Randomized trial of manual aspiration Thrombectomy + PCI vs. PCI Alone in STEMI (TOTAL)

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on behalf of the TOTAL Investigators

TOTAL

Population Health Research Institute
Health Through Knowledge
PHRI

Disclosures

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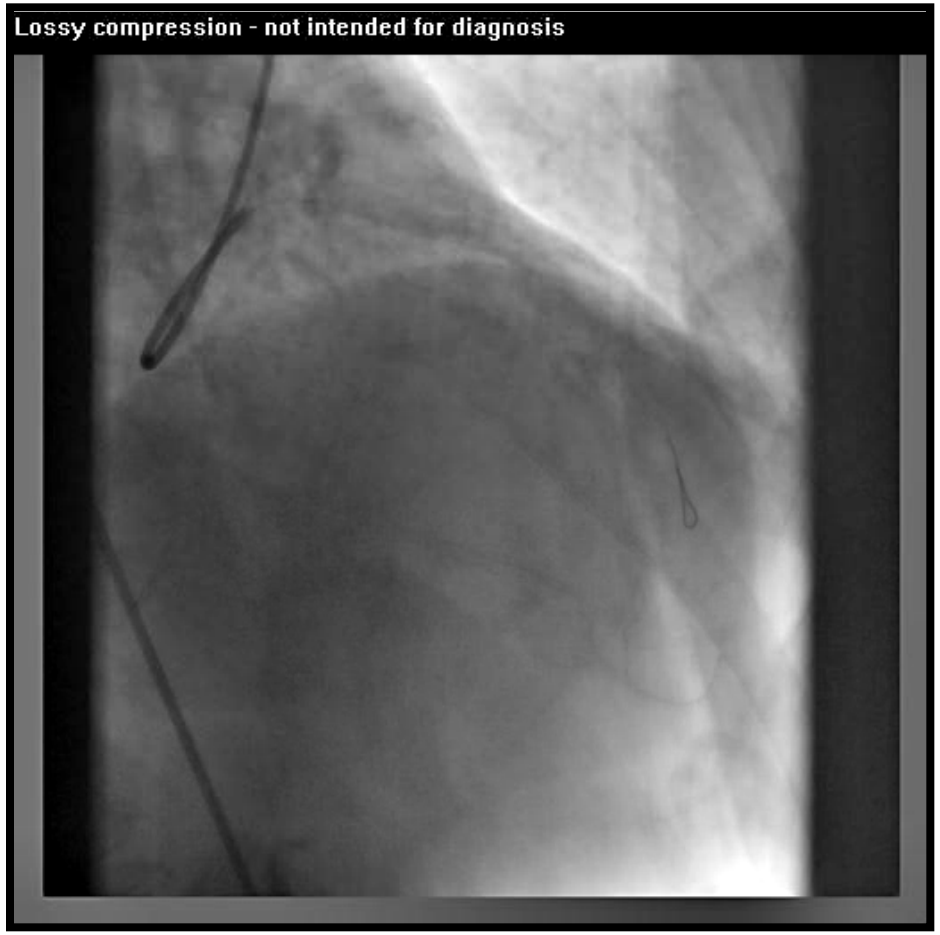
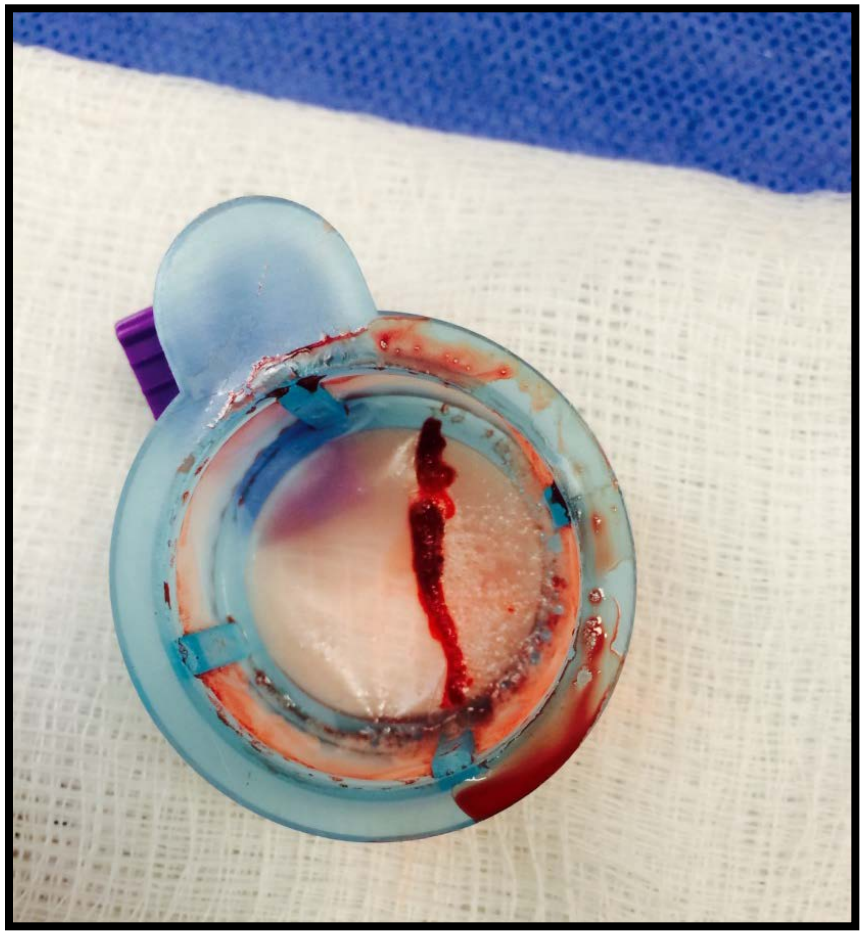
- Canadian Network and Centre for Trials Internationally (CANNeCTIN)
- Medtronic Inc.

Rationale for Thrombectomy



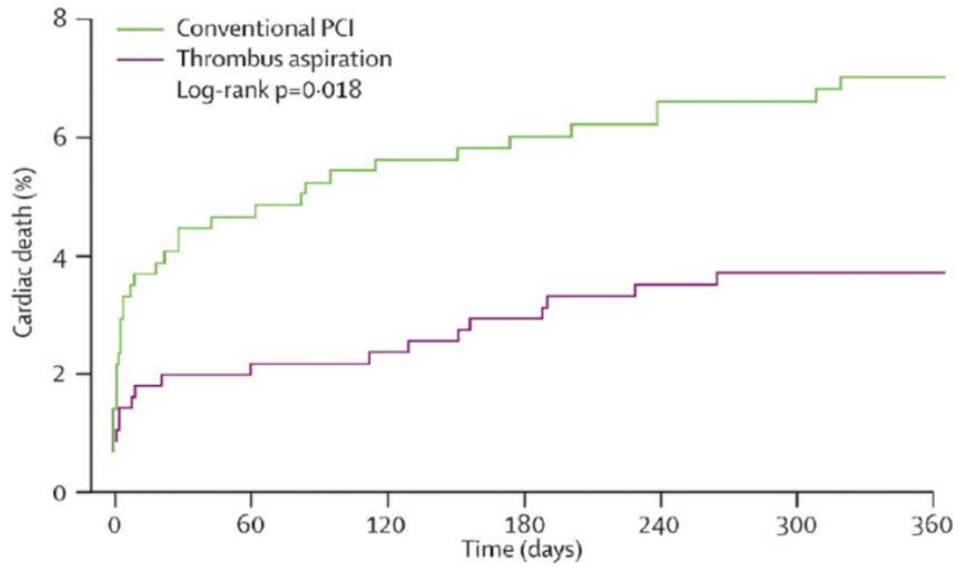
Major Limitation of Primary PCI:
Distal Embolization and Reduced Flow



Hypothesis: Aspiration thrombectomy may reduce embolization and improve clinical outcomes

Background

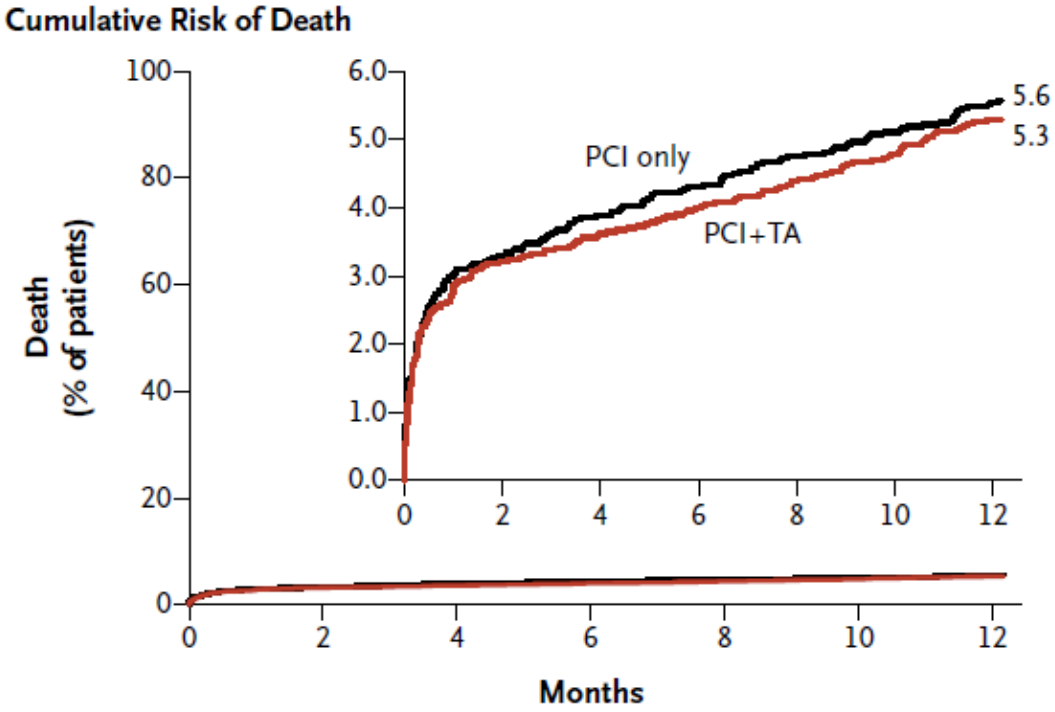
Large effect size in TAPAS (2008)



University Medical Center Groningen

Vlaar P, et al. TAPAS 1-year clinical outcome. Lancet 2008;371:1915-20

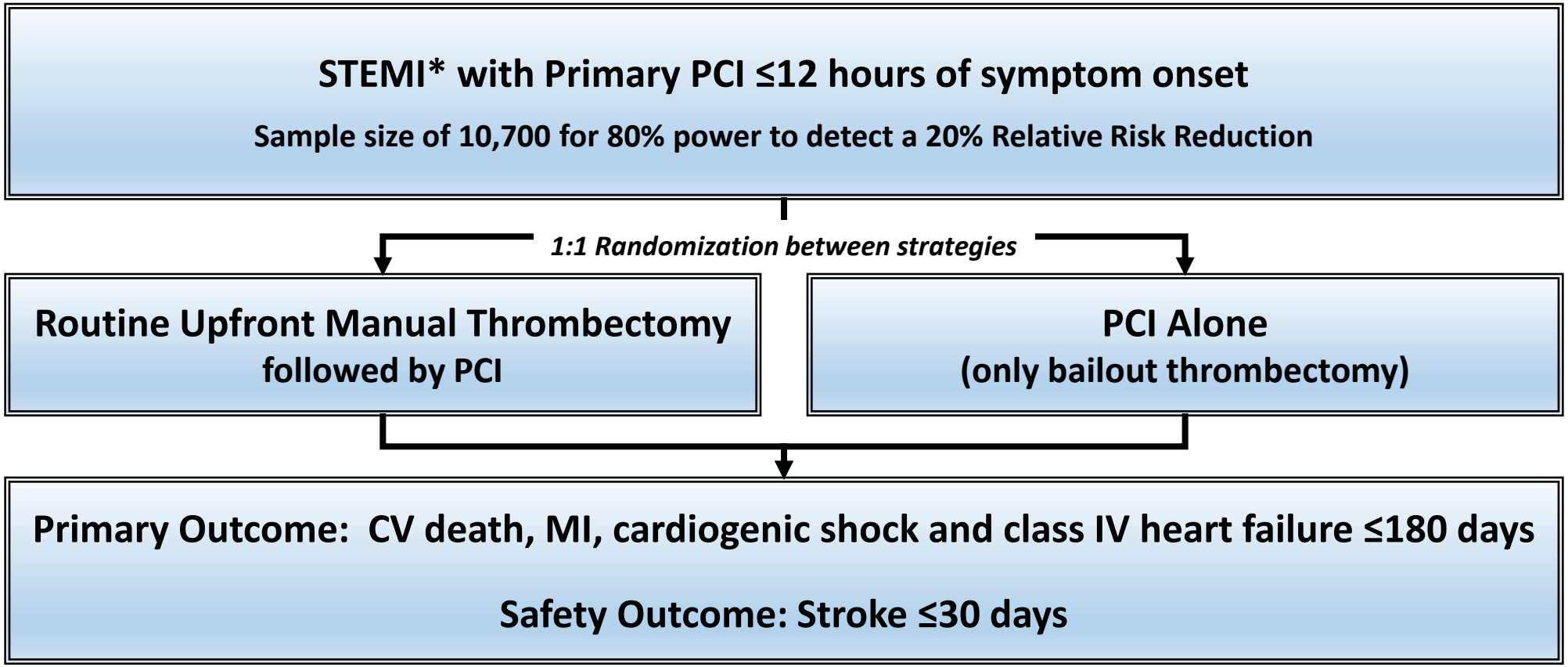
No difference in TASTE (2013)



TAPAS trial (N=1071) showed a large benefit
vs. TASTE (N=7244) showed no benefit of thrombus aspiration

Vlaar PJ, et al. Lancet 2008;371:1915-20.
Frobert O, et al. N Engl J Med 2013.
Lagerqvist B, et al. N Engl J Med. 2014.

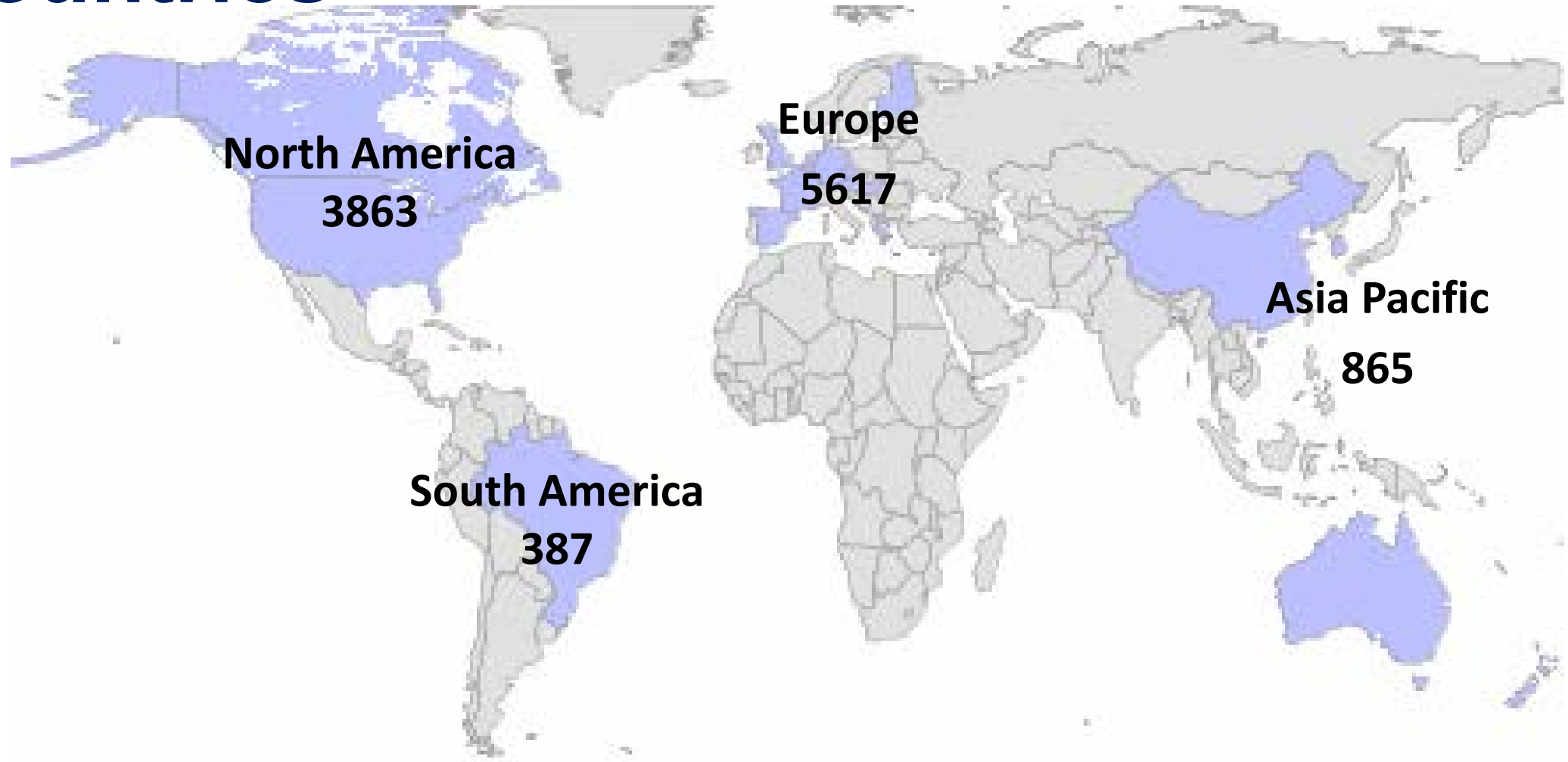
The TOTAL Trial Study Design



Bailout Thrombectomy allowed if PCI alone strategy fails:

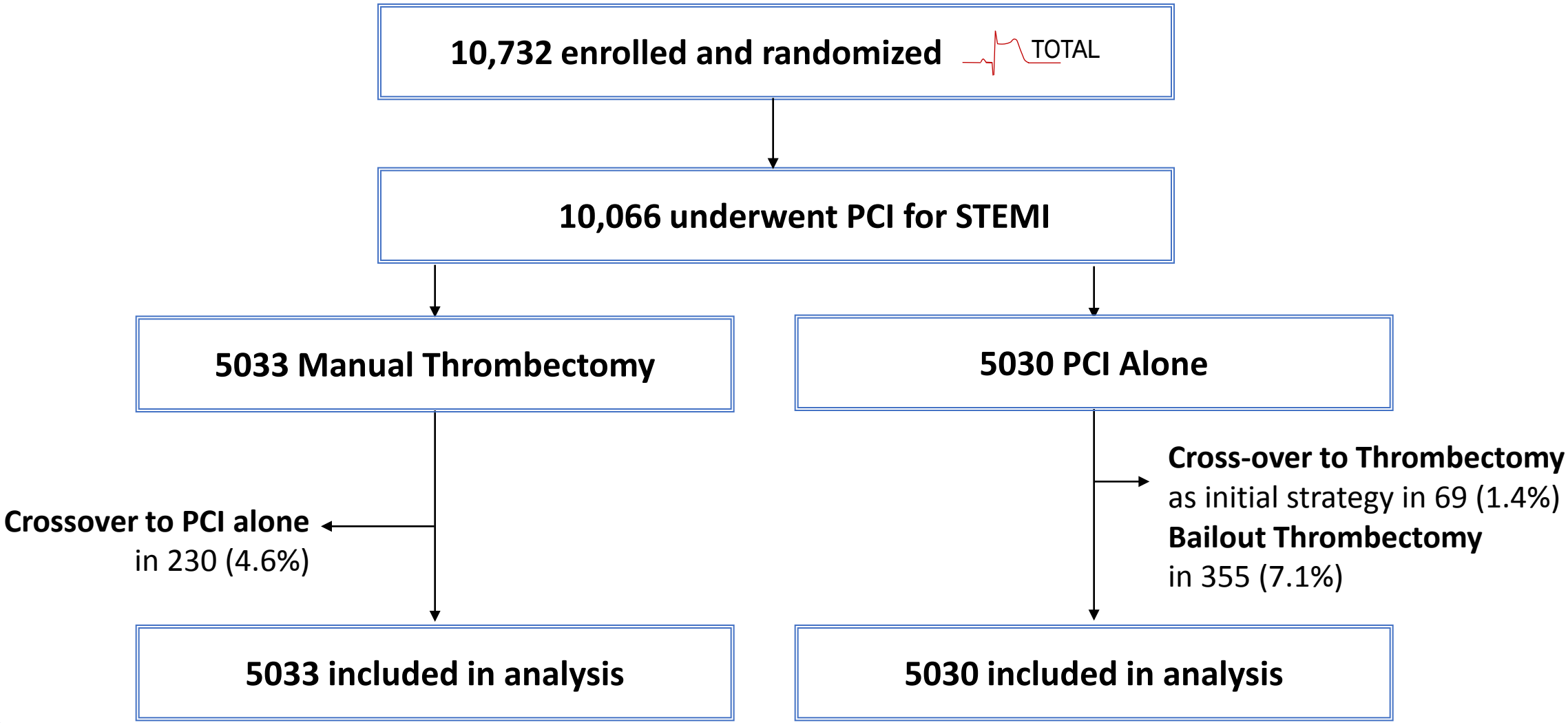
- Persistent TIMI 0 or 1 flow with large thrombus after balloon pre-dilatation
- Persistent large thrombus after stent deployment at target lesion

TOTAL Recruitment from 87 sites in 20 countries



10,732 patients randomized between August 2010 and July 2014

TOTAL Trial Flow and Adherence



Baseline Characteristics

	Thrombectomy N=5033	PCI alone N=5030
Mean Age	61.0 years	61.0 years
Male	76.8%	78.2%
Killip Class ≥2	4.3%	4.2%
Anterior MI	39.0%	40.9%
Symptom onset to hospital arrival*	128 min	120 min
Door to Device time	53.0 min	53.0 min

*P=0.024

PCI Procedural Details

	Thrombectomy N=5033	PCI alone N=5030
Pre PCI TIMI 0 flow	66.3%	67.8%
TIMI thrombus grade ≥3	90.8%	89.1%
Unfractionated Heparin	80.8%	81.6%
Bivalirudin	18.7%	17.3%
Upfront Glycoprotein IIb/IIIa**	22.7%	25.4%
Drug Eluting Stents	44.7%	45.0%
Radial Access	68.3%	68.2%

**P=0.0002

PCI Variables and Surrogate Outcomes

	Thrombectomy N=5033	PCI alone N=5030	P
PCI Procedure time (median)	39 min	35 min	<0.001
Direct Stenting	38.3%	21.3%	<0.001
Final TIMI 3 flow*	93.1%	93.1%	0.12
Distal Embolization*	1.6%	3.0%	<0.001
ST segment Resolution <70%*	27.0%	30.2%	<0.001

* Investigator Reported Outcomes. Core laboratory analysis is ongoing.

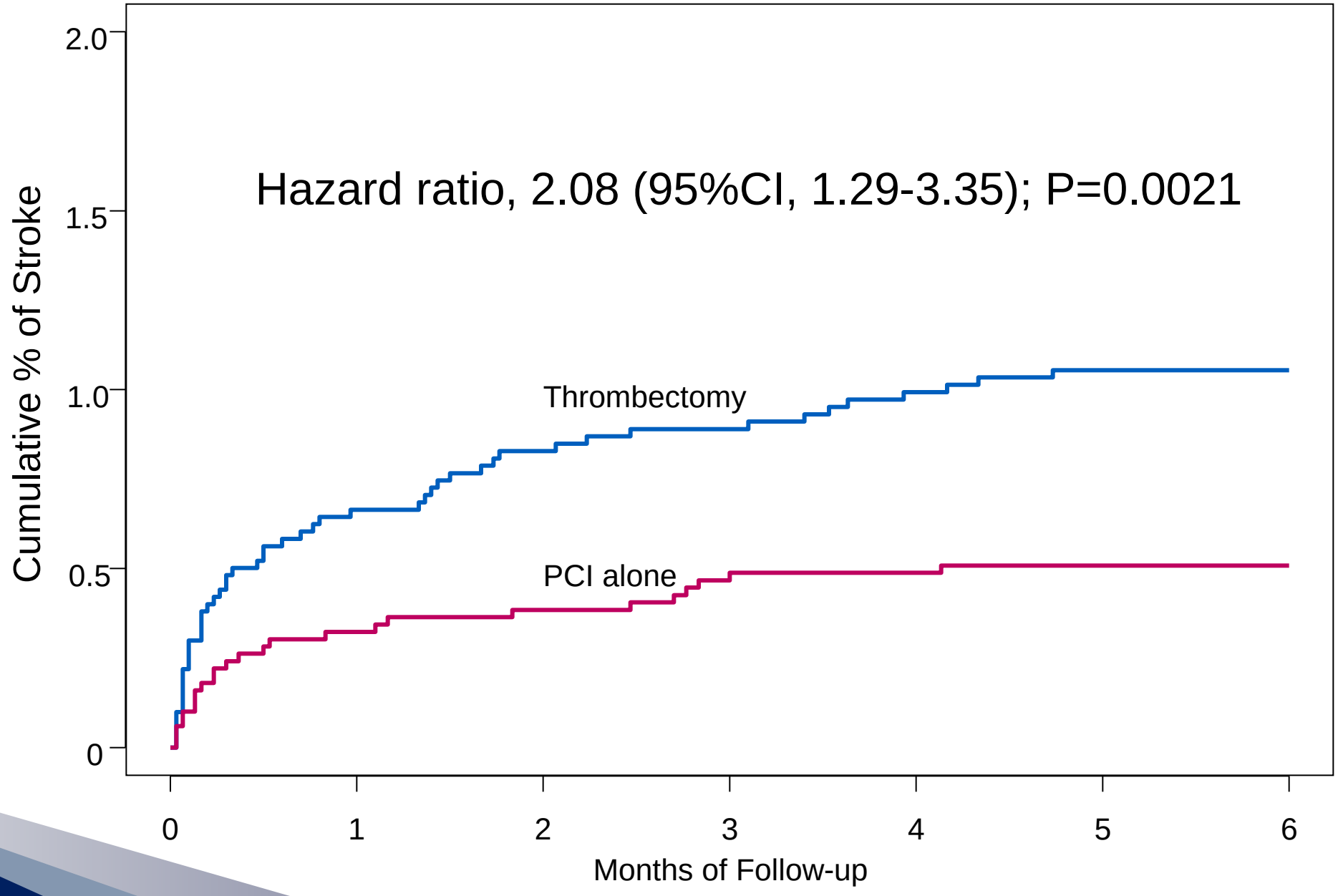
Primary Outcome

Day 180	Thrombectomy (N=5033) (%)	PCI alone (N=5030) (%)	HR	95% CI	p
CV death, MI, shock or class IV heart failure	347 (6.9%)	351 (7.0%)	0.99	0.85-1.15	0.86
CV death	157 (3.1%)	174 (3.5%)	0.90	0.73-1.12	0.34
Recurrent MI	99 (2.0%)	92 (1.8%)	1.07	0.81-1.43	0.62
Cardiogenic Shock	92 (1.8%)	100 (2.0%)	0.92	0.69-1.22	0.56
Class IV heart failure	98 (1.9%)	90 (1.8%)	1.09	0.82-1.45	0.57

Safety Outcomes

	Thrombectomy (N=5033) (%)	PCI alone (N=5030) (%)	HR	95% CI	p
Stroke within 30 days	33 (0.7%)	16 (0.3%)	2.06	1.13-3.75	0.015
Stroke or TIA within 30 days	42 (0.8%)	19 (0.4%)	2.21	1.29-3.80	0.003
Stroke within 180 days	52 (1.0%)	25 (0.5%)	2.08	1.29-3.35	0.002

Time to Stroke

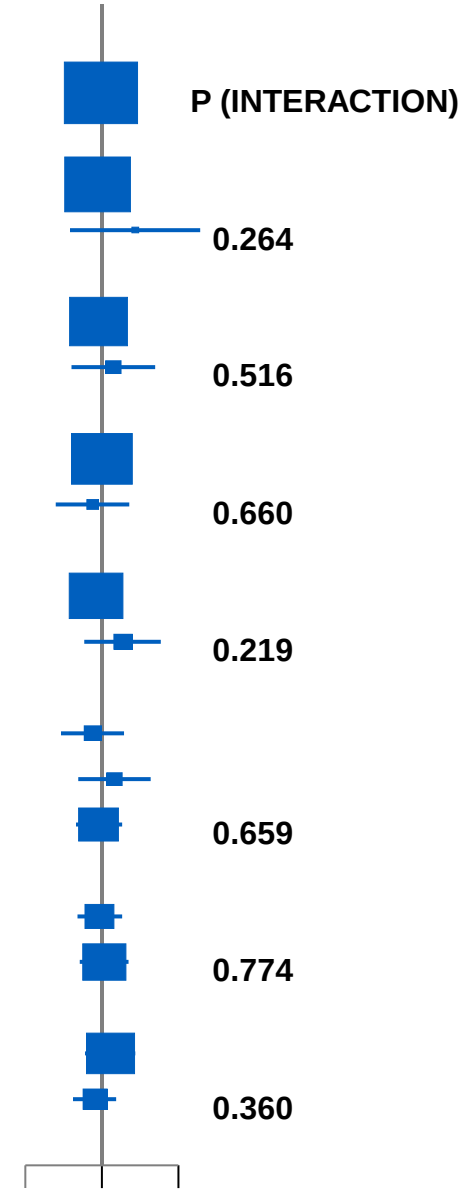


Outcomes at 30 days

	Thrombectomy (N=5033) (%)	PCI alone (N=5030) (%)	HR	95% CI	p
CV Death, MI, shock or class IV heart failure	281 (5.6%)	287 (5.7%)	0.98	0.83-1.15	0.79
Stent Thrombosis	59 (1.2%)	69 (1.4%)	0.85	0.60-1.21	0.37
Target Vessel Revascularization	126 (2.5%)	132 (2.6%)	0.95	0.75-1.22	0.69

Subgroup Analysis Primary Outcome

		Thrombectomy (%)	PCI Alone (%)	
OVERALL	10063	6.9	7.0	P (INTERACTION)
TIMI Thrombus Grade:				
≥3	9052	7.0	7.3	
<3	998	5.2	3.9	0.264
TIMI Thrombus Grade:				
≥4	7943	7.3	7.5	
<4	2107	5.3	4.8	0.516
Symptom Onset:				
<6 hrs	8375	6.6	6.6	
6-12 hrs	1665	8.1	8.8	0.660
Initial TIMI Flow:				
0-1	7443	7.4	7.8	
2-3	2519	5.6	4.7	0.219
Site Primary PCI Volume:				
Tertile 1	2450	7.3	7.9	
Tertile 2	2139	7.2	6.5	
Tertile 3	5474	6.6	6.7	0.659
MI Type:				
Anterior	4016	9.0	9.2	
Non-Anterior	6037	5.6	5.5	0.774
Age:				
≤65 yrs	6662	4.7	4.3	
>65 yrs	3401	11.4	12.1	0.360



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Limitations

- **Operators not blinded**
  Slightly lower use of GP IIb/IIIa inhibitors in Thrombectomy group

- **Strategy trial of routine thrombectomy**
  Cannot rule out a benefit of selective thrombectomy

- **Control Arm had Bailout thrombectomy (7%) when PCI alone strategy failed**
  Not designed to test effectiveness of bailout. Clinical judgement still needed.

- **Stroke findings are unexpected**
  Requires confirmation in other studies
  Analyses are ongoing to understand etiology

TOTAL

Conclusions

- **Routine thrombectomy compared to PCI alone with only bailout thrombectomy did not reduce CV death, MI, shock or heart failure within 180 days**

- **Routine thrombectomy was associated with increased risk of stroke within 30 days**

- **TOTAL and TASTE emphasize the need to conduct large randomized trials of common interventions even when small trials appear positive**

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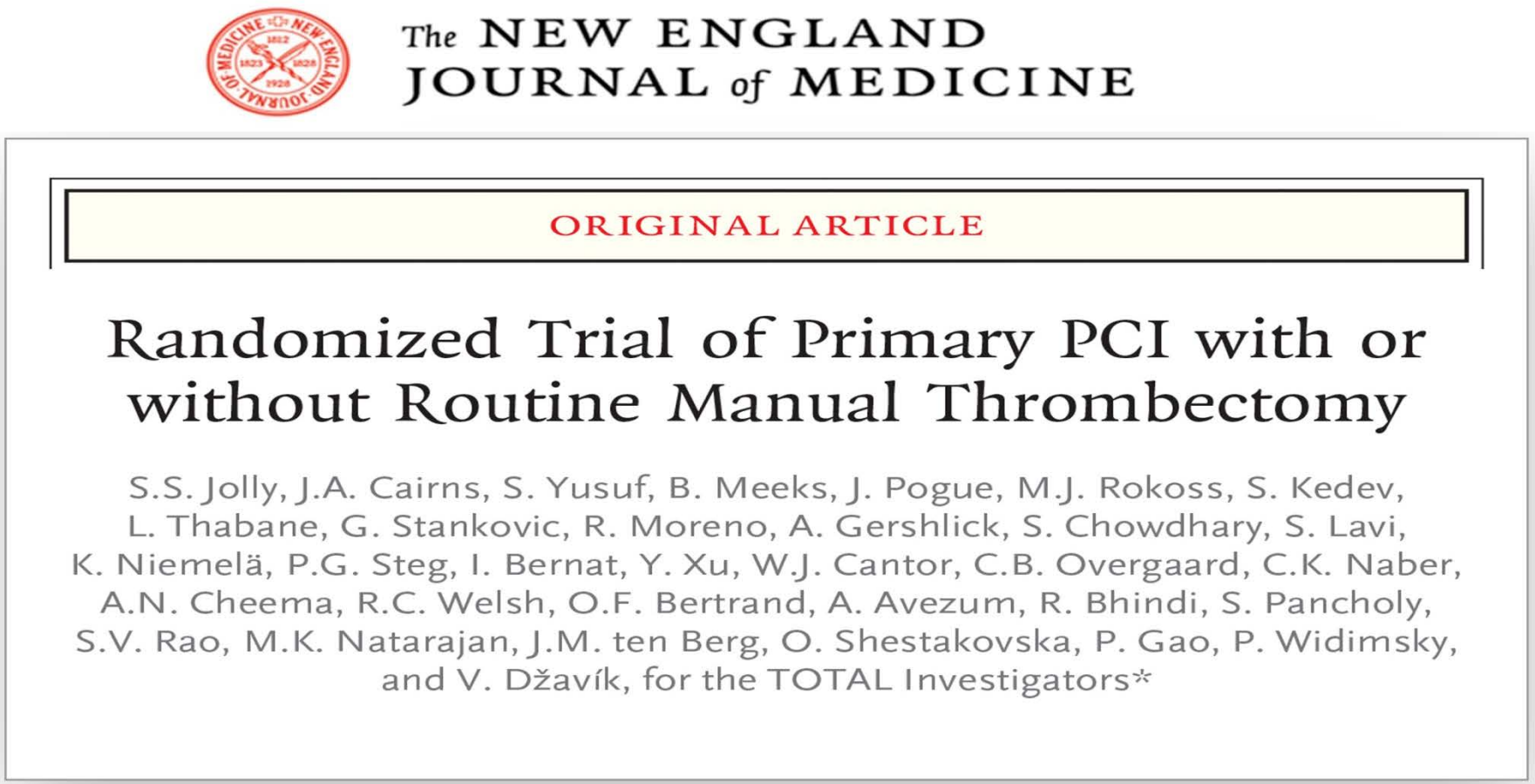

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