

EXPORT STUDY

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On behalf of the study investigators

EXPORT Study



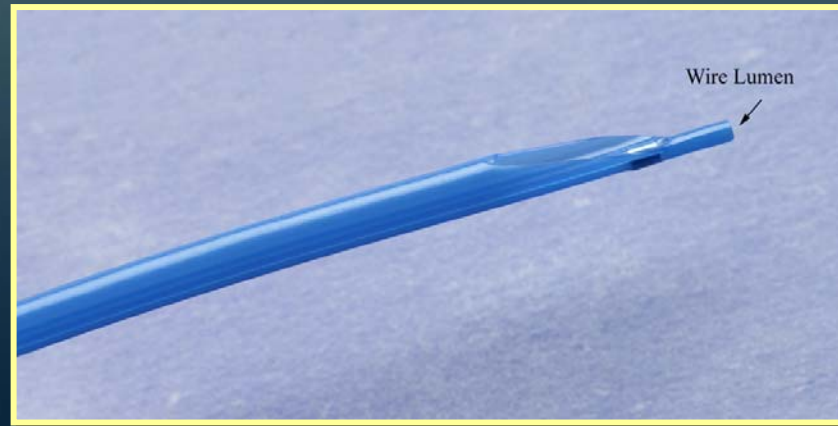
Declaration disclosure

- Grant / research support
 - Abbott vascular, Medtronic, Terumo
- Consulting fees
 - Abbott vascular, Boston scientific, Cordis J&J, Medtronic, Terumo

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Study Device

Medtronic Export® Aspiration Catheter



CE Mark and FDA approved device, with the following indication for use in central and peripheral circulatory system:

- **Contain and aspirate embolic material (thrombus/debris) while performing transluminal angioplasty or stenting procedures**
- **To sub selectively infuse/deliver diagnostic or therapeutic fluids.**

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Primary Objective

- To evaluate flow improvement in patients with Acute Myocardial Infarction undergoing either conventional stenting or a strategy of primary aspiration followed by stenting using the EXPORT[®] Aspiration Catheter

Background

Why a « Surrogate Endpoint » ?

- Hypothesis: if a technique reduces by 33% the risk of no-reperfusion (basis: Claeys et al.)
- Hard endpoint: mortality
 - 6.7% versus 5.1%
 - ...7056 patients

Background

ST Regression Analysis



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Background

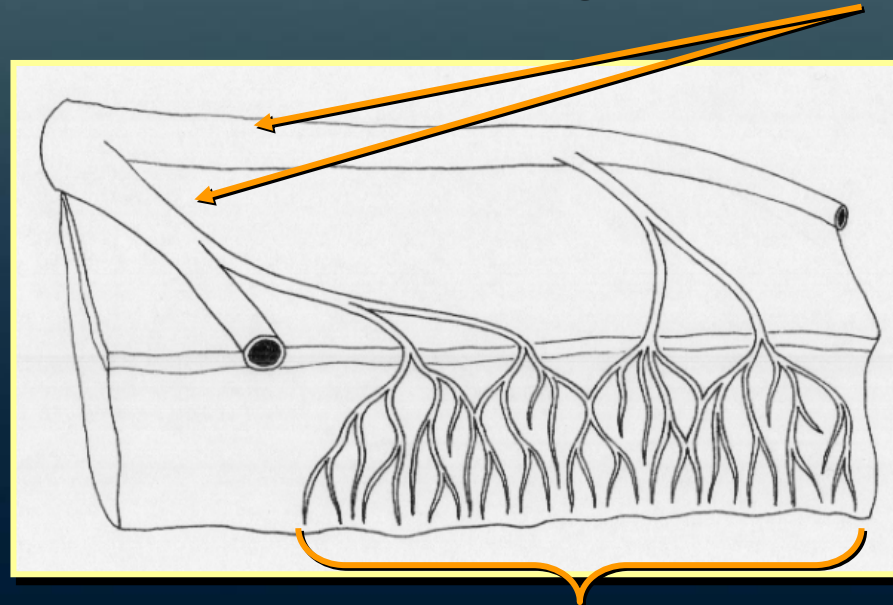
Correlation Mortality–ST Regression (PCI)

Author	# pts	Mortality (ST reg)	Odds ratio
Claeys 1999	91	2 / 15 (1 y.)	
Matetzky 1999	117	–	1 / 7.3 (1 y.)
Domingo 2002	116	8.3 / 30 (1 y)	
Van't Hof 1997	403	–	1 / 3.6 / 8.7 (1 y.)
Dong 2002	243	2.4 / 6.2 / 12.8 (6m)	

Background

TIMI Flow vs Myocardial Blush

TIMI Flow Grade assesses flow in the large epicardial coronary vessels



...but myocardial perfusion takes place at the microvascular level

Myocardial blush assesses contrast filling in these distal microvessels as a measure of myocardial perfusion.

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Background

Myocardial Blush Score

Blush 0

- No appearance of blush or opacification of the myocardium

Blush 1

- Presence of blush but no clearance of contrast (stain is present on the next injection)

Blush 2

- Blush clears slowly – clears minimally or not at all during three cardiac cycles

Blush 3

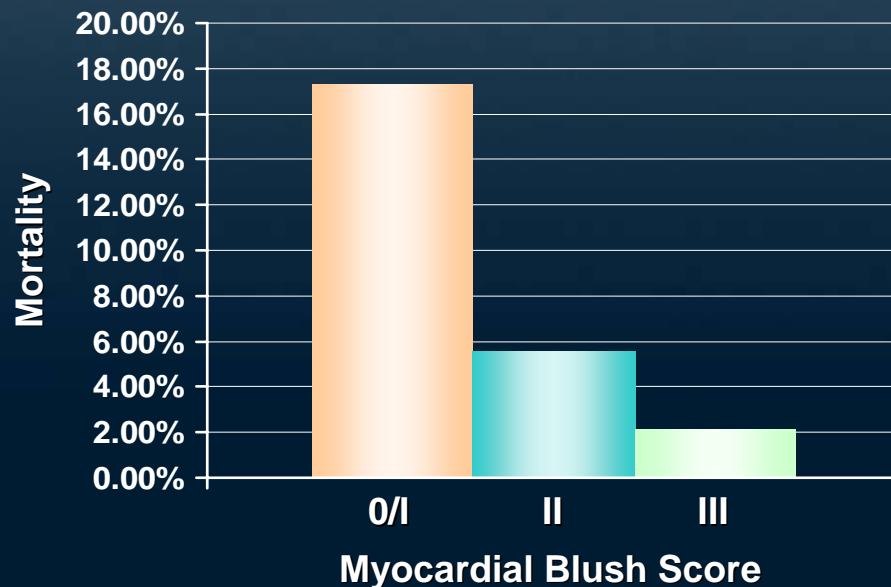
- Blush begins to washout and is only minimally persistent after three cardiac cycles

Background

Myocardial Blush Score

TIMI-3 flow was restored in 94% of patients treated with PTCA after acute MI – in contrast, normal perfusion was restored in only 28%:

Myocardial Blush Scores Following PTCA in AMI	0/I	II	III
	30%	42%	28%



Impaired perfusion despite normal epicardial coronary flow is consistent with microvascular obstruction due to microembolization.

Reduced myocardial blush correlates with an increased risk of death.

Stone GW, et al. *Abstract AHA*. November 1999.

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Background

Blush and ST are Poorly Correlated

	Blush 0-1	Blush 2	Blush 3	<i>P value</i>
Sum ST Regression	40±40%	45±40%	63±50%	<0.05
ST Max Regression	42±30%	48±30%	54±40%	NS

T. Lefevre et al. XAMINE trial. JACC 2005.

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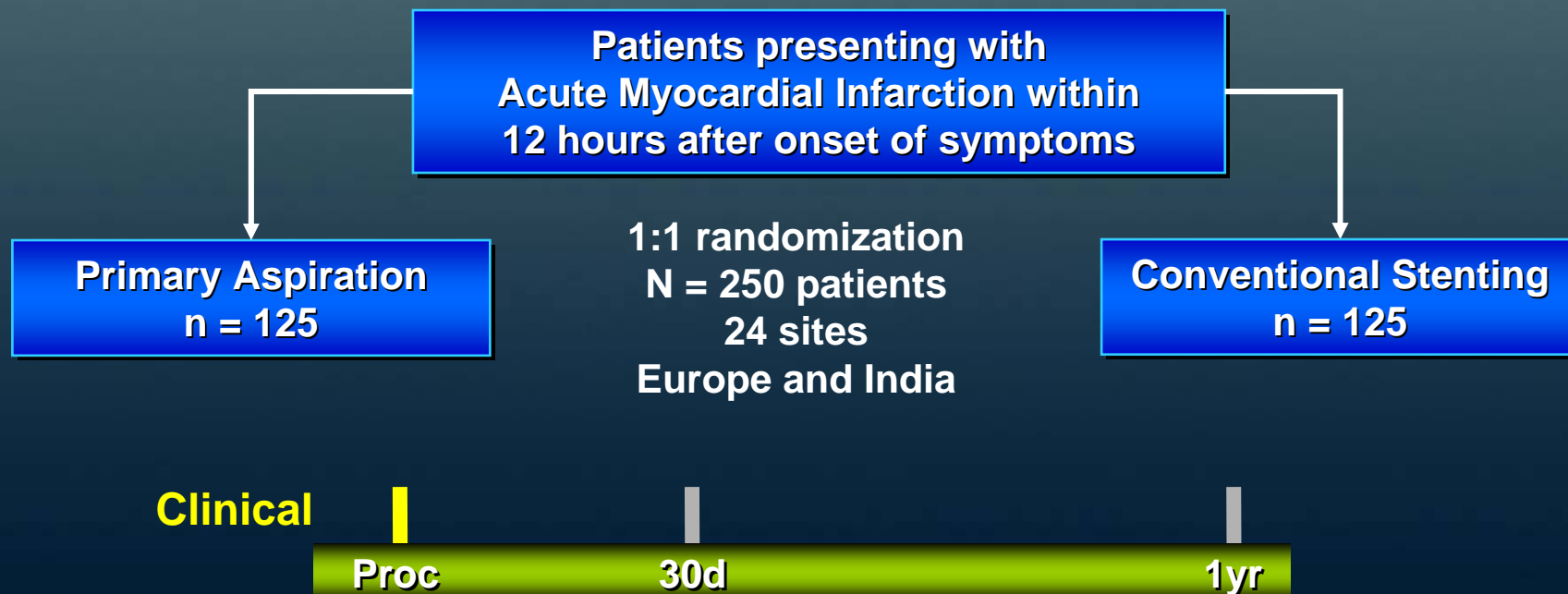
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Statistical Hypothesis

- Primary endpoint: Rates of ST segment resolution >50% (60 minutes post procedure) and/or Myocardial Blush grade III
- Null hypothesis: $H_0: P_{\text{conventional}} = P_{\text{export}}$
- Alternative hypothesis: $H_1: P_{\text{conventional}} \neq P_{\text{export}}$
- Assumptions:
 - Two-sided alpha level: 0.05
 - Power: 80%
 - An expected clinical difference of 18% in rate of patients with ST segment resolution and/or Myocardial Blush grade III
 - Lost to follow-up: 8%
- The calculated number of patients for this two-sided significance testing is 230; a total of 250 patients will be enrolled to account for those lost to follow-up

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Randomized, Open Label, Multicenter Trial



Primary Endpoint: Rate of ST segment resolution >50% (60 minutes post procedure) and/or myocardial blush grade III (immediately post procedure)

Secondary Endpoints: Magnitude of ST resolution, improvement in TIMI flow, corrected TIMI frame count, MACCE at 30 days and at 1 year, distal visible emboli/Distal embolization, rate required bail-out techniques (IIb/IIIa antagonist or aspiration or protection devices bail-out use)

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Main Inclusion Criteria

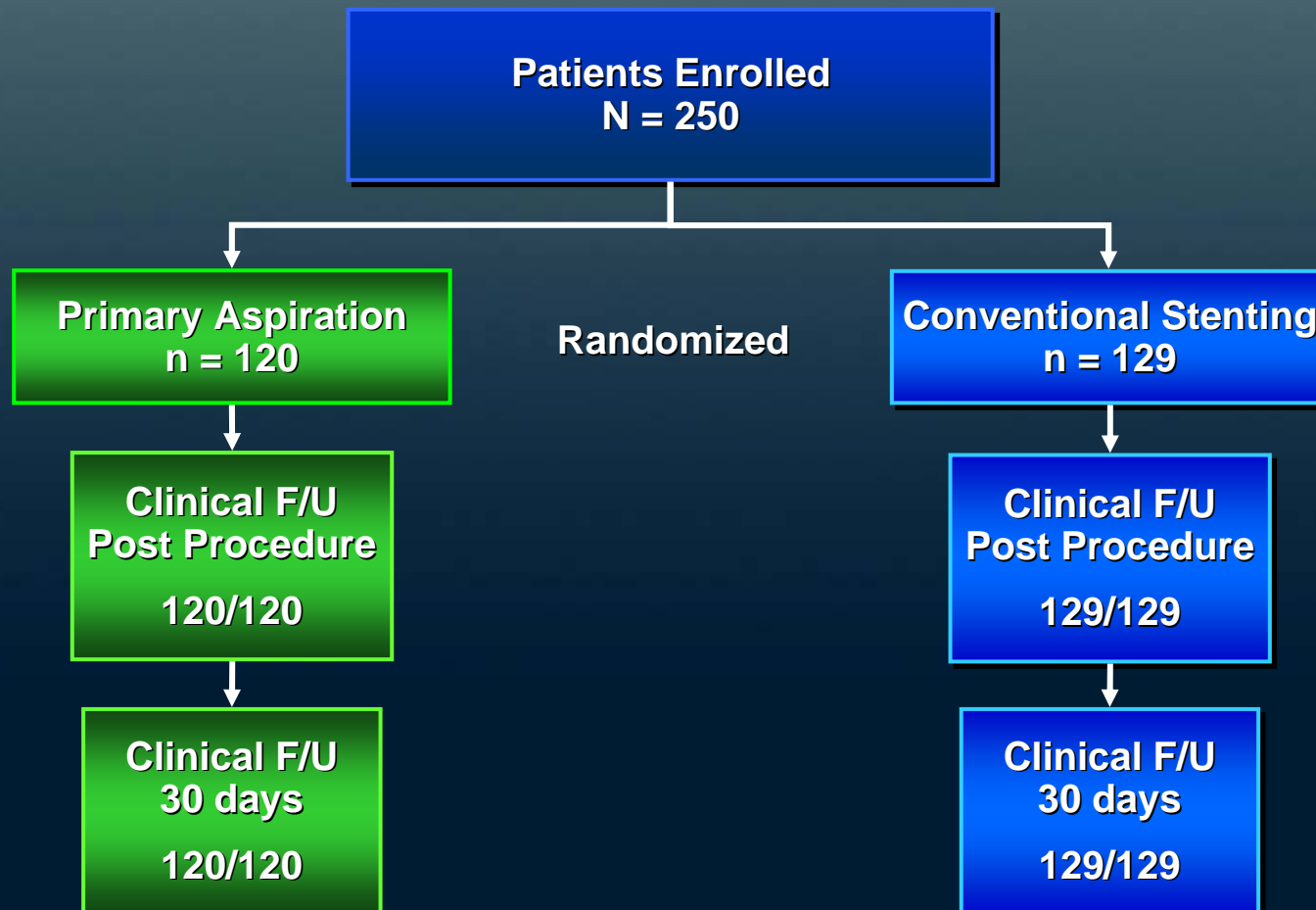
- ST-segment elevation of ≥ 2 mm in ≥ 2 contiguous leads
- De novo lesions in mid or proximal segments of native coronary vessels
- A visual estimated reference vessel diameter ≥ 2.5 mm
- TIMI flow of 0 or 1 before wiring

Main Exclusion Criteria

- Pre-cathlab use of lytic therapy or IIb/IIIa antagonist
- Patients presenting with a cardiogenic shock (blood pressure <90 mmHg)
- Patients presenting with cardiac arrest at any time before intervention
- Patients previously treated with a pacemaker or with left/right bundle branch block
- Any planned use of distal protection device
- Multivessel coronary artery disease with planned non-target artery PCI or treated with emergent coronary artery bypass surgery

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Patient Flowchart



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Data Analysis

- **QCA and ECG Core Lab**
 - Diagram B.V., Zwolle, Netherlands
 - Dr. H. Suryapranata
- **Clinical Event Committee**
 - Isala Klinieken, Zwolle, Netherlands
 - Dr. H. Suryapranata / Dr. M.J. De Boer / Dr. A.W.J. van't Hof
- **Data Coordinating Center**
 - Diagram B.V., Zwolle, Netherlands

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Patient Enrollment

Country	Hospital	Investigator	# Patients
India	The Heart Care Clinic, Gujarat	Dr. K. Parikh	49
France	Hopital De La Cavale Blanche, Brest	Dr. M. Gilard	37
Austria	Allgemeines Krankenhaus der Stadt Wien, Vienna	Prof. I. Lang	25
France	Polyclinique Les Fleurs, Ollioules	Dr. P. Commeau	15
Belgium	AZ Imelda, Bonheiden	Dr. J. Roosen	14
France	CHG Haguenau, Haguenau	Dr. M. Hanssen	11
France	Institut Hospitaliers Jacques Cartier, Massy	Dr. T. Lefevre	11
France	CHU Toulouse, Toulouse	Prof. D. Carrie	10
France	Groupe Hospitalier La Pitie Salpetriere, Paris	Dr. G. Montalescot	10
Italy	Centro Cardiologico Monzino, Milan	Prof. A. Bartorelli	10
France	Hopital Lariboisiere, Paris	Dr. V. Stratiev	9
France	Hopital du Bocage - CHU Dijon, Dijon	Prof. J.E. Wolf	7

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Patient Enrollment

Country	Hospital	Investigator	# Patients
France	Hopital Cardologique du Haut Leveque, Pessac	Prof. P. Coste	7
Portugal	Hospital de Santa Marta, Lisboa	Dr. D. Cacela	6
Italy	Ulss 9 Ospedale Ca'Foncello, Treviso	Dr. Z. Olivari	5
UK	King's College Hospital, London	Dr. P. MacCarthy	5
France	Nouvelles Cliniques Nantaises, Nantes	Dr. P. Brunel	4
Belgium	CHU Brugmann, Brussels	Dr. J. Castro Rodriguez	4
Netherlands	Amphia Ziekenhuis, Breda	Dr. P. den Heijer	3
Belgium	AZ Middelheim, Antwerpen	Dr. P. Vermeersch	2
Portugal	Centro Hospitalar de Coimbra	Dr. A.L. Marques	2
Italy	Ospedale Sasdro Pertini, Rome	Dr. P. Loschiavo	1
France	Centre Cardiologique du Nord, Saint-Denis	Dr. B. Chevalier	1
Poland	SPZOZ University Hospital Krakow	Dr. D. Dudek	1
		Total	249

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Patient Demographics

	Conventional Stenting	Primary Aspiration	<i>P value</i>
Age (mean ± SD)	61.2±12.9	59.2±12.8	0.18
Male Gender (%)	81.4	80.8	0.91
Fulfills In and Exclusion (%)	95.3	92.5	0.35
Prior Q-wave MI (%)	8.5	9.2	0.86
Prior Non Q-wave MI (%)	2.3	1.7	1.00
Prior CABG (%)	0.0	0.8	0.48
Prior Non Target Vessel PCI (%)	2.3	3.3	0.71
Prior Target Vessel PCI (%)	3.1	5.0	0.53

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Risk Factors

	Conventional Stenting	Primary Aspiration	<i>P value</i>
Smoking (%)	35.7	42.5	0.18
Diabetes (%)	13.2	16.7	0.44
NIDDM	94.1	65.0	0.05
IDDM	5.9	35.0	
Hypertension (%)	44.2	41.7	0.69
Hypercholesterolemia (%)	41.9	36.7	0.40
Family history CVD (%)	25.6	32.5	0.23

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Description Current MI

	Conventional Stenting	Primary Aspiration	<i>P value</i>
Killip I (%)	89.1	88.3	0.69
Killip II (%)	10.1	10.0	
Killip III (%)	0.8	0.8	
Killip IV (%)	0.0	0.8	
Left Ventricular Dysfunction (%)	19.4	20.0	0.90
Atrial Fibrillation at Study Entry (%)	6.2	2.5	0.16
Location Infarct Inferior/Posterior (%)	44.2	51.7	0.24
Location Anterior/Lateral	55.8	49.2	0.29

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Target Lesion Description

	Conventional Stenting	Primary Aspiration	<i>P value</i>
Target Vessel (%)			
LAD	51.9	47.5	0.70
LCX	10.9	10.0	
RCA	37.2	42.5	
TIMI Flow Before Wiring (%)			
0	89.1	85.0	0.33
1	10.9	14.2	
2	0	0.8	
3	0	0	
Pre Corrected Timi Frame Count*	46.73±25.44	52.57±54.56	0.75
Lesion Type			
A	14.8	10.8	0.53
B	55.5	61.7	
C	29.7	27.5	
Other Significant Lesions (%)	33.3	42.5	0.14

* Estimated from core lab

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Procedure

	Conventional Stenting	Primary Aspiration	<i>P</i> value
Time Onset of Symptoms – Randomization			
Mean ± SD (min.)	271.4±197.6	321.7±413.5	0.53
Median Q1-Q3 (min.)	219 (145-362.5) (n=129)	225 (149-333) (n=119)	
Procedure Time			
Mean ± SD (min.)	34.5±21.5	36.7±18.0	0.08
Median Q1-Q3 (min.)	30 (20-45) (n=129)	32 (25-45) (n=120)	
Pre Dilatation Performed (%)	55.8	28.3	<0.001
Post Dilatation Performed (%)	18.6	8.3	0.02
Number Of Stents Used	1.17±0.58	1.28±0.58	0.08

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Procedural Medications

	Conventional stenting	Primary aspiration	P value
GP IIb/IIIa – n (%)	90/129 (69.8)	79/120 (65.8)	0.51
Heparin – n (%)	91/129 (70.5)	90/120 (75.0)	0.43
ASA – n (%)	56/129 (43.4)	52/120 (43.3)	0.99
Clopidogrel – n (%)	51/129 (39.5)	53/120 (44.2)	0.46

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Aspiration Details

	#	%
*Primary Aspiration performed	117	
– Export device crossed occlusion	113	96.6
– Debris present	99	85.3
– Number of aspiration runs	2.42±1.15	
– Amount aspiration (cc)	38.08±26.51	

*Data only for patients randomized to primary aspiration.

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Peri Procedural Events

	Conventional Stenting	Primary Aspiration	<i>P value</i>
Vessel Spasm (%)	0.0	0.8	0.48
Slow Reflow (%)	4.7	3.3	0.42
No Flow (%)	10.1	3.3	0.04
Side Branch Occlusion (%)	1.6	1.7	1.00

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Primary /Secondary Endpoint Results*

	Conventional Stenting	Primary Aspiration	P value
Rate of ST segment resolution >50% (60 minutes post-procedure) and/or Myocardial Blush grade III (immediately post-procedure)	71.9	85.0	0.025
Rate of ST segment resolution > 50% (n=196) (%)	64.8	73.5	0.218
Magnitude of ST segment resolution (%)	52.5±46.1	59.5±49.2	0.132
Myocardial Blush Grade (%)			
0	7.9	2.8	0.089
1	23.7	24.8	0.850
2	43.0	36.7	0.338
3	25.4	35.8	0.094

*All endpoints calculated by core lab

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Angiographic Secondary Endpoints*

	Conventional Stenting	Primary Aspiration	P value
TIMI Flow Post Procedure (%)			0.42
0	0.8	1.6	
1	3.1	0.8	
2	19.2	15.6	
3	76.9	82.0	0.32
Post Corrected TIMI Frame Count	22.82±13.97	20.06±14.87	0.02
Distal Embolization Post (%)	16.8	9.3	0.10

*All endpoints calculated by core lab

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Other Secondary Endpoints

	Conventional Stenting	Primary Aspiration	<i>P value</i>
Bailout Performed (%(N))	14.7(19)	5.8(7)	0.02
Reason for Bailout			
Thrombus	5.4	0.8	
Slow reflow	5.4	1.7	
Distal embolization	2.3	3.3	
Lack of ST resolution	0.8	1.7	
Other	3.9	0.8	
Techniques for Bailout (%(N)):			
Rescue IIb/IIIa antagonist	73.7(14)	57.1(4)	
Rescue distal protection	0	0	
Rescue aspirations	42.1(8)	42.9(3)	

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MACCE at 30 Days

	Conventional Stenting	Primary Aspiration	<i>P</i> value
MACCE* (%)	4.7	5.8	0.675
Cardiac Death (%)	3.9	2.5	0.538
Non Cardiac Death (%)	0.0	0.8	0.482
Non Q-wave MI (%)	0.8	1.7	0.610
Q-wave MI (%)	0.0	0.8	0.482
Repeat Revascularization TL	0.8	1.7	0.610
Repeat Revascularization TV	0.0	0.0	
Emergent CABG	0.0	0.8	0.482
CVA	0.0	1.7	0.231

*MACCE defined as Death, (re) infarction (Q- and non-Q wave), emergent bypass surgery, and target lesion revascularization (coronary artery bypass surgery (CABG), or repeat percutaneous transluminal coronary angioplasty (PTCA) and cerebrovascular accidents (CVA; disabling stroke).

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Conclusion

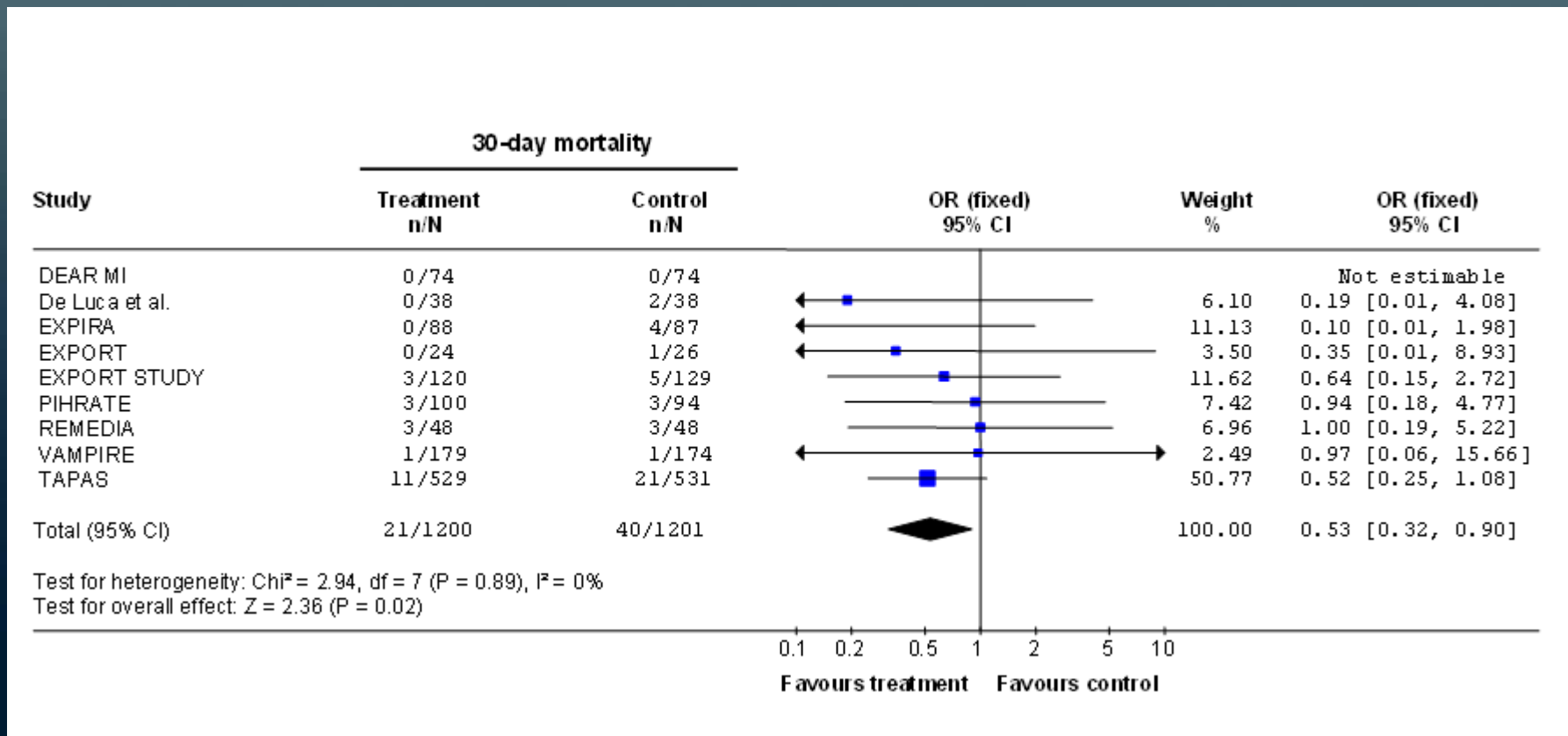
- In patients with an Acute Myocardial Infarction and TIMI 0/I flow, primary aspiration using the Export catheter is associated with:
 - Higher rate of ST segment resolution >50% (60 minutes post-procedure) and/or Myocardial Blush grade III (immediately post-procedure)
 - Higher corrected TIMI frame count post procedure
 - Lower requirement for bail-out technique
 - Lower rate of noflow
 - A trend for reducing distal embolization
- No difference in both groups concerning 30 day MACCE

Meta analysis for power issue?

Study	Period	Study device and design (number of patients)
REMEDIA... [19]	2004	Diver (n = 50) vs Control (n = 49)
De Luca et al [24]	2004	Diver (n = 28) vs Control (n = 34)
DEAR MI [22]	2004-2005	Pronto catheter (n = 74) vs control (n = 74)
EXPORT [20]	2004-2005	Export catheter (n = 24) vs control (n = 26)
VAMPIRE [23]	2004-2005	TVAC (n = 180) vs control (n = 175)
EXPORT study	Export catheter (n = 120) control (n = 129)
EXPIRA	Export catheter (n = 88) control (n = 87)
PIHRATE	Diver (n = 102) vs Control (n = 94)
TAPAS	2005-2006	Export catheter (n = 535) control (n = 536)

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Improvement in distal embolization, TIMI III, MBG III rates but....



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Primary Endpoint Results

Per protocol analysis

	Conventional Stenting	Primary Aspiration	P-value
Rate of ST segment resolution >50% (60 minutes post-procedure) and/or Myocardial Blush grade III (immediately post-procedure)* (n=196) (%)	72.5	85.9	0.026
ST resolution > 50% (%)	66.7	75.0	0.248
ST resolution	53.0 _± 46.4	59.2 _± 51.0	0.139
Myocardial blush grade III (%)	34.1	41.9	0.303