Angiographic Sub-study of the TOTAL trial: a randomized trial of manual thrombectomy during PCI for STEMI

CB Overgaard, V Sharma, T Hameed, D Sharma, J Chiha, W Chan, F Fuchs, S Kassam, R Leung, D Horak, H Romppanen, M El Omar, S Chowdhary, G Stankovic, S Kedev, M Rokoss, T Sheth, V Džavík, SS Jolly

on behalf of the TOTAL Investigators



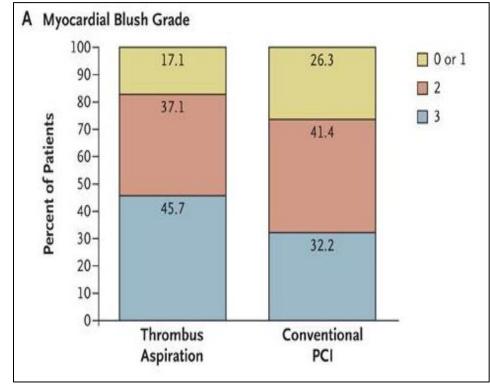
Disclosures

TOTAL trial was funded by:

- Canadian Institutes of Health Research
- Canadian Network and Centre for Trials Internationally (CANNeCTIN)
- Medtronic Inc.

Background

- Myocardial blush grade has been shown to predict mortality after primary percutaneous coronary intervention (PPCI)¹
- Small trials have shown improvement in myocardial blush grade with manual thrombectomy²



Svilaas T et al. N Engl J Med 2008;358:557-567.

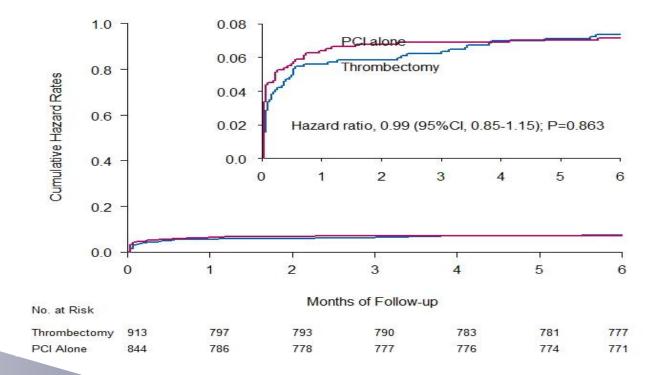
- 1. Van 't Hof AW et al Circulation 1998; 97(23):2302-2306
- 2. Svilaas T et al NEJM 2008; 358 (96): 557-567

TOTAL

Background

 The TOTAL trial is an international, prospective randomized (multicenter) trial of manual thrombus aspiration (using the Export[®] catheter, Medtronic CardioVascular, Santa Rosa, CA) in STEMI patients versus PPCI alone

TOTAL demonstrated no benefit to routine aspiration in patients undergoing PPCI for STEMI



TOTAL

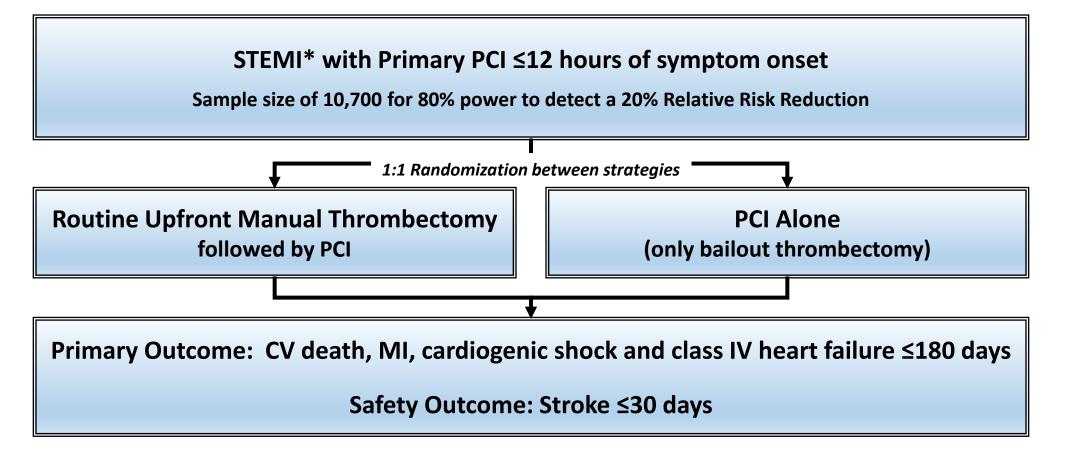
Study Questions

1) Does manual thrombectomy compared to PCI alone impact:

- Myocardial blush grade 0/1
- Final TIMI flow
- Distal embolization and other angiographic complications

2) Are these angiographic outcomes associated with mortality?

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



Methods

• The sub-study randomly selected 1610 patients (791 thrombectomy, 819 PCI only) from the TOTAL cohort (80% power to detect 25% RR reduction MBG 0 or 1 for manual thrombectomy)

 Angiographic parameters were blinded to treatment assignment at the angiographic core lab (Peter Munk Cardiac Centre, Toronto, Canada)

Primary Outcome

	Thrombectomy (N=791) (%)	PCI alone (N=819) (%)	p value
Myocardial Blush Grade 0,1	221 (28%)	246 (30%)	0.38
Myocardial Blush Grade 2,3	567 (72%)	573 (70%)	0.38
Post PCI TIMI Flow 0	9 (1.1%)	6 (0.7%)	0.4
Post PCI TIMI Flow 1	11 (1.4%)	10 (1.2%)	0.76
Post PCI TIMI Flow 2	59(7.5%)	70 (8.5%)	0.42
Post PCI TIMI Flow 3	712 (90%)	733 (89.5%)	0.73

Secondary Outcomes

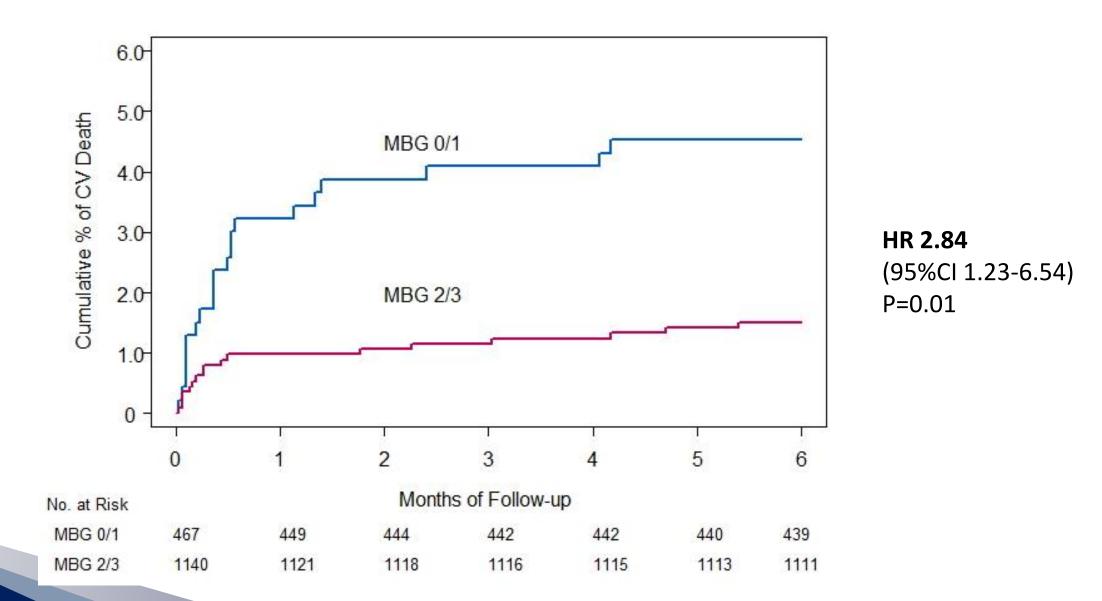
	Thrombectomy (N=791) (%)	PCI alone (N=819) (%)	p value	
PPCI Complications	94 (11.9%)	126 (15.5%)	0.04	
Distal Embolization	56 (7.1%)	87 (10.7%)	0.01	
Abrupt IRA Closure	7 (0.9%)	1 (0.1%)	0.02	
Perforation	4 (0.5%)	5 (0.6%)	0.78	
Dissection	26 (3.3%)	22 (2.7%)	0.48	
IRA Sidebranch Closure	7 (0.9%)	9 (1.1%)	0.66	
Thrombus Formation	6 (0.8%)	6 (0.7%)	0.95	
Transient No-reflow	o-reflow 14 (1.8%) 11 (1.3)		0.49	
Left Main Dissection	1 (0.1%)	0 (0 %)	-	

Subgroup Analysis for MBG 0/1

	N	Thrombectomy	PCI Alone	Odds Ratio(95%CI)	P	Ĩ
		no. of even	ts/total no. (%)			
OVERALL	1607	221/788 (28.05)	246/819 (30.04)	0.91(0.73-1.13)	0.3795	P(INTERACTION)
FIMI Thrombus Grade:						
<3	275	22/129 (17.05)	31/146 (21.23)	0.76(0.42-1.4)	0.3806	
>=3	1332	199/659 (30.2)	215/673 (31.95)	0.92(0.73-1.16)	0.4904	0.5679
IMI Thrombus Grade:						
<4	388	36/192 (18.75)	42/196 (21.43)	0.85(0.51-1.39)	0.5104 -	
>=4	1219	185/596 (31.04)	204/623 (32.74)	0.92(0.73-1.18)	0.5233	0.7536
Symptom Onset:						
<6 hrs	1368	182/670 (27.16)	206/698 (29.51)	0.89(0.7-1.13)	0.3353	
6-12 hrs	237	39/117 (33.33)	40/120 (33.33)	1(0.58-1.72)	1 -	0.7003
nitial TIMI Flow:						
0-1	1162	171/574 (29.79)	200/588 (34.01)	0.82(0.64-1.05)	0.1227	
2-3	426	49/203 (24.14)	45/223 (20.18)	1.26(0.8-1.99)	0.3251	0.1096
Site PCI Volume:						
Tertile 1	317	33/154 (21.43)	35/163 (21.47)	1(0.58-1.71)	0.9924	-
Tertile 2	302	54/146 (36.99)	45/156 (28.85)	1.45(0.89-2.35)	0.1321	
Tertile 3	988	134/488 (27.46)	166/500 (33.2)	0.76(0.58-1)	0.0498 -	0.0695
AI Type:						
Anterior	600	79/289 (27.34)	91/311 (29.26)	0.91(0.64-1.3)	0.6011 -	-
Non-Anterior	1005	142/497 (28.57)	155/508 (30.51)	0.91(0.69-1.19)	0.5003 -	0.9943
Age:						
<=65 yrs	1089	151/550 (27.45)	155/539 (28.76)	0.94(0.72-1.22)	0.6326	c 0 ⁻
>65 yrs	518	70/238 (29.41)	91/280 (32.5)	0.87(0.6-1.26)	0.4492 -	0.7319

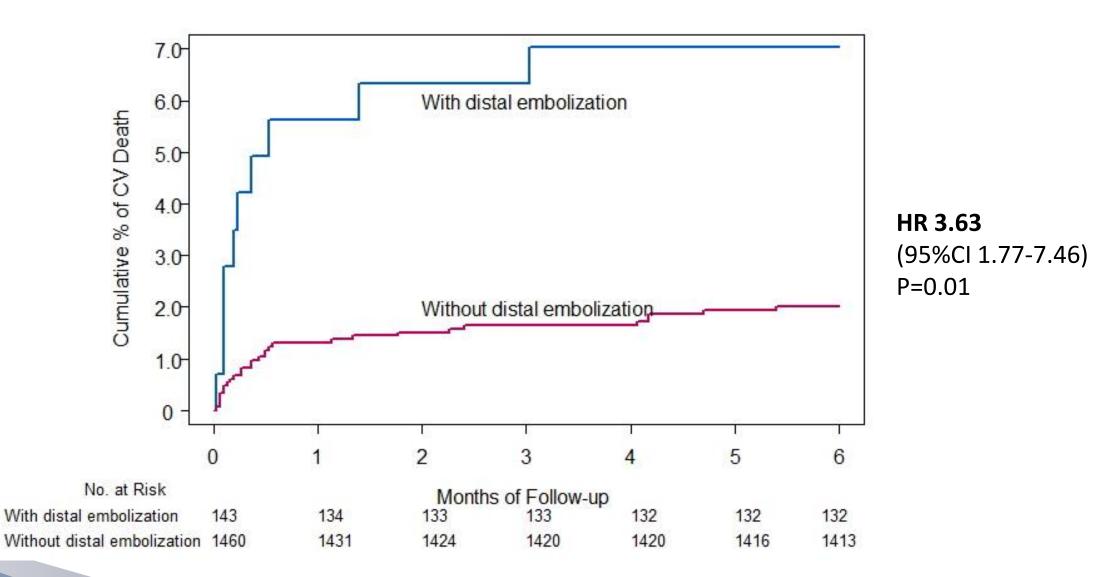
Favours Thrombectomy

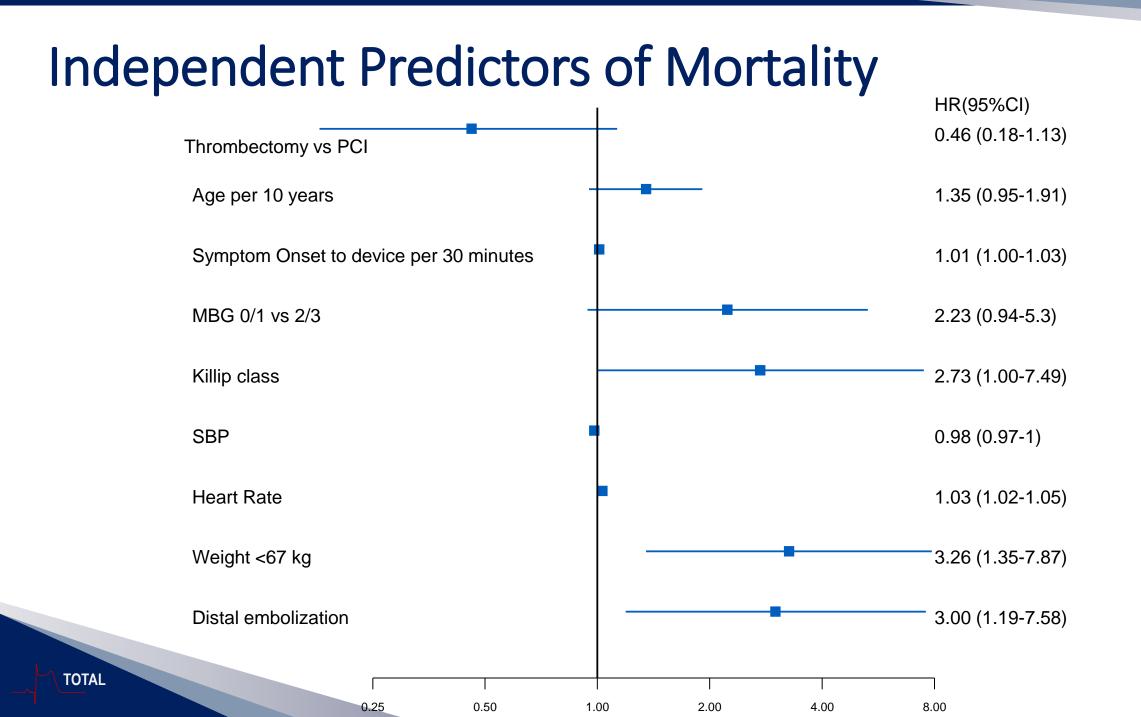
Myocardial Blush Grade and Mortality



TOTAL

Distal Embolization and Mortality





Conclusions

- Routine thrombectomy did not result in an improvement in final myocardial blush or TIMI Flow following PPCI for STEMI
- Routine thrombectomy reduced angiographic distal embolization
- Distal embolization was independently associated with mortality in multivariable analysis
- distal embolization is a important surrogate endpoint which is less subjective than blush and should be considered in future trials evaluating therapies for STEMI management