INSTITUT CARDIOVASCULAIRE PARIS SUD

TASTE trial: No benefit, time to rethink

Bernard Chevalier,

ICPS Massy

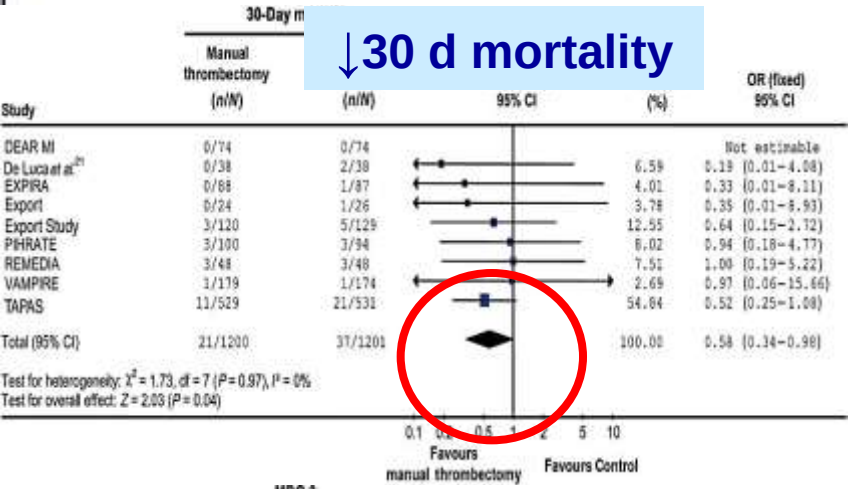
France

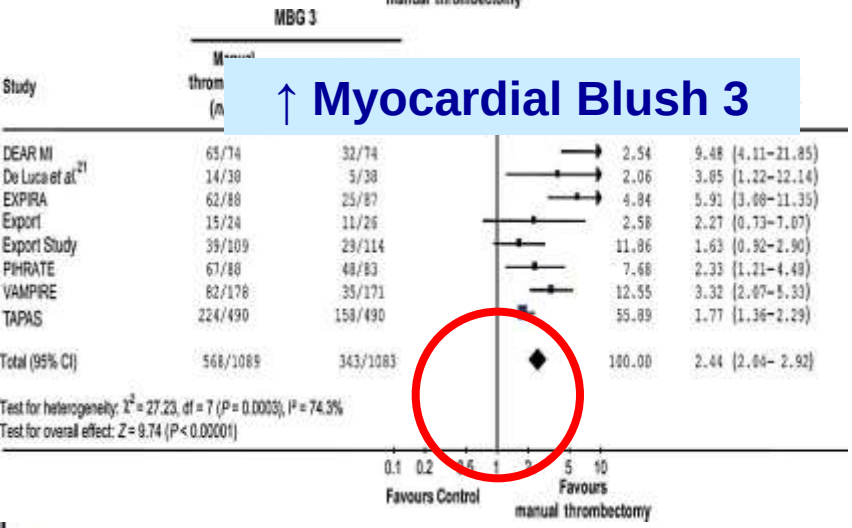
GÉNÉRALE DE SANTÉ

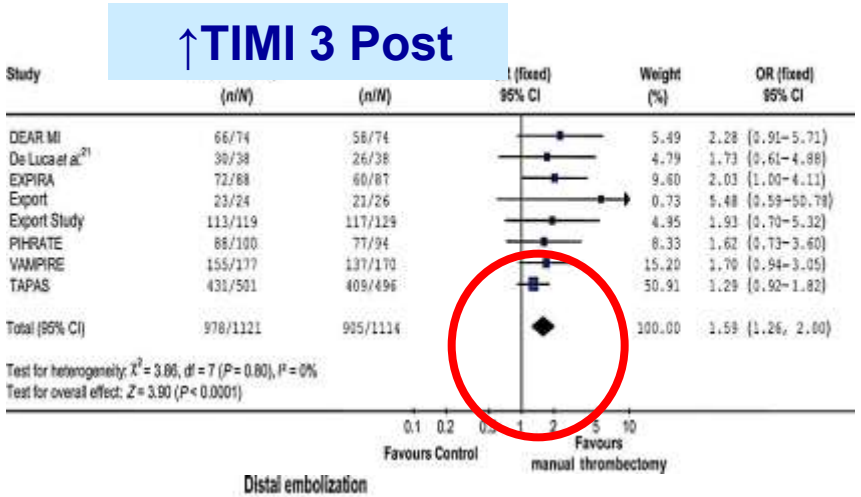
In the last five years , I received research grants or speaker fees or I am/was consultant for: Abbott Vascular, Asahi, Astra Zeneca, AVI, Boston Scientific, Biotronik, Colibri, Cook, Cordis, Daichi-Sankyo, Eli-Lilly, Iroko, Medtronic, Terumo. I am currently minor shareholder & general mamager of CERC (CRO)

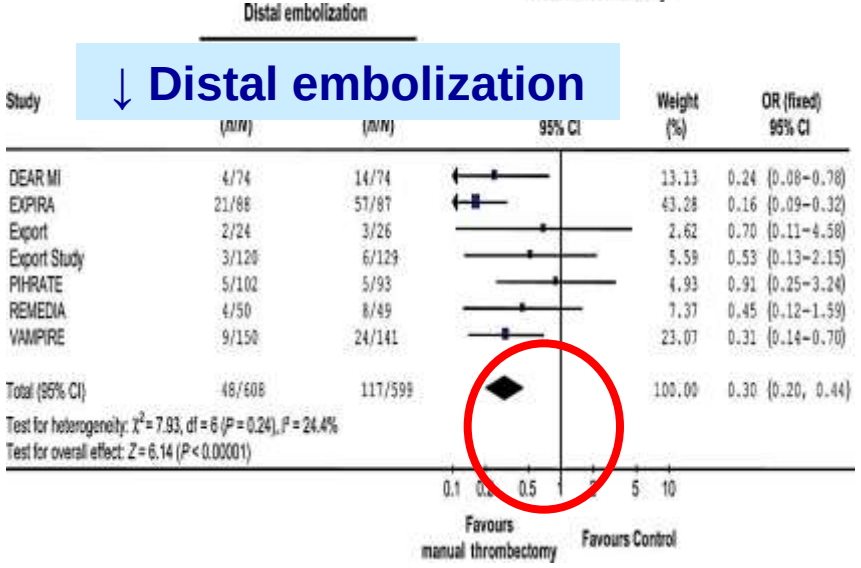
. Metanalysis.

9 randomized trials with 2417 patients









De Luca et al. EHJ 2008;29:3002-3010

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 24, 2013 VOL. 369 NO. 17

Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

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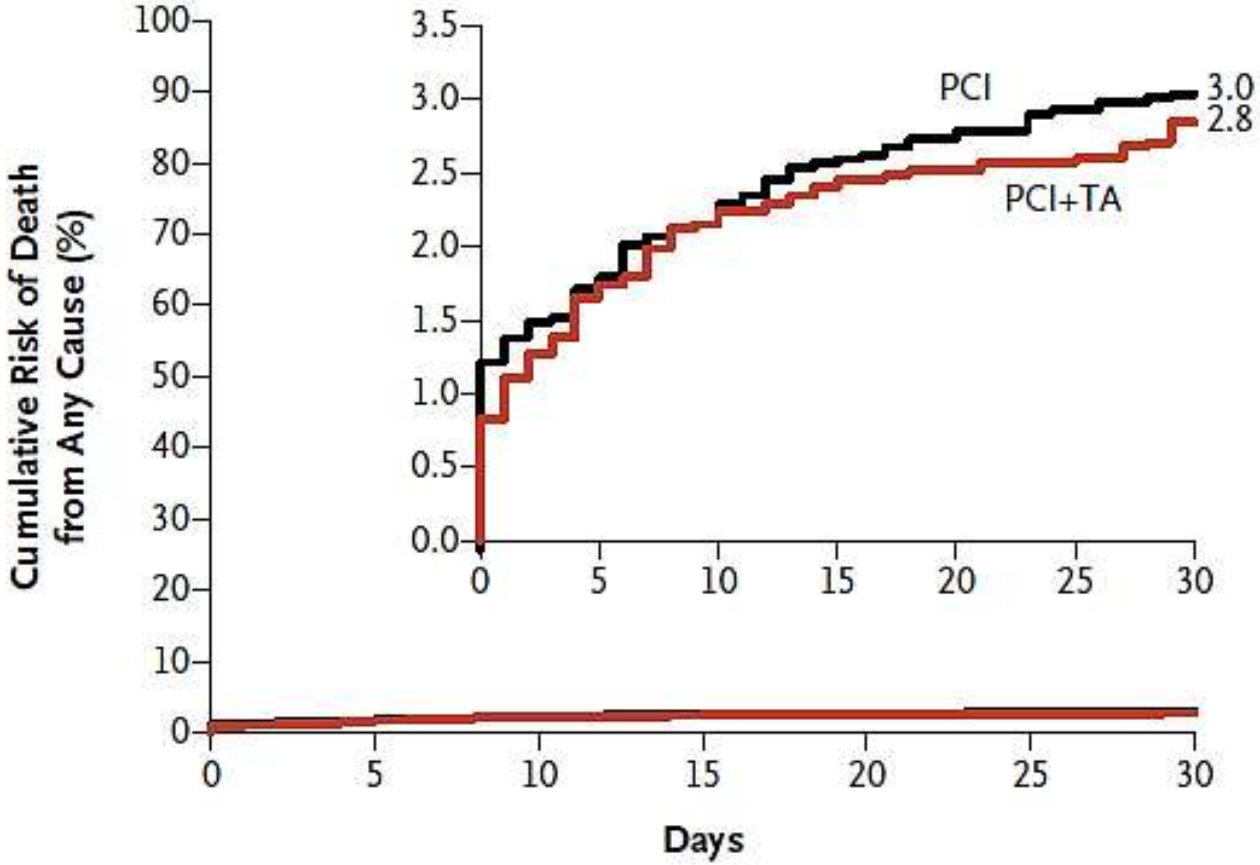
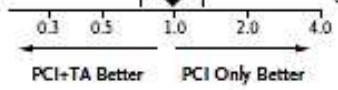
A

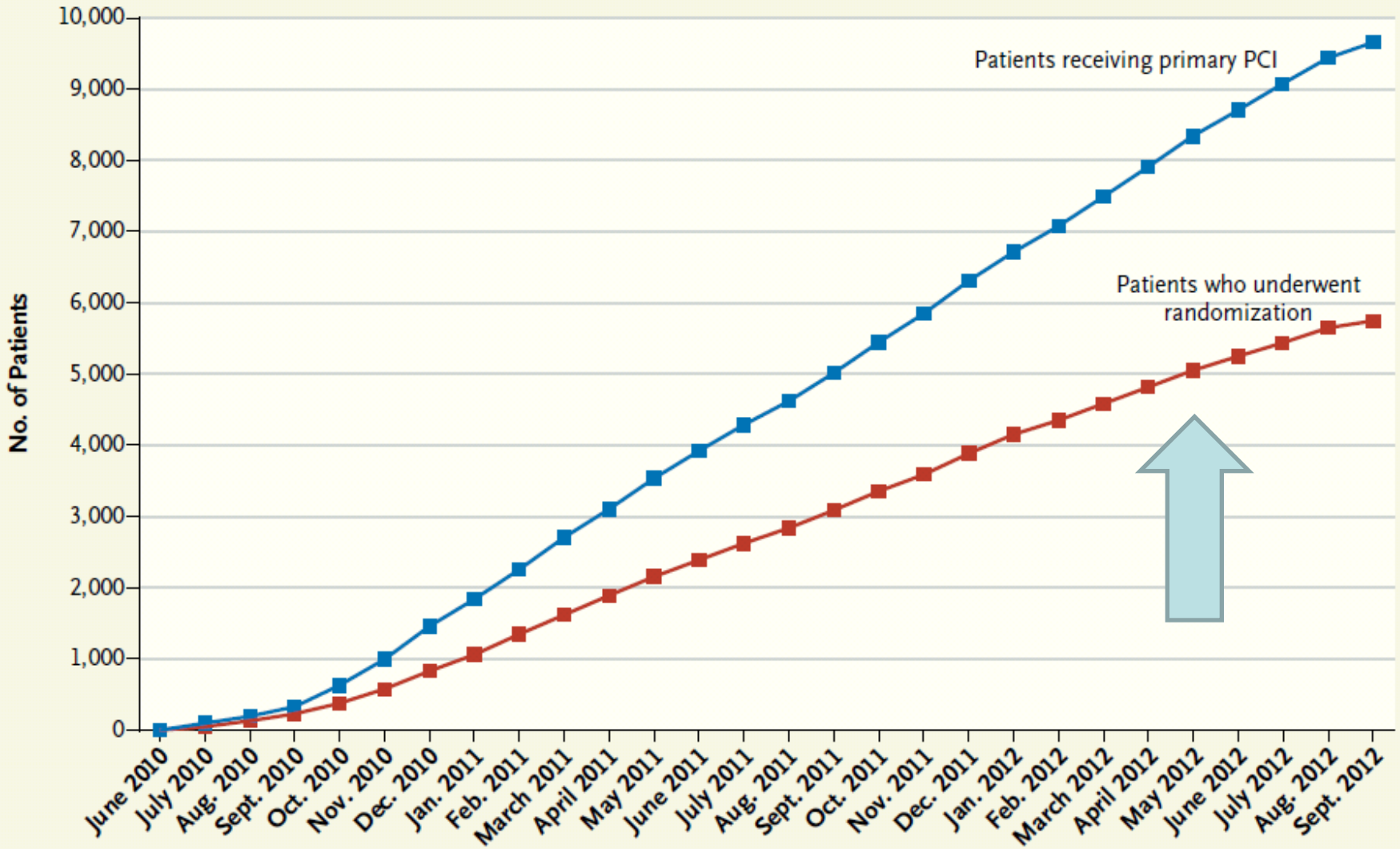


No. at Risk							
PCI+TA	3621	3568	3540	3532	3526	3524	3519
PCI	3623	3567	3545	3530	3523	3517	3513

Subgroup	PCI+TA	PCI Only	Hazard Ratio (95% CI)	P Value for Interaction
	no. of deaths/total no. of patients			
All patients	103/3621	110/3623	0.94 (0.72–1.22)	
Sex				0.51
Female	37/900	45/920	0.84 (0.54–1.29)	
Male	66/2721	65/2703	1.01 (0.72–1.42)	
Age				0.09
<65 yr	95/1955	92/1875	0.99 (0.74–1.32)	
≥65 yr	8/1666	18/1748	0.47 (0.20–1.07)	
Diabetes				0.55
Yes	23/448	21/453	1.11 (0.61–2.00)	
No	78/3155	86/3155	0.91 (0.67–1.23)	
Smoker				0.46
Yes	14/1083	23/1173	0.66 (0.34–1.28)	
No	70/2336	76/2211	0.87 (0.63–1.20)	
Previous myocardial infarction				0.81
Yes	13/402	14/439	1.01 (0.48–2.15)	
No	85/3172	92/3138	0.91 (0.68–1.23)	
Previous PCI				0.60
Yes	6/337	9/362	0.71 (0.25–2.00)	
No	97/3284	101/3261	0.95 (0.72–1.26)	
Time from symptom onset to PCI				0.98
>2 hr	73/2308	77/2308	0.95 (0.69–1.30)	
≤2 hr	13/800	14/805	0.94 (0.44–1.99)	
Time from ECG to PCI				0.66
>Median	61/1765	61/1732	0.98 (0.69–1.40)	
≤Median	42/1816	49/1843	0.87 (0.58–1.31)	
Target vessel				0.73
Left anterior descending artery	60/1467	58/1449	1.02 (0.71–1.16)	
Left circumflex artery	10/494	13/471	0.73 (0.32–1.67)	
Right coronary artery	24/1436	28/1443	0.86 (0.50–1.49)	
Proximal lesion				0.29
Yes	94/2903	96/2935	0.99 (0.74–1.32)	
No	9/718	14/688	0.62 (0.27–1.42)	
Thrombus grade				0.93
4–5	41/1138	41/1078	0.95 (0.61–1.46)	
0–3	61/2451	64/2499	0.97 (0.68–1.38)	
TIMI grade before PCI				0.36
0–1	91/2821	92/2811	0.98 (0.74–1.32)	
2–3	12/792	18/809	0.68 (0.33–1.41)	
Bivalirudin therapy				0.85
Yes	86/2874	92/2835	0.92 (0.69–1.24)	
No	17/746	18/782	0.99 (0.51–1.92)	
Glycoprotein IIb/IIIa blocker therapy				0.36
Yes	10/558	17/630	0.66 (0.30–1.44)	
No	93/3063	93/2993	0.98 (0.73–1.30)	



The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?



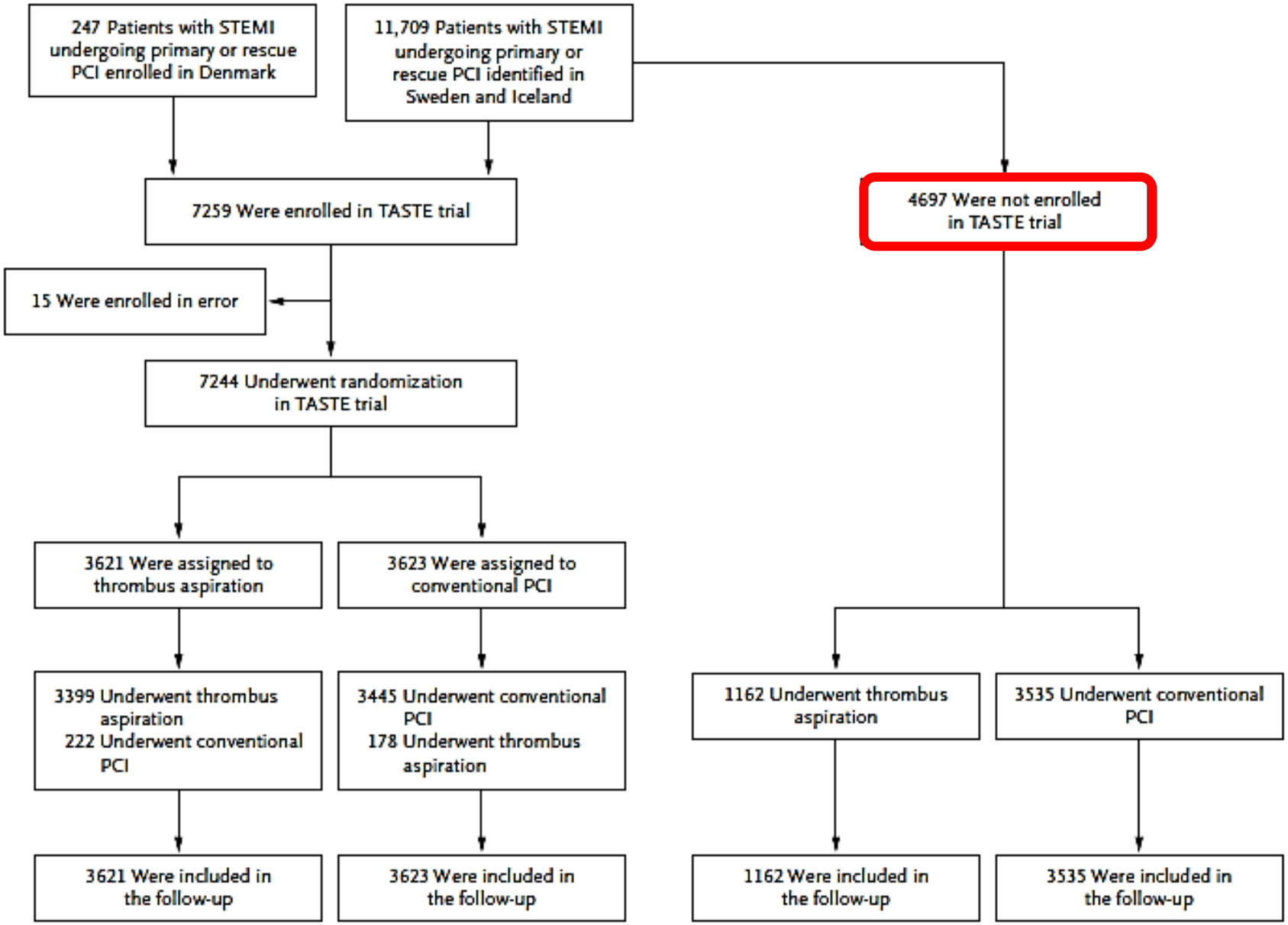

247 Patients with STEMI undergoing primary or rescue PCI enrolled in Denmark
11,709 Patients with STEMI undergoing primary or rescue PCI identified in Sweden and Iceland
7259 Were enrolled in TASTE trial
4697 Were not enrolled in TASTE trial
15 Were enrolled in error
7244 Underwent randomization in TASTE trial
3621 Were assigned to thrombus aspiration
3623 Were assigned to conventional PCI
3399 Underwent thrombus aspiration
222 Underwent conventional PCI
3445 Underwent conventional PCI
178 Underwent thrombus aspiration
1162 Underwent thrombus aspiration
3535 Underwent conventional PCI
3621 Were included in the follow-up
3623 Were included in the follow-up
1162 Were included in the follow-up
3535 Were included in the follow-up

Table 1. Baseline Characteristics of the Patients According to Randomization Status and Treatment Group.*

Characteristic	Patients Who Underwent Randomization		Patients Who Did Not Undergo Randomization	
	Thrombus Aspiration (N=3621)	PCI Only (N=3623)	Thrombus Aspiration (N=1162)	PCI Only (N=3535)
Age — yr†	66.5±11.5	65.9±11.7	66.8±13.5	69.4±12.5
Male sex — no. (%)	2721 (75.1)	2703 (74.6)	829 (71.3)	2360 (66.8)
Body-mass index‡	27.2±7.1	27.1±5.2	27.1±8.6	27.0±8.8
Diabetes mellitus — no. (%)	448 (12.4)	453 (12.5)	162 (13.9)	635 (18.0)†
Smoking status — no. (%)†				
Never smoked	1299 (35.9)	1153 (31.8)	362 (31.2)	1259 (35.6)
Former smoker				
Current smoker				
Unknown				
Hyperlipidemia — no. (%)				
Hypertension — no. (%)				
Previous myocardial infarction — no.				
Previous PCI — no. (%)				
Previous CABG — no. (%)				
Therapy before PCI — no. (%)				
Warfarin	60 (1.7)	52 (1.4)	35 (3.0)	86 (2.4)
Heparin	1481 (40.9)	1460 (40.3)	310 (26.7)	1187 (33.6)†
Thrombolysis	69 (1.9)	68 (1.9)	16 (1.4)	100 (2.8)†
Time from symptom onset to PCI — min				
Median	185	182	180	210
Interquartile range	120–330	120–315	116–350	125–412
Time from diagnostic ECG to PCI — min				
Median	67	66	65	72
Killip class ≥II — no. (%)	198 (5.5)	183 (5.1)	195 (16.8)	533 (15.1)

End Point	Patients Who Underwent Randomization				Patients Who Did Not Undergo Randomization	
	Thrombus Aspiration (N=3621)	PCI Only (N=3623)	Point Estimate (95% CI)	P Value	Thrombus Aspiration (N=1162)	PCI Only (N=3535)
30 days						
All-cause death — no./total no. (%)	103/3621 (2.8)	110/3623 (3.0)	Hazard ratio, 0.94 (0.72–1.22)	0.63	124/1138 (10.9)*	362/3442 (10.5)*

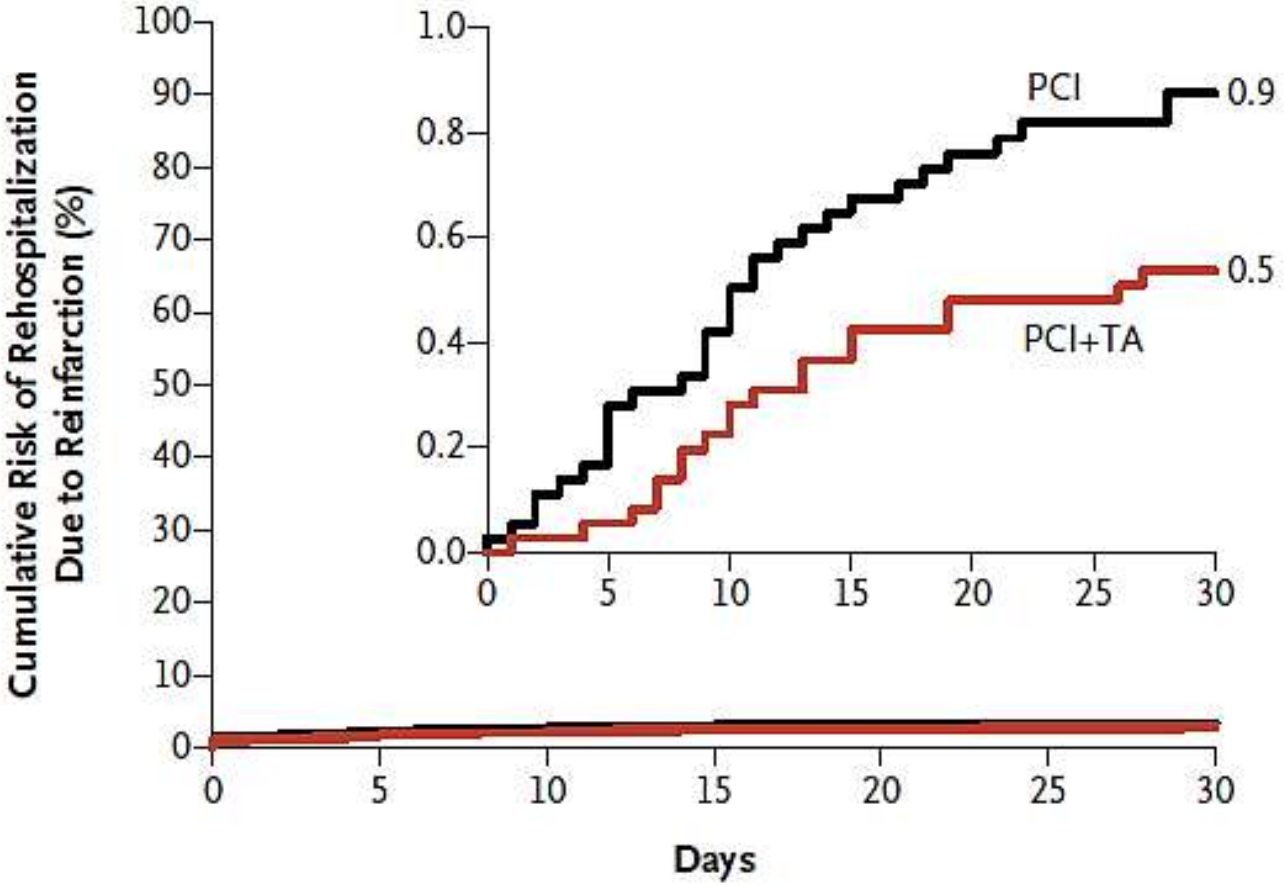
Pitfalls in methodology

- No data on presence/amount of debris
- No dedicated monitoring
  - Management of missing data?
- No CEC
  - Under-reporting for endpoints except mortality?
- No corelab
  - Angiographies (Blush, DE, TIMI)
  - EKG (ST resolution)

Systematic use?

Authors (Study name)	Diagnosis (Onset time)	Type of devices	*N*	Methods for evaluating clinical outcome (primary endpoint) and *p*-value	Result
Thrombus aspiration vs. conventional PCI					
Svilaas *et al.*[45] (TAPAS trial)	STEMI (<12 hours)	6Fr Export Catheter (Medtronic)	1071	MBG 0 or 1 (17.1% vs. 26.3%, $p<0.001$)	better
Kaltoft *et al.*[48]	STEMI (<12 hours)	Rescue Catheter (Boston Scientific/Scimed)	215	Myocardial salvage assessed by Tc 99m sestamibi imaging (13% vs. 18%, $p=0.12$)	n.s
Ali *et al.*[49] (AIMI study)	STEMI (<12 hours)	AngioJet RT Catheter (Possis Medical)	480	Infarct size assessed by Tc 99m sestamibi imaging (9.8 ± 10.9% vs. 12.5 ± 12.1%, $p=0.03$)	worse
Beran *et al.*[54]	(N) STEMI	7 or 8Fr X-Sizer Catheter (EndiCOR Medical)	66	Postprocedural TIMI 3 flow (90% vs. 84%)	n.s
				CTFC (18.3 ± 10.2 vs. 24.7 ± 14.1, $p<0.05$)	better
				STR >50% (83% vs. 52%, $p<0.03$)	better
Antoniucci *et al.*[55]	STEMI	AngioJet RT Catheter	100	Ratio of early STR (90% vs. 72%, $p=0.022$)	better
Ikari *et al.*[56] (VAMPIRE trial)	STEMI (<24 hours)	7Fr TransVascular Aspiration Catheter (TVAC) (Nipro)	355	TIMI myocardial perfusion grade <3 (12.4% vs. 19.4%, $p=0.07$)	n.s
Napondano *et al.*[57]	STEMI (<12 hours)	X-Sizer Catheter (ev3)	92	Postprocedural MBG 3 (71.7% vs. 36.9%, $p=0.006$)	better
Burzotta *et al.*[58] (REMEDIA trial)	STEMI (<12 hours)	6Fr Diver CE Catheter (Invatec)	99	MBG ≥ 2 and STR ≥ 70% (46.0% vs. 24.5%, $p=0.025$)	better
Lefévre *et al.*[59] (X AMINE ST trial)	STEMI (<12 hours)	X-Sizer Catheter	201	Magnitude of STR (7.5 mm vs. 4.9 mm, $p=0.033$)	better
Silva-Orrego *et al.*[60] (DEAR-MI study)	STEMI (<12 hours)	6Fr Pronto Catheter (Vasc.solutions)	148	Complete (>70%) STR (68% vs. 50%, $p<0.05$)	better
				MBG 3 (2.84 ± 0.32 vs. 2.38 ± 0.59, $p<0.001$)	better
Chevalier *et al.*[61] (Export study)	STEMI (<12 hours)	Export Catheter	249	MBG 3 and/or STR >50% (85.0% vs. 71.9%, $p=0.025$)	better
Sardella *et al.*[62] (EXPIRA trial)	STEMI (<9 hours)	Export Catheter	175	MBG ≥ 2 (88% vs. 59%, $p<0.0001$)	better
				Magnitude of STR (63% vs. 39%, $p=0.001$)	better
Dudek *et al.*[63] (PIHRATE trial)	STEMI (<6 hours)	6Fr Diver CE Catheter	196	STR ≥70% (60 min: 53.7% vs. 35.1%, $p=0.27$;	n.s
				immediately after PCI: 41% vs. 26%, $p=0.037$)	better
De Luca *et al.*[64]	STEMI (<12 hours)	7Fr Diver CE Catheter	76	MBG 3 (36.8% vs. 13.1%, $p=0.03$)	better
				STR >70% (81.6% vs. 55.3%, $p=0.02$)	better
				LV remodeling (11% vs. 39%, $p=0.006$)	better
Liistro *et al.*[65]	STEMI (<12 hours)	6Fr Export Catheter	111	STR ≥ 70% (71% vs. 39%, $p=0.001$)	better
				LV remodeling (4% vs. 18%, $p=0.02$)	better
Vlaar *et al.*[68] (TAPAS sub-study)	STEMI (<12 hours)	6Fr Export Catheter	1071 (1060)	Cardiac death or non-fatal reinfarction at 1 year (5.6% vs. 9.9%, $p=0.009$)	better

B



No. at Risk							
PCI+TA	3621	3567	3533	3520	3512	3508	3501
PCI	3623	3562	3533	3509	3498	3489	3483

TASTE

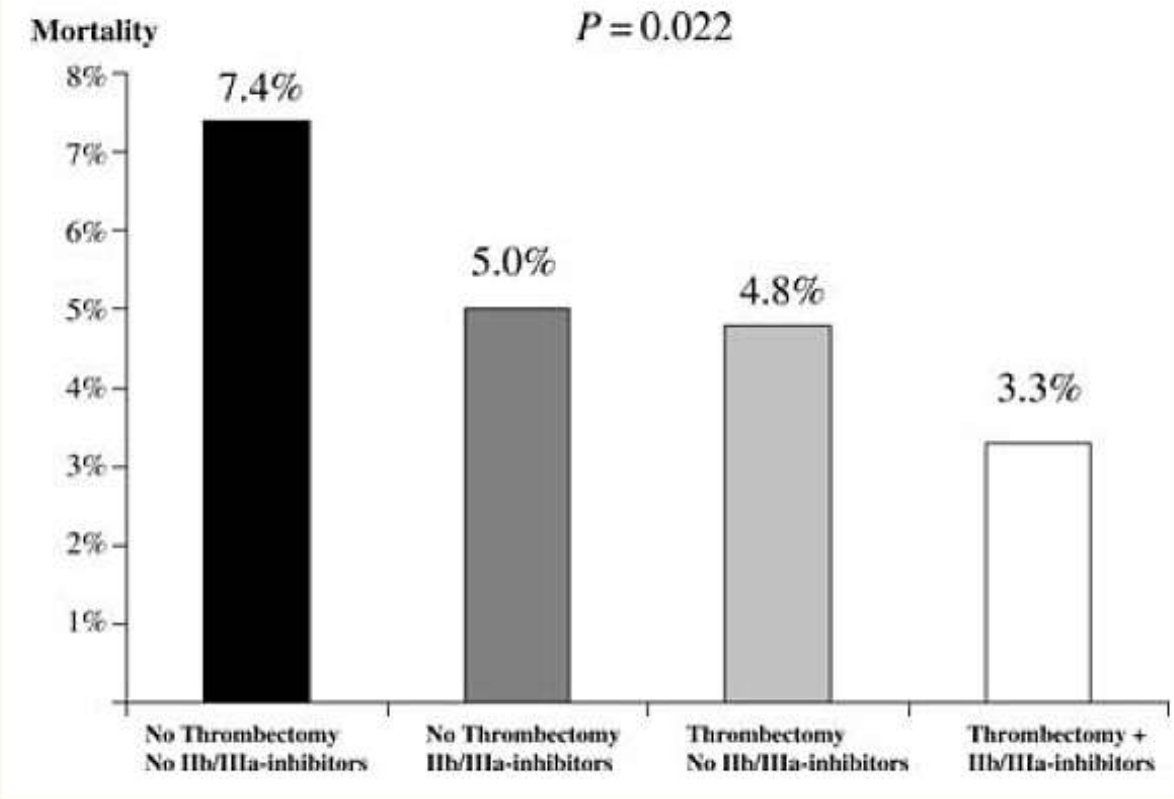
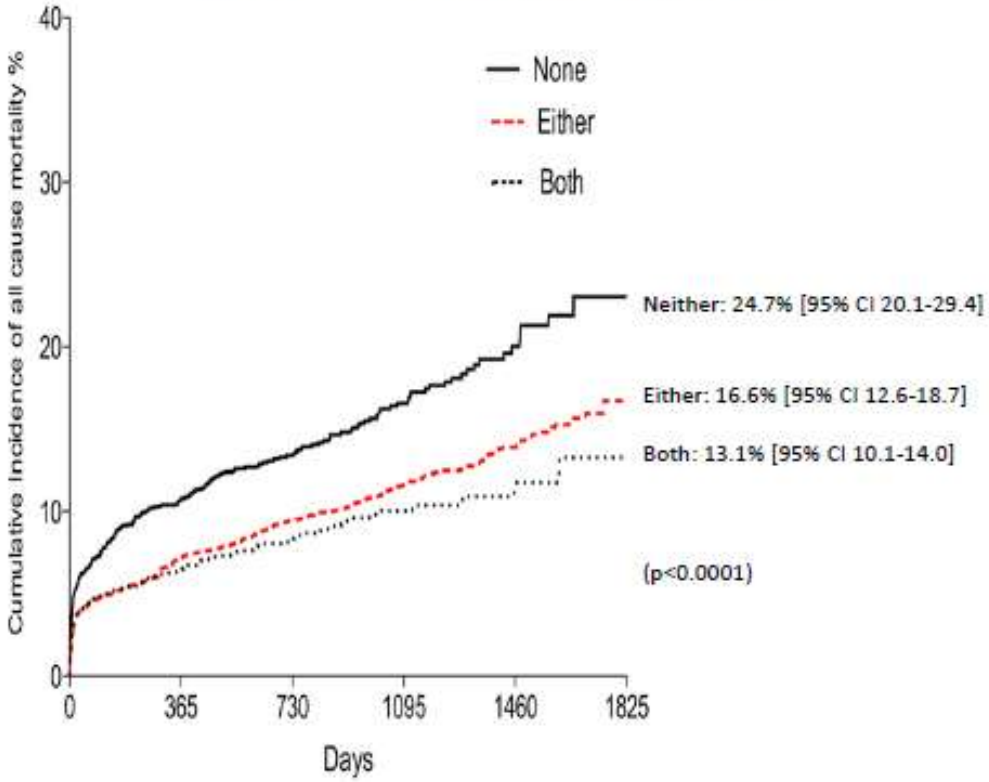


Figure 6 Mortality rates observed in the ATTEMPT database according to thrombectomy and to administration of IIb/IIIa-inhibitors. Comparison between four treatment subgroups performed by Fisher test.

9266 Pts from London Heart Attack Group

Kaplan Meier curve showing cumulative incidence of all cause mortality after PPCI comparing the different groups



Cox Analysis:

•After multivariable adjustment, thrombectomy use with adjunctive GPIIb/IIIa was still associated with significantly decreased mortality rates when compared with those that had neither therapy (hazard ratio: 0.77, 95% confidence interval: 0.62-0.96, p = 0.02).

•Other independent predictors of mortality were

Age:

Cardiogenic shock

Diabetes mellitus

Procedural success

M Akhtar et al. ESC 2013

Selective use

Procedural aspects of primary PCI			
Stenting is recommended (over balloon angioplasty alone) for primary PCI.	I	A	101, 102
Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion.	IIa	B	75, 103–105
If performed by an experienced radial operator, radial access should be preferred over femoral access.	IIa	B	78, 79
If the patient has no contraindications to prolonged DAPT (indication for oral anticoagulation, or estimated high long-term bleeding risk) and is likely to be compliant, DES should be preferred over BMS.	IIa	A	80, 82, 106, 107
Routine thrombus aspiration should be considered.	IIa	B	83–85
Routine use of distal protection devices is not recommended.	III	C	86, 108
Routine use of IABP (in patients without shock) is not recommended.	III	A	97, 98

	Stand-alone pPCI n=867	Thrombus aspiration n=671	P
Time to first call	75 [30; 201]	70 [30; 240]	0.99
Time to pPCI	285 [180; 640]	245 [165; 500]	0.001
Radial approach	69	73.5	0.07
TIMI 0/1 flow before	52	79	<0.001
High thrombus burden	21	73	<0.001
DES	31	22	<0.001
BMS	67	74	0.015
TIMI 3 flow after	95.5	93	0.035
Biva before/during CAG	6.5	6.7	0.13
LMWH before/during CAG	43.5	43	0.44
UFH before/during CAG	58	59.5	0.74
GP IIb-IIIa	52	66.5	<0.001
Prasugrel first	22	27	0.02

Puymirat et al. ESC 2013

Embolisation predicatibility

NNT for saving one blush 0/1	
TIMI 0/1	11
TIMI 2/3	15

			Value
TIMI flow grade before PCI			
0 or 1	62/275	96/306	0.43
2 or 3	22/210	31/179	0.34
Thrombus seen on angiography			
Yes	39/236	60/221	0.09
No	44/241	68/262	

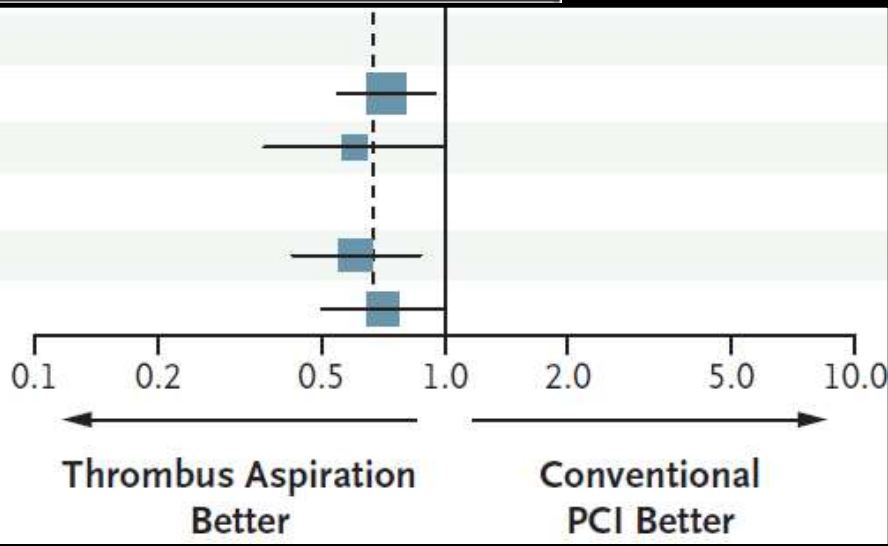
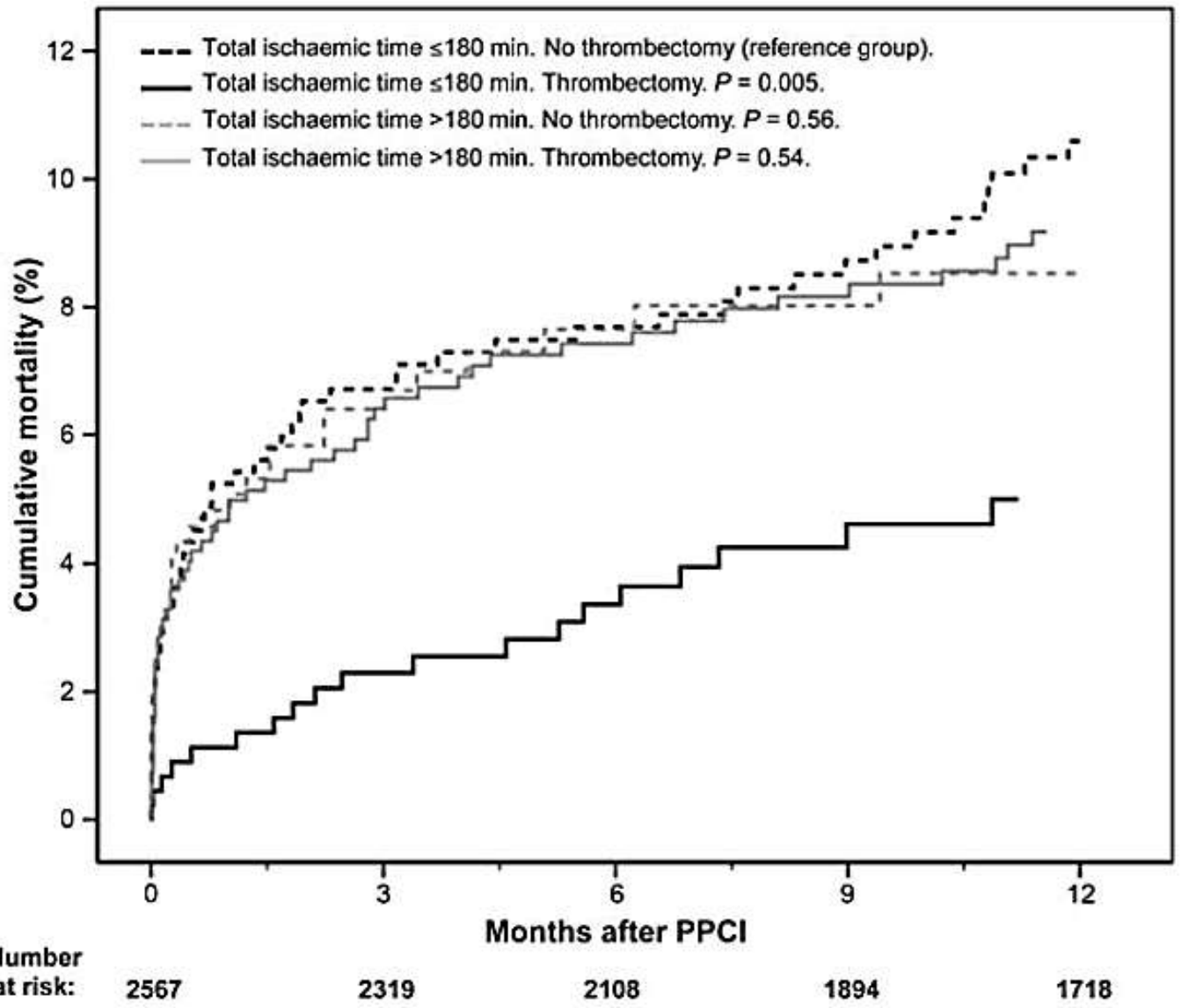


Figure 3. Risk Ratios for the Primary End Point, According to Prespecified Clinical or Angiographic Subgroup.
Data are reported for the patients who had clinical and coronary angiographic data at baseline. PCI denotes percutaneous coronary intervention, RCA right coronary artery, and TIMI Thrombolysis in Myocardial Infarction.

Svilaas et al. NEJM 2008; 358: 557-567

European Heart Journal (2012) 33, 3054–3061

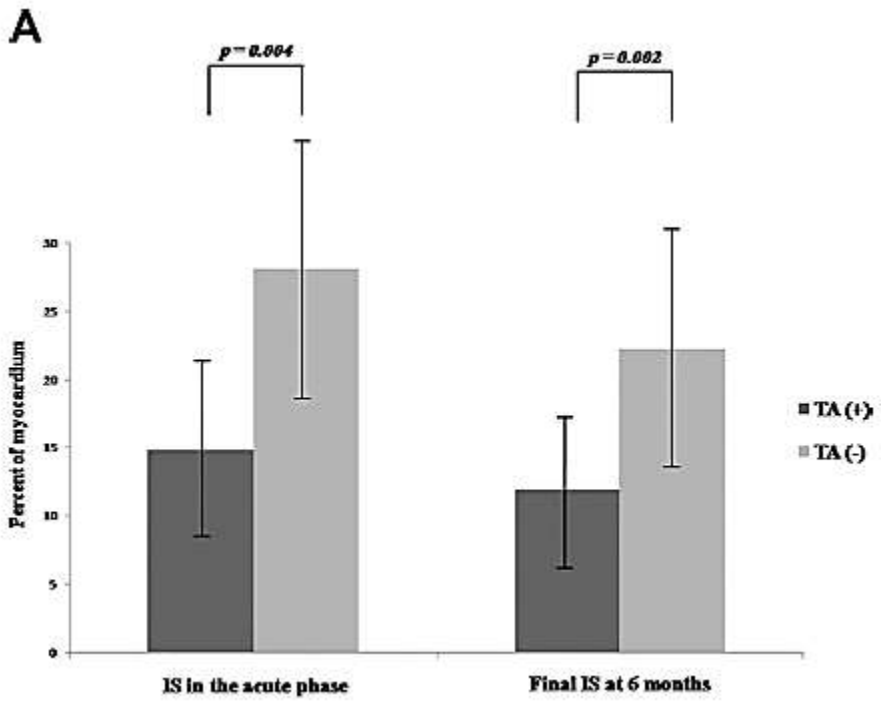


In summary

- Efficacy depends on
  - Thrombus volume (versus plaque volume)
  - Thrombus composition
  - Age of thrombus
  - Visible thrombus
  - Flow
  - And quality of aspiration technique!

Effect of Macroscopic-Positive Thrombus Retrieval During Primary Percutaneous Coronary Intervention With Thrombus Aspiration on Myocardial Infarct Size and Microvascular Obstruction

Romain Chopard, MD[a,*], Philoktimon Plastaras, MD[a], Jerome Jehl, MD[b], Sebastien Janin, MD[a], Vincent Descotes Genon, MD[a], Marie-France Seronde, MD[a], Siamak Davani, MD, PhD[c], Bruno Kastler, MD[b], Francois Schiele, MD, PhD[a], and Nicolas Meneveau, MD, PhD[a]



Am J Cardiol 2013

Do a good job !

- A lot of catheters
- …but no comparative data!
  - Bench test versus clinical trial

Tip							
Cross Section							
Distal Lumen (in) [a, b]	0.043	0.041	0.050	0.047	0.033	0.041	0.044
Shaft Lumen (in) [a]	0.043	0.041	0.050	0.049	0.039	0.039	0.044
Wire Lumen (in) [a]	0.015	0.015	0.016	0.017	0.016	0.016	0.016
Outer Diameter (in) [a, c]	0.068	0.068	0.078	0.066	0.062	0.060	0.055

Conclusions

- No mortality benefit @ 30 days after systematic use
  - Some effects on secondary endpoints
  - MI size reduction may not necessarily be translated into a 30 d mortality benefit
- Aspiration technique influences results
- A selective use has to be considered
  - TIMI 0
  - Visible thrombus
  - Short ischemic time