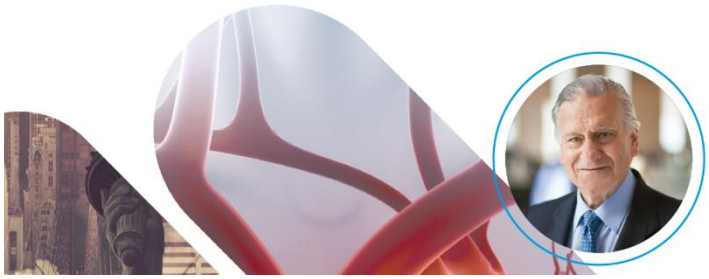
New York Cardiovascular Symposium



STEMI 1: Timing, Mechanical Type and Pharmacology of Reperfusion: The Three Main Challenges to Decrease Infarct Size and Increase Viability

Borja Ibanez, MD PhD FESC.

- Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC).
- Fundación Jiménez Díaz Hospital.

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MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

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Grupo quirónsalud

ciber cv

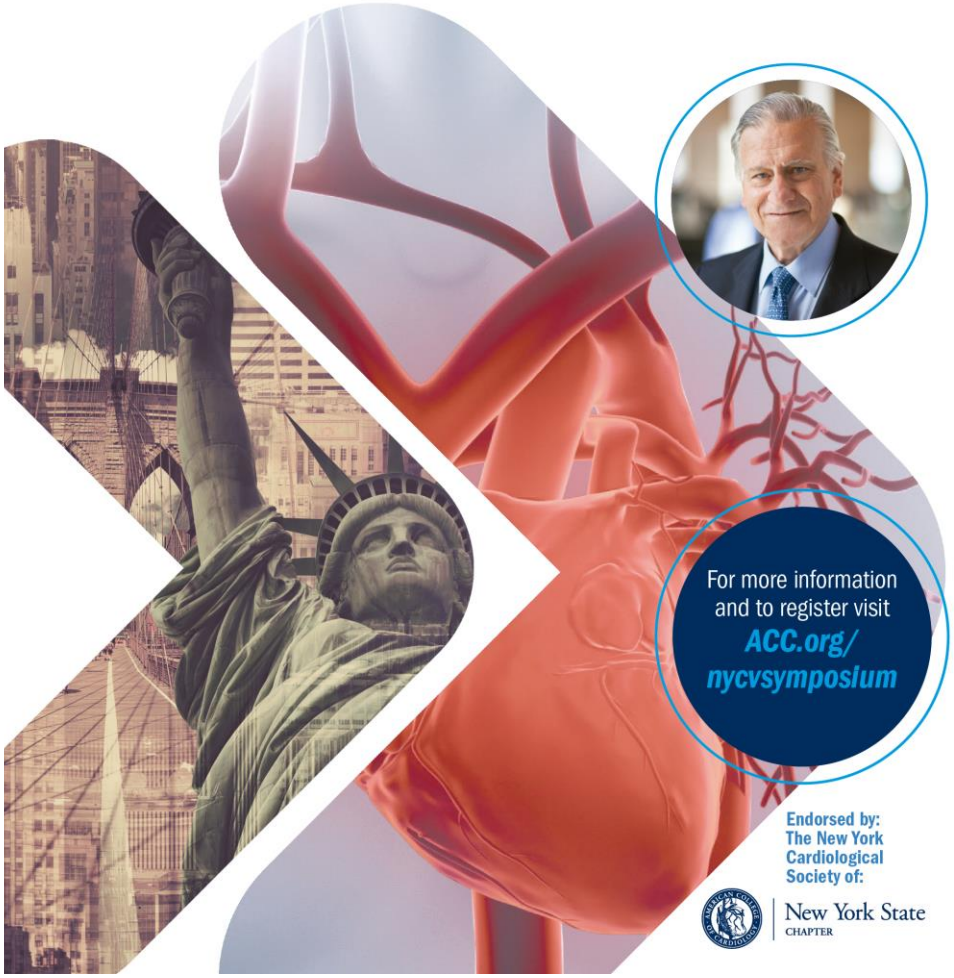
Centro de Investigación Biomédica en Red

Enfermedades Cardiovasculares

AMERICAN C

CONFLICTS OF INTEREST

B Ibanez has no conflicts to declare



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1) Reperfusion: a paradigm shift → from mortality to HF.

2) Next goal: Infarct size limitation in reperfused STEMI.

3) Ischemia/Reperfusion injury.

4) Therapies to reduce infarct size:
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   - Metoprolol

5) Impact of timing of intervention on infarct size reduction

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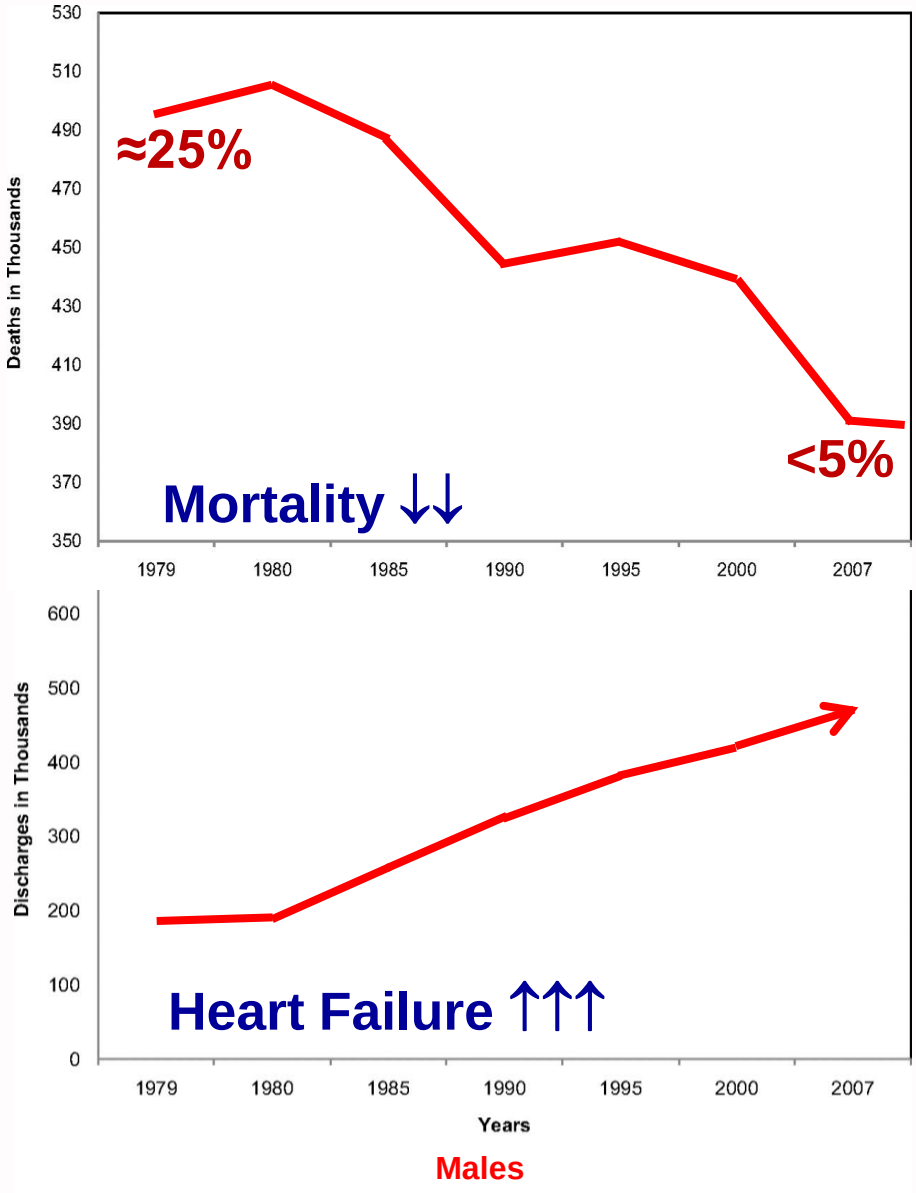
STEMI: A paradigm shift

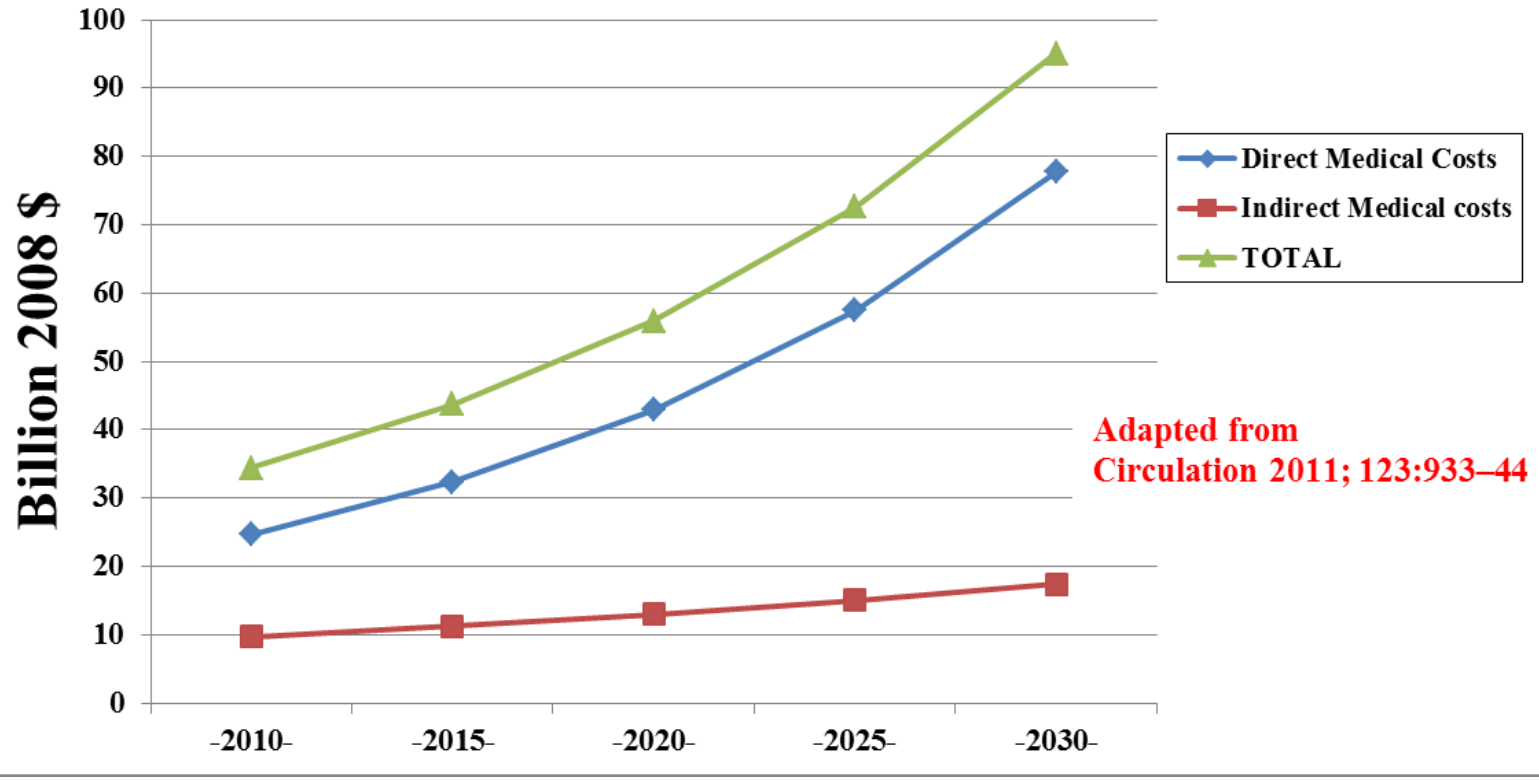


Adapted from Roger VL et al. ***Circulation*** 2011;123:e18-e209

STEMI→ Heart Failure

•Figure 2:

Projected Heart Failure direct medical costs and indirect (lost productivity) costs.



Adapted from Circulation 2011; 123:933–44

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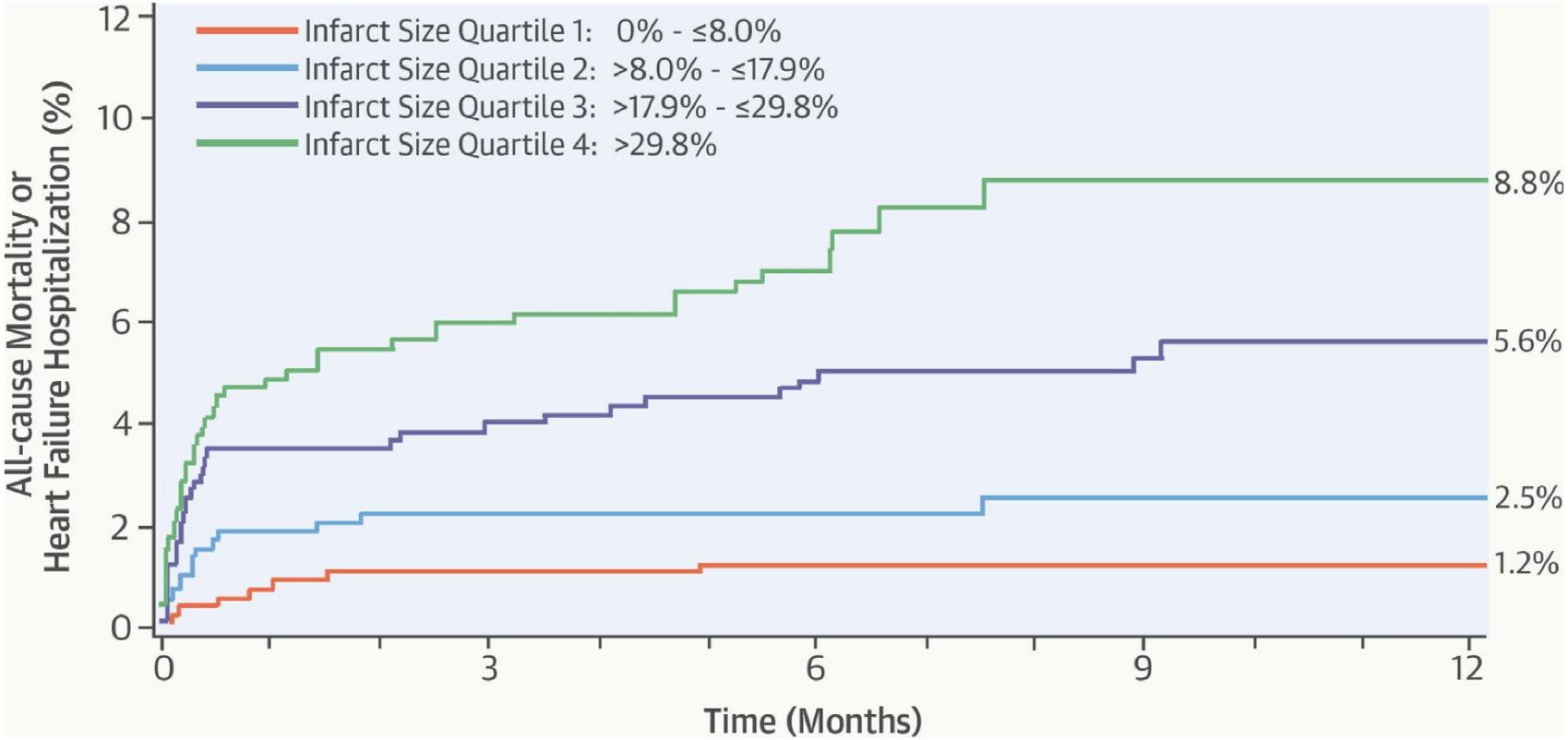
Surrogate markers: predictors

CENTRAL ILLUSTRATION IS and Prognosis After Primary PCI: All-Cause Mortality or HF Hospitalization



Stone, G.W. et al. J Am Coll Cardiol. 2016;67(14):1674-83.

Infarct size is a strong determinant of long-term mortality and chronic heart failure

Therapies to reduce MI size

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction : A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Patrick T. O'Gara, Frederick G. Kushner, Deborah D. Ascheim, Donald E. Casey, Jr, Mina K. Chung, James A. de Lemos, Steven M. Ettinger, James C. Fang, Francis M. Fesmire, Barry A. Franklin, Christopher B. Granger, Harlan M. Krumholz, Jane A. Linderbaum, David A. Morrow, L. Kristin Newby, Joseph P. Ornato, Narith Ou, Martha J. Radford, Jacqueline E. Tamis-Holland, Carl L. Tommaso, Cynthia M. Tracy, Y. Joseph Woo and David X. Zhao

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC)

Authors/Task Force Members: Borja Ibanez* (Chairperson) (Spain), Stefan James*

ESC
European Society of Cardiology

No therapy to reduce MI size
→ URGENT clinical need

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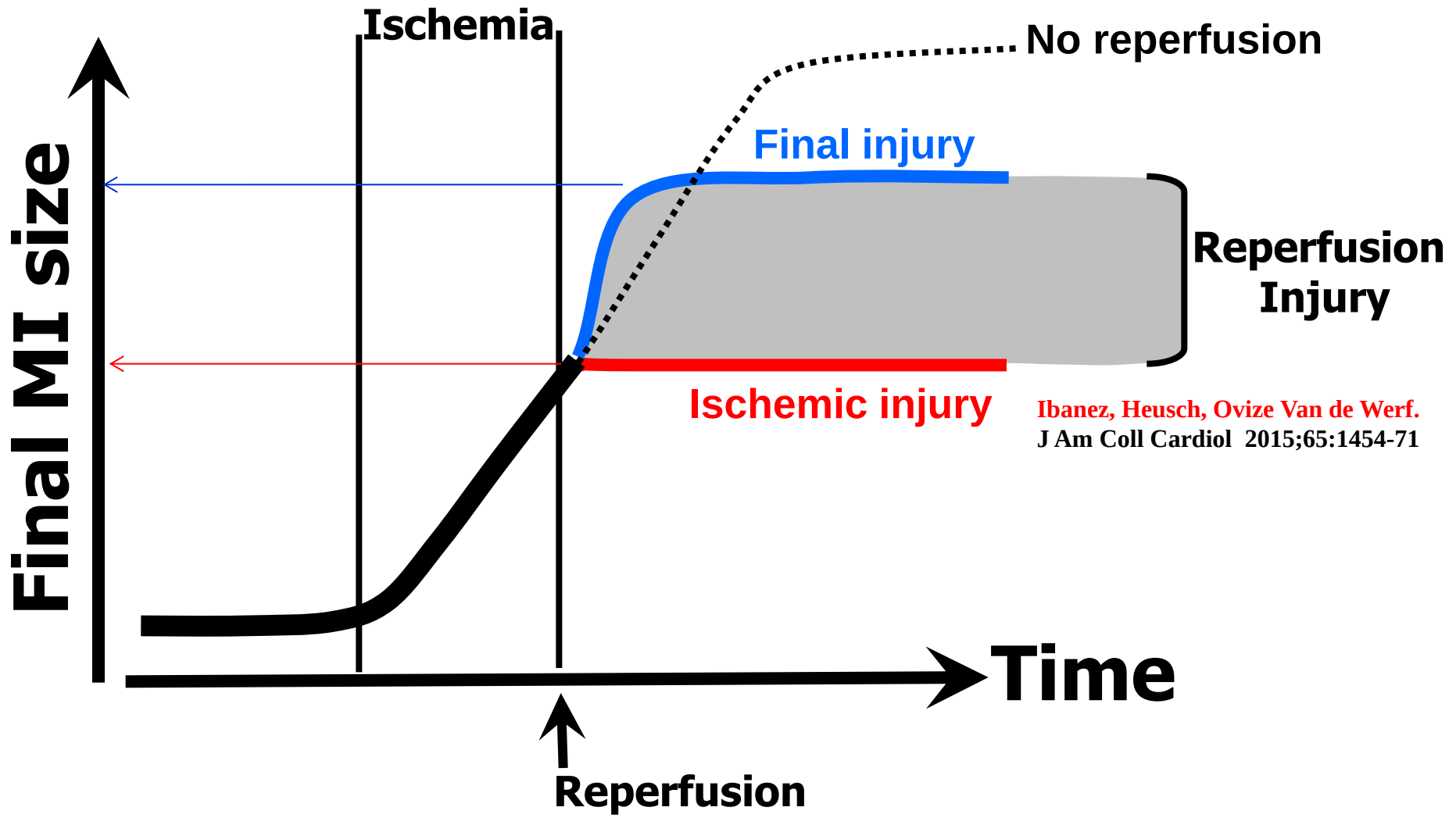
Reperfusion

+ Conditioning.

+ β-blockers.

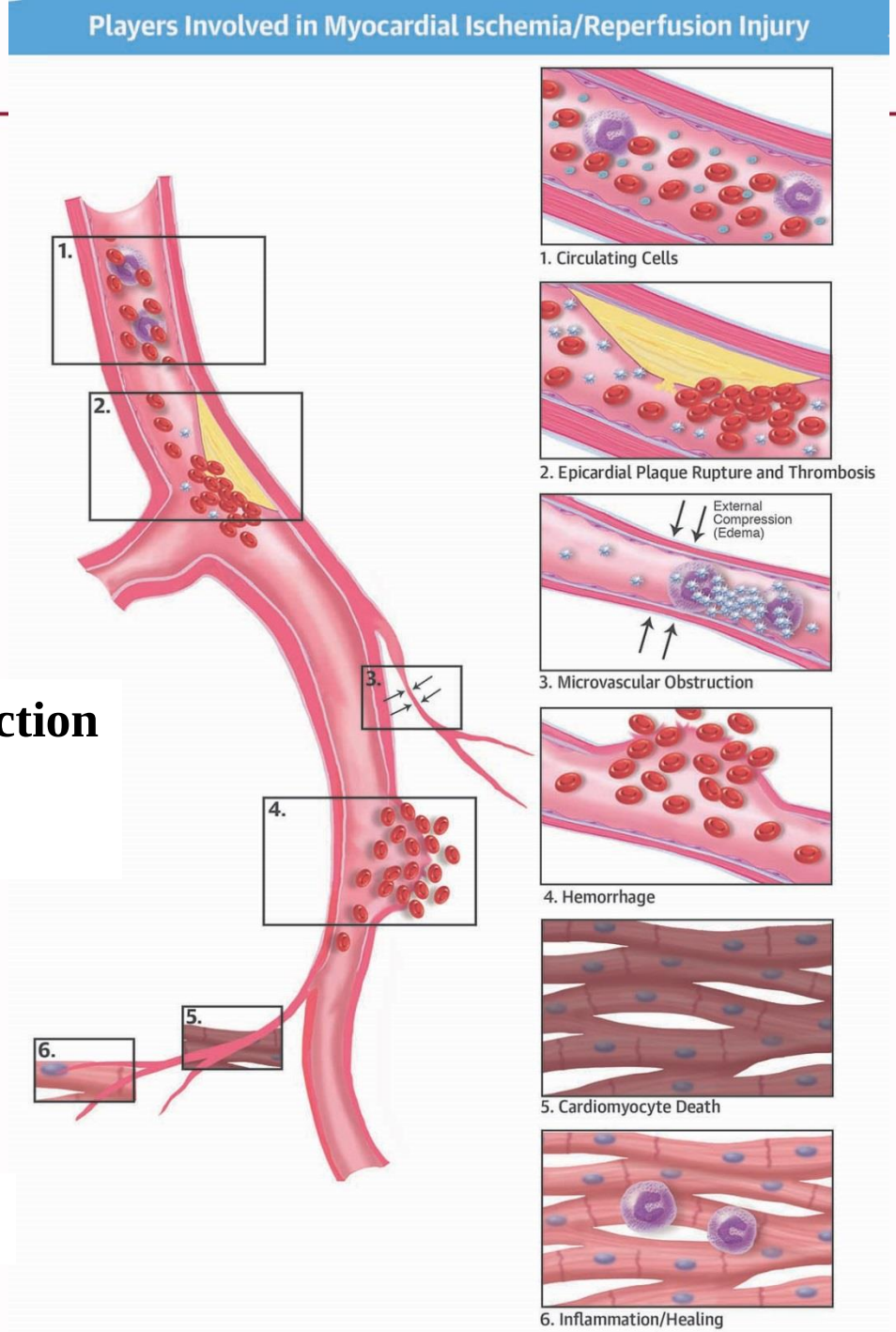
5) Impact of timing of intervention on infarct size reduction.

Ischemia/Reperfusion injury



Ibanez, Heusch, Ovize Van de Werf.
J Am Coll Cardiol 2015;65:1454-71

Microvascular Obstruction Myocardial Healing : critical players



State of the art review

J Am Coll Cardiol 2015;65:1454-71

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Type of Reperfusion: PCI Vs Lysis

Head to head PCI >>Thrombolysis (Up to 120 min PCI-delay)

Do early presenters without immediate PCI benefit from Lysis?

STREAM trial (STEMI ≤3 hours evolution) → No differences between transfer to PCI and immediate thrombolysis

PCI when STEMI diagnosis to PCI ≤120min... **even for early presenters**

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC)

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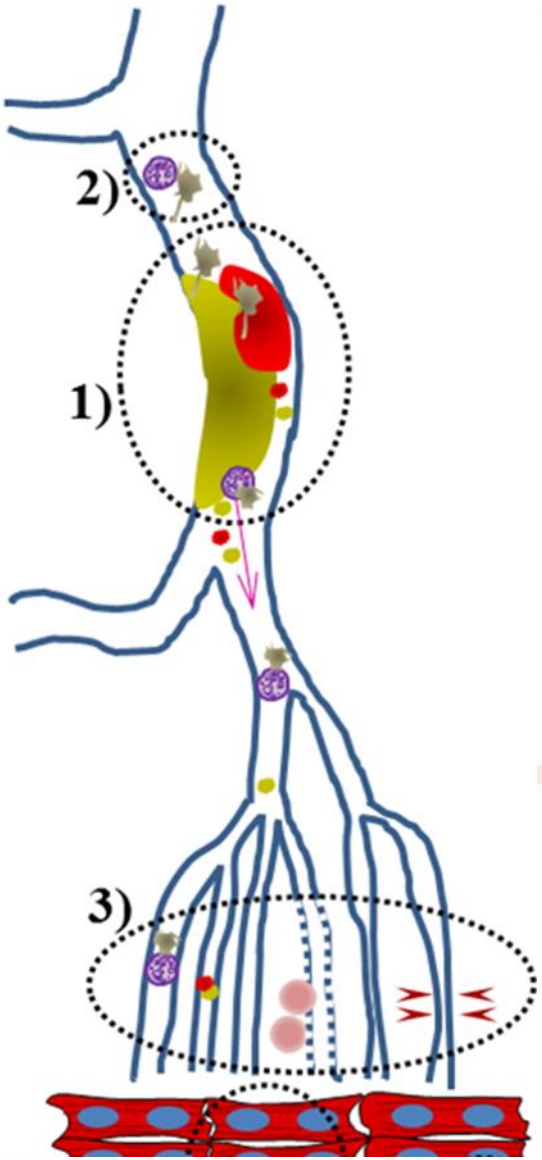
DEFER Stenting



SOTA Review on reperfusion injury
J Am Coll Cardiol 2015;65:1454-71

High thrombus burden→risk of embolization and microvascular obstruction

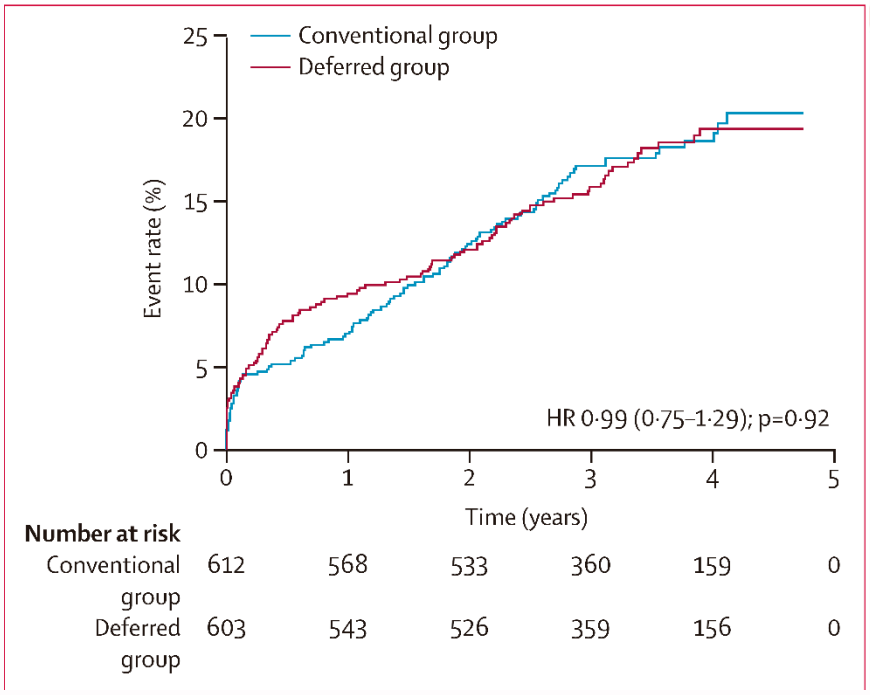
Is there a role of deferred stenting (under intense antithrombotic therapy)?

DEFER Stenting

Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER): an open-label, randomised controlled trial

Henning Kelbæk, Dan Eik Høfsten, Lars Køber, Steffen Helqvist, Lene Kløvgaard, Lene Holmvang, Erik Jørgensen, Frants Pedersen, Kari Saunamäki, Ole De Backer, Lia E Bang, Klaus F Kofoed, Jacob Lønborg, Kiril Ahtarovski, Niels Vejlstrup, Hans E Bøtker, Christian J Terkelsen, Evald H Christiansen, Jan Ravkilde, Hans-Henrik Tilsted, Anton B Villadsen, Jens Aarøe, Svend E Jensen, Bent Raungaard, Lisette O Jensen, Peter Clemmensen, Peer Grande, Jan K Madsen, Christian Torp-Pedersen, Thomas Engstrøm

Lancet 2016; 387: 2199–206



N= 1215

Primary outcome: "death, HF admission, re-MI, unplanned TVR"

median F-Up 42 months

DEFER Stenting

Myocardial Damage in Patients With Deferred Stenting After STEMI

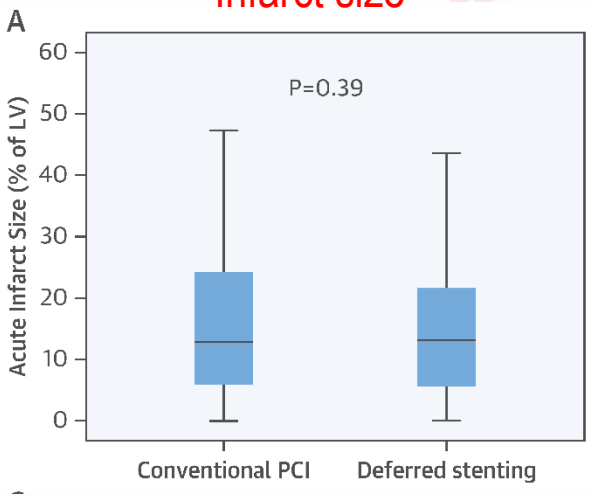
A DANAMI-3–DEFER Substudy

Jacob Lønborg, MD, PhD, DMSc,[a] Thomas Engstrøm, MD, PhD, DMSc,[a] Kiril Aleksov Ahtarovski, MD, PhD,[a] Lars Nepper-Christensen, MD,[a] Steffen Helqvist, MD, DMSc,[a] Niels Vejlstrup, MD, PhD,[a] Kasper Kyhl, MD,[a] Mikkel Malby Schoos, MD, PhD,[a] Ali Ghotbi, MD,[a] Christoffer Göransson, MD,[a] Litten Bertelsen, MD,[a] Lene Holmvang, MD, DMSc,[a] Frants Pedersen, MD, PhD,[a] Erik Jørgensen, MD,[a] Kari Saunamäki, MD, DMSc,[a] Peter Clemmensen, MD, DMSc,[b,c] Ole De Backer, MD, PhD,[a] Lene Kløvgaard, RN,[a] Dan Eik Høfsten, MD, PhD,[a] Lars Køber, MD, DMSc,[a] Henning Kelbæk, MD, DMSc,[d] for the DANAMI-3 Investigators

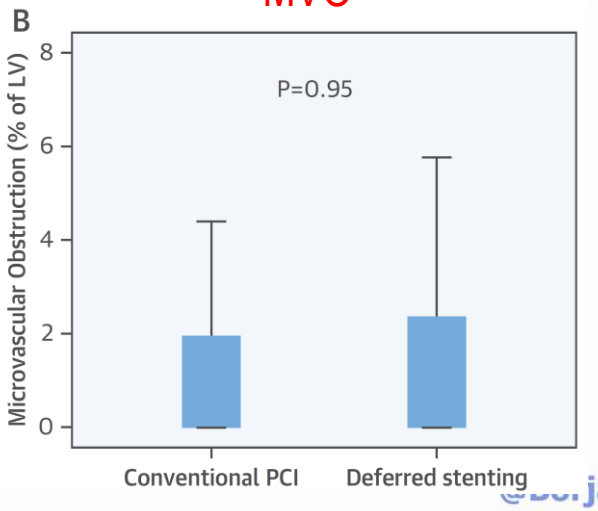
J Am Coll Cardiol 2017;69:2794–804

N=510 (out of 1215)
2 CMR (predischarge, 3 months

Infarct size



MVO



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Ischemic Conditioning

Preinfarction angina confers protection

Ischemic preconditioning protect the heart

Ischemic Conditioning

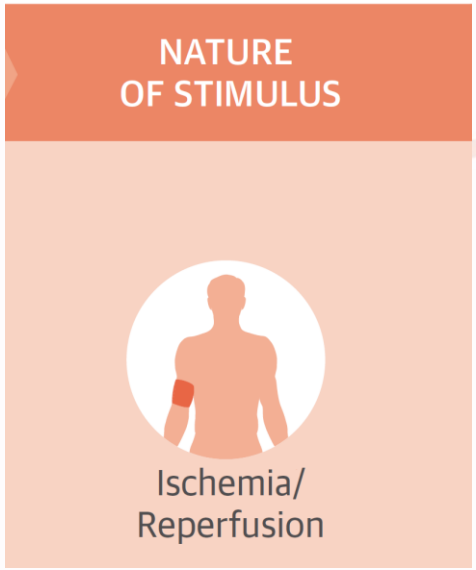
THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

J Am Coll Cardiol 2015;65:177-95

Remote Ischemic Conditioning

Gerd Heusch, MD,* Hans Erik Bøtker, MD, PhD,† Karin Przyklenk, PhD,‡ Andrew Redington, MD,§ Derek Yellon, PhD, DSc||



Brief episodes of occlusion/ reperfusion in a distant organ protects the heart

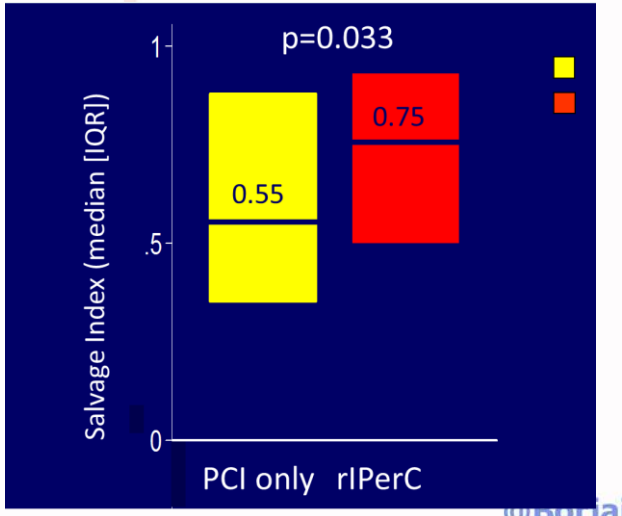
CONDI trial

Remote ischaemic conditioning before hospital admission, as a complement to angioplasty, and effect on myocardial salvage in patients with acute myocardial infarction: a randomised trial

Lancet 2010;375:727-734

Hans Erik Bøtker, Rajesh Kharbanda, Michael R Schmidt, Morten Bøttcher, Anne K Kaltoft, Christian J Terkelsen, Kim Munk, Niels H Andersen, Troels M Hansen, Sven Trautner, Jens Flensted Lassen, Evald Høj Christiansen, Lars R Krusell, Steen D Kristensen, Leif Thuesen, Søren S Nielsen, Michael Rehling, Henrik Toft Sørensen, Andrew N Redington, Torsten T Nielsen

333 patiens with first STEMI. RIC (4 cycles arm cuff inflation) or regular PCI



RIC and thrombolysis

Letters

J Am Coll Cardiol. 2015;65:2764-70

JACC JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Remote Ischemic Conditioning Reduces Myocardial Infarct Size in STEMI Patients Treated by Thrombolysis

CrossMark

N=519

No access to PCI at all

TABLE 1 Patient Characteristics and AUC Cardiac Enzymes

	Control (n = 258)	RIC (n = 261)	p Value
Enzymatic MI size, ng.h/ml			
24-h AUC CK-MB	2,894 ± 2,306	2,378 ± 2,089	
	2,381 (980-4,690)	1,928 (780-3,289)	0.026
24-h AUC Troponin T	105.9 ± 69.5	90.0 ± 67.6	
	109.0 (41.1-162.7)	74.6 (28.5-149.0)	0.020

RIC large trial

CONDI-2 trial, Denmark, Spain, Serbia.

-2,000 STEMI patients
-conventional PCI vs. RIC+PCI
-Combined end-point:
all-cause mortality /heart failure @ 2 years

ONGOING TRIAL

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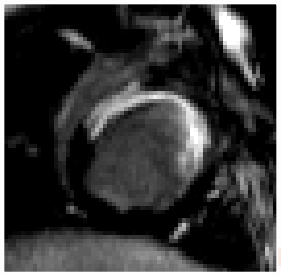
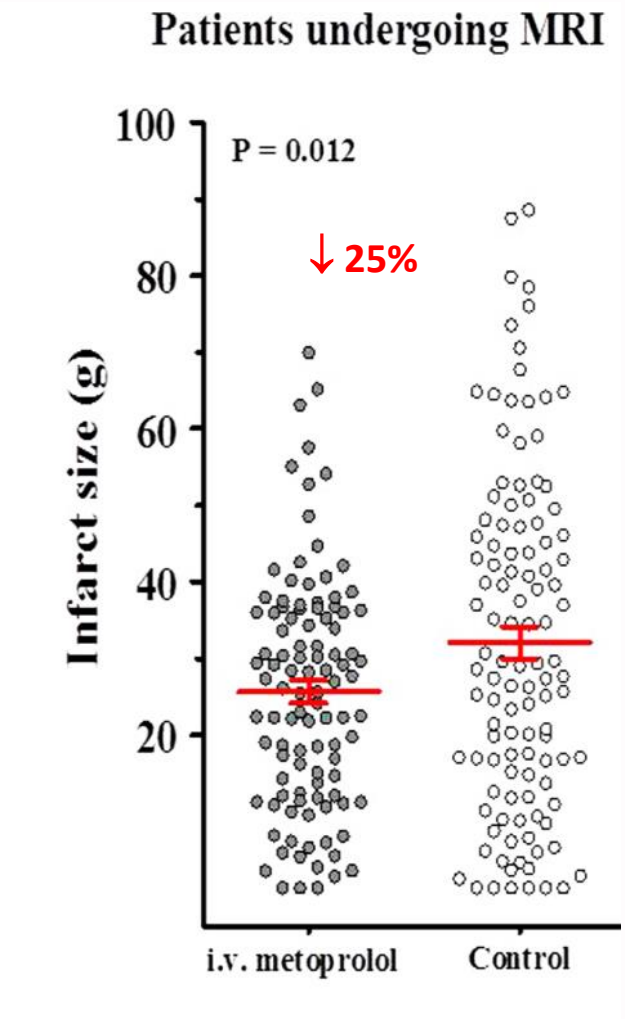
EARLY METOPROLOL

i.v. metoprolol before pPCI → ↓↓↓ infarct size

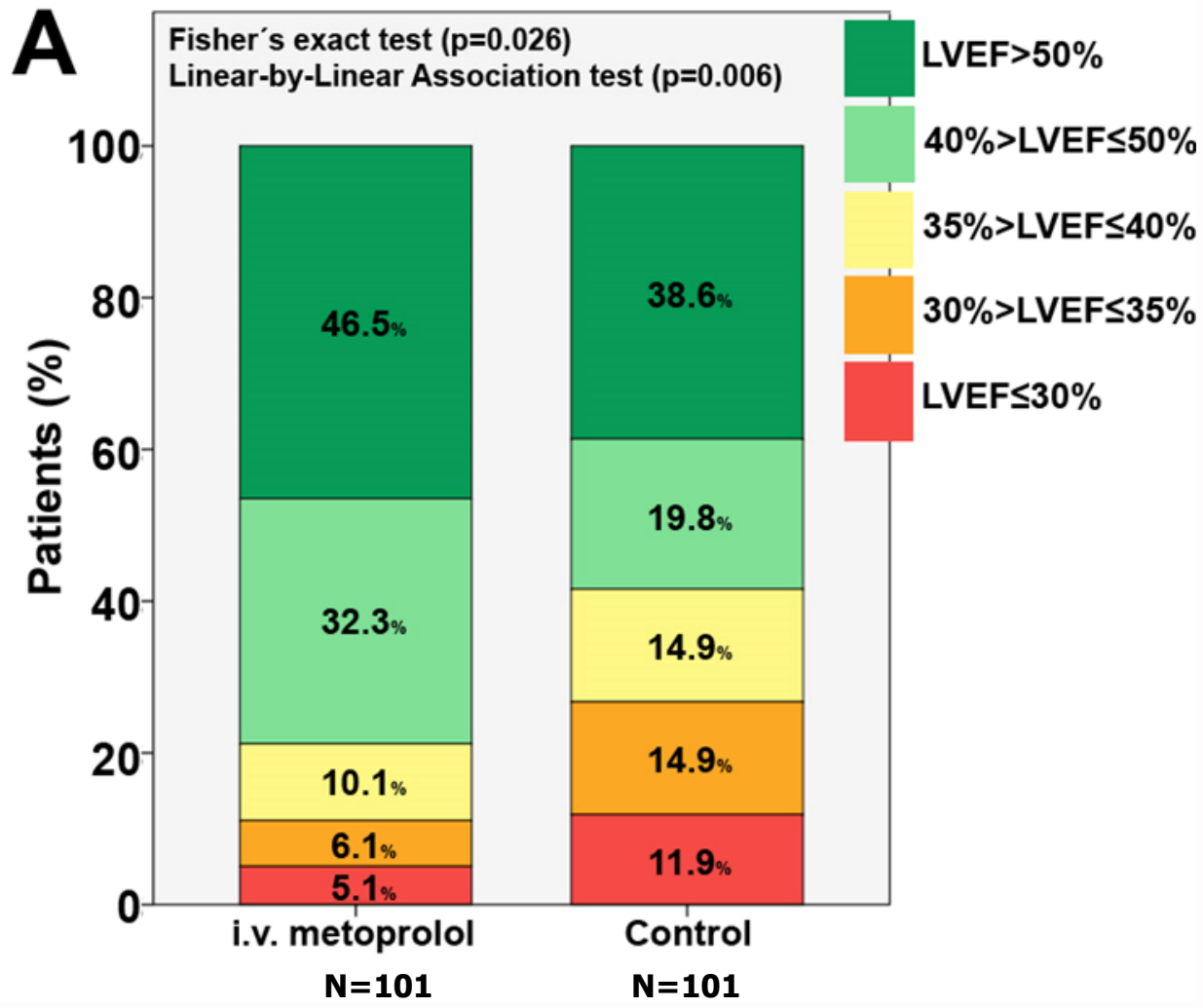




Ibanez B, Fuster V et al. ***Circulation*** 2013;128:1495-1503

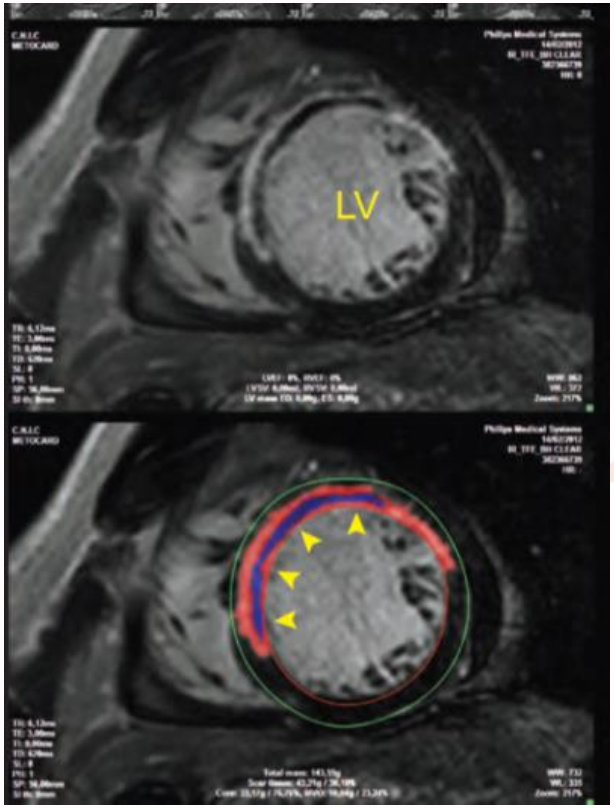
EARLY METOPROLOL

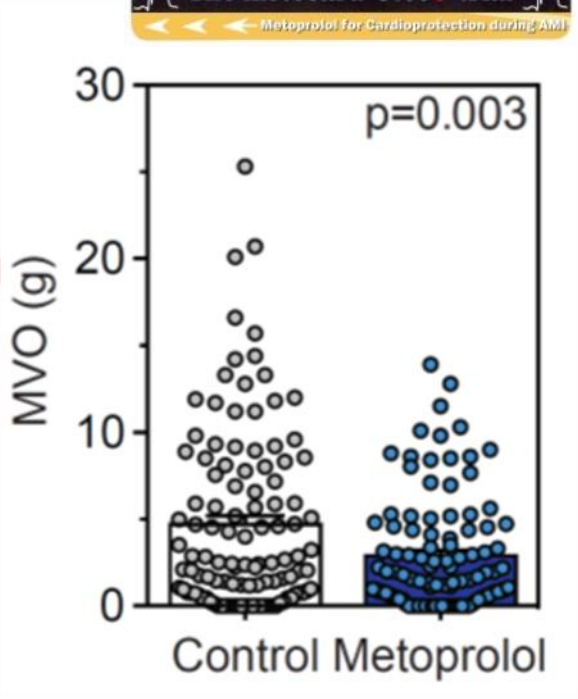
Mean LVEF (6 mo CMR):
48.7±9% vs. 45.0±11%



G Pizarro, V Fuster, B Ibanez et al.
J Am Coll Cardiol 2014; 63: 2356-62.

EARLY METOPROLOL





Metoprolol reduces Microvascular Obstruction in STEMI patients.

García-Prieto J, Fuster V, Ibanez B et al ***Nature Commun*** 2017

Cellular mechanism

nature COMMUNICATIONS

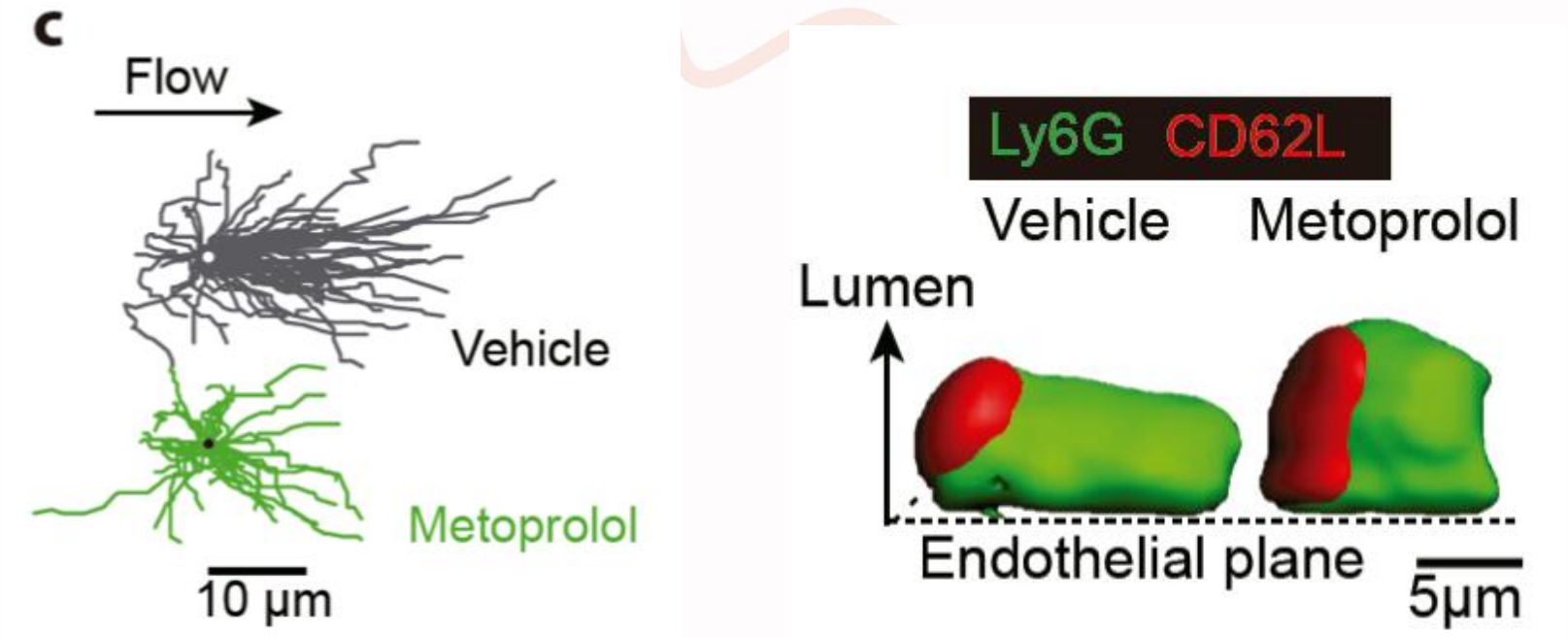
ARTICLE

Received 22 Mar 2016 | Accepted 30 Jan 2017 | Published 18 Apr 2017

DOI: 10.1038/ncomms14780 OPEN

Neutrophil stunning by metoprolol reduces infarct size

García-Prieto et al
Nature Commun 2017



Metoprolol stuns neutrophils to protect the heart

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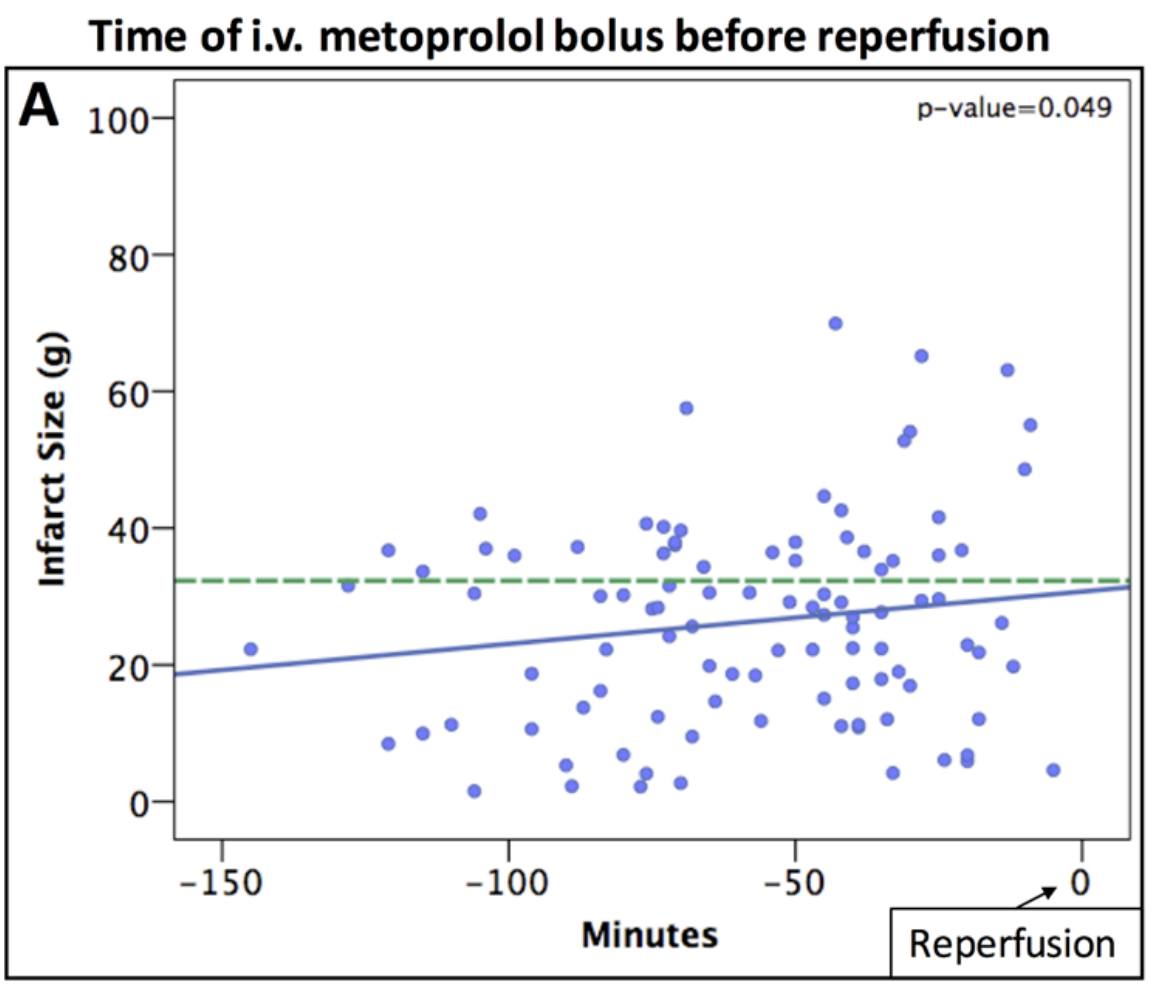
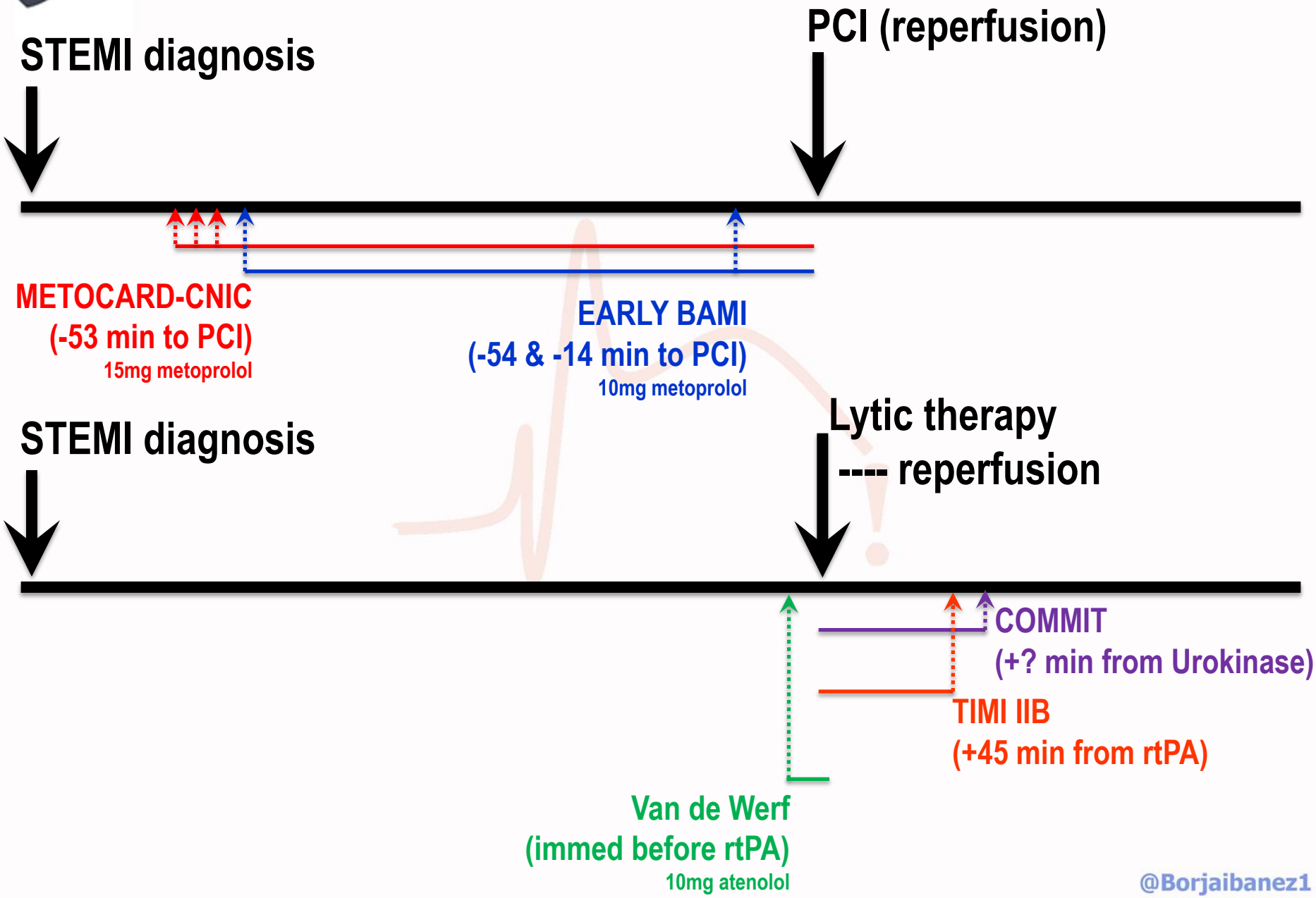
Timing of metoprolol admin



The longer the "on board" metoprolol duration at reperfusion, the higher the cardioprotection

Garcia-Ruiz et al ***J Am Coll Cardiol*** 2016;67:2093-104

Window β-blk admin in trials



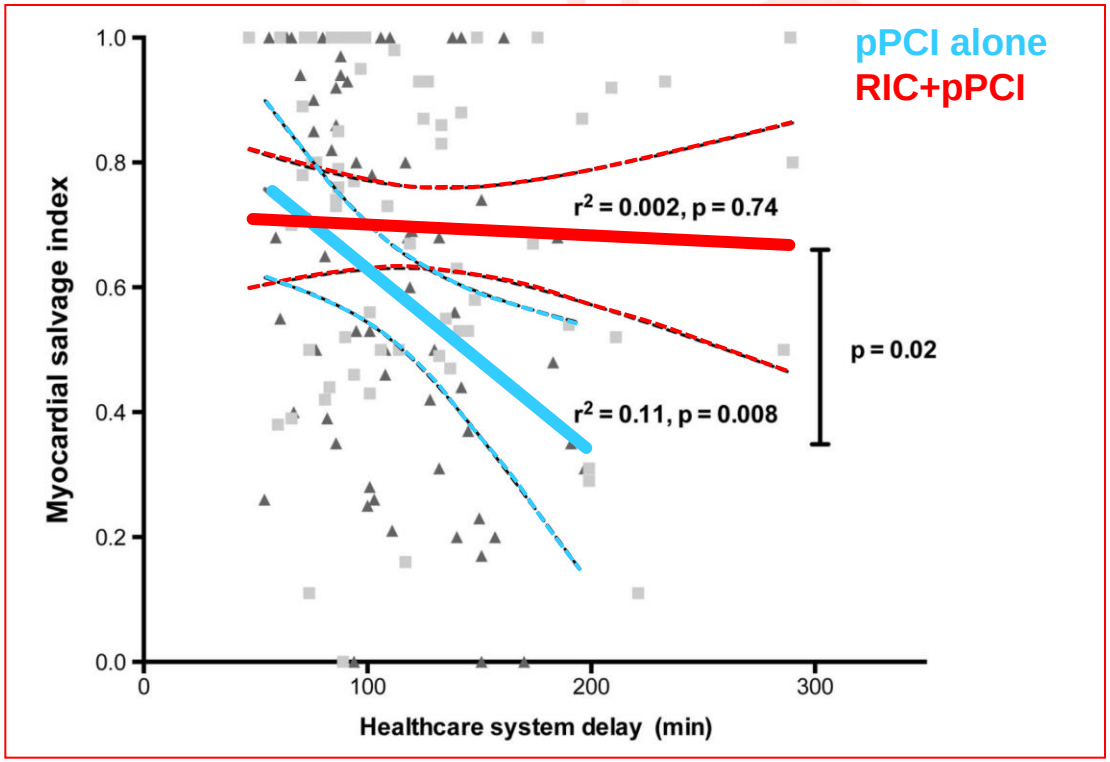
Timing of RIC initiation

ORIGINAL ARTICLE

Remote ischaemic conditioning and healthcare system delay in patients with ST-segment elevation myocardial infarction

Kasper Pryds,[1,2] Christian Juhl Terkelsen,[1] Astrid Drivsholm Sloth,[1,2] Kim Munk,[1] Søren Steen Nielsen,[3] Michael Rahbek Schmidt,[1] Hans Erik Bøtker,[1] CONDI Investigators

Heart. 2016 *Feb 24. pii: heartjnl-2015-308980.*

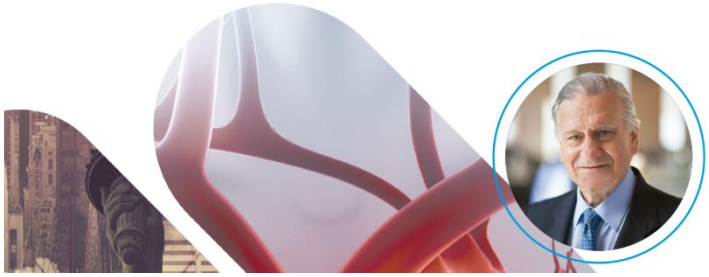


Conclusions

1) Timely reperfusion widespread use has resulted in a massive reduction of acute mortality during STEMI.
2) The next goal is to reduce infarct size to reduce chronic post-MI HF
3) Reperfusion injury reduction is a relevant target. Preserve microvascular integrity!
4) Metoprolol and remote ischemic conditioning are promising therapies
5) Timing of administration of therapies to reduce infarct size seem to play a critical role in its ability to protect from ischemia/reperfusion.

STEMI 1: Timing, Mechanical Type and Pharmacology of Reperfusion: The Three Main Challenges to Decrease Infarct Size and Increase Viability

New York Cardiovascular Symposium



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