Seoul, 27 April
TCT AP 2010

ANGIOPLASTY SUMMIT
TCTAP2011
TRANSCATHETER CARDIOVASCULAR THERAPEUTICS ASIA PACIFIC

Thrombus Aspiration before PCI:
Routine Mandatory

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Academic Medical Center
University of Amsterdam

Case # 1:

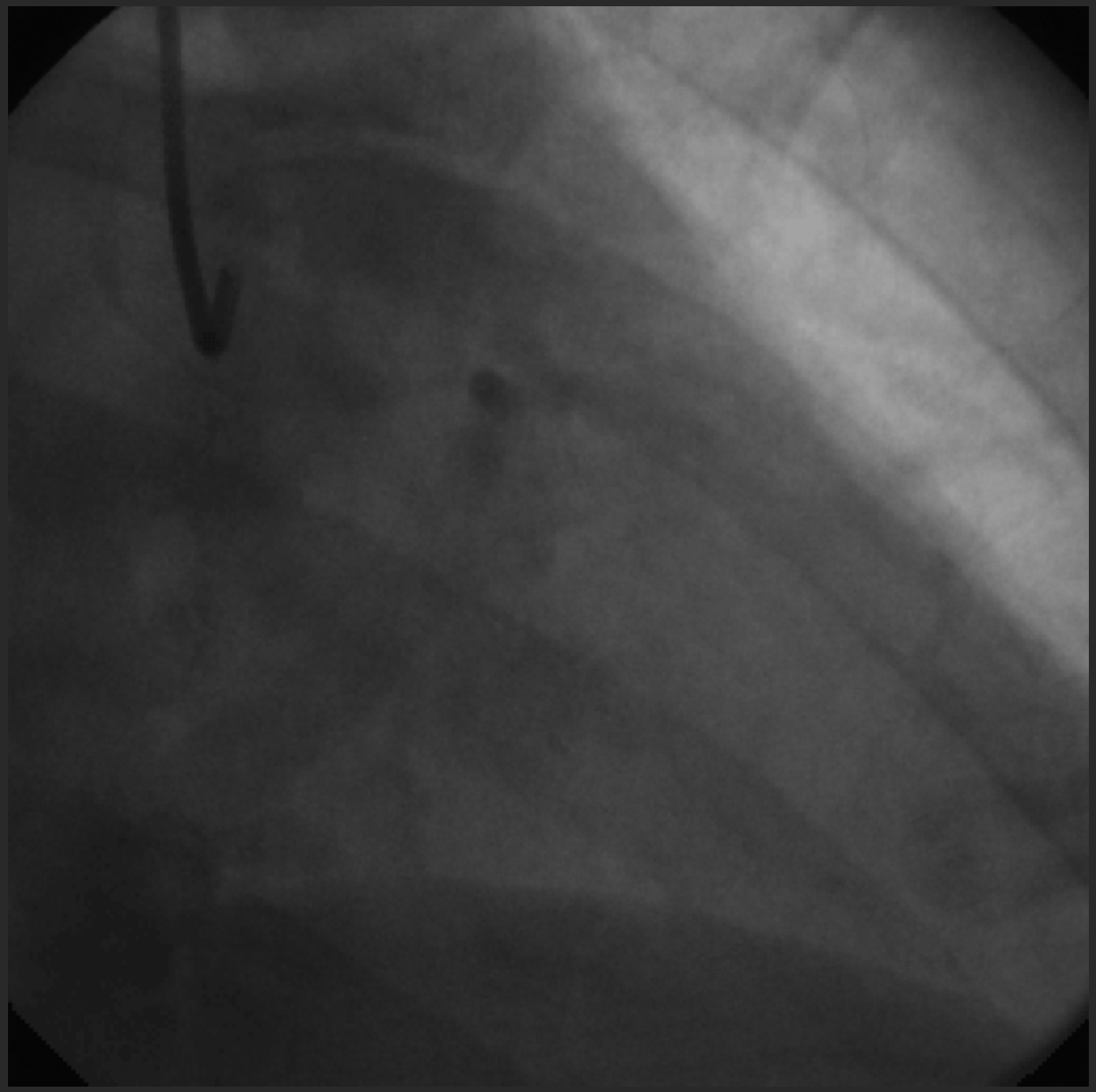
- ♥ male, 43 yrs
- ♥ Hypertension, Smoking, Positive family history
- ♥ No prior cardiac history
- ♥ Morning run 10 miles without complaints
- ♥ Chest pain while cooling down
- ♥ Sweating, nausea, near fainting

Thrombectomy in primary PCI

Male 43 yrs
Acute ischemia

Urgent CAG

- heparin 75IU/kg
- aspirin iv
- clopidogrel
- abciximab



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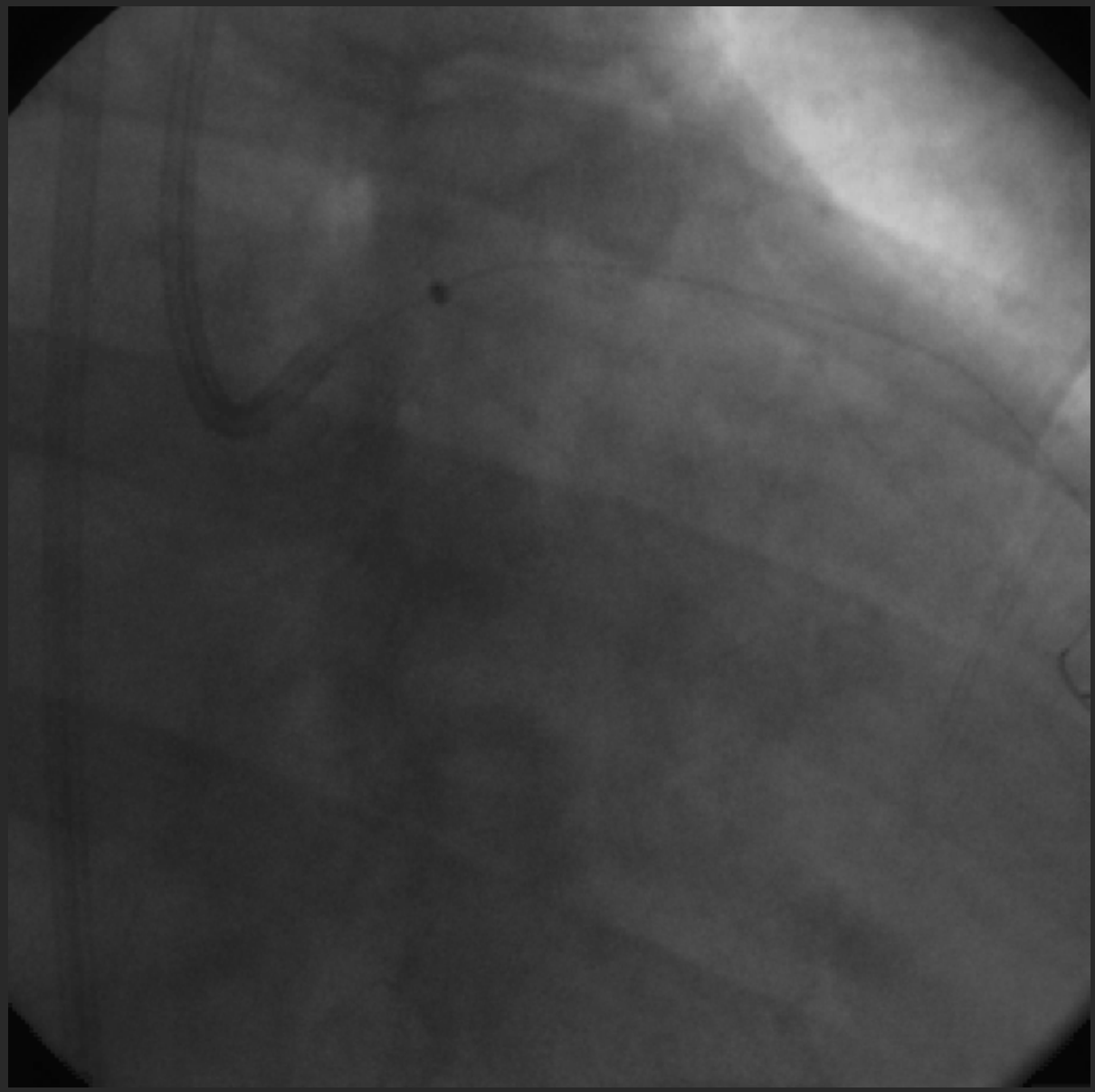

Thrombectomy in primary PCI

Male 43 yrs
Acute ischemia

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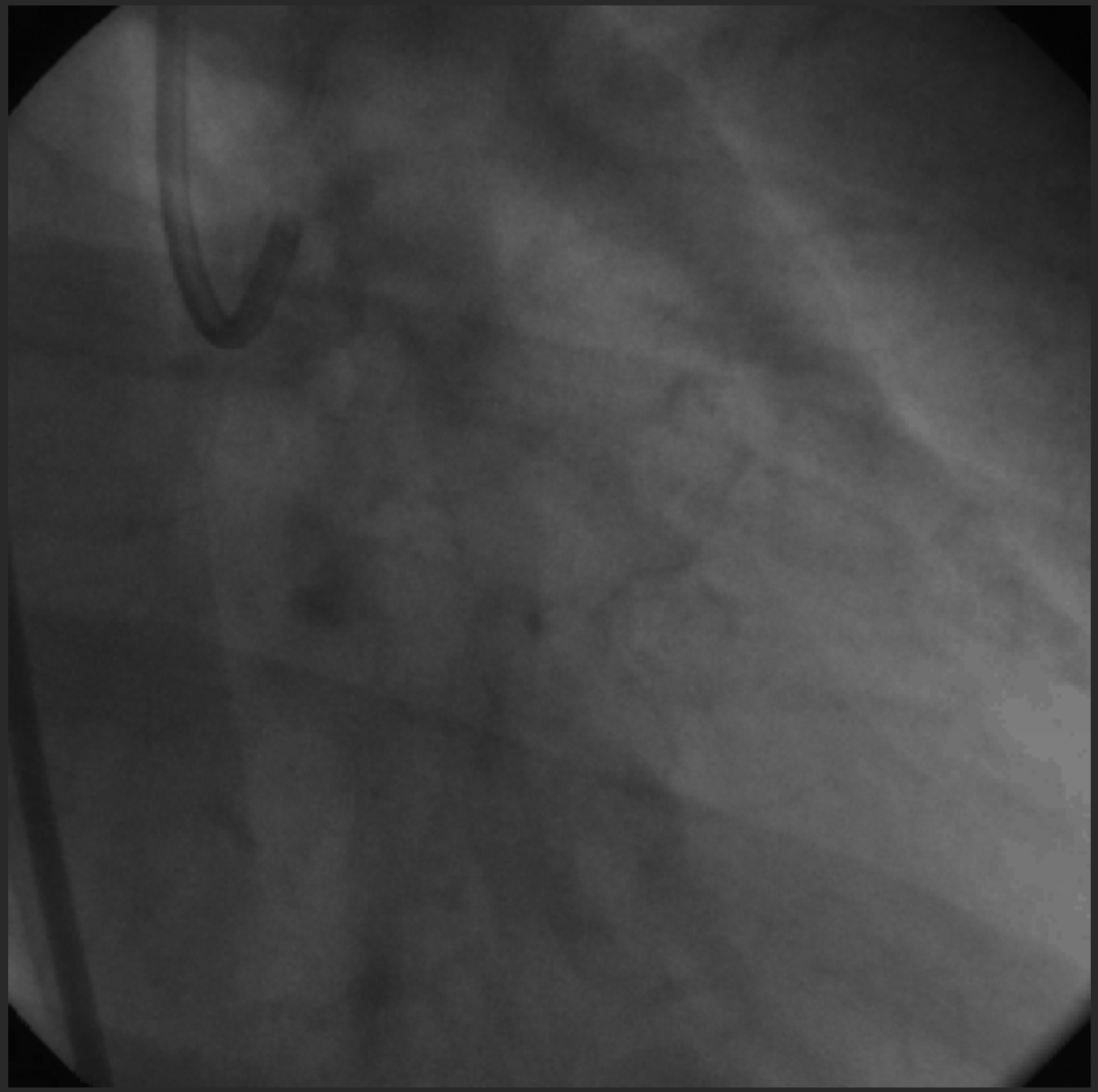
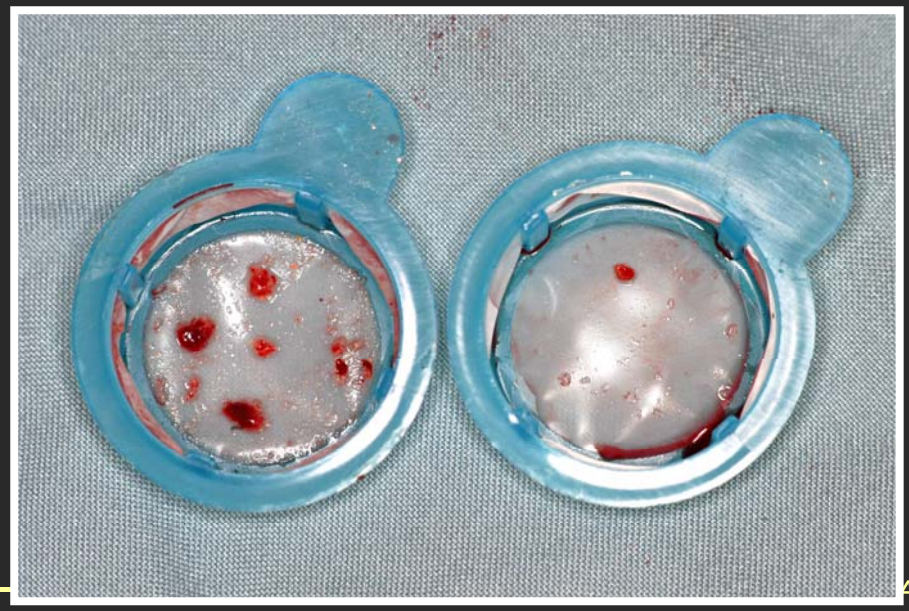
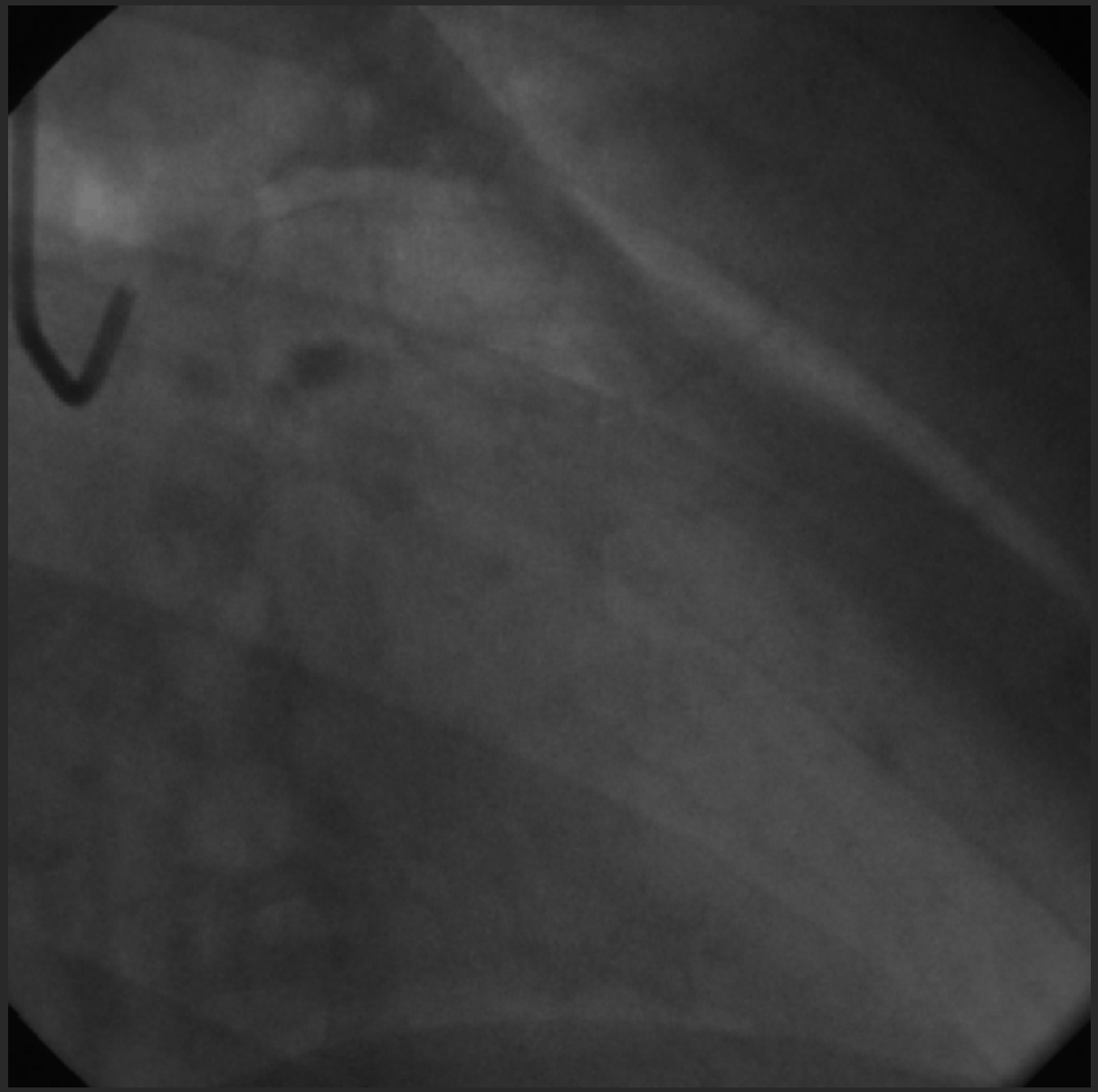


Result after thrombectomy



Thrombectomy in primary PCI

Result after 5 days
- UFH i.v.
- ASA
- Clopidogrel



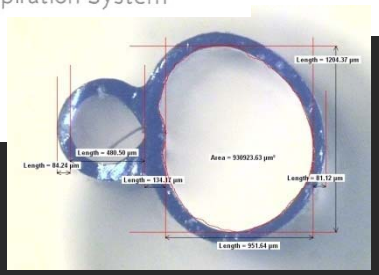
Case # 1:

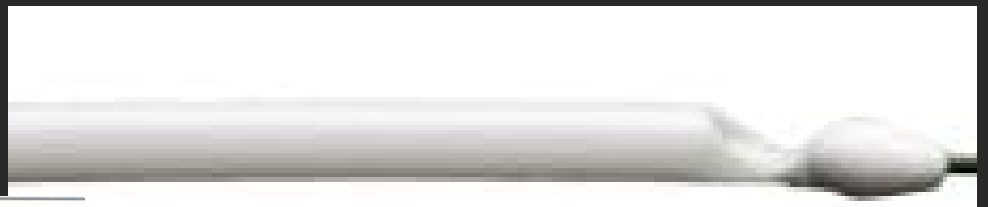
- ♥ male, 43 yrs
- ♥ Anterior AMI
- ♥ Large thrombus burden
- ♥ Thrombectomy effective (no additional stenting) in addition to anti-platelet and anti-thrombotic Rx

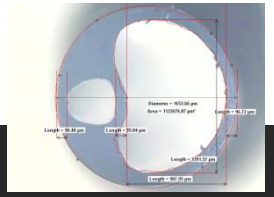
Rationale of Thrombectomy and Embolic Protection

- pPCI preferred treatment in STEMI
- 85% - 93% restoration epicardial flow
- Frequent suboptimal myocardial perfusion
  - Distal embolization
  - Slow flow / no-reflow
  - Microvascular obstruction
- Occurring in up to 33% of patients
- Reduction of thrombus burden and distal embolization may improve microvascular perfusion, reduce infarct size and possibly clinical outcome

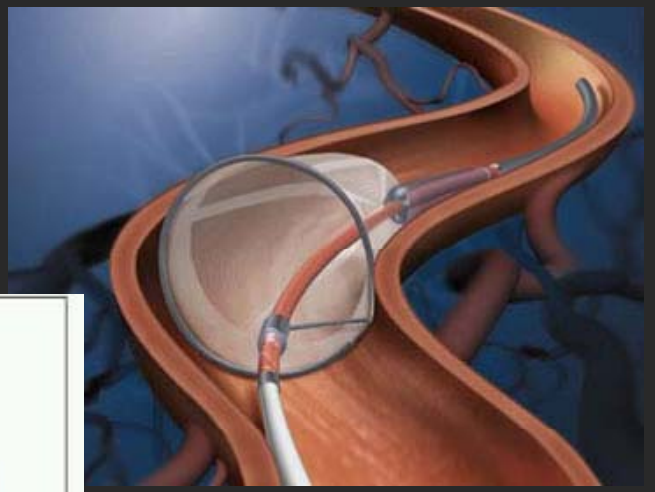
EXPORT
Aspiration System

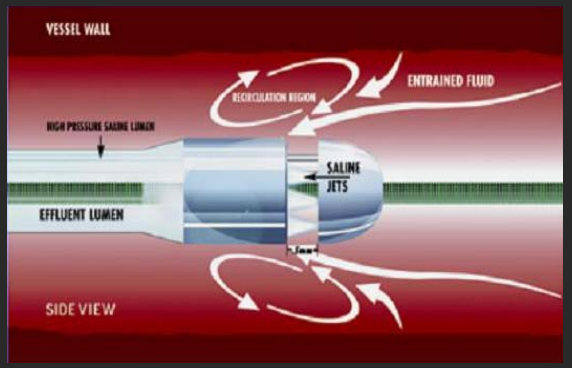


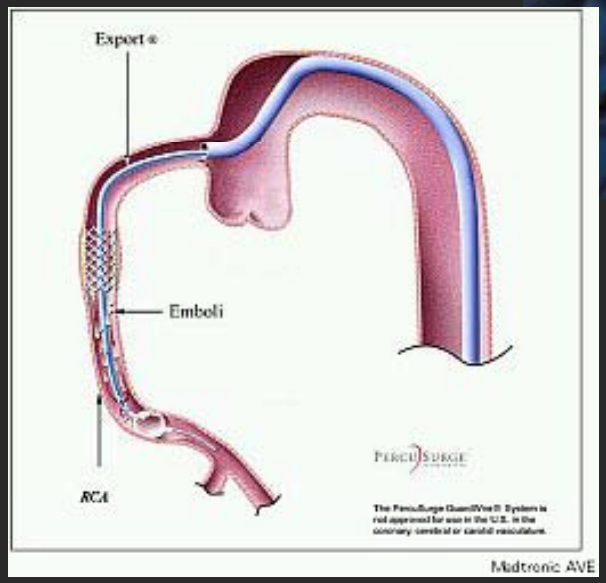




PRONTO



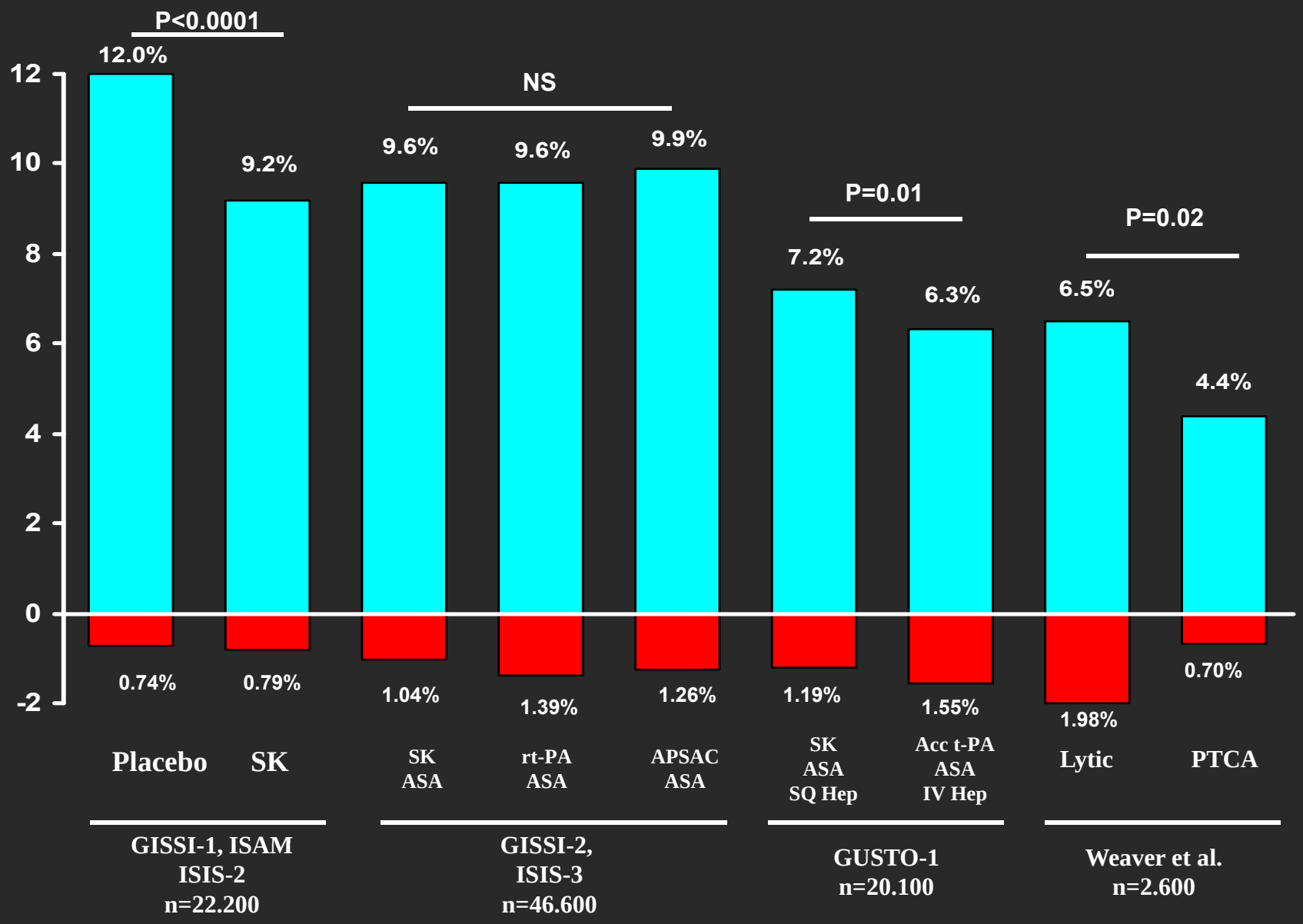




Treatment of STEMI

Why has it been so difficult to demonstrate beneficial effects of thrombus aspiration?

30-day mortality and stroke rate after reperfusion therapy



Treatment of STEMI

A randomized controlled trial demonstrating a significant reduction in mortality of adjuvant treatment in primary PCI in STEMI, with conventional pPCI 30-day mortality ~4%, would require > 2000 patients

Evidence largely based on meta-analyses

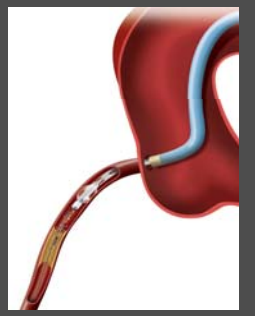
Rationale of Thrombectomy and Embolic Protection

- Smaller studies underpowered for clinical endpoints
- Surrogate endpoints associated with outcome
- Measures of incomplete reperfusion
  - Distal embolization
  - TIMI-grade flow post PCI
  - Myocardial Blush Grade MBG
  - ST-recovery
  - Infarct size
  - Myocardial salvage

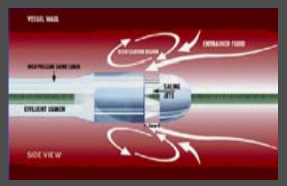
Thrombectomy and Embolic Protection Devices

- Distal embolic protection devices

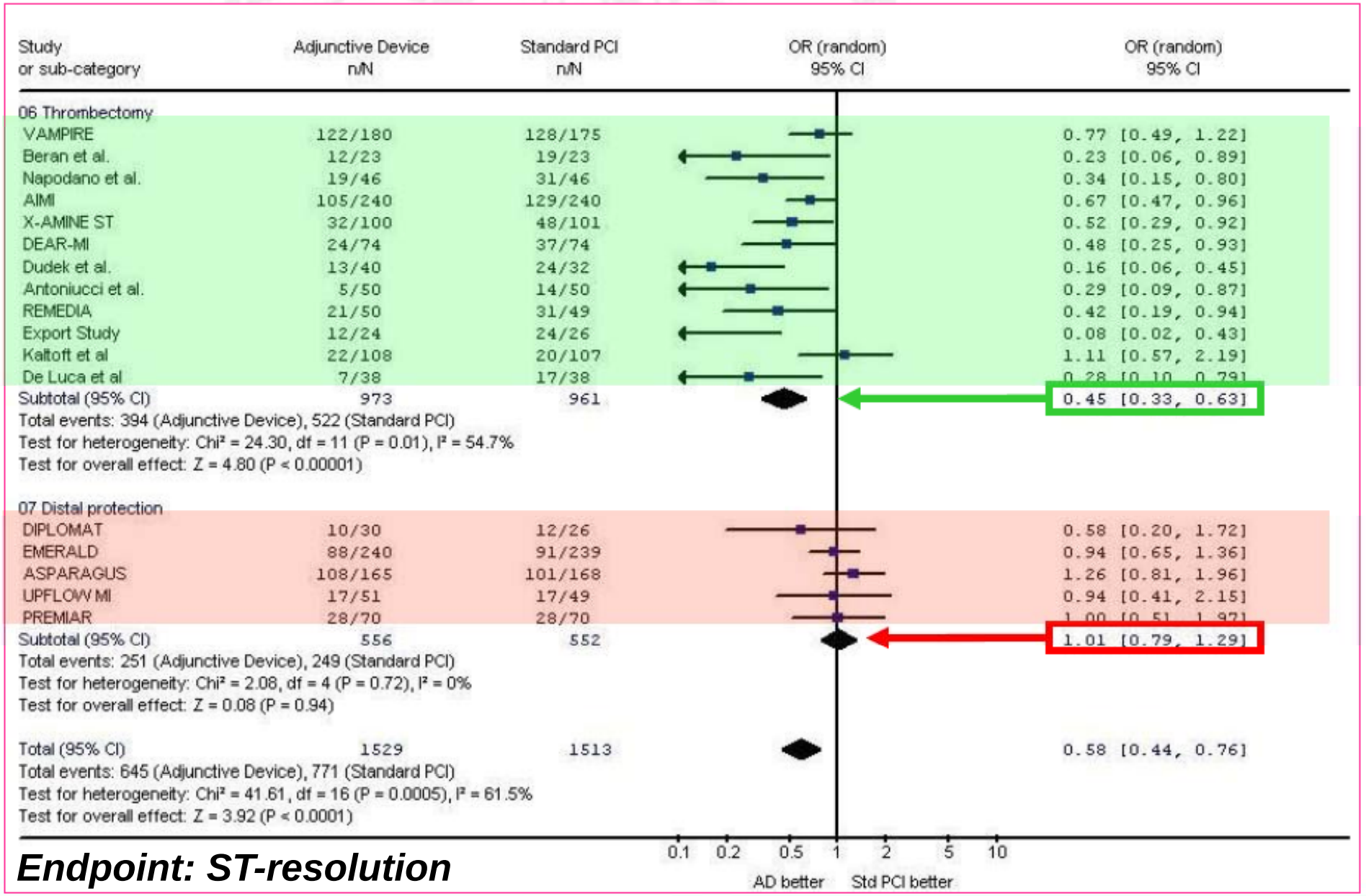
- Proximal embolic protection devices



- Thrombus aspiration catheters
  - *Mechanical*
  - *Non-manual (vacuum)*
  - *Manual*



Thrombectomy, but not distal protection, reduce no-reflow as compared to standard PCI



Endpoint: ST-resolution

INCLUDED TRIALS

MANUAL ASPIRATION

DIVER CE

REMEDIA | De Luca | PIHRATE

PRONTO

DEAR-MI

EXPORT

EXPORT | EXPIRA | TAPAS

NON-MANUAL THROMBECTOMY

ANGIOJET

Antoniucci

X-SIZER

X-AMINE ST

RESCUE

Kaltoft

TVAC

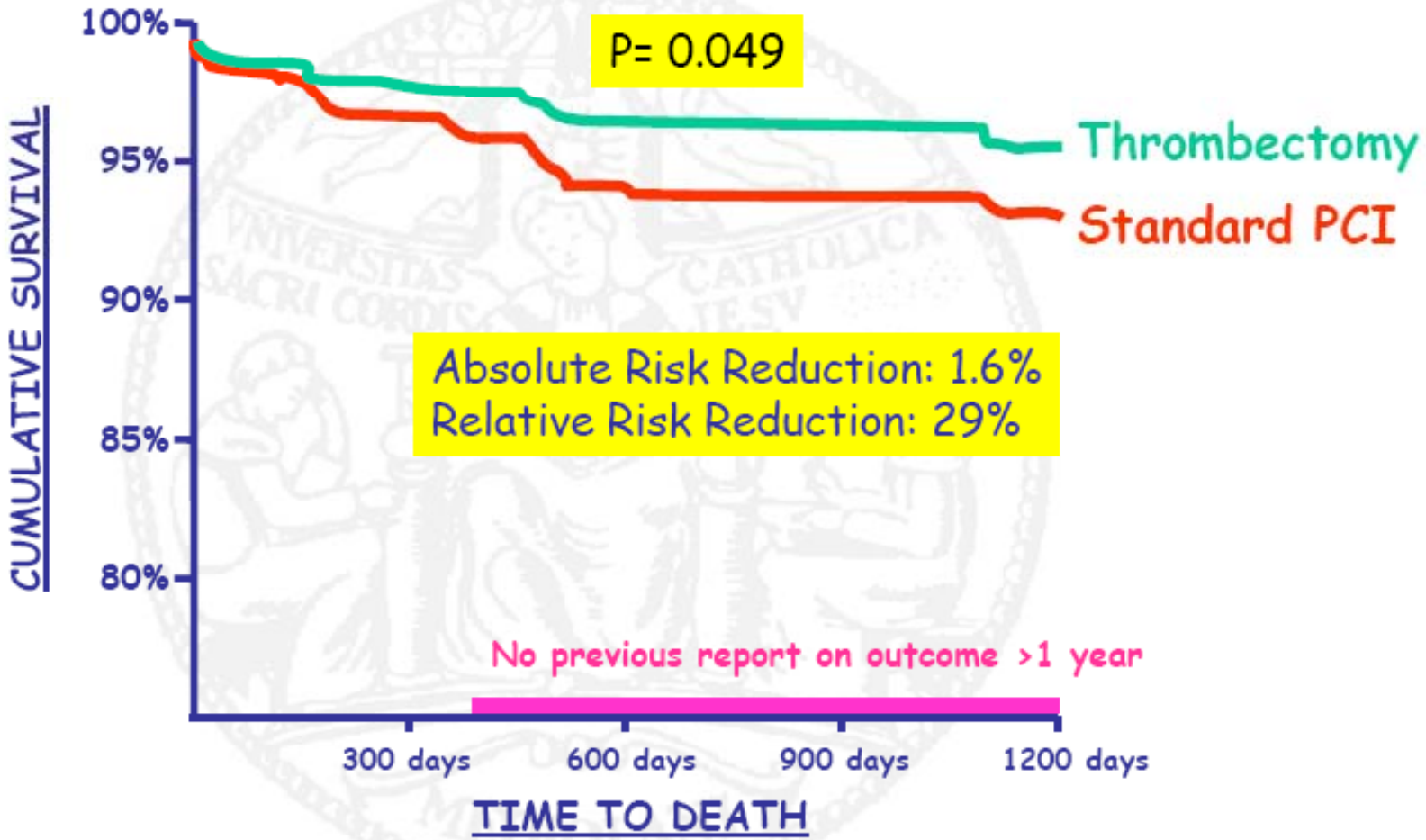
VAMPIRE

2686 pts

Median FU available for ATTEMPT study: 365 days
(significantly extended compared to published median FU of included trials: 135 days)

Burzotta et al. Eur Heart J 2009;30:2193-2203

PRIMARY END-POINT

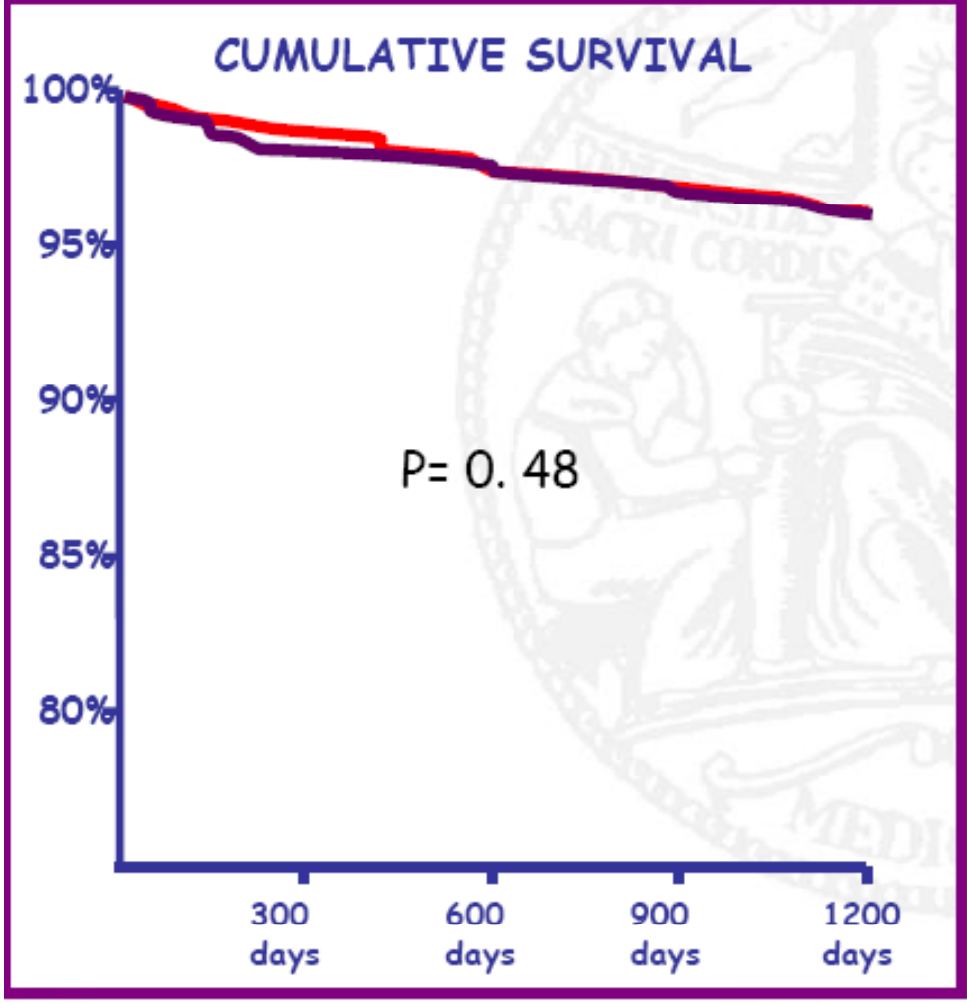


Patients at risk					
Standard PCI	1333	857	167	97	37
PCI with thrombectomy	1339	864	164	101	48

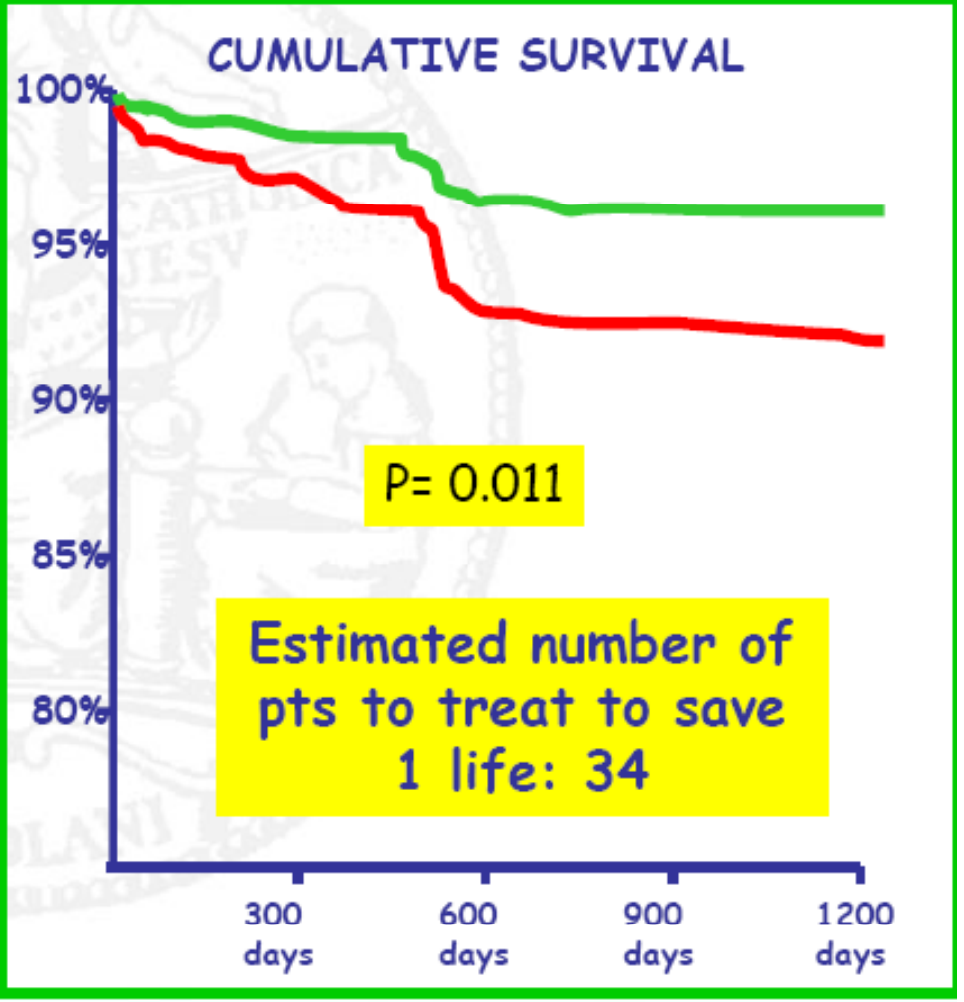
Burzotta et al. Eur Heart J 2009;30:2193-2203

TYPE OF THROMBECTOMY

NON- MANUAL THROMBECTOMY TRIALS



MANUAL ASPIRATION TRIALS

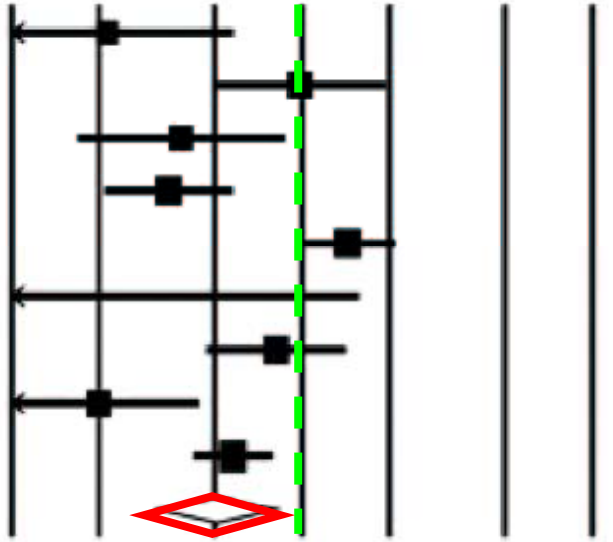


Burzotta et al. Eur Heart J 2009;30:2193-2203

Meta-analysis MBG 0-1

Study name	Device type	Year	Myocardial blush grade 0-1/Total	
			Thrombectomy	Control
Napodano	Mechanical	2003	7 / 46	21 / 46
X-AMINE ST	Mechanical	2005	23 / 92	23 / 91
REMEDIA	Manual	2005	16 / 50	27 / 49
VAMPIRE	Vacuum	2005	30 / 178	63 / 171
AIMI	Mechanical	2006	105 / 234	85 / 235
DEAR-MI	Manual	2006	0 / 74	5 / 74
Chevalier	Manual	2007	33 / 120	41 / 129
EXPIRA	Manual	2007	10 / 88	34 / 87
Svilaas	Manual	2008	84 / 490	129 / 490

Odds ratio and 95% CI

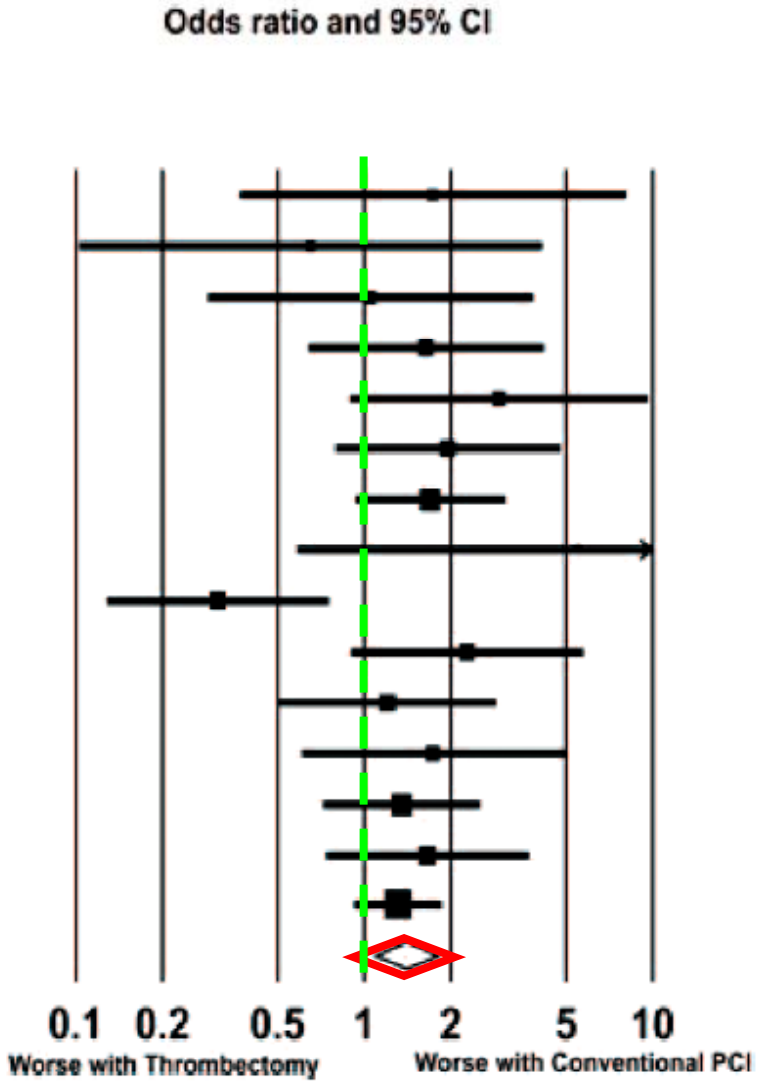


Test for heterogeneity Q= 43.23 , dF = 8, P <0.001, I^2 = 81.5%

Meta-analysis TIMI-3 flow

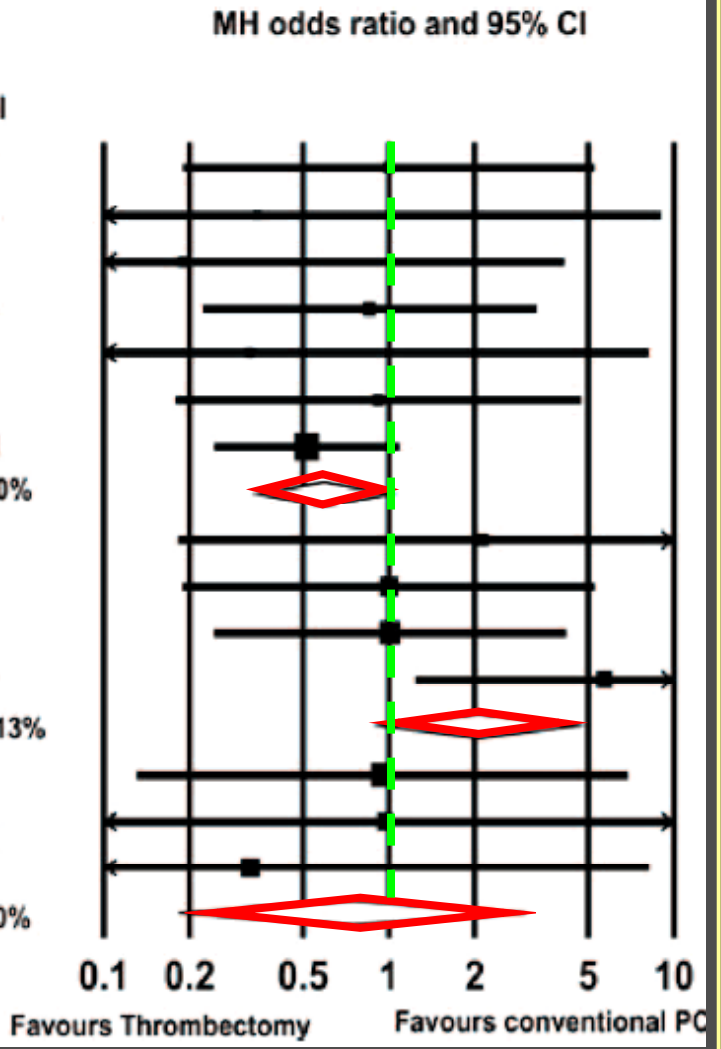
Study name	Device type	Year	TIMI-3 flow / Total	
			Thrombectomy	Control
Beran G	Mechanical	2002	27 / 30	26 / 31
Napodano	Mechanical	2003	43 / 46	44 / 46
Dudek	Vacuum	2004	34 / 40	27 / 32
NON STOP	Vacuum	2004	130 / 138	119 / 131
X-AMINE ST	Mechanical	2005	96 / 100	90 / 101
REMEDIA	Manual	2005	37 / 48	31 / 49
VAMPIRE	Vacuum	2005	155 / 177	137 / 170
Export	Manual	2005	23 / 24	21 / 26
AIMI	Mechanical	2006	213 / 234	228 / 235
DEAR-MI	Manual	2006	66 / 74	58 / 74
Kaltoft	Vacuum	2006	93 / 104	91 / 104
De Luca	Manual	2006	30 / 38	26 / 38
Chevalier	Manual	2007	98 / 120	99 / 129
PIHRATE	Manual	2007	90 / 102	77 / 94
Svilaas	Manual	2008	431 / 501	409 / 496

Test for heterogeneity Q= 17.94 , dF = 14, P =0.21, I^2 = 22%



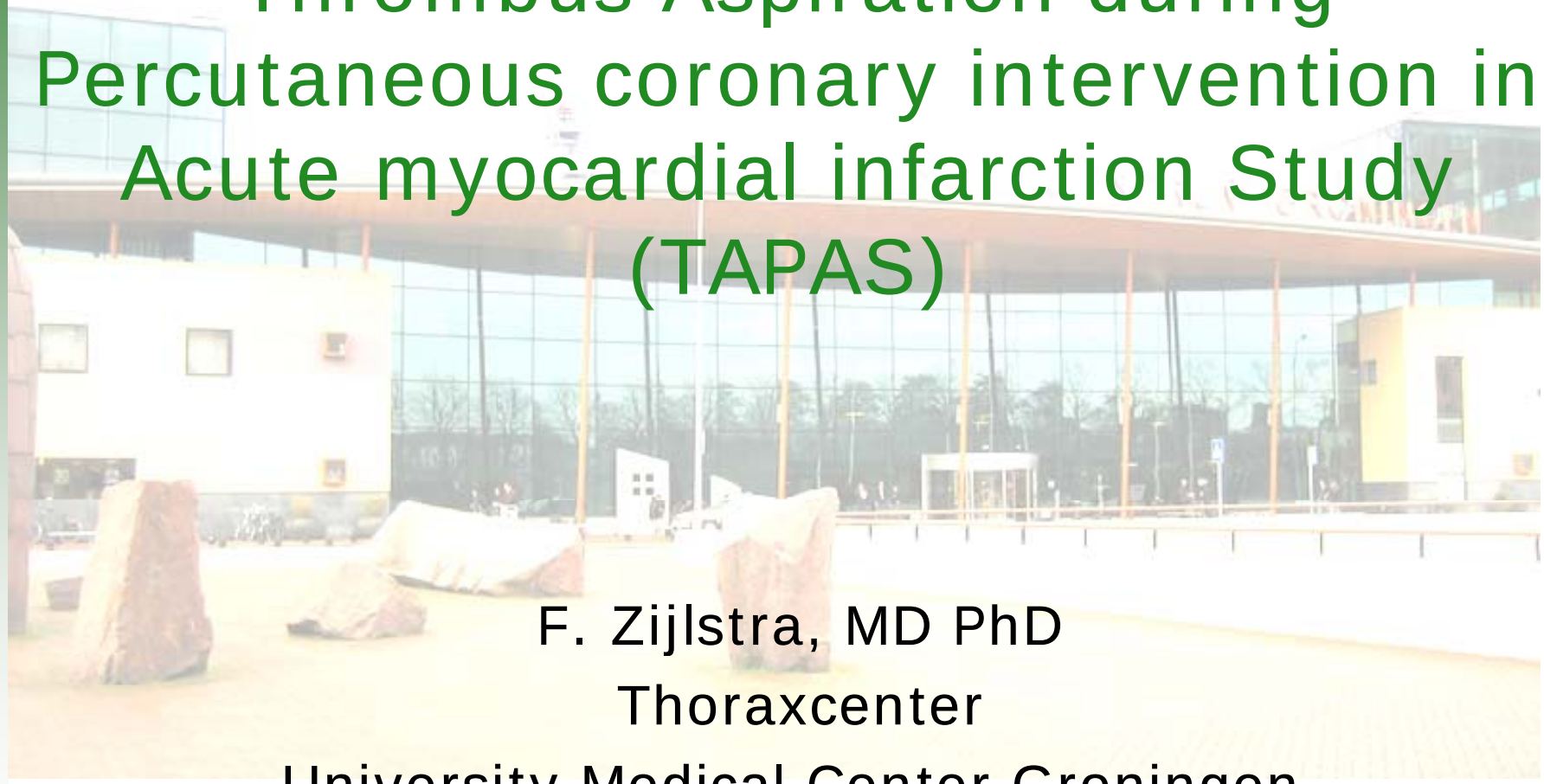
Meta-analysis Mortality

Study name	Device type	Year	Death / Total	
			Thrombectomy	Control
REMEDIA	Manual	2005	3 / 48	3 / 48
Export	Manual	2005	0 / 24	1 / 26
De Luca	Manual	2006	0 / 38	2 / 38
Chevalier	Manual	2007	4 / 120	5 / 129
EXPIRA	Manual	2007	0 / 88	1 / 87
PIHRATE	Manual	2007	3 / 102	3 / 94
Svilaas	Manual	2008	11 / 529	21 / 531
Odds ratio 0.59 (0.35-1.01; p= 0.05)	Test for heterogeneity Q= 1.86, dF = 6, P =0.93, I^2 = 0%			
Beran G	Mechanical	2002	2 / 30	1 / 31
Napodano	Mechanical	2003	3 / 46	3 / 46
X-AMINE ST	Mechanical	2005	4 / 100	4 / 101
AIMI	Mechanical	2006	11 / 240	2 / 240
Odds ratio 2.07 (0.95-4.48; p= 0.07)	Test for heterogeneity Q= 3.45, dF = 3, P =0.33, I^2 = 13%			
NON STOP	Vacuum	2004	2 / 138	2 / 131
VAMPIRE	Vacuum	2005	1 / 179	1 / 174
Kaltoft	Vacuum	2006	0 / 108	1 / 107
Odds ratio 0.75 (0.18-3.05; p= 0.69)	Test for heterogeneity Q= 0.34, dF = 2, P =0.84, I^2 = 0%			

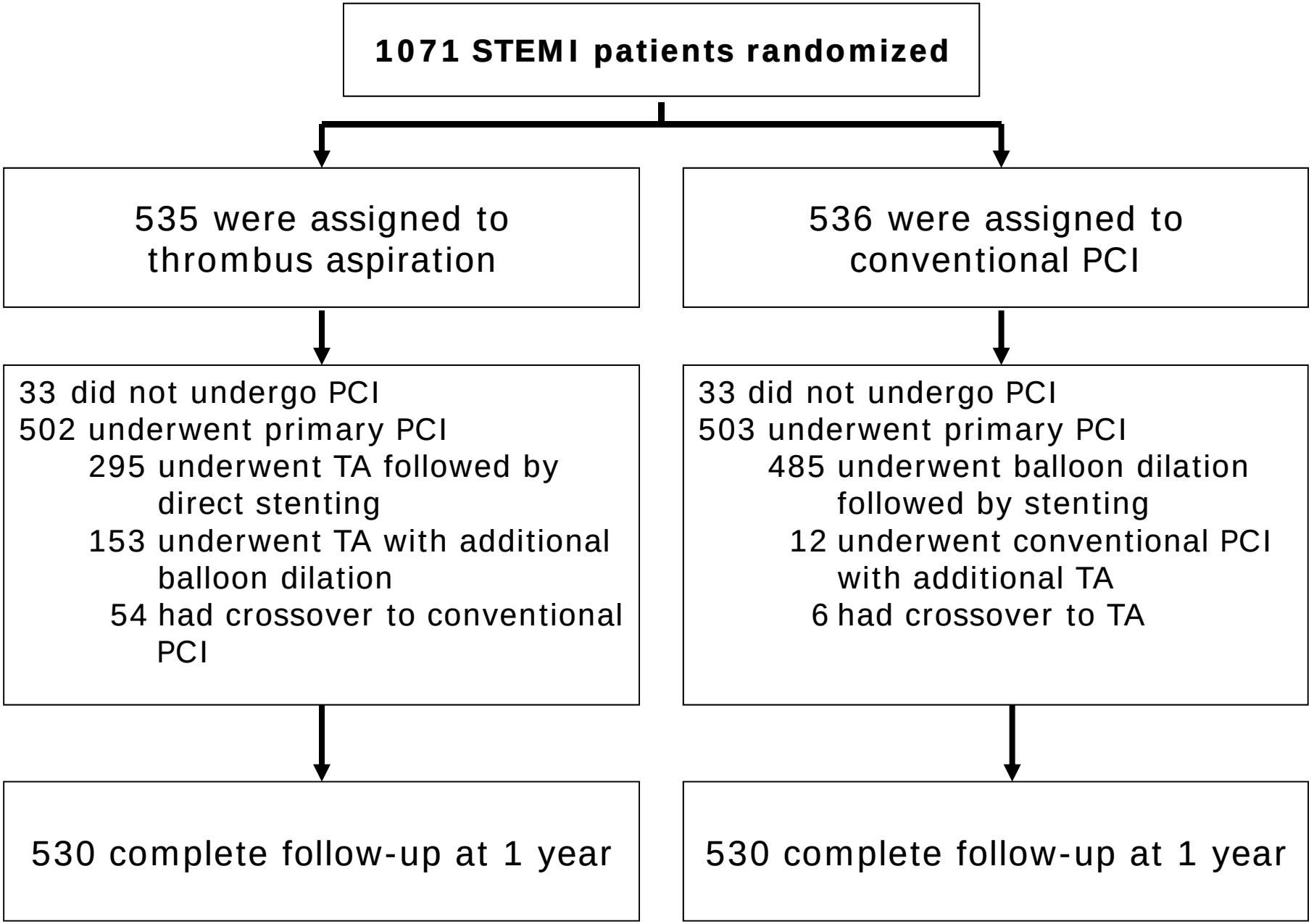


Tamhane et al. BMC Cardiovasc Disord 2010;10:10

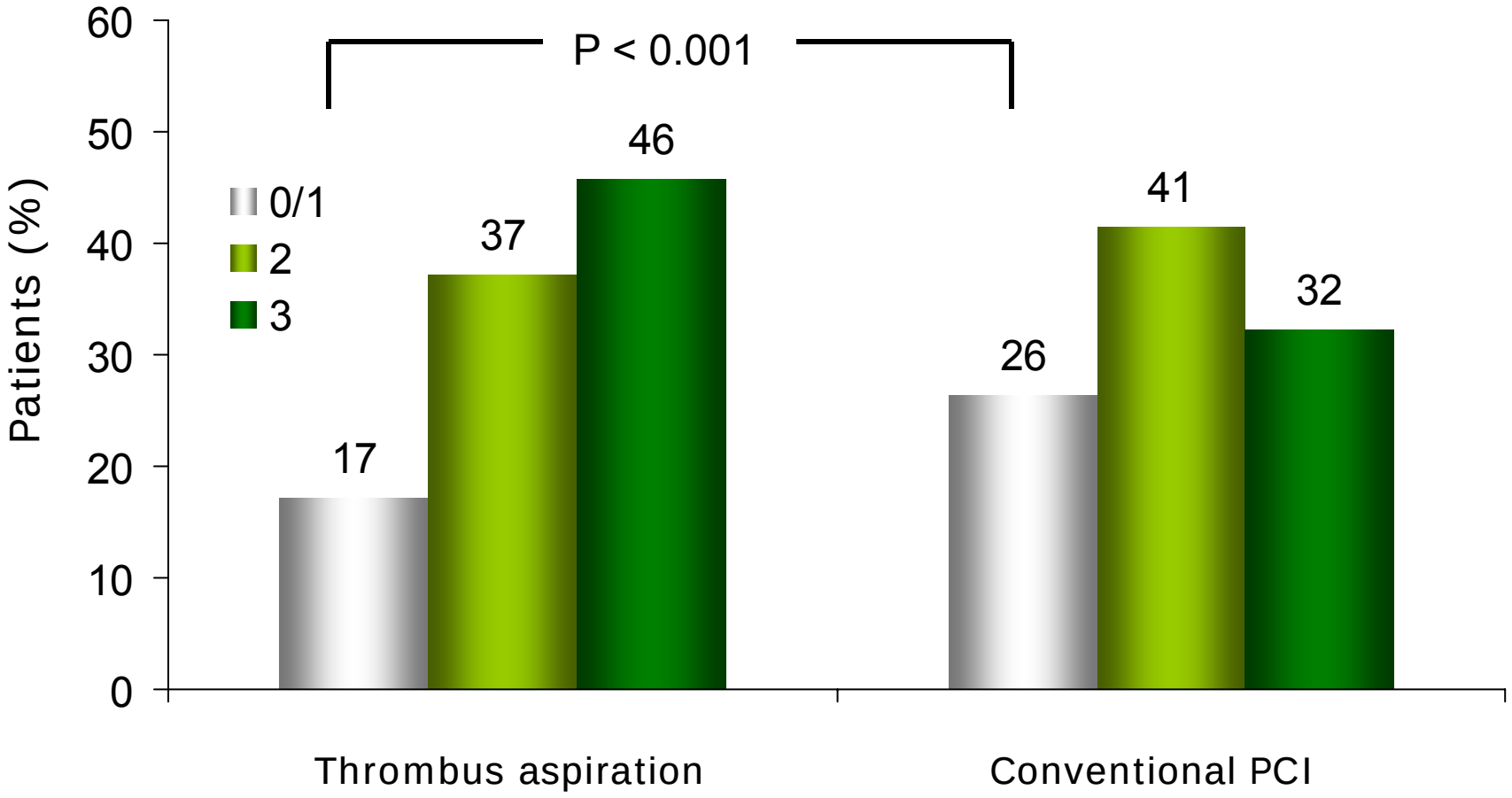
Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS)



F. Zijlstra, MD PhD
Thoraxcenter
University Medical Center Groningen,
The Netherlands

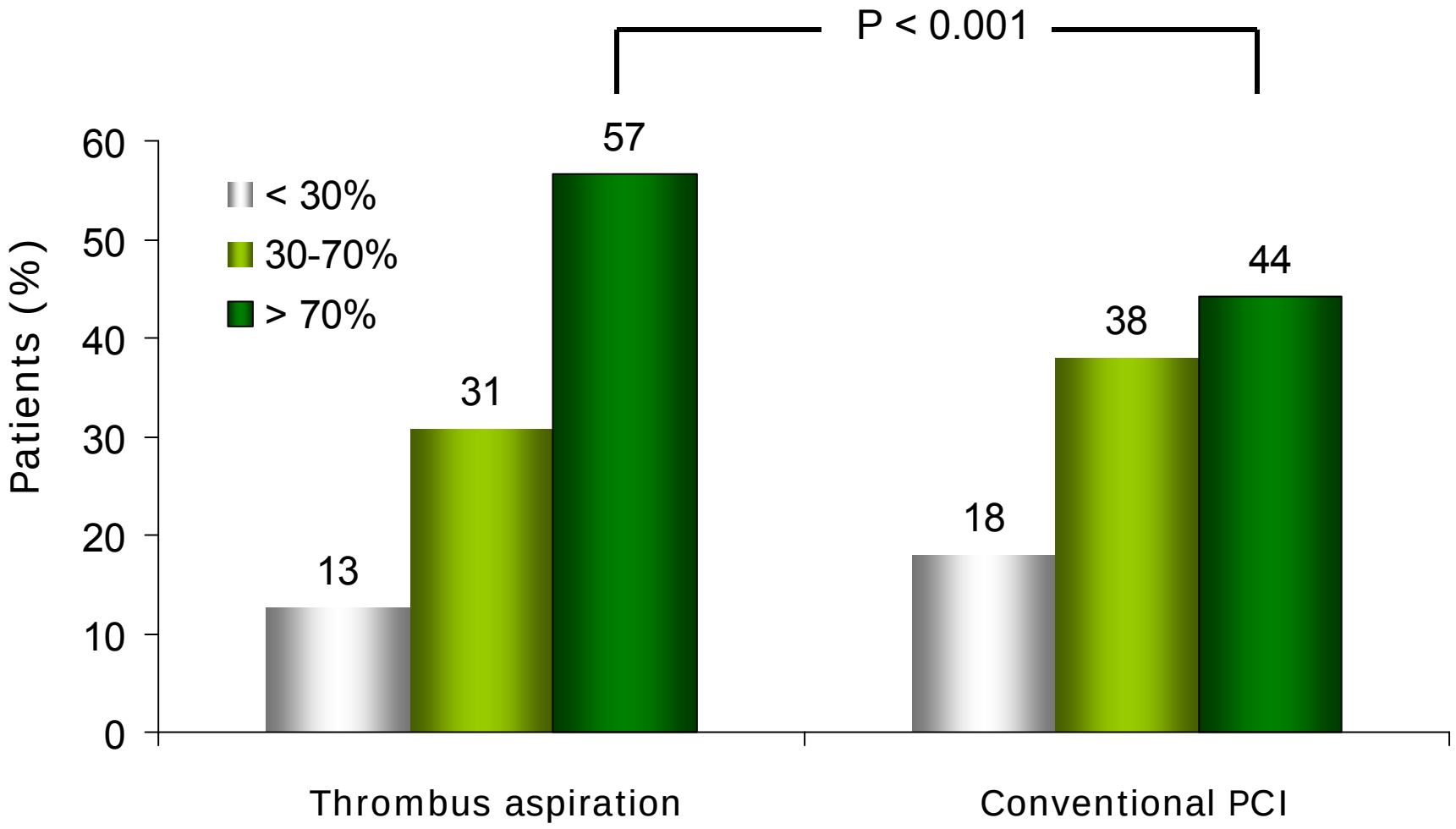

1071 STEMI patients randomized
535 were assigned to thrombus aspiration
536 were assigned to conventional PCI
33 did not undergo PCI
502 underwent primary PCI
295 underwent TA followed by direct stenting
153 underwent TA with additional balloon dilation
54 had crossover to conventional PCI
33 did not undergo PCI
503 underwent primary PCI
485 underwent balloon dilation followed by stenting
12 underwent conventional PCI with additional TA
6 had crossover to TA
530 complete follow-up at 1 year
530 complete follow-up at 1 year

Primary endpoint: Myocardial blush grade



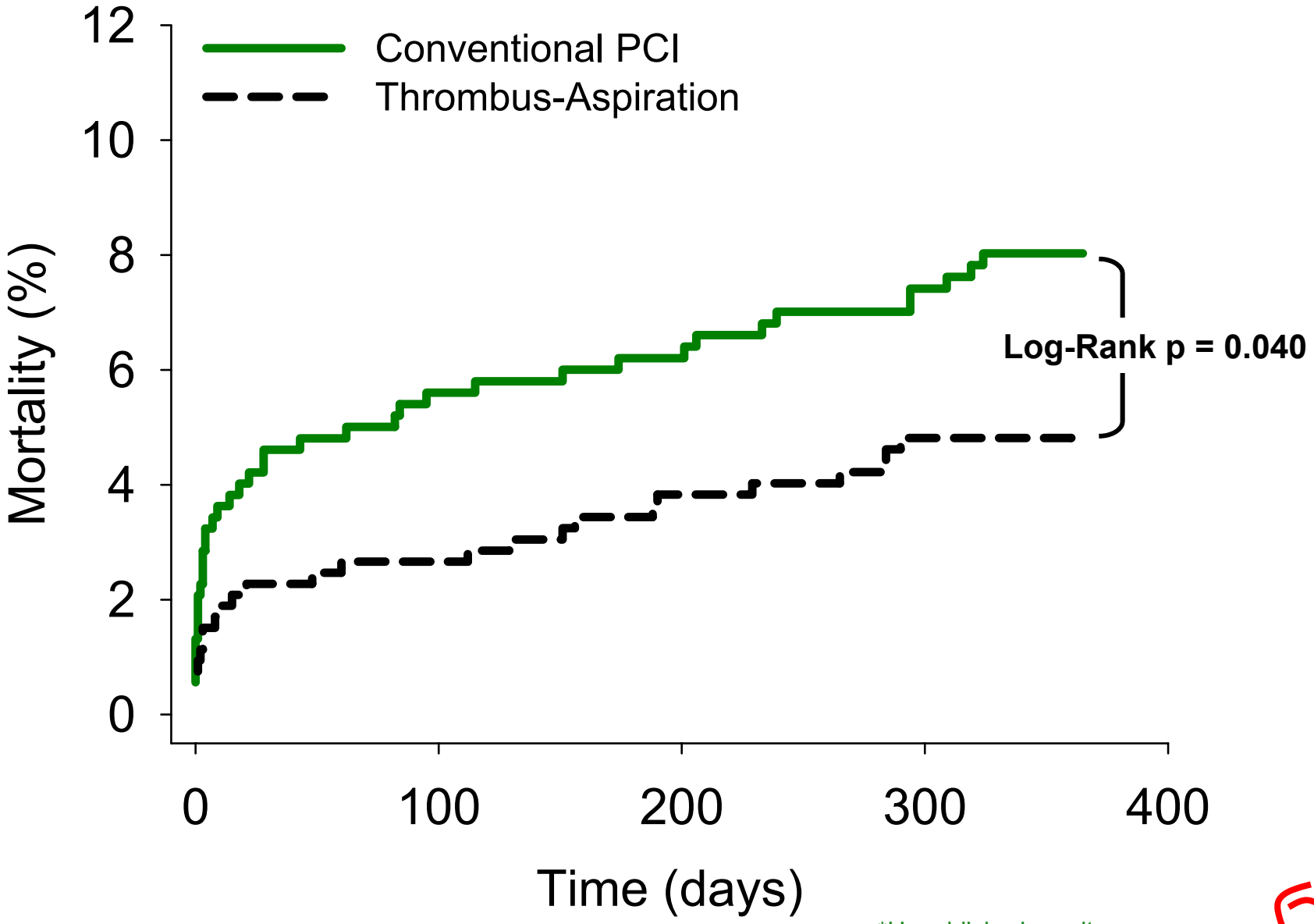
Svilaas T et al. NEJM 2008;358:557 - FZ 2008-8

ST-segment elevation resolution



Svilaas T et al. NEJM 2008;358-557 - FZ 2008-9

Mortality at 1 year



*Unpublished results

Comparison of Angio*JET* Rheolytic Thrombectomy Before Direct Infarct Artery *STENT*ing with Direct Stenting Alone in Patients with Acute Myocardial Infarction: the *JETSTENT trial*

David Antoniucci on behalf of the JETSTENT Investigators

ACC.10 i2 summit 2010

Study Design

Pts with STEMI admitted within 12 hours from symptom onset

- Lysis
- Stroke < 30 days
- Surgery < 6 weeks
- Pre-stented IRA

After angiography and IRA wiring: thrombus grade 3 to 5

Randomization 1:1
N = 500

Direct Stenting (DS)

Rheolytic Thrombectomy +DS

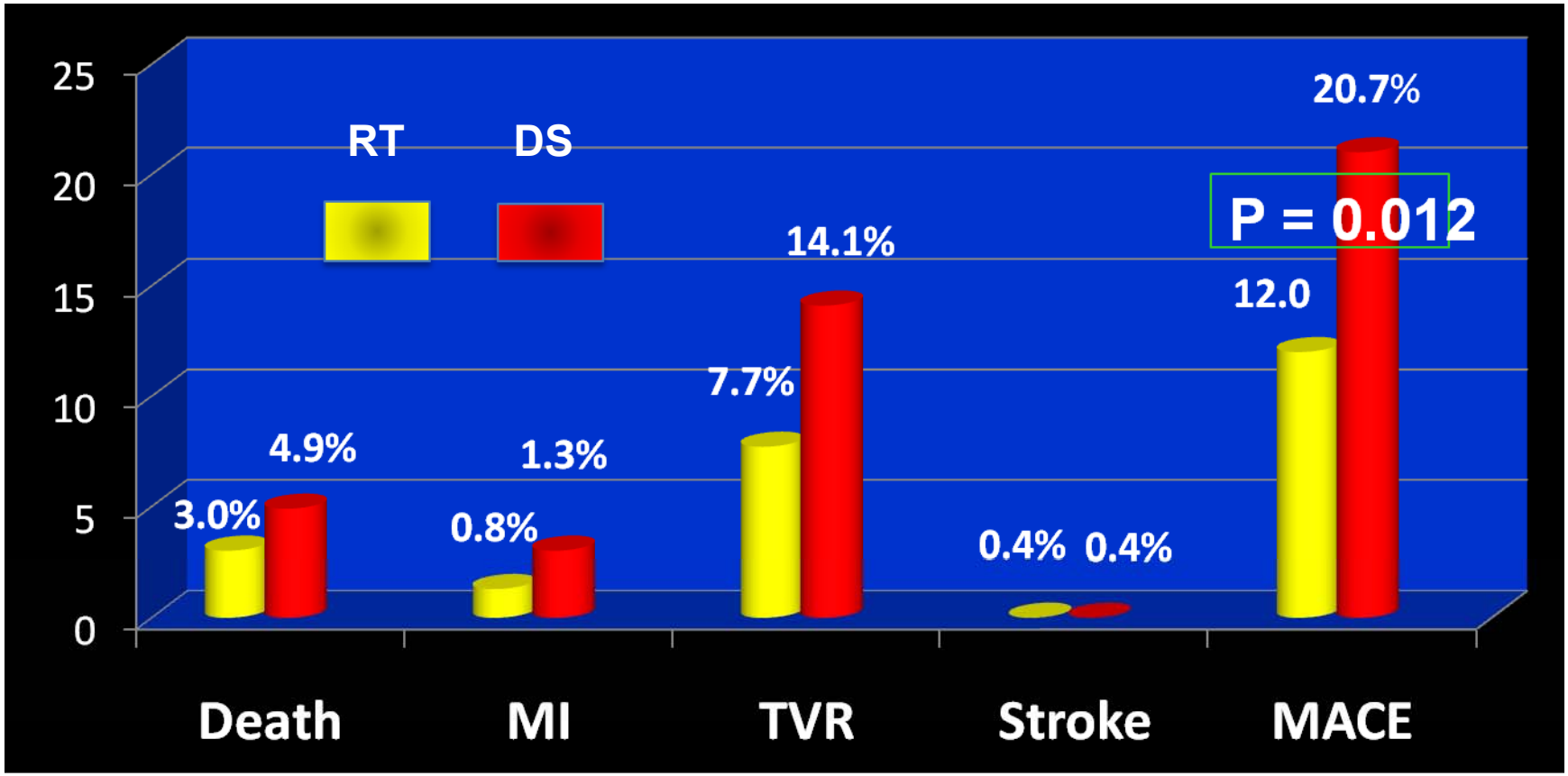
Technique for AngioJet Use and DS

- **Single pass anterograde technique**
  (activate AngioJet proximal to thrombus)
- Angiographic check after first AngioJet pass.
- **Temporary pacemaker strongly discouraged.**
- Balloon pre-dilation strongly discouraged.
- **DS had to be attempted in all cases in both arms.**
- **Routine Abciximab in both arms.**

Surrogate Endpoints

	RT	DS	p value
STR ≥ 50% at 30 min	n=246 211 (85.8)	n=240 189 (78.8)	.043
Infarct Size (%)	n=217 11.8 [3.1-23.7]	n=208 12.7 [4.7-23.3]	.398
Final TIMI 3 flow	n=252 203 (80.6)	n=241 207 (85.9)	.113
cTFC	n=228 20 [15.0-27.2]	n=216 20 [14.0-25.7]	.357
Blush grade	n=215	n=211	.207
0-1	17 (8)	11 (5)	
2	43 (20)	33 (16)	
3	155 (72)	167 (79)	

6-Month Outcome



Primary PCI: Adjunctive Therapies

Recommendations	Class	LOE
▪ Antiplatelet co-therapy		
❑ Aspirin	I	B
❑ NSAID and COX-2 selective inhibitors	III	B
❑ Clopidogrel loading dose	I	C
❑ GPIIb/IIIa antagonist		
▪ abciximab	IIa	A
▪ tirofiban	IIb	B
▪ eptifibatide	IIb	C
▪ Antithrombin co-therapy		
❑ heparin	I	C
❑ bivalirudin	IIa	B
❑ fondaparinux	III	B
▪ Adjunctive devices		
❑ Thrombus aspiration	IIb	B

2009 Focused Updates: STEMI and PCI Guidelines

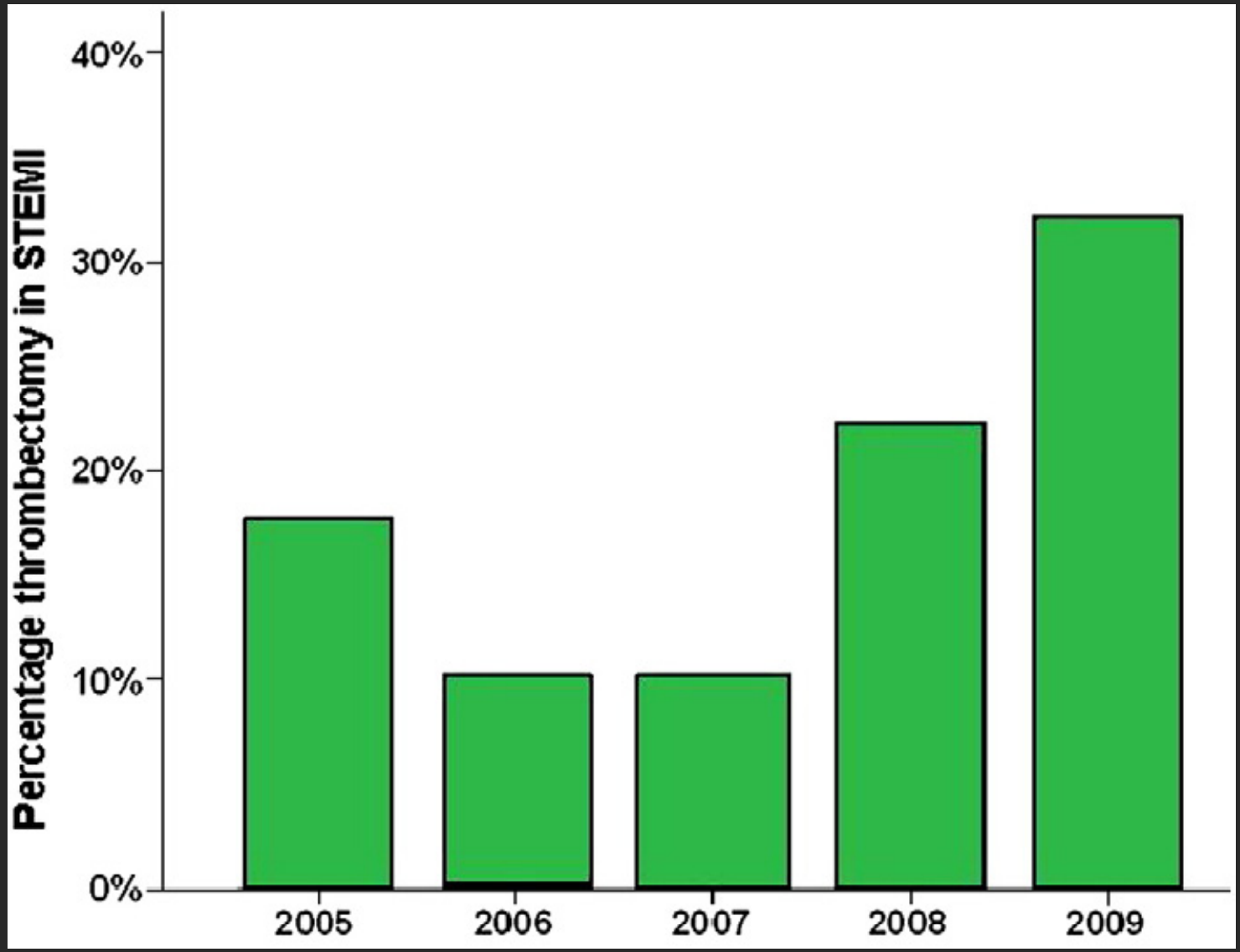
2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update)

- **upgrade of the recommendation for PCI in unprotected left main disease from a class III to a class IIb indication.**

- **the use of aspiration thrombectomy in primary PCI.**
  IIa, LOE **B**

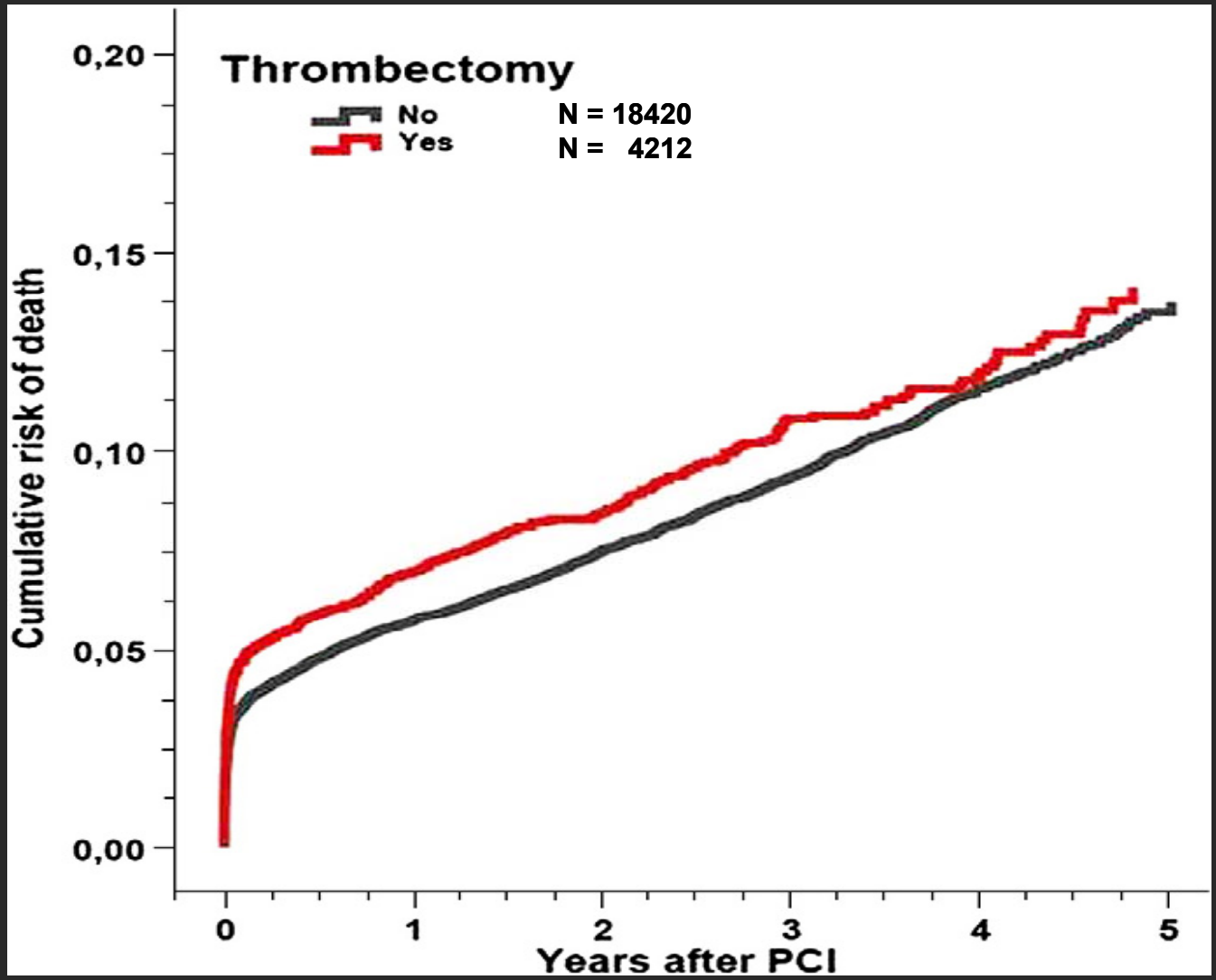
CCI on line; 18 november 2009

Thrombus Aspiration in the SCAAR registry



Frobert et al. Int J Cardiol 2010;145:572-3

Thrombus Aspiration in the SCAAR registry



Frobert et al. Int J Cardiol 2010;145:572-3

Thrombus Aspiration Trials in Progress

Rationale and design of the INFUSE-AMI study: A 2 × 2 factorial, randomized, multicenter, single-blind evaluation of intracoronary abciximab infusion and aspiration thrombectomy in patients undergoing percutaneous coronary intervention for anterior ST-segment elevation myocardial infarction

C. Michael Gibson, MS, MD,[a,j] Akiko Maehara, MD,[b,j] Alexandra J. Lansky, MD,[b,j] Jochen Wohrle, MD,[c,j] Tom Stuckey, MD,[d,j] Rajesh Dave, MD,[e,j] David Cox, MD,[f,j] Cindy Grines, MD,[g,j] Dariusz Dudek, MD,[h,j] Gabriel Steg, MD,[i,j] Helen Parise, ScD,[i,j] Steven D. Wolff, MD, PhD,[b,j] Ecaterina Cristea, MD,[b,j] and Gregg W. Stone, MD[b,j] *Boston, MA; New York, NY; Ulm, Germany; Greensboro, NC; Harrisburg, and Allentown, PA; Royal Oak, MI; Krakow, Poland; and Paris, France*

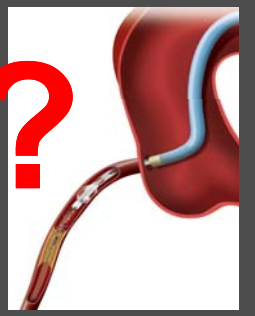
Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE trial). A multicenter, prospective, randomized, controlled clinical registry trial based on the Swedish angiography and angioplasty registry (SCAAR) platform. Study design and rationale

Ole Fröbert, MD, PhD,[a] Bo Lagerqvist, MD, PhD,[b] Thórarinn Gudnason, MD, PhD, FESC,[c] Leif Thuesen, MD, PhD,[d] Roger Svensson, MSci,[e] Göran K. Olivecrona, MD, PhD,[f] and Stefan K. James, MD, PhD[b] *Örebro, Uppsala and Lund, Sweden; Reykjavik, Iceland; and Aarhus, Denmark*

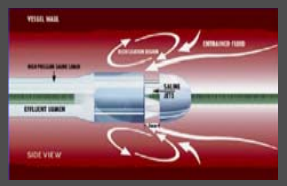
Thrombectomy and Embolic Protection Devices

- Distal embolic protection devices ?

- Proximal embolic protection devices ?



- Thrombectomy catheters ?!
  - *Mechanical*
  - *Non-manual (vacuum)* ?
  - *Manual*



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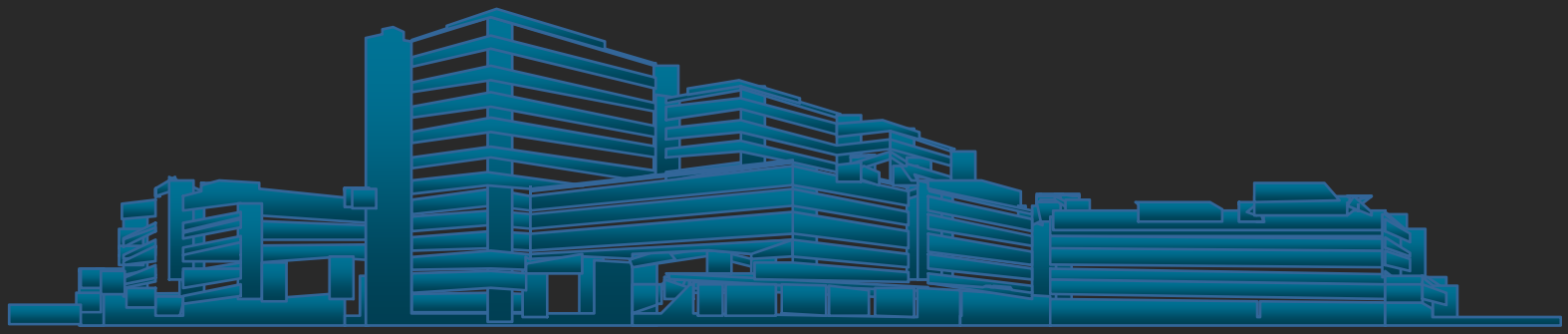
Paris, 28 mei, EuroPCR 2010

Should we perform Thrombus Aspiration in all STEMI Patients undergoing primary PCI?

YES




Academisch Medisch Centrum
Thank You

Table 1

One-year clinical outcomes in selected randomized ST segment myocardial infarction trials from 2000 to 2010

Study	Yr	Intervention	Control	*n*	All-cause death (%)		Cardiac mortality (%)		MI (%)	
					C	S	C	S	C	S
NORDISTEMI[16]	2010	All PCI	Selective	276	3.0	2.2	NA	NA	9.0	3.0
HORIZONS AMI[17]	2009	Bivalurudin	Hep/Gp	3602	4.8	3.5	3.8	2.1	NA	NA
TAPAS[5]	2008	TA + PCI	PCI/no TA	1071	7.6	4.7	6.7	3.6	4.3	2.2
DANAMI-2[18]	2008	PCI	Lytic	1424	1.3	1.4	NA	NA	0.9	1.3
Transfer with Tirofiban for PCI	2007	Transfer/PCI	Lytic	401	NA	NA	12.5	7.0	7.5	3.5
Thrombolysis with STEMI[19]										
SESAMI[20]	2007	DES	BMS	320	4.3	1.8	NA	NA	1.8	1.8
TYPHOON[21]	2006	DES	BMS	712	2.2	2.3	1.4	2.0	1.4	1.1
PASSION[22]	2006	DES	BMS	619	NA	NA	6.5	4.5	1.9	1.6
ADMIRAL[23]	2004	Abciximab + PCI	PCI	400	12.5	6.0	10.5	5.0	6.0	1.0
STENTIM-2[24]	2000	BMS	BA	211	1.9	3.0	NA	NA	5.5	4.0

BA: Balloon angioplasty; BMS: Bare metal stent; C: Control group; DES: Drug-eluting stent; Gp: Glycoprotein IIb/IIIa inhibitors; Hep: Heparin; MI: Myocardial infarction; NA: Not applicable; S: Study (intervention) coronary interventio

Table 2

Randomized studies utilizing manual aspiration devices in ST segment myocardial infarction and primary percutaneous coronary intervention[1]

Study	Yr	*n*	Device	Primary endpoint(s)	Outcomes[1]
EXPIRA[14]	2009	175	Export (Medtronic, Minneapolis, MN, USA)	MBG > 2, STR	Improvement
VAMPIRE[11]	2008	355	TVAC (Nipro, Osaka, JP)	SR or NR	Trend to improvement
TAPAS[5]	2008	1071	Export (Medtronic, Minneapolis, MN, USA)	MBG	Improvement
De Luca *et al*[8]	2006	76	Diver CE (Invatec, Brescia, IT)	MBG > 2, STR	Improvement
Kaltoft et al[9]	2006	215	Rescue (BSC, Maple Grove, MN, USA)	Myocardial salvage	No improvement
DEAR-MI[10]	2006	148	Pronto (Vascular Solutions, Minneapolis, MN, USA)	STR, MBG 3	Improvement
REMEDIA[6]	2005	99	Diver CE (Invatec, Brescia, IT)	MBG > 2, STR	Improvement

[1]Please see text for study data. MBG: Myocardial blush grade; NR: No reflow; SR: Slow reflow; STR: ST segment resolution.