



SABATO 9 OTTOBRE

Angioplastica primaria tardiva (oltre le 12 ore): siamo certi vada evitata?

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Rationale for the 12-hour limit

- Fibrinolysis is unable to reduce mortality in late-presenting STEMI patients (LATE and EMERAS Studies 1993)
- Animal models showed loss of all jeopardized myocardium before 12 hours of coronary occlusion (Reimer 1977)

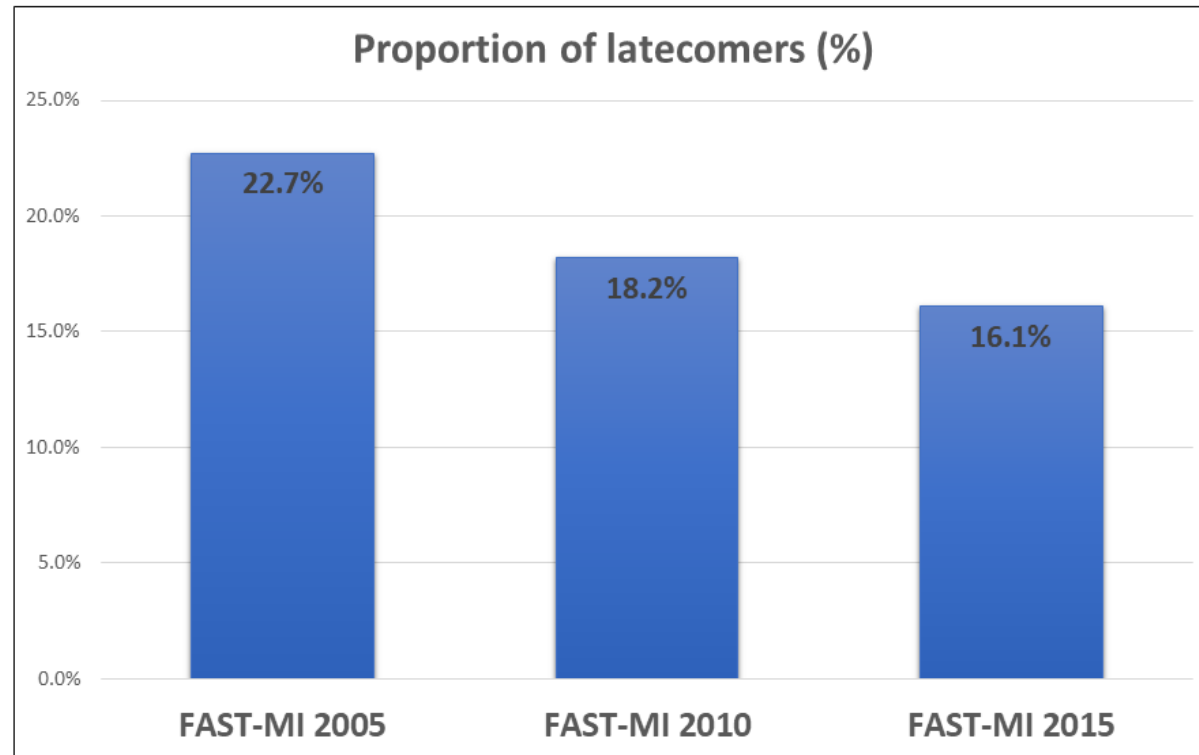


Late STEMI presenters: a challenging population

- Heterogeneous population
- It is becoming increasingly rare
- Different demographic and clinical characteristics as compared to early presenters
- Less likely to undergo primary PCI
- Remarkably worse clinical outcomes
- Paucity of data indicating a strong correlation between S2DT and clinical outcomes
- The “survivor cohort effect”

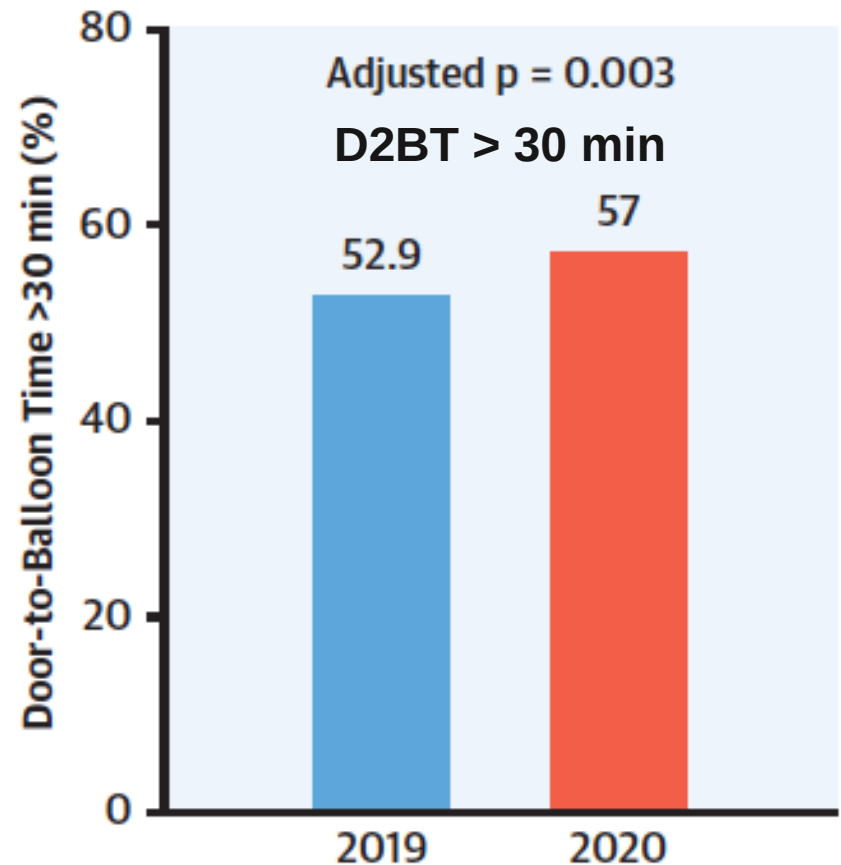
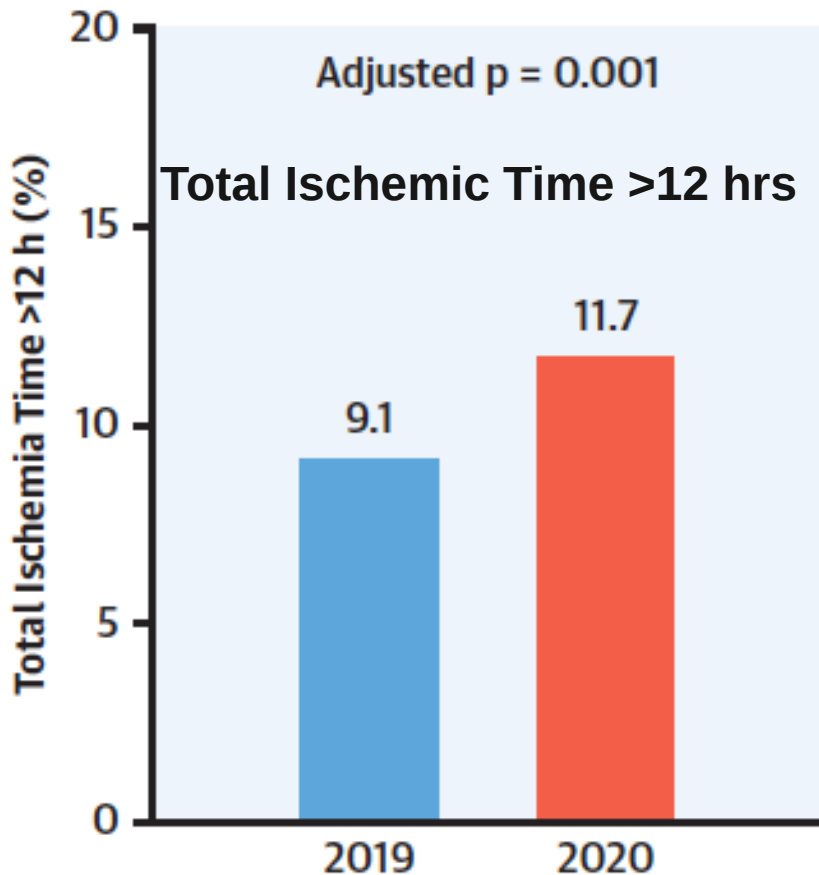


Proportion of latecomers according to the year of inclusion in the FAST-MI program



Bouisset, F. et al. J Am Coll Cardiol. 2021;78:1291–1305

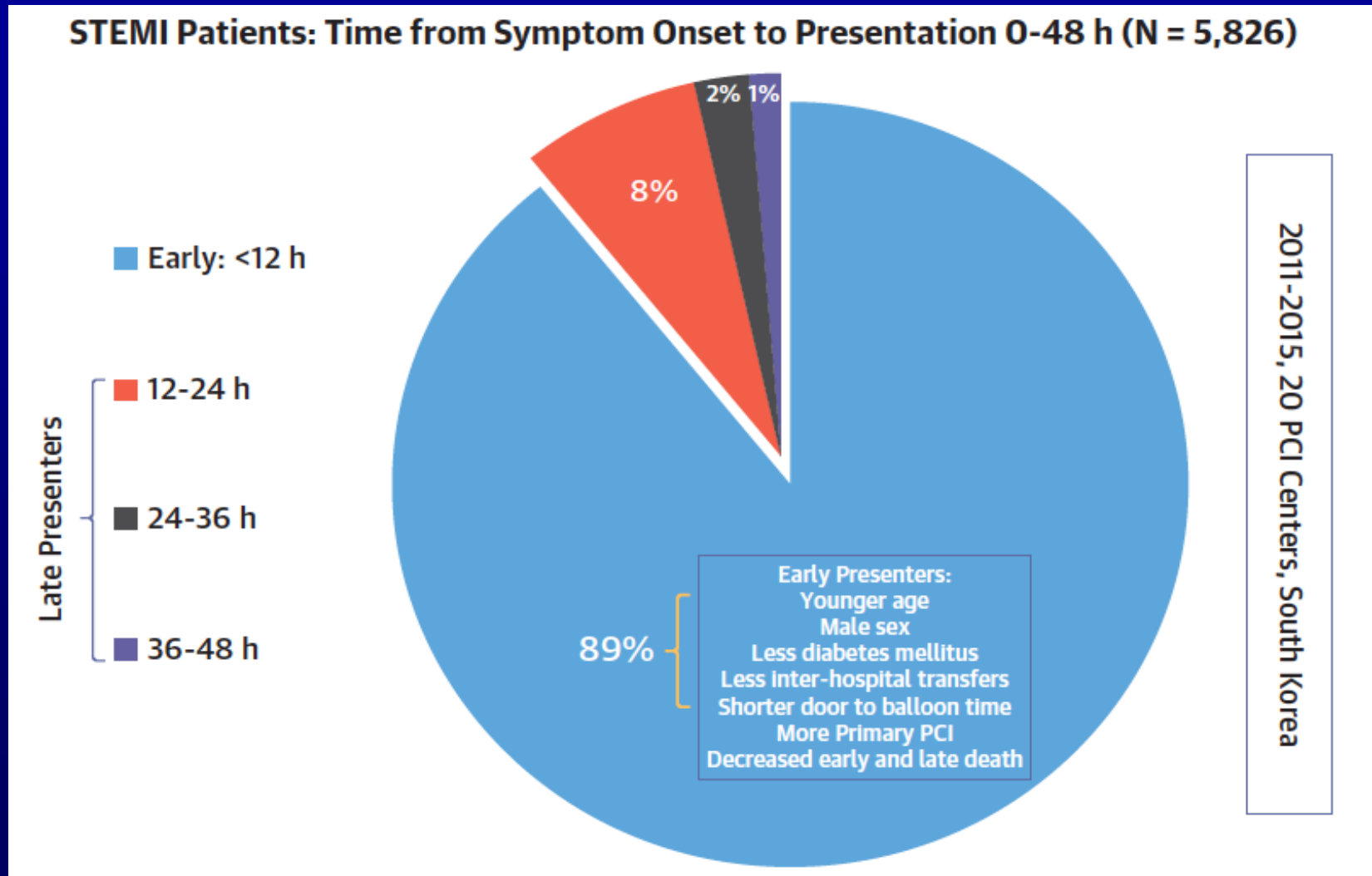
Impact of COVID-19 Pandemic on Mechanical Reperfusion for Patients With STEMI



De Luca, G. et al. J Am Coll Cardiol. 2020;76:2321–30

Incidence and Characteristics of Patients Presenting Early and Late With STEMI

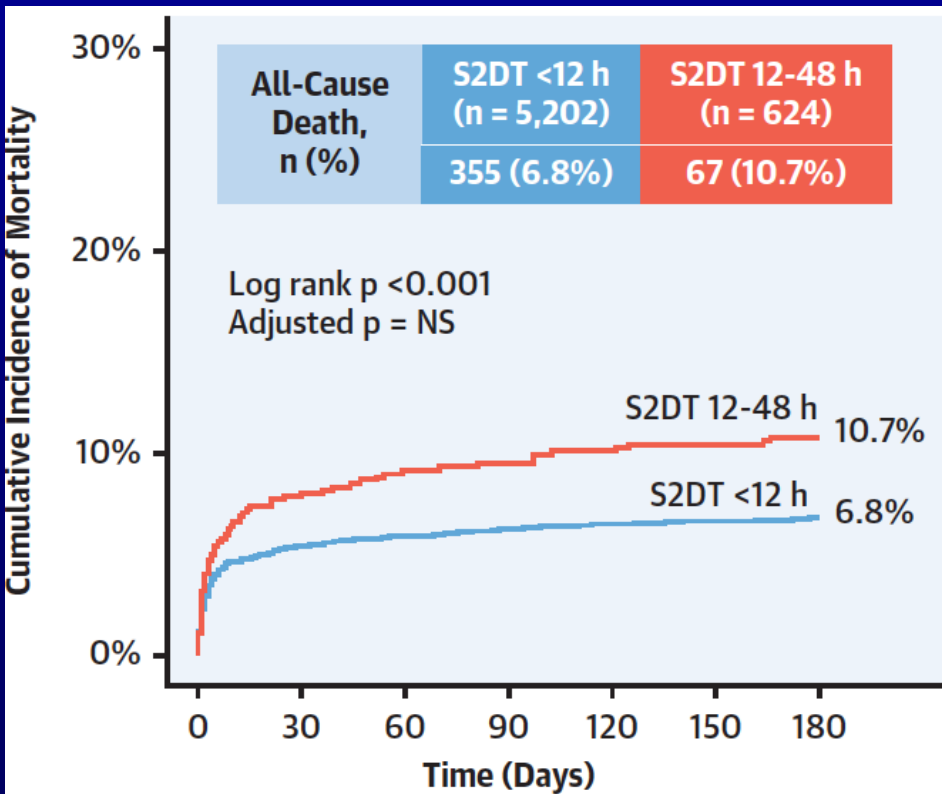
The Korea Acute Myocardial Infarction Registry



Incidence and Characteristics of Patients Presenting Early and Late With STEMI

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Mortality over 180 days



Adjusted Prognostic Values of Variables for 180-Day Mortality

	Hazard Ratio (95% CI)	p Value
Age, years	1.04 (1.03 - 1.05)	<0.001
LVEF, %	0.96 (0.95 - 0.97)	<0.001
Killip IV	4.45 (3.29 - 6.01)	<0.001
Killip III	2.45 (1.78 - 3.38)	<0.001
Killip II	1.43 (0.99 - 2.08)	0.059
SBP <100	1.92 (1.47 - 2.52)	<0.001
eGFR <60	1.89 (1.53 - 2.34)	<0.001
No PPCI strategy	1.82 (1.37 - 2.43)	<0.001
Heart rate >100	1.74 (1.37 - 2.19)	<0.001
Anemia	1.71 (1.39 - 2.12)	<0.001
Ant. STE or LBBB	1.25 (1.03 - 1.53)	0.027
S2DT ≥12 h	1.14 (0.87 - 1.48)	0.354

Hazard Ratio for 180-Day Mortality



PPCI >12 Hours in Patients With STEMI

- Potential Benefits of Late Reperfusion of Infarcted Myocardium
- Myocardial salvage from PCI in late presenting STEMI
- Evidence on the PCI strategy for late STEMI



The “Late” open artery hypothesis

Reperfusion of an occluded IRA at a time too late for myocardial salvage

- Prevention of ventricular remodeling
- Prevention of the late development of arrhythmias
- Prevention of interstitial collagen turnover
- Prevention of apoptosis among cardiomyocytes



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Infarct size and myocardial salvage after PPCI in pts presenting with symptoms for <12 h vs. 12–72 h

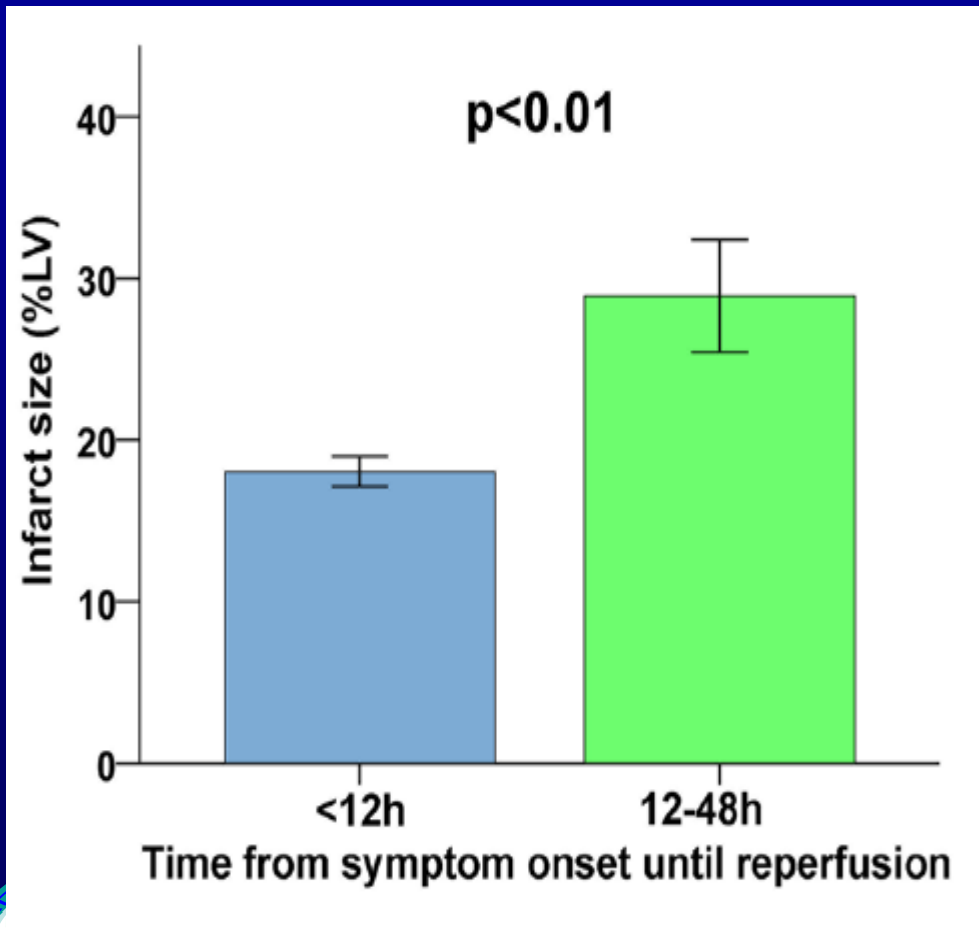
	Infarct-related artery patent				
	<12 h (n = 125)	12–72 h (n = 24)	P-value	Adjusted estimate ^a	Adjusted P-value
Area at risk (%)	23 (13–31)	26 (19–35)	0.047	5.3 (–0.9 to 11.5)	0.10
Infarct size (%)	3 (0–8)	6 (1–23)	0.05	7.2 (3.3–11.1)	<0.001
Salvage index (%)	81 (55–100)	71 (46–95)	0.42	–6.4 (–20.0 to 7.1)	0.36
LVEF (%)	55 (49–61)	53 (45–60)	0.23	–4.1 (–8.8 to 0.6)	0.09
LV EDV (mL)	107 (87–133)	109 (80–137)	0.90	1.06 (0.93–1.21)	0.36
LV ESV (mL)	48 (34–66)	52 (32–69)	0.61	1.16 (0.93–1.44)	0.19
Peak troponin T (μg/L)	2.7 (1.1–4.9)	3.3 (1.1–4.6)	0.51	1.21 (0.73–2.00)	0.46



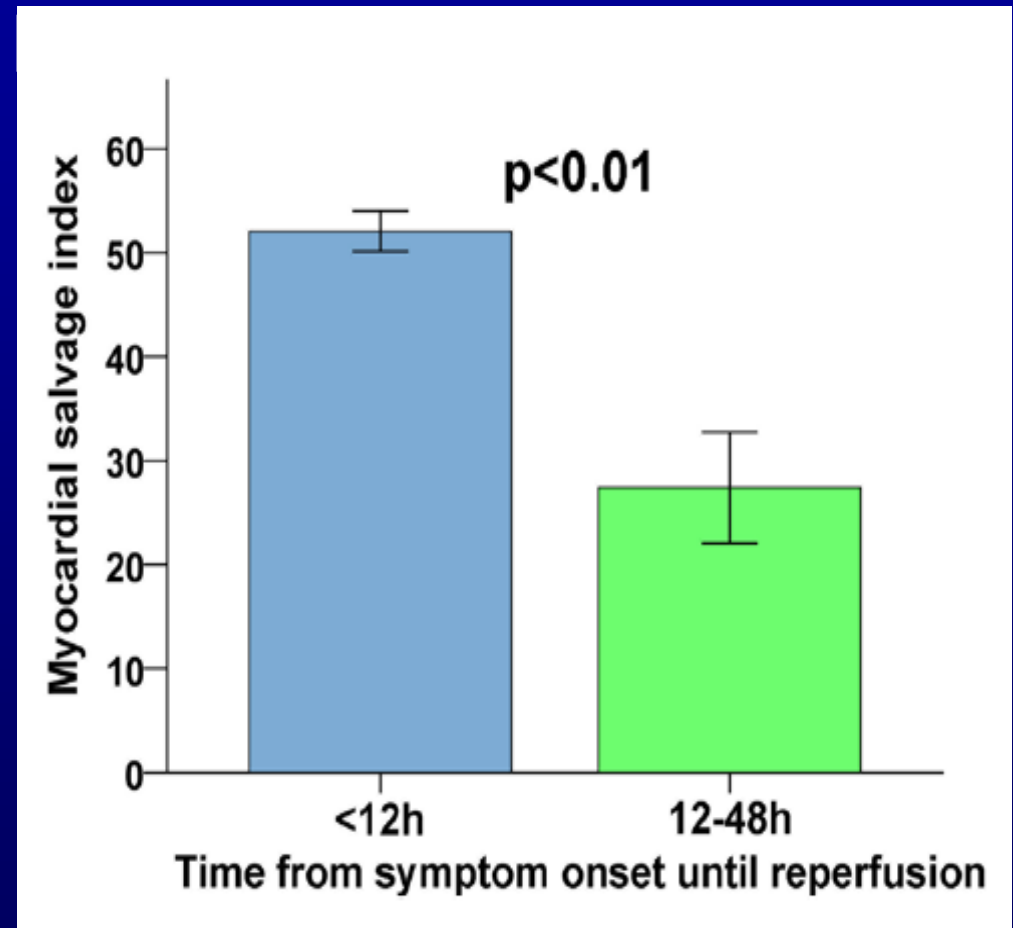
Busk M et al. Eur Heart J 2009;30:1322–30

Myocardial salvage after PPCI in pts with STEMI presenting early versus late after symptom onset

Infarct Size



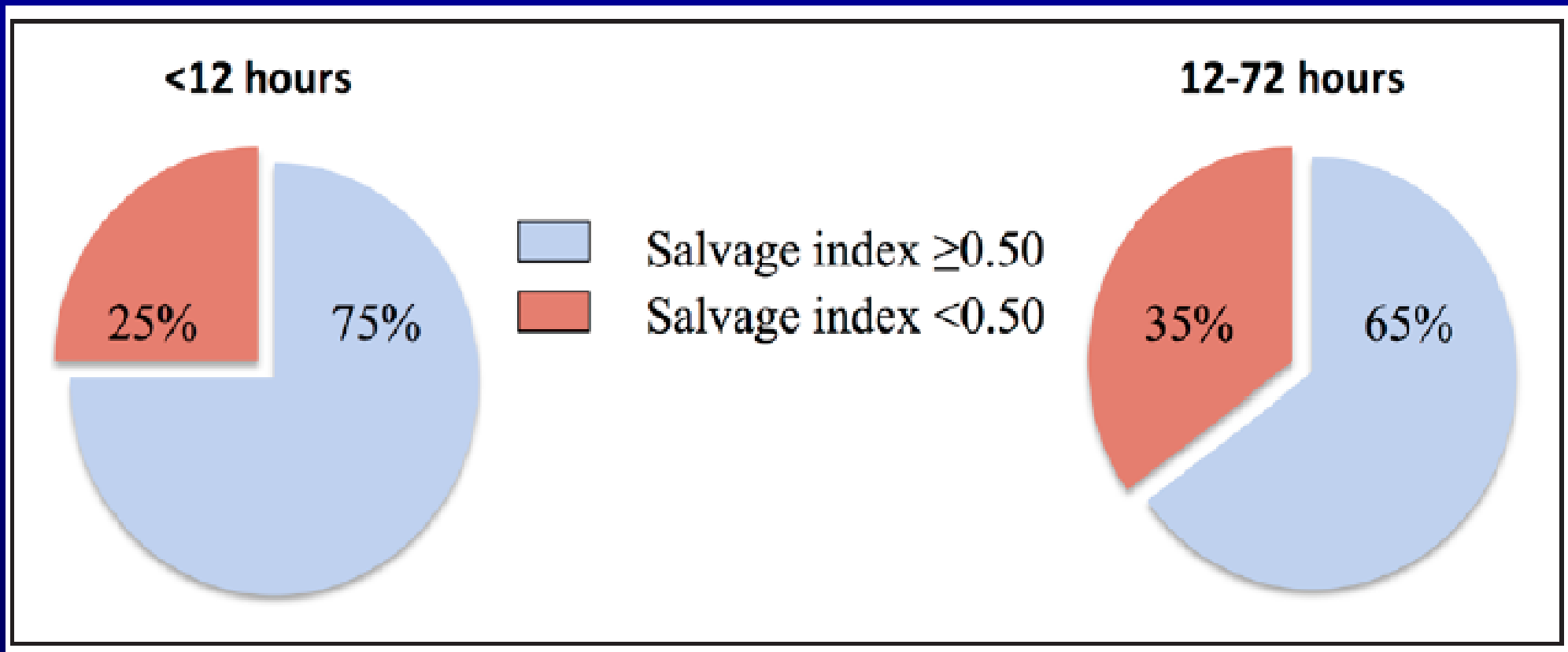
Myocardial salvage Index



Stiermaier T et al. Int J Cardiovasc Imaging 2017;33:1571–9



Benefit From PPCI >12 Hours in Patients With STEMI



Nepper-Christensen L et al. *Circ Cardiovasc Interv* 2018;11: e006842

Myocardial salvage from PCI in late presenting STEMI

While myocardial salvage is less with late presenters than early presenters, substantial myocardial salvage may be observed when PCI is performed at the 12 to 48-h outer edge of time limits for STEMI PCI



Myocardial salvage from PCI in late presenting STEMI: Potential Mechanisms

- Incomplete coronary occlusion with preservation of a minimal blood flow
- Collateral circulation
- Dynamic coronary occlusion and reperfusion with consequent ischemic pre-conditioning and a resulting delay of progression to irreversible myocardial injury



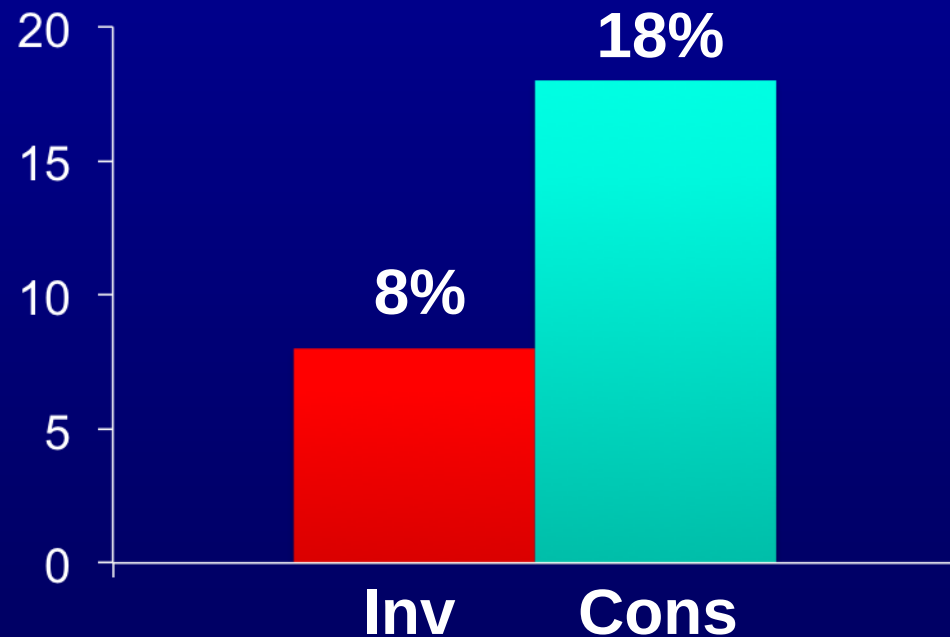
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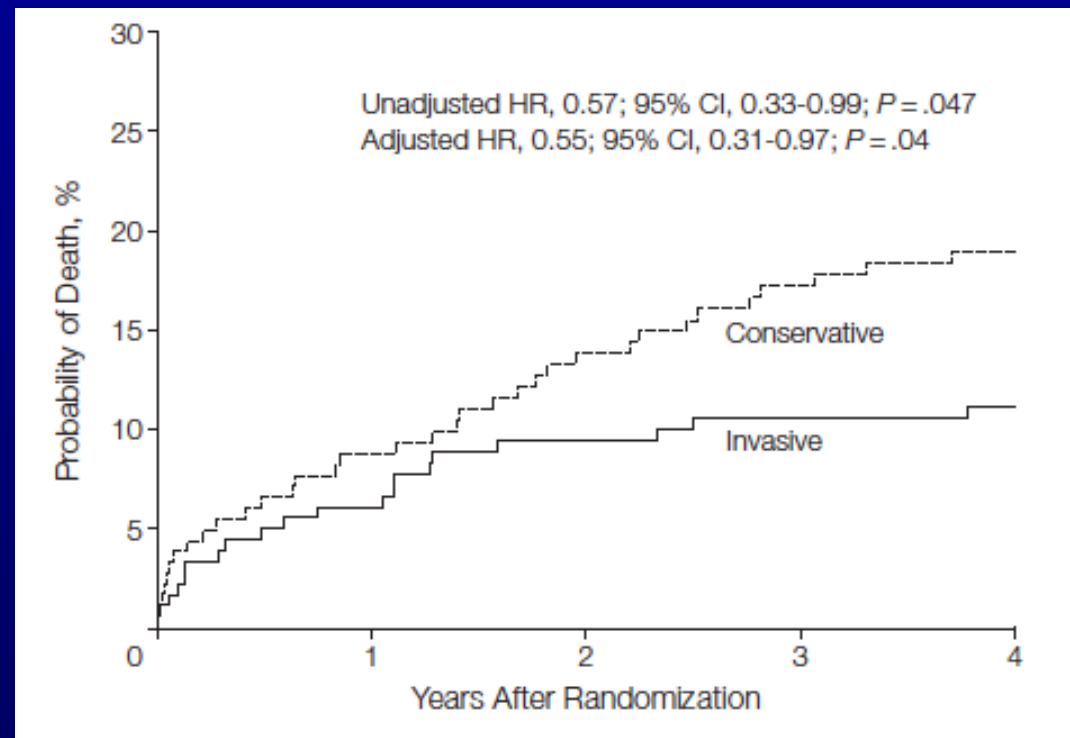


Mechanical Reperfusion in Pts With AMI Presenting >12 Hours From Symptom Onset: The BRAVE 2 Trial

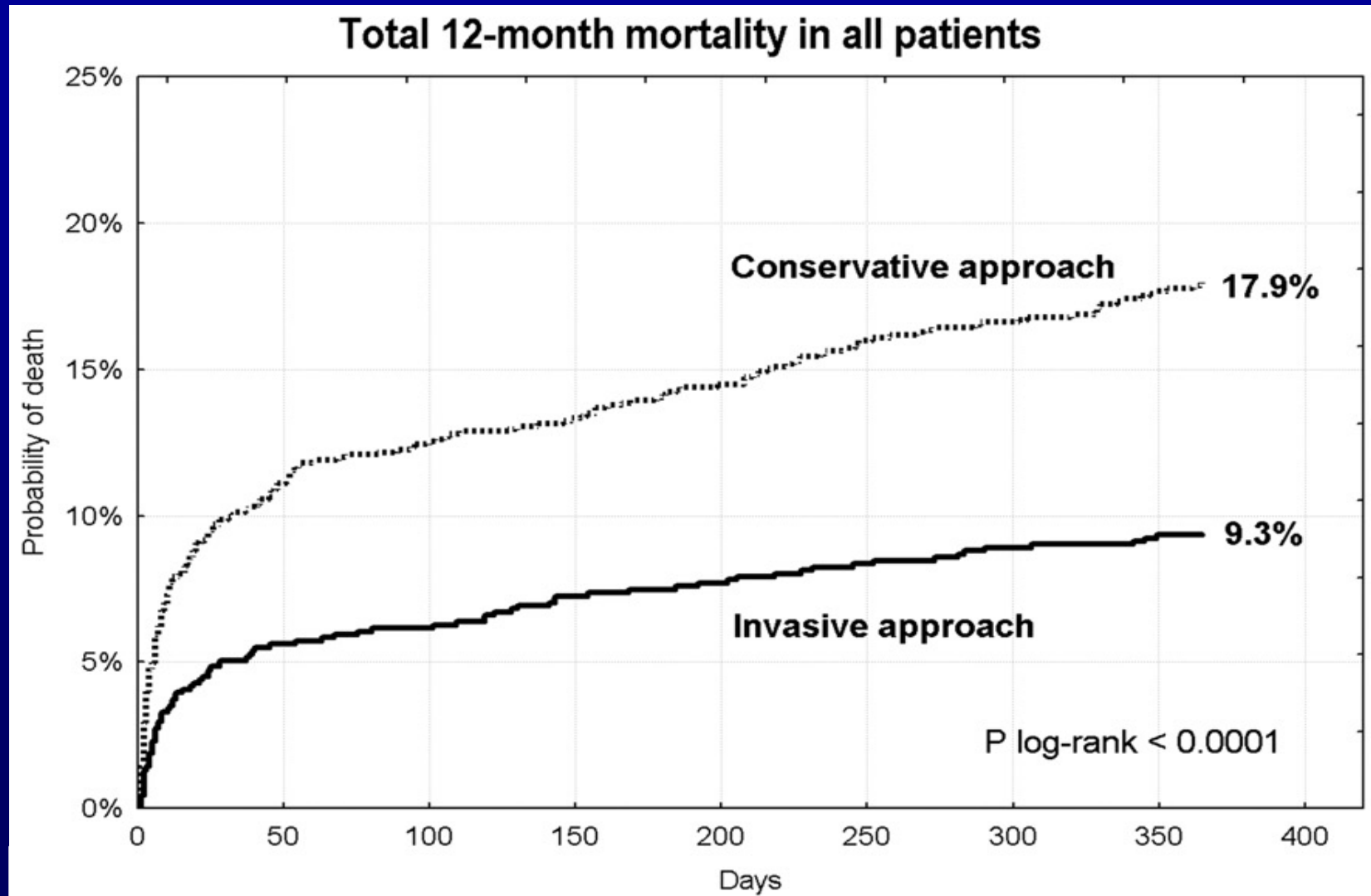
Final LV infarct size



4-year Mortality



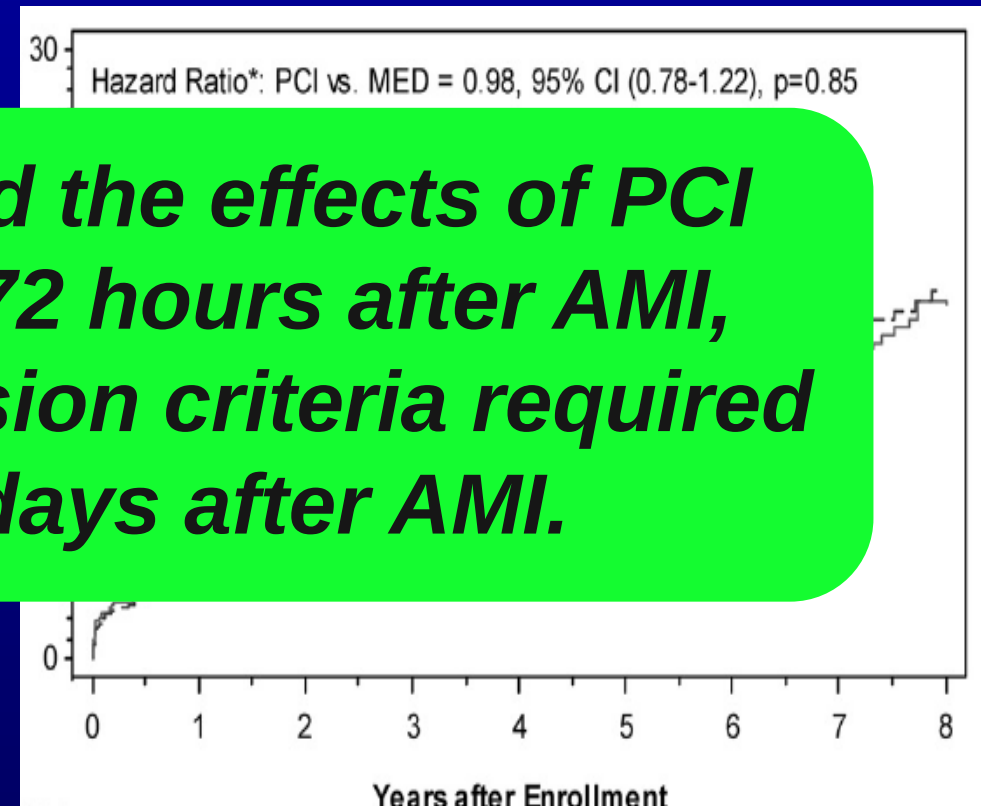
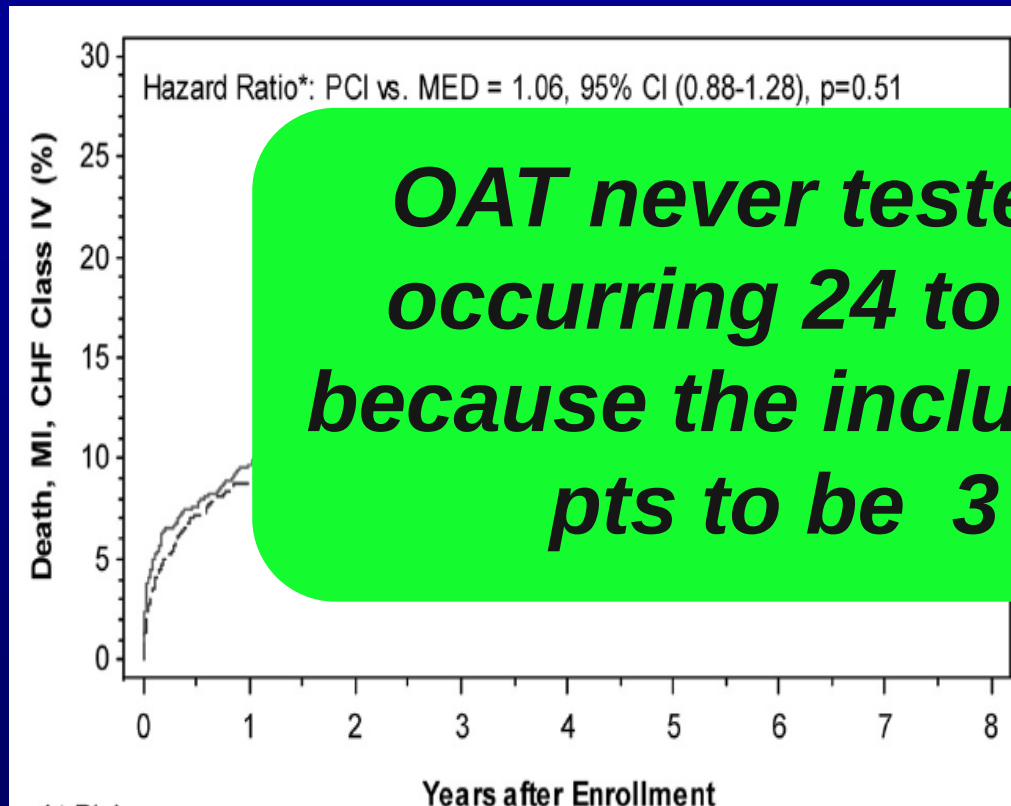
Reperfusion by PPCI in pts With STEMI Within 12 to 24 Hours of the Onset of Symptoms



The Occluded Artery Trial: 4-year follow-up

Death, MI, CHF

Death



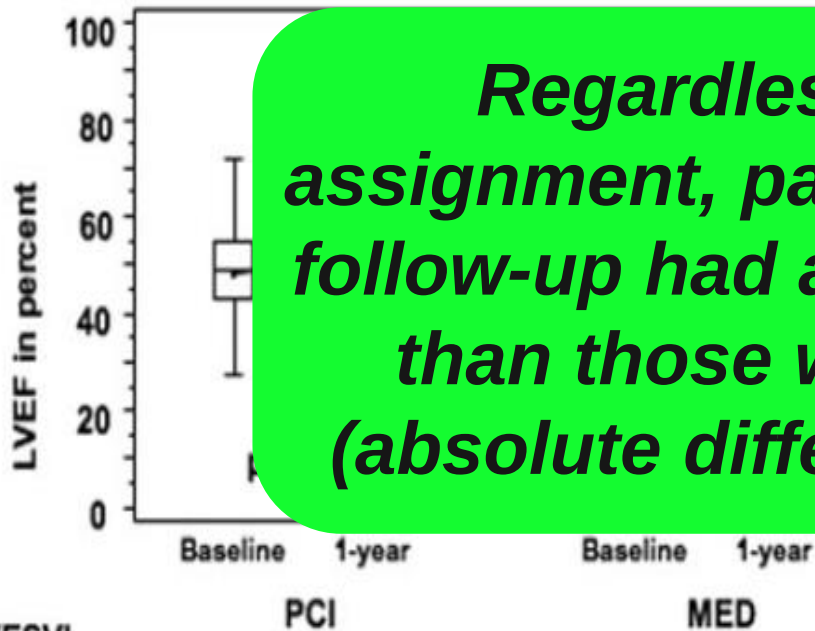
OAT never tested the effects of PCI occurring 24 to 72 hours after AMI, because the inclusion criteria required pts to be 3 days after AMI.



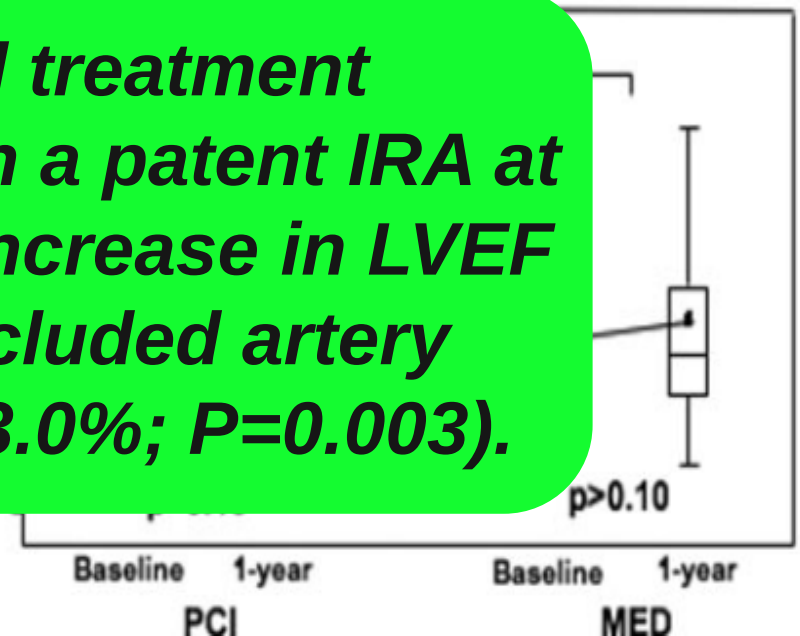
Hochman JS et al Circulation. 2011;124:2320-2328

The Total Occlusion Study of Canada (TOSCA)-2 Trial

A LVEF - primary endpoint



B LVESVI PCI MED



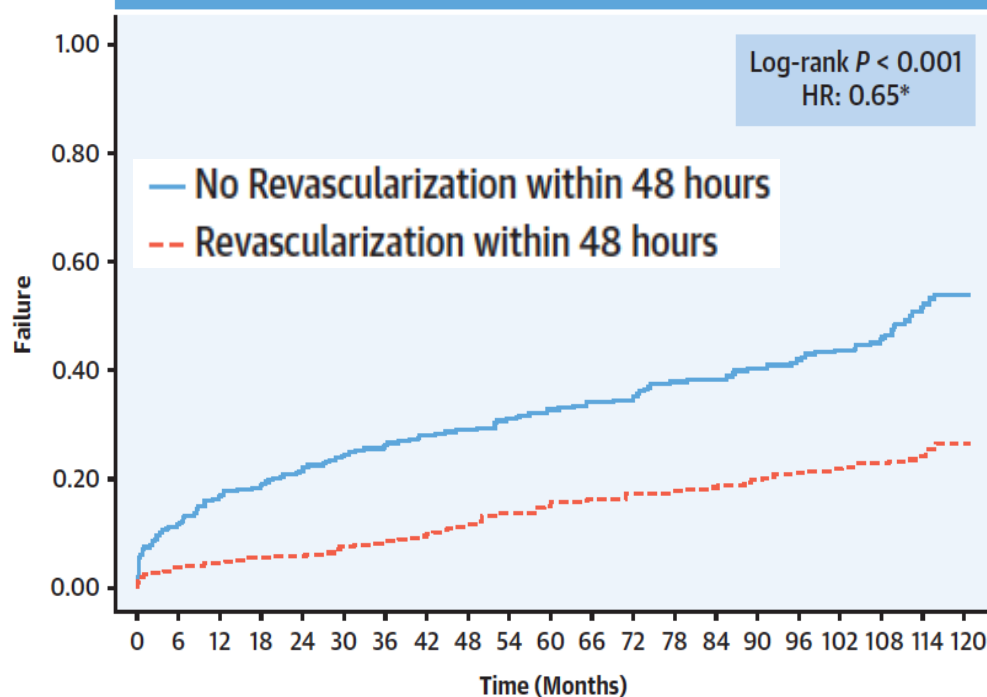
Regardless of initial treatment assignment, patients with a patent IRA at follow-up had a greater increase in LVEF than those with an occluded artery (absolute difference of 3.0%; $P=0.003$).



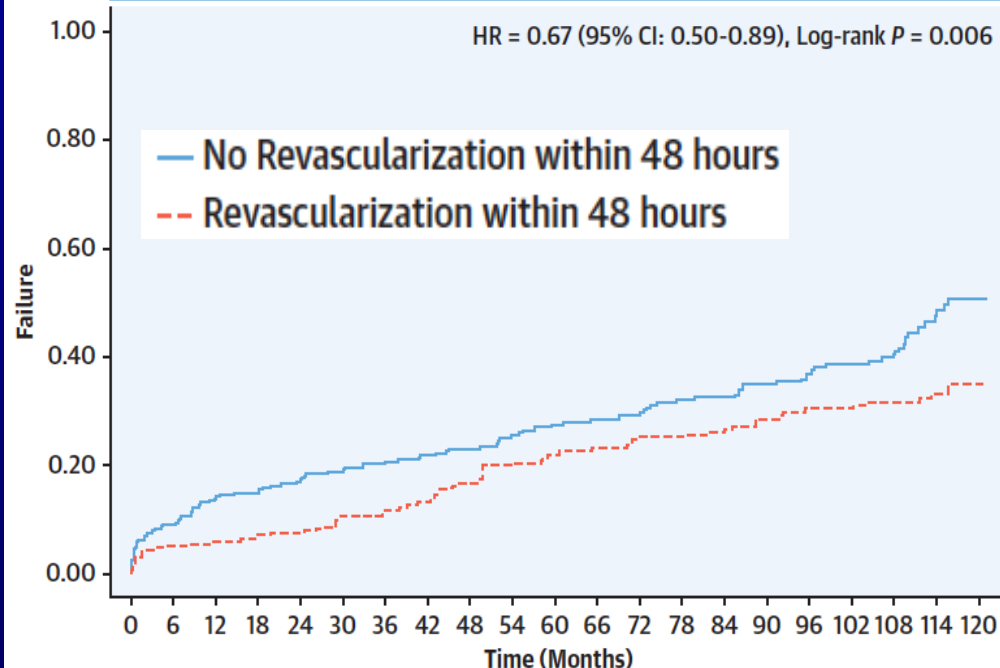
PPCI in Late-Presenting Patients With STEMI

The FAST-AMI Registry

Long-Term All-Cause Mortality



All-Cause Mortality
Propensity Matched Analysis (n = 534)



Bouisset, F. et al. *J Am Coll Cardiol.* 2021;78:1291–1305

2017 ESC GL for the management of pts presenting with STEMI

Recommendations for reperfusion therapy

Recommendation	Class ^a	Level ^b
In patients with time from symptom onset >12 h, a primary PCI strategy is indicated in the presence of ongoing symptoms suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias. ¹⁴¹	I	C
A routine primary PCI strategy should be considered in patients presenting late (12–48 h) after symptom onset. ^{133,134,142}	IIa	B
In asymptomatic patients, routine PCI of an occluded IRA >48 h after onset of STEMI is not indicated. ^{135,137}	III	A

How late is too late for primary percutaneous coronary intervention in patients with STEMI?

“It is never too late to do the right thing!”



Take-home Messages

- Late STEMI presenters are a heterogeneous population, and the clinical decision regarding PCI should not be the same for all.
- Late presentation is associated with increased death
- Presence of hemodynamic or electrical instability, and ongoing ischemia tip the scales toward PCI
- Also pts who are still early in the course of STEMI (12-48 hours) should undergo PCI
- Those beyond 48 hours with evidence of silent ischemia or viability should also undergo PCI
- Pts who are truly stable and asymptomatic > 48 hours from symptom onset, with no evidence of silent ischemia or viability, can safely be treated with medical therapy

