

SURGICAL ABLATION OF ATRIAL FIBRILLATION DURING MITRAL VALVE SURGERY

THE CARDIOTHORACIC SURGICAL TRIALS NETWORK

Marc Gillinov, M.D.

For the CTSN Investigators

**ACC Late Breaking Clinical Trials
March 16, 2015**



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



Disclosures

- **Consultant/Speaker**
 - AtriCure
 - Medtronic
 - On-X
 - Edwards
 - Tendyne
- **Research Funding**
 - St. Jude Medical
- **Equity Interest**
 - Clear Catheter
- **Cleveland Clinic**
 - Right to receive royalties from AtriCure for a left atrial appendage occlusion device

AF and Mitral Valve Surgery Patients

Case Study

- 69 year old woman
- 4+ MR (Degenerative Disease)
- Long-standing persistent AF
- NYHA Class 2

How should the surgeon treat the AF?

2014 AHA/ACC/HRS Guidelines

Surgical AF Ablation

Recommendation	COR	LOE
An AF surgical ablation procedure is reasonable for selected patients with AF undergoing cardiac surgery for other indications	Ia	C

J Am Coll Cardiol. 2014;64(21):2246-80

Clinical Trial

Purpose

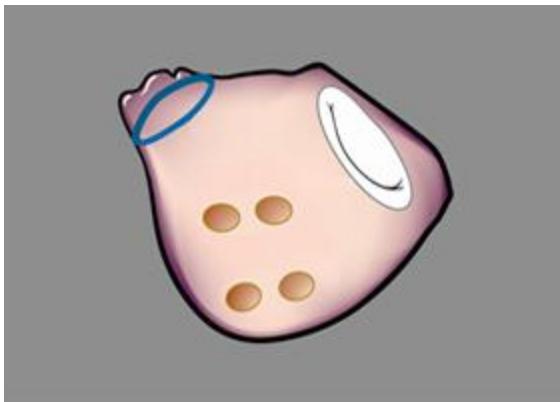
- **To assess the safety and effectiveness of ablation in patients presenting for mitral valve surgery who have persistent or long-standing persistent AF**
- **To compare two different lesion sets**
 - ✓ **Pulmonary vein isolation (PVI)**
 - ✓ **Biatrial Maze**

Persistent and Long-Standing Persistent AF

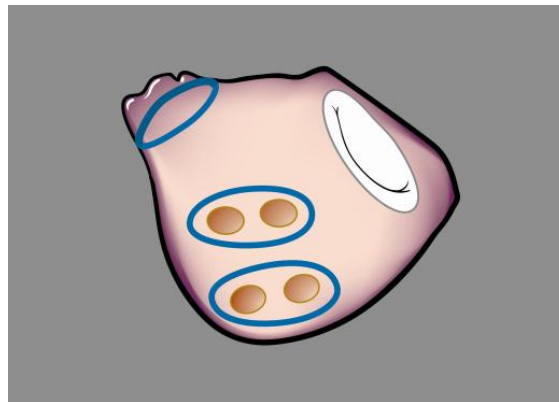
- **Persistent AF**
 - **Non-self-terminating AF lasting more than 7 days or less than 7 days if cardioverted**
- **Long-Standing Persistent AF**
 - **Continuous AF of more than one year's duration**

Surgical Ablation Options

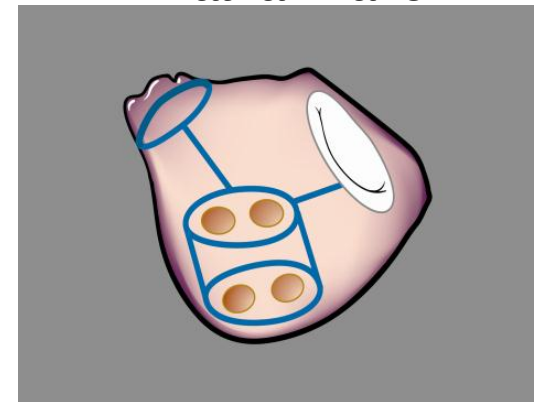
No Ablation



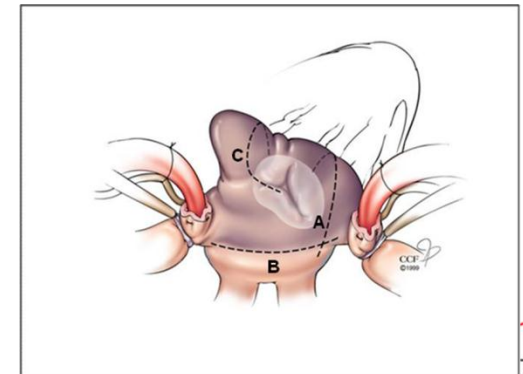
PVI



Bilateral Maze



LAA closure performed in all patients



Primary Endpoint

- Freedom from AF at both 6 and 12 months by 3-day Holter monitor
- Powered (90%) to detect an increase of 20% in the proportion of patients free of AF with ablation therapy
- Pts who died before 12 month assessment or had subsequent ablation were considered treatment failures

Secondary Endpoints

- Mortality
- MACCE
- Quality of life
- Serious adverse events

CTSN Surgical AF Ablation Trial Design

Enrollment

Assessed for Eligibility
(n=3502)

Excluded (n=3242)

Randomized (n=260)

Allocation

Allocated to MVS Alone (n=127)

Allocated to MVS + Ablation (n=133)

- Pulmonary Vein Isolation (PVI) (n=67)
- Biatrial Maze (n=66)

Follow-Up

- Withdrawal or lost to follow-up (n=10)
- Death before month 12 (n=11)

- Withdrawal or lost to follow-up (n=8)
- Death before month 12 (n=9)

Analysis

Primary Endpoint Analysis (n=127)

- **Primary Endpoint Data (n=102)**
 - 6 & 12 Month Holter (n=88)
 - Died (n=11)
 - Underwent Ablation (n=3)
- **Imputed (n=25)**

Primary Endpoint Analysis (n=133)

- **Primary Endpoint Data (n=106)**
 - 6 & 12 Month Holter (n=96)
 - Died (n=9)
 - Underwent Ablation (n=1)
- **Imputed (n=27)**

Baseline Characteristics

	MVS Alone (N=127)	MVS & Ablation (N=133)
Female –no. (%)	63 (49.6)	57 (42.9)
Age (yr)	69.4 ± 10.0	69.7 ± 10.4
NYHA Class III & IV –no. (%)	62 (49.2)	56 (42.1)
Atrial fibrillation duration –med (IQR)	29 (3, 96)	18.5 (3, 65)
Atrial fibrillation type	28 (18.7)	24 (16.0)
Longstanding Persistent	71 (55.9)	70 (52.6)
Persistent	56 (44.1)	63 (47.4)
Anticoagulants –no. (%)	97 (76.4)	105 (79.0)
Anti-arrhythmic Drugs (Class III)	15 (11.8)	14 (10.5)
Mitral disease etiology		
Organic	73 (57.5)	75 (56.4)
Functional non-ischemic	48 (37.8)	43 (32.3)
Ischemic	6 (4.7)	15 (11.3)

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Operative Characteristics

	MVS Alone (N=127)	MVS & Ablation (N=133)
Mitral Valve Surgery		
Replacement	61 (48.4)	54 (40.6)
Repair	65 (51.6)	79 (59.4)
Concomitant Procedures		
Tricuspid Valve Surgery	48 (38.1)	50 (37.6)
Aortic Valve Replacement	20 (15.9)	14 (10.5)
CABG	25 (19.8)	27 (20.3)
Cardiopulmonary Bypass Time (min)*	132.5 $\pm$ 51	147.8 $\pm$ 63.3
Cross-Clamp Time (min)	95.9 $\pm$ 36.3	102.9 $\pm$ 41.5

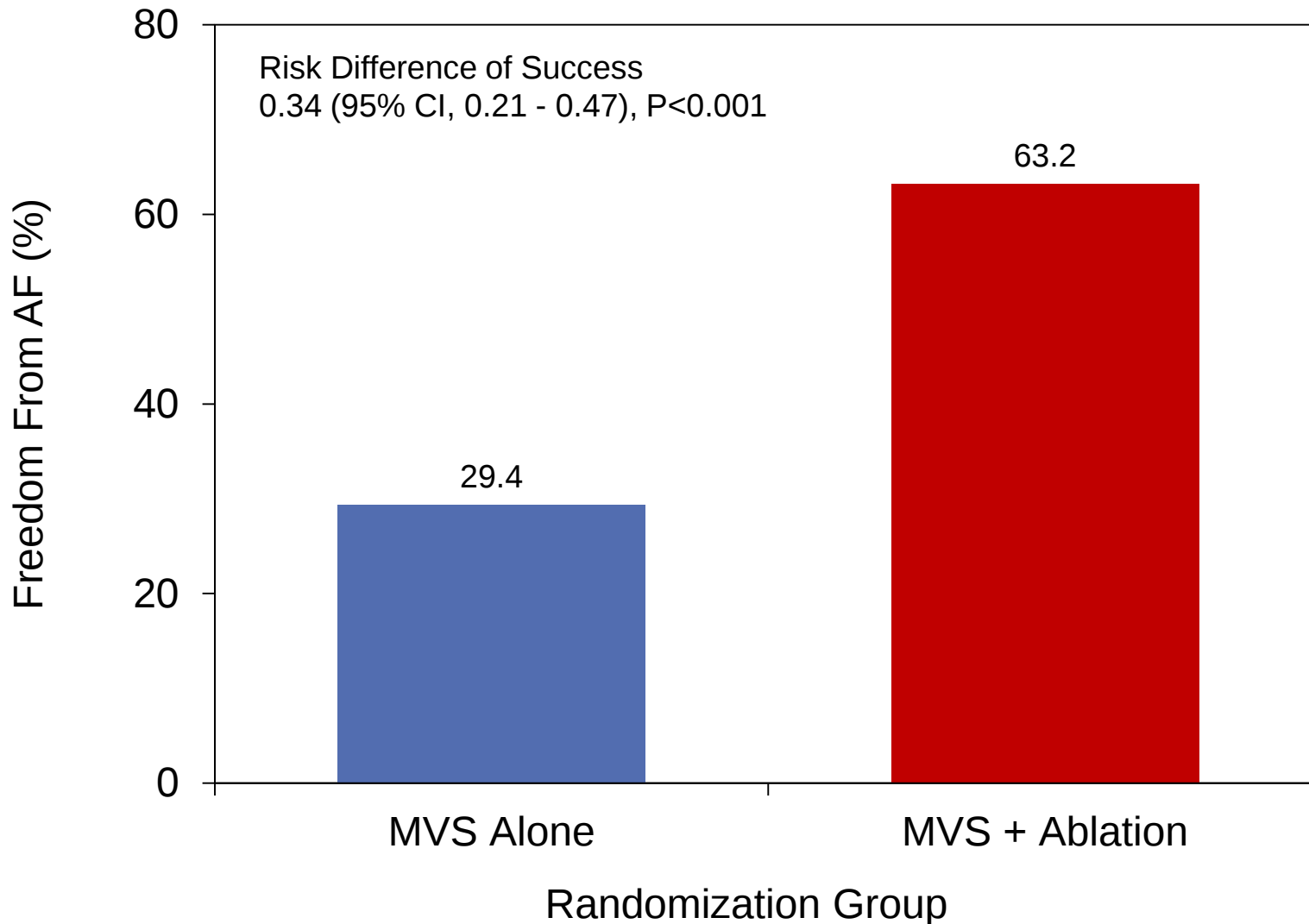
*P-Value for Cardiopulmonary Bypass Time = 0.03

Operative Characteristics

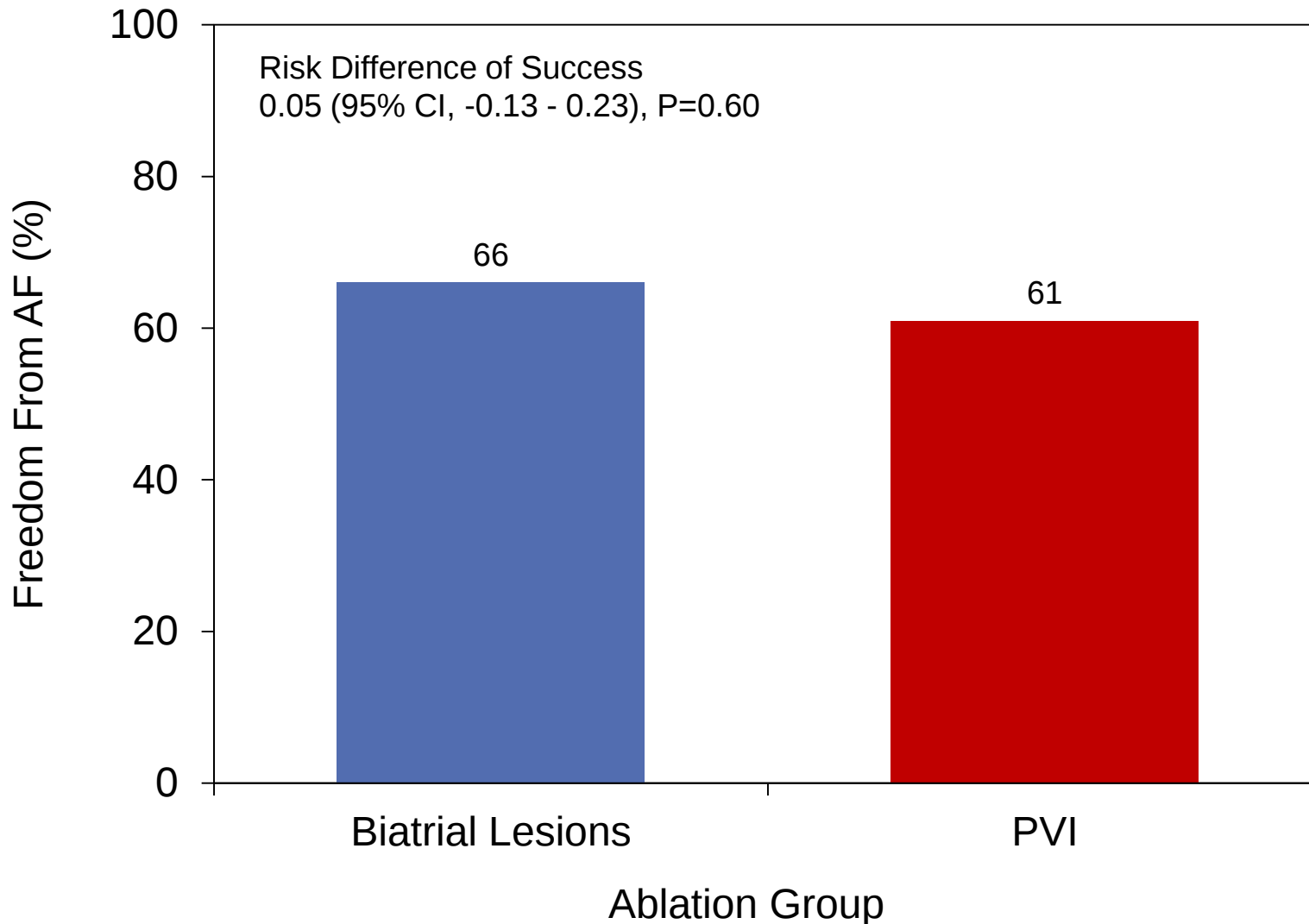
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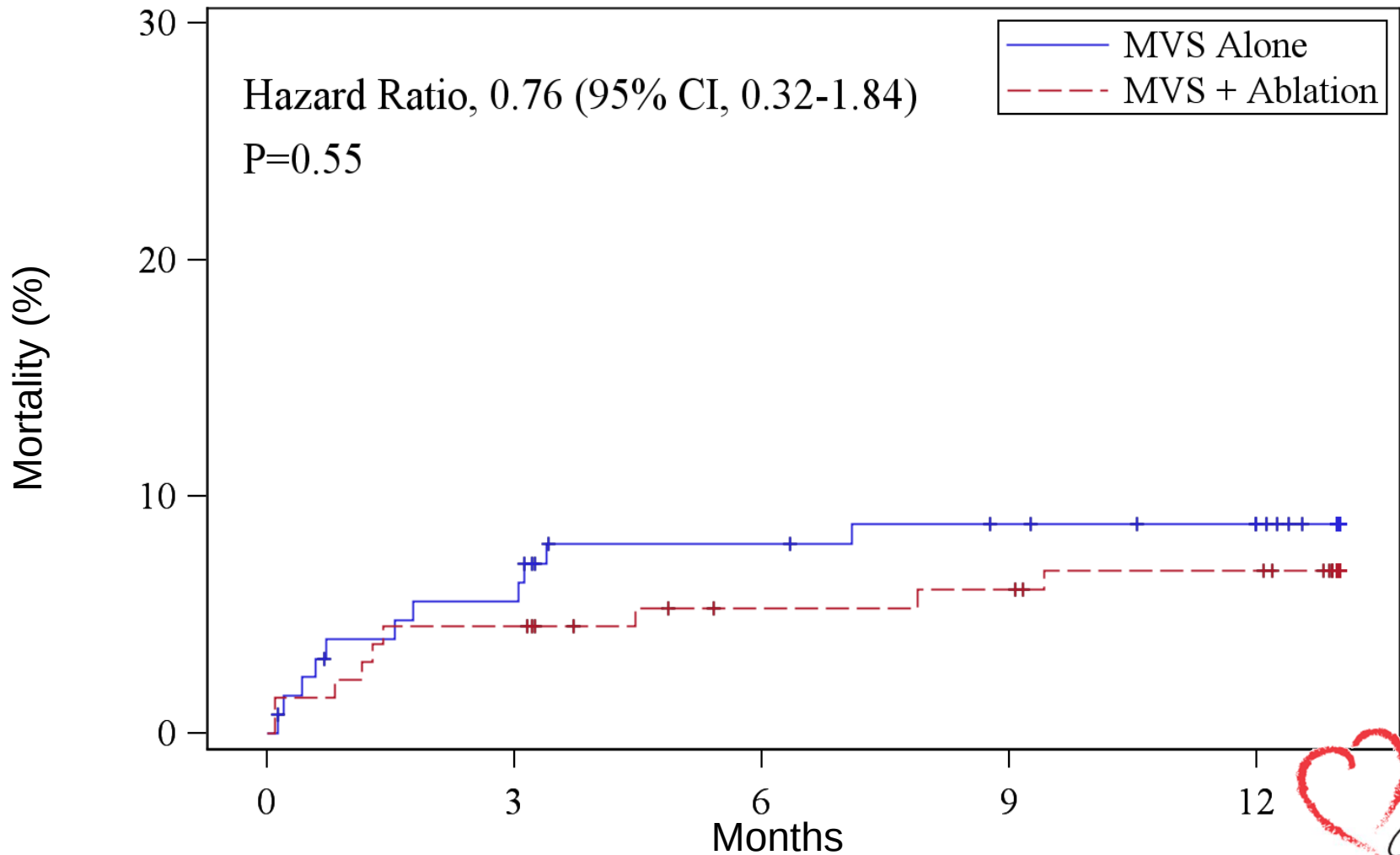
Primary Endpoint



Biatrial Maze vs. PVI



Mortality



MVS Alone

127

118

111

108

104

MVS + Ablation

133

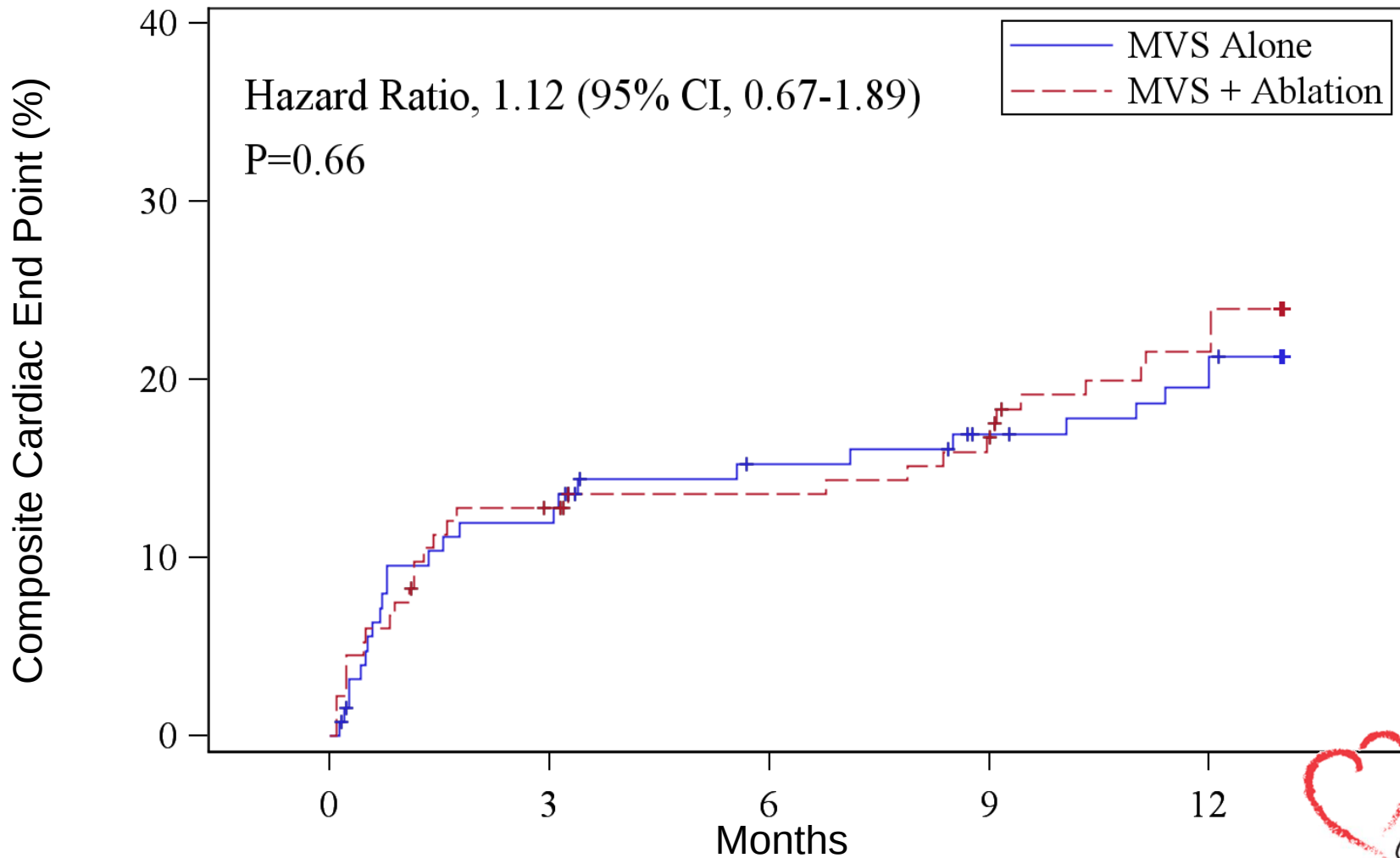
127

120

119

116

MACCE



MVS Alone

127

110

101

96

90

MVS + Ablation

133

114

110

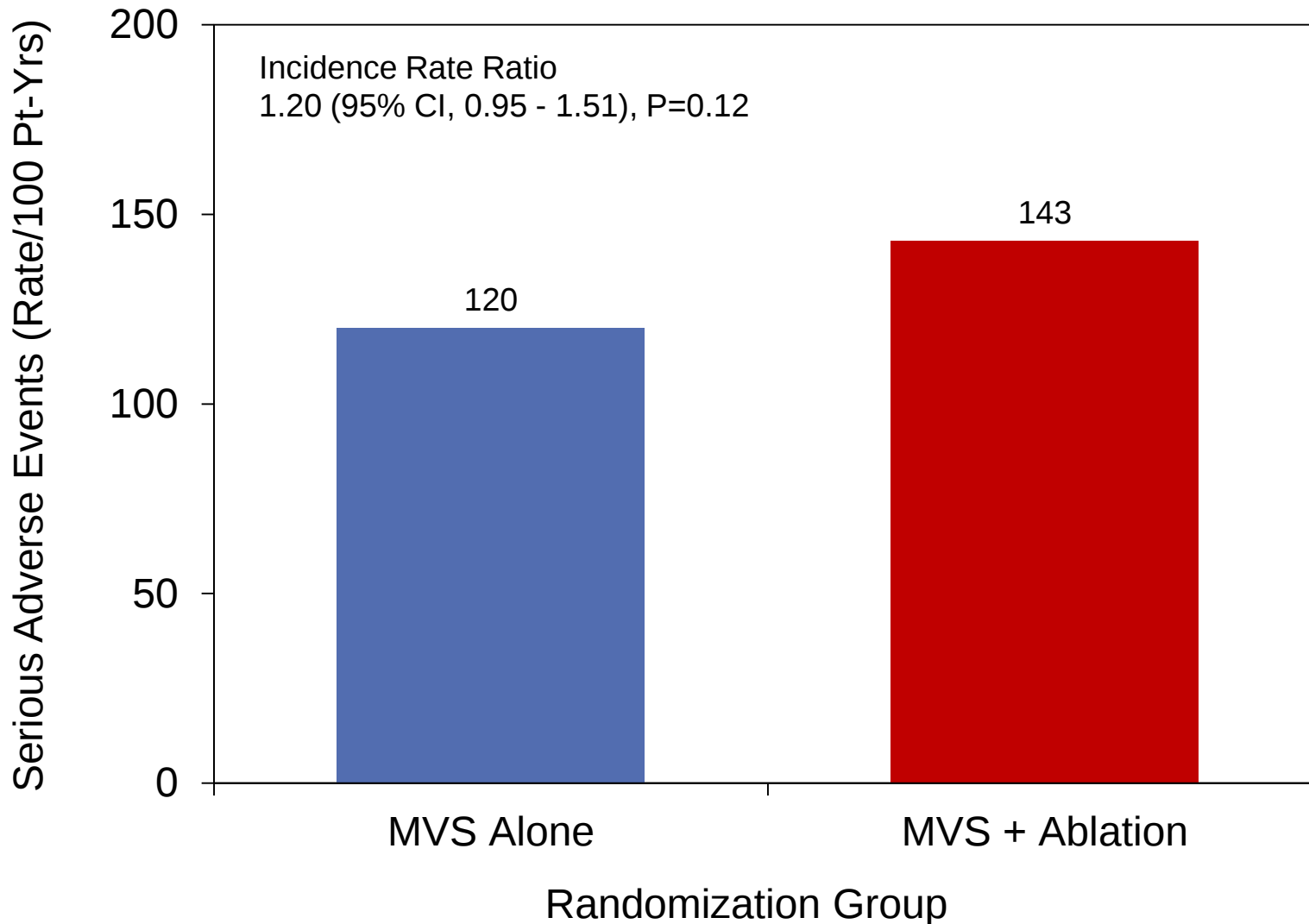
106

97

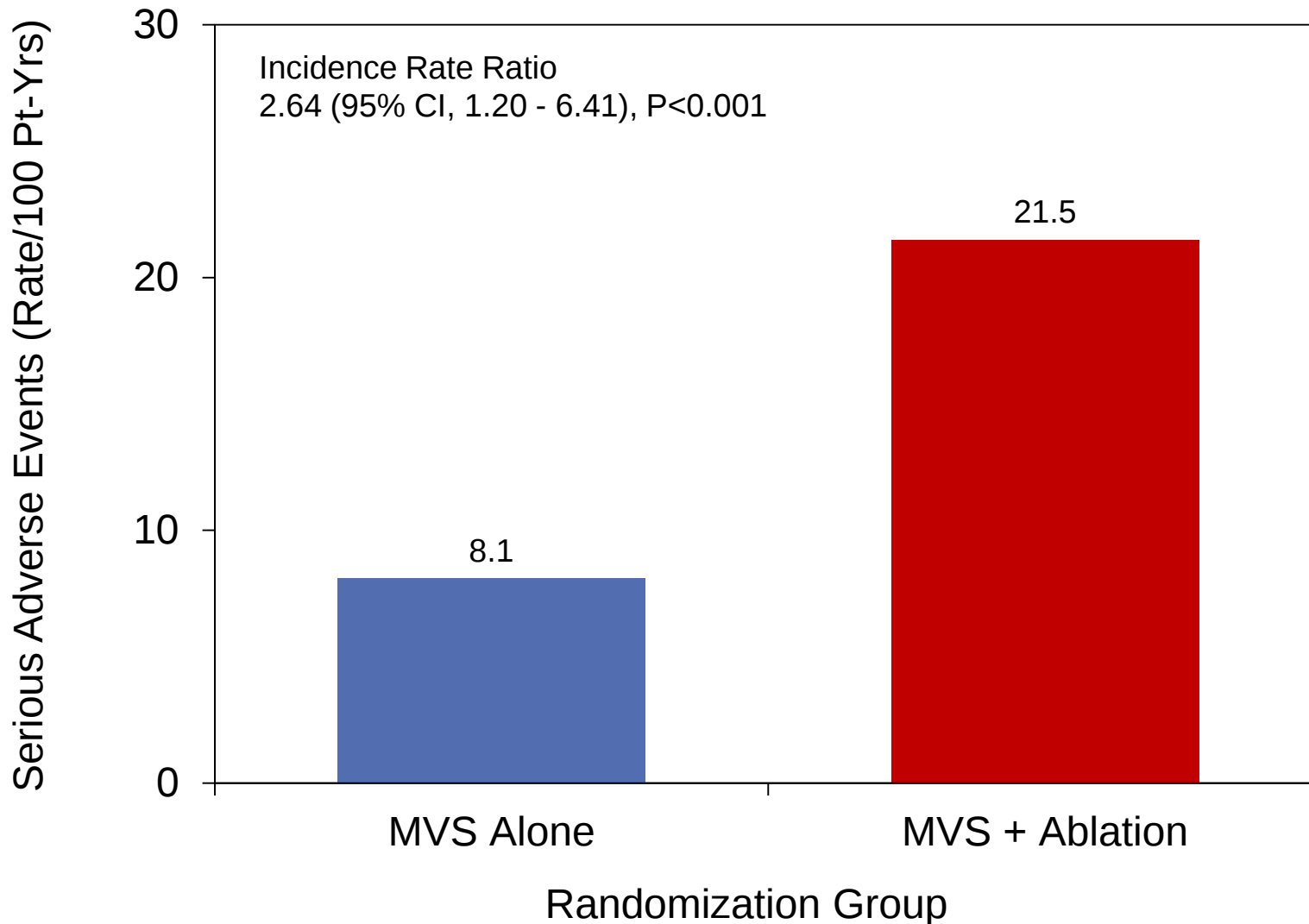
Quality of Life

	MVS Alone (N=127)	MVS & Ablation (N=133)	P-Value
SF-12			
Physical Function	45.3 ±7.9	44.3 ±9.0	0.38
Mental Function	48.5 ±6.5	48.0 ±6.3	0.56
AF Severity Scale			
Daily AF –no. (%)	42 (45.2)	20 (19.8)	<0.001
Life Rating (1-10, median)	8.0 (7,9)	8.0 (7,9)	0.45
NYHA Class III + IV –no. (%)	3 (2.9)	8 (7.0)	0.17

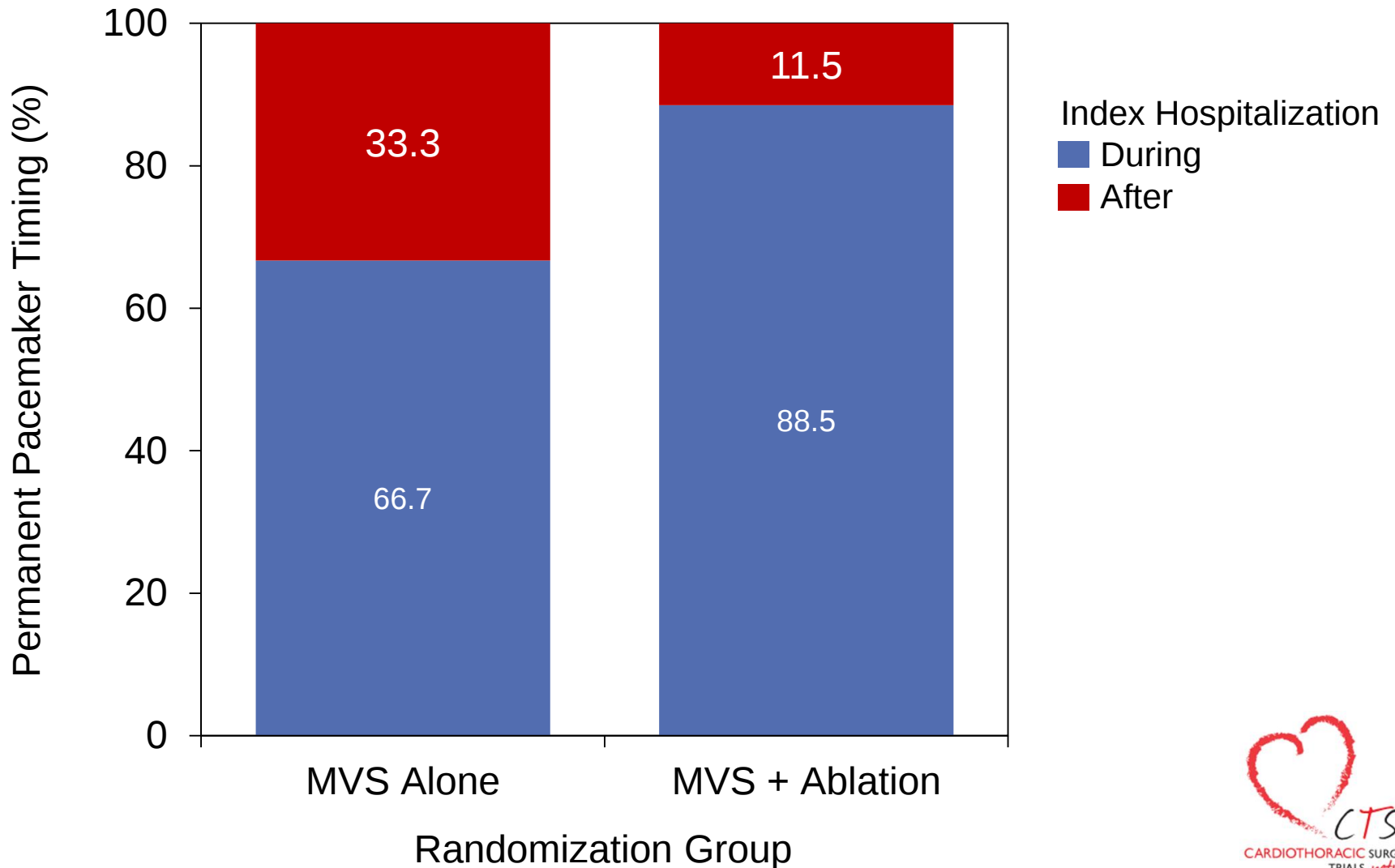
Serious Adverse Events



Pacemaker Implantation



Pacemaker Timing



Unique Trial Features

- **Largest RCT of surgical ablation for AF**
- **Mitral valve patients**
- **Persistent and long-standing persistent AF**
- **Stringent heart rhythm endpoint**
 - **3-day Holter monitor**
 - **Both 6 and 12 months**
 - **Repeat ablation procedures and death considered treatment failures**

Limitations

- **Primary endpoint not a clinical endpoint**
 - Trial with mortality or stroke endpoint would require more than one thousand patients and many years of follow up
- **Twenty percent of patients did not have primary endpoint data (Holter recordings, death or subsequent ablation)**

Summary

- Ablation significantly increased 1-year freedom from AF (63% vs. 29%)
- No difference between PVI and biatrial maze lesion sets
- Ablation did not increase mortality or major adverse cardiac or cerebrovascular events
- Ablation was associated with increased risk of permanent pacemaker implantation

Conclusion

- **Surgical ablation improves rhythm control in mitral valve patients with persistent and long-standing persistent AF**
- **Establishing the impact of ablation on long-term survival, freedom from stroke and need for anticoagulation will require further investigation**

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
- Sunnybrook Health Sciences Centre
- Aarhus University

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(CTSN)
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 - National Heart, Lung, and Blood Institute
 - National Institute of Neurological Disorders and Stroke
 - Canadian Institutes for Health Research



ORIGINAL ARTICLE

Surgical Ablation of Atrial Fibrillation during Mitral-Valve Surgery

A. Marc Gillinov, M.D., Annetine C. Gelijns, Ph.D., Michael K. Parides, Ph.D.,
Joseph J. DeRose, Jr., M.D., Alan J. Moskowitz, M.D., Pierre Voisine, M.D.,
Gorav Ailawadi, M.D., Denis Bouchard, M.D., Peter K. Smith, M.D.,
Michael J. Mack, M.D., Michael A. Acker, M.D., John C. Mullen, M.D.,
Eric A. Rose, M.D., Helena L. Chang, M.S., John D. Puskas, M.D.,
Jean-Philippe Couderc, Ph.D., Timothy J. Gardner, M.D., Robin Varghese, M.D.,
Keith A. Horvath, M.D., Steven F. Bolling, M.D., Robert E. Michler, M.D.,
Nancy L. Geller, Ph.D., Deborah D. Ascheim, M.D., Marissa A. Miller, D.V.M.,
Emilia Bagiella, Ph.D., Ellen G. Moquete, R.N., Paula Williams, M.S.,
Wendy C. Taddei-Peters, Ph.D., Patrick T. O'Gara, M.D., Eugene H. Blackstone, M.D.,
and Michael Argenziano, M.D., for the CTSN Investigators*

Parked Slides

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Surgical Ablation of Atrial Fibrillation during Mitral-Valve Surgery

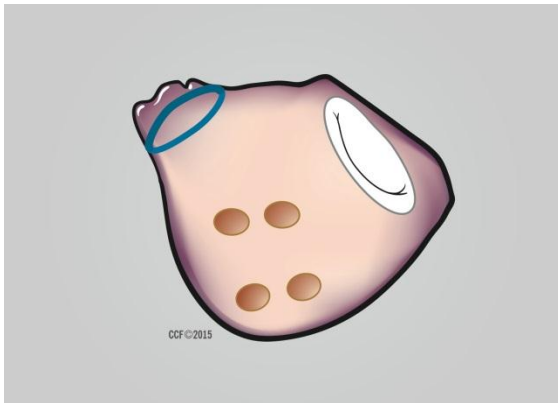
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AF and Mitral Valve Surgery Patients

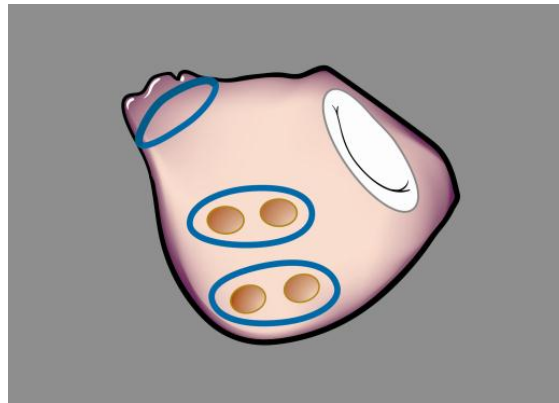
- Present in 30% to 50%
- Associated with adverse outcomes
- How should surgeons treat the AF?

Surgical Treatment Options

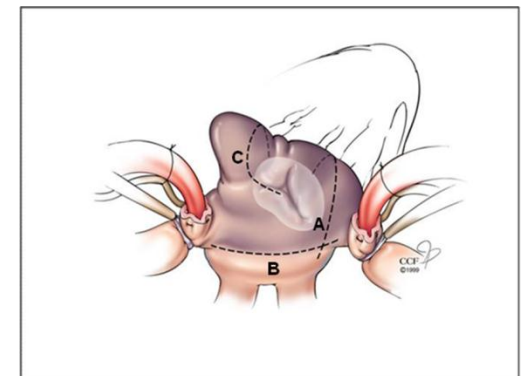
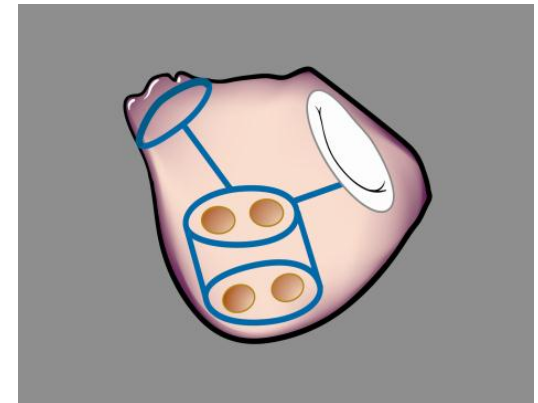
No Ablation



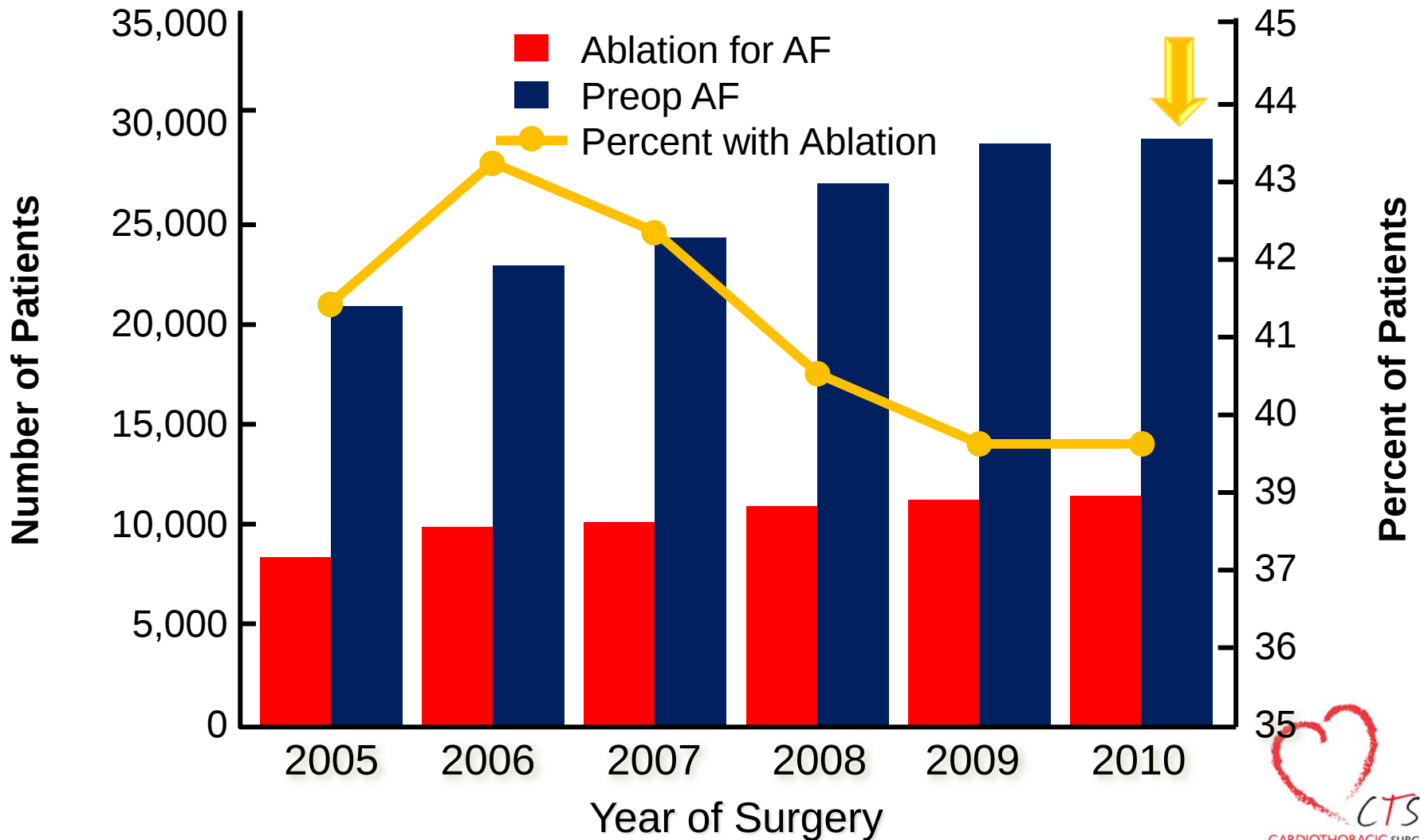
PVI



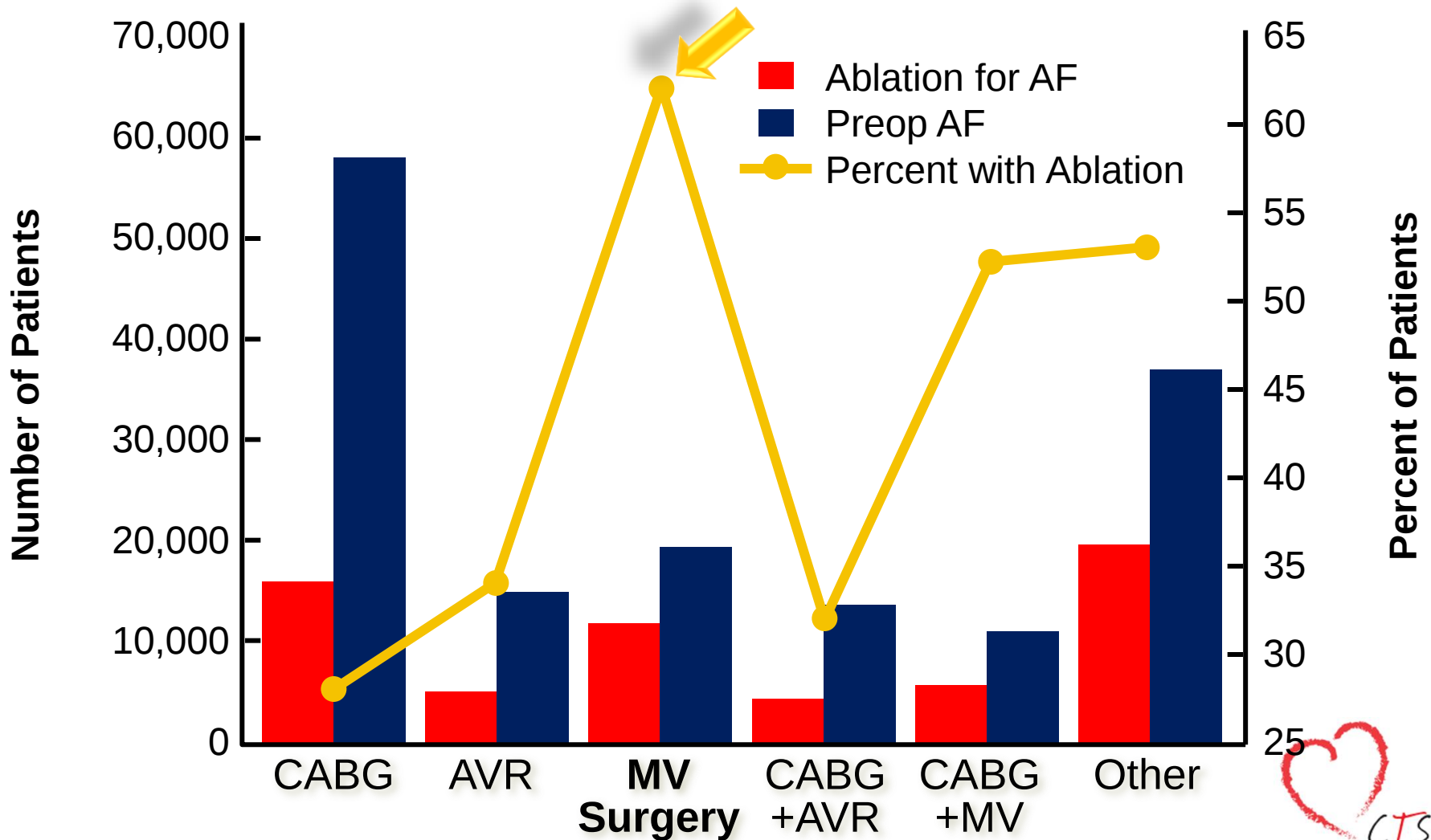
Bilateral Maze



AF Ablation in Cardiac Surgery



Concomitant Surgical Ablation



Heart Rhythm Interventions

	MVS Alone (N=127)	MVS & Ablation (N=133)	P-Value
Cardioversion (3 mths post-randomization) –no. (%)	12 (9.5)	8 (6.0)	0.30
AADs (1 year) –no. (%)	15 (14.6)	15 (13.2)	0.76
Ablation –no. (%)	3 (2.4)	1 (0.8)	0.36
Pacemaker –no. (rate/100 Pt-yrs)	9 (8.1)	26 (21.5)	0.01

Pacemaker Indications

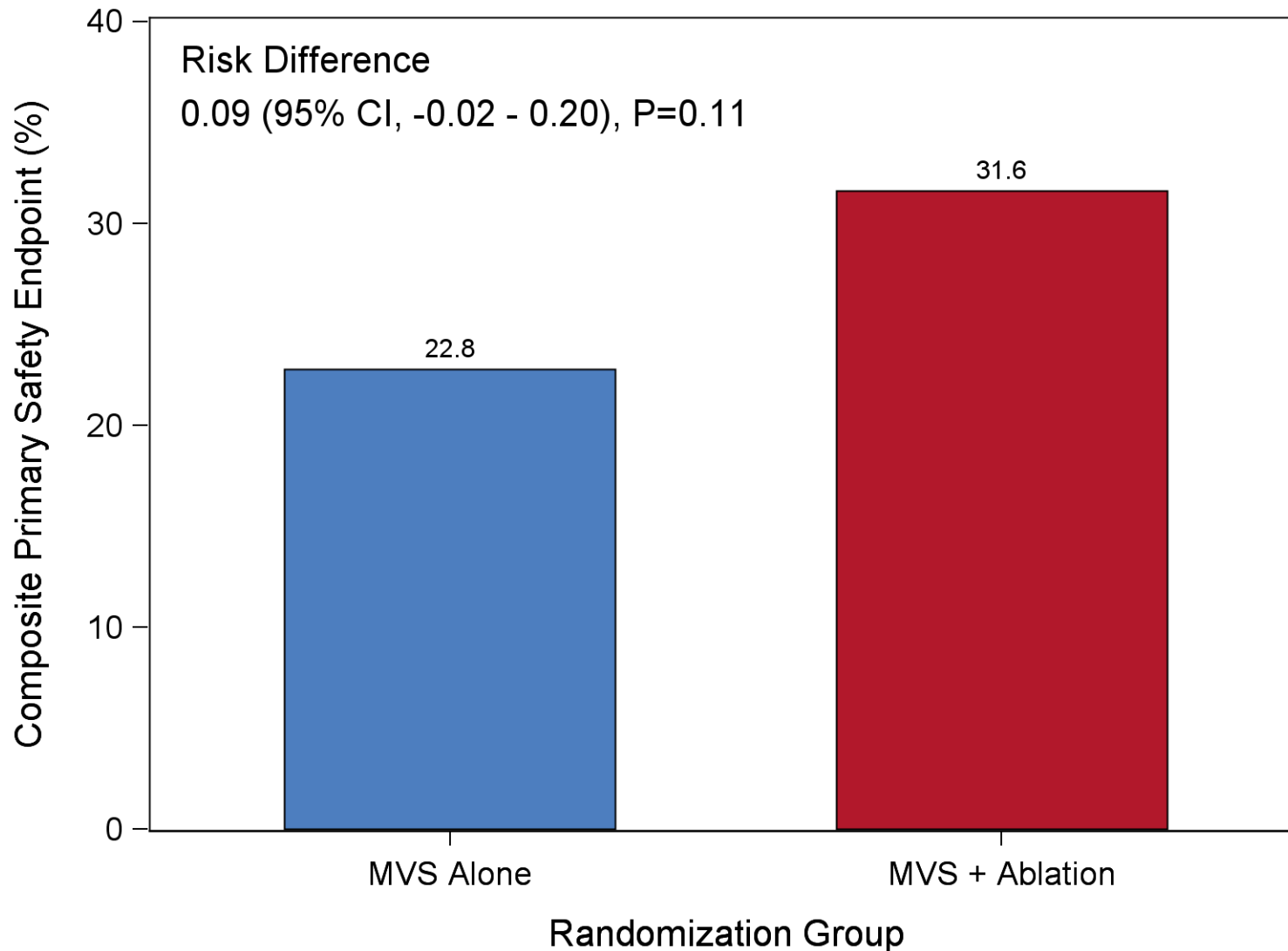
	MVS Alone (N=9 PPM)	MVS & Ablation (N=26 PPM)
Heart Block –no. (%)	4 (44.4)	14 (53.9)
Sinus Node Dysfunction –no. (%)	3 (33.3)	9 (34.6)
Control AF –no. (%)	2 (22.2)	0 (0.0)
Unknown –no. (%)	0 (0.0)	3 (11.5)

Primary Safety Endpoint (Composite)

At 30 days post index surgery / hospital discharge
(whichever is first)

- Death
- Stroke
- Heart failure
- MI
- Cardiac Readmissions
- Pulmonary embolism
- Peripheral embolism
- Excessive bleeding
- DSWI/Mediastinitis
- Permanent pacemaker
- Damage to adjacent structures
- TIA

Primary Safety Endpoint



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- Pulmonary Vein Isolation (PVI) (n=67)
- Biatrial Maze (n=66)

Follow-Up

- Withdrawal before month 12 (n=6)
- Lost to follow-up before month 12 (n=4)
- Death before month 12 (n=11)

- Withdrawal before month 12 (n=6)
- Lost to follow-up before month 12 (n=2)
- Death before month 12 (n=9)

Analysis

Primary Endpoint Analysis (n=127)

- **Primary Endpoint Data (n=102)**
 - 6 & 12 Month Holter (n=88)
 - Died (n=11)
 - Underwent Ablation (n=3)
- **Imputed (n=25)**

Primary Endpoint Analysis (n=133)

- **Primary Endpoint Data (n=106)**
 - 6 & 12 Month Holter (n=96)
 - Died (n=9)
 - Underwent Ablation (n=1)
- **Imputed (n=27)**

Explore Two Different Lesion Sets

- Ablation arm further randomized to pulmonary vein isolation vs. biatrial maze
- Lesion set randomization for exploratory analysis only