

SURGICAL TREATMENT OF MODERATE ISCHEMIC MITRAL REGURGITATION: *THE CARDIOTHORACIC SURGICAL TRIALS NETWORK*

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For the CTSN Investigators

AHA Late Breaking Clinical Trials
November 18, 2014

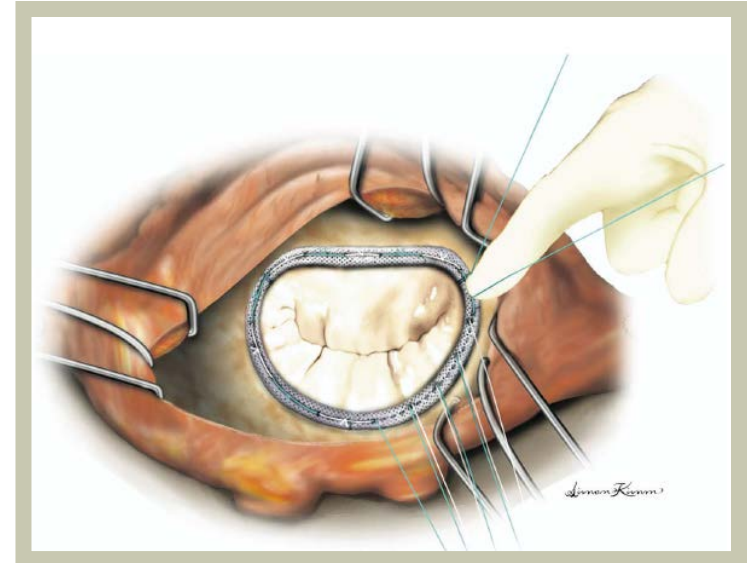
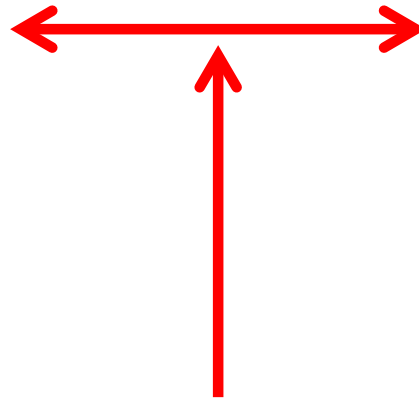
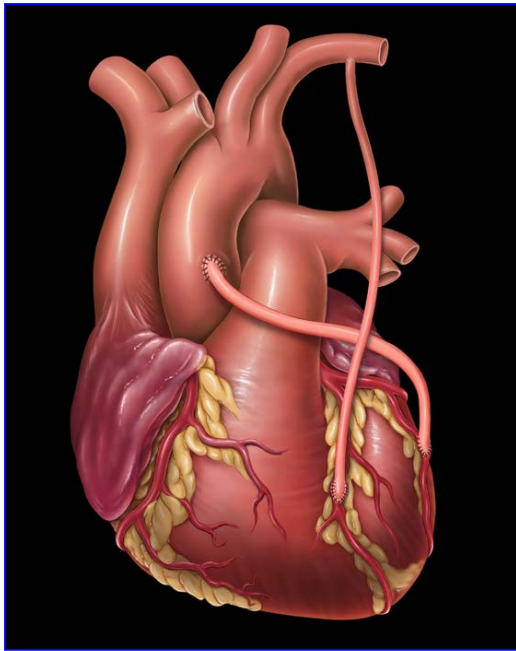
The Many Faces of MR

- Primary MR
 - Structural (degenerative) valve and sub-valvular disease
- Secondary MR
 - Functional Impairment of the LV
 - Ischemic
 - Non-Ischemic

Epidemiology of Ischemic MR

- 50% of MI's are associated with some degree of ischemic MR
- 10% of MI's are associated with moderate ischemic MR
- Ischemic MR is associated with reduced event-free survival

Surgical Treatment Options



Considerations:
CABG alone: improves LV function and MR
CABG + MVr: persistent adverse consequences of MR

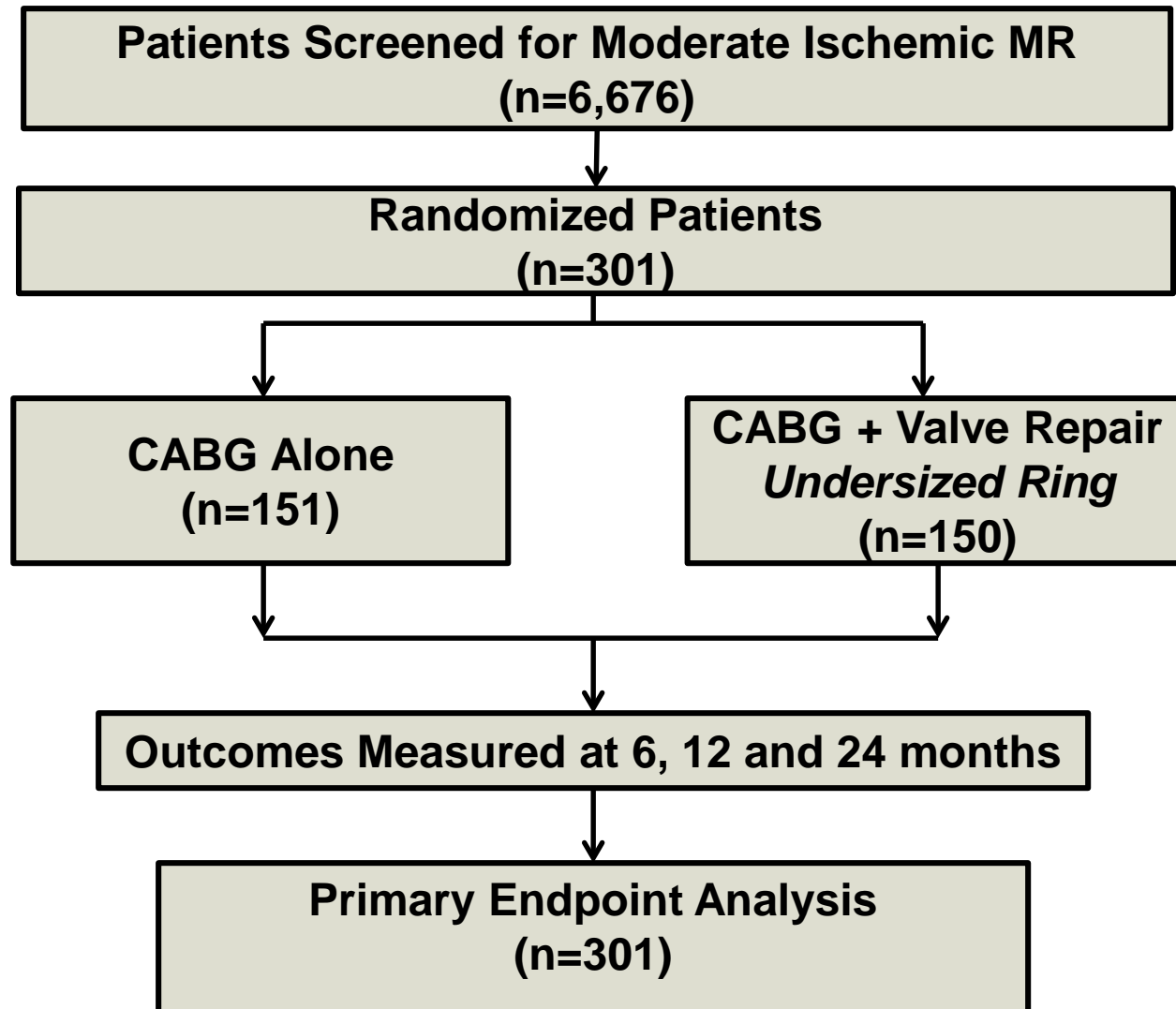
2014 AHA/ACC Guidelines

Chronic Moderate Secondary MR

Recommendations	COR	LOE
MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery	IIb	C

J Am Coll Cardiol. 2014;63(22):e57-e185. doi:10.1016/j.jacc.2014.02.536

CTSN Moderate MR Trial Design



Primary Endpoint

- Degree of left ventricular reverse remodeling as measured by changes in LVESVI
- Powered (90%) to detect a decrease in LVESVI of 12 mL/m² with repair compared to CABG alone at 12 months

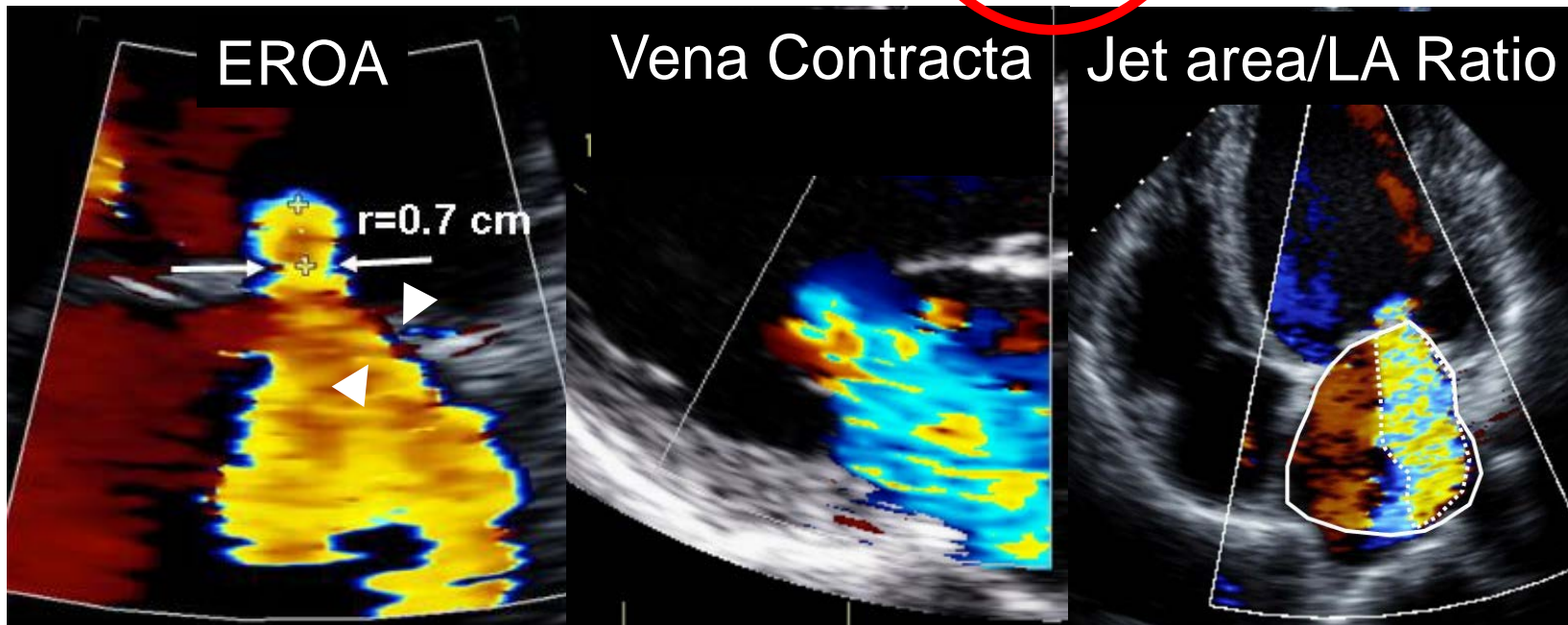
Secondary Endpoints

- MACCE
- Mortality
- Residual MR
- Serious adverse events
- Hospitalizations
- Quality of life

Integrative Method of MR Grading

(ASE Guidelines: Zoghbi W. et al. JASE 2003; 16:777-802)

Parameter	Mild	Moderate	Severe
EROA(cm ²)	<0.2	0.2 - 0.39	≥0.4
VC width (mm)	<3	3 - 6.9	≥7
Jet/LA area	<20%	20-39%	≥ 40%

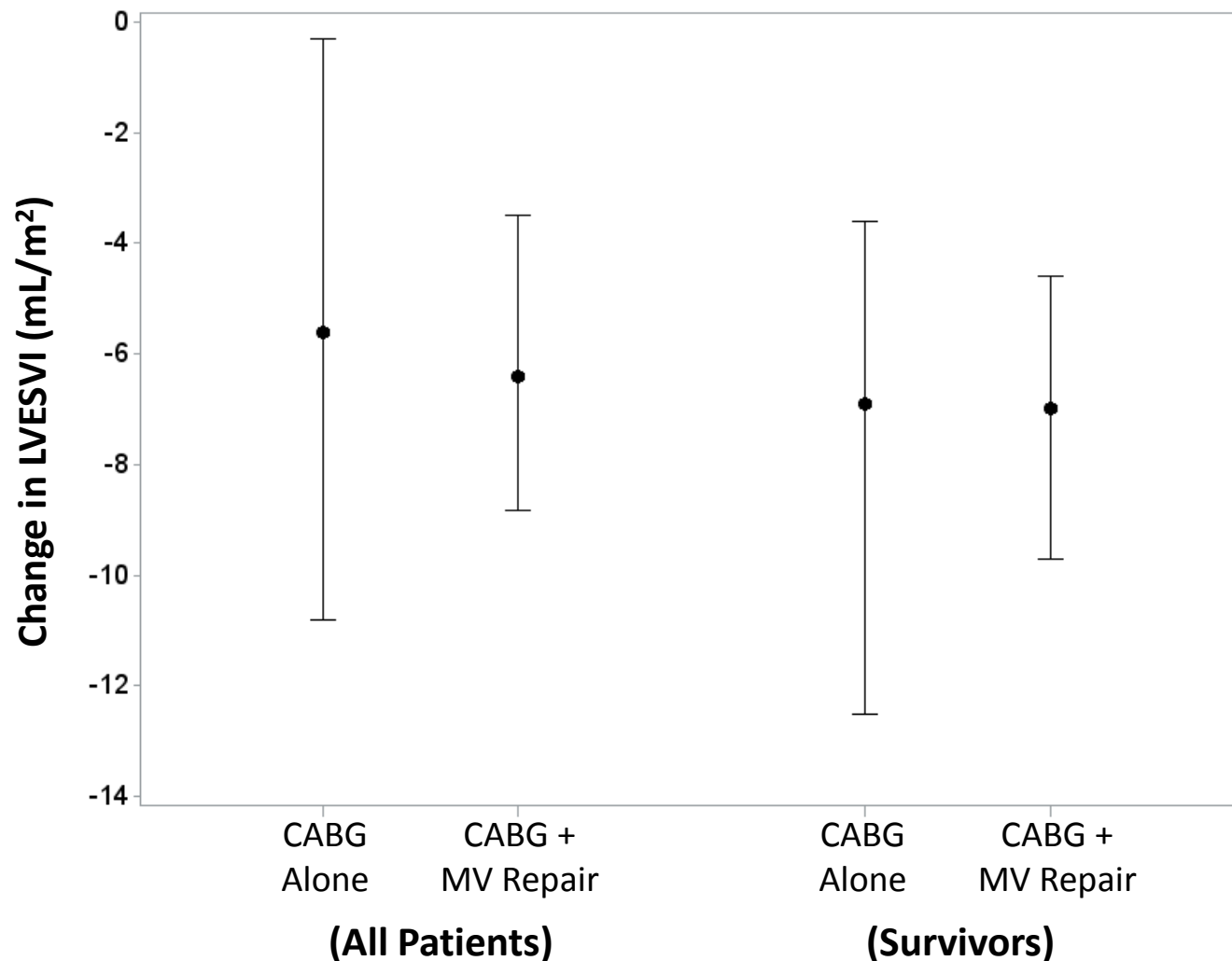


Baseline Characteristics

	CABG Alone (N=151)	CABG + Repair (N=150)
Male –no. (%)	99 (65.6)	106 (70.7)
Age (yr)	65.2 ± 11.3	64.3 ± 9.6
White –no. (%)	122 (80.8)	115 (76.7)
Hispanic–no. (%)	14 (9.3)	12 (8.0)
Diabetes –no. (%)	66 (43.7)	76 (50.7)
Medical and Surgical History –no. (%)		
Renal Insufficiency	28 (18.7)	24 (16.0)
Prior CABG	4 (2.8)	4 (2.8)
Prior PCI	24 (15.9)	26 (17.3)
Heart Failure	76 (50.3)	82 (54.7)
Myocardial Infarction	97 (64.2)	103 (68.7)
Atrial Fibrillation	35 (23.3)	19 (12.8)
ICD	6 (4.0)	6 (4.0)
Stroke	9 (6.0)	15 (10.0)

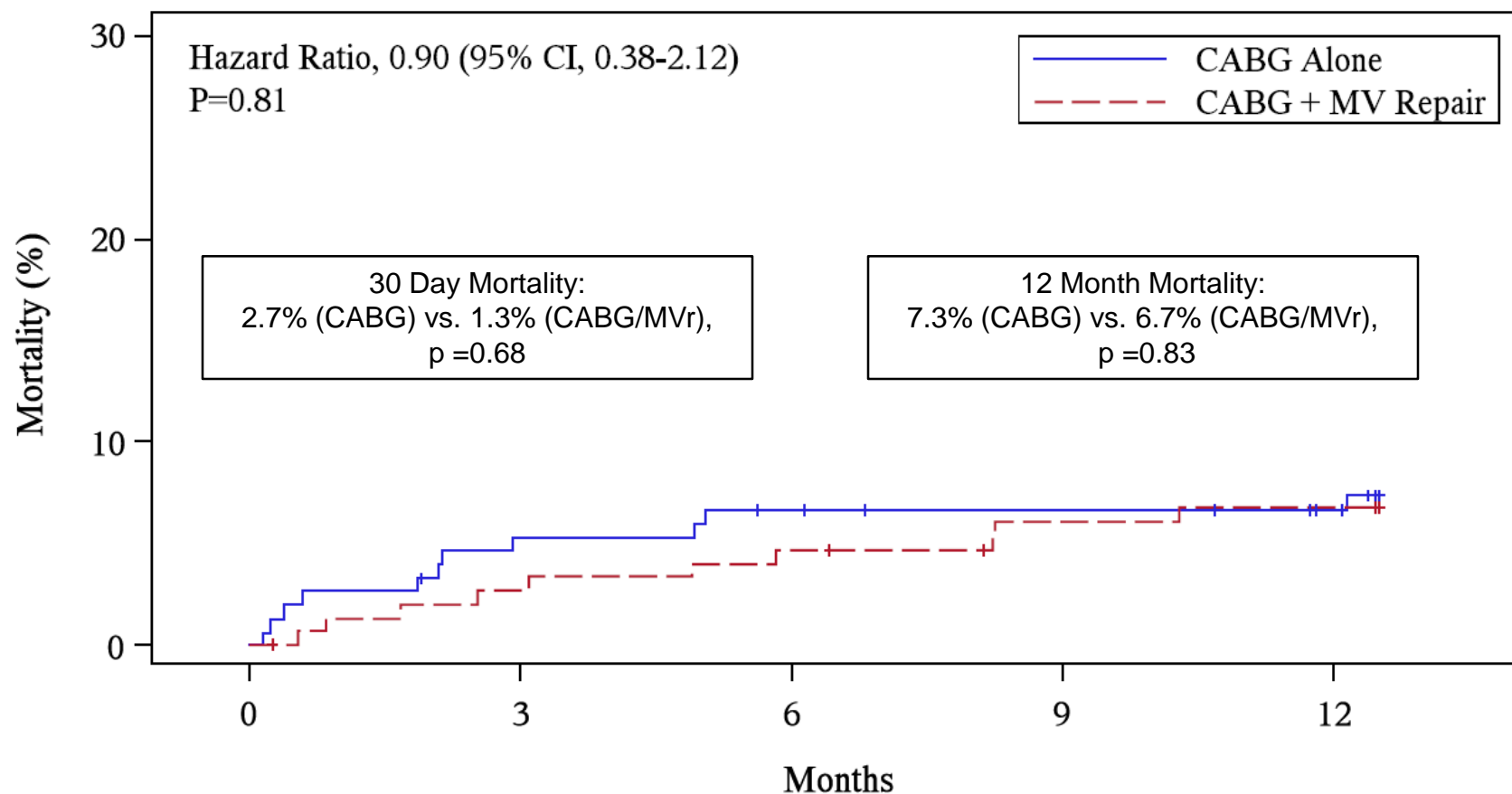
Change in LVESVI at 1 Year

Median with 95% CI for change in LVESVI (1 Year – baseline)



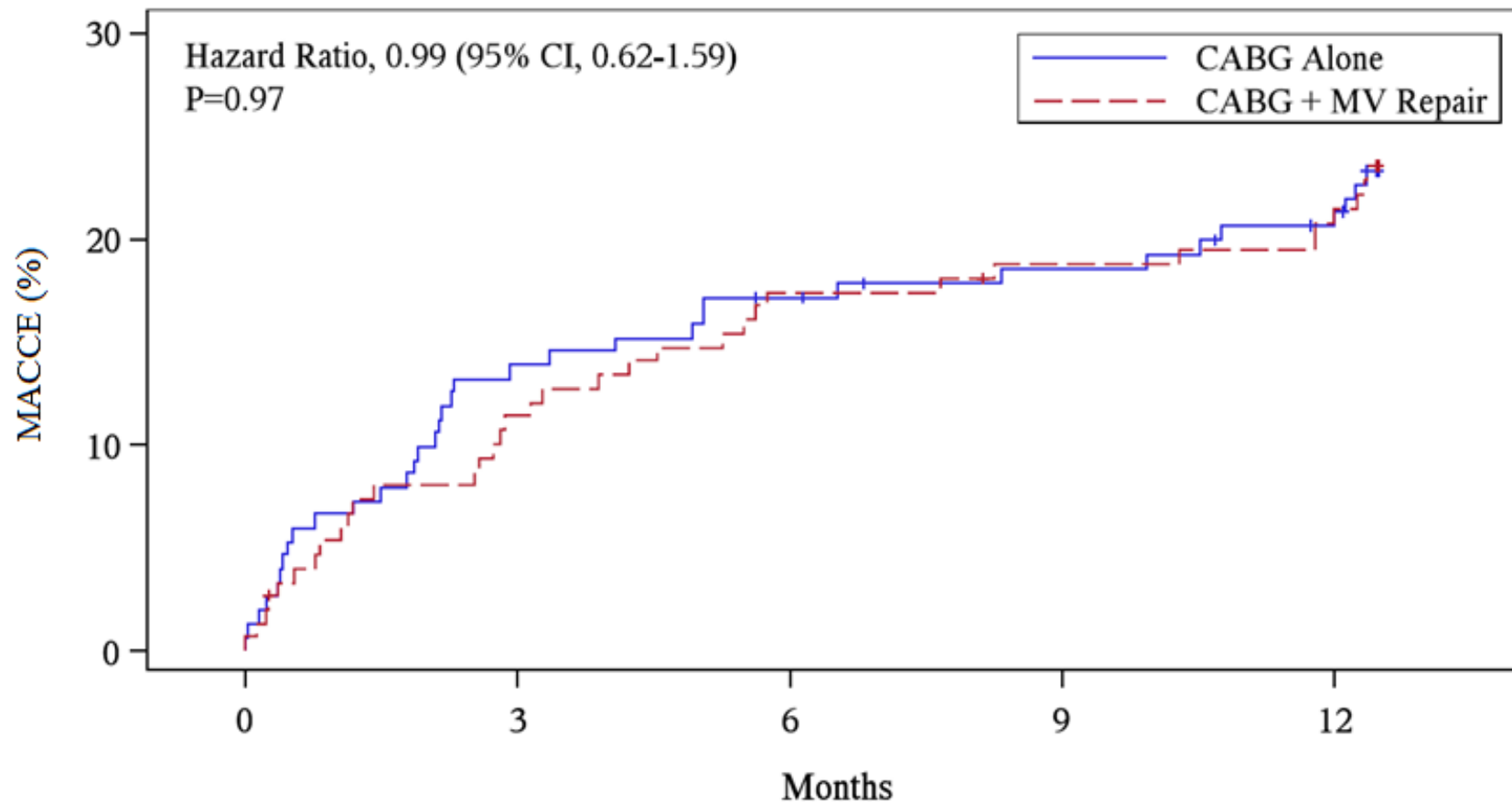
Z=0.50, p=0.61
(All patients)

Mortality



CABG Alone	151	142	139	137	134
CABG + MV Repair	150	145	142	138	137

MACCE at 12 Months



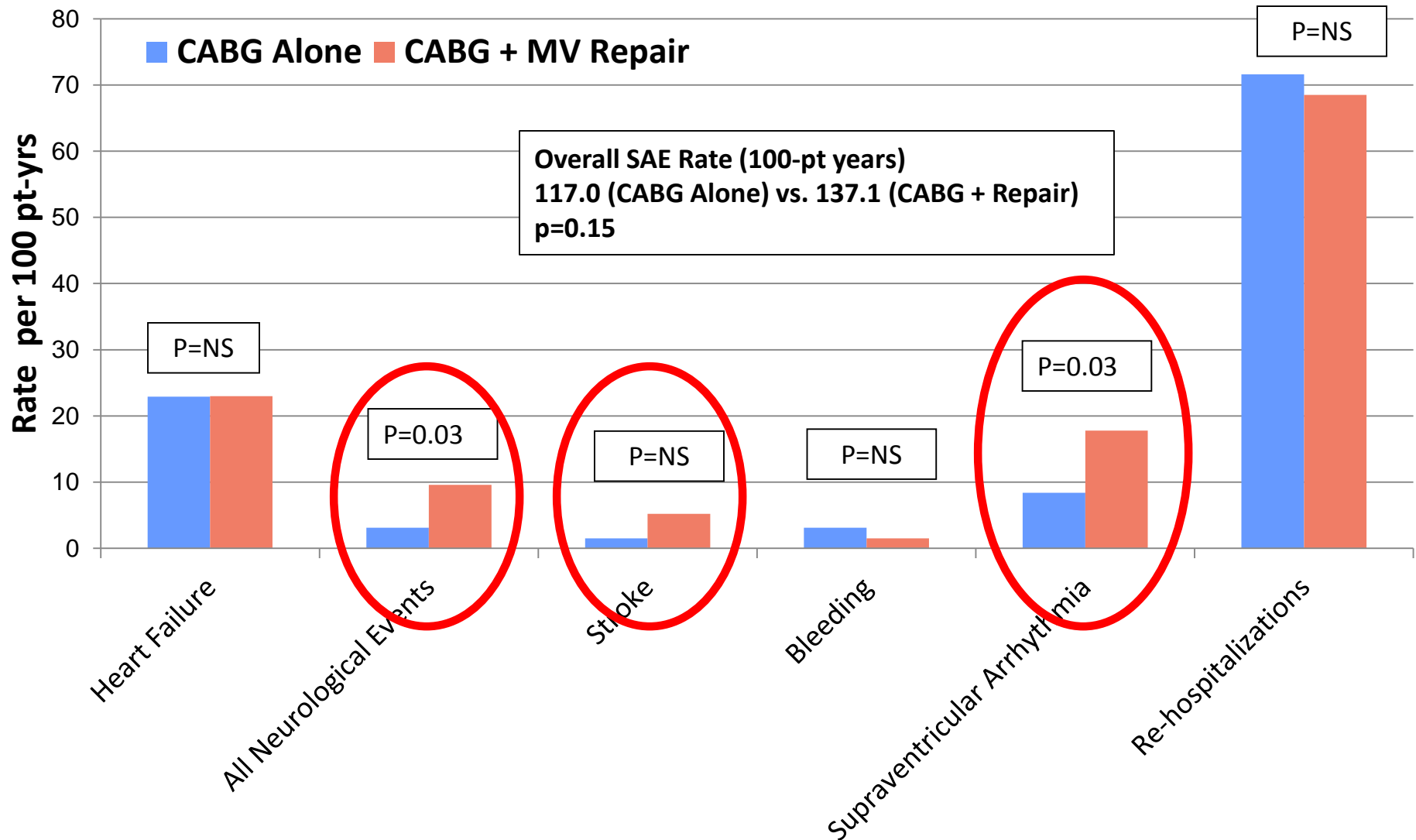
CABG Alone	151	130	124	120	114
CABG + MV Repair	150	132	123	120	116

Operative Conduct and Length of Stay

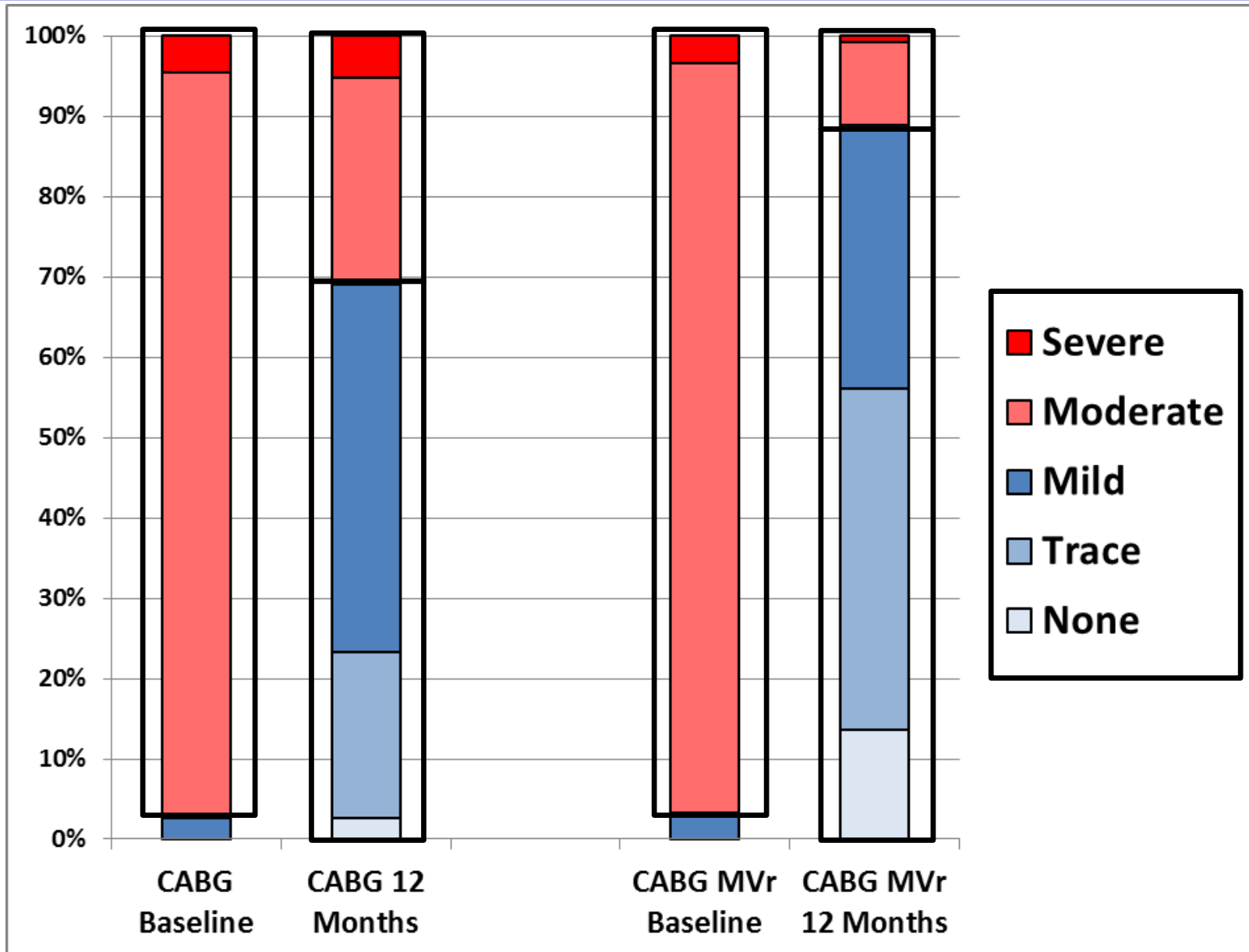
	CABG Alone	CABG + MV Repair	P-value
No. of Grafts	3.3±0.9	3.2±0.9	NS
Aortic XClamp (min)	74.7±36.7	117.2±35.4	<0.001
CPB time (min)	106.8±49.7	163.1±54.9	<0.001
ICU stay	4.0±5.7	4.8±6.1	0.006
Postoperative LOS	9.4±5.9	11.3±8.2	0.002

Data presented as mean±std

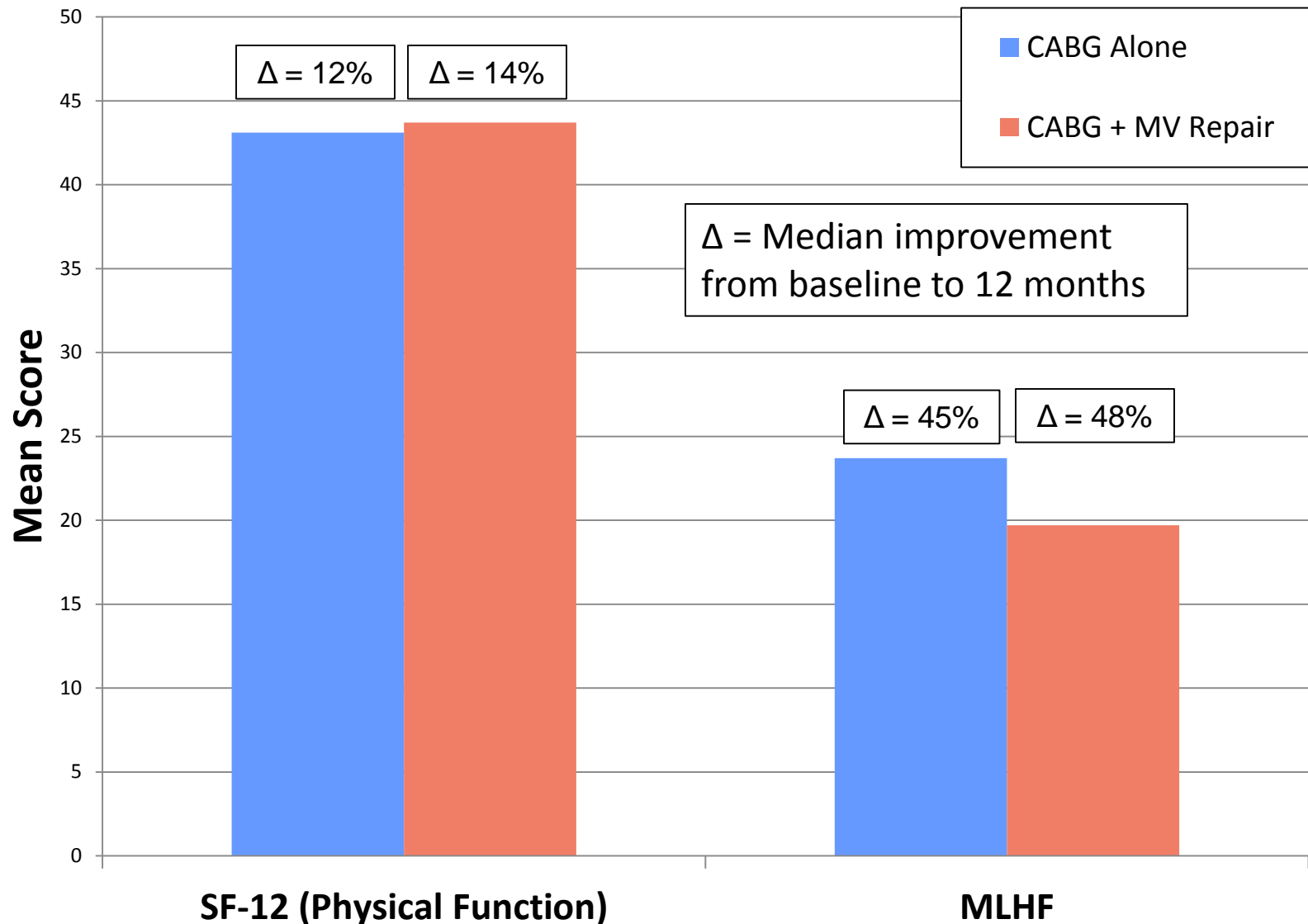
Rates of Serious Adverse Events and Re-hospitalization



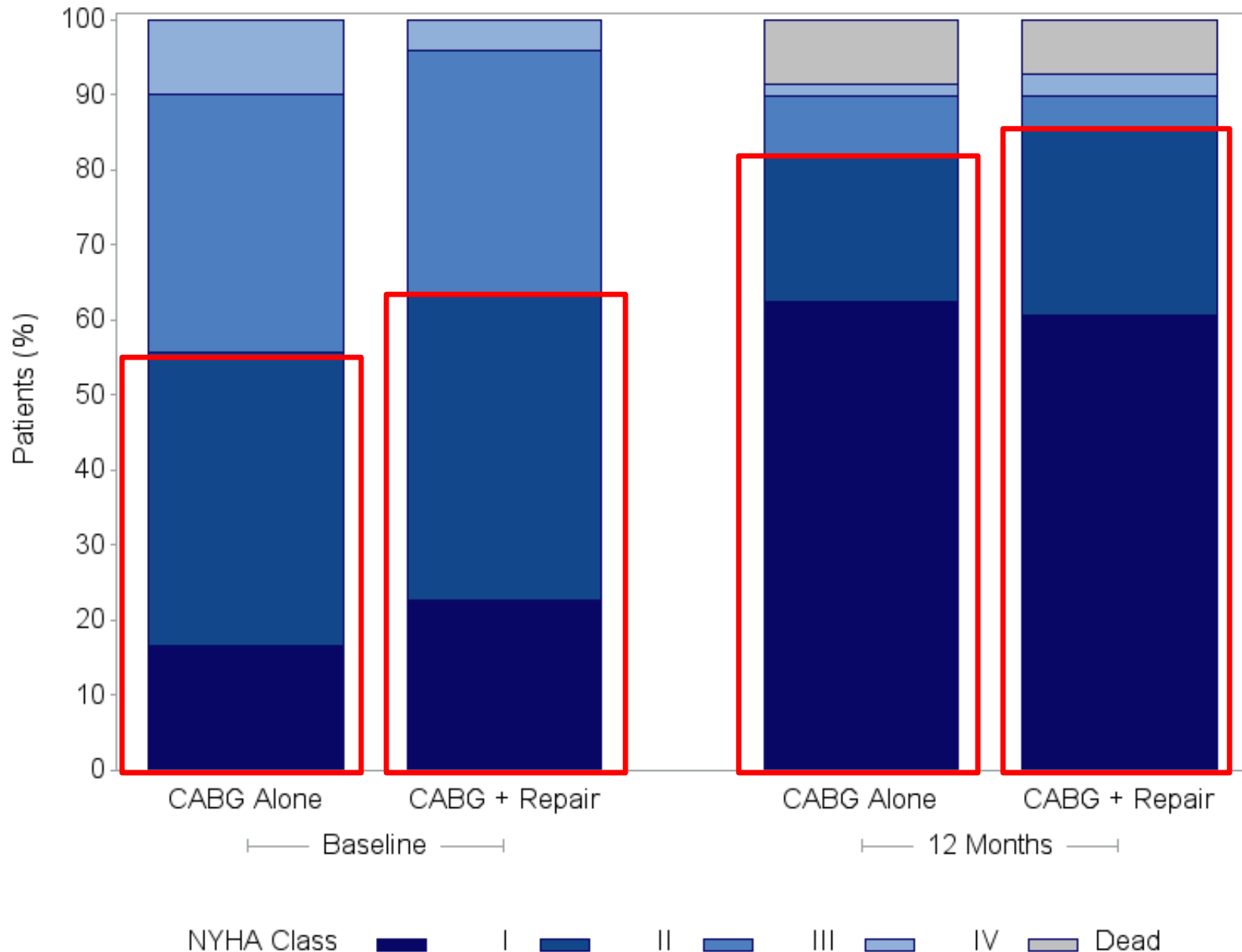
Mitral Regurgitation



Quality of Life at 1 year



NYHA Classification & Death



Unique Features

- MR was consistently measured using an integrative method in an echo core lab
 - Trial represents a study population with Moderate Ischemic MR
- 30 day and 1 year mortality excellent

Limitations

- Primary end point not a clinical endpoint
 - Trial with mortality endpoint would require several thousand patients and multiple years of follow up
- Only 1 year results reported
 - 2 year follow up pending

Summary

- No difference at 1 year:
 - in the degree of reverse remodeling
 - in mortality
 - in MACCE, hospital readmission, or QOL
- CABG + MV repair associated with more:
 - neurologic events
 - increased cross clamp and cardiopulmonary bypass time
 - longer ICU and hospital LOS
- At 1 year, higher degree of moderate and severe MR in the CABG alone group

Conclusion

- The trial did not demonstrate a clinically meaningful advantage to the routine addition of MVr to CABG
- Longer-term follow-up is ongoing
 - Will the lower incidence of moderate or severe MR at one-year translate into a net clinical benefit for patients undergoing CABG + mitral repair?

MMR Investigators

- Data Coordinating Center: InCHOIR
- Montefiore – Einstein
- Emory University
- Duke University
- Hôpital Laval
- University of Virginia Health System
- Montreal Heart Institute
- University of Pennsylvania
- Columbia University Medical Center
- Cleveland Clinic Foundation
- University of Maryland
- Brigham and Women's Hospital
- Sacré-Cœur de Montréal
- Ohio State University Medical Center
- East Carolina Heart Institute
- Wellstar / Kennestone
- Baylor Research Institute
- University of Southern California
- St. Michael's Hospital
- Toronto General Hospital
- Mission Hospital
- NIH Heart Center at Suburban Hospital
- Inova Heart & Vascular Institute
- University of Alberta Hospital
- Centre Hospitalier de l'Université de Montréal
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- Aarhus University

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 - Canadian Institutes for Health Research



National Institutes of Health

National Heart, Lung, and Blood Institute
National Institute of Neurological Disorders and Stroke



CIHR IRSC
Canadian Institutes of Health Research
Institut de recherche en santé du Canada



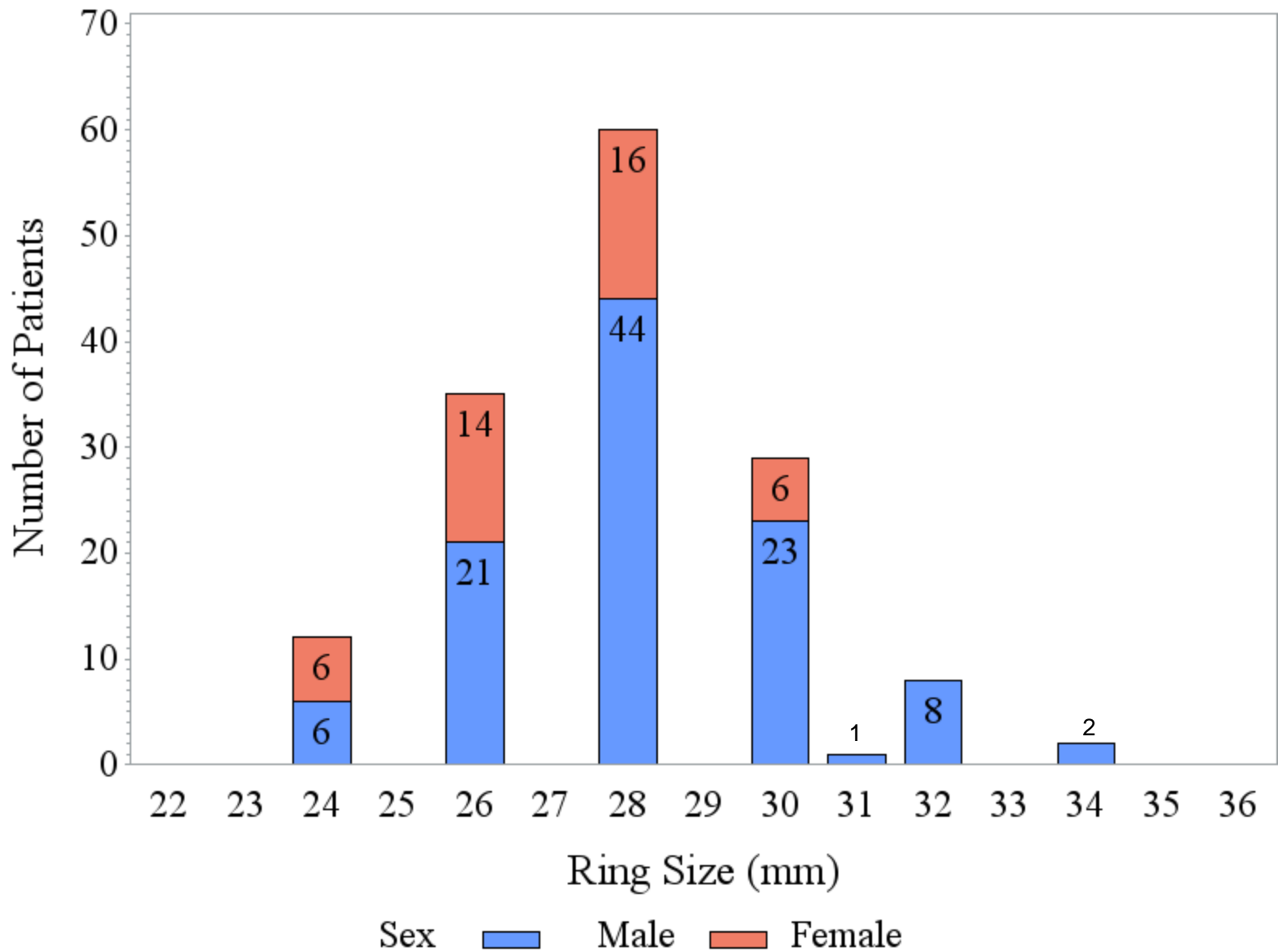
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ORIGINAL ARTICLE

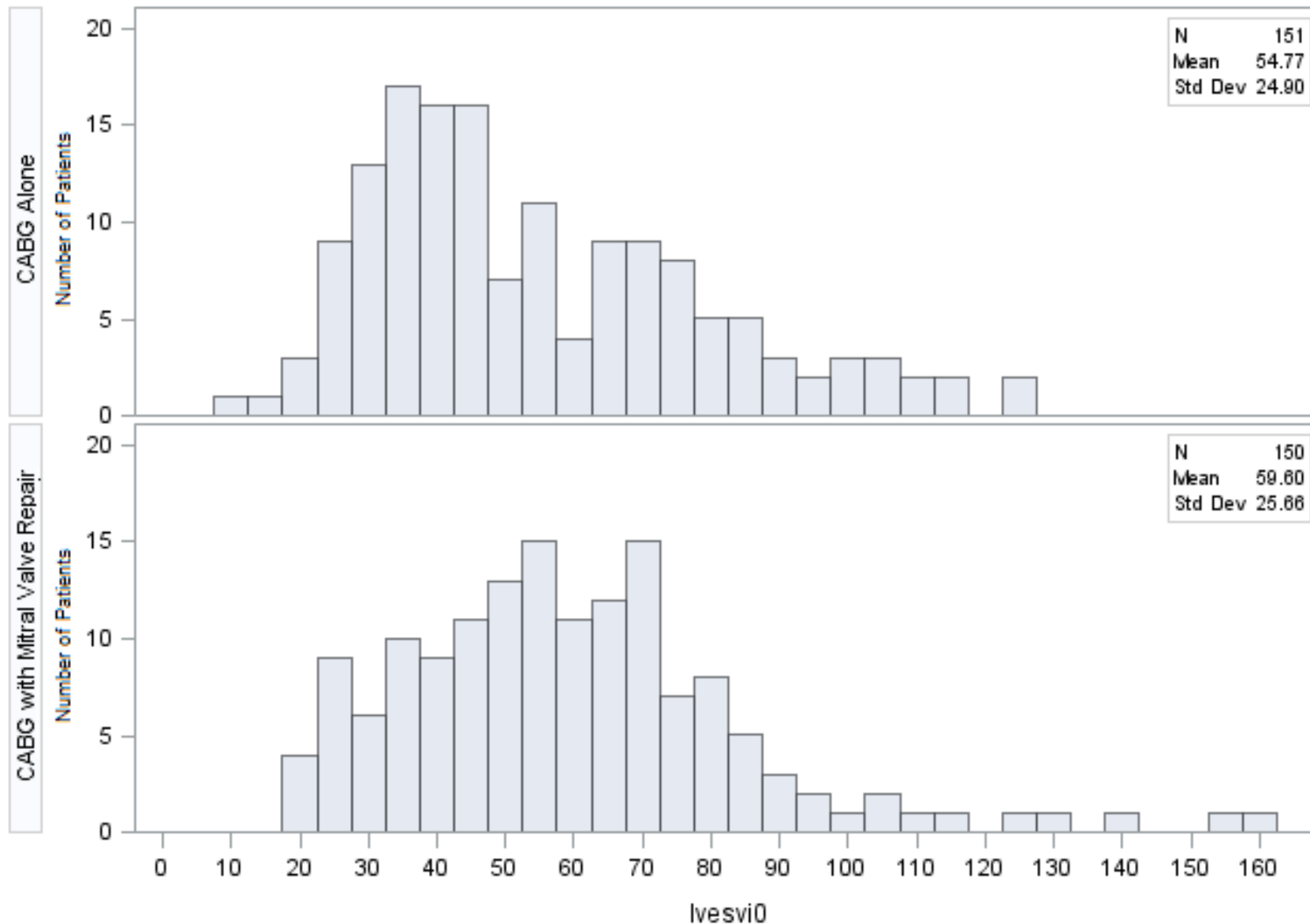
Surgical Treatment of Moderate Ischemic Mitral Regurgitation

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Distribution of Ring Size



LVESVI Distribution at Baseline



History of MI and LVESVI Change

		12 Month LVESVI – Baseline LVESVI					
		N	Mean	<u>Std</u>	Median	Min	Max
History of MI	Randomization Assignment						
No	CABG Alone	45	-11.31	22.46	-8.90	-78.80	40.10
	CABG with Mitral Valve Repair	38	-5.75	17.12	-4.30	-44.10	32.80
Yes	CABG Alone	72	-7.93	23.39	-5.55	-78.90	71.80
	CABG with Mitral Valve Repair	88	-11.05	25.51	-8.85	-96.20	133.00

MR at 1 Year and LVESVI Change

			N	Mean	Std	Median	Min	Max
	MR at 12 Months							
CABG Alone	None, Trace or Mild	Baseline LVESVI	80	59.62	26.30	55.80	16.00	124.90
		12 Month LVESVI	80	44.48	19.68	40.50	17.40	104.50
		Change (12 Month – Baseline)	80	-15.14	22.53	-10.40	-78.90	21.40
	Moderate or Severe	Baseline LVESVI	36	46.48	19.34	41.60	10.20	115.60
		12 Month LVESVI	36	50.44	26.71	47.70	14.00	141.00
		Change (12 Month – Baseline)	36	3.97	18.65	0.50	-16.20	71.80
CABG with Mitral Valve Repair	None, Trace or Mild	Baseline LVESVI	111	56.92	24.00	54.10	19.00	139.10
		12 Month LVESVI	111	45.08	21.39	39.60	15.00	121.50
		Change (12 Month – Baseline)	111	-11.84	19.93	-7.90	-96.20	32.80
	Moderate or Severe	Baseline LVESVI	14	73.33	32.72	68.05	33.90	161.00
		12 Month LVESVI	14	82.62	66.53	63.20	33.70	294.00
		Change (12 Month – Baseline)	14	9.29	38.21	0.50	-32.20	133.00