Complete vs. Culprit-Only Revascularization in Older Patients with MI with or without ST-segment elevation

A FIRE trial sub-analysis

Simone Biscaglia
University Hospital of Ferrara
On behalf of the FIRE investigators

August 31, 2024

Background

- Complete revascularization is the recommended strategy in patients with STEMI with multivessel disease
- No dedicated trial has compared complete revascularization with culprit-only PCI in NSTEMI patients
- The FIRE trial enrolled 1445 patients aged ≥75 years with MI and multivessel disease. The trial included both STEMI and NSTEMI patients

Research question

To investigate the consistency of risks and benefits of complete revascularization based on coronary physiology over a culprit-only revascularization strategy with respect to the initial clinical presentation (STEMI vs. NSTEMI)

Organization

3 countries: Italy, Spain, Poland

34 centers

Study PI: Simone Biscaglia

Study Chair: Gianluca Campo

Executive Committee: Javier Escaned, Dariusz Dudek, Raul Moreno, Matteo Tebaldi, Emanuele Barbato

CEC: Rita Pavasini, Paolo Cimaglia

CRC: Veronica Lodolini, Martina Viola

Stats: Elisa Maietti, Anna Zanetti, Nicola Pesenti

CROs: AdvicePharma, Impulsae Consulting, KCRI

Investigator-driven trial

FIRE TRIAL

CFR Consorzio Futuro in Ricerca

Università degli Studi di Ferrara

Contributors

SMT

Medis Medical Imaging Systems

EUKON Future Healthcare Now

SIEMENS Healthineers

GE Healthcare

Insight Lifetech

AMGEN

Design

FIRE TRIAL

All comers, prospective, randomized, multicenter, open-label trial with blinded adjudicated evaluation of outcomes (PROBE).

Pts ≥75 ys hospitalized for MI (STE or NSTE) with indication to invasive management

Multivessel disease at coronary artery angiography

Culprit lesion clearly identifiable and successfully treated

R

Physiology-guided Complete Revascularization

- **STEMI** n=253
- **NSTEMI** n=467

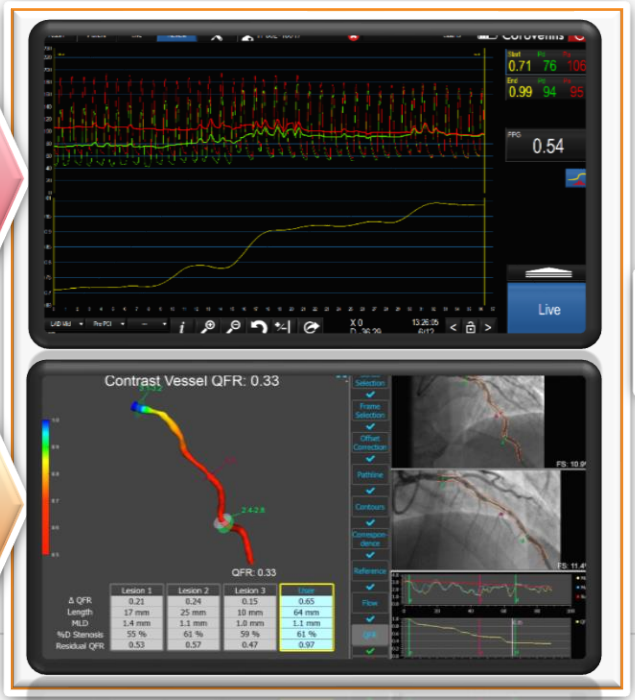
Culprit-only Revascularization

- **STEMI** n=256
- **NSTEMI** n=469

Coronary Physiology & Stents

- **Non-culprit lesions were assessed with either wire-based FFR, resting index or angiography-derived FFR**
- **Flow-limiting lesions (FFR≤0.80, resting ≤0.89) had to be revascularized with biodegradable-polymer sirolimus ultra-thin stent(s)**

OR



Endpoints

Primary

Death, any MI, any stroke, or ID-revascularization

Key secondary

Cardiovascular death or MI

Safety

CA-AKI, stroke, or BARC type 3-5 bleeding

Baseline Characteristics

Characteristic	STEMI (N=509)	NSTEMI (N=936)	P
Age (IQR) – yr	81.2±5	80.8±4	0.164
Female sex	212 (42)	316 (38)	**0.003**
Comorbidities			
Hypertension	399 (78)	786 (84)	**0.010**
Diabetes	125 (24)	338 (36)	**<0.001**
Prior MI	43 (8)	177 (19)	**<0.001**
eGFR<60 ml/min	221 (43)	441 (47)	0.196
PAD	69 (13)	180 (19)	**0.007**
LVEF	46.1±10	50.8±11	**<0.001**
Killip class ≥2	164 (32)	248 (26)	**0.011**

Characteristic	STEMI (n=509)	NSTEMI (n=936)	p
Culprit vessel			
Left main	12 (2)	64 (7)	**<0.001**
LAD artery	222 (44)	437 (47)	
LCx artery	75 (15)	194 (21)	
RCA	195 (38)	218 (23)	
RI artery	5 (1)	23 (2)	
Physiological assessment			
Wire-based index	155 (30)	296 (32)	0.913
QFR	86 (17)	163 (17)	

NSTEMI patients were more complex in terms of clinical and procedural characteristics

Baseline Characteristics

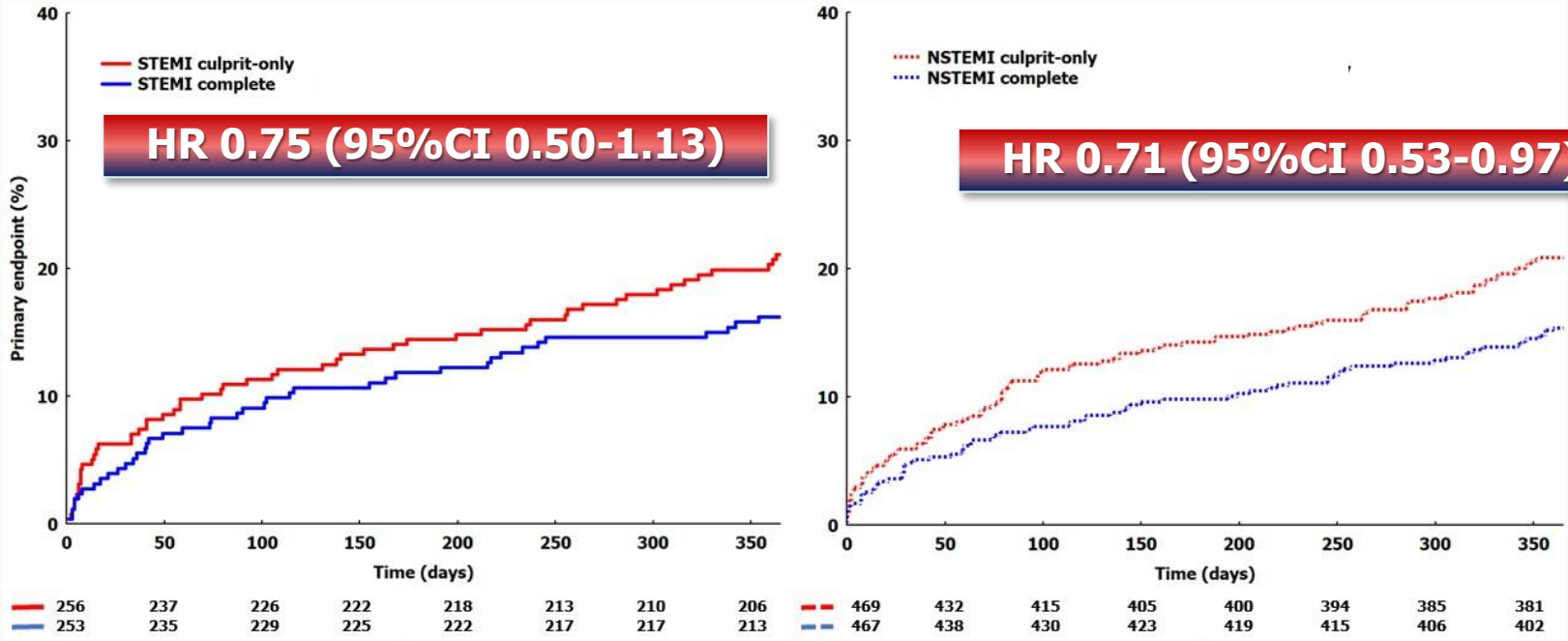
Characteristic	NSTEMI		
	Culprit Only (n=469)	Physio-guided Complete (n=467)	p
Age (IQR) – yr	80.8±4	80.8±4	0.864
Female sex	158 (34)	158 (34)	0.982
Comorbidities			
Hypertension	387 (82)	399 (85)	0.258
Diabetes	168 (36)	170 (36)	0.906
Prior MI	94 (20)	83 (18)	0.421
eGFR<60 ml/min	216 (46)	225 (48)	0.558
PAD	93 (20)	87 (18)	0.701
LVEF	50.4±11	51.2±10	0.246
Killip class ≥2	126 (27)	122 (26)	0.901

Characteristic	NSTEMI		p
Culprit vessel	**Culprit Only (n=469)**	**Physio-guided Complete (n=467)**	
Left main	36 (8)	28 (6)	0.644
LAD artery	222 (47)	215 (46)	
LCx artery	97 (21)	97 (21)	
RCA	105 (22)	113 (24)	
RI artery	9 (2)	14 (3)	
Physiological assessment			
Wire-based index	/	296	NA
QFR	/	163	

No differences between the two study groups also in STEMI patients

Primary endpoint

All-cause death, any MI, stroke, or ID-revascularization

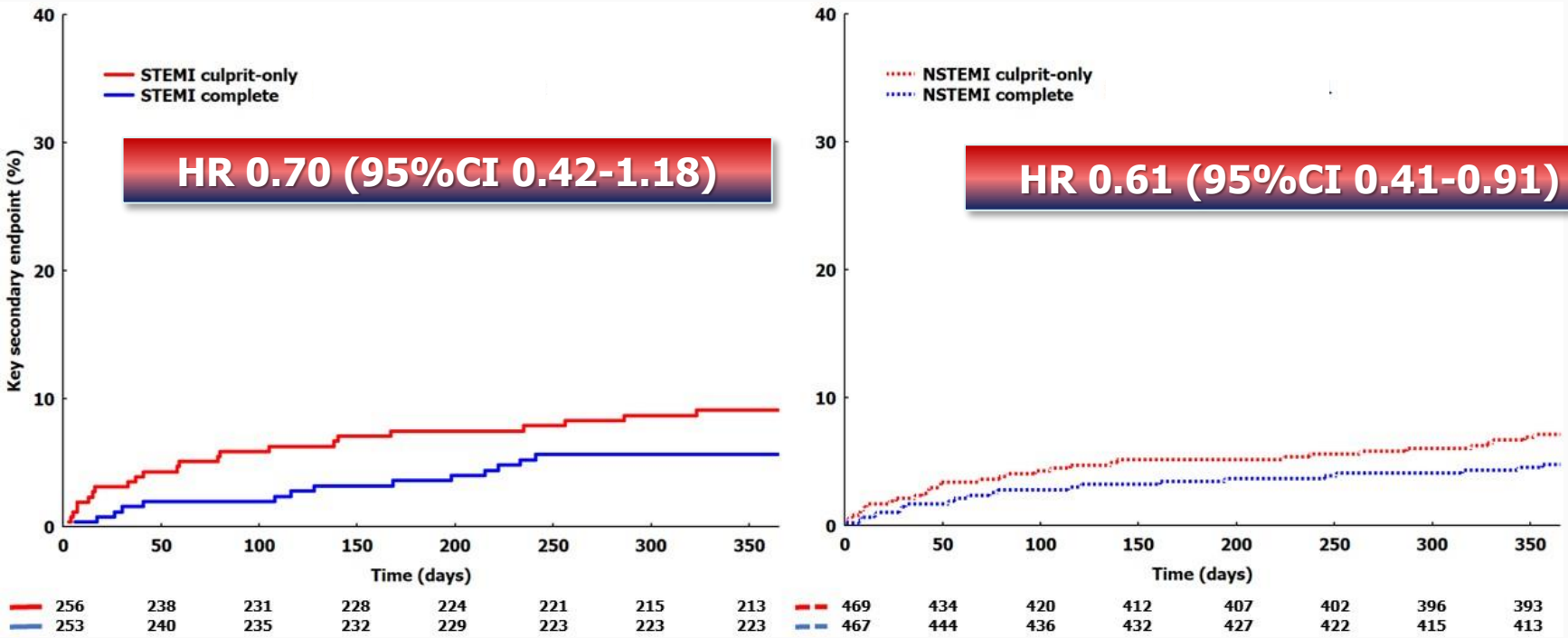


p for interaction 0.846

Culprit-only
Physio-guided Complete

Key secondary endpoint

CV death or MI



p for interaction 0.526

Culprit-only
Physio-guided Complete

Safety and Secondary Endpoints

	STEMI (n=509)		NSTEMI (n=936)		
Outcome	Culprit only (n=256)	Physio-guided complete (n=253)	Culprit only (n=469)	Physio-guided complete (n=467)	p for interaction
Death	0.65 [0.38-1.09]		**0.73 [0.49-1.09]**		**0.72**
CV Death	0.60 [0.31-1.16]		**0.66 [0.39-1.13]**		**0.82**
Myocardial infarction	0.93 [0.41-2.10]		**0.57 [0.31-1.05]**		**0.35**
Stroke	1.02 [0.14-7.20]		2.69 [0.72-10.14]		**0.42**
ID revascularization	0.89 [0.43-1.81]		**0.46 [0.24-0.88]**		**0.18**
Stent thrombosis	1.01 [0.21-8.32]		1.23 [0.35-6.44]		**0.97**
BARC 3-5 bleeding	1.15 [0.44-2.96]		0.80 [0.42-1.55]		**0.55**

Limitations

- Need to clearly identify culprit lesion
- Angio-guided complete revascularization may solve the culprit identification issue, but it is associated with overtreatment
- In NSTEMI patients the integration of physiology and imaging tools could be the best solution
- COMPLETE-2 trial is comparing physio vs angio-guided complete revascularization including also NSTEMI patients

Conclusions

- In older MI patients, physiology-guided complete revascularization strategy provided consistent benefits across the entire spectrum of MI
- In the presence of a clearly identifiable culprit lesion, physiology-guided complete revascularization should be pursued in both older STEMI and NSTEMI patients

ARTICLE IN PRESS

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2024 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. ■, NO. ■, 2024

Complete vs Culprit-Only Revascularization in Older Patients With Myocardial Infarction With or Without ST-Segment Elevation

Marta Cocco, MD,[a] Gianluca Campo, MD,[a] Vincenzo Guiducci, MD,[b] Gianni Casella, MD,[c] Caterina Cavazza, MD,[d] Enrico Cerrato, MD,[e] Giorgio Sacchetta, MD,[f] Raul Moreno, MD,[g] Alberto Menozzi, MD,[h] Ignacio Amat Santos, MD,[i] José Luis Díez Gil, MD,[j] Roberto Scarsini, MD,[k] Andrea Picchi, MD,[l] Giuseppe Vadalà, MD,[m] Gerlando Pilato, MD,[n] Iginio Colaiori, MD,[o] Marco Barbierato, MD,[p] Manfredi Arioti, MD,[q] Rita Pavasini, MD,[a] Valerio Lanzilotti, MD,[c] Mila Menozzi, MD,[d] Ferdinando Varbella, MD,[e] Andrea Erriquez, MD,[a] Simone Biscaglia, MD[a]

ABSTRACT

BACKGROUND The effectiveness of complete revascularization is well established in patients with ST-segment elevation myocardial infarction (STEMI), but it is less investigated in those with non-ST-segment elevation myocardial infarction (NSTEMI).

OBJECTIVES This study aimed to assess whether complete revascularization, compared with culprit-only revascularization, was associated with consistent outcomes in older patients with STEMI and NSTEMI.

METHODS In the FIRE (Functional Assessment in Elderly MI Patients with Multivessel Disease) trial, 1,445 older patients with myocardial infarction (MI) were randomized to culprit-only or physiology-guided complete revascularization, stratified by STEMI (n = 256 culprit-only vs n = 253 complete) and NSTEMI (n = 469 culprit-only vs n = 467 complete). The primary outcome comprised a composite of death, MI, stroke, or revascularization at 1 year. The key secondary outcome included a composite of cardiovascular death or MI at 1 year.

RESULTS In the overall study population, physiology-guided complete revascularization reduced both primary and key secondary outcomes. The primary outcome occurred in 54 (21.1%) STEMI patients randomized to culprit-only vs 41 (16.2%) STEMI patients of the complete group (HR: 0.75; 95% CI: 0.50-1.13) and in 98 (20.9%) NSTEMI patients randomized to culprit-only vs 72 (15.4%) NSTEMI patients of the complete group (HR: 0.71; 95% CI: 0.53-0.97), with negative interaction testing (*P* for interaction, 0.846). Similarly, no signal of heterogeneity with respect to the initial clinical presentation was observed for the key secondary endpoint (*P* for interaction, 0.654).

CONCLUSIONS Physiology-guided complete revascularization, compared with culprit-only revascularization, provided consistent benefit across the whole spectrum of patients with MI. (FIRE [Functional Assessment in Elderly MI Patients With Multivessel Disease]; NCT03772743) (*JACC*. 2024;■:■-■) © 2024 by the American College of Cardiology Foundation.

From the [a]Cardiology Unit, Azienda Ospedaliero Universitaria di Ferrara, Ferrara, Italy; [b]Cardiology Unit, Azienda USL-IRCCS Reggio Emilia, S. Maria Nuova Hospital, Reggio Emilia, Italy; [c]Cardiology Unit, Ospedale Maggiore, Bologna, Italy; [d]Cardiovascular Department, Infermi Hospital, Rimini, Italy; [e]Interventional Cardiology Unit, San Luigi Gonzaga University Hospital, Orbassano, and Rivoli Infermi Hospital ASLTO3, Rivoli, Turin, Italy; [f]Cardiology Unit, Umberto I Hospital, ASP Siracusa, Siracusa, Italy; [g]Centro de Investigación Biomédica en Red en Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain, Instituto de Investigación Hospital La Paz (IDIPAZ), University Hospital La Paz, Madrid, Spain; [h]S.C. Cardiologia, Ospedale Sant'Andrea, La Spezia, Italy; [i]Centro de Investigación Biomédica en Red en Enfermedades Cardiovasculares (CIBERCV), Cardiology Department, Hospital Clínico Universitario, Valladolid, Spain; [j]Centro de Investigación Biomedica end Red en Enfermedades Cardiovasculares, Cardiology Department, H. Universitario y Politécnico La Fe, Valencia, Spain; [k]Azienda Ospedaliero Universitaria Integrata di Verona, Verona, Italy; [l]Cardiovascular Department, Azienda Unità Sanitaria Locale (USL) Toscana Sud-Est, Misericordia Hospital, Grosseto, Italy; [m]Azienda Ospedaliero Universitaria Policlinico Paolo Giaccone, Palermo, Italy; [n]Department of Interventional Cardiology, San Giovanni Di Dio Hospital, Agrigento, Italy; [o]Cardiology Unit, Ospedale Santa Maria Goretti, Latina, Italy; [p]Interventional Cardiology, Department of Cardio-Thoracic and Vascular Sciences, Ospedale dell'Angelo, Mestre, Venice, Italy; and [q]Ospedale Santa Maria delle Croci, ASL Romagna, Ravenna, Italy.

ISSN 0735-1097/$36.00

https://doi.org/10.1016/j.jacc.2024.07.028

Simultaneously published in *JACC*

JACC®