The MASTER Trial

A Prospective, Randomized, Multicenter Evaluation of a PET Micronet Mesh Covered Stent (MGuard) in STEMI

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CARDIOVASCULAR RESEARCH FOUNDATION
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Disclosure Statement of Financial Interest

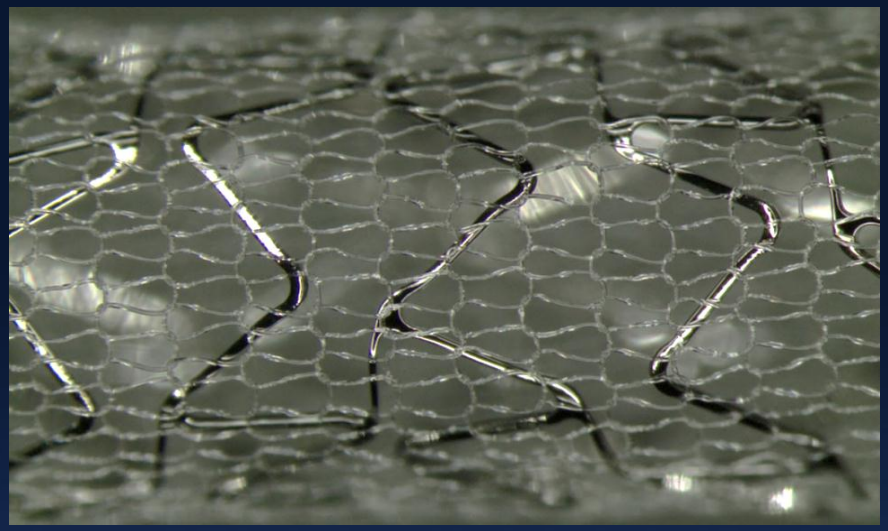
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria	• Abbott Vascular, Boston Scientific, Medtronic, InspireMD, Atrium

Background

- Suboptimal myocardial reperfusion after PCI in STEMI is common, and results in increased infarct size and mortality
- The MGuard Embolic Protection Stent (EPS) s a novel thin-strut metallic stent with a PET micronet covering designed to trap and exclude thrombus and friable atheromatous debris to prevent distal embolization

The MGuard and MGuard Prime Embolic Protection Stent (EPS)

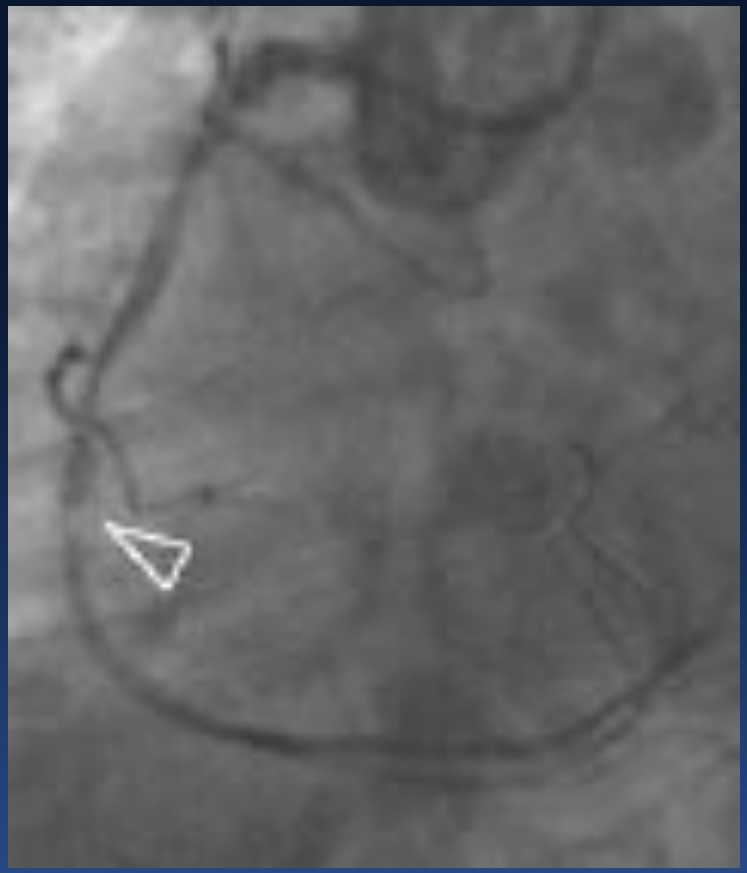


	MGuard	MGuard Prime
Metallic frame	316L stainless steel	L605 cobalt chromium
Strut width	100 µm	80 µm
Crossing profile	1.1 – 1.3 mm	1.0 – 1.2 mm
Shaft dimensions	0.65 – 0.86 mm	0.65 – 0.86 mm
Mesh sleeve	PET**	PET**
- Fiber width	20 µm	20 µm
- Net aperture size	150 - 180 µm	150 - 180 µm

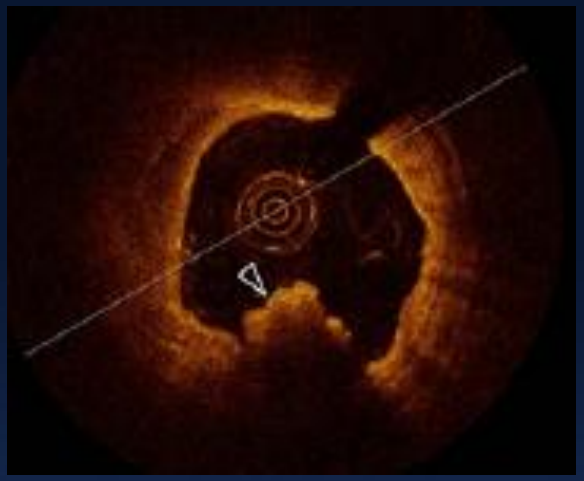
*InspireMD, Tel Aviv, Israel; **Polyethyleneterephthalate

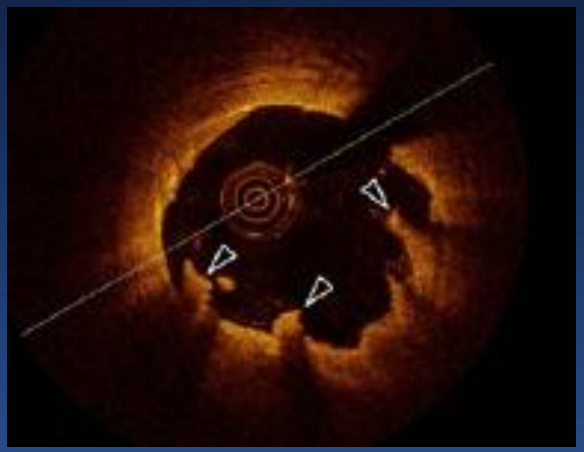
Thrombus Entrapment by the MGuard in STEMI

Pre



Post aspiration

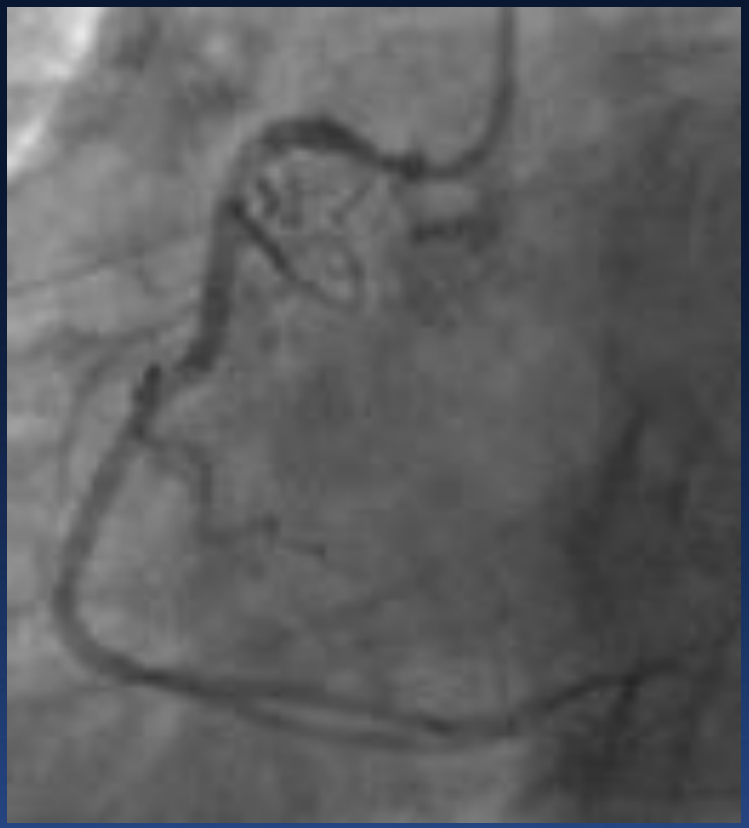




Residual thrombus

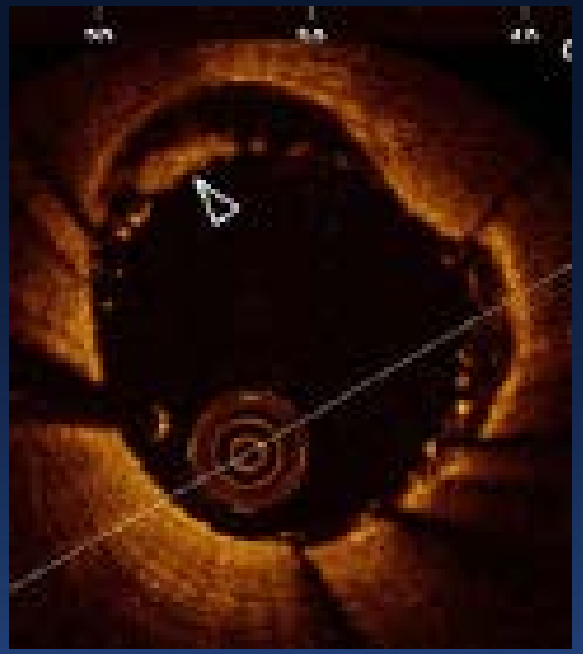
Jain AK and Rothman MT. JACC 2011;58;e39

Thrombus Entrapment by the MGuard in STEMI



Post MGuard

Mesh

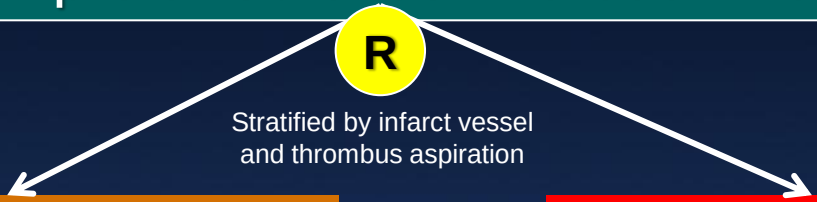


Thrombus trapped behind mesh

Jain AK and Rothman MT. JACC 2011;58;e39

MGUARD for Acute ST Elevation Reperfusion
The MASTER Trial

STEMI with symptom onset within 12 hours at 432 pts at 50 sites in 9 countries



Follow-up: 30 days, 6 months, 1 year

Primary endpoint: ST-segment resolution at 60-90 minutes

Substudies:

Cardiac MRI: 60 pts (30 pts in each arm) at 3-5 days

Angio FU: 50 pts in MGuard arm at 13 months

Principal Inclusion Criteria

- Symptoms consistent with STEMI within 12 hours of symptom onset
- ≥2 mm of ST-segment elevation in ≥2 contiguous leads
- PCI of a single de novo lesion with RVD ≥3.0 to ≤4.0 mm and length ≤33 mm (capable of being covered by a single study stent)

Principal Exclusion Criteria

- LBBB, paced rhythm, etc.
- Prior PCI within 6 months or prior CABG anytime
- LVEF ≤20%, cardiogenic shock or CPR
- ≥50% left main stenosis present
- Infarct lesion ostial or bifurcation with ≥2.0 mm sidebranch
- Target vessel or infarct lesion excessively tortuous, angulated or with moderate to heavy calcification
- Prior stent proximal or w/i 10 mm distal to the target

Primary Endpoint and Power

- Primary endpoint: Complete ST-segment resolution (STR), defined as ≥70% reduction in the summed 12-lead extent of ST-segment elevation from the baseline to the post-procedure (60-90') ECG as determined by a blinded, independent electrocardiographic core laboratory
- Power: With 412 pts, 80% power is present to demonstrate a 21.7% relative improvement in complete STR from 60% to 73% (2-sided α=0.05)
  - Assuming 95% evaluable paired ECGs, enrollment was planned for 432 pts

Study Organization

Principal investigators:	Alexandre Abizaid, Dariusz Dudek, Sigmund Silber
Study chairman:	Gregg W. Stone
Executive committee:	GW Stone, A Abizaid, D Dudek, S Silber, C Lotan, MB Leon, E Bar, E Yaacoby, M Ivenshitz
Data monitoring:	KCRI, Poland; MedPass Int, France; CRC, Brazil; Tal Yerushalmi, Israel; Modestas Jarutis, Ireland; Adele Liebenberg and Brendalynne Bezuidenhout, South Africa
Data management:	InspireMD, Tel Aviv, Israel.
Data analysis and biostatistics:	Cardiovascular Research Foundation (CRF), NY, NY; Helen Parise (Director), Ovidiu Dressler
Event adjudication:	Cardiovascular Research Center (CRC), Sao Paulo, Brazil; Andrea Abizaid, MD (Director)
STR and MRI core labs:	CRF; S Wolff, A Maehara, E Cristea, P Genereux (Directors)
Angio core labs:	CRC; Ricardo Costa (Director), and CRF; Sorin J. Brener (myocardial blush analysis)
DSMB:	B Gersh (Chair), D Faxon, S Pocock
Sponsor and funding:	InspireMD, Tel Aviv, Israel

Top 12 Enrolling Sites

Between July 22, 2011 and May 29, 2012, 433 pts were randomized at 50 sites in 9 countries

1. Bela Merkely, Semmelweis University, Budapest, Hungary	37
2. Dariusz Dudek, University Hospital in Krakow, Krakow, Poland	33
3. Ran Kornowski, Rabin Medical Center, Petach Tiqva, Israel	31
4. Roman Wojdyła, Krakow Center of Invasive Cardiology, Electrotherapy and Angiology, Krakow, Poland	23
5. Dezső Apró, State Hospital for Cardiology, Balatonfured, Hungary	19
6. Haim Danenberg, Hadassah U Medical Center, Jerusalem, Israel	19
7. Itzhak Herz, Laniado Hospital, Netanya, Israel	18
8. Bogdan Januś, E. Szczeklik Specialized Hospital, Tarnow, Poland	16
9. Marc A. Ohlow, Zentralklinik Bad Berka, Bad Berka, Germany	15
10. Krystrof Żmudka, John Paul II Hospital, Krakow, Poland	15
11. Jacek Legutko, INTERCARD, Nowy Targ, Nowy Targ, Poland	15

Baseline Characteristics

	MGuard stent (n=217)	Control stent (n=216)
Age (years)	60 [52, 68]	58 [51, 67]
Male	75.1%	76.9%
Hypertension	42.3%	47.4%
Hyperlipidemia	27.4%	27.1%
Diabetes mellitus	12.0%	18.1%
Cigarette smoking	55.3%	46.8%
Prior MI	3.7%	8.8%
Prior PCI	3.7%	5.6%
Symptoms to device, mins	207 [156, 308]	240 [140, 383]
Infarct artery = LAD	40.1%	40.3%
Baseline TIMI flow = 0/1	66.5%	74.0%
Baseline RVD, mm	3.15 [2.87, 3.38]	3.06 [2.87, 3.40]
Baseline DS %	100 [85, 100]	100 [88, 100]

Procedural Medications

	MGuard stent (n=217)	Control stent (n=216)	*P* value
Anti-platelet agents, peri-procedural			
– Aspirin	98.6%	99.1%	1.0
– ADP antagonists	95.4%	95.8%	0.82
– Clopidogrel	72.9%	70.0%	0.51
– Ticlopidine	0.5%	0.0%	1.0
– Prasugrel	21.7%	20.8%	0.81
– Ticagrelor	4.8%	9.2%	0.08
Anticoagulation, peri-procedural			
– Unfractionated heparin	96.8%	96.3%	0.79
– Glycoprotein IIb/IIIa inhibitor	82.9%	83.3%	0.92
– Bivalirudin	11.1%	12.5%	0.64

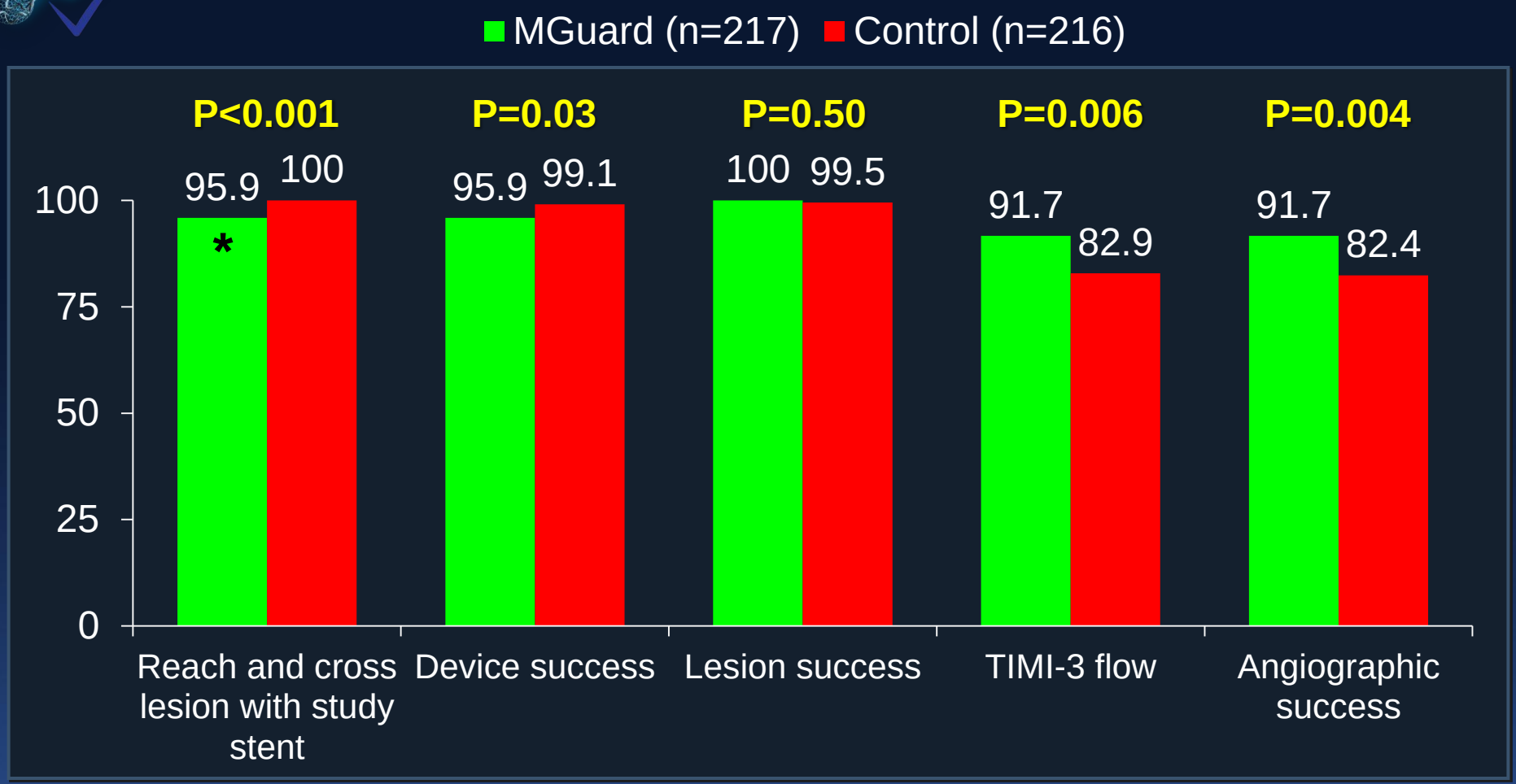
Procedures

	MGuard stent (n=217)	Control stent (n=216)	*P* value
Aspiration performed	65.9%	67.1%	0.79
Balloon pre-dilatation performed	50.2%	44.9%	0.27
Direct stenting	12.0%	10.6%	0.66
≥1 stent implanted	99.5%	100.0%	1.0
≥2 stents implanted	12.9%	10.6%	0.47
Stent type			
– MGuard	96.3%*	0.5%	<0.0001
– Bare metal stent	1.4%	59.7%	<0.0001
– Drug-eluting stent	2.3%	39.8%	<0.0001
Total stent length, mm	19 [15, 24]	20 [15, 24]	0.64
Post stent dilatation performed	36.4%	30.6%	0.20
Maximal device size, mm	3.5 [3.0, 3.5]	3.5 [3.0, 3.5]	0.78
Maximal dilatation pressure, atm	16 [14, 18]	16 [14, 18]	0.02**

*191 MGuard, 26 MGuard Prime

**Marginally higher in the MGuard group

Device Success



Device success: <50% final residual stenosis using only the randomized stent

Lesion success: <50% final residual stenosis using any percutaneous method

Angiographic success: <50% final residual stenosis and final TIMI 3 flow

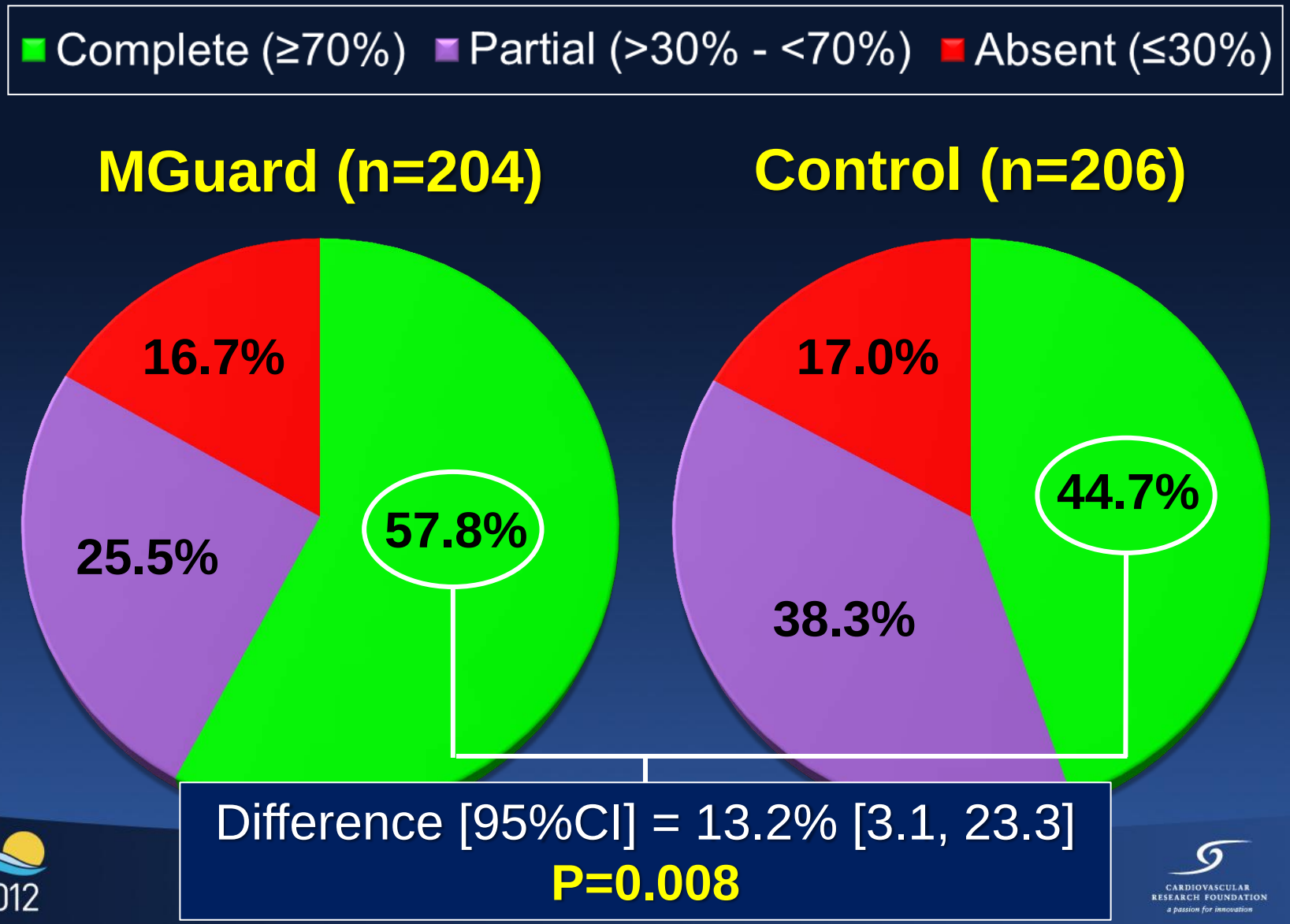
*9/217 cases (4.1%), including 9/191 (4.7%) and 0/26 (0%) cases in which the original MGuard and MGuard Prime devices were used, respectively

Procedural Results

	MGuard stent (n=217)	Control stent (n=216)	*P* value
TIMI flow = 3	91.7%	82.9%	0.006
TIMI flow = 2	6.5%	11.6%	0.06
TIMI flow = 0/1	1.8%	5.6%	0.01
Corrected TIMI frame count	17 [12, 23]	18 [13,22]	0.23
Myocardial blush = 2/3	83.9%	84.7%	0.81
IPTE	21.7%	22.3%	0.87
RVD, mm	3.20 [2.90, 3.46]	3.16 [2.91, 3.46]	0.99
MLD, in-stent, mm	2.99 [2.73, 3.25]	2.99 [2.69, 3.31]	0.91
MLD in-lesion, mm	2.64 [2.40, 2.96]	2.64 [2.36, 2.95]	0.82
DS%, in-stent	6.9 [4.2, 10.5]	6.4 [3.9, 10.3]	0.56
DS%, in-lesion	15.3 [9.6, 21.2]	15.4 [10.8, 21.2]	0.66

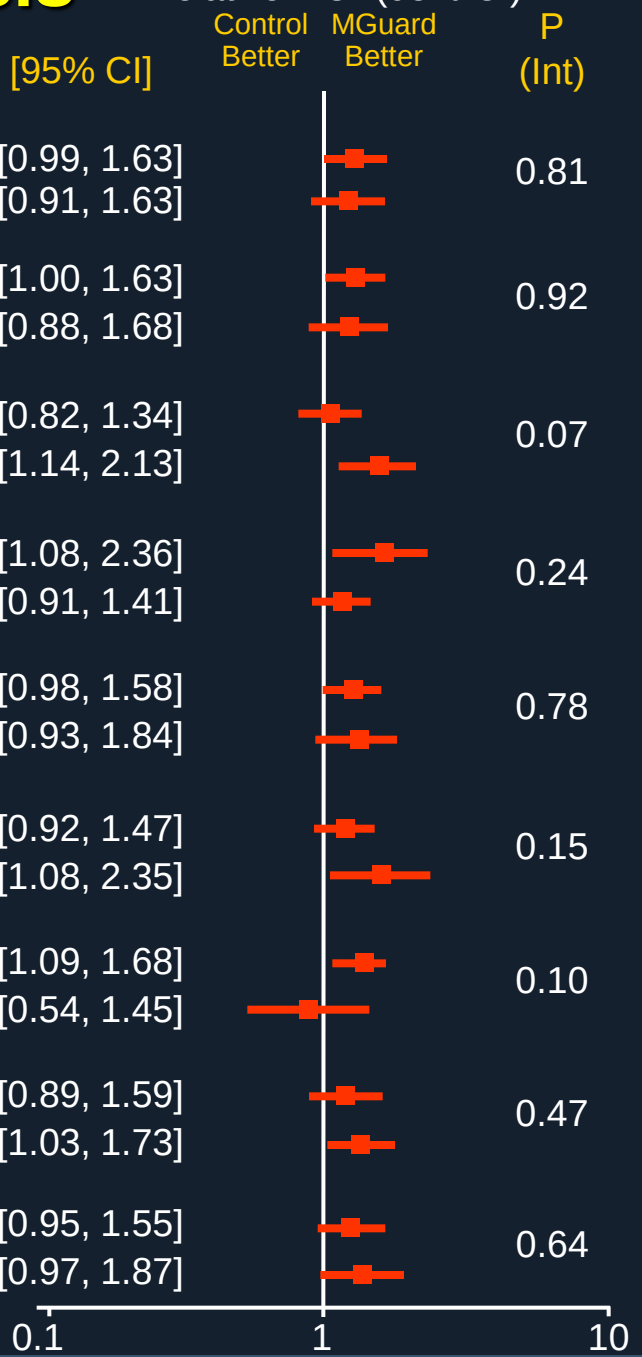
IPTE = intraprocedural thrombotic events

Primary Endpoint:
Complete ST-segment resolution



Complete STR: Subgroup Analysis

Group	MGuard	Control	RR [95% CI]	P (Int)
Sex				
Male	80/163 (49.1%)	64/166 (38.6%)	1.27 [0.99, 1.63]	0.81
Female	38/54 (70.4%)	29/50 (58.0%)	1.21 [0.91, 1.63]	
Age				
≤65 years	78/149 (52.3%)	63/154 (40.9%)	1.28 [1.00, 1.63]	0.92
>65 years	40/68 (58.8%)	30/62 (48.4%)	1.22 [0.88, 1.68]	
Symptom onset to balloon time				
<Median (220 min)	63/114 (55.3%)	54/102 (52.9%)	1.04 [0.82, 1.34]	0.07
>Median	55/102 (59.2%)	39/113 (34.5%)	1.56 [1.14, 2.13]	
Infarct vessel				
LAD	41/87 (47.1%)	26/88 (29.5%)	1.60 [1.08, 2.36]	0.24
Non-LAD	77/130 (59.2%)	67/128 (52.3%)	1.13 [0.91, 1.41]	
Aspiration				
Used	77/143 (53.8%)	63/145 (43.4%)	1.24 [0.98, 1.58]	0.78
Not used	41/74 (59.2%)	30/71 (42.3%)	1.31 [0.93, 1.84]	
Initial TIMI flow				
0/1	74/143 (51.7%)	71/159 (44.7%)	1.16 [0.92, 1.47]	0.15
2/3	43/72 (59.7%)	21/56 (37.5%)	1.59 [1.08, 2.35]	
Vessel diameter				
<3.5 mm	102/179 (57.0%)	74/176 (42.0%)	1.36 [1.09, 1.68]	0.10
≥3.5 mm	16/38 (42.1%)	19/40 (47.5%)	0.89 [0.54, 1.45]	
Lesion length				
≤Median (7.8 mm)	54/109 (49.5%)	45/108 (41.7%)	1.19 [0.89, 1.59]	0.47
<Median	64/108 (59.3%)	48/108 (44.4%)	1.33 [1.03, 1.73]	
Maximum device size				
≤3.5 mm	73/135 (54.1%)	60/135 (44.4%)	1.22 [0.95, 1.55]	0.64
<3.5 mm	45/82 (54.9%)	33/81 (40.7%)	1.35 [0.97, 1.87]	



Clinical Events at 30 Days

	MGuard stent (n=217)	Control stent (n=214)	*P* value
MACE	4 (1.8%)	5 (2.3%)	0.75
– Cardiac mortality*	0 (0.0%)	4 (1.9%)	0.06
– Reinfarction	3 (1.4%)	2 (0.9%)	1.00
– TLR, ischemia-driven	4 (1.8%)	1 (0.5%)	0.37
TVR, ischemia-driven	6 (2.8%)	1 (0.5%)	0.12
Stent thrombosis, def/prob	3 (1.4%)	2 (0.9%)	1.00
Stroke	1 (0.5%)	0 (0.0%)	1.00
TIMI bleeding, major/minor	4 (1.8%)	4 (1.9%)	1.00

Mortality at 30 days occurred in 0/211 pts with complete STR and in 4/198 pts with partial or absent STR (0% vs 2.0%, p=0.05)

* There were no non-cardiac mortalities

3-5 Day MRI Substudy Results

	MGuard stent (n=30)	Control stent (n=29)	*P* value
Total LV myocardial mass, gms	141 [117, 163]	147 [118, 174]	0.41
Infarct mass, grams	17.1 [10.0, 30.0]	22.3 [15.7, 30.1]	0.27
Infarct mass (% total LV mass)	13.3 [7.9, 25.0]	16.6 [10.0, 22.6]	0.48
Total MVO, grams	0.3 [0.0, 1.6]	1.0 [0.2, 2.8]	0.14
MVO (% total LV mass)	0.4 [0.0, 1.4]	0.8 [0.2, 1.9]	0.39
Abnormal wall motion score	22.5 [20.0, 26.0]	25.0 [21.0, 27.0]	0.48
LVEF (%)	48.3 [44.5, 52.3]	47.3 [42.0, 54.5]	0.79

MVO = microvascular obstruction

Limitations

- Single-blind only
- Underpowered for infarct size and clinical events, and subgroup analyses should be considered hypothesis-generating.
- More experience with the MGuard Prime in STEMI is required
- Long-term clinical and angiographic follow-up is ongoing
- Discordance between TIMI flow, STR, infarct size, and death (improvement) vs. blush and IPTE (no significant change) is noted

Conclusions and Implications

- Among pts with acute STEMI undergoing emergent PCI, the MGuard micronet mesh covered stent compared to conventional metallic stents resulted in superior rates of epicardial coronary flow and complete STR
- A larger randomized trial is warranted to verify these findings, and determine whether these benefits result in reduced infarct size and/or improved clinical outcomes (MASTER II)

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Journal of the American College of Cardiology
© 2012 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 60, No. 19, 2012
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.09.004

EXPEDITED PUBLICATION

Prospective, Randomized, Multicenter Evaluation of a Polyethylene Terephthalate Micronet Mesh–Covered Stent (MGuard) in ST-Segment Elevation Myocardial Infarction

The MASTER Trial

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