

COMPARE-ACUTE



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**Randomised trial of
FFR-guided complete revascularization
versus
infarct artery only treatment
in
multivessel STEMI patients**

On behalf of all COMPARE-ACUTE investigators

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COMPARE-ACUTE is an investigator initiated, multicenter, prospective randomized trial



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Haga Ziekenhuis, Den Haag

Atrium Medisch Centrum, Heerlen

Rijnstate Ziekenhuis, Arnhem

Universitair Medisch Centrum, Groningen

Sweden

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Klinikum Links der Weser, Bremen

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Zala Megyei Korhaz, Zalaegerszeg

Poland

MSWiA w Warszawie, Warsaw

4 Wojskowy Szpital, Wroclaw

Miedziowe Centrum Zdrowia, Lubin

Kliniki Kardiologii Allenort, Warsaw



Trial Organization



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Steering committee

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DSMB

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Diagram (Zwolle, The Netherlands): core lab and clinical event adjudication

Statistic analysis

Bianca Boxma - de Klerk

Sponsor

Maasstad Cardiovascular Research Organisation (Rotterdam, The Netherlands), receiving research grants from Abbott Vascular and St. Jude Medical





Introduction

- **Approximately 50% of the STEMI patients have multivessel disease at presentation; meaning 50% or more diameter stenosis in one or more non-infarct-related arteries (non-IRAs)**
- **What and when to do with these non-infarct-related artery (non-IRA) lesions remains a unresolved clinical dilemma**



MV-STEMI Patients

Aggressive
MV-PCI acutely

Intermediate
Non-IRA staged

Conservative
Medication

Revasc. based on **angio**

Revasc. based on FFR

Revasc. based on **angio**

Revasc. based on FFR

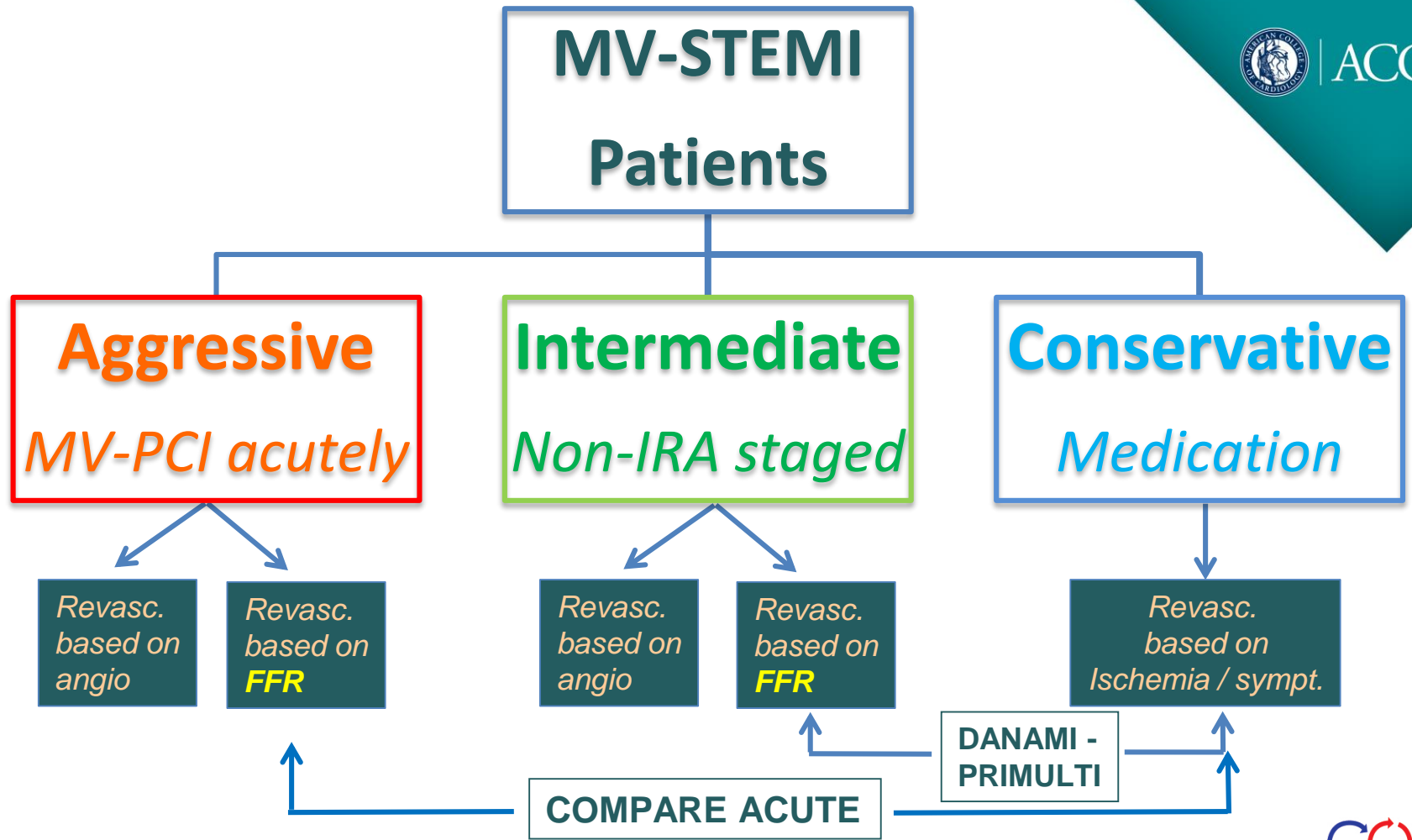
Revasc. based on Ischemia / sympt.

PRAMI
CvLPRIT

PRAMI: Wald et al. NEJM 2013; 369: 1115-23

CvLPRIT: Gerschlick et al. JACC 2015; 65: 963-72





Trial design



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Acute STEMI patients
undergoing primary PCI

885 stable multivessel
STEMI pts. randomized

1 : 2 randomization

FFR was
measured
by Pd/Pa in
rest and after
adenosine iv
or ic

295 pts

Acute FFR-guided complete
revascularization of non-IRA lesions

590 pts

Infarct related artery only treatment
+ blinded FFR of non-IRA lesions

45 day treatment window for
elective clinically indicated PCI

Follow-up at 30 days, 12, 24 and 36 months



Key In- and Exclusion Criteria

Inclusion Criteria

- Pts. between 18-85 years old
- Presenting with STEMI within 12 hours of onset of complaints with an indication for primary PCI
- And of which the non-IRAs - or their major side branches of ≥ 2.0 mm in diameter - demonstrated lesions with $\geq 50\%$ stenosis by quantitative coronary angiography (QCA) or visual assessment and were judged feasible for PCI by the operator

Exclusion Criteria

- Left main disease
- Chronic total occlusion or severe stenosis with TIMI flow \leq II of the non-IRA lesion
- Suboptimal result or complications after treatment of IRA
- Severe valve dysfunction
- Killip Class III or IV



Endpoints

Primary endpoint:

The composite of all-cause death, recurrent myocardial infarction, recurrent revascularization and cerebrovascular event (MACCE) at 12 months follow-up

Secondary endpoints:

- The primary endpoint (MACCE) at 24 and 36 months
- The components of the primary endpoint at 12, 24 and 36 months
- The composite of all-cause death and myocardial infarction at 12, 24 and 36 months
- The composite of cardiac death, myocardial infarction, revascularization, cerebrovascular event and major bleeding (NACE) at 12, 24 and 36 months
- Major bleeding at 48 hours and 12 months
- Stent thrombosis at 12, 24 and 36 months
- Treatment costs at 12, 24 and 26 months



Endpoint adjudication

- All events were independently monitored and adjudicated
- Recurrent revascularizations were adjudicated for indication (clinically indicated or not) and setting (urgent or elective)
- Clinically indicated revascularization was defined as:
 1. Stenosis of $\geq 50\%$ by QCA and one of the following: recurrent angina pectoris, ischemic ECG changes, ischemic non-invasive or invasive test findings, all presumably related to the target vessel
 2. Stenosis of $\geq 70\%$ by QCA, without objective signs of angina or ischemia
- Elective, clinically indicated revascularizations performed within 45 days after the primary PCI procedure in the IRA only group were not counted as an event

Baseline characteristics



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	FFR guided Complete Revascularization (n=295)	Infarct Artery Only Revascularization (n=590)	p-value
Mean age (sd) - yr	62 (10)	61 (10)	0.22
Male – no. (%)	233 (79.0%)	450 (76.3%)	0.37
Medical history – no. %			
Diabetes	43 (14.6%)	94 (15.9%)	0.60
Hypertension	136 (46.1%)	282 (47.8%)	0.63
Current Smoker	120 (40.8%)	287 (48.7%)	0.03
Hypercholesterolemie	95 (32.2%)	176 (29.8%)	0.47
Family history of premature CAD	103 (35.0%)	223 (37.8%)	0.42
Previous Stroke	10 (3.4%)	26 (4.4%)	0.47
Previous MI	22 (7.5%)	48 (8.1%)	0.73
Previous PCI	25 (8.5%)	44 (7.5%)	0.60
Renal impairment *	3 (1.0%)	7 (1.2%)	0.82
Peripheral vessel disease	10 (3.4%)	23 (3.9%)	0.71

* A creatinine value of more than 133 μmol/l or patients in dialysis





Baseline characteristics

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only Revascularization (n=590)	p-value
Location of infarct - no. (%)†			
Posterior MI	53 (18.0%)	96 (16.3%)	0.53
Anterior MI	105 (35.6%)	206 (34.9%)	0.84
Inferior MI	149 (50.5%)	307 (52.0%)	0.67
Lateral MI	41 (13.9%)	86 (14.6%)	0.79
Impossible to determine	3 (1.0%)	4 (0.7%)	0.59
Primary PCI within 6 / 6-12 / >12 hours of onset symptoms - no.(%)	<6h: 225 (76.3%) 6-12h: 47 (15.9%) >12h: 23 (7.8%)	<6h: 462 (78.3%) 6-12h: 84 (14.2%) >12h: 44 (7.5%)	0.58
Arteries with stenosis –no. (%)			
2	204 (69.2%)	396 (67.1%)	0.54
3	91 (30.8%)	194 (32.9%)	
Killip class ≥2 – no. (%)	15 (5.1%)	30 (5.1%)	1.00
Median maximum CK (range) – IU/l	1040 (102-8182)	1125 (112-11052)	0.62

† The location of the infarct was determined on the basis of electrocardiography

Procedural data: infarct artery lesions



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	FFR guided Complete Revascularization (295 pts, 327 lesions)	Infarct Artery Only Revascularization (590 pts, 645 lesions)	p-value
Mean IRA lesions per patient	1.11 ± 0.35	1.10 ± 0.33	0.32
Mean ref.vessel diameter IRA - mm	3.1 ± 0.5	3.2 ± 0.5	0.08
Mean IRA lesions length – mm	21.1 ± 12.1	22.3 ± 13.1	0.15
RCA – no. (%)	147 (45.0%)	296 (45.9%)	0.25
LAD – no. (%)	110 (33.6%)	233 (36.1%)	
RCX – no. (%)	69 (21.1%)	115 (17.8%)	
LM – no. (%)	1 (0.3%)	1 (0.2%)	
Pre-procedure TIMI flow (0-3) – no. (%)	0: 172 (52.6%) 1: 25 (7.6%) 2: 63 (19.3%) 3.:67 (20.5%)	0: 364 (56.4%) 1: 57 (8.8%) 2: 109 (16.9%) 3:115 (17.8%)	0.16
ACC/AHA Classification – no. (%)	A: 35 (10.7%) B1: 69 (21.1%) B2: 112 (34.3%) C:111 (33.9%)	A: 73 (11.3%) B1: 148 (22.9%) B2:189 (29.3%) C: 235 (36.4%)	0.93
Treatment (DES) – no. (%)	312 (95.4%)	620 (96.1%)	0.62



Procedural data: non-infarct artery lesions

	FFR guided Complete Revascularization (295 pts, 451 non-IRA lesions)	Infarct Artery Only Revascularization (590 pts, 856 non-IRA lesions)	p-value
Mean non-IRA lesions per patient	1.54 ± 0.81	1.56 ± 0.85	0.91
RCA – no. (%)	118 (26.2%)	206 (24.1%)	0.71
LAD – no. (%)	184 (40.8%)	360 (42.1%)	
RCX – no. (%)	149 (33.0%)	290 (33.9%)	
LM – no. (%)	0 (0.0%)	0 (0.0%)	
Pre-procedure TIMI flow (0-3) – no. (%)	0: NA 1: NA 2: 9 (2.0%) 3: 441 (98.0%)	0: 5 (0.6%) 1: 4 (0.5%) 2: 10 (1.2%) 3: 831 (97.3%)	0.19
ACC/AHA Classification – no. (%)	A: 102 (26.0%) B1: 124 (31.7%) B2: 93 (23.8%) C: 72 (18.4%)	NA	NA
Treatment (DES) – no. (%)	209 /216 (96.8%)	NA	NA

Procedural data



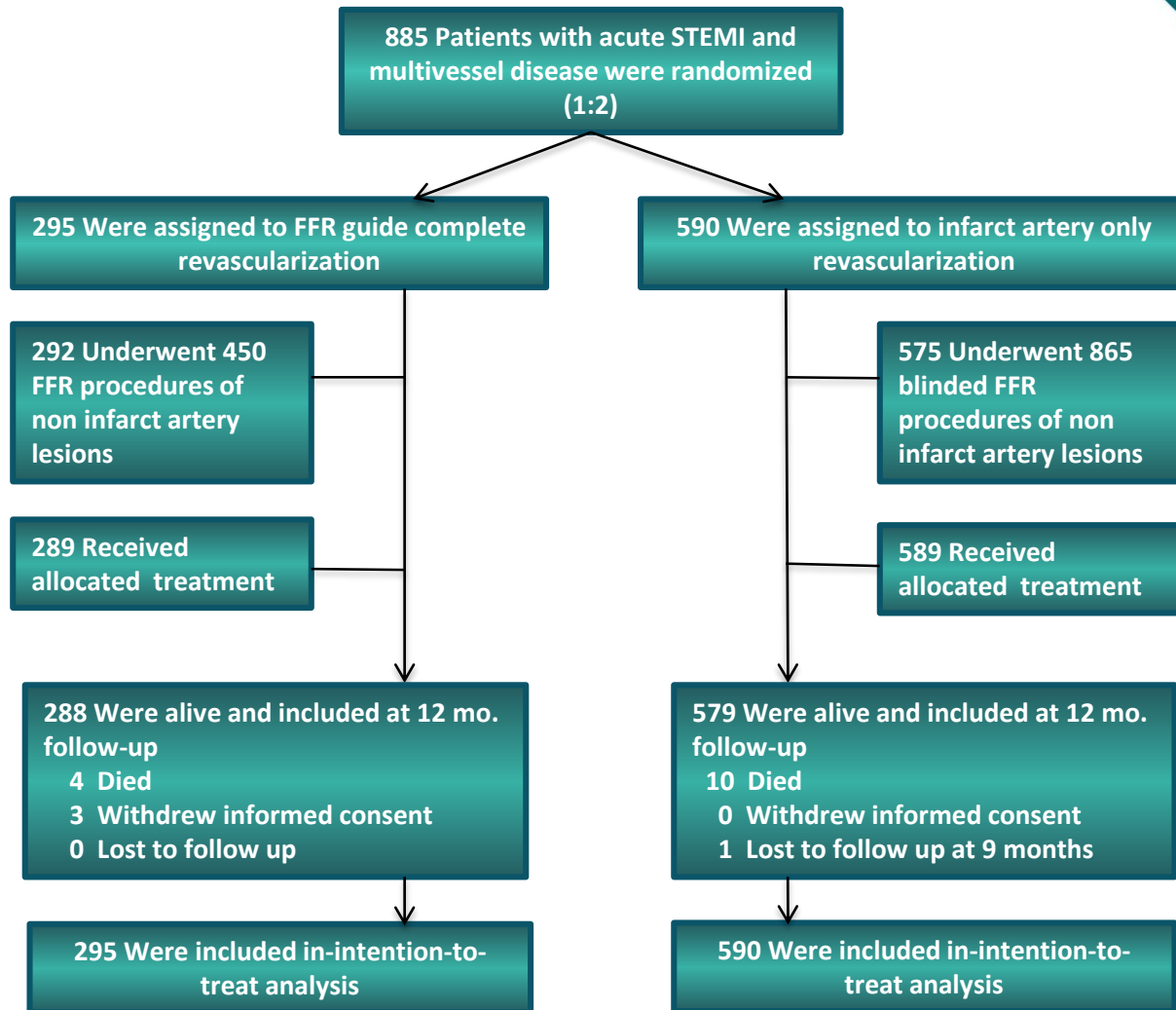
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	FFR guided complete Revascularization (295 pts.)	Infarct Artery Only Revascularization (590 pts.)	p-value
Pts. with treated (FFR guided) non-IRA lesions – no.(%)	163 (55.3%) [¶]	NA	
during index PCI procedure	136 (83.4%)		
delayed during index hospitalization	27 (16.6%) [§]		
Mean index procedure time – min	65 ± 31	59 ± 28	0.001
Mean contrast volume during index PCI procedure – ml	224 ± 104	202 ± 75	0.007
Median (range) hospital stay - days	4 (1 – 35)	4 (1 -71)	0.36
Pre-discharge non-invasive stress tests – no.(%)	21 (7.1%)	71 (12.0%)	0.03

¶ 158 pts. FFR guided + 5 pts without FFR guidance underwent non-IRA treatment

§ mean delay of 2.1 ± 1.0 days





FFR outcome



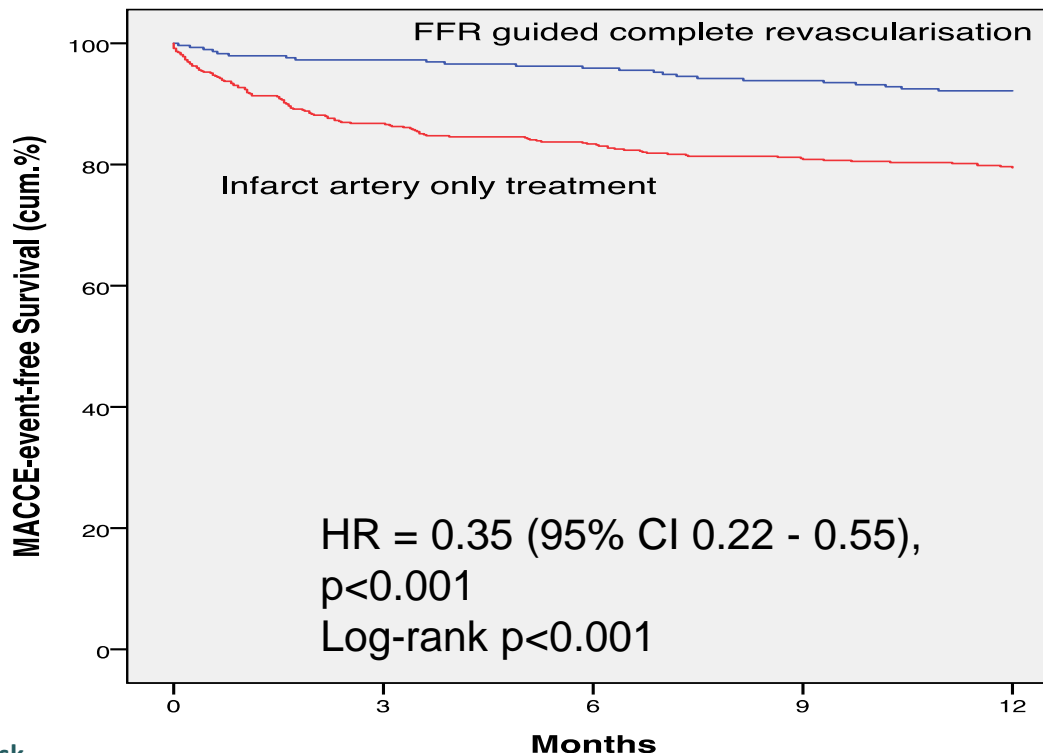
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	FFR-guided Complete n=295 pts (450 lesions)	IRA-only n=590 pts (856 lesions)	P value
FFR measurements	292 (99.0%)	575 (97.5%)	0.13
Min. FFR (mean \pm SD)	0.78 \pm 0.12	0.79 \pm 0.12	0.42
Positive FFR value (\leq 0.80)	158/292 (54.1%)	275/575 (47.9%)	0.08
Negative FFR value ($>$ 0.80)	134/292 (45.9 %)	300/575 (52.1%)	

Primary outcome



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7.8%

20.5%

No. at risk	0	3	6	9	12
FFR guided complete	295	286	281	264	215
Culprit lesion only	590	512	492	457	371



Primary outcome and its components

* MACCE = the composite of all-cause mortality, non-fatal myocardial infarction, any revascularization and cerebrovascular events.

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only treatment (n=590)	HR	95% CI	P value
Primary endpoint	Number of events (%)				
MACCE* (any first event)	23 (7.8%)	121 (20.5%)	0.35	0.22 – 0.55	<0.001
Death, all cause	4 (1.3%)	10 (1.7%)	0.80	0.25 – 2.56	0.70
Cardiac	3 (1.0%)	6 (1.0%)			
Myocardial infarction (MI)	7 (2.4%)	28 (4.7%)	0.50	0.22 - 1.13	0.10
Spontaneous	5 (1.6%)	17 (2.9%)	0.59	0.22 – 1.59	0.29
Peri-procedural	2 (0.6%)	11 (1.9%)	0.36	0.08 – 1.64	0.19
Revascularization	18 (6.1%)	103 (17.5%)	0.32	0.20 – 0.54	<0.001
PCI	15 (5.1%)	98 (16.6%)	0.37	0.24 – 0.57	<0.001
CABG	3 (1.0%)	5 (0.8%)	1.20	0.29 – 5.02	0.80
Cerebrovascular event	0 (0.0%)	4 (0.7%)	NA	NA	NA

Secondary endpoints

** NACE = Net Adverse Clinical Events; the composite of cardiac death, myocardial Infarction, any revascularization, stroke and major bleeding.

	FFR guided Complete Revascularization (n=295)	Infarct Artery Only treatment (n=590)	HR	95% CI	P value
Secondary endpoints	Number of events (%)				
NACE** (any first event)	25 (8.5%)	174 (29.5%)	0.25	0.16– 0.38	<0.001
Death (all cause) or MI	11 (3.7%)	38 (6.4%)	0.57	0.29 – 1.12	0.10
Major bleeding	3 (1.0%)	8 (1.4%)	0.75	0.20 – 2.84	0.67
Any bleeding at 12months	9 (3.1%)	28 (4.7%)	0.64	0.30 – 1.36	0.25
Any bleeding at 48h	5 (1.7%)	8 (1.4%)	1.25	0.41 – 3.83	0.69
Hospitalization for heart failure, unstable angina and chest pain	13 (4.4%)	47 (8.0%)	0.54	0.29 – 0.99	0.04
Any revascularization	19 (6.4%)	161 (27.3%)	0.47	0.29 – 0.76	0.002
Stent thrombosis	2 (0.7%)	1 (0.2%)	0.58	0.12 – 2.80	0.50



Conclusions

- **In multivessel STEMI patients, FFR-guided complete revascularization of non-infarct-related lesions in the acute phase of primary PCI significantly reduced the risk of the composite MACCE outcome as compared with a strategy of treatment of the infarct-related artery only**
- **This reduction was mainly driven by the decreased need for subsequent revascularization**



Conclusions

- **Approximately half of the lesions in non infarct-related arteries considered significant on coronary angiograms had an FFR value >0.8 and were therefore not physiologically significant**
- **Deferring treatment of angiographically significant coronary lesions in non-infarct related arteries with an FFR > 0.8 is safe and efficient**



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ORIGINAL ARTICLE

Fractional Flow Reserve–Guided Multivessel Angioplasty in Myocardial Infarction

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Online today 18 March 2017 @ www.nejm.org
To be published 30 March 2017

