Towards Holistic & Comprehensive Cardiac Care

Restoring Heart Health:

- Role of Percutaneous Coronary Interventions

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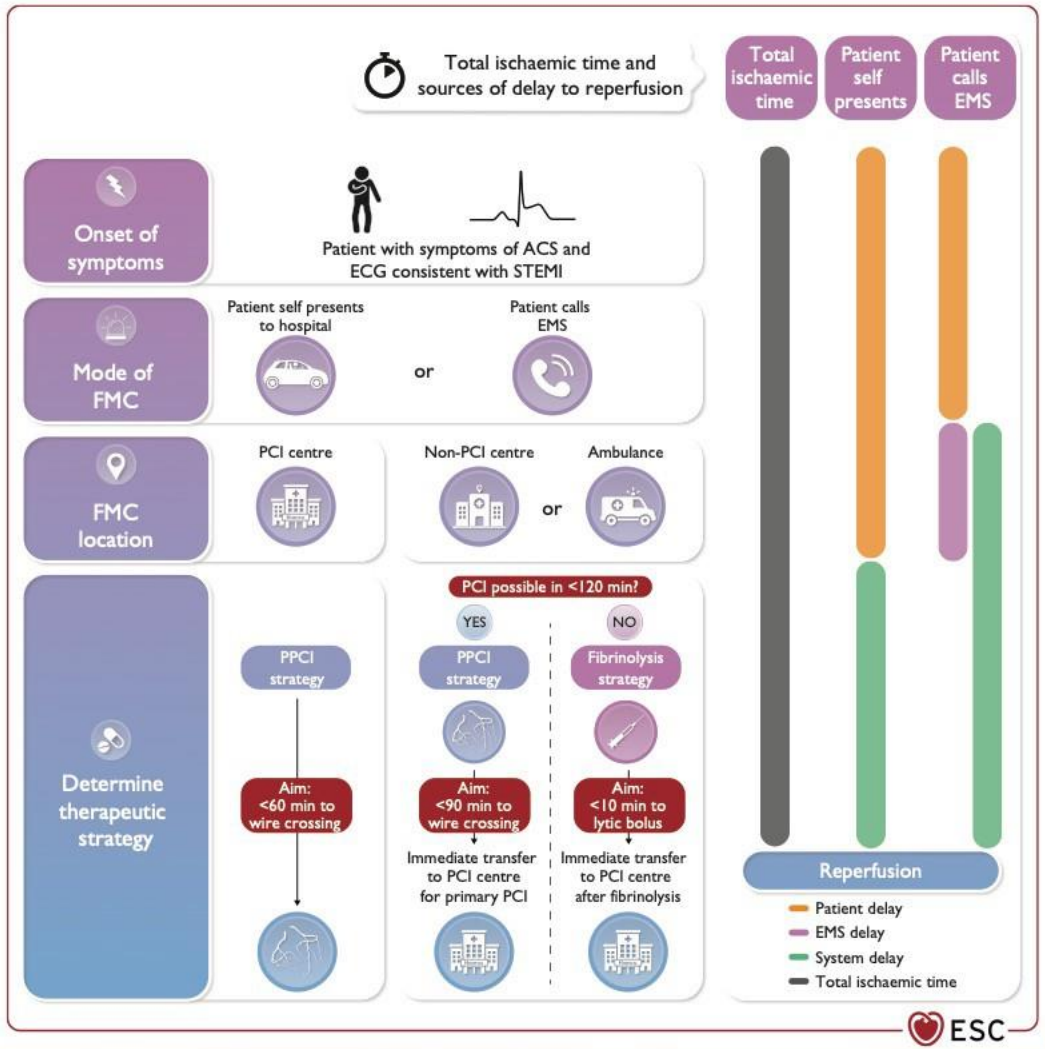
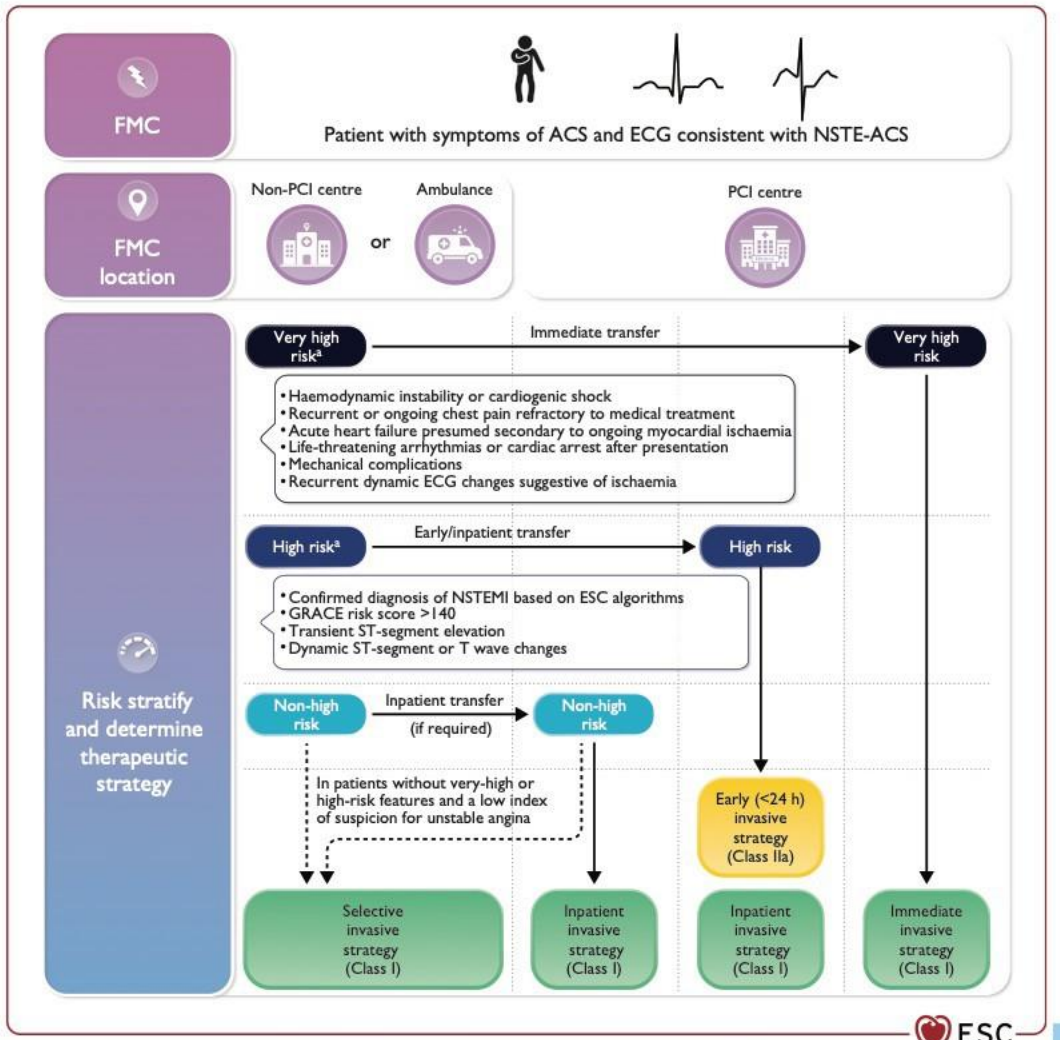
ACS required prompt revascularization

- *The higher the risk, the sooner PCI should be performed!*

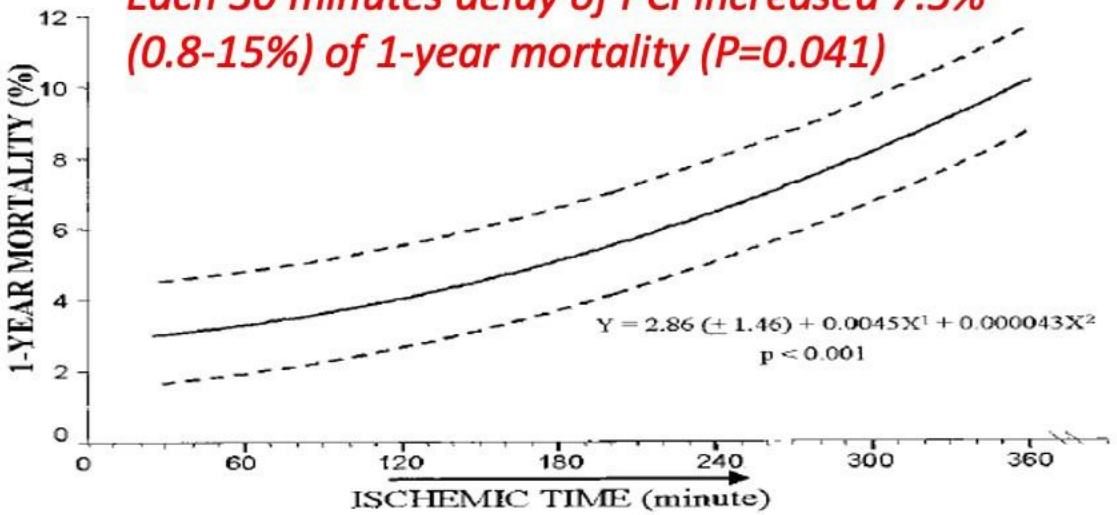




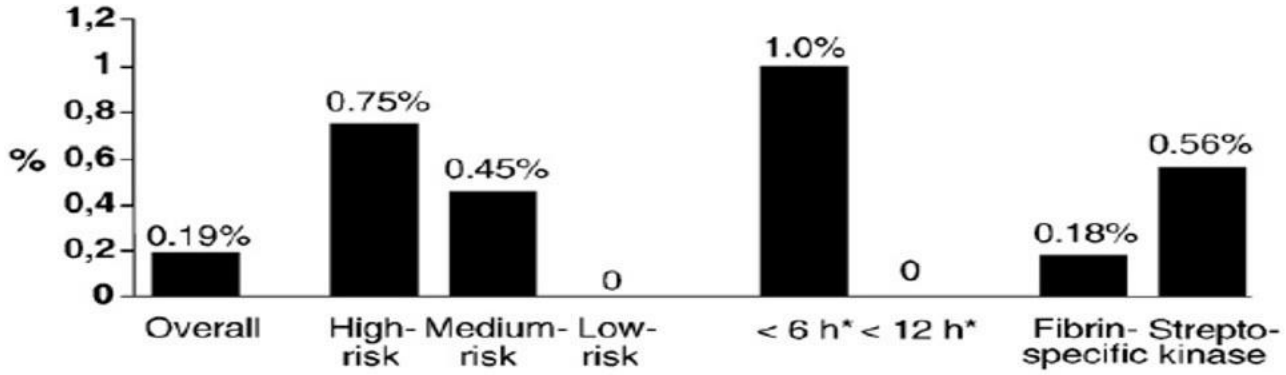
Byrne RA, et al. Eur Heart J. 2023 Oct 12;44(38):3720-3826. doi: 10.1093/eurheartj/ehad191.

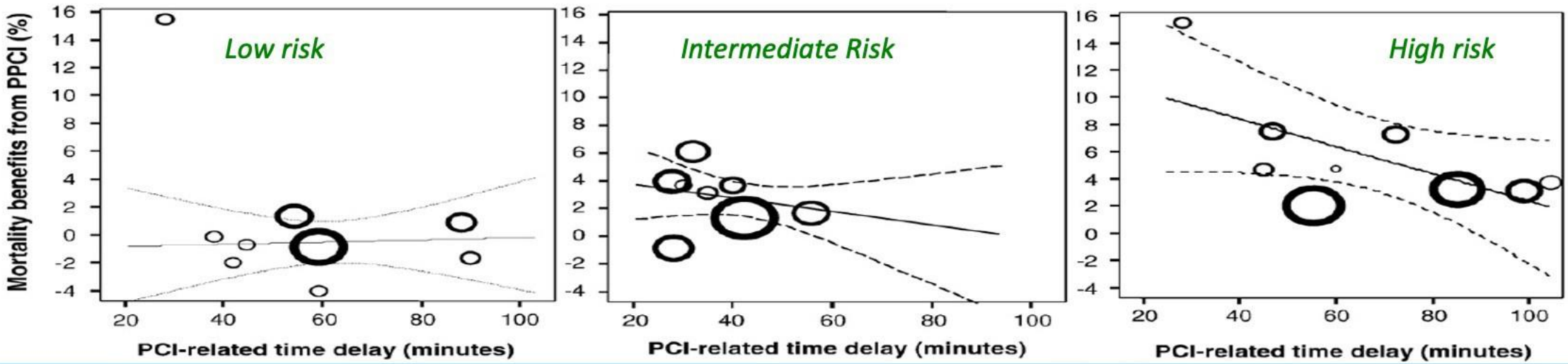
“Time is muscle!” for STEMI

Each 30 minutes delay of PCI increased 7.5% (0.8-15%) of 1-year mortality (P=0.041)



Reduction of mortality benefits with PPCI with per each 10 minutes of PCI-related time delay

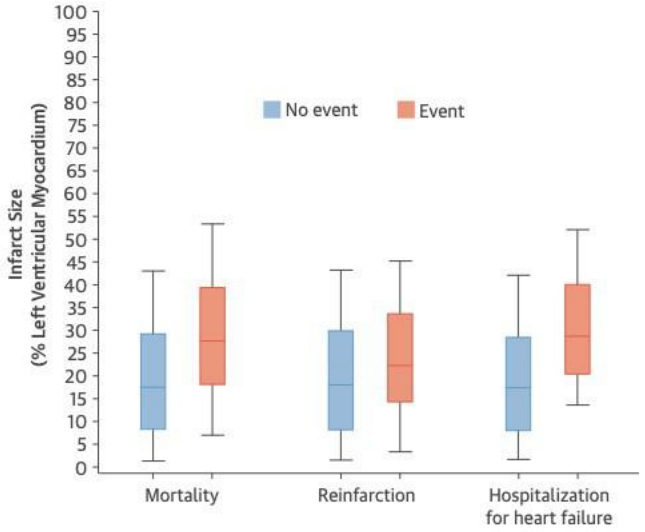


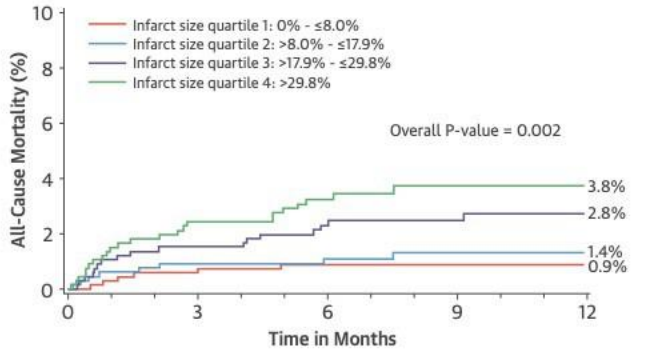


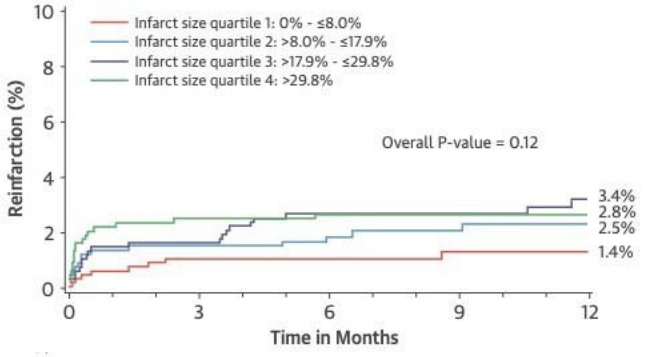
De Luca G. Circulation, 2004;109:1223-5. De Luca G. Am J Emerg Med, 2009;27:712-9.

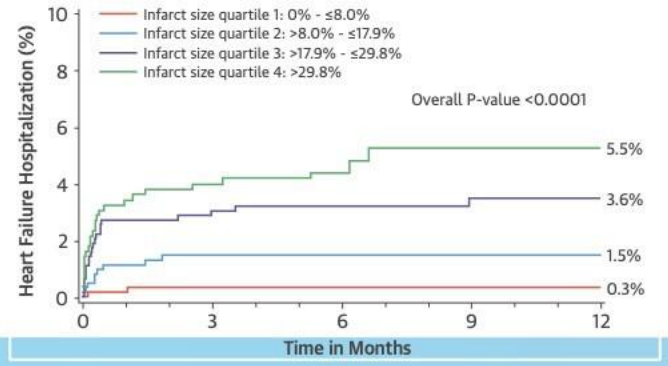
Infarct size and outcomes following primary PCI

1-Year Endpoint	C-Statistic (95% CI)
All-cause mortality (n = 2,630)	0.66 (0.58-0.73)
CMR (n = 1,887)	0.64 (0.56-0.73)
SPECT (n = 743)	0.71 (0.52-0.90)
Reinfarction (n = 2,592)	0.58 (0.51-0.65)
CMR (n = 1,886)	0.59 (0.50-0.67)
SPECT (n = 706)	0.60 (0.47-0.72)
Heart failure hospitalization (n = 2,340)	0.71 (0.65-0.77)
CMR (n = 1,884)	0.70 (0.64-0.76)
SPECT (n = 456)	0.72 (0.58-0.86)



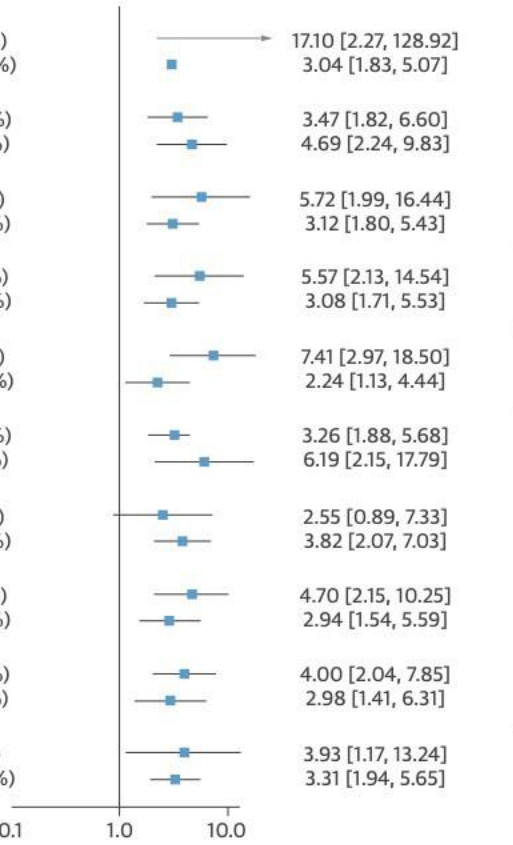






Pooled patient-level analysis from 10 RTC (n=2,632)
Infarct size assessed (1 month) by CMR or Te99m SPECT

	Infarct Size >17.9%	Infarct Size ≤17.9%	HR [95% CI]	P-Value for Interaction
	No. of Events/Total No.			
Age < vs ≥ median				0.10
<60 years	16/571 (2.8%)	1/592 (0.2%)	17.10 [2.27, 128.92]	
≥60 years	59/577 (10.2%)	20/600 (3.3%)	3.04 [1.83, 5.07]	
Gender				0.53
Male	43/911 (4.7%)	12/896 (1.3%)	3.47 [1.82, 6.60]	
Female	32/237 (13.5%)	9/296 (3.0%)	4.69 [2.24, 9.83]	
Diabetes				0.32
Yes	25/222 (11.3%)	4/195 (2.1%)	5.72 [1.99, 16.44]	
No	50/925 (5.4%)	17/994 (1.7%)	3.12 [1.80, 5.43]	
Current smoker				0.30
Yes	25/472 (5.3%)	5/508 (1.0%)	5.57 [2.13, 14.54]	
No	46/639 (7.2%)	15/653 (2.3%)	3.08 [1.71, 5.53]	
LAD vs non-LAD				0.04
LAD	58/824 (7.0%)	5/517 (1.0%)	7.41 [2.97, 18.50]	
Non-LAD	17/323 (5.3%)	16/669 (2.4%)	2.24 [1.13, 4.44]	
Hypertension				0.30
Yes	50/578 (8.7%)	17/647 (2.6%)	3.26 [1.88, 5.68]	
No	25/569 (4.4%)	4/542 (0.7%)	6.19 [2.15, 17.79]	
Hyperlipidemia				0.51
Yes	11/185 (5.9%)	5/211 (2.4%)	2.55 [0.89, 7.33]	
No	52/829 (6.3%)	13/796 (1.6%)	3.82 [2.07, 7.03]	
Symptom onset to first device < vs ≥ median				0.37
<198 minutes	31/541 (5.7%)	8/655 (1.2%)	4.70 [2.15, 10.25]	
≥198 minutes	41/569 (7.2%)	12/477 (2.5%)	2.94 [1.54, 5.59]	
Baseline TIMI flow				0.58
0 or 1	56/810 (6.9%)	10/577 (1.7%)	4.00 [2.04, 7.85]	
2 or 3	18/296 (6.1%)	11/528 (2.1%)	2.98 [1.41, 6.31]	
Final TIMI flow				0.80
≤2	22/147 (15.0%)	3/81 (3.7%)	3.93 [1.17, 13.24]	
3	53/985 (5.4%)	18/1077 (1.7%)	3.31 [1.94, 5.65]	



Stone GW, et al. J Am Coll Cardiol. 2016 Apr 12;67(14):1674-83. doi: 10.1016/j.jacc.2016.01.069.

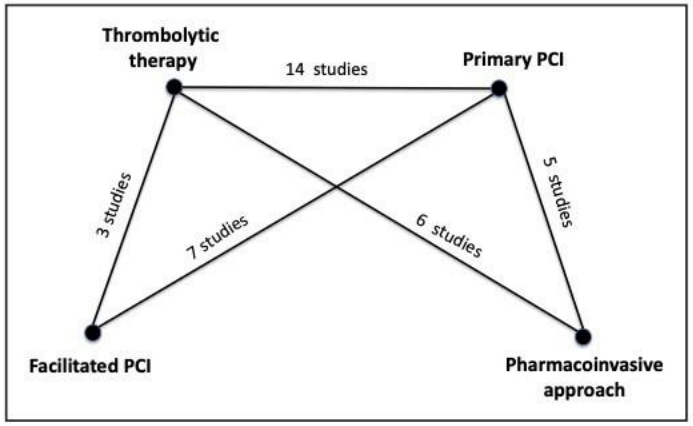
Reperfusion strategies for STEMI

Journal of the American Heart Association

SYSTEMATIC REVIEW AND META-ANALYSIS

Comparison of Reperfusion Strategies for ST-Segment–Elevation Myocardial Infarction: A Multivariate Network Meta-analysis

Reza Fazel, MD, MSc; Timothy I. Joseph, MD; Mullasari A. Sankardas, MD; Duane S. Pinto, MD, MPH; Robert W. Yeh, MD, MSc; Dharam J. Kumbhani, MD, SM; Brahmajee K. Nallamothu, MD, MPH



Outcome	Fibrinolytic Therapy	Primary PCI		Pharmacoinvasive Approach		Faciliated PCI	
		OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Death	Reference	0.73 (0.61–0.89)	0.002	0.79 (0.59–1.08)	0.14	0.90 (0.66–1.24)	0.53
Reinfarction	Reference	0.38 (0.29–0.50)	<0.001	0.53 (0.37–0.75)	<0.001	0.52 (0.36–0.76)	0.001
Stroke	Reference	0.38 (0.24–0.60)	<0.001	0.70 (0.38–1.29)	0.25	0.71 (0.33–1.53)	0.38
Major bleeding	Reference	1.03 (0.72–1.49)	0.86	1.19 (0.81–1.74)	0.36	1.51 (0.93–2.46)	0.10

CLINICAL PERSPECTIVE

What Is New?

- Combining fibrinolytic therapy with immediate transfer for percutaneous coronary intervention (PCI) has been proposed as a management strategy for ST-segment–elevation myocardial infarction at centers without PCI capability; this approach is termed facilitated PCI when fibrinolytic to PCI time interval is shorter (<2 hours) and a pharmacoinvasive approach when this interval is longer (2–24 hours).
- To date no published trials of have directly compared a pharmacoinvasive approach and facilitated PCI for treatment of ST-segment–elevation myocardial infarction.
- We performed a multivariate network meta-analysis comparing 4 main strategies for treating ST-segment–elevation myocardial infarction: fibrinolytic therapy, primary PCI, a pharmacoinvasive approach, and facilitated PCI.

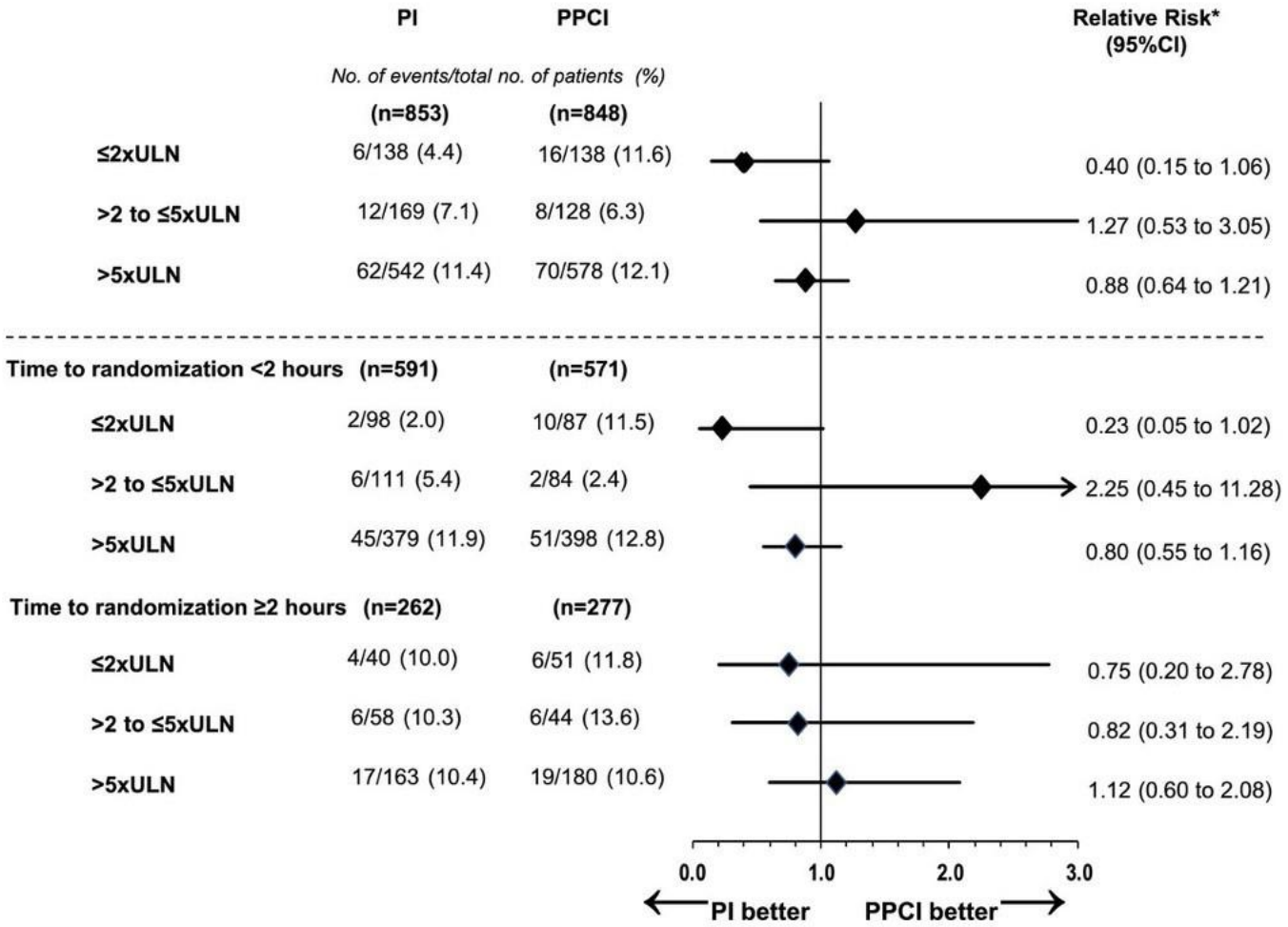
What Are the Clinical Implications?

- Primary PCI is the preferred treatment for ST-segment–elevation myocardial infarction.
- The key finding of this study is that, in settings where timely primary PCI is not available, a pharmacoinvasive approach is safer and more effective than facilitated PCI or fibrinolytic therapy alone.

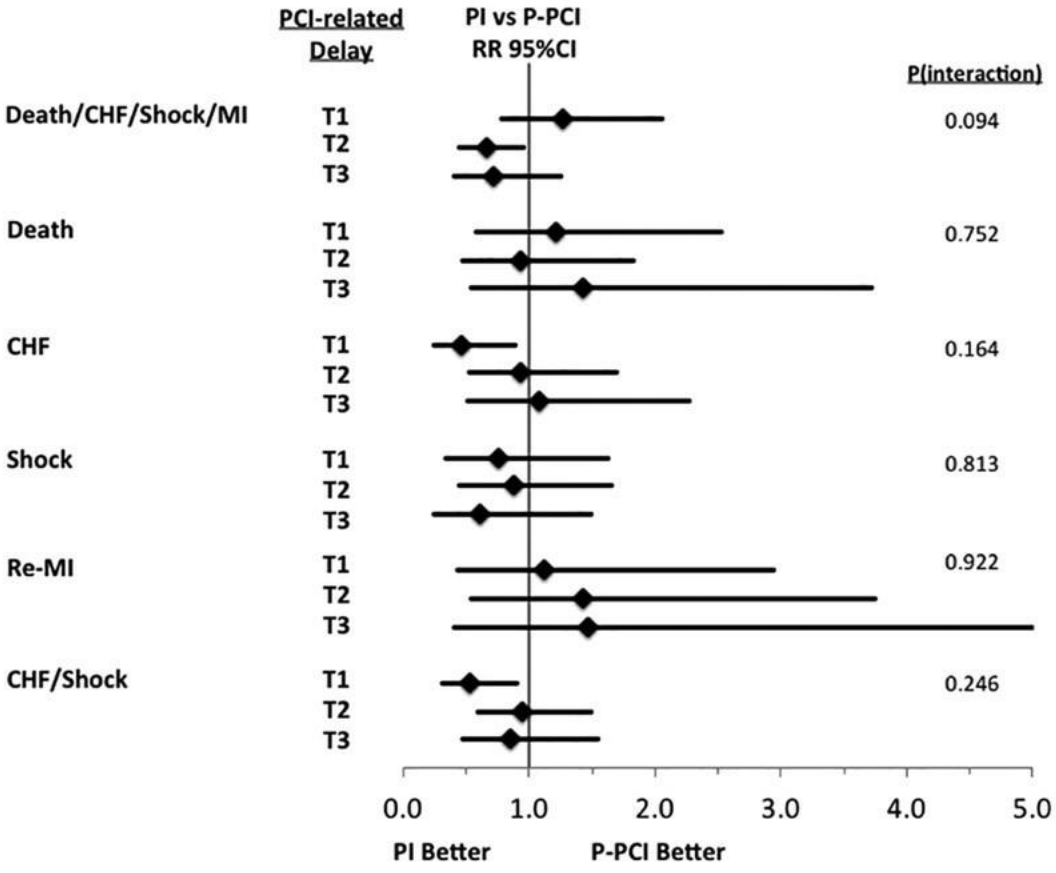
Fazel R, et al. J Am Heart Assoc. 2020 Jun 16;9(12):e015186. doi: 10.1161/JAHA.119.015186.

Potential benefits of pharmacoinvasive strategy on HF

P-I strategy: more medium, fewer large infarct



P-I strategy: better outcome of heart failure



Shavadia J. J Am Heart Assoc, 2015;4(8):e002049. Gershlick AH. Heart 2015;101:692–8.

Pharmacoinvasive therapy benefits more for delayed pts

Circulation

ON MY MIND

The Future of Pharmacoinvasive Therapy for ST-Segment–Elevation Myocardial Infarction Reperfusion in the Post-STREAM Era

Thomas Alexander, MD, DM; Dharam J. Kumbhani, MD, SM; Ajit Mullasari Sankardas, MD, DM

Coming on the heels of the STREAM trial (STREAM-Strategic Reperfusion [With Tenecteplase and Antithrombotic Treatment] Early After Myocardial Infarction),[1] the recently concluded STREAM-2 trial (Strategic Reperfusion in Elderly Patients Early After Myocardial Infarction)[2] has provided additional data in pharmacoinvasive (PI) reperfusion as a reperfusion strategy in ST-segment–elevation myocardial infarction (STEMI) when time delays are expected. To summarize the findings of these 2 trials, patients with STEMI within 3 hours of chest pain and with expected delays of >1 hour to primary percutaneous coronary intervention (PCI) were randomly assigned to PI versus primary PCI. STREAM was conducted with full-dose tenecteplase in the PI arm, which was amended after one-fifth of expected randomization to half-dose tenecteplase in patients >75 years of age due to an increased risk of intracranial bleeding. STREAM-2, on the other hand, randomly assigned patients >60 years of age (mean age, 71 years) and used half-dose tenecteplase in the PI group from the outset. Both studies showed similar results for PI versus primary PCI for the primary composite end point of death, shock, reinfarction, and heart failure at 30 days (STREAM-1: 12.4% versus 14.3%; relative risk, 0.86 [95% CI, 0.68–1.09]; STREAM-2: 12.8% versus 13.3%; relative risk, 0.96 [95% CI, 0.62–1.48]).

However, there are 2 areas of concern. The first is the issue of intracranial hemorrhage. In STREAM, more intracranial hemorrhages occurred in the fibrinolysis group than in the primary PCI group (1.0% versus 0.2%, *P*=0.04). The rates of nonintracranial bleeding were similar in the 2 groups. In STREAM-2, despite the use of half-dose tenecteplase, intracranial hemorrhage was numerically higher in the PI arm (1.5% [6 events] versus 0%). This could be a real finding because it is concordant with the STREAM data, although it could also be due to a protocol violation, for instance, use of additional heparin during the PCI. The second area of concern is the issue of failed reperfusion with tenecteplase and the need for emergent rescue PCI, 36% in STREAM and 34% in STREAM-2.

So, to summarize, the Achilles heel of a PI strategy is failed reperfusion and increased intracranial bleeding. The best strategy to deal with failed reperfusion is to institute fibrinolysis within the golden first hour where reperfusion results can be similar to primary PCI.[3] There is also an added advantage of increased percentage of aborted myocardial infarction if fibrinolysis is initiated early; however, this may only be feasible in a small minority of patients, because most patients with STEMI present >1 hour from the onset of ischemic symptoms. The issue of increased bleeding risk, however, will require different strategies and studies. Ischemic times in the PI arms of both STREAM trials were similar and fairly short (100–110 minutes). In this setting, pre-PCI baseline TIMI II/III flow rates in the PI arms were fairly similar (74.1% in STREAM-1, 71.6% in STREAM-2) despite the use of half-dose tenecteplase in the latter. Could half-dose tenecteplase in younger patients or even lower doses in the elderly patients produce similar reperfusion rates without increased bleeding rates? Could avoiding the standard strategy of coadministration of heparin reduce bleeding rates? These strategies need to be studied in future PI trials.

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For Sources of Funding and Disclosures, see page 733.

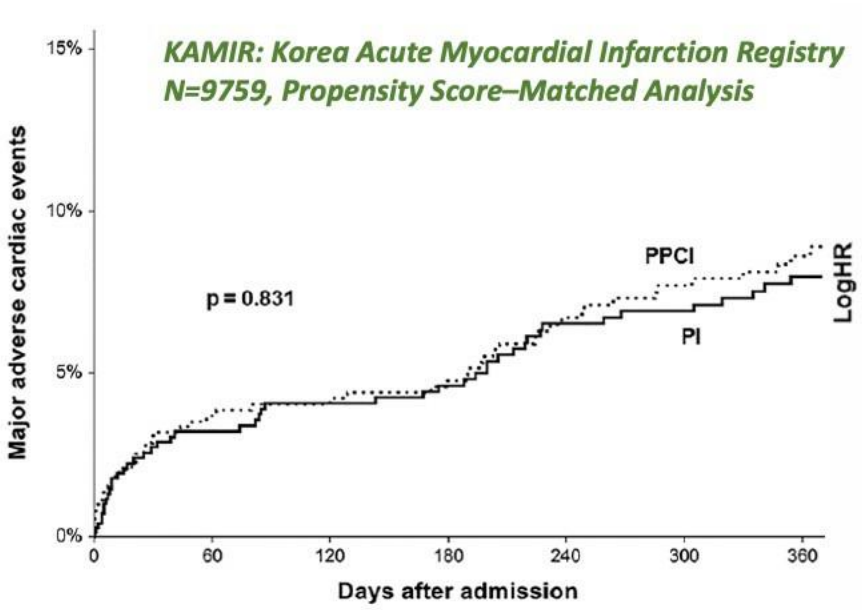
Circulation is available at www.ahajournals.org/journal/circ

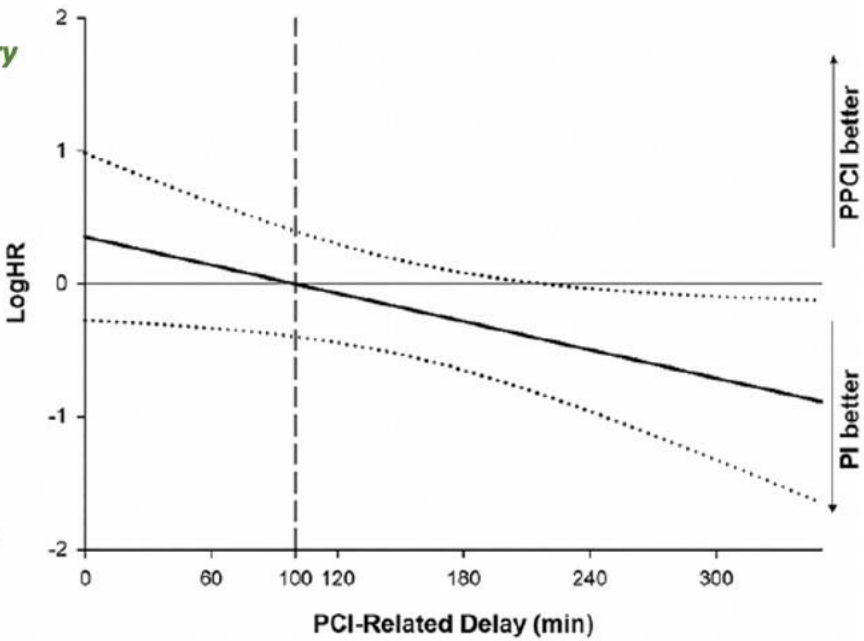
Intracranial hemorrhage in fibrinolysis

- *1.0% vs 0.2%, p=0.04) in STREAM*
- *1.5% [n=6] vs 0% in STREAM-2 (half-dose TNK)*

Failed reperfusion with TNK → emergent rescue PCI,

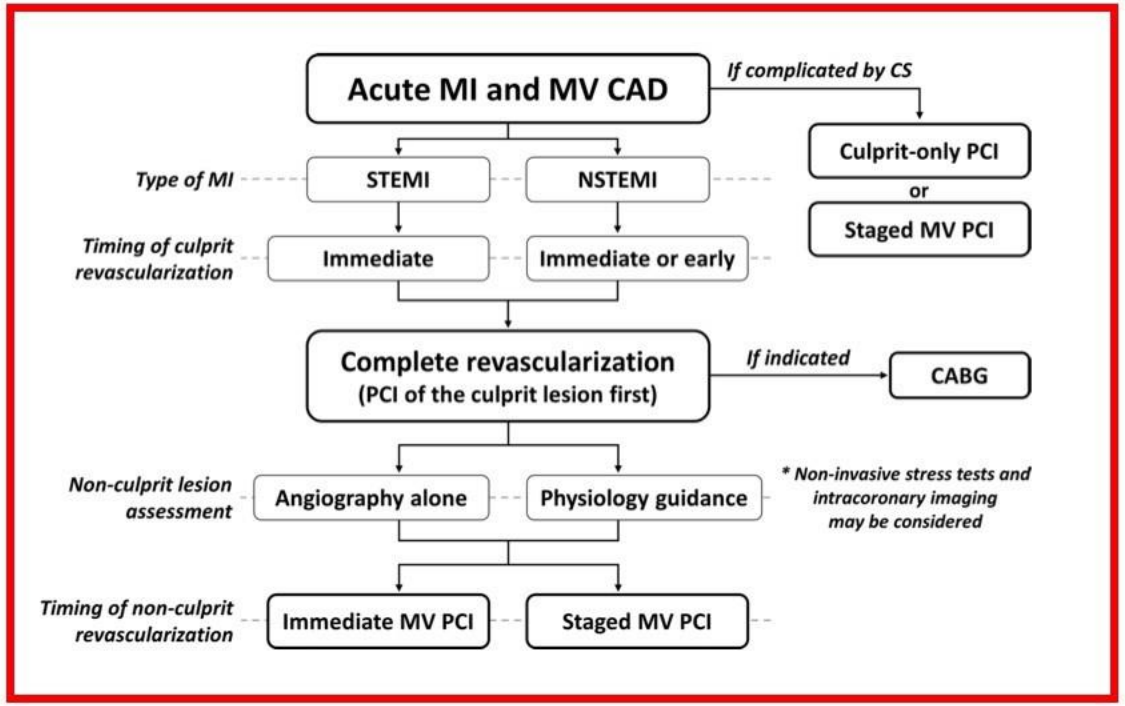
- *36% in STREAM*
- *34% in STREAM-2*

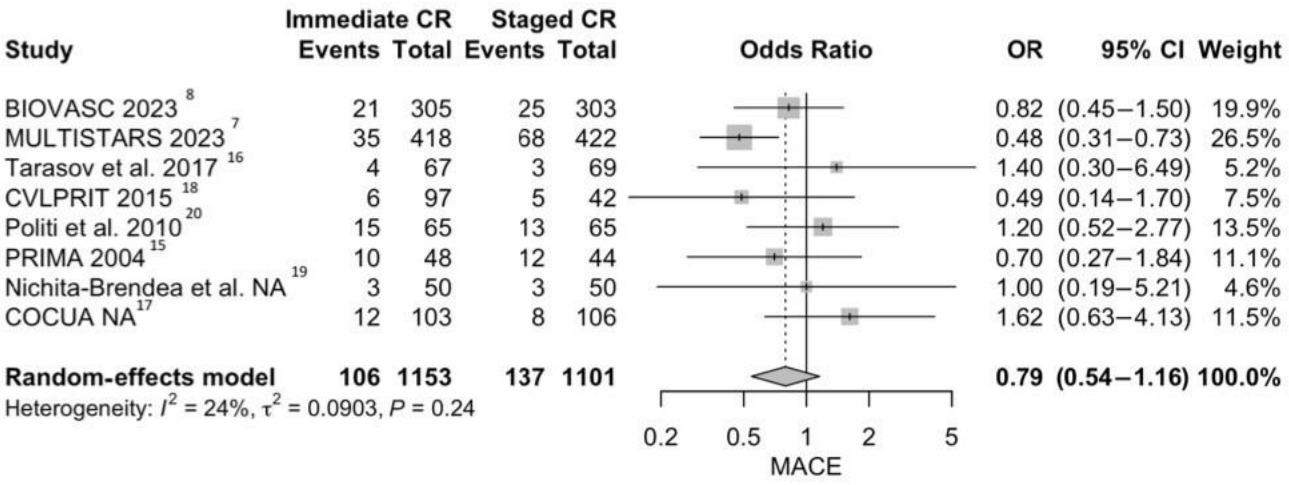


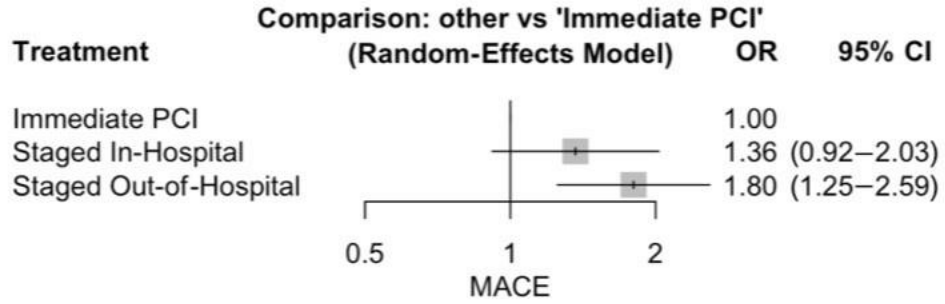


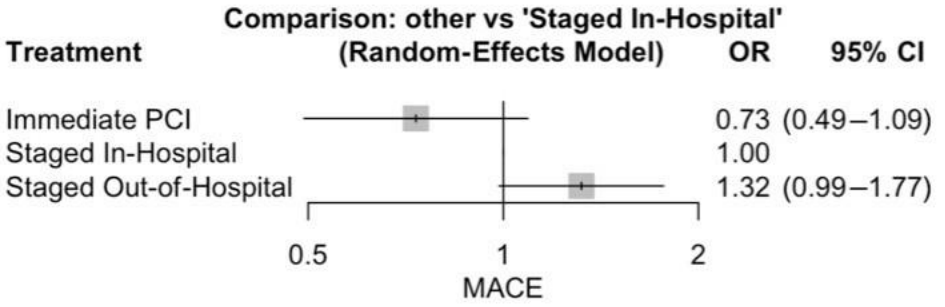
Alexander T, et al. Circulation. 2024 Mar 5;149(10):732-733.
Sim DS, et al. Circ Cardiovasc Interv. 2016 Sep;9(9):e003508

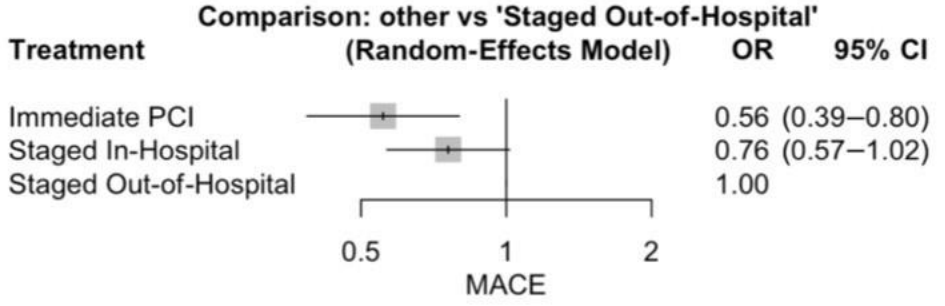
Immediate or stage PCI for MV-ACS











Elbadawi A et al. J Am Heart Assoc. 2024 Nov 5;13(21):e035535.

PCI for elderly ACS patients

2024 EARTH-STEMI meta-analysis #ESCCongress

Complete vs. culprit-only revascularisation in older STEMI patients

Conclusion
Complete vs. culprit-only revascularisation reduced CV events in the first 4 years after a ST-segment elevation myocardial infarction (STEMI) in older patients with multivessel disease.

Impact on clinical practice
The benefits of complete revascularisation were confirmed, but longer-term data are needed after 4 years.

Study objectives
The EARTH-STEMI meta-analysis investigated the long-term benefits of complete vs. culprit-only revascularisation in older STEMI patients with multivessel disease.

Study population

- Individual patient data from 7 randomised controlled trials
- Patients aged ≥75 years with multivessel disease admitted for STEMI
- 20% had follow-up data at 4 years

Who and what?

Complete revascularisation

816 patients

Culprit-only revascularisation

917 patients

Primary endpoint

Death, MI or ischaemia-driven revascularisation

Complete vs. culprit-only revascularisation

At 4 years	At longest follow-up
22%	17%
↓ reduction	↓ reduction
adjusted HR 0.78; 95% CI 0.63-0.96; p=0.005	adjusted HR 0.83; 95% CI 0.69-1.01; p=0.063

Secondary endpoints

Complete vs. culprit-only revascularisation

CV death or MI At longest follow up	Ischaemia-driven revascularisation At longest follow-up
24%	48%
↓ reduction	↓ reduction
adjusted HR 0.76; 95% CI 0.58-0.99; p=0.046	HR 0.52; 95% CI 0.34-0.85; p=0.002

ESC

British Heart Foundation SENIOR-RITA Trial

RESULTS: In older adults with NSTEMI, an invasive approach did not significantly reduce the risk of cardiovascular death or nonfatal myocardial infarction compared to a conservative approach over a median follow-up of 4.1 years.

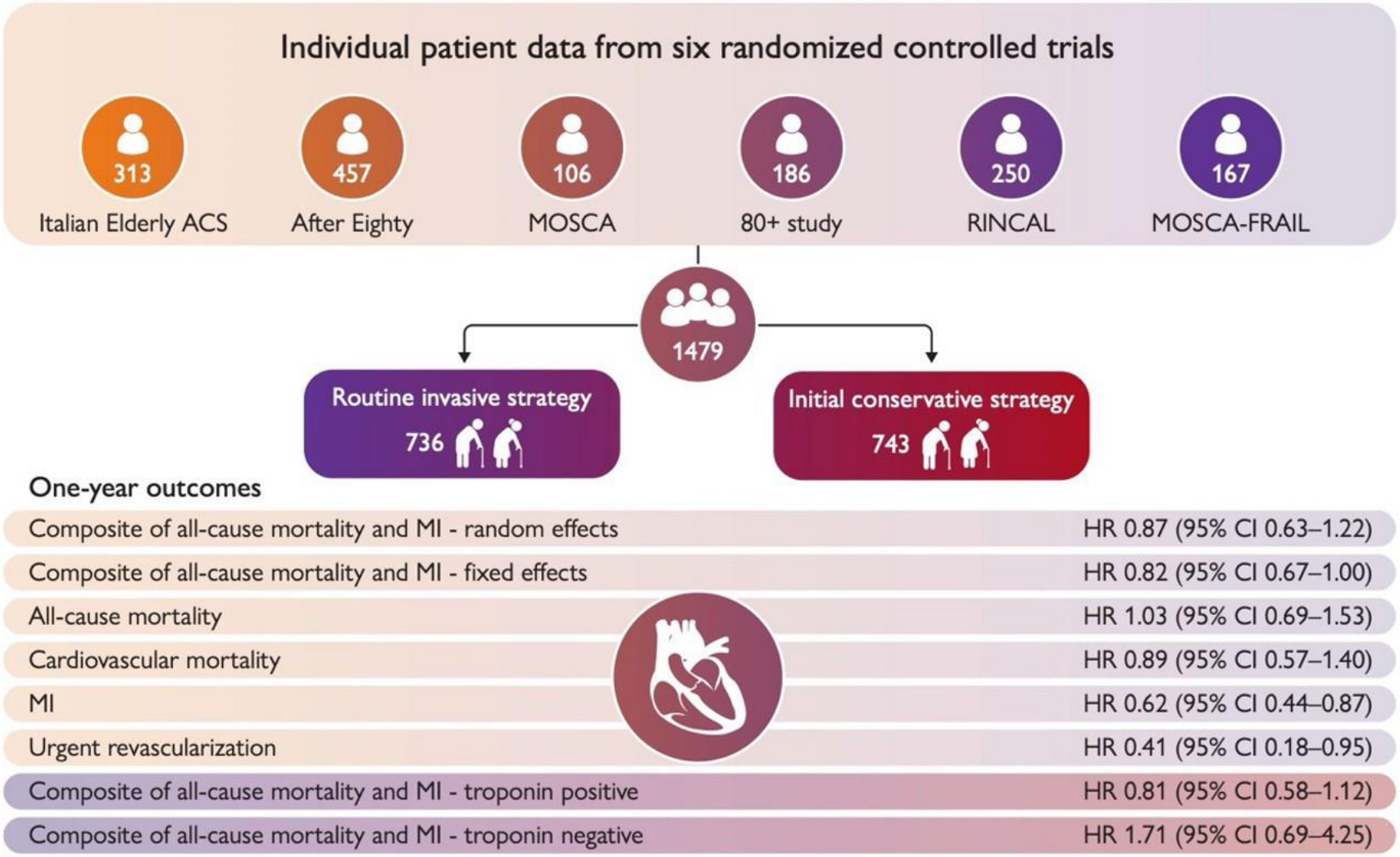
PURPOSE: To assess if a routine invasive treatment, including coronary revascularization and medical therapy, is more effective than medical therapy alone in reducing cardiovascular (CV) death or nonfatal MI in older adults with NSTEMI.

TRIAL DESIGN: Prospective, multicenter, open label, RCT, N= 1518

	Invasive Strategy (N= 753)	Conservative Strategy (N=765)	Hazard Ratio for Treatment Effect (95%CI)
Primary outcome: CV death or non-fatal MI	193 (25.6)	201 (26.3)	0.94 (0.77-1.14)
Cardiovascular death	119 (15.8)	109 (14.2)	1.11 (0.86-1.44)
Nonfatal MI	88 (11.7)	115 (15.0)	0.75 (0.57-0.99)
Secondary outcome			
Composite of death from any cause or nonfatal MI	319 (42.4)	321 (42.0)	0.97 (0.83–1.13)
Death from any cause	272 (36.1)	247 (32.3)	1.13 (0.95 – 1.34)

Key Takeaways: An invasive strategy did not significantly reduce the risk of the primary outcome—cardiovascular death or nonfatal myocardial infarction—compared to a conservative approach in older adults with NSTEMI.

PCI strategy for elderly NSTE-ACS patients



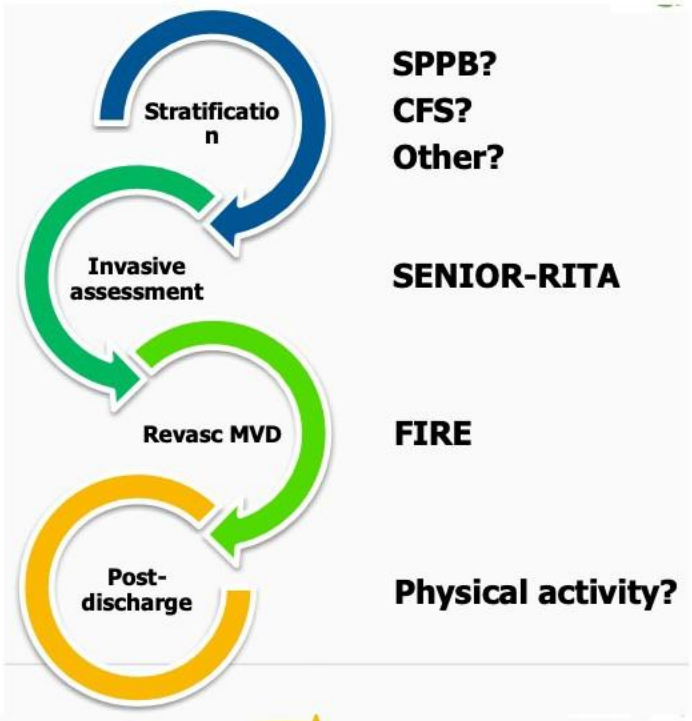
SENIOR-RITA
1518

No evidence was found that routine invasive treatment for NSTEACS in older patients reduces the risk of a composite of all- cause mortality and MI within 1 year compared with conservative management.

However, there is convincing evidence that invasive treatment significantly lowers the risk of repeat MI or urgent revascularisation.

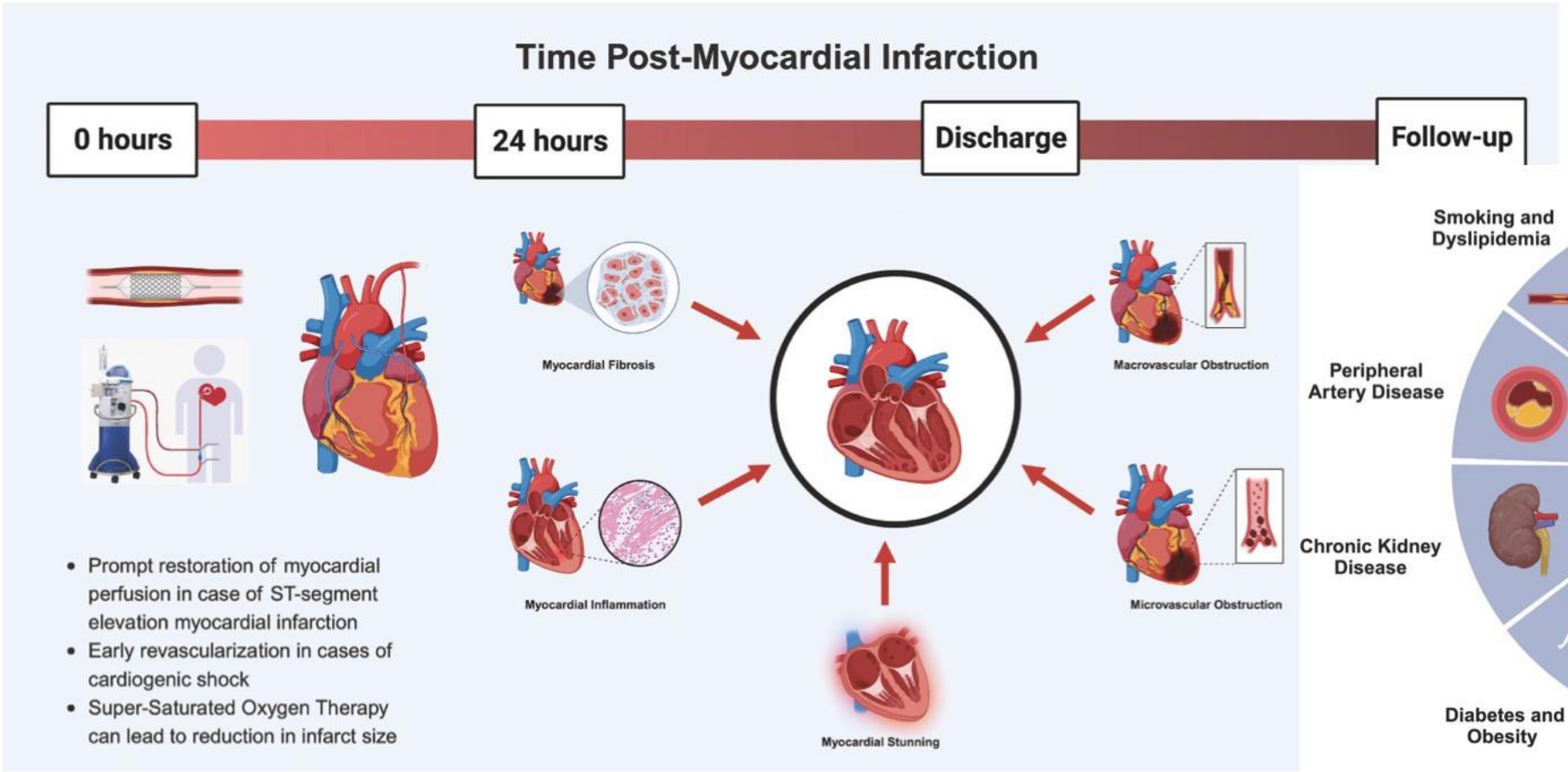
Kotanidis CP, et al. Eur Heart J. 2024 Jun 14;45(23):2052-2062. doi: 10.1093/eurheartj/ehae151.

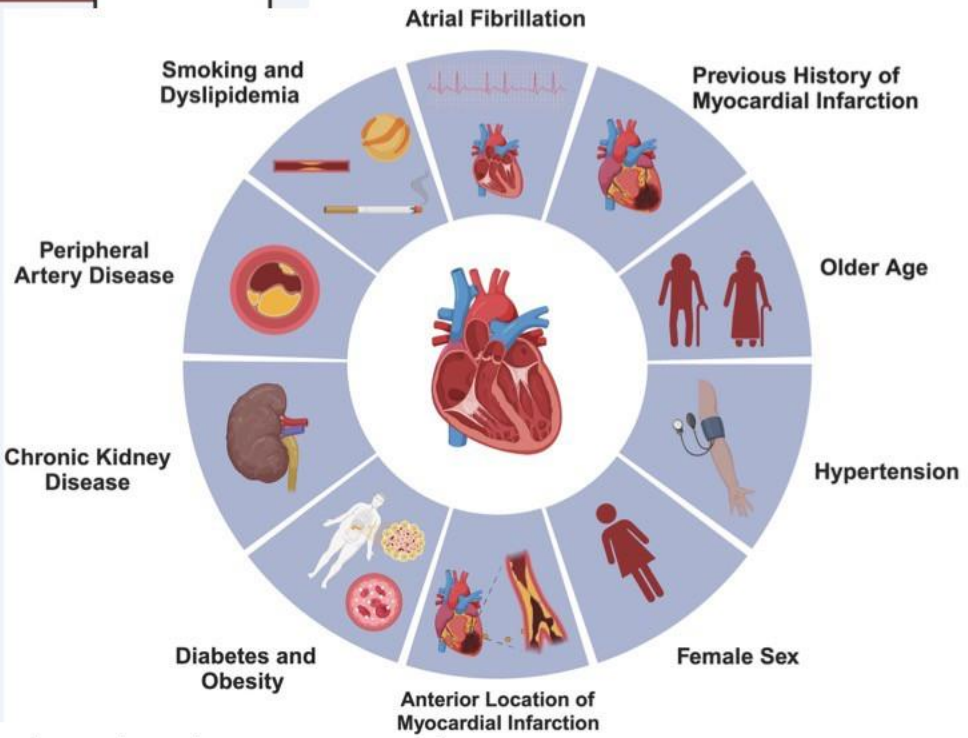
PCI strategy for elderly NSTE-ACS patients



	FIRE NSTEMI	SENIOR-RITA
Age	82	82
Comorbidities	2	3
Frailty	10%	20-30%
Female	35%	45%
Cognitive impairment	<10%	60%
GRACE score	180	135
MVD	100%	55%
Time to angiography	1 day	5 days
Complete revasc	≈100%	≈54%
CV death	↓ 1 year	=4 years
MI	↓ 1 year	↓ 4 years
Revascularization	↓ 1 year	↓ 4 years

ACS care: Switch from acute ischemia to heart failure!





- *Early revascularization should be performed in STEMI pts to improve survival and reduce HF incidence*
- *Early revascularization is crucial to improve survival in patients with cardiogenic shock*
- *In MVD-CS patients with, culprit lesion-only PCI should be performed in the acute setting*

Akhtar KH, et al. Prog Cardiovasc Dis. 2024 Jan-Feb;82:15-25. doi: 10.1016/j.pcad.2024.01.017.

New strategies for myocardial salvage in STEMI

LV UNLOADING

- STEMI-DTU trial (NCT03947619)

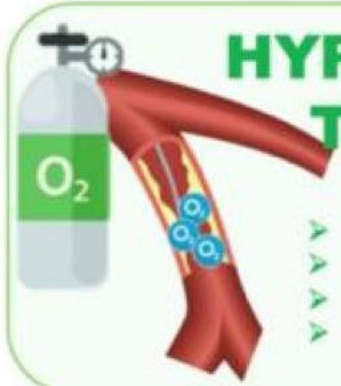
STENT RETRIEVER – ASSISTED THROMBECTOMY

- RETRIEVE-AMI (NCT05307965)

Myocardial salvage strategies

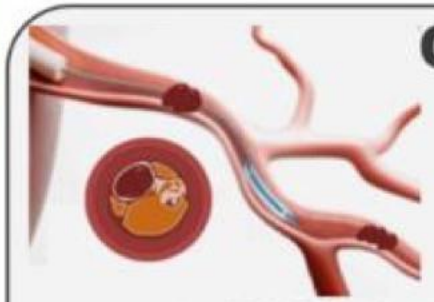
CORONARY MECHANICAL THROMBECTOMY CatRx

- CHEETAH study
  - More science is needed



HYPEROXEMIC THERAPY

- AMIHOT I
- AMIHOT II
- IC HOT
- AMI HOT III



Controlled Flow Infusion (CoFI)

- MOCA I study (NCT03654573)

Zuccarelli V, et al. J Clin Med. 2024 May 15;13(10):2923. doi: 10.3390/jcm13102923.

Promising of cell therapy for AMI

Lee *et al. Stem Cell Research & Therapy* (2024) 15:290
https://doi.org/10.1186/s13287-024-03891-1

Stem Cell Research & Therapy

REVIEW **Open Access**

Mid- to long-term efficacy and safety of stem cell therapy for acute myocardial infarction: a systematic review and meta-analysis

Hyeongsuk Lee[1], Hyun-Jai Cho[2], Yeonjung Han[1] and Seon Heui Lee[1*]

Abstract

Background This comprehensive systematic review and meta-analysis investigated the mid- to long-term efficacy and safety of stem cell therapy in patients with acute myocardial infarction (AMI).

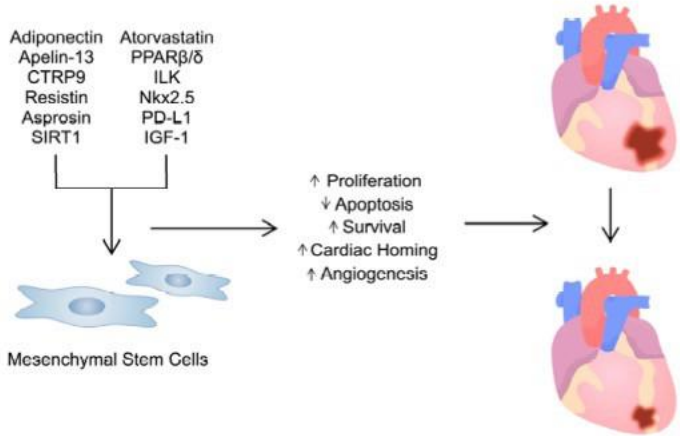
Methods The study encompassed 79 randomized controlled trials with 7103 patients, rendering it the most up-to-date and extensive analysis in this field. This study specifically focused on the impact of stem cell therapy on left ventricular ejection fraction (LVEF), major adverse cardiac events (MACE), and infarct size.

Results Stem cell therapy significantly improved LVEF at 6, 12, 24, and 36 months post-transplantation compared to control values, indicating its potential for long-term cardiac function enhancement. A trend toward reduced MACE occurrence was observed in the intervention groups, suggesting the potential of stem cell therapy to lower the risk of cardiovascular death, reinfarction, and stroke. Significant LVEF improvements were associated with long cell culture durations exceeding 1 week, particularly when combined with high injected cell quantities (at least 10^8 cells). No significant reduction in infarct size was observed.

Conclusions This review highlights the potential of stem cell therapy as a promising therapeutic approach for patients with AMI, offering sustained LVEF improvement and a potential reduction in MACE risk. However, further research is required to optimize cell culture techniques, determine the optimal timing and dosage, and investigate procedural variations to maximize the efficacy and safety of stem cell therapy in this context.

Keywords Cell therapy, Acute myocardial infarction, Systematic review

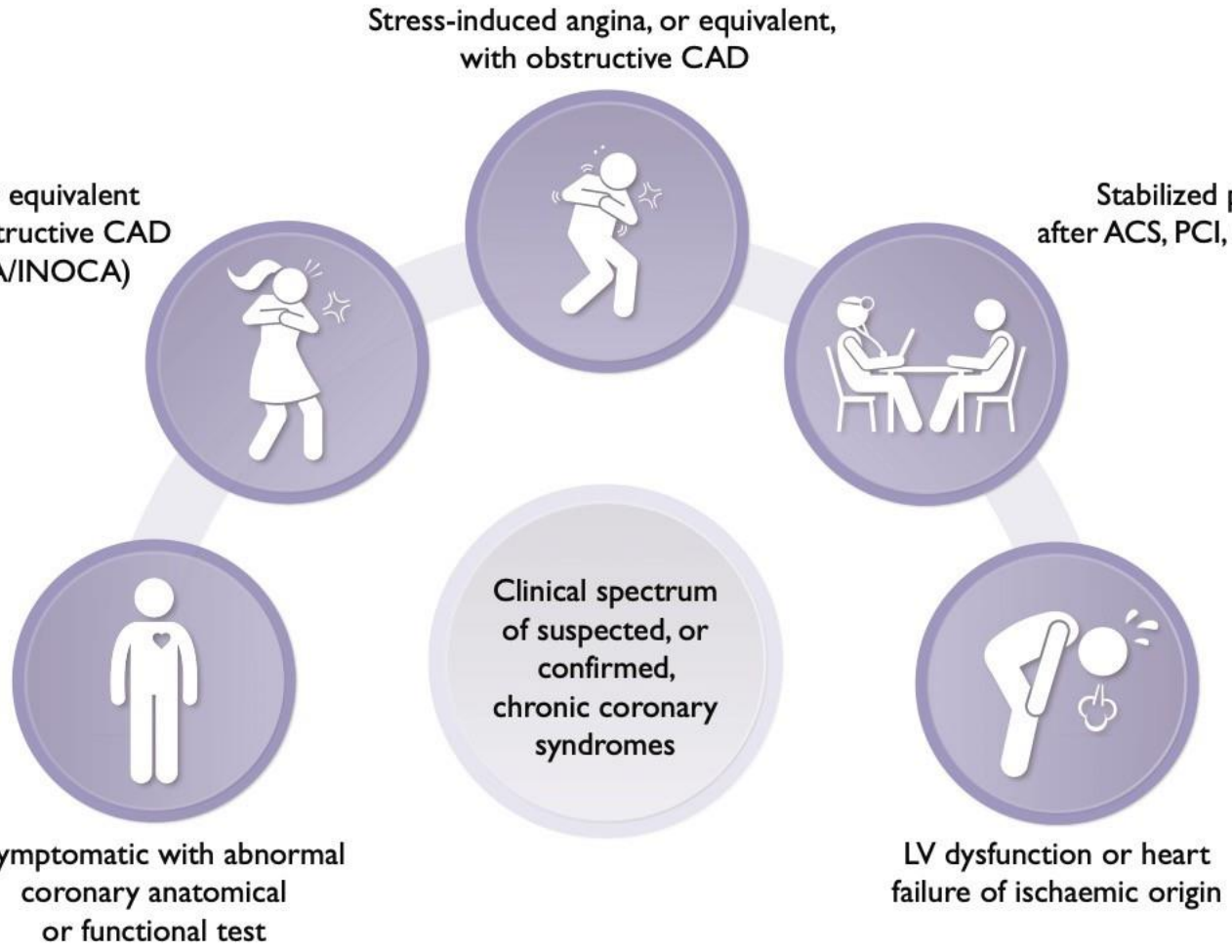
Methods to improve the functionality of mesenchymal stem cells.



Agent/Molecule	Mechanisms Mediating the Functionality of Stem Cells
Adiponectin	Stimulation of circulating adiponectin promotes the beneficial effects of MSCs in HF.
	Adiponectin further enhanced the beneficial effects of MSCs in the treatment of animal models with cardiac infarction.
	Adiponectin transduction into BM-MSCs could enhance the positive effects on left ventricle and fibrosis in diabetic rats.
Apelin-13	MSCs pretreated with apelin-13 were associated with improved viability and could further increase cardiac repair after infarction in animal models.
CTRP9	Injection of AD-MSCs into CTRP9-knockdown mice with myocardial infarction was associated with reduced engraftment.
	CTRP9-281, a C-terminal polypeptide, stimulates stem cells to produce exosomes with a pro-angiogenic cargo and further enhances cardioprotection.
	Inhibition of miR-34a-5p, an upstream inhibitor of CTRP9, could further enhance the cardioprotective role of adipose-derived stem cells.
Resistin	Resistin promotes homing of MSCs towards cardiac tissue and thereby improves their cardioprotective potential.
Asprosin	Pretreatment of MSCs with asprosin stimulated the ERK1/2 pathway to upregulate antioxidant molecules and suppress apoptosis, which could translate into elevated cardioprotection of pretreated stem cells.
SIRT1	SIRT1-knockdown cells demonstrate reduced efficacy in the treatment of HF.
	Pretreatment of stem cells with resveratrol enhanced the expression of survival proteins in the hearts of rats with diabetes.
	Pretreatment of stem cells with resveratrol promoted the expression of proangiogenic mediators in hearts after infarction.
	Aged MSCs pretreated with SRT1720, a SIRT1 activator, had significantly enhanced cardiac function after infarction in animal models.
	Stem cells with melatonin enhances the expression of SIRT1 and stimulates animal hearts recovery after infarction.
IGF-1/IGF-1R	Stimulation of BM-MSCs with IGF-1 enhances their differentiation into cardiomyocyte-like cells
Rapamycin	Pretreatment of MSCs with rapamycin enhanced the cardioprotective properties of these cells, improved their survival, and enhanced angiogenesis at the area of infarct in the rats model of myocardial infarction.
PPARβ/δ	PPARβ/δ knockdown or the use of its antagonist suppressed the ability of MSCs to reduce infarct size.
	The use of PPARβ/δ agonist enhances the cardioprotective role of MSCs.
Integrin-linked kinase	MSCs overexpressing integrin-linked kinase demonstrated greater viability. Transplantation of these cells into an animal model of myocardial infarction was associated with reduced fibrosis and number of apoptotic cells.
	Integrin-linked kinase modifies the paracrine properties of MSCs, as the condition medium of modified cells could significantly improve cardiac function.
Atorvastatin	Pretreatment of MSCs with atorvastatin upregulated CXCR4 and resulted in improved cardiac homing of stem cells. Furthermore, the use of pretreated cells could significantly improve cardiac function and lower fibrosis and inflammation.
	Atorvastatin enhanced the secretion of lncRNA H19 in stem cell-derived exosomes, which was associated with improved cardiac function.
	Atorvastatin significantly changed the profile of miRNAs secreted by MSCs in exosomes, which could promote the M2 macrophage polarization.

Lee H, et al. Stem Cell Res Ther. 2024 Sep 11;15(1):290. doi: 10.1186/s13287-024-03891-1.
Bakinowska E, et al. Int J Mol Sci. 2024 Mar 31;25(7):3901. doi: 10.3390/ijms25073901.

Various scenarios of chronic coronary syndromes



Lifestyle and risk factor modification
- To improve prognosis

Disease-modifying medical treatment
- To improve prognosis

Revascularization
- To reduce symptoms
- To improve prognosis in patients with obstructive CAD who are at high risk of adverse events

Antianginal medical treatment
- To reduce symptoms

Vrints C, et al. Eur Heart J. 2024 Sep 29;45(36):3415-3537. doi: 10.1093/eurheartj/ehae177.

Revascularization for CCS patients

Revascularization if:

- high risk of adverse events
- GDMT fails to relieve symptoms

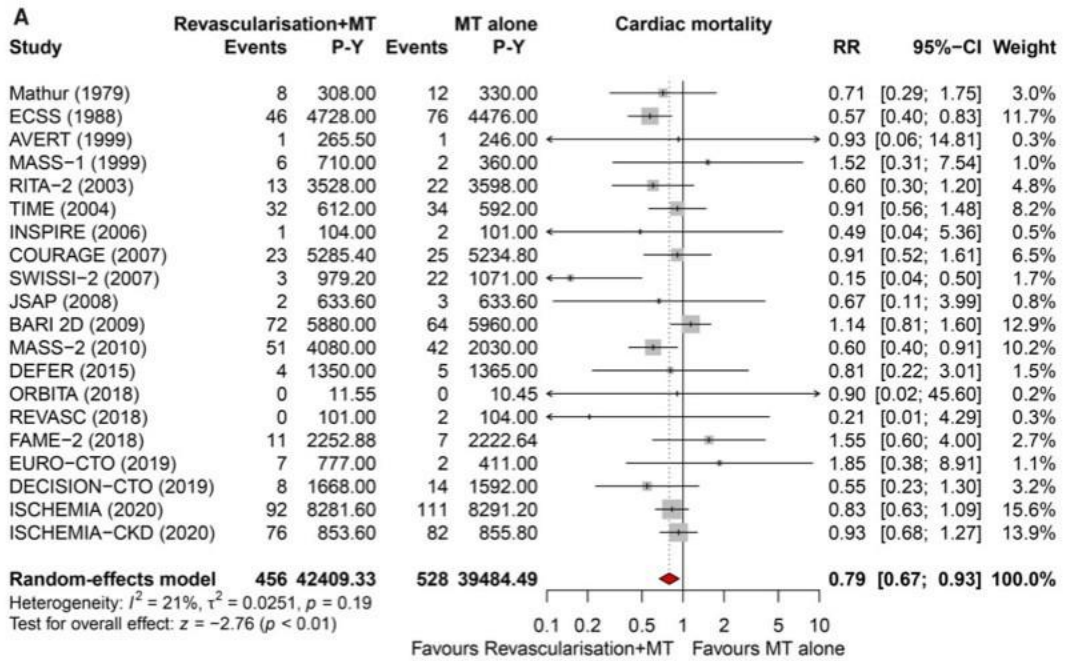
Revascularization

- To reduce symptoms
- To improve prognosis in patients with obstructive CAD who are at high risk of adverse events

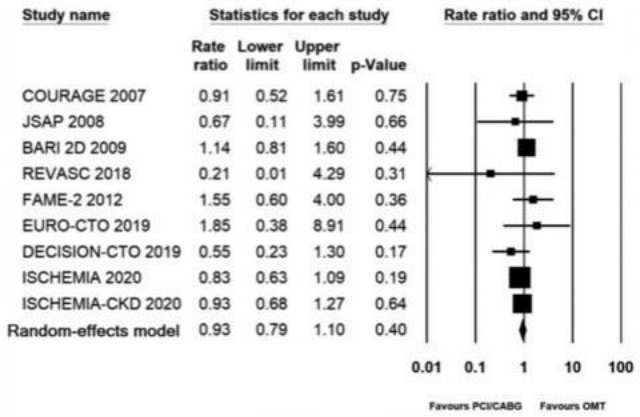
Revascularization to improve outcomes		
In CCS patients with LVEF >35%, myocardial revascularization is recommended, in addition to guideline-directed medical therapy, for patients with functionally significant left main stem stenosis to improve survival.	I	A
In CCS patients with LVEF >35%, myocardial revascularization is recommended, in addition to guideline-directed medical therapy, for patients with functionally significant three-vessel disease to improve long-term survival and to reduce long-term cardiovascular mortality and the risk of spontaneous myocardial infarction.	I	A
In CCS patients with LVEF >35%, myocardial revascularization is recommended, in addition to guideline-directed medical therapy, for patients with functionally significant single- or two-vessel disease involving the proximal LAD, to reduce long-term cardiovascular mortality and the risk of spontaneous myocardial infarction.	I	B
In CCS patients with LVEF ≤35%, it is recommended to choose between revascularization or medical therapy alone, after careful evaluation, preferably by the Heart Team, of coronary anatomy, correlation between coronary artery disease and LV dysfunction, comorbidities, life expectancy, individual risk-to-benefit ratio, and patient perspectives.	I	C
In surgically eligible CCS patients with multivessel CAD and LVEF ≤35%, myocardial revascularization with CABG is recommended over medical therapy alone to improve long-term survival.	I	B
In selected CCS patients with functionally significant MVD and LVEF ≤35% who are at high surgical risk or not operable, PCI may be considered as an alternative to CABG.	IIb	B
Revascularization to improve symptoms		
In CCS patients with persistent angina or anginal equivalent, despite guideline-directed medical treatment, myocardial revascularization of functionally significant obstructive CAD is recommended to improve symptoms.	I	A

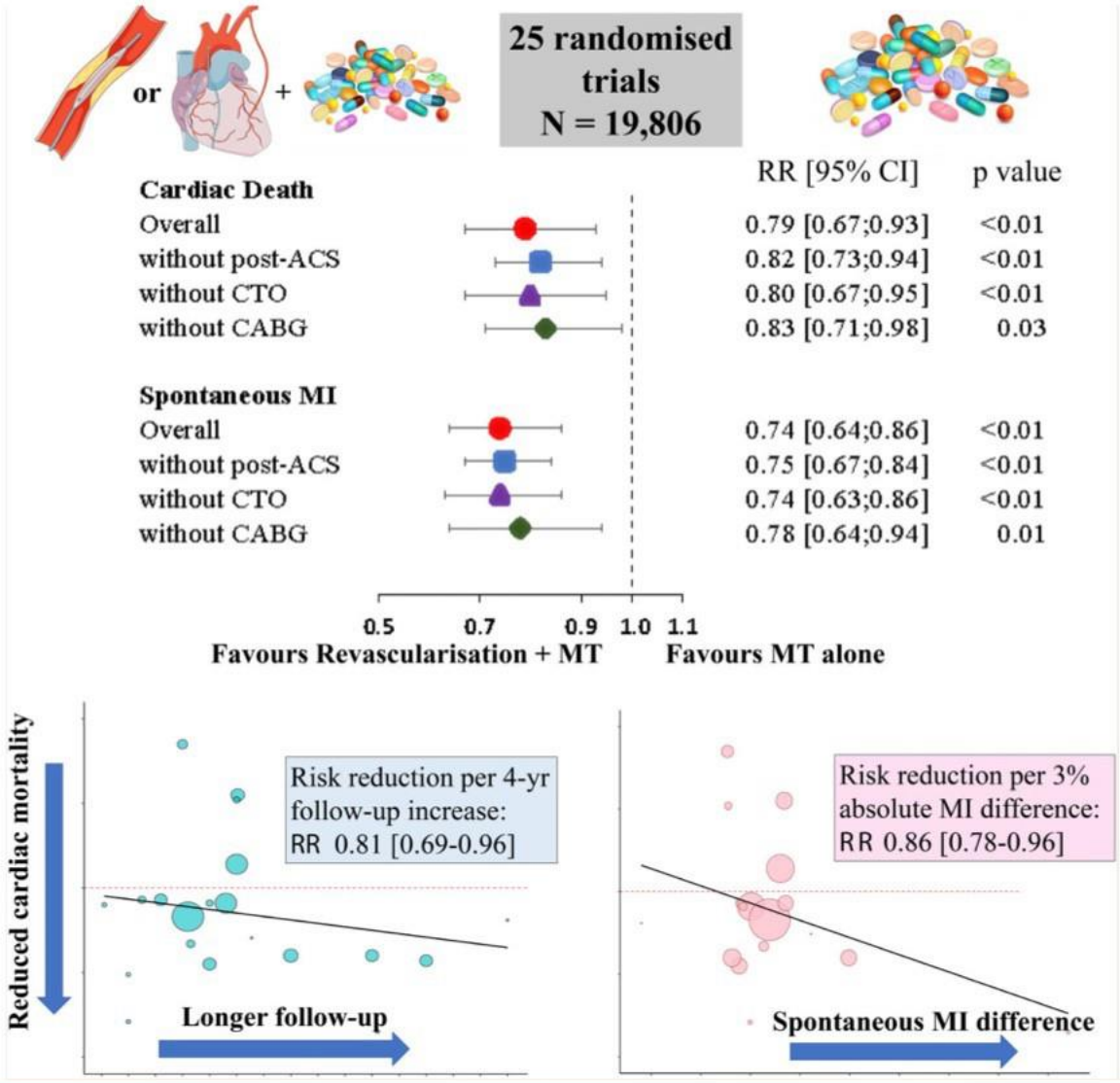
Vrints C, et al. Eur Heart J. 2024 Sep 29;45(36):3415-3537. doi: 10.1093/eurheartj/ehae177.

Revascularization + OMT versus OMT for CCS



After OMT





Navarese EP, et a. Eur Heart J. 2021 Dec 1;42(45):4638-4651.
Brown DL, et al Eur Heart J. 2021 Dec 1;42(45):4652-4655

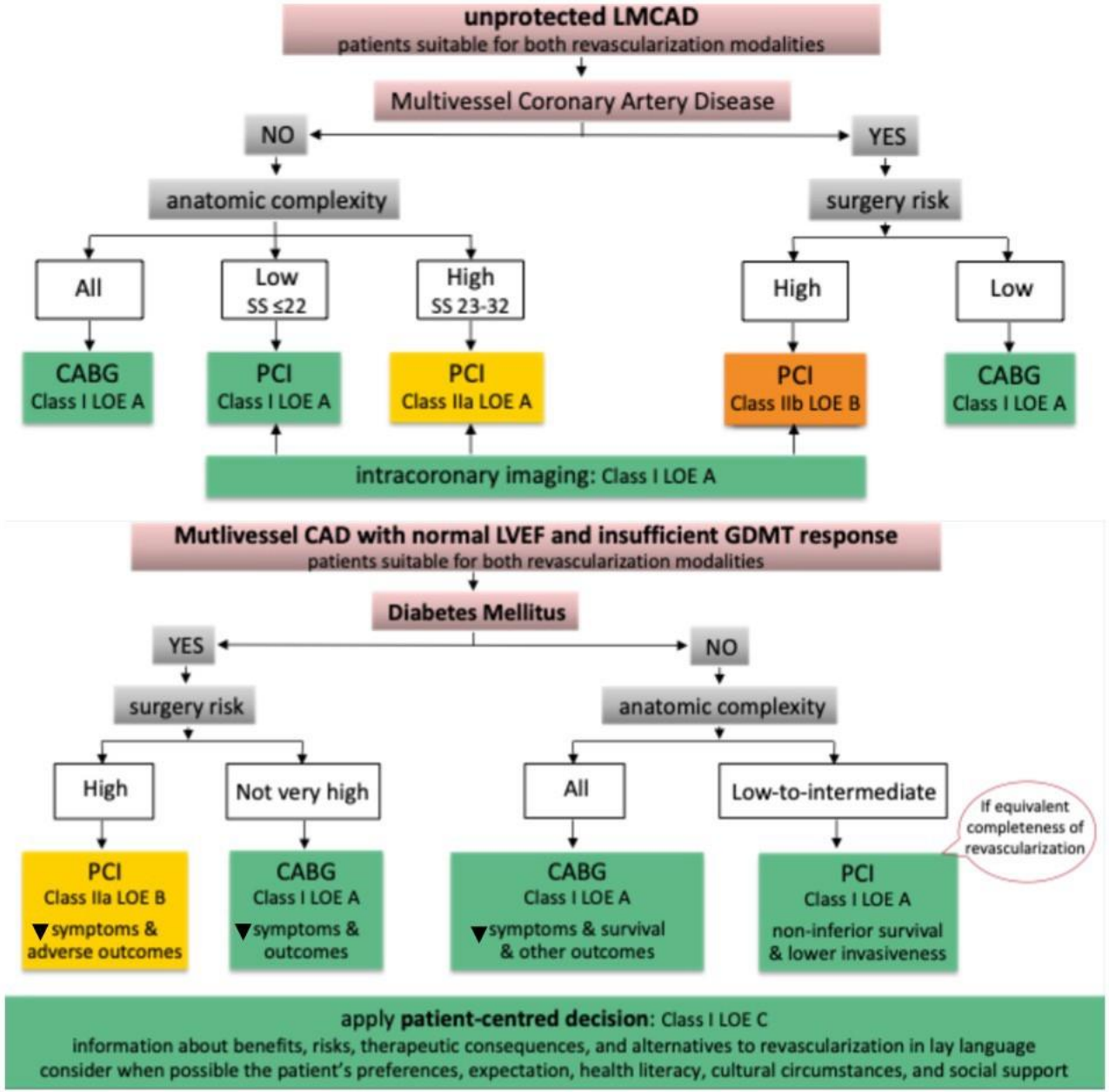
Roles of PCI for CCS patients

Revascularization

- To reduce symptoms
- To improve prognosis in patients with obstructive CAD who are at high risk of adverse events

FAVOURS PCI
Clinical characteristics
Presence of severe co-morbidity (not adequately reflected by scores)
Advanced age/frailty/reduced life expectancy
Restricted mobility and conditions that affect the rehabilitation process
Anatomical and technical aspects
MVD with SYNTAX score 0–22
Anatomy likely resulting in incomplete revascularization with CABG due to poor quality or missing conduits
Severe chest deformation or scoliosis
Sequelae of chest radiation
Porcelain aorta[a]

FAVOURS CABG
Clinical characteristics
Diabetes
Reduced LV function (EF ≤35%)
Contraindication to DAPT
Recurrent diffuse in-stent restenosis
Anatomical and technical aspects
MVD with SYNTAX score ≥23
Anatomy likely resulting in incomplete revascularization with PCI
Severely calcified coronary artery lesions limiting lesion expansion
Need for concomitant interventions
Ascending aortic pathology with indication for surgery
Concomitant cardiac surgery

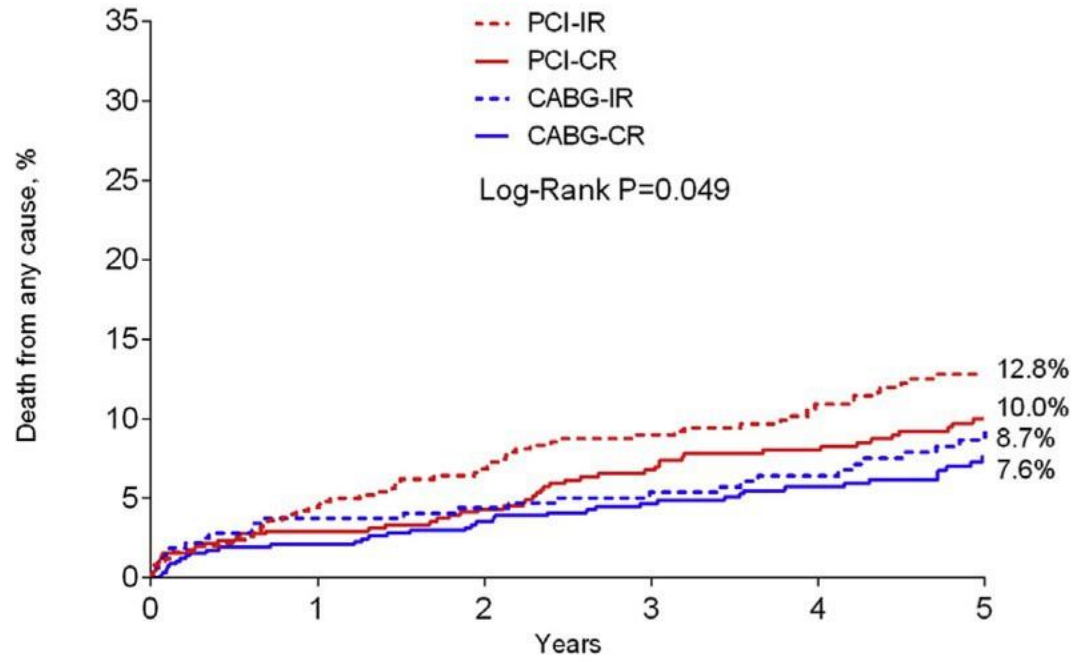


Windecker S, et al. Eur Heart J, 2019;40:204–12.
Neumann FJ, et al. Eur Heart J, 2019;40(2):87-165.
Vrints C, et al. Eur Heart J. 2024 Sep 29;45(36):3415-3537.

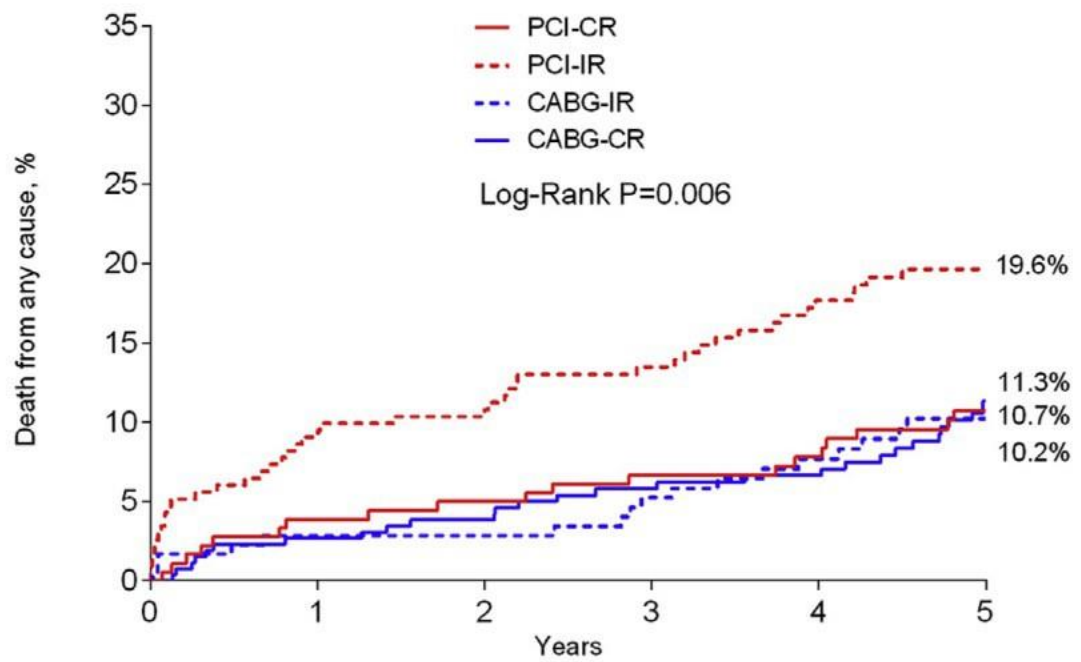
PCI is non inferior CABG if complete revascularization

Patient-Level Pooled Analysis of the SYNTAX, PRECOMBAT, and BEST Trials, n=3.212 (~1/3 ACS)

Multivessel Coronary Artery Disease



High SYNTAX score (>32)



Risk for Death From Any Cause in Subgroup	Crude Incidence					Adjusted Hazard Ratio (95% Confidence Interval)*				
	CABG CR	CABG IR	PCI CR	PCI IR	p Value	CABG CR	CABG IR	PCI CR	PCI IR	p Value
Left main disease	44 (10.1%)	22 (12.2%)	38 (8.3%)	28 (12.6%)	0.28	1.00 (reference)	1.06 (0.63–1.80)	0.88 (0.56–1.39)	1.10 (0.67–1.80)	0.85
Multivessel disease	40 (6.9%)	27 (8.3%)	48 (9.4%)	59 (11.8%)	0.044	1.00 (reference)	1.00 (0.60–1.65)	1.28 (0.83–1.96)	1.65 (1.10–2.48)	0.005
High SYNTAX score	29 (10.9%)	17 (9.6%)	19 (10.5%)	44 (19.0%)	0.01	1.00 (reference)	0.83 (0.45–1.53)	0.93 (0.51–1.72)	1.68 (1.02–2.76)	0.032
Diabetes	28 (9.2%)	21 (12.3%)	35 (11.8%)	40 (15.3%)	0.17	1.00 (reference)	1.23 (0.68–2.23)	1.32 (0.79–2.23)	1.70 (1.02–2.84)	0.23

Ahn JM, et al. JACC Cardiovasc Interv, 2017;10(14):1415-1424. doi: 10.1016/j.jcin.2017.04.037.

PCI versus OMT in CCS

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DOI: 10.1111/eci.14303

ORIGINAL ARTICLE

WILEY

Percutaneous coronary revascularization versus medical therapy in chronic coronary syndromes: An updated meta-analysis of randomized controlled trials

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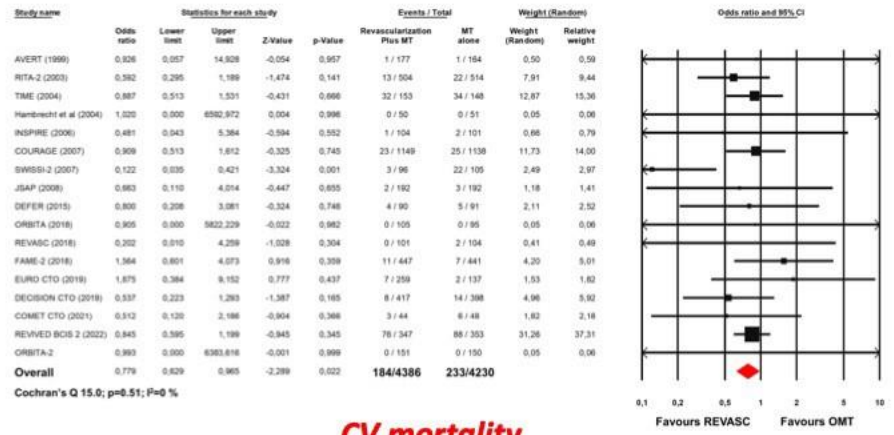
Abstract

Introduction: Coronary artery disease (CAD) is a main cause of morbidity and mortality. The effectiveness of coronary revascularization in chronic coronary syndromes (CCS) is still debated. Our recent study showed the superiority of coronary revascularization over optimal medical therapy (OMT) in reducing cardiovascular (CV) mortality and myocardial infarction (MI). The recent publication of the ORBITA-2 trial suggested superiority of percutaneous coronary revascularization (PCI) in reducing angina and improving quality of life. Therefore, we aimed to provide an updated meta-analysis evaluating the impact of PCI on both clinical outcomes and angina in CCS.

Methods: Relevant studies were screened in PubMed/Medline until 08/01/2024. Randomized controlled trials (RCTs) comparing PCI to OMT in CCS were selected. The primary outcome was CV death. Secondary outcomes were MI, all-cause mortality, stroke, major bleeding and angina severity.

Results: Nineteen RCTs involving 8616 patients were included. Median follow-up duration was 3.3 years. Revascularization significantly reduced CV death (4.2% vs. 5.5%; OR = .77; 95% CI .62–.96, $p = .02$). Subgroup analyses favoured revascularization in patients without chronic total occlusions (CTOs) ($p = .052$) and those aged <65 years ($p = .02$). Finally, a follow-up duration beyond 3 years showed increased benefit of coronary revascularization ($p = .04$). Secondary outcomes analyses showed no significant differences, except for a lower angina severity in the revascularization group according to the Seattle Angina Questionnaire (SAQ) ($p = .04$) and to the Canadian Cardiovascular Society (CCS) classification ($p = .005$).

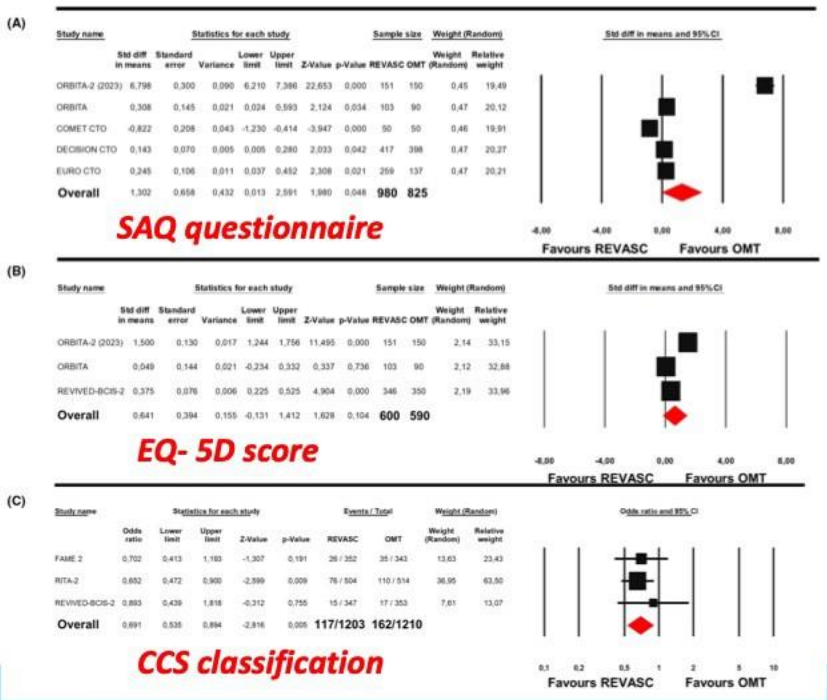
Conclusions: PCI compared to OMT significantly reduces CV mortality and angina severity, improving quality of life in CCS patients. This benefit was larger without CTOs, in patients aged <65 years and with follow-up duration beyond 3 years.



CV mortality

Benefit was larger

- Without CTO
- < 65 years
- F/u beyond 3 year



SAQ questionnaire

EQ- 5D score

CCS classification

Panuccio G, et al. Eur J Clin Invest. 2024 Dec;54(12):e14303. doi: 10.1111/eci.14303.

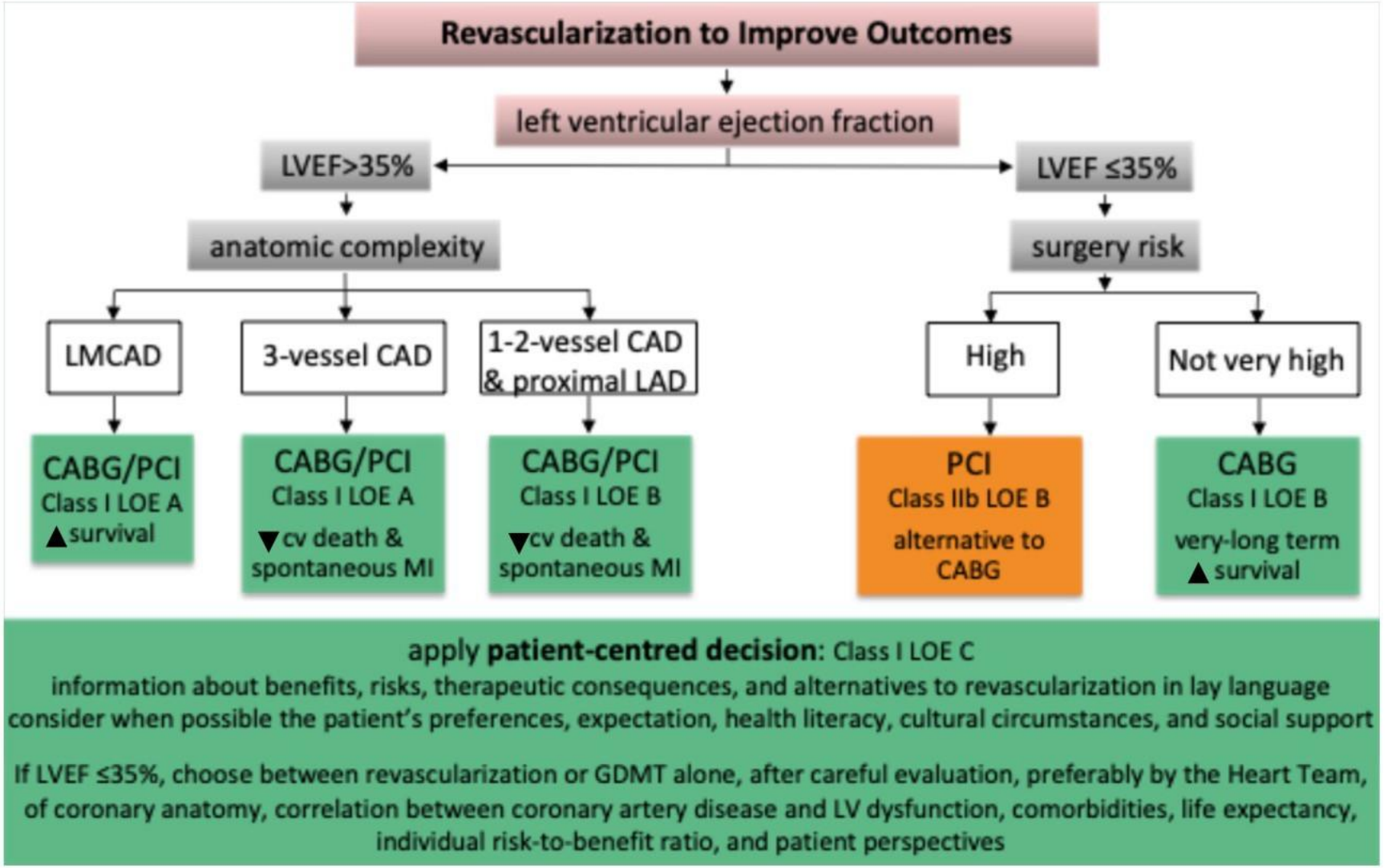
Roles of PCI for CCS patients

Revascularization if:

- high risk of adverse events
- GDMT fails to relieve symptoms

Revascularization

- To reduce symptoms
- To improve prognosis in patients with obstructive CAD who are at high risk of adverse events



Vrints C, et al. Eur Heart J. 2024 Sep 29;45(36):3415-3537. doi: 10.1093/eurheartj/ehae177.

Does PCI benefit CCS patients with low LVEF?

2022 REVIVED-BCIS2 trial #ESCCongress

Percutaneous revascularisation for ischaemic ventricular dysfunction

Conclusion

Percutaneous coronary intervention (PCI) does not reduce all-cause mortality or heart failure hospitalisation in patients with severe left ventricular (LV) dysfunction and extensive coronary artery disease.

Impact on clinical practice

PCI should not be offered to stable patients with ischaemic LV dysfunction if the sole aim is to provide prognostic benefit. However, it is important to note that REVIVED-BCIS2 excluded patients with limiting angina or recent acute coronary syndromes, and PCI is still an option in these contexts.

Study objectives

REVIVED-BCIS2 is the first adequately powered randomised trial to examine the efficacy and safety of PCI in patients with LV systolic dysfunction.

Who and what?

Population

Patients with
- severe LV dysfunction (ejection fraction ≤35%)
- extensive coronary disease
- demonstrable viability in at least 4 dysfunctional myocardial segments that could be revascularised by PCI

700 patients

randomised 1:1

PCI group: PCI + optimal medical therapy

Control group: optimal medical therapy alone

Median follow-up → 3.4 years

Primary endpoint

Composite of all-cause death or hospitalisation for heart failure

	Rate%
PCI group	37.2%
Control group	38.0%

Hazard ratio 0.99
95% CI 0.78–1.27; p=0.96

Secondary outcomes

LV ejection fraction at 6 and 12 months:

No differences between groups

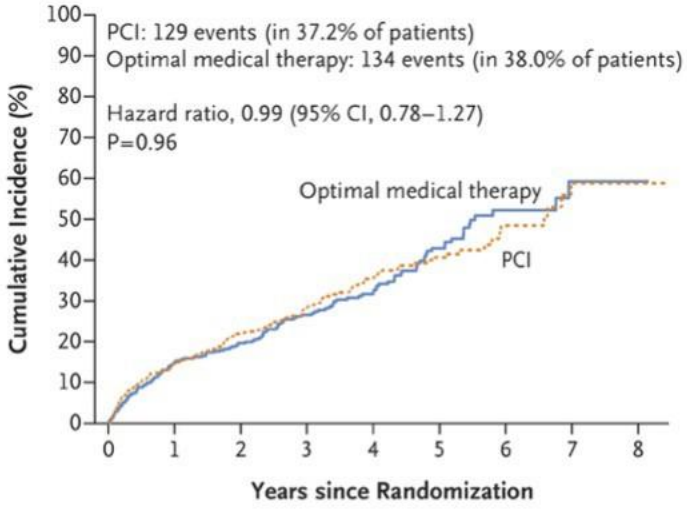
Quality of life measures:

Favoured PCI at 6 and 12 months

No difference between groups at 24 months

ESC

	HEART[9]	PARR-2[10,11]	STICH[12,13]	REVIVED-BCIS2[14]
Number of enrolled patients	138	430	1,212	700
Primary outcome	All-cause mortality	Cardiac death, MI or hospitalisation for cardiac cause	All-cause mortality	All-cause mortality, hospitalisation for HF
LVEF at enrolment	24%	27%	28%	27%
Revascularisation method	CABG and PCI	CABG and PCI	CABG	PCI
Follow-up (median)	59 months	5 years	4.7 years[12] 9.8 years[13]	41 months
Outcome	No significant benefit of revascularisation over OMT	No significant difference between PET-guided and standard strategies	No benefit of CABG over OMT at 5 years After 10 years CABG was associated with a lower all-cause mortality than OMT (0.72; 95% CI [0.64–0.82]; p<0.001)	No significant benefit of revascularisation over OMT



Increase of LVEF after PCI can improve late outcome!

ORIGINAL ARTICLE

Change in Left Ventricular Ejection Fraction With Coronary Artery Revascularization and Subsequent Risk for Adverse Cardiovascular Outcomes

Raghava S. Velagaleti, MD, MPH; Joy Vetter, MA, MPH; Rachel Parker, MPH; Katherine E. Kurgansky, MPH; Yan V. Sun, PhD; Luc Djousse, MD, DSc; J. Michael Gaziano, MD; David Gagnon, MD, PhD*; Jacob Joseph, MD*

BACKGROUND: Coronary revascularization is recommended to treat ischemic cardiomyopathy. However, the relations of revascularization-associated ejection fraction (EF) change to subsequent outcomes have not been elucidated.

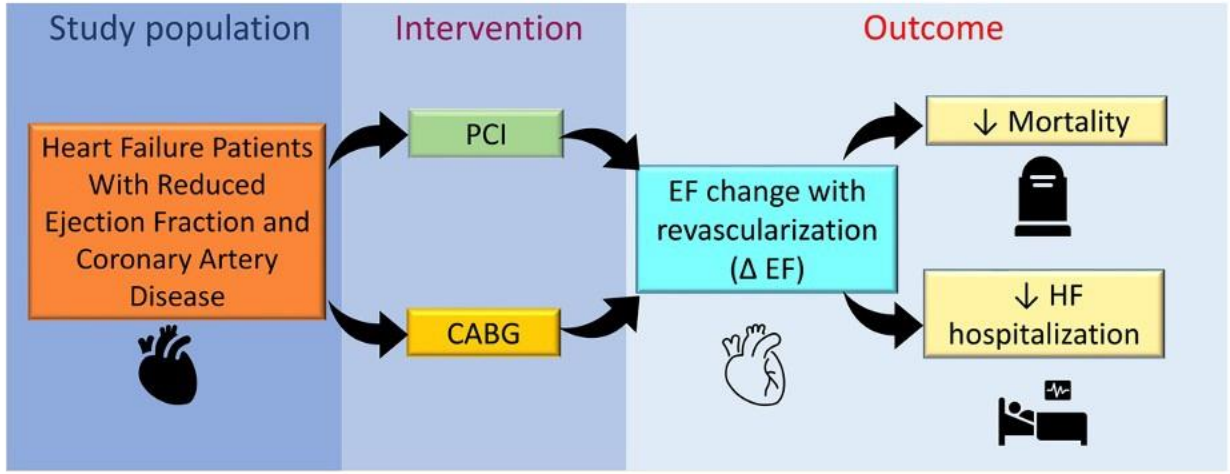
METHODS: In 10 071 veterans (mean age 67 years; 1% women; 15% non-White) who underwent a first percutaneous coronary intervention (PCI) or coronary artery bypass grafting between January 1, 1995, and December 31, 2010, and had prerevascularization and postrevascularization EF measured, we calculated delta-EF (postprocedure EF−preprocedure EF). We related delta-EF as a continuous measure and as categories (≤−5, −5<delta-EF<0, delta-EF=0, 0<delta-EF<5, and delta-EF≥5) to death (using Cox regression) and heart failure hospitalization days (using negative binomial regression) in multivariable-adjusted models, for total sample, and PCI and coronary artery bypass grafting strata.

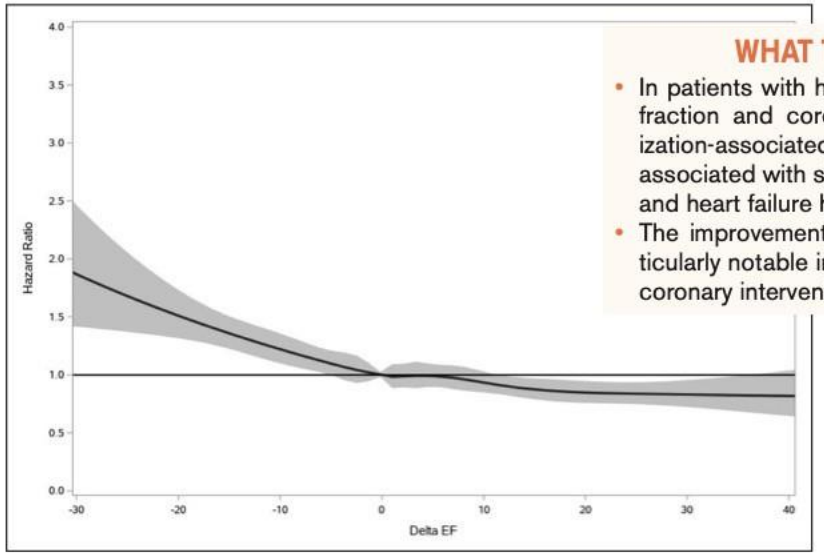
RESULTS: Over follow-up (mean/maximum 5/14 years) 56% died. Each 5% improvement in delta-EF was associated with statistically significant reductions in death and heart failure hospitalization days of 5% (95% CI, 3%–7%) and 10% (95% CI, 5%–15%), respectively, in the total sample and 6% (95% CI, 4%–8%) and 10% (95% CI, 5%–16%), respectively, in the PCI subgroup. Patients in the highest delta-EF category had 27% (95% CI, 19%–34%) lower mortality (30% [95% CI, 21%–37%] lower in PCI stratum) and ≈40% lower heart failure hospitalization days in total sample and PCI stratum, compared with those in the lowest category. Relations of delta-EF and outcomes in coronary artery bypass grafting subgroup did not reach statistical significance.

CONCLUSIONS: Revascularization-associated EF improvement was associated with significant reductions in mortality and heart failure hospitalization burden, particularly in the PCI subgroup.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: coronary artery bypass ■ heart failure ■ hospitalization ■ mortality ■ percutaneous coronary intervention



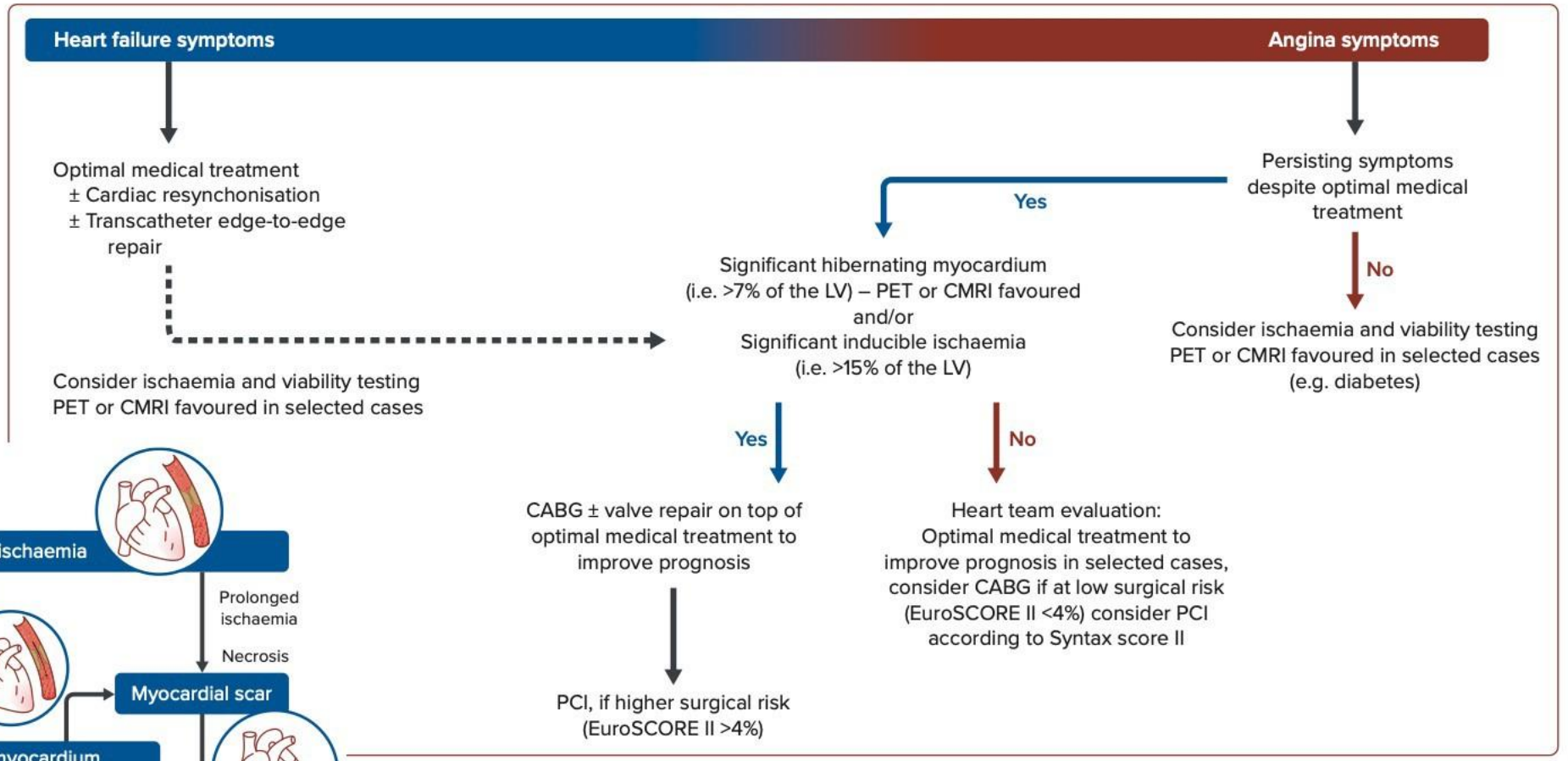


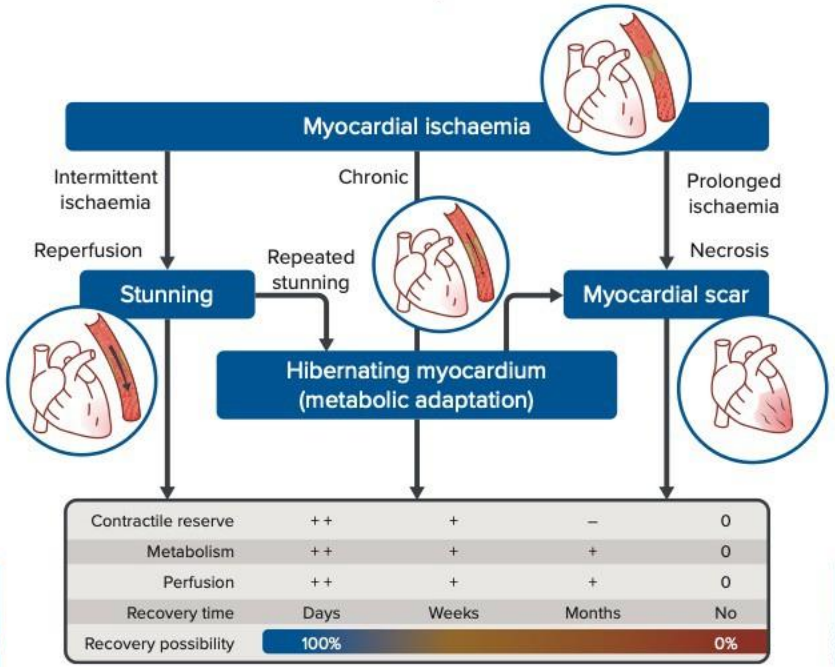
WHAT THE STUDY ADDS

- In patients with heart failure with reduced ejection fraction and coronary artery disease, revascularization-associated change in ejection fraction was associated with significantly lower rates of mortality and heart failure hospitalization burden.
- The improvements in clinical outcomes were particularly notable in those undergoing percutaneous coronary intervention.

Velagaleti RS, et al. Circ Cardiovasc Interv. 2022 Apr;15(4):e011284.

Management for HFrEF with Ischaemic Cardiomyopathy



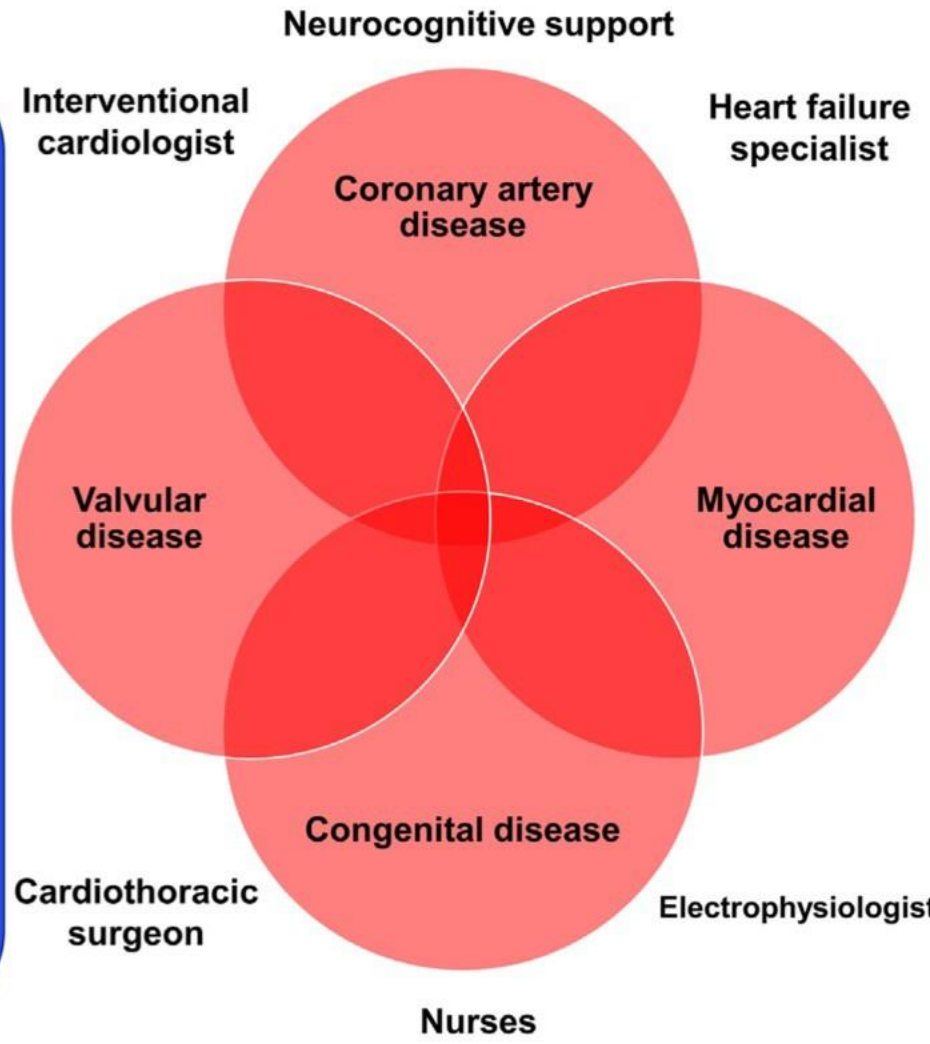


J of Asian Pacific Society of Cardiology 2024;3:e14doi: 10.15420/japsc.2024.05

PCI is only one part of all HF transcatheter interventions

Acute Heart Failure Treatment

- Medical therapy
- Coronary artery revascularization
- Transvalvular left ventricular support/unloading
- Intra-aortic hemodynamic support
- Extracorporeal membrane oxygenation
- Right ventricular support



Chronic Heart Failure Treatment

- Medical therapy
- Coronary artery revascularization
- Cardiac resynchronization therapy
- Transcatheter valve therapy
- Shunt therapy
- Left ventricular remodeling
- Cardiorenal axis therapy
- Cardiac contractility modulation
- Neuromodulation
- Lymphatic drainage enhancement

doi: 10.1016/j.jscai.2023.101214

PCI can be considered as a preventive tool?

AMERICAN COLLEGE of CARDIOLOGY

PREVENT

Preventive Percutaneous Coronary Intervention (PCI) vs. Optimal Medical Therapy (OMT) Alone For the Treatment of Vulnerable Atherosclerotic Coronary Plaques

Investigator-Initiated, Multicenter, Open-Label, Randomized, Controlled Trial

2024

OBJECTIVE: To evaluate the effects of preventive PCI with OMT vs. OMT alone on major adverse cardiovascular events in patients with non-flow-limiting, high-risk, vulnerable plaques.

1,606 PATIENTS

INCLUSION CRITERIA: Adults with non-flow limiting (fractional flow reserve >0.80) vulnerable coronary plaques identified by intracoronary imaging.

PCI + OMT (N=803) vs. OMT (N=803)

PRIMARY ENDPOINT

COMPOSITE OF DEATH FROM CARDIAC CAUSES, TARGET-VESSEL MYOCARDIAL INFARCTION (MI), ISCHEMIA-DRIVEN TARGET-VESSEL REVASCULARIZATION, OR HOSPITALIZATION FOR UNSTABLE OR PROGRESSIVE ANGINA ASSESSED AT TWO YEARS.

3 PATIENTS (0.4% IN PCI GROUP) vs. **27 PATIENTS (3.4% IN OMT GROUP)**

SECONDARY ENDPOINT

DEATH FROM ANY CAUSE:
HAZARD RATIO (HR), 0.61 (95% CI, 0.35-1.06)

COMBINED DEATH FROM ANY CAUSE, ALL MIs, ANY REVASCULARIZATION: HR, 0.69 (95% CI, 0.50-0.95)

CONCLUSION

In patients with non-flow limiting vulnerable coronary plaques, preventive PCI reduced major adverse cardiac events arising from high-risk vulnerable plaques compared with OMT alone.

Park S-J, Ahn J-M, Kang D-Y, et al. Preventive Percutaneous Coronary Intervention Versus Optimal Medical Therapy Alone For The Treatment Of Vulnerable Atherosclerotic Coronary Plaques (PREVENT): A Multicentre, Open-Label, Randomised Controlled Trial. Presented at ACC.24.

Developed and reviewed by: Raymond Yeow, MD, and Kent Brummel, MD

PREVENT Trial

Any Epicardial Coronary Stenosis with *FFR >0.80* and with *Two* of the following

1. TCFA by OCT or VH-IVUS
2. IVUS MLA ≤4.0mm²
3. IVUS Plaque Burden >70%
4. Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>315)

R

BVS or DES +OMT N=800

OMT N=800

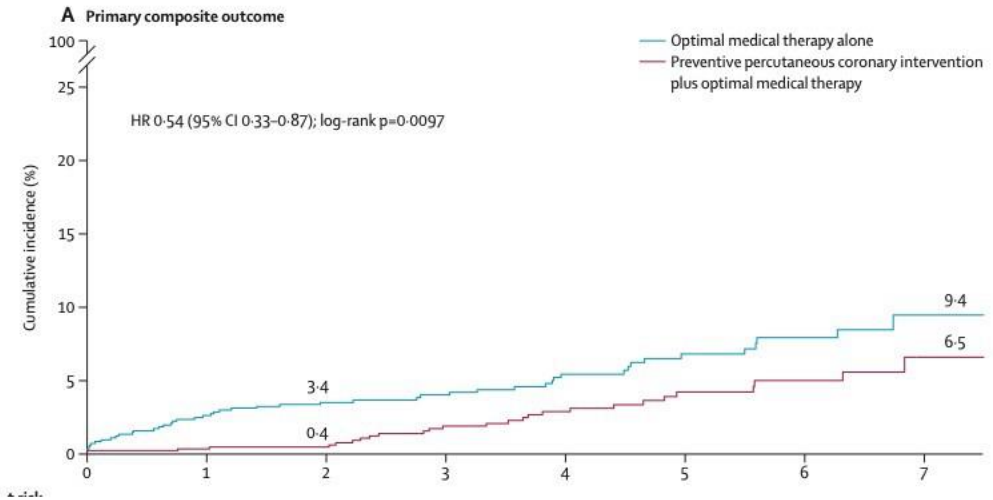
Primary endpoint : *Target Vessel Failure at 2 years*
(A Composite of death from cardiac causes, target-vessel MI, ischemia-driven target-vessel revascularization, or hospitalization for unstable or progressive angina)

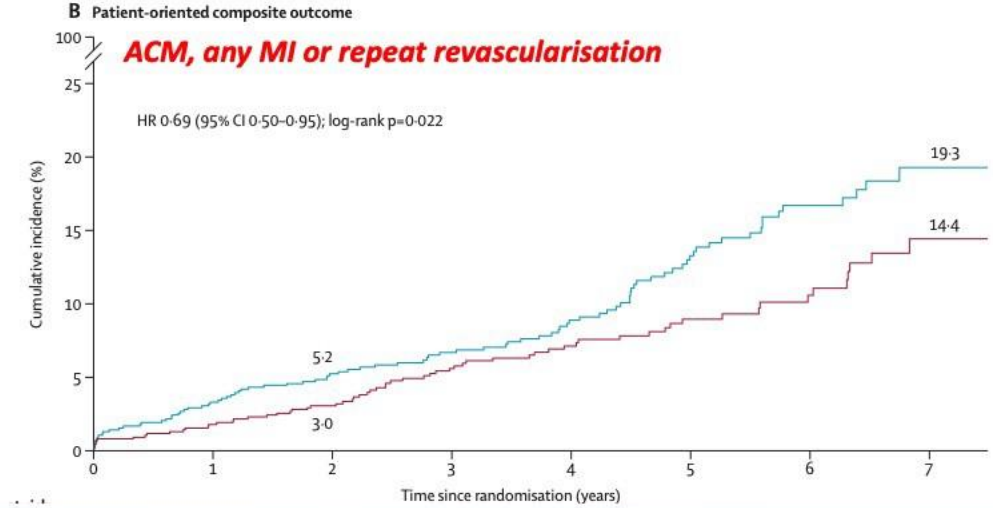
WHAT IS KNOWN?

- Vulnerable plaque is defined as atherosclerotic coronary plaque responsible for future acute coronary syndrome.
- Vulnerable plaques can be identified by invasive intracoronary imaging such as IVUS, OCT, and NIRS or noninvasive coronary CT angiography.
- Vulnerable plaques have morphologic characteristics of large plaque burden, small minimal luminal area, lipid-rich plaque, and thin fibrous cap.
- Medical treatment using lipid-lowering therapy has been a cornerstone of the treatment of the vulnerable plaque.

WHAT IS UNKNOWN?

- The association between changes in plaque composition and thickness of fibrous cap and long-term cardiovascular outcomes.
- The effect of local preventive PCI on the vulnerable plaque should be examined in a large-sized randomized controlled trial with longer-term follow-up.





Park SJ, et al. Lancet. 2024 May 4;403(10438):1753-1765. doi: 10.1016/S0140-6736(24)00413-6.

Conclusions

Towards Holistic & Comprehensive Cardiac Care

PCI plays a very important role in restoring heart health:

- In acute settings: PCI obviously saves lives and preserves heart function.
- In chronic settings: PCI can improve patients outcomes and angina symptoms.
- *However, the benefits of PCI diminish when the ischemic burden is low, and the comorbidity burden, including heart failure, is high.*

PCI has the ability to both treat and prevent MI.

- Nevertheless, PCI cannot stand alone without optimal medical therapy.
- Despite its importance, PCI remains only one component of transcatheter therapy.

Thank you very much for your attention!