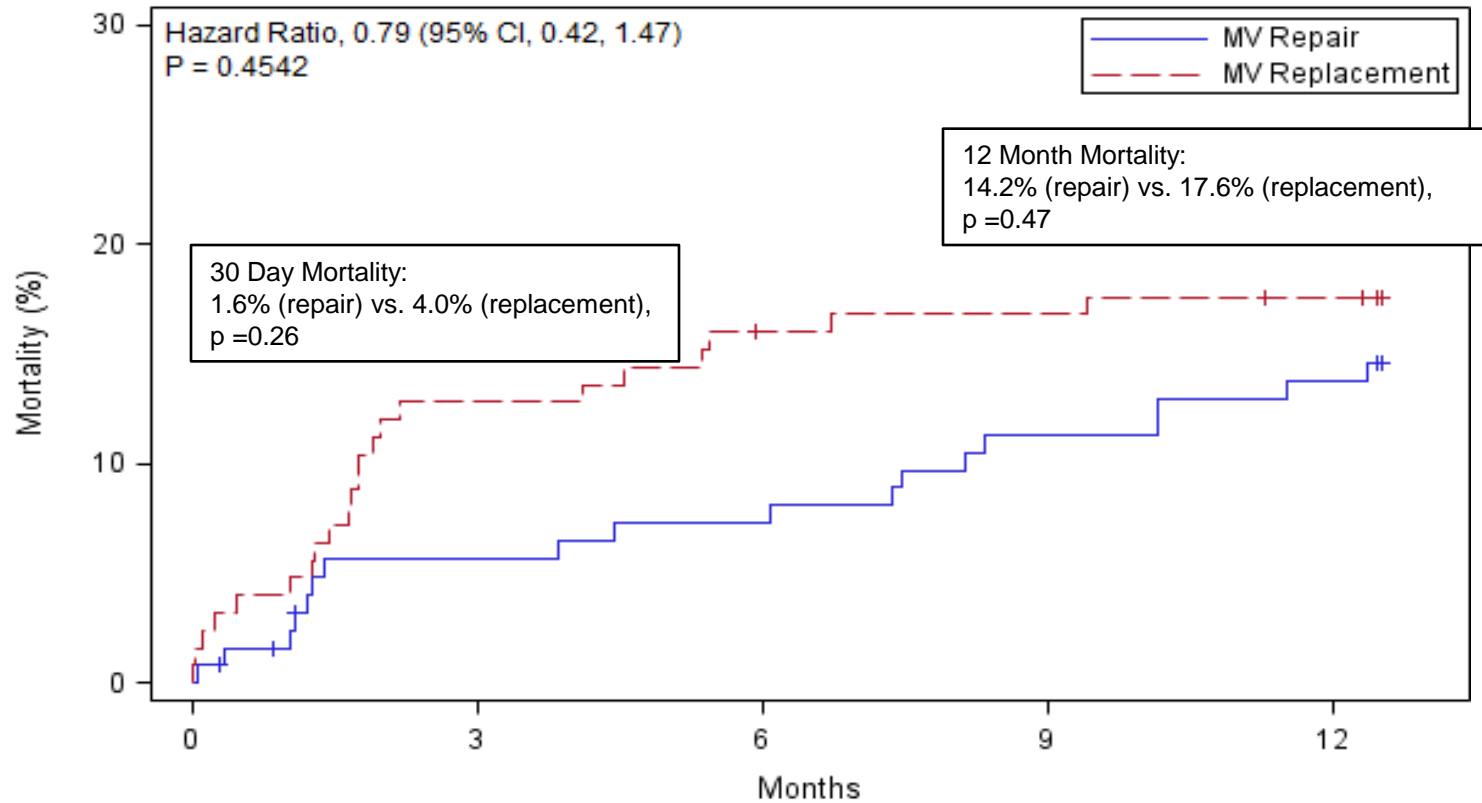


# LVESVI with Recurrent MR

Mean LVESVI for Patients Undergoing Repair

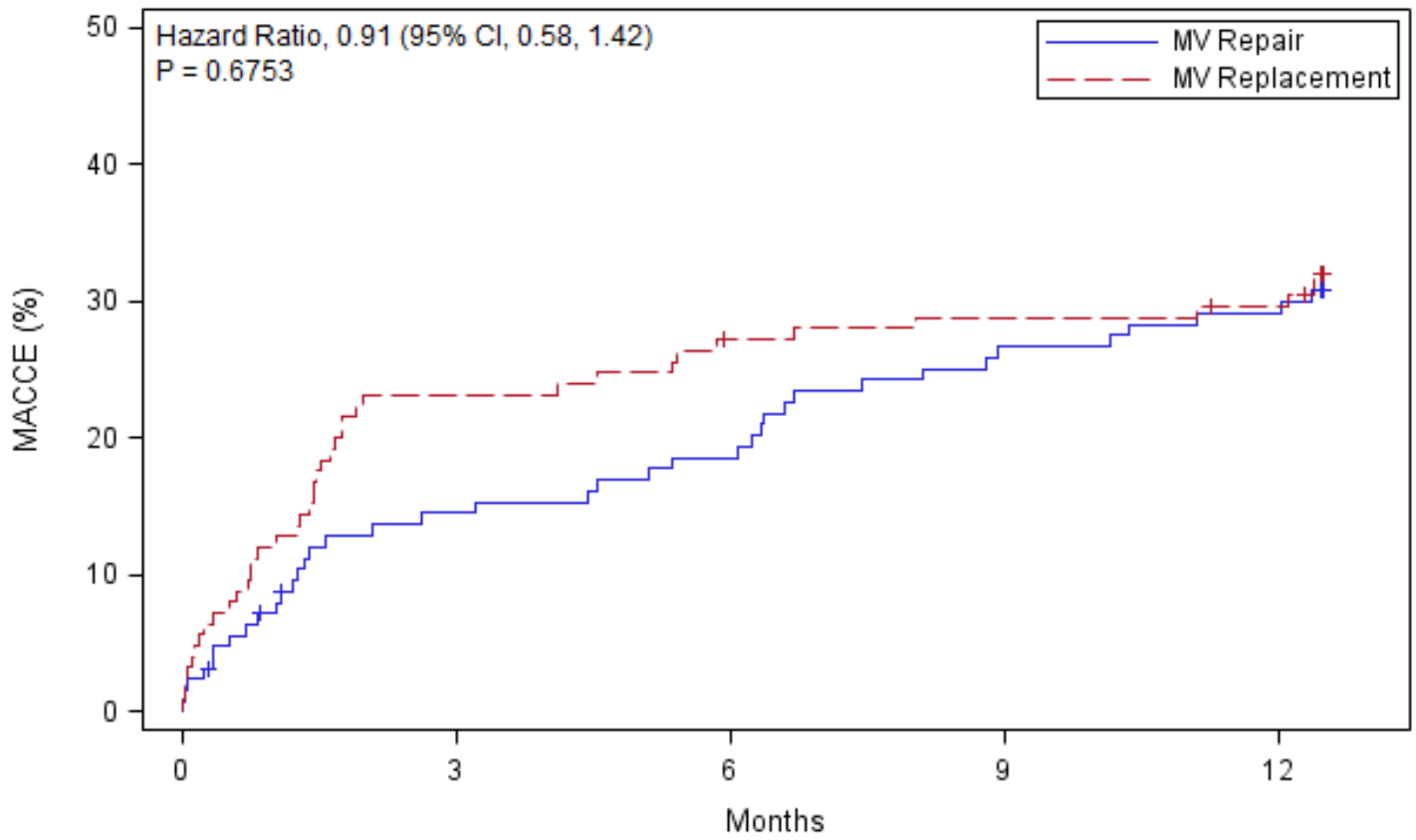


# Mortality



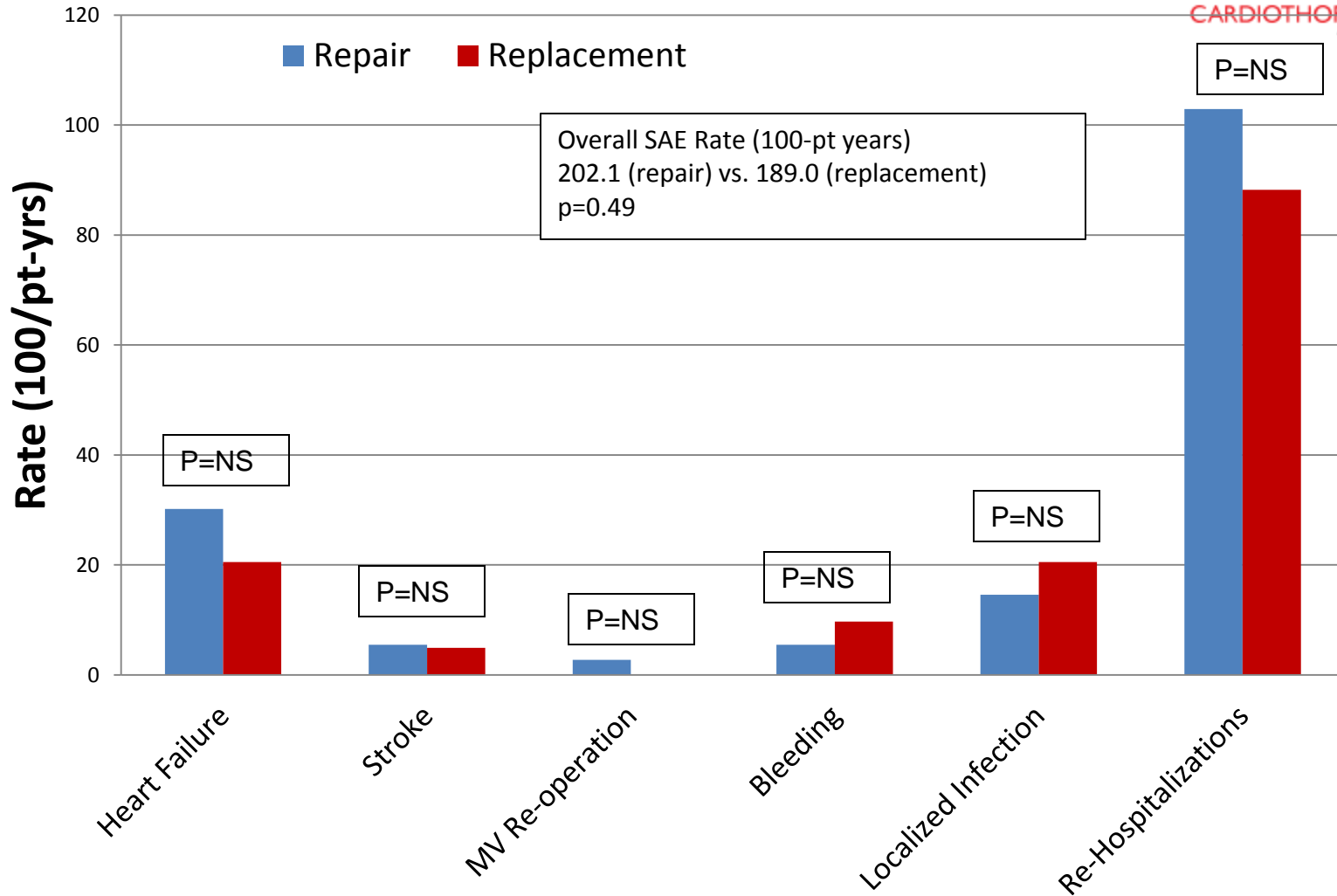
MV Repair	126	116	114	109	106
MV Replacement	125	109	104	103	101

# MACCE at 12 Months



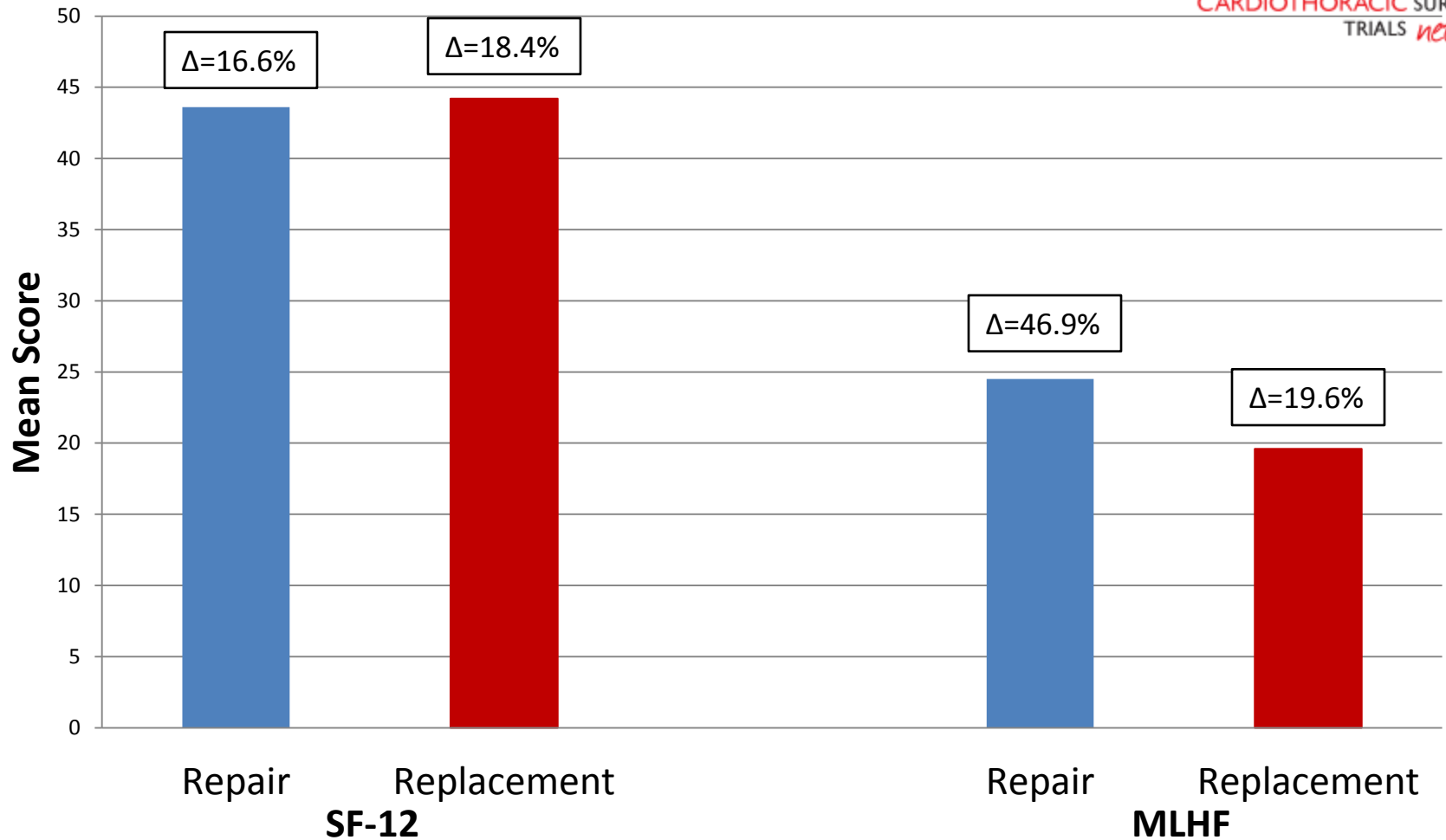
MV Repair	126	105	100	90	87
MV Replacement	125	96	90	88	86

# Serious Adverse Events

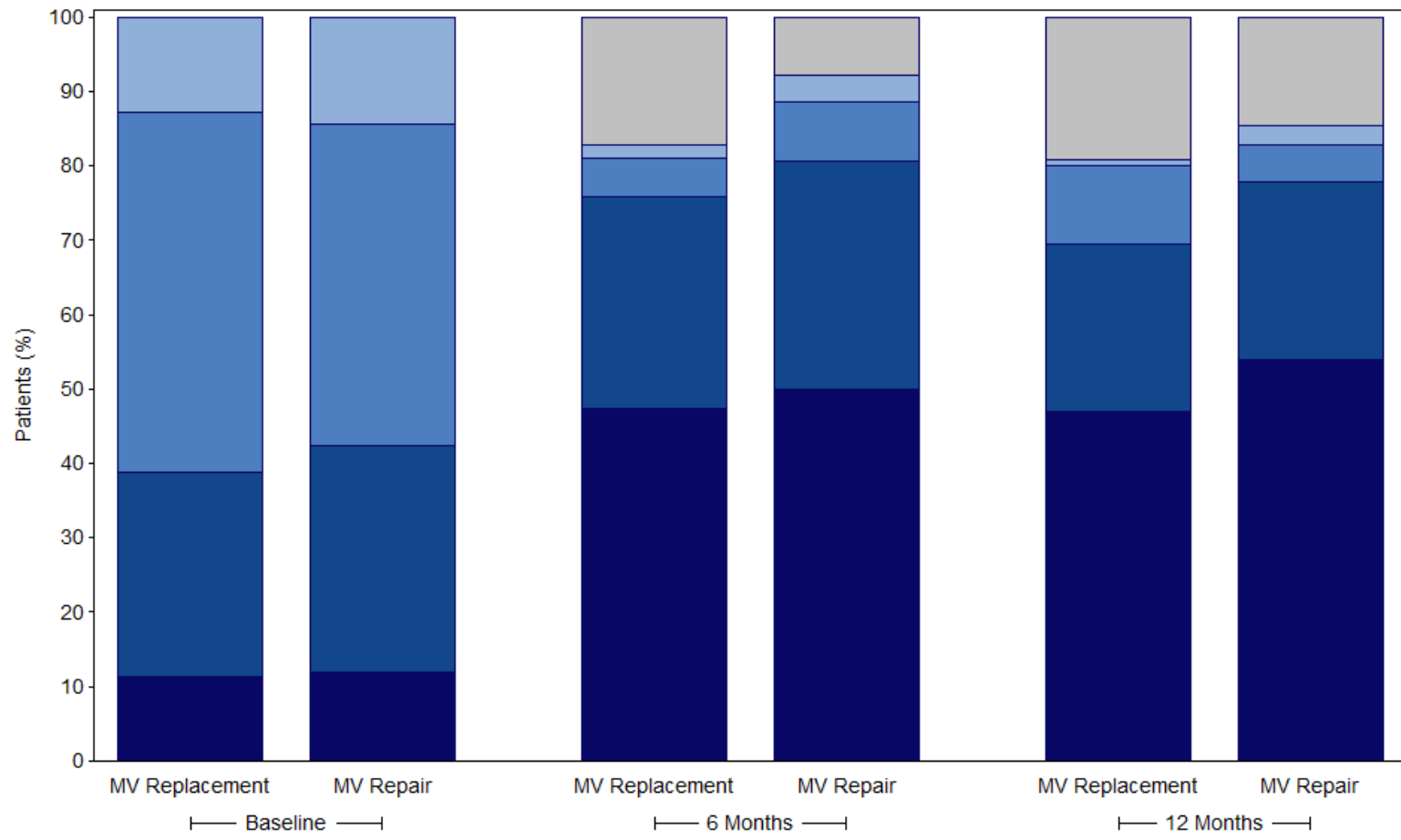




# Quality of Life at 1 year



# NYHA Classification & Death



NYHA Class I II III IV Dead



# Limitations

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- Trial does not include revascularization alone arm
  - Lack of equipoise with severe MR given current guidelines
  - Revascularization alone currently studied in ongoing CTSN trial (MMR)
- Primary end point measures LV remodeling not a clinical endpoint
  - Abundant evidence correlates LVESVI with clinical outcomes
  - Trial with mortality endpoint requires several thousand pts
- Only 1 year results reported
  - Pts will be followed for 2 yrs

# Summary

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- There was no difference in the degree of reverse remodeling and mortality

Mortality	Repair	Replacement
30 day	1.6%	4.0%
1 year	14.3%	17.6%

- Significantly more recurrent MR at 1 year (32.6% vs 2.3%) with MV repair compared to chordal sparing MV replacement
- No difference in MACCE, overall SAEs, NYHA Class and QOL

# Conclusions



- Chordal-sparing MV Replacement provides a more durable correction of severe IMR with no differences seen in reversal of LV remodeling or clinical outcomes – MR recurrence may have an important effect on long-term outcomes
- Additional follow-up and subset analysis may provide insight about predictors and clinical impact of MR recurrence optimizing therapeutic decisions for individual patients

# Investigators

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- Coordinating Center: InCHOIR
- University of Pennsylvania
- Montefiore - Einstein
- Montreal Heart Institute
- University of Virginia Health System
- Hôpital Laval
- Cleveland Clinic Foundation
- Emory University
- Columbia University Medical Center
- University of Maryland
- Baylor Research Institute
- Duke University
- East Carolina Heart Inst
- Brigham and Women's Hospital
- Ohio State University Medical Center
- Sacre-Coeur de Montreal
- University of Southern California
- Inova Heart & Vascular Institute
- Mission Hospital
- NIH Heart Center at Suburban Hospital
- Jewish Hospital
- Sunnybrook Health Sciences Centre
- Wellstar / Kennestone