Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Michler RE, Smith PK, Parides MK, et al. Two-year outcomes of surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med. DOI: 10.1056/NEJMoa1602003

SUPPLEMENTARY APPENDICES

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Cardiothoracic Surgical Trials Network (CTSN)

The members of the Cardiothoracic Surgical Trials Network (CTSN) involved in this study are as follows:

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Canadian Institutes of Health Research: Ilana Kogan Gombos, Jennifer Ralph;

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Protocol Review Committee: David A. Bull (Chair); Patrice Desvigne-Nickens, Executive Secretary; Dennis O. Dixon, Mark Haigney, Richard Holubkov, Alice Jacobs, Frank Miller, John M. Murkin, John Spertus, Andrew S. Wechsler;

Data and Safety Monitoring Board: Frank Sellke (Chair); Cheryl L. McDonald, Executive Secretary; Robert Byington, Neal Dickert, Dennis O. Dixon, John S. Ikonomidis, David O. Williams, Clyde W. Yancy;

Medical Monitors: James C. Fang, Nadia Giannetti, Wayne Richenbacher;

Overall Event Adjudication Committee: Vivek Rao (Chair); Karen L. Furie, Rachel Miller, Sean Pinney, William C. Roberts, Mary N. Walsh;

Cardiopulmonary Exercise Core Lab, Henry Ford Hospital: Stephen J. Keteyian, Clinton A. Brawner, Heather Aldred;
Echo Core Lab, Massachusetts General Hospital: Judy Hung, Xin Zeng;

Neurocognitive Core Lab, Duke University Medical Center: Joseph P. Mathew, Jeffrey Browndyke, Yanne Toulgoat-Dubois.

**John D. Puskas has subsequently moved to Mount Sinai Beth Israel, New York*

Characterization of Patient Population
The patient population for this trial consists of patients with moderate ischemic mitral regurgitation and clinically significant coronary artery disease with a clinical indication for coronary artery bypass grafting (CABG). All patients who meet the eligibility criteria may be included in the study regardless of gender, race or ethnicity.

Inclusion Criteria

1. Moderate mitral regurgitation in the judgment of the clinical site echocardiographer, assessed by transthoracic echocardiogram. Assessment of mitral regurgitation will be performed using an integrative method (Zoghbi W. et al. J. American Society of Echocardiography. 2003:16:777-802. see appendix). Quantitative guidelines as proposed would be: ERO between 0.2 cmsq to 0.39 cmsq. If ERO < 0.2, then the degree of mitral regurgitation will be guided by other color Doppler quantitative methods (jet area/left atrial area ratio, vena contracta, supportive criteria in an integrated fashion (See Appendix I).

2. Coronary artery disease amenable to coronary artery bypass grafting and a clinical indication for revascularization

3. Age ≥ 18 years

4. Able to sign Informed Consent and Release of Medical Information forms

Exclusion Criteria

1. Any evidence of structural (chordal or leaflet) mitral valve disease

2. Inability to derive ERO and ESVI by transthoracic echocardiography

3. Planned concomitant intra-operative procedures (with the exception of closure of patent foramen ovale [PFO] or atrial septal defect [ASD], left atrial appendage ligation/excision or Maze procedure)

4. Prior surgical or percutaneous mitral valve intervention

5. Contraindication to cardiopulmonary bypass (CPB)

6. Clinical signs of cardiogenic shock at the time of randomization

7. Treatment with chronic intravenous inotropic therapy at the time of randomization

8. Severe, irreversible pulmonary hypertension in the judgment of the investigator

9. ST segment elevation MI requiring intervention within 7 days prior to randomization

10. Congenital heart disease (except PFO or ASD)

11. Evidence of cirrhosis or hepatic synthetic failure

12. Recent history of psychiatric disease (including drug or alcohol abuse) that is likely to impair compliance with the study protocol, in the judgment of the investigator

13. Therapy with an investigational intervention at the time of screening, or plan to enroll patient in additional investigational intervention study during participation in this trial

14. Any concurrent disease with life expectancy < 2 years

15. Pregnancy at the time of randomization

Figure S1 Consort Diagram

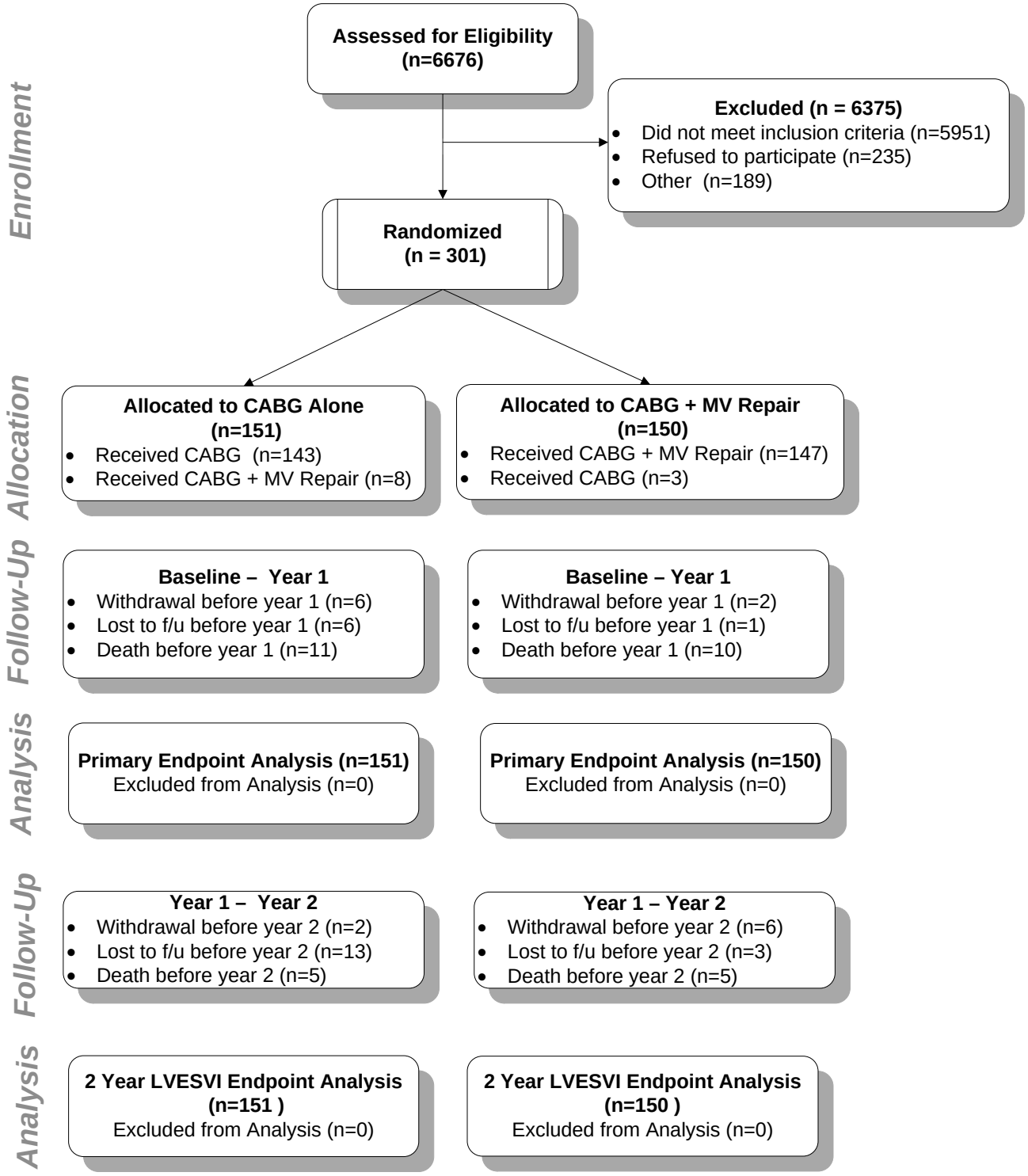


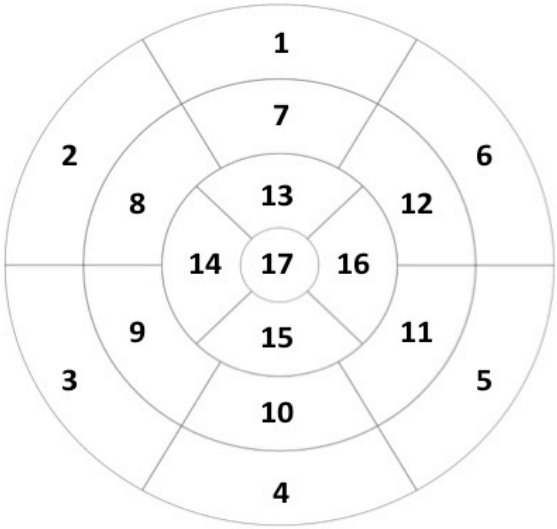
Table S1. Baseline and Operative Characteristics of the Patients*

Characteristic	CABG Alone (N=151)	CABG + MV Repair (N=150)	P-value
Male	99 (65.6)	106 (70.7)	0.34
Age (yr)	65.2 ± 11.3	64.3 ± 9.6	0.49
White	122 (80.8)	115 (76.7)	0.38
Hispanic	14 (9.3)	12 (8.0)	0.69
Diabetes	66 (43.7)	76 (50.7)	0.23
Renal Insufficiency	27/150 (18.0)	24 (16.0)	0.64
Prior CABG	4 (2.8)	4 (2.8)	1.00
Prior PCI	24 (15.9)	26 (17.3)	0.74
Heart Failure	75 (50.0)	82 (54.7)	0.39
Myocardial Infarction	97 (64.2)	103 (68.7)	0.42
Atrial Fibrillation	35/150 (23.3)	19/149 (12.8)	0.02
ICD	6 (4.0)	6 (4.0)	0.99
Stroke	9 (6.0)	15 (10.0)	0.20
LVESVI (ml/m^2)	54.8 (24.9)	59.6 (25.7)	0.10
LVEF (%)	41.2 ± 11.6	39.3 ± 10.9	0.13
EROA (cm^2)	0.2 ± 0.1	0.2 ± 0.1	0.17
BSA (m^2)	1.9 ± 0.2	1.9 ± 0.3	0.93
Angina Scale (CCSC)[‡] – None	45/150 (30.0)	50/149 (33.6)	0.77
Angina Scale (CCSC)[‡] – Class III & IV	51/150 (34.0)	46/149 (30.9)	
NYHA[‡] – Class III & IV	67 (44.4)	55 (36.7)	0.17
MLHF[‡]	43.0 ± 27.2	40.4 ± 27.5	0.44
Concomitant procedure – LAA Management	8 (5.3)	12 (8.0)	0.35
Concomitant procedure – Atrial Maze	10 (6.6)	11 (7.3)	0.81
Number of Grafts	3.3 ± 0.9	3.2 ± 0.9	0.26
Aortic Cross Clamp Time (minutes)	74.7 ±36.7	117.1 ± 35.4	<0.001
Cardiopulmonary Bypass Time (minutes)	106.8 ±49.7	163.1 ±54.9	<0.001

*Plus-minus values are means ± SD, categorical values are n (%); [‡]CSCC = Canadian Cardiovascular Society Classification; NYHA = Median New York Heart Association Functional Class: 1(best) – 4 (worst); MLHF= Minnesota Living with Heart Failure questionnaire: 0 (best) – 105 (worst)

Wall Motion Segments

This figure depicts the 17 segment model of wall motion scores. We considered segments 3, 4, 5, 9, 10, 11 and 15 as the inferior-posterior-lateral segments, which are the segments correspond to the right coronary and circunflex distribution that supply the papillary muscles.



1- Basal anterior
2- Basal anteroseptal
3- Basal inferoseptal
4- Basal inferior
5-Basal Inferolateral
6- Basal anterolateral
7- Mid anterior
8- Mid anteroseptal
9- Mid inferoseptal
10- Mid inferior
11-Mid Inferolateral
12- Mid anterolateral
13-Apical anterior
14- Apical septal
15- Apical inferior
16- Apical lateral
17- Apex