Giảm suy tim sau nhồi máu cơ tim

- Từ điều trị trước viện đến tối ưu ngay trong giai đoạn cấp

PGS.TS.BS. Nguyễn Ngọc Quang, FASCC, FSCAI

Bộ môn Tim mạch – Trường Đại học Y Hà Nội

Đơn vị Chăm sóc Mạch vành C7 – Viện Tim mạch Việt Nam

Email: quangtm@gmail.com

HỘI TIM MẠCH HỌC VIỆT NAM

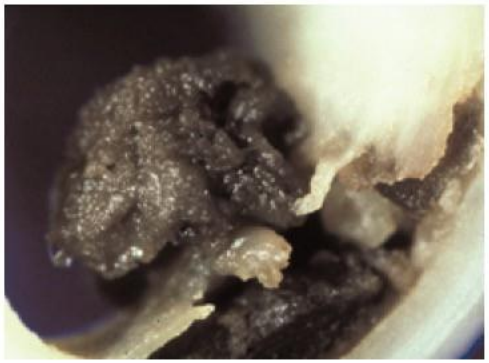
HỘI NGHỊ KHOA HỌC TIM MẠCH TOÀN QUỐC 2017

Thông báo về xung đột lợi ích

Trong 12 tháng qua, tôi, Nguyễn Ngọc Quang, có thể có một số xung đột lợi ích với các nội dung trình bày trong bài báo cáo này:

Liên quan/lợi ích	Công ty
• Báo cáo viên	• AstraZeneca, Sanofi, Novartis, MSD, Servier, Merck, Abbott
• Tư vấn/ Ban cố vấn	• N/A

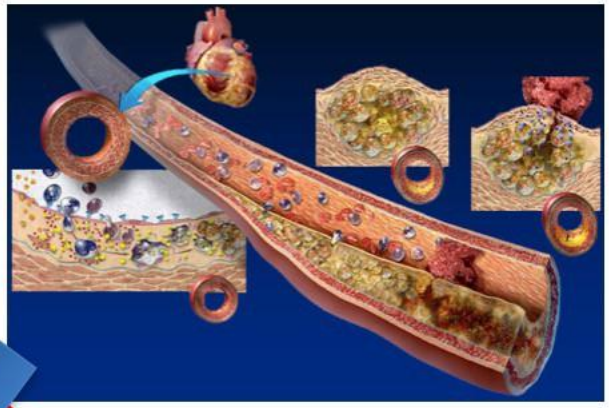
Huyết khối trên mảng xơ vữa nứt/loét/vôi là trung tâm của nhồi máu cơ tim

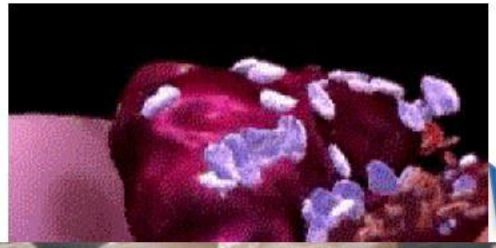


Nứt loét mảng xơ vữa

↓

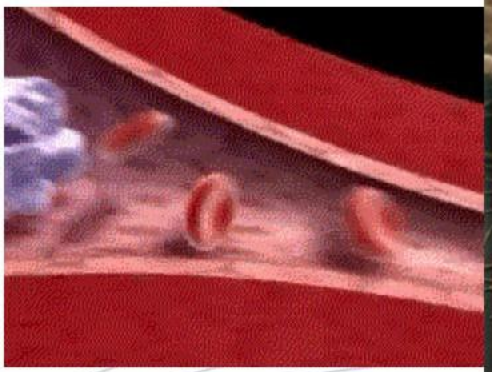
Hình thành huyết khối





Cơ học

Hoá học

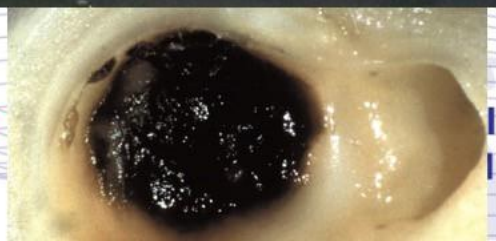


Tắc mạch đoạn xa

Phóng thích Serotonin

↓

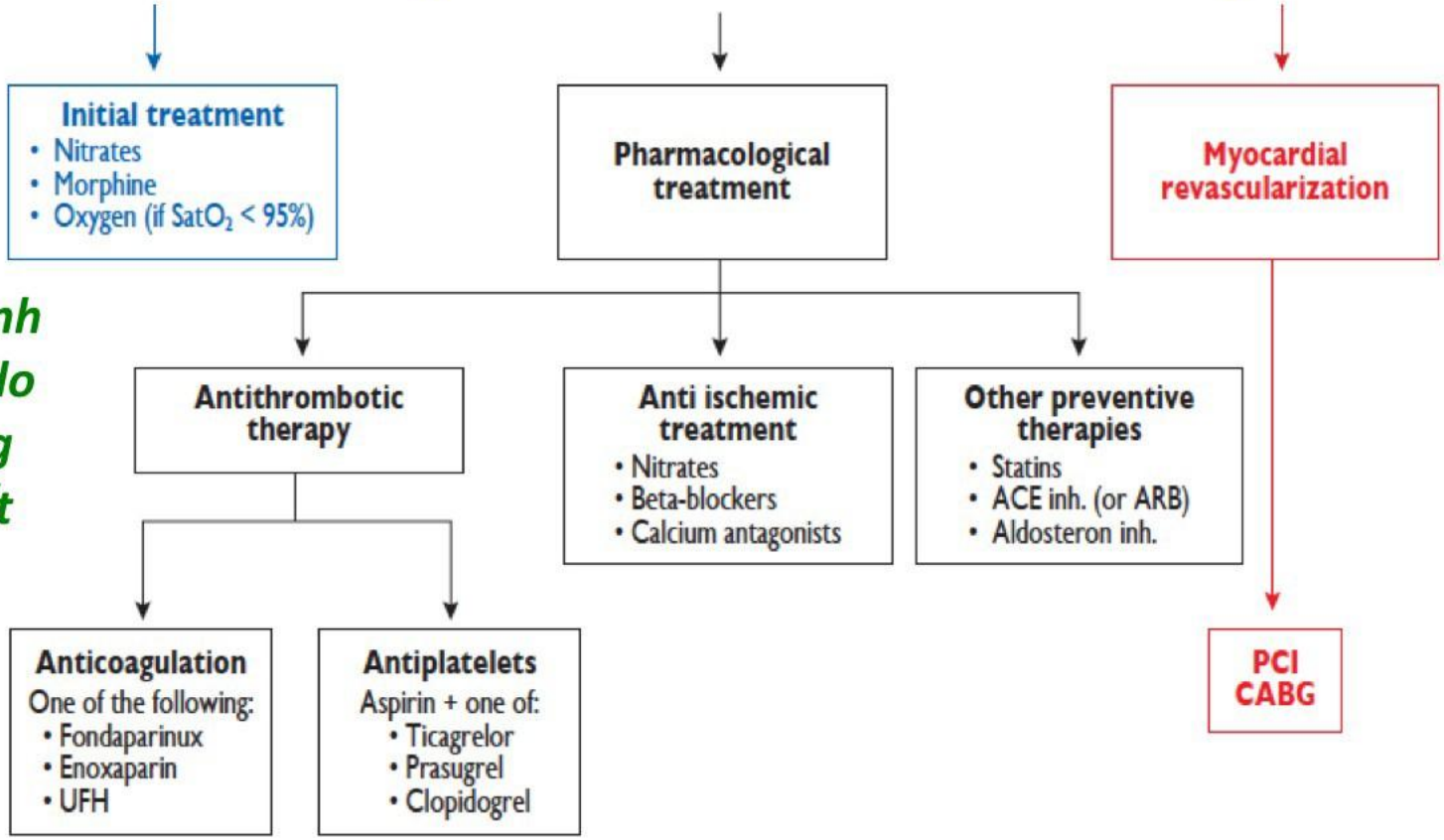
Tắc nghẽn cơ học

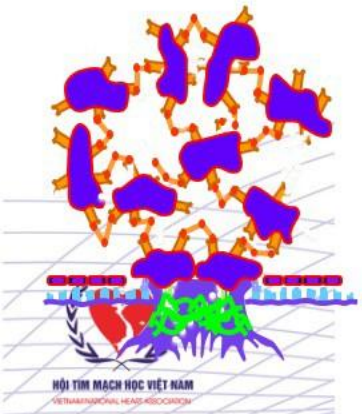


Co thắt mạch

Mục đích điều trị nhồi máu cơ tim cấp

Mục đích để ổn định tình trạng bất ổn do mảng xơ vữa đang nứt loét kèm huyết khối gây ra !!!



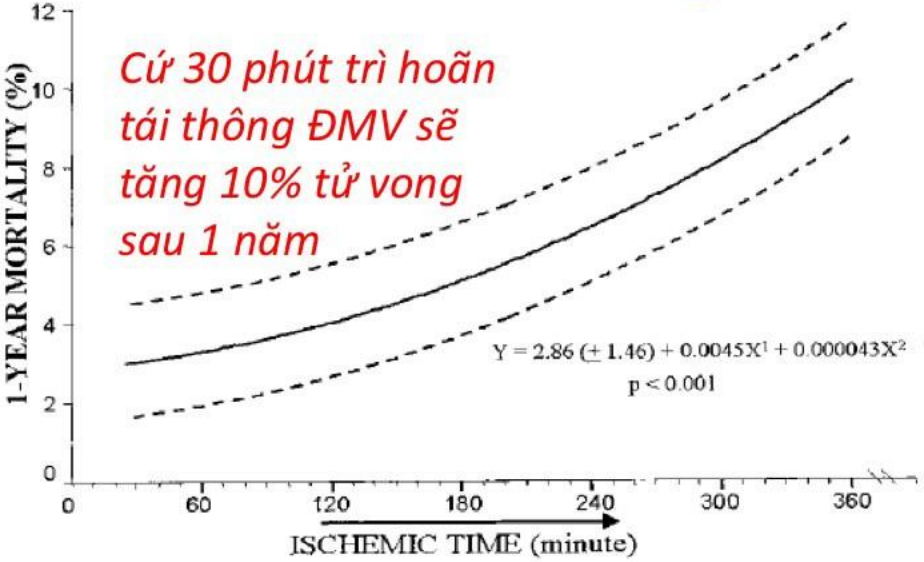


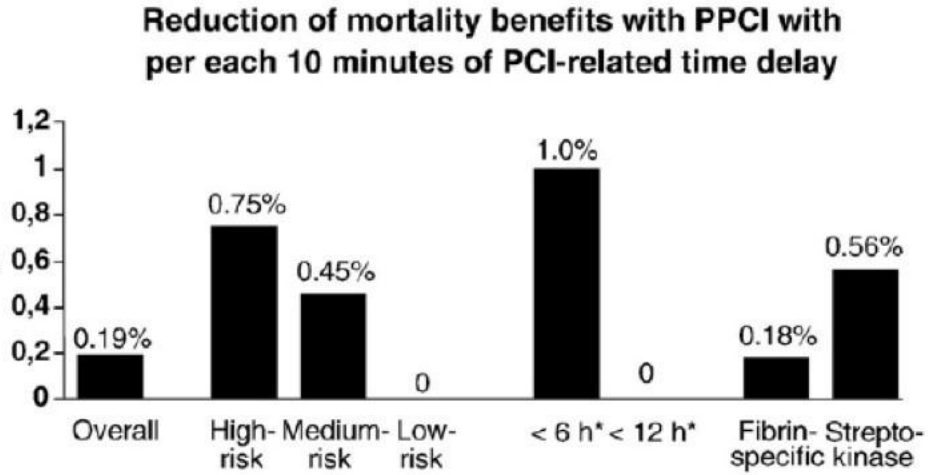
Kháng ngưng tập tiểu cầu	*Aspirin + Ticagrelor/Prasugrel/Clopidogrel*
Kháng đông	*Enoxaparin/Heparin/Fondaparinux/Bivalirudin*
Hạ lipid và ổn định xơ vữa	*Statins tích cực*
Tái thông động mạch vành	***Can thiệp qua da/Phẫu thuật bắc cầu chủ vành***
Giảm tải thất và tái cấu trúc thất	*Kháng hệ RAS (ACEI/ARB/MRA)/Chẹn beta*
Chống thiếu máu (đau thắt ngực)	*Nitroglycerin/Chẹn beta/Chẹn kênh canxi/….*

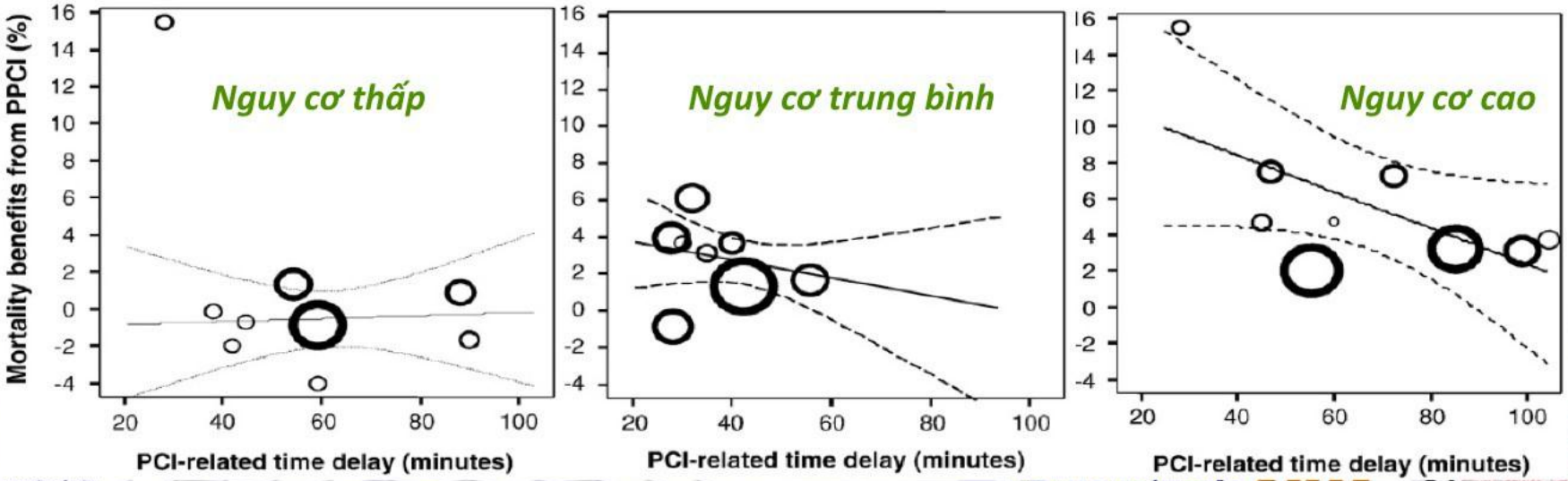
Trì hoãn tái thông mạch máu lớn sẽ gây hại

Với STEMI: Thời gian là cơ tim và Cơ tim là sự sống!

Cứ 30 phút trì hoãn tái thông ĐMV sẽ tăng 10% tử vong sau 1 năm







De Luca G, et al. Circulation, 2004;109(10):1223-5.
De Luca G, et al. Am J Emerg Med, 2009;27(6):712-9.

Thúc đẩy tiêu sợi huyết phối hợp can thiệp cho *STEMI* khi có nguy cơ trì hoãn tái thông

STEMI < 12 giờ

Can thiệp mạch vành chậm > 90-120 phút

→ **Tiêu sợi huyết tức thời và can thiệp ĐMV sau 3-24 giờ nếu không chống chỉ định****

NMCT đến sớm < 3 giờ

NMCT lớn hoặc thành trước

*Nguy cơ chảy máu thấp**

Can thiệp mạch vành chậm > 60 phút

→ ***Tiêu sợi huyết tức thời và can thiệp ĐMV sau 3-24 giờ nếu không chống chỉ định****

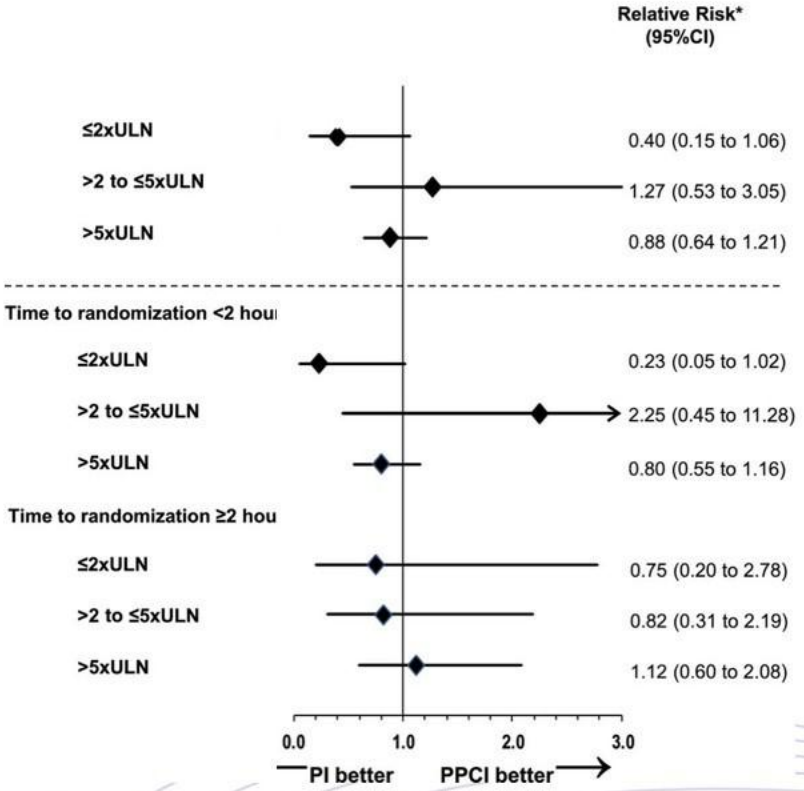
Can thiệp mạch vành ngay < 90-120 phút

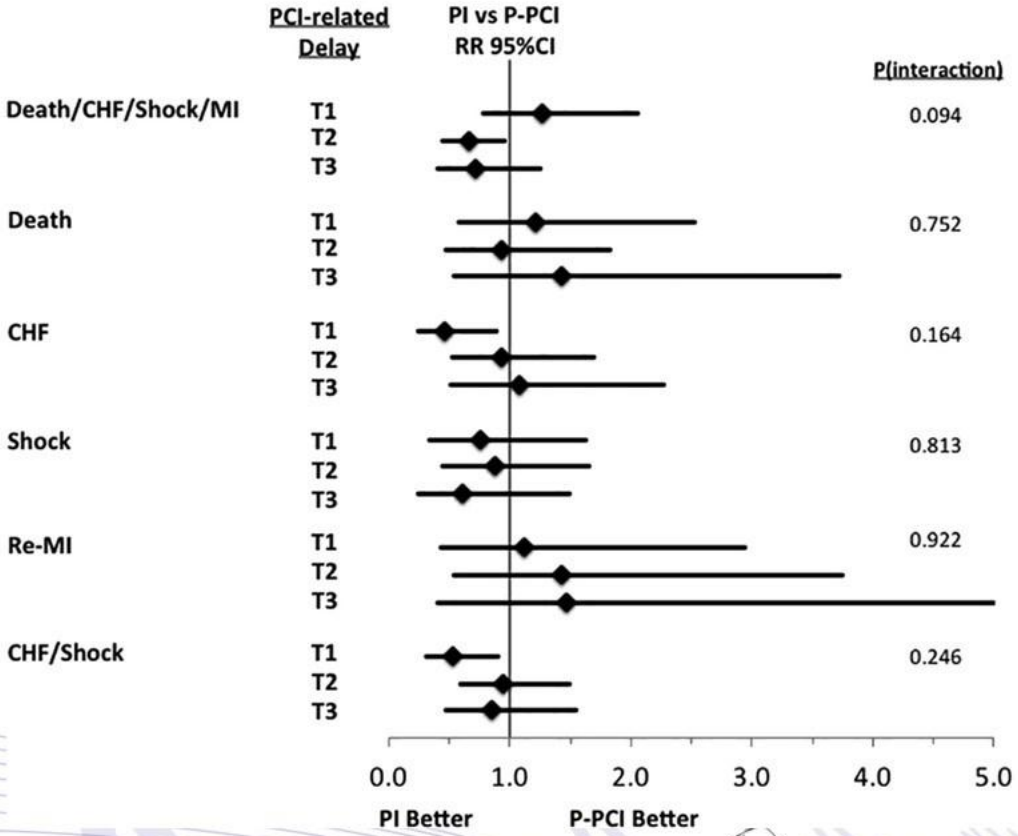
→ **Can thiệp mạch vành cấp thì đầu**

** Người bệnh trẻ tuổi < 75, không có tiền sử chảy máu từ trước*

*** Chỉnh liều thuốc tiêu sợi huyết giống thử nghiệm STREAM*

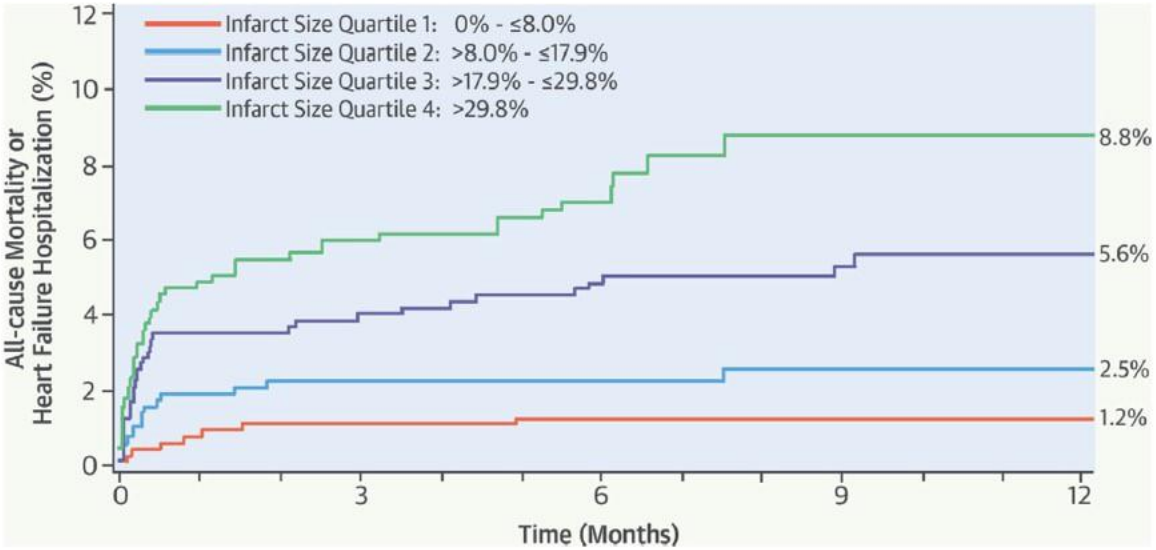
Tiêu sợi huyết phối hợp can thiệp cho STEMI giảm ổ nhồi máu lớn, giảm suy tim/sốc tim

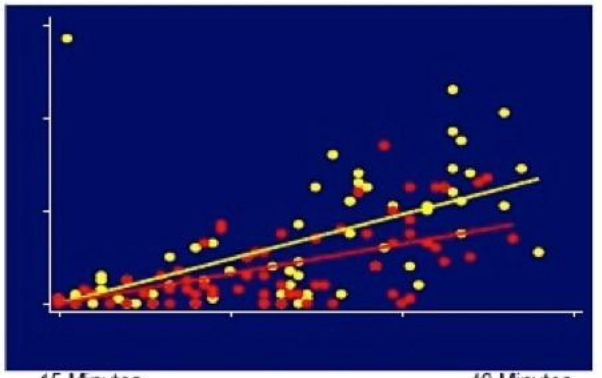


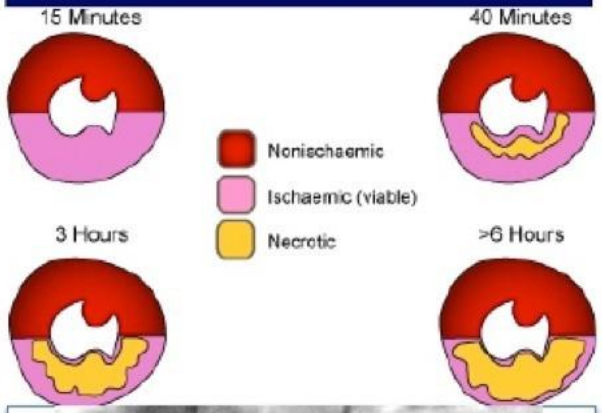


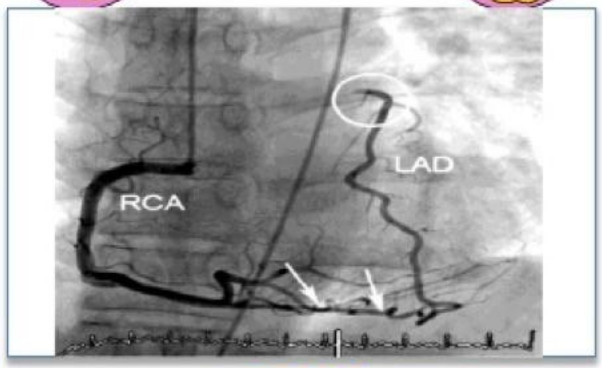
Shavadia J, et al. J Am Heart Assoc, 2015;4(8):e002049.
Gershlick AH, et al. Heart 2015;101:692–8.

Tiên lượng dài sẽ phụ thuộc vào diện tích sẹo









Các yếu tố xác định kích thước ổ nhồi máu

- Vùng cơ tim có nguy cơ
- Thời gian thiếu máu
- Tưới máu cho vùng nguy cơ (mạng lưới bàng hệ...)
- Huyết động đại tuần hoàn

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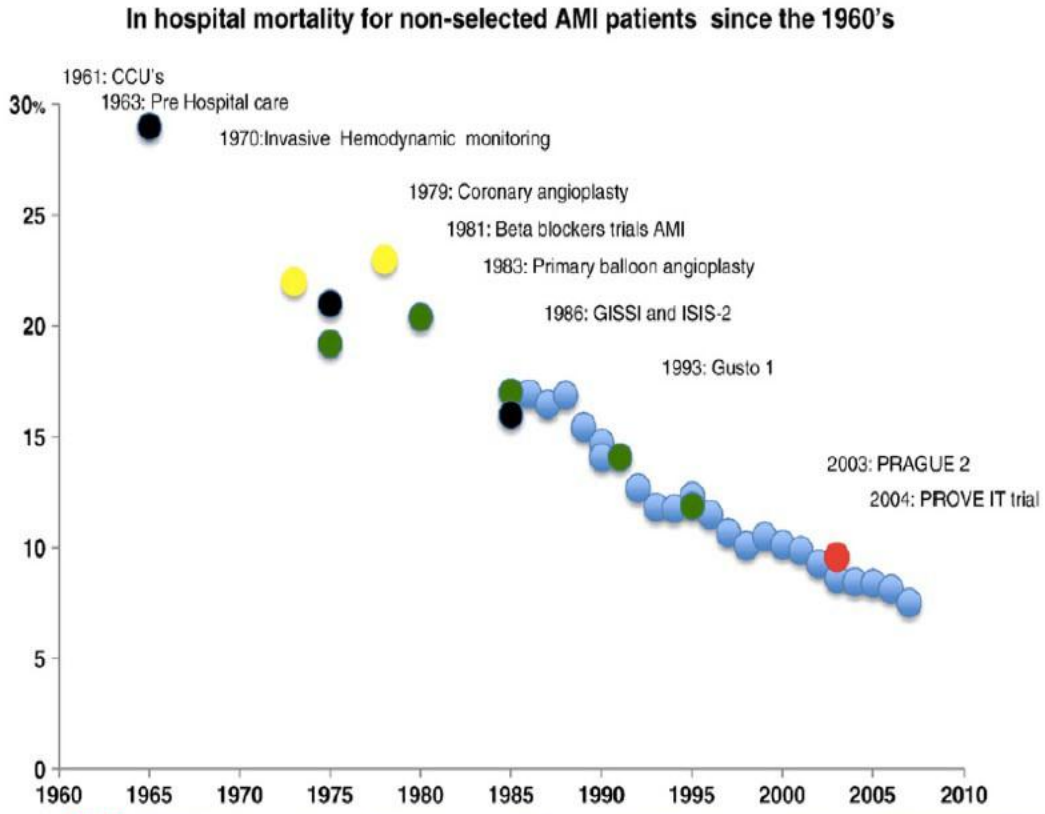
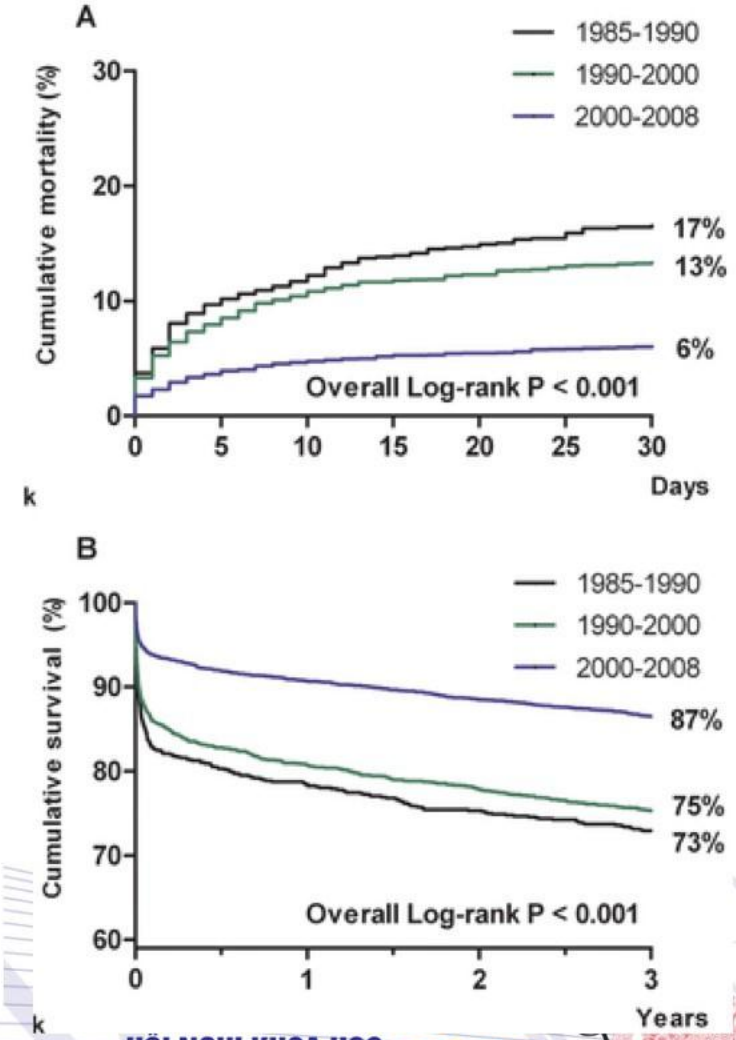
Stone GW et al. J Am Coll Cardiol, 2016;67(14):1674–83.

Nhu cầu giảm biến cố ngoài việc giảm tử vong trong nhồi máu cơ tim cấp

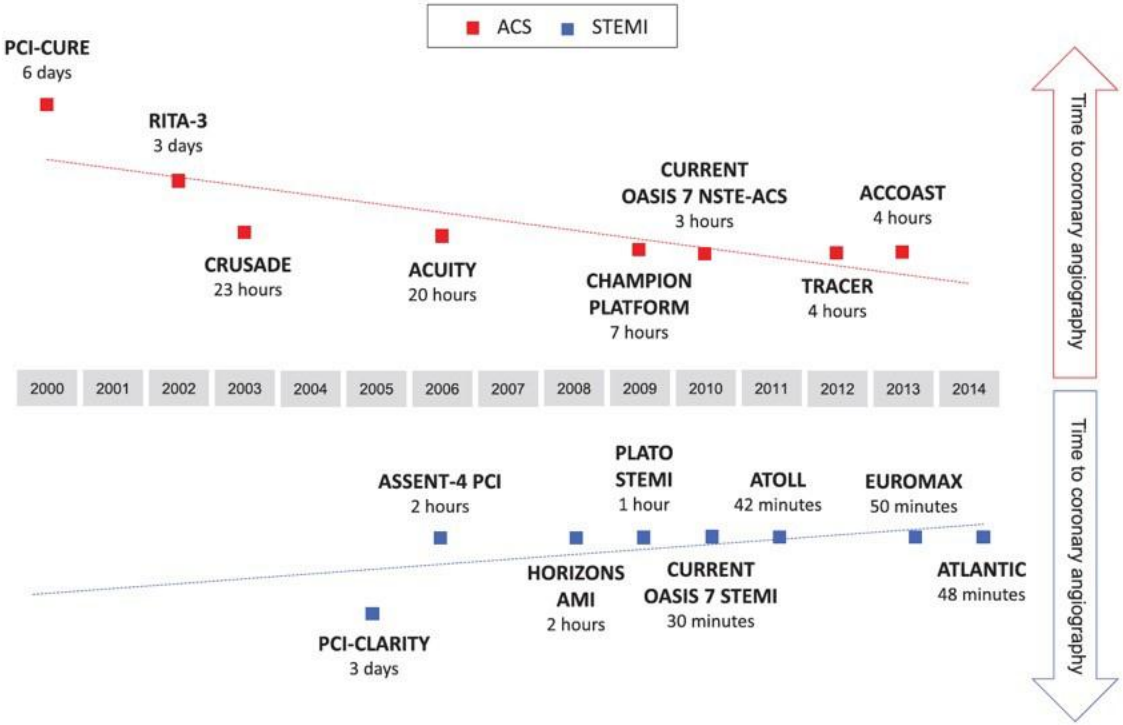
Tử vong trong viện do NMCT ngày càng giảm nhờ tối ưu điều trị trong giai đoạn cấp

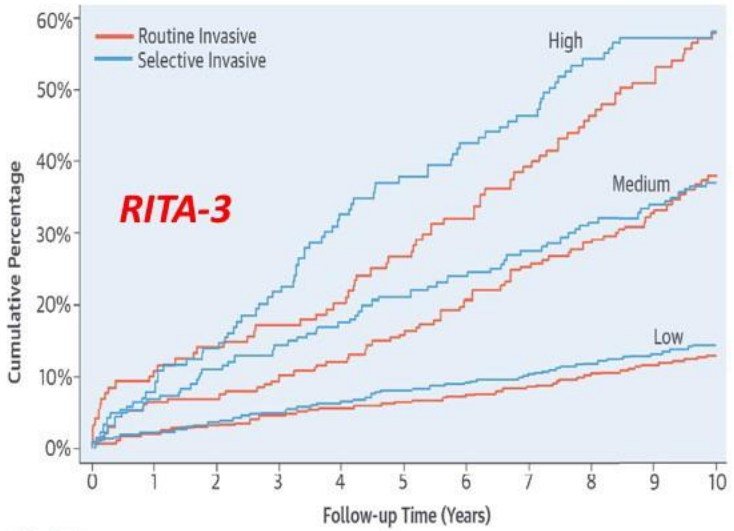


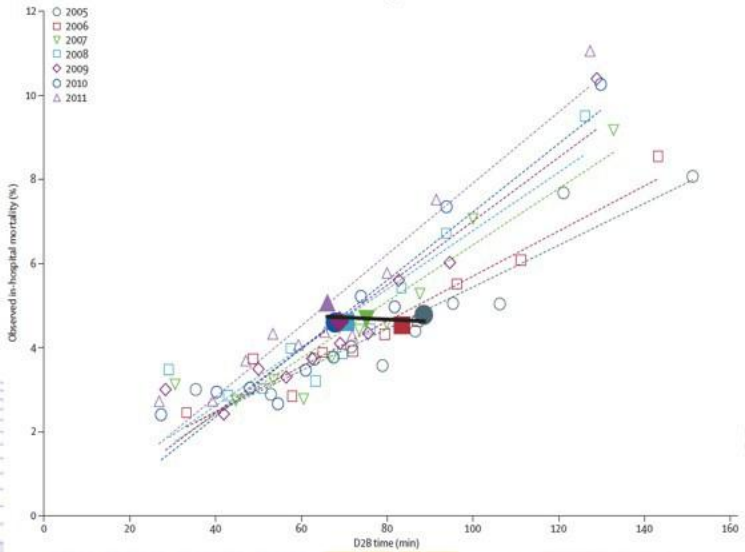


Teixeira R, et al. Int J Cardiol, 2013;167(5):1825-34.
Nauta ST et al. PLoS One 2011;6:e26917

Tái thông sớm ĐMV cải thiện rõ tỷ lệ sống còn







Capodanno D, et al. Circ Cardiovasc Interv, 2015;8(3):e002301.
Nallamothu BK, et al. Lancet, 2015;385(9973):1114-22.
Henderson RA, et al. J Am Coll Cardiol, 2015;66(5):511–20.

Thời điểm can thiệp ĐMV được đẩy sớm lên

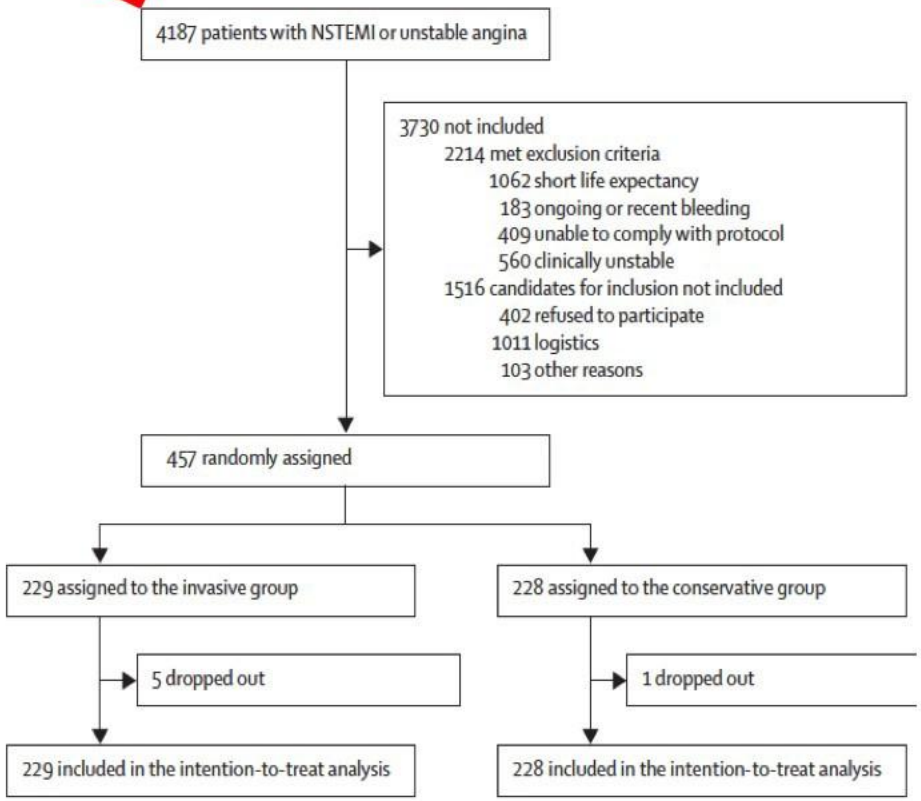
COR	LOE	*2007 AHA/ACC NSTE-ACS Guideline. J Am Coll Cardiol, 2007;50(7):e1-e157.*
I	B	An early invasive strategy is indicated in UA/NSTEMI patients who have refractory angina or hemodynamic or electrical instability
I	A	An early invasive strategy is indicated in initially stabilized UA/NSTEMI patients who have an elevated risk for clinical events
IIa	B	In initially stabilized patients, an ischemia-guided strategy may be considered for patients with NSTE-ACS who have an elevated risk for clinical events

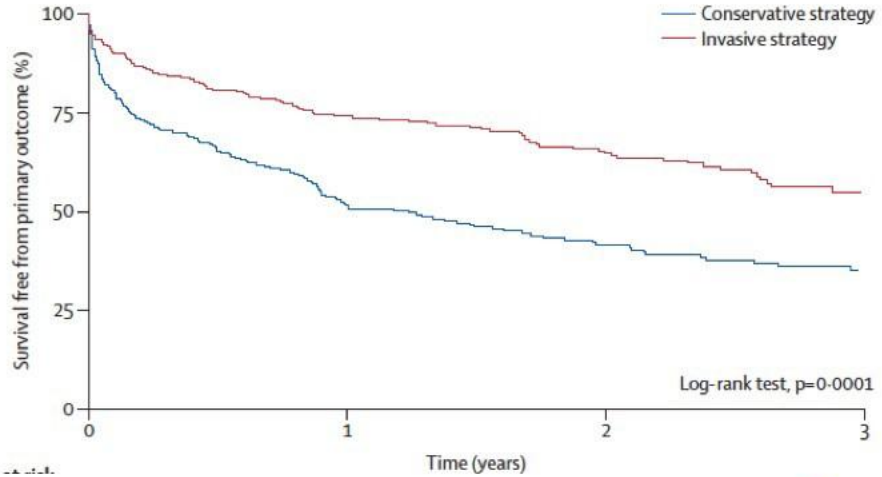
COR	LOE	*2014 AHA/ACC NSTE-ACS Guideline. J Am Coll Cardiol, 2014;64(24):e139-228*
I	A	An urgent/immediate invasive strategy (within 2 hours) is indicated in patients with NSTE-ACS who have refractory angina or hemodynamic or electrical instability
I	B	An early invasive strategy (within 24 hours) is indicated in initially stabilized patients with NSTE-ACS who have an elevated risk for clinical events
IIa	B	In initially stabilized patients, an ischemia-guided strategy may be considered for patients with NSTE-ACS who have an elevated risk for clinical events

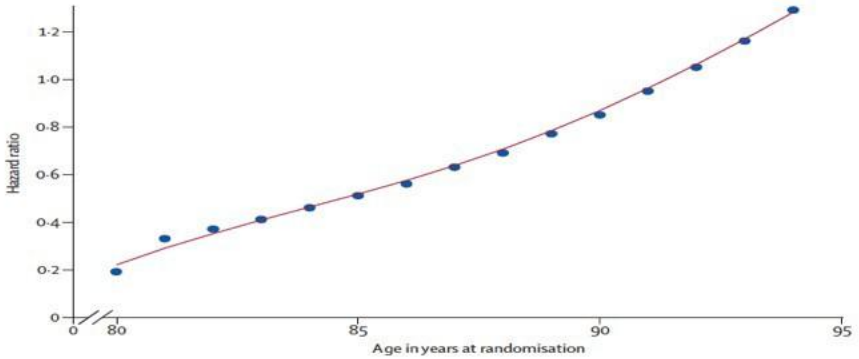
Can thiệp sớm kể cả cho người cao tuổi mắc ACS

Thử nghiệm After Eighty

NEW







Interpretation In patients aged 80 years or more with NSTEMI or unstable angina, an invasive strategy is superior to a conservative strategy in the reduction of composite events. Efficacy of the invasive strategy was diluted with increasing age (after adjustment for creatinine and effect modification). The two strategies did not differ in terms of bleeding complications.

Tegn N, et al. Lancet, 2016;387(10023):1057-65.

STEMI không chỉ tái thông sớm mà còn toàn bộ

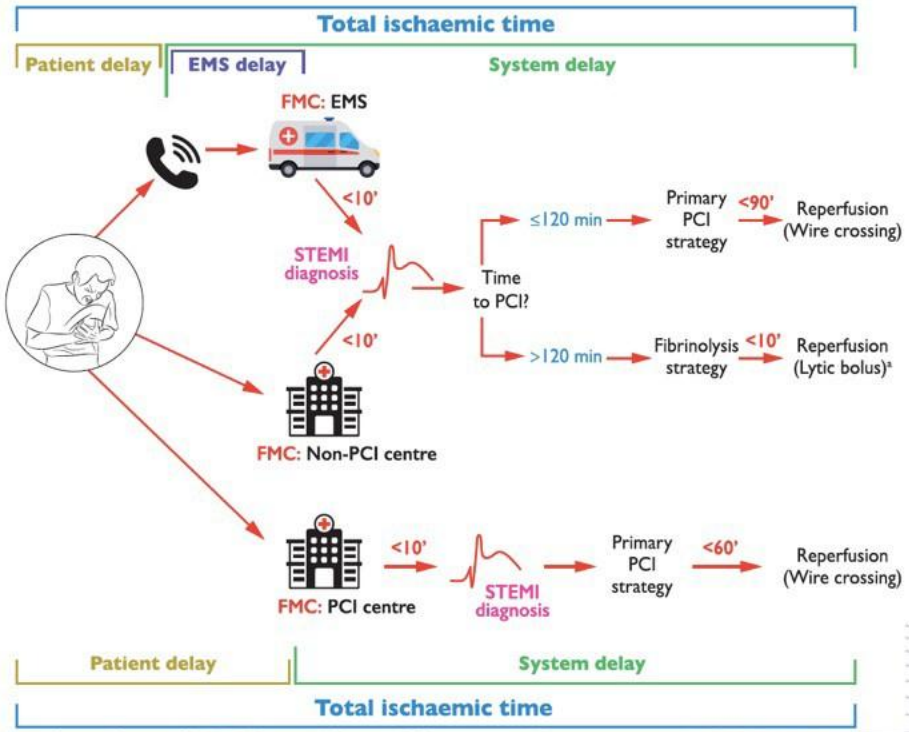
Xu thế mở thông ĐM kô thủ phạm trong STEMI

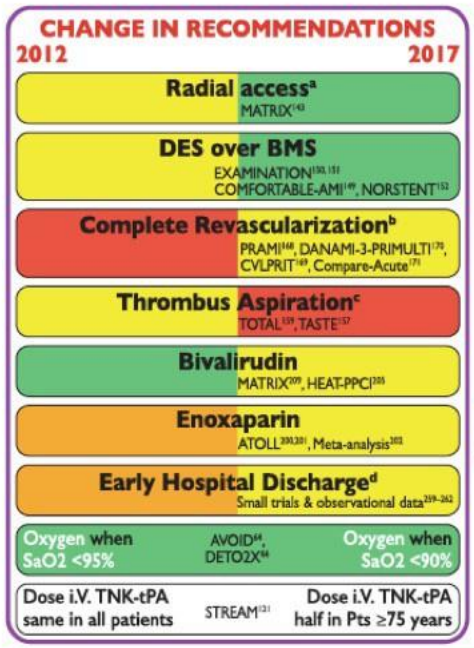
COR	LOE	*2013 AHA/ACC STEMI Guideline. J Am Coll Cardiol, 2013;61:e78–140*
III - Harm	B	PCI should not be performed in a noninfarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable

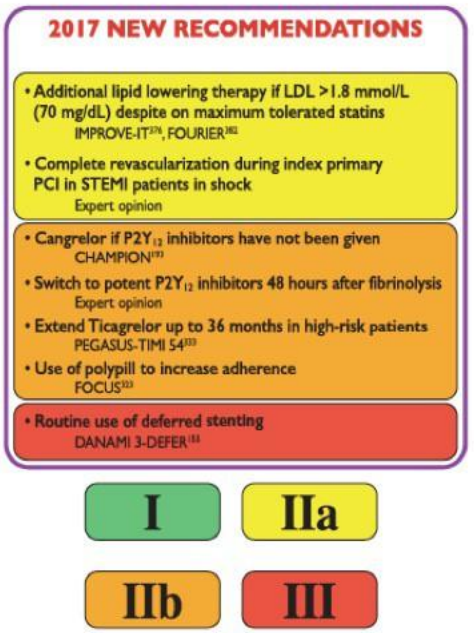
PRAMI
CvLPRIT
DANAMI-3
PRIMULTI
(PRAGUE-13)

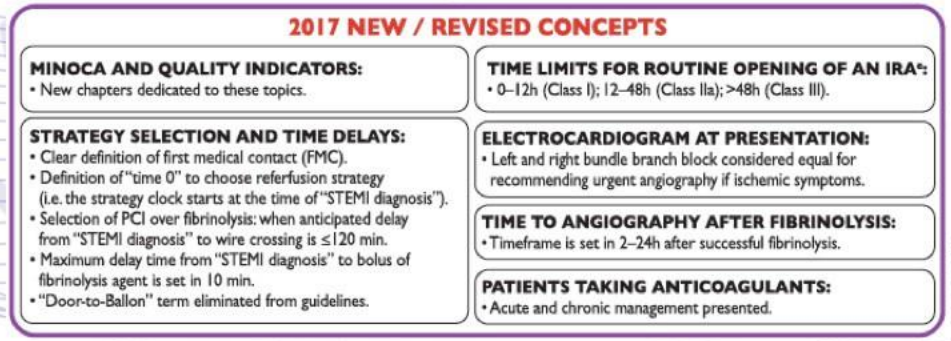
COR	LOE	*2015 AHA/ACC STEMI Guideline. J Am Coll Cardiol, 2016;67:1235–50.*
IIb	B-R	PCI of a noninfarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned staged procedure

Xác định ngay có hay không NMCT cấp để can thiệp sớm và toàn diện, giảm thiểu tác hại của huyết khối, *giảm tử vong và diện tích NMCT!*









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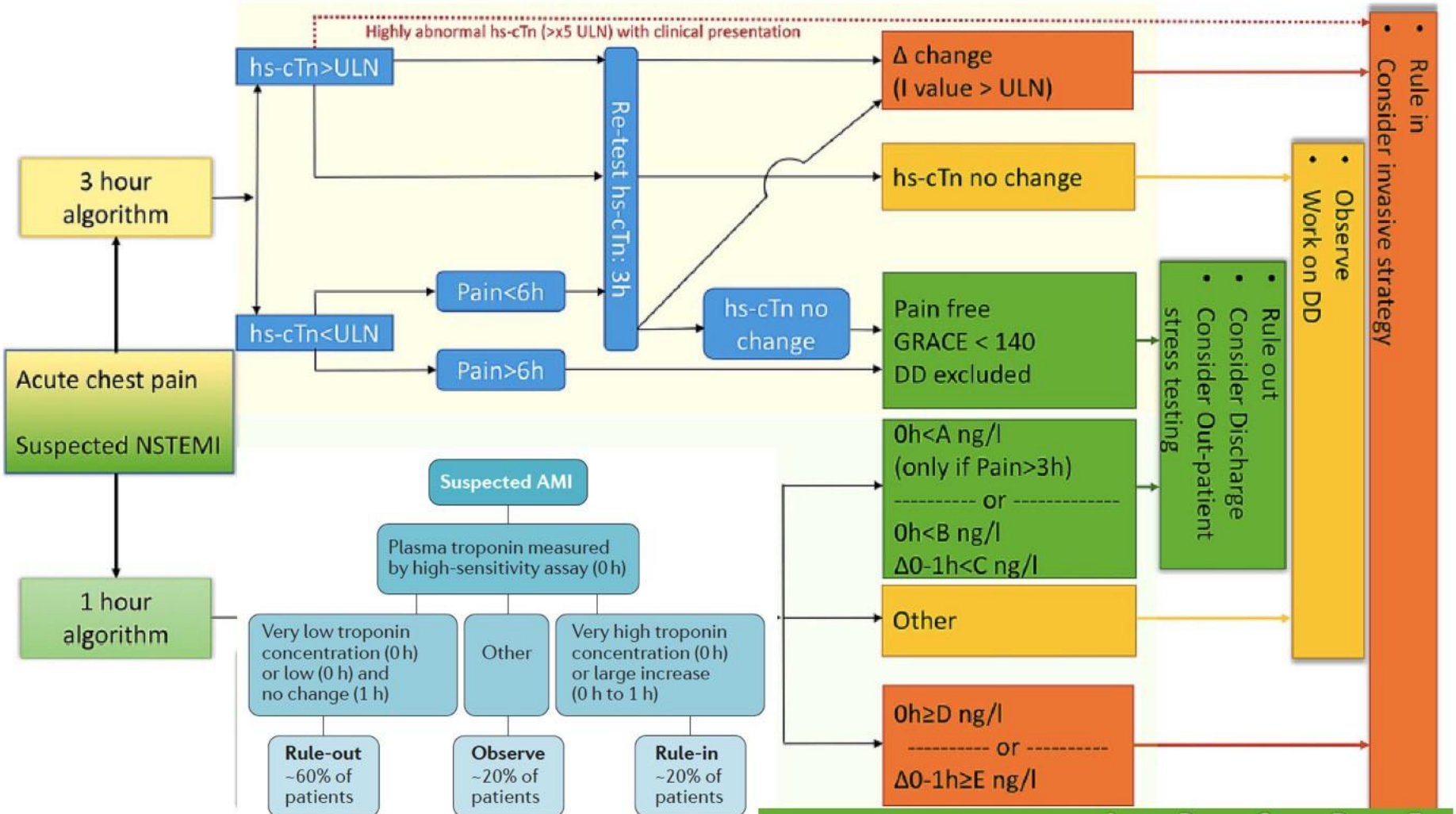
Ibanez B, et al. Eur Heart J, 2017.
doi:10.1093/eurheartj/ehx393

Xác định/loại trừ NMCT bằng chỉ điểm sinh học

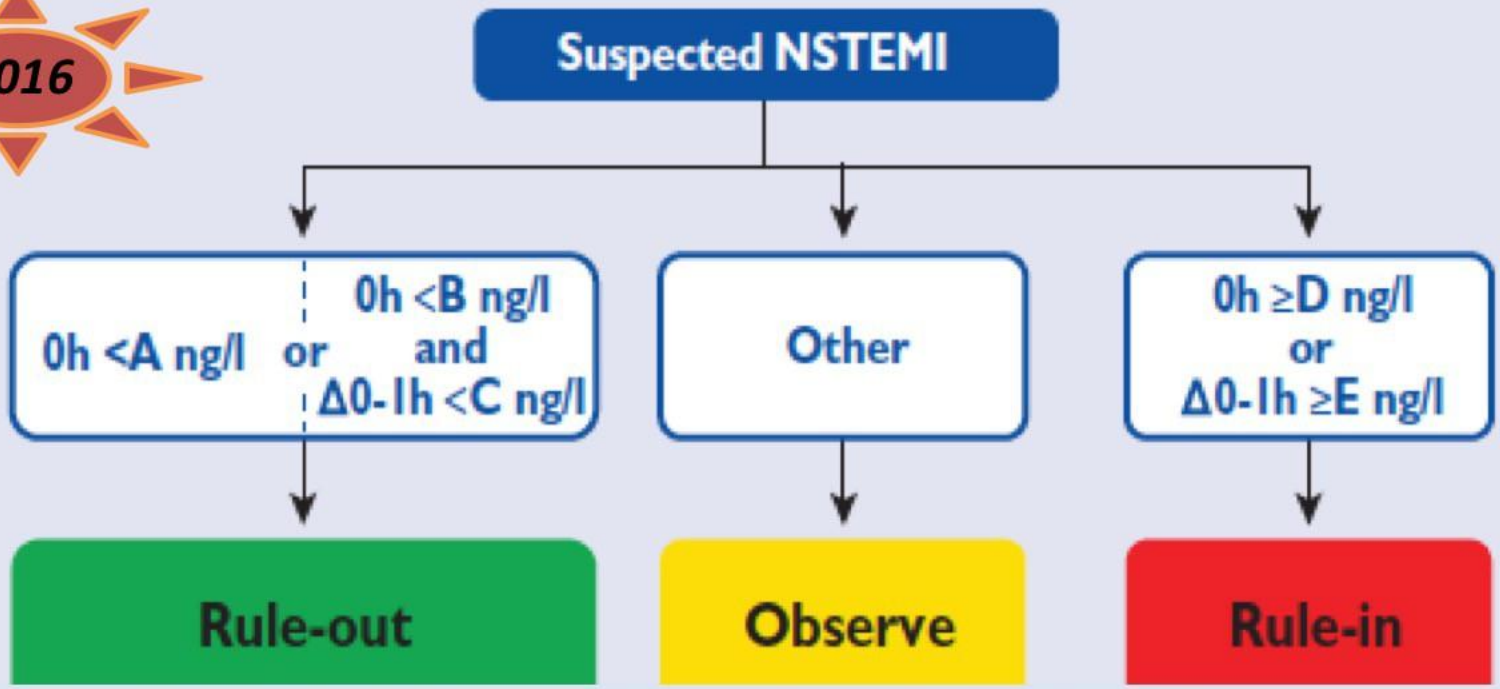


	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)	0.5	5	2	107	19

Garg P, et al. Intern Emerg Med, 2017;12:147–55.
Westermann D, et al. Nat Rev Cardiol, 2017;14(8):472-83.

Phác đồ 1 giờ chẩn đoán nhanh NSTE-ACS

2016



Giá trị dự báo âm tính >98%, dự báo dương tính 75-80% đối với NMCT cấp

	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)	0.5	5	2	107	19

Thấp — Ít thay đổi — Cao — Thay đổi rõ

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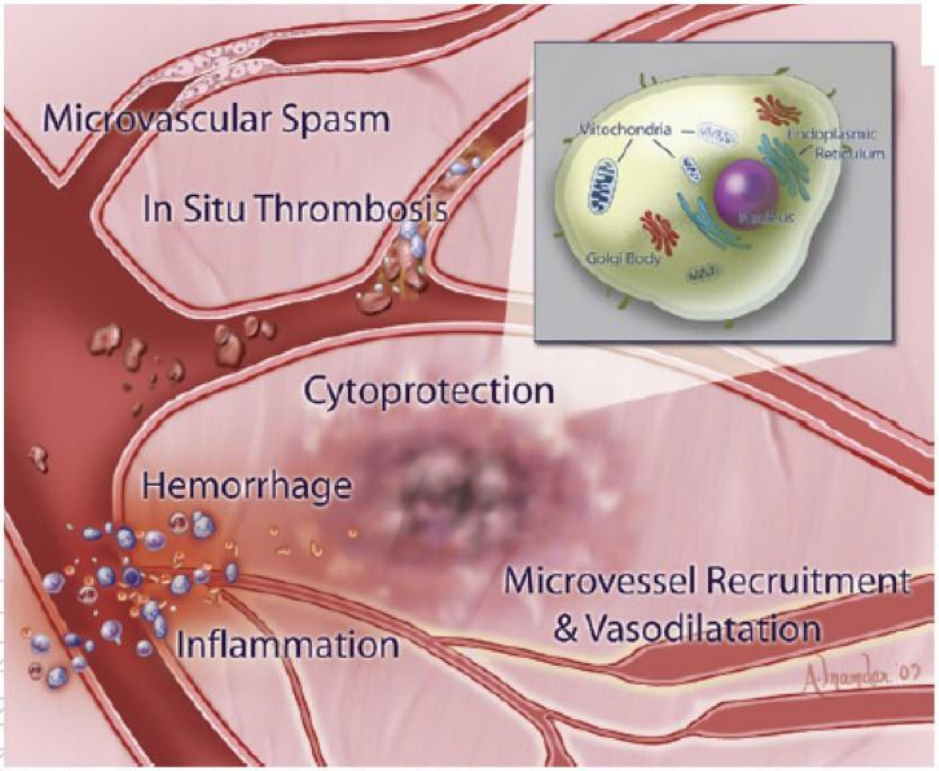
Roffi M, et al. Eur Heart J, 2016;37(3):267-315.

Can thiệp không giải quyết hết được hậu quả của bậc thang đông máu khi đã kích hoạt

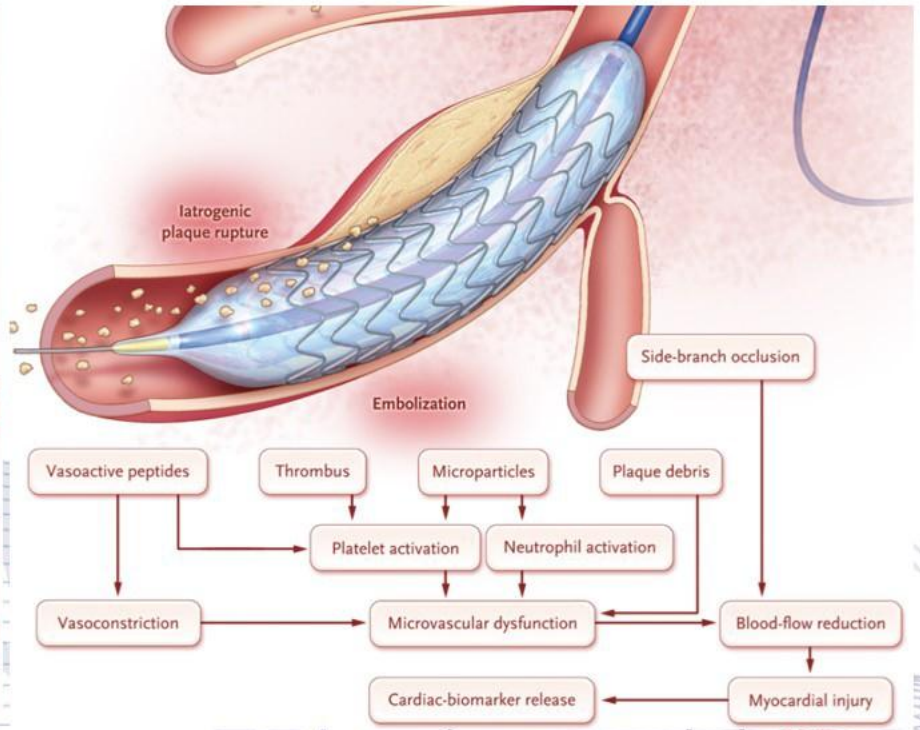
Nhồi máu cơ tim cấp gây biến cố:

- *Co thắt mạch*
- *Tắc mạch đoạn xa*
- *Hoại tử cơ tim*
- *Tổn thương do tái tưới máu*



Bản thân can thiệp gây biến cố:

- *Bong huyết khối gây tắc mạch đoạn xa*
- *Can thiệp gây viêm và tổn thương thành mạch, giải phóng yếu tố mô và các yếu tố kết dính → Hoạt hóa và kết tập tiểu cầu, tăng tạo Thrombin*

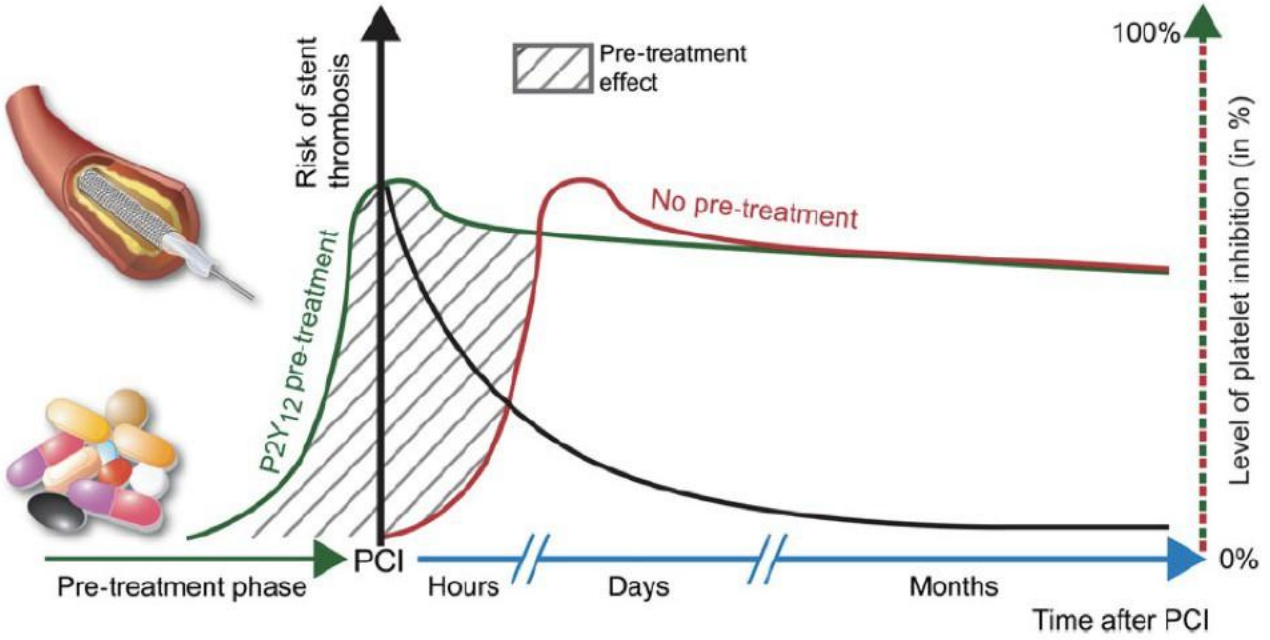


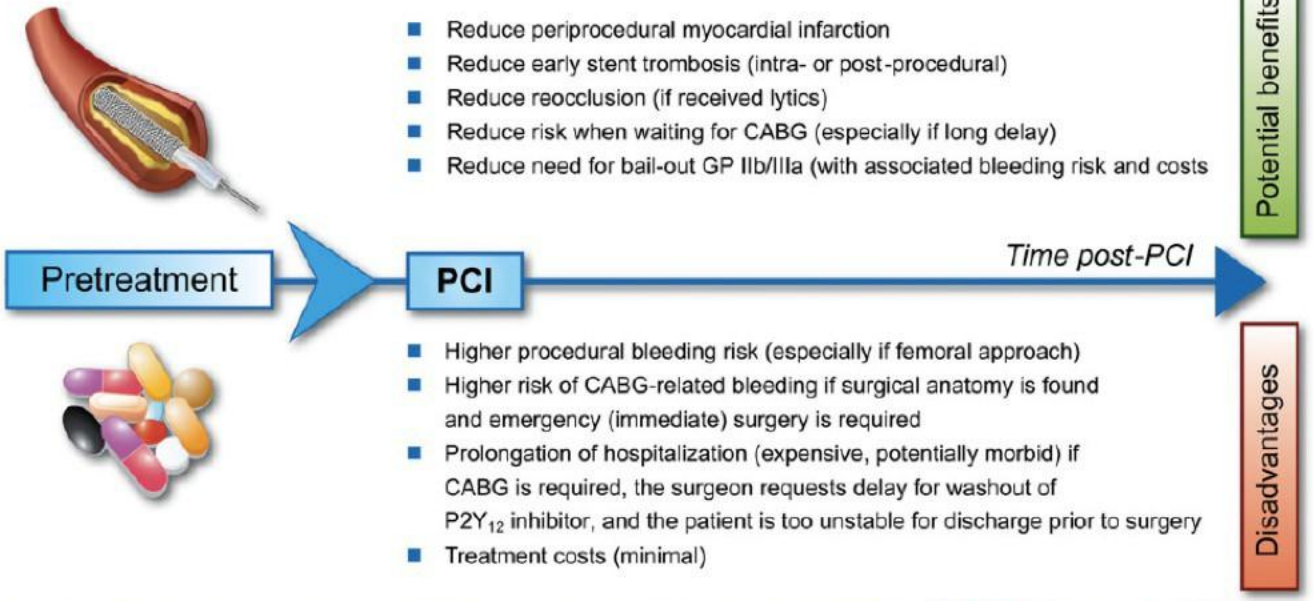
Jaffe R, et al. JACC Cardiovasc Interv, 2010;3(7):695-704.

Prasad A, et al. N Engl J Med, 2011;364(5):453-64.

Giảm thiểu gánh nặng đông máu trong ACS:

dùng sớm các thuốc kháng tiểu cầu và kháng đông





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TIM MẠCH TOÀN QUỐC 2017

Sibbing D, et al. Eur Heart J, 2016;37:1284-95.

Nên dùng kháng tiểu cầu kép trước viện ngay khi chẩn đoán hội chứng vành cấp

Guideline/country	Recommendations on P2Y12 pre-treatment	Class	LOE
Europe—NSTEMI			
2014 ESC/EACTS guidelines for myocardial revaascularization	Pre-treatment with prasugrel in patients in whom coronary anatomy is not known, is not recommended	III	B
2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation	The optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated. No recommendation for or against pre-treatment with these agents can be formulated		
	Pre-treatment with prasugrel is not recommended	III	B
USA—NSTEMI			
2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes	A loading dose of a P2Y12 receptor inhibitor should be given before the procedure in patients undergoing PCI with stenting	I	A
Europe—STEMI			
2014 ESC/EACTS guidelines for myocardial revaascularization	It is recommended to give P2Y12 inhibitors at the time of first medical contact	I	B
2012 ESC Guidelines for the management of STEMI	Patients undergoing primary PCI should receive a combination of DAPT with aspirin and an ADP receptor blocker, as early as possible before angiography		
USA—STEMI			
2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction:	A loading dose of a P2Y12 receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI. Options include clopidogrel 600 mg, prasugrel 60, ticagrelor 180 mg	I	B

Sibbing D, et al. Eur Heart J, 2016;37:1284-95.

Nhu cầu giảm biến cố và tử vong trong ACS

Xu thế sử dụng các kháng tiểu cầu mạnh mới

Biến cố	CURE	TRITON-TIMI 38	PLATO	CHAMPION gộp
	Clopidogrel (so với giả dược) RR (95% CI)	**Prasugrel** (so với clopidogrel) RR (95% CI)	**Ticagrelor** (so với clopidogrel) RR (95% CI)	**Cangrelor** (so với clopidogrel) RR (95% CI)
Biến cố tim mạch chính	**9.3% và 11.4% 0.80 (0.72-0.90)**	**9.9% và 12.1% 0.81 (0.73-0.90)**	**9.8% và 11.7% 0.84 (0.77-0.92)**	**5.3% và 6.1% 0.87 (0.78-0.97)**
NMCT	**5.2% và 6.7% 0.77 (0.67-0.89)**	**7.3% và 9.5% 0.76 (0.67-0.85)**	**5.8% và 6.9% 0.84 (0.75-0.95)**	**3.4% và 3.9% 0.85 (0.74-0.97)**
TBMMN	1.2% và 1.4% 0.86 (0.63-1.18)	1.0% và 1.0% 1.02 (0.71-1.45)	1.5% và 1.3% 1.17 (0.91-1.52)	-
Tử vong chung	5.7% và 6.2% 0.93 (0.81-1.07)	3.0% và 3.2% 0.95 (0.78-1.16)	**4.5% và 5.9% 0.78 (0.69-0.89)**	1.1% và 1.1% 0.97 (0.76-1.23)
Tử vong do n/n tim mạch	5.1% và 5.5% 0.93 (0.79-1.08)	2.1% và 2.4% 0.89 (0.70-1.12)	**4.0% và 5.1% 0.79 (0.69-0.91)**	-
Chảy máu nặng	**3.7% và 2.7% 1.38 (1.13-1.67)**	**2.5% và 1.7% 1.45 (1.15-1.83)**	11.6% và 11.2% 1.04 (0.95-1.13)	0.3% và 0.2% 1.14 (0.69-1.90)

N Engl J Med, 2001;345:494–502; N Engl J Med, 2007;357:2001-15;
N Engl J Med, 2009;361:1045–57; Lancet, 2013;382:1981–92.

Vai trò dùng sớm kháng tiểu cầu trong ACS

Dùng sớm clopidogrel:
Liều 600mg có hiệu quả khi dùng trước đến viện

Dùng sớm kháng P2Y12 mới:
Hiệu quả không khác so với dùng khi đến viện

Study	Study drug	Cohort	*n*	Design	Pre-treatment approach	Key results
CREDO	Clopidogrel	ACS and non-ACS	2116	Randomized	300 mg upstream vs. placebo	No significant benefit for the primary ischaemic endpoint, benefit observed with longer pre-treatment durations (>6 h)
PCI-CURE	Clopidogrel	NSTEMI	2658	Pre-specified analysis of randomized trial	300 mg upstream vs. placebo	Clopidogrel pre-treatment followed by long-term therapy was beneficial in reducing major cardiovascular events
PCI-CLARITY	Clopidogrel	STEMI	1863	Pre-specified analysis of randomized trial	300 mg upstream vs. placebo	Significant reduction of ischaemic events without a significant increase in major bleeding
ARMYDA-5	Clopidogrel	ACS and non-ACS	409	Ramdomized	600 mg upstream vs. 600 mg in cath lab	No significant benefit for upstream treatment on ischaemic events
CIPAMI	Clopidogrel	STEMI	654	Randomized	600 mg upstream vs. 300 mg downstream	No significant benefit for upstream treatment on TIMI flow
LOAD & GO	Clopidogrel	STEMI	168	Randomized	600/900 mg upstream vs. 300 downstream	No significant benefit for upstream treatment on TIMI flow
de Waha et al.	Clopidogrel	STEMI	423	Randomized	600 mg loading dose pre- or post-catheterization laboratory arrival	Upstream clopidogrel treatment was associated with a significant decrease in the prevalence and extent of microvascular obstruction
ACCOAST	Prasugrel	NSTEMI	4033	Randomized	30 mg upstream plus 30 mg in cath lab vs. 60 mg in cath lab	No reduction of ischaemic events, increased rate for major bleeding
Bonello et al.	Prasugrel/ Ticagrelor	NSTEMI	213	Randomized	180 mg ticagrelor after admission and before PCI vs. 60 mg prasugrel given at the time of PCI	Less periprocedural myonecrosis in ticagrelor arm, simialar rates of MACE and bleeding in both arms
De Backer et al.	Prasugrel/ Ticagrelor/ Clopidogrel	STEMI	3497	Non-randomized, observational	Pre-treatment with prasugrel vs. ticagrelor vs. clopidogrel	No differences between the three groups for TIMI flow or ischaemic events
ATLANTIC	Ticagrelor	STEMI	1862	Randomized	180 mg pre-hospital vs. 180 mg in hospital	No benefit on TIMI flow or ST segment resolution, no benefit on MACE, no increase in bleeding risk

Sibbing D, et al. Eur Heart J, 2016;37:1284-95.

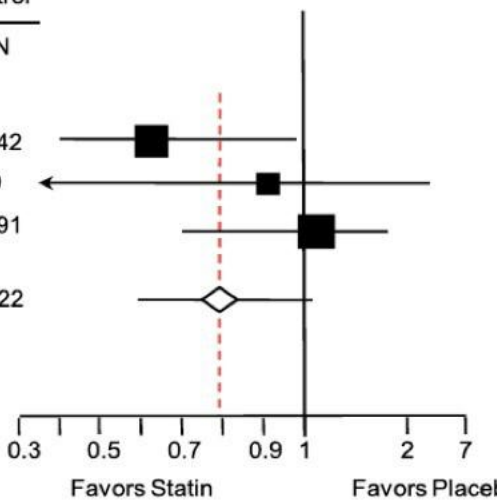
Statin mạnh liều cao có lợi trong NMCT cấp

Atorvastatin 80mg
Rosuvastatin 40mg

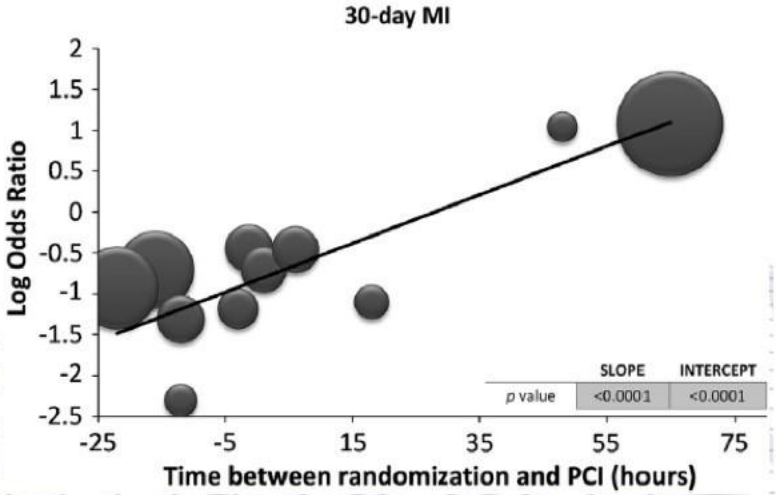
Tử vong ngắn hạn (trong viện)

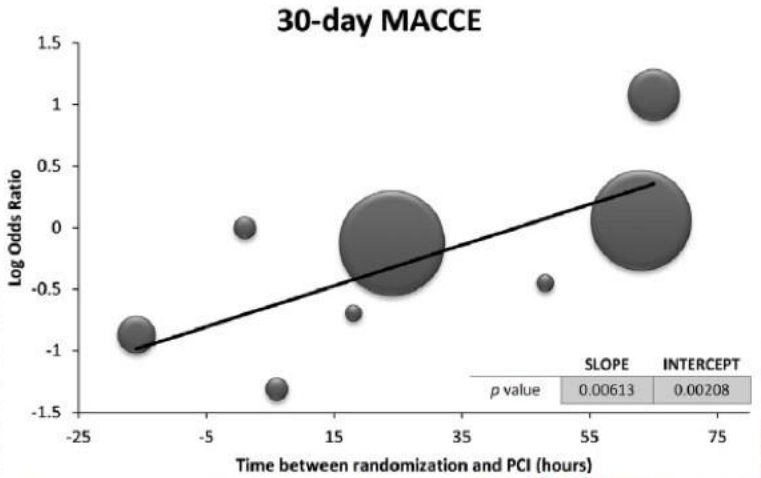
Sub-group	Number of Trials	Statin n/N	Control n/N	Odds Ratio (95% CI)	P-value
Mean time for initiation of statin					
1 day	5	32/1946	51/1942	0.63 (0.41, 0.99)	0.047
2 days	3	2/503	2/489	0.92 (0.16, 5.26)	0.925
3 days	2	32/1581	30/1591	1.07 (0.65, 1.77)	0.779
Overall	10	66/4030	83/4022	0.81 (0.58, 1.12)	

Test of Overall Effect p=0.198
I^2 = 0%



20 RCTs với 8750 bệnh nhân ACS-PCI



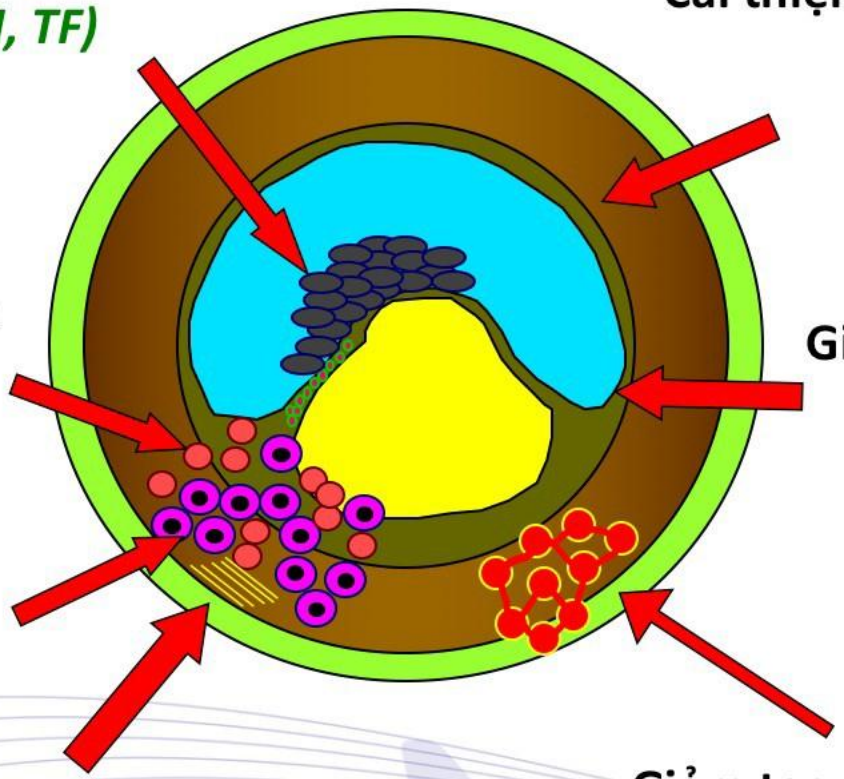


Angeli F, et al. Acute Card Care, 2012;14(1):34-9.
Navarese EP, et al. Am J Cardiol, 2014;113(10):1753-64.

Statin giảm thiểu tổn thương sau can thiệp

Giảm kết dính tiểu cầu,
Hình thành huyết khối
(TM, PAI, TF)

Cải thiện chức năng nội mạc
(NO)



Tác dụng chống viêm
(cytokines, GFs)

Giảm sự bài xuất của các
phân tử kết dính
(CAMs, selectins)

Giảm chết chu kỳ

Giảm tạo mảng xơ
(↓tích lũy đại thực bào và tế bào T,
↓giảm tổng hợp men metalloproteinases)

Giảm tạo lớp áo ngoài mạch
máu mới

Điều trị trước viện hội chứng vành cấp 2017

từ MONAC
thành *mon*APES

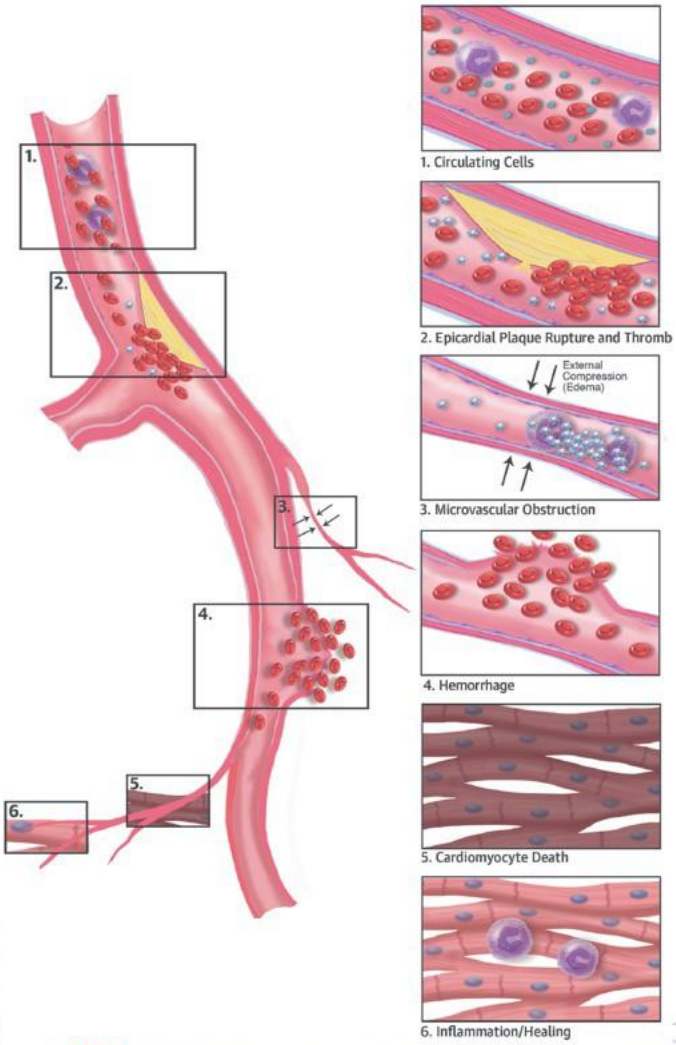
	Class of recommendation	LOE
NSTEMI		
AHA/ACCF		
2014	Class 2b: In the absence of contraindications, it may be reasonable to administer morphine sulfate intravenously to patients with NSTE-ACS if there is continued ischemic chest pain despite treatment with maximally tolerated anti-ischemic medications.	B
ECS		
2015	No formal recommendation given. However, the committee advise that morphine be administered exclusively in the context of resistant chest pain after nitrate and beta blocker therapy administration.	
STEMI		
AHA/ACCF		
2013	No formal recommendation given. However, the committee advise that in the absence of history of hypersensitivity, morphine sulfate is the drug of choice for pain relief in this cohort.	
ESC		
2012	Class 1: Relief of pain is of paramount importance, not only for humane reasons but because the pain is associated with sympathetic activation that causes vasoconstriction and increases the workload of the heart. Titrated intravenous opioids (e.g., morphine) are the analgesics most commonly used in this context.	C

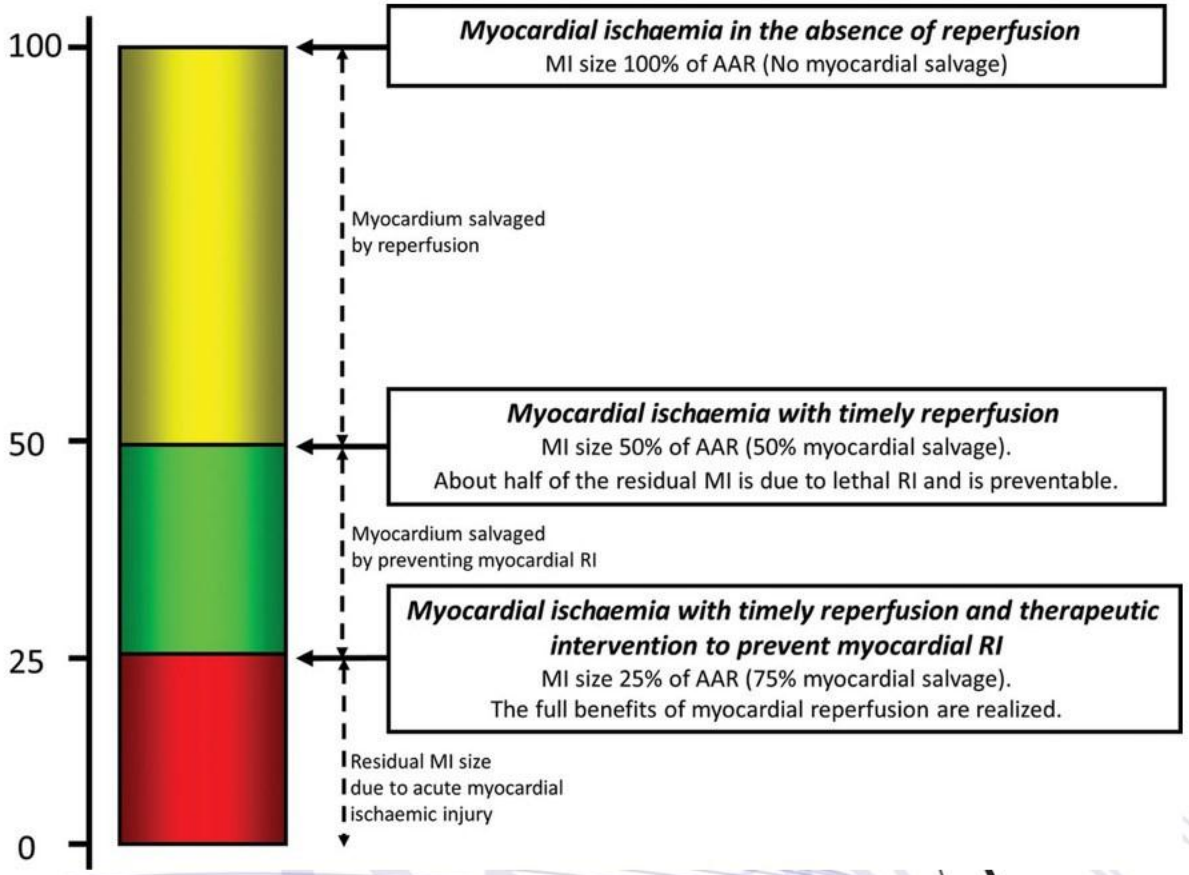
	Class of recommendation	LOE
NSTEMI		
AHA/ACCF		
2014	Class 1 recommendation for oxygen therapy in patients with an oxygen saturation <90% and in patients with respiratory distress, or other high-risk features of hypoxemia.	C
ECS		
2015	No formal recommendation given. However, the committee advise that oxygen should be administered when blood oxygen saturation is <90% or if the patient is in respiratory distress.	
STEMI		
AHA/ACCF		
2013	No formal recommendation given. However, the committee advise that oxygen therapy is appropriate for patients who are hypoxemic (oxygen saturation <90%) and acknowledge the need for more research on its utility in ACS patients.	
ESC		
2012	No formal recommendation is provided. However, the committee recommend oxygen administration to those who are breathless, hypoxic, or who have heart failure.	

	Class of recommendation	LOE
NSTEMI		
AHA/ACCF		
2014	Class 1 recommendation for sublingual nitrates for patients with continuing ischemic pain up to three doses, after which intravenous nitroglycerin should be considered.	C
ECS		
2015	Provide a Class l recommendation for nitrates for the relief of angina, uncontrollable hypertension or heart failure in NSTEMI patients.	C
STEMI		
AHA/ACCF		
2013	No formal recommendation provided. However, the committee advise that nitrates may be useful to treat patients with STEMI and hypertension or heart failure but they should be avoided in a number of situations including hypotension, marked bradycardia, or tachycardia, RV infarction, or 5′phosphodiesterase inhibitor use within the previous 24–48 h.	
ESC		
2012	No formal recommendation given. However, the committee advise that nitrates are a valuable anti-anginal agent in this setting.	

McCarthy CP, et al. Trends Cardiovasc Med, 2017 May 9. pii: S1050-1738(17)30055-5.

Giảm tổn thương do tái tưới máu với STEMI





Fröhlich GM et al. Eur Heart J, 2013;34:1714-22.
Ibáñez B, et al. J Am Coll Cardiol, 2015;65(14):1454-71.

Các biện pháp bảo vệ cơ tim trong NMCT cấp

Therapeutic intervention	Pre-clinical knowledge	Surrogate outcome studies	Clinical outcome results	Potential reasons for neutral results in the clinical setting
Nicorandil	Nicorandil given just before IRI reduced IS in a dog model [85] *Main mechanism: combination of ATP-sensitive potassium channel opener and nitrate preparation*	J-WIND-KTP trial [86] tested the administration of nicorandil started after reperfusion, demonstrating no difference in myocardial IS measured using biomarkers or 6 month LVEF	No data	– Not only anterior STEMI – Treatment started after reperfusion
Glucose–insulin–potassium	GIK slows the progression of IRI in many experimental settings [87] *Main mechanism: promotion of glucose metabolism*	IMMEDIATE trial [34] demonstrated a reduction in myocardial IS with no difference in progression to myocardial infarction	CREATE-ECLA [88] showed no differences in mortality at 30 days	– IV GIK infusion for 24 h started after reperfusion in the majority of cases – Not only anterior STEMI – Prior TIMI flow grade not used as selection criteria
Atrial natriuretic peptide	ANP given just prior to reperfusion reduced IS in rabbit hearts [89] *Main mechanism: ANP targets prosurvival kinase pathways such as the cGMP and RISK pathways*	J-WIND-ANP: Intravenous carperitide (an ANP analogue) starting prior PPCI reduced IS measured by biomarker release and showed a slight increase in LVEF [86]	No data	– Further studies are needed to determine whether carperitide has an impact in clinical outcomes
Adenosine	Prior to index ischemia, adenosine reduces IS in animal models of acute IRI [90]. Whether it can also be effective when administered at the time of reperfusion is less clear. *Main mechanism: nitric oxide and protein kinase G*	AMISTAD study reported reductions in IS with high-dose intravenous administration [91], whilst PROMISE study [92] failed to show reproduce the results using lower doses of intracoronary adenosine	No data	– Doses and route of administration (intravenous vs. intracoronary)
IPOST	IPOST has demonstrated to be capable of reduce both myocardial IS and coronary microvascular obstruction [93] *Main mechanism: delayed reversal of acidosis and activation of pro-survival cascades*	Significant reduction in biomarkers release, increase in LVEF and reduction in myocardial IS by SPECT [94,95]	DANAMI 3-iPOST has failed to demonstrate clinical benefit using a composite endpoint of all-cause mortality and hospitalization for congestive heart failure[a]	– Risk of coronary microembolization – Potential influence of concomitant co-morbidities and co-treatment on the ischemic conditioning response
RIC	Consistent evidence among diverse models and species that RIC confers cytoprotection against IRI [96] *Main mechanism: neural and/or humoral signalling*	Increase in the myocardial salvage index at 30 days when applied in the ambulance [33]	CONDI2/ERIC-PPCI study [97] is expected to recruit 4300 patients (NCT01857414)	
Cyclosporin	Cyclosporin has demonstrated to reduce IS in many studies, with some contentious results [19] *Main mechanism: inhibition of MPTP opening*	Significant reduction in 72 h AUC, increase in LVEF and reduction in myocardial IS by CMR [98], although very recently the CYCLE study [99] failed to demonstrate enzymatic IS reduction and ST-segment resolution	CIRCUS trial [40] failed to improved clinical outcomes at 1 year in anterior STEMI patients	– Total ischemic times were relatively prolonged (4.5 h) – Dose and route of administration
Exenatide	Exenatide has resulted cardioprotective in both small and large animal models [100,101] *Main mechanism: GLP-1 analogy, NO/cGMP signalling pathway*	Increase in the myocardial salvage index at 90 days by CMR [102]	No data	– Further studies are needed to determine whether exenatide has an impact in clinical outcomes
Metoprolol	Metoprolol reduced myocardial IS and preserve LV systolic function in a swine model [103] *Main mechanism: unknown, although it seems to extend beyond their effect on hemodynamics and oxygen consumption*	METOCARD-CNIC trial [31] administered in the ambulance reduced IS and preserved LV systolic function EARLY BAMI trial [32] has recently reported that early intravenous metoprolol before PPCI was not associated with a reduction in infarct size in a non-restricted STEMI population	Move On! Trial [104] plans to investigate the effect of metoprolol on mortality and heart failure hospitalization	– The largest trial has been performed in all AMI locations, whilst the positive effects had been shown in anterior infarcts – The timing of drug administration might be of major importance, as a substudy reveals that the sooner metoprolol is administered in the course of infarction, the smaller is the infarct and the higher the LVEF [36]
Hypothermia	Hypothermia can reduce IS either starting before ischemia, during ischemia or immediately at reperfusion [105] *Main mechanism: energy preservation (reduction of metabolic demands)*	CHILL-MI trial [106] failed to demonstrated an overall IS reduction using hypothermia, although patients with an anterior STEMI presenting within 4 h benefited from the therapy	No data	– The main limitation to translate the therapy is the technology: further devices capable of inducing hypothermia at a faster rate are needed
TRO40303	Reduction of myocardial IS when administered at time of reperfusion in small-animal model [107], although failing in a large-animal model [108] *Main mechanism: inhibition of MPTP opening by attenuating ROS production*	MITOCARE study [109] failed to show IS reduction and increased myocardial salvage, using biomarkers and CMR respectively	No data	– Not enough pre-clinical evidence – Formulation and dosage of TRO40303 used in the clinical setting differed from pre-clinical studies – Difference between groups in TIMI-flow of culprit artery after PCI (12.1% in the TRO40303-group vs 6.3% in the placebo-group)

Rossello X, et al. Int J Cardiol, 2016;220:176-84.

Tạo *"thích nghi cơ tim"* khi can thiệp cấp ĐMV

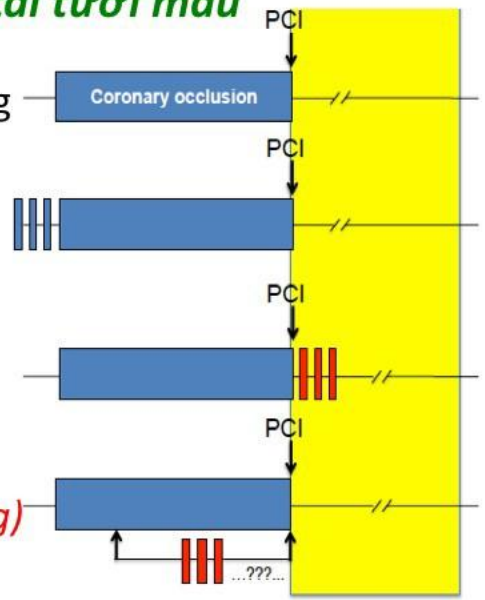
Tổn thương do tái tưới máu

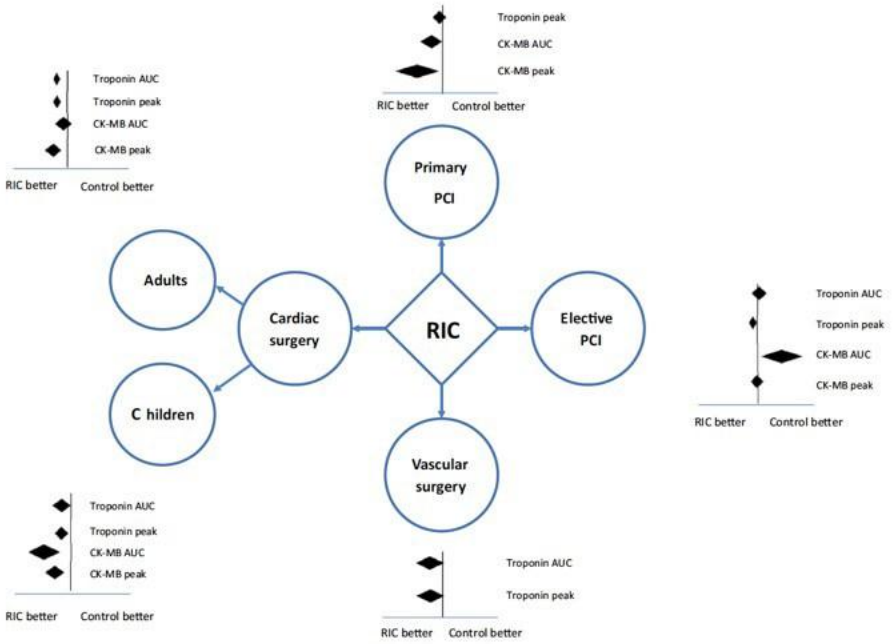
Điều trị thông thường

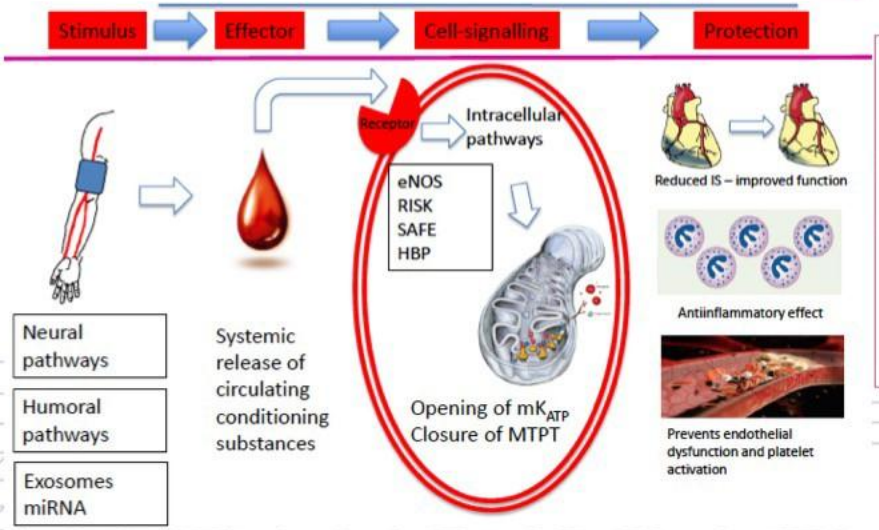
Tiền thích nghi
(Pre-Conditioning)

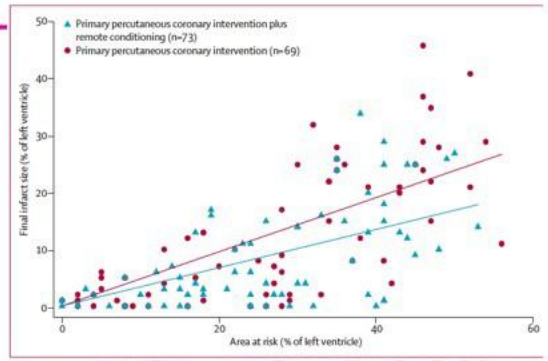
Hậu thích nghi
(Post-Conditioning)

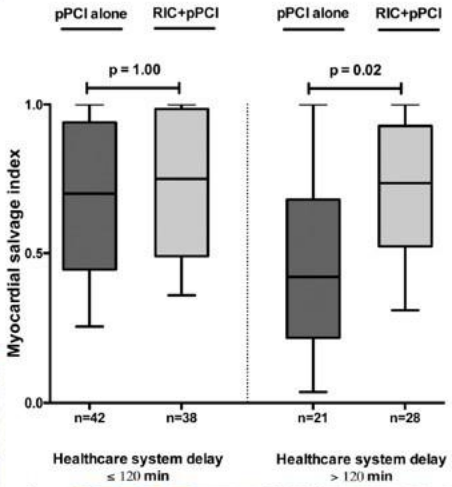
Viễn thích nghi
(Remote-Conditioning)





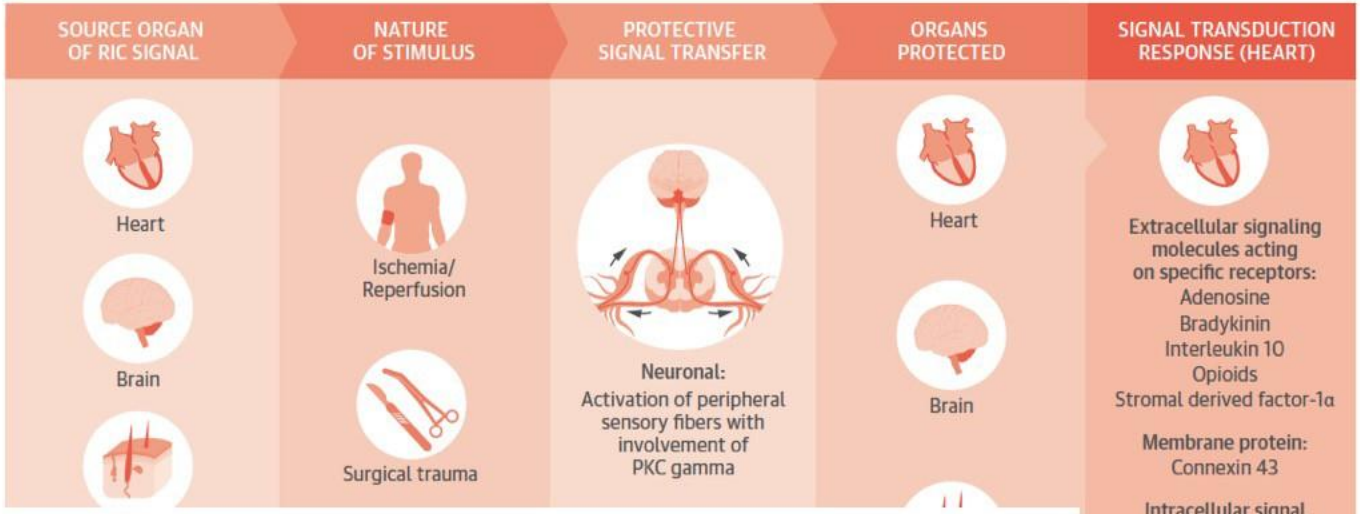






Basic Res Cardiol, 2015;110(2):11.
Lancet 2010;375:727-34.
Heart 2016;102(13):1023-8.

Hiệu quả của thích nghi từ xa trong STEMI



First Author, Year (Ref. #)	Patients, n (Control/RIC)	RIC Regimen	Endpoint	Outcome
Bøtker et al., 2010 (28)	69/73	Upper limb 4 cycles I/R (5/5 min)	Salvage index (SPECT)	20% increase in salvage index
Munk et al., 2010 (141)	110/108	Upper limb 4 cycles I/R (5/5 min)	LVEF at 30 days	5% increase in LVEF in anterior infarcts
Rentoukas et al., 2010 (142)	30/33	Upper limb 3 cycles I/R (5/5 min)	ST-segment resolution	20% increase in proportion of patients achieving full ST-segment resolution
Crimi et al., 2013 (143)	50/50	Lower limb 3 cycles I/R (5/5 min)	CK-MB (AUC 72 h after PCI)	20% reduction of CK-MB release
Prunier et al., 2014 (144)	17/18	Upper limb 4 cycles I/R (5/5 min)	CK-MB (AUC 72 h after PCI)	31% reduction of CK-MB release
Sloth et al., 2014 (145)	167/166	Upper limb 4 cycles I/R (5/5 min)	MACCE at 4 years	12% reduction in MACCE
Hausenloy et al., 2014 (147)	260/260	Upper limb 4 cycles I/R (5/5 min)	TnT (AUC 24 h after PCI)	17% reduction of TnT release
White et al., 2014 (146)	40/43	Upper limb 4 cycles I/R (5/5 min)	CMR	27% reduction of infarct size

Heusch G, et al. J Am Coll Cardiol, 2015;65(2):177–95.

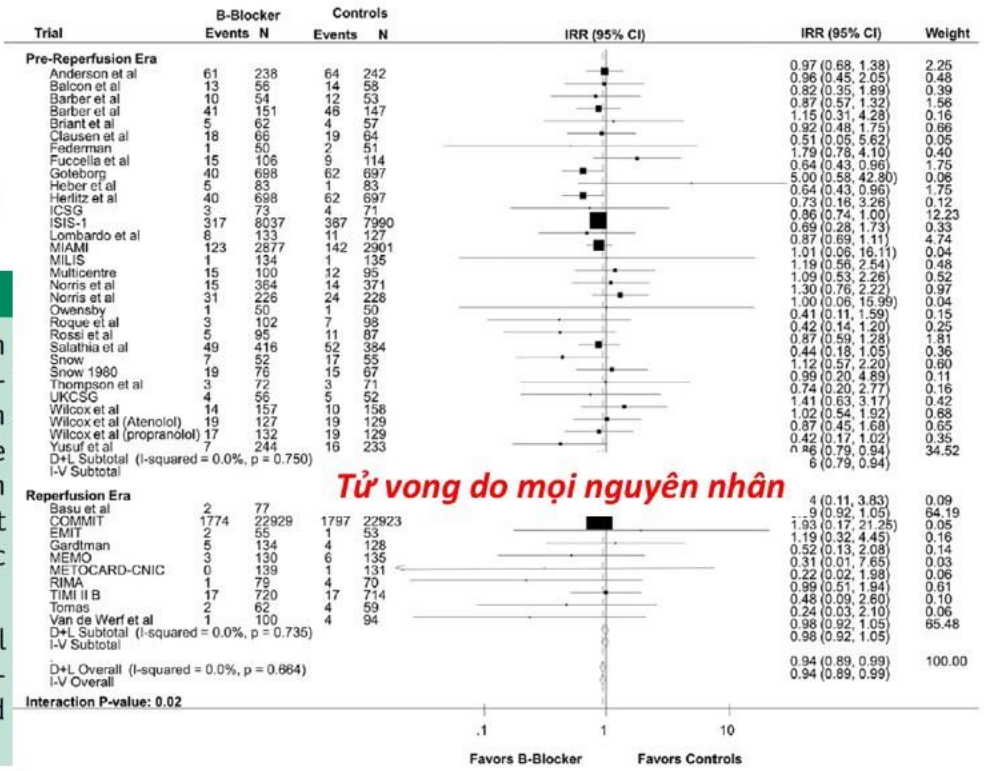
Chẹn beta trong nhồi máu cơ tim cấp

Cải thiện tiên lư

- *Giảm thiểu m*
- *Chống rối loạ*
- *Chống tái cấu*

CLINICAL SIGNIFICANCE

- In the treatment of patients with myocardial infarction, β-blockers reduced mortality in the pre-reperfusion but not in the reperfusion era, where there was reduction (short-term) in myocardial infarction and angina, but increase in heart failure, cardiogenic shock, and drug discontinuation.
- The benefit for recurrent myocardial infarction and angina reduction by β-blockade in the reperfusion era appeared to be short term (30 days).



Tử vong do mọi nguyên nhân

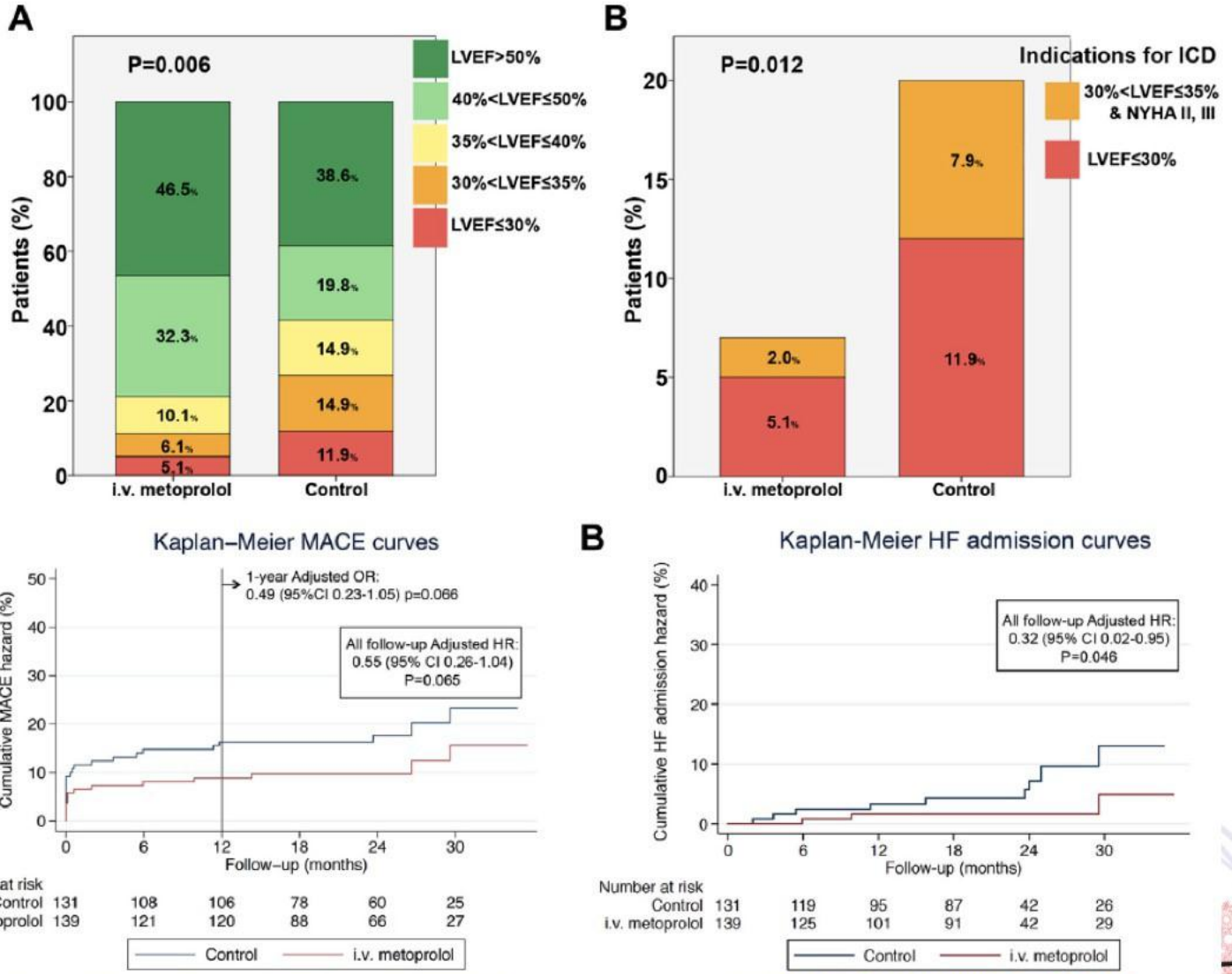
60 TNLS, n=102,003

	Death	CV Death	Sudden Death	MI	Angina	Stroke	Heart Failure	Cardiogenic Shock
Events at 30 days								
Pre-reperfusion	0.87 (0.79, 0.96)	0.86 (0.77, 0.96)	0.82 (0.59, 1.13)	0.81 (0.63,1.04)	0.89 (0.83, 0.95)	2.96 (0.47, 18.81)	1.06 (0.97, 1.16)	1.03 (0.87, 1.21)
Reperfusion era	0.98 (0.92, 1.05)	1.00 (0.91,1.10)	0.94 (0.86, 1.01)	0.72 (0.62, 0.84)	0.81 (0.66, 1.00)	1.09 (0.91, 1.30)	1.10 (1.05, 1.16)	1.29 (1.18, 1.41)
Events between 30 days and 1 year								
Pre-reperfusion	0.79 (0.71, 0.88)	0.84 (0.71, 1.00)	0.61 (0.49, 0.76)	0.77 (0.64, 0.91)	0.94 (0.75, 1.18)	1.54 (0.60, 3.95)	1.07 (0.91, 1.27)	1.88 (0.51, 6.96)
Reperfusion era	1.50 (0.53, 4.21)	1.50 (0.53, 4.21)	NA	0.71 (0.23, 2.25)	1.03 (0.72, 1.48)	4.00 (0.45, 35.79)	3.83 (1.56, 9.41)	NA
Events > 1 year								
Pre-reperfusion	0.81 (0.66, 0.98)	0.73 (0.48, 1.11)	0.64 (0.43, 0.97)	0.81 (0.62, 1.06)	NA	0.20 (0.01, 4.20)	0.25 (0.03, 2.25)	NA
Reperfusion era	NA	NA	NA	NA	NA	NA	NA	NA

Bangalore S, et al. Am J Med, 2014;127:939-53.

Chẹn beta làm giảm suy tim sau nhồi máu

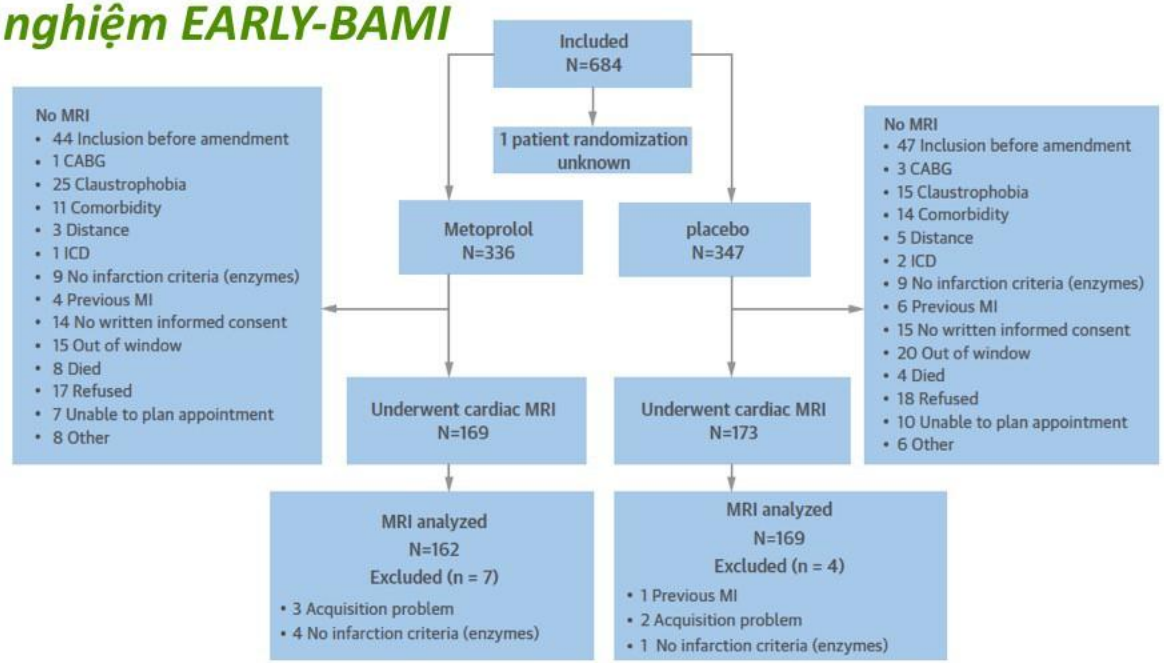
Kết quả dài hạn của thử nghiệm METOCARD-CNIC



Pizarro G, et al. J Am Coll Cardiol, 2014;63:2356–62.

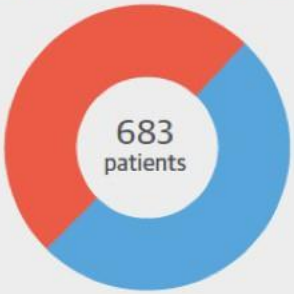
Chẹn beta làm giảm suy tim sau nhồi máu

Kết quả thử nghiệm EARLY-BAMI



Early Beta-blocker Administration before primary PCI in patients with ST-elevation Myocardial Infarction (EARLY-BAMI) trial

336 patients: 10 mg metoprolol



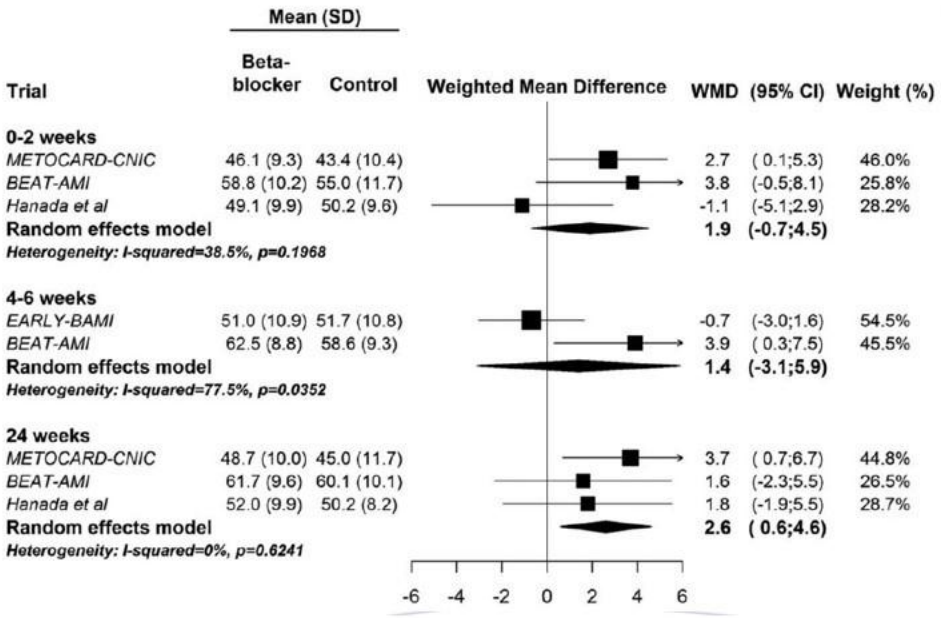
346 patients: placebo

	Significant improvement with metoprolol?
Baseline characteristics	✖
Infarct size	✖ 15.3% vs. 14.9% placebo
Peak and area under creatine kinase (CK) curve	✖
Left ventricular ejection fraction	✖ 51% vs. 51.6%
Incidence of adverse events	✖
Incidence of malignant arrhythmias	✔ 3.6% vs. 6.9%

Roolvink V, et al. J Am Coll Cardiol, 2016;67(23):2705–15.

Dùng chẹn beta đường tĩnh mạch trong STEMI

presenting in Killip classes 1 and 2, IV beta-blocker use in conjunction with PCI were associated with improved LVEF at 24 weeks post-infarct relative to PCI alone. Rates of VA, any arrhythmia, and cardiogenic shock were numerically lower with IV beta-blockers during index hospitalization, but 95% CI were wide. Further, larger RCTs are required to more precisely determine IV beta-blockers' role in STEMI in the era of PCI.



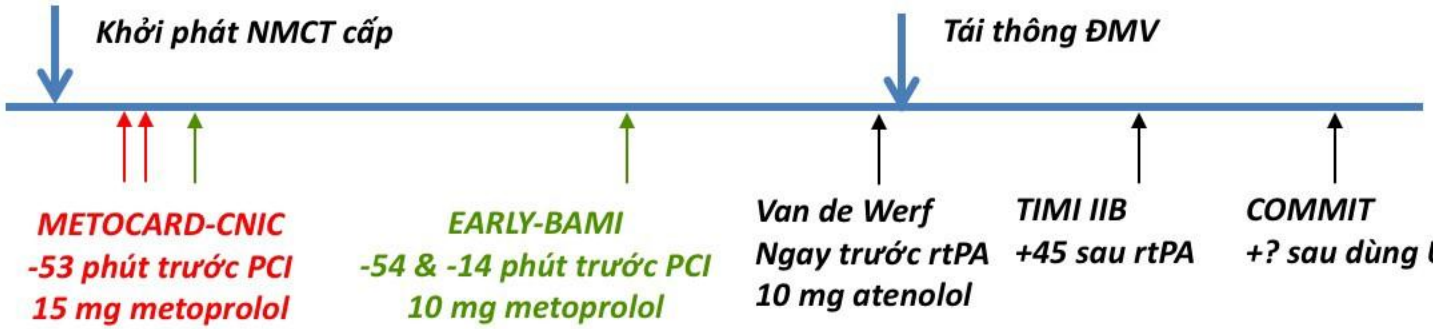
Intravenous beta-blockers in STEMI patients (Killip class I or II), undergoing primary PCI appear to be safe. This therapy was associated with a reduced risk of ventricular arrhythmias. Due to the small number of included subjects in this analysis, the impact of intravenous beta-bl ıls ar a- bl

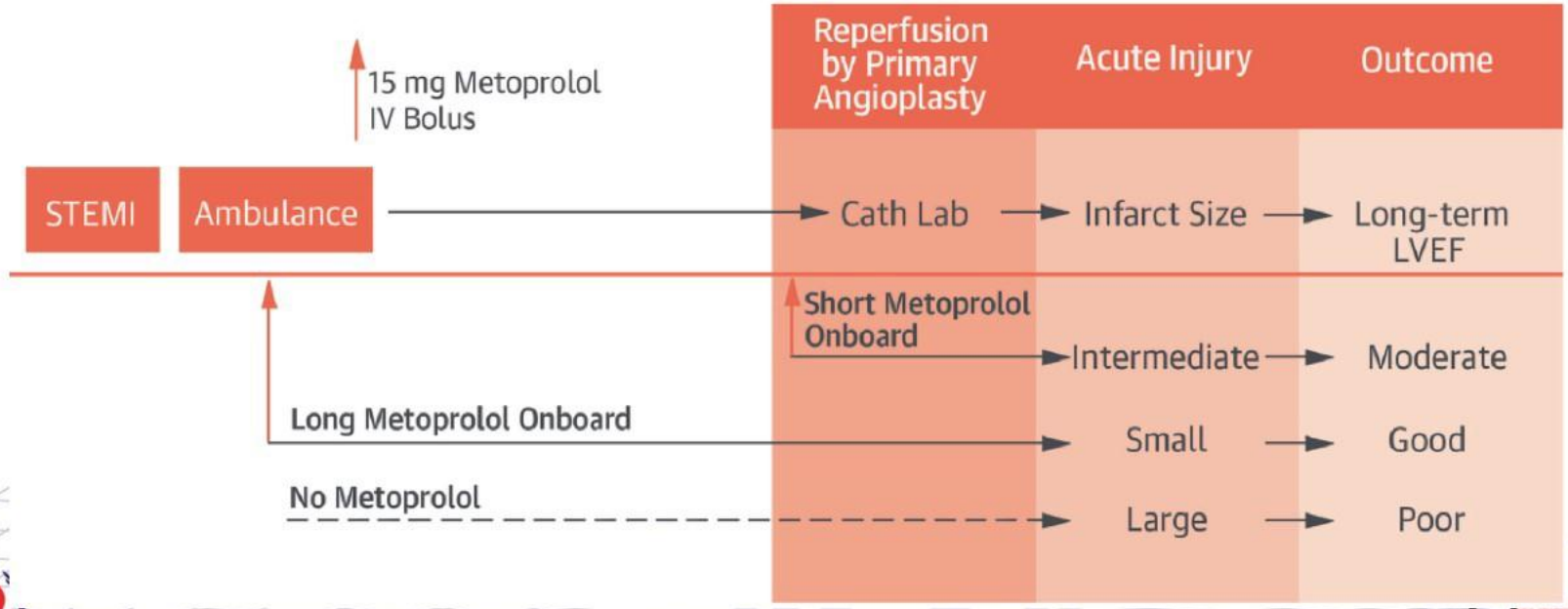
Outcome	Incidence IV Intravenous β-blockers%/control%	Model	RR[a]	95% CI	P-value	I²%
Efficacy outcomes						
Short-term						
Ventricular arrhythmia	3.7/8.8	DL	0.42	0.26–0.69	0.001	0
		Peto	0.40	0.25–0.65	<0.001	6
Re-infarction	0.7/0.7	DL	1.13	0.28–4.50	0.86	0
		Peto	1.02	0.25–4.08	0.98	37
All-cause mortality	1.3/1.7	DL	0.77	0.19–3.17	0.72	0
		Peto	0.71	0.16–3.17	0.66	0
Cardiovascular mortality	1.6/1.8	DL	0.93	0.35–2.48	0.88	0
		Peto	0.90	0.32–2.50	0.84	0
Long-term						
Heart failure hospitalization	1.6/5.6	DL	0.32	0.10–1.05	0.06	0
		Peto	0.31	0.10–0.94	0.04	0
Re-infarction	0.4/2.6	DL	0.29	0.06–1.37	0.12	0
		Peto	0.23	0.05–1.02	0.05	0
All-cause mortality	2.5/3.0	DL	0.84	0.30–2.40	0.75	0
		Peto	0.81	0.27–2.44	0.70	0
Safety outcomes						
Cardiogenic shock	1.4/1.9	DL	0.78	0.31–1.97	0.61	0
		Peto	0.70	0.28–1.74	0.44	32
Bradycardia	1.4/0.9	DL	1.54	0.35–6.81	0.57	14
		Peto	1.54	0.44–5.35	0.50	49

Study	EARLY BAMI [15]	BEAT-AMI [16]	METOCARD-CNIC [17,27]	Hanada et al. [18]
Single/multicenter	Multicenter	Single center	Multicenter	Single center
Blinding assessment	Double blinded	PROBE	PROBE	PROBE
Generation of treatment assignment	Random blocks	Opaque, sealed envelopes	Random blocks	Opaque, sealed envelopes
Follow-up completion%	55[a]	97	81[a]	100
Primary outcome	Infarct size on MRI after 30 days	Maximum change in troponin T from baseline to 48 h	Infarct size on MRI after 5–7 days	LVEF by ventriculogram in 2 weeks

Elgendy IY, et al. Int J Cardiol, 2016;223:891-897. Sterling LH, et al. Int J Cardiol, 2017;228:295-302.

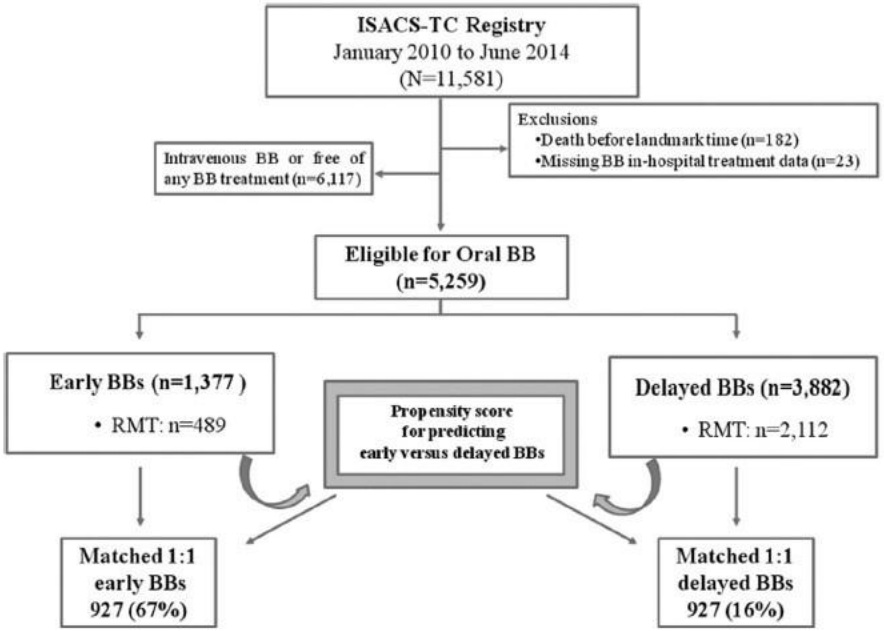
Hiệu quả bảo vệ cơ tim của chẹn beta tuỳ thuộc thời điểm dùng trong bệnh cảnh NMCT

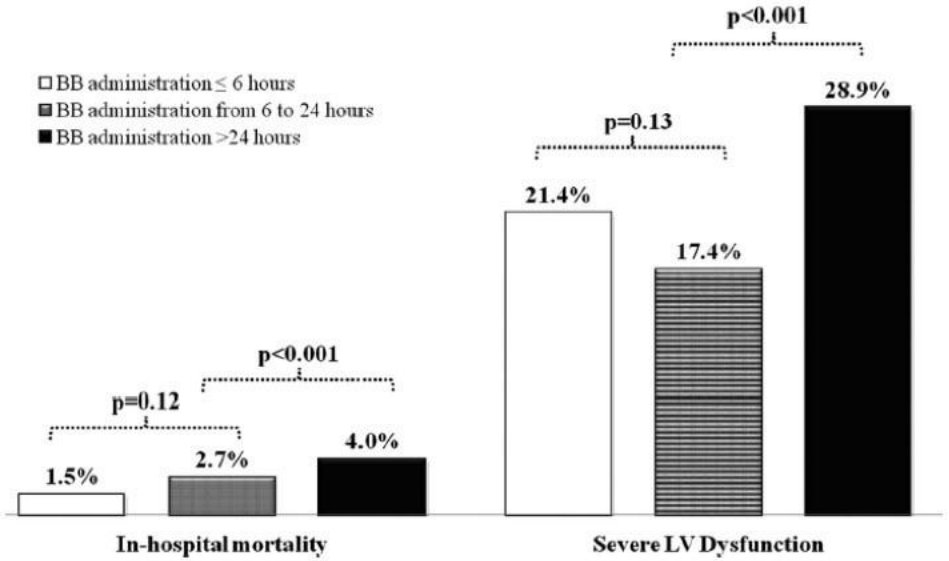




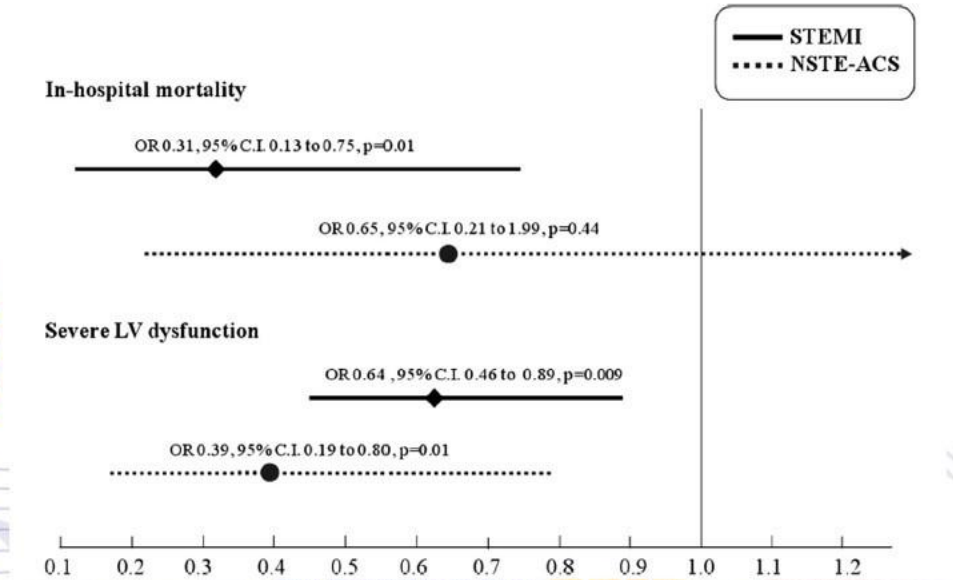
García-Ruiz JM, et al. J Am Coll Cardiol. 2016;67(18):2093–104.

Dùng chẹn beta đường uống trong STEMI





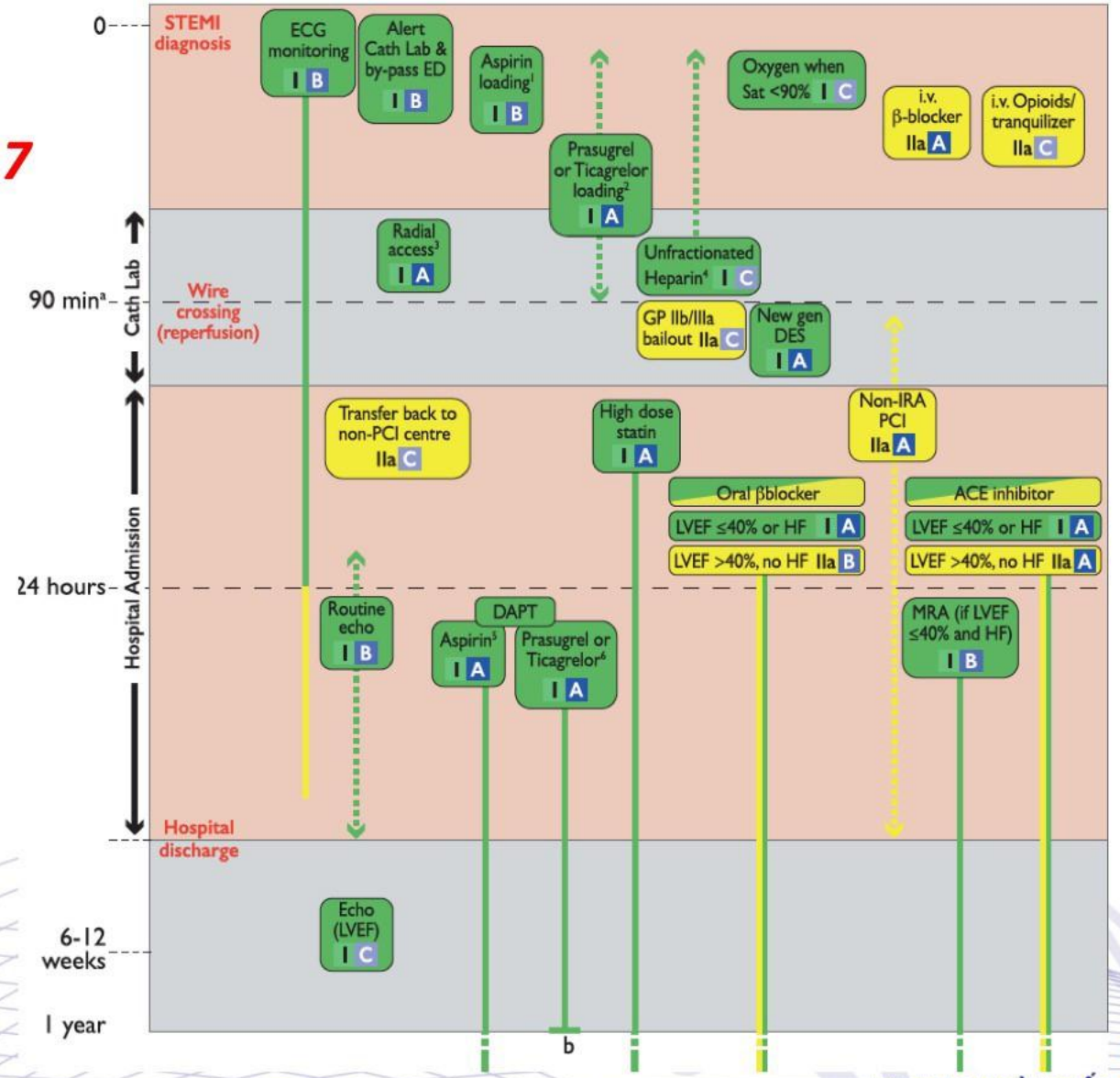
0.42 to 0.78). Significant mortality benefits with early β blocker therapy disappeared when patients with Killip class III/IV were included as dummy variables. The results were confirmed by propensity score–matched analyses. In conclusion, in patients with ACSs, earlier administration of oral β blocker therapy should be a priority with a greater probability of improving LV function and in-hospital survival rate. Patients presenting with acute pulmonary edema or cardiogenic shock should be excluded from this early treatment regimen. (Am J Cardiol 2016;117:760–767)



Bugiardini R, et al. Am J Cardiol, 2016;117:760-7.

Thời gian dùng chẹn beta trong/sau NMCT

STEMI
ESC 2017



Ibanez B, et al. Eur Heart J, 2017. doi:10.1093/eurheartj/ehx393

Chẹn beta với NSTE-ACS ACC 2014

Recommendations	COR	LOE
Oxygen		
Administer supplemental oxygen only with oxygen saturation <90%, respiratory distress, or other high-risk features for hypoxemia	I	C
Nitrates		
Administer sublingual NTG every 5 min × 3 for continuing ischemic pain and then assess need for IV NTG	I	C
Administer IV NTG for persistent ischemia, HF, or hypertension	I	B
Nitrates are contraindicated with recent use of a phosphodiesterase inhibitor	III: Harm	B
Analgesic therapy		
IV morphine sulfate may be reasonable for continued ischemic chest pain despite maximally tolerated anti-ischemic medications	IIb	B
NSAIDs (except aspirin) should not be initiated and should be discontinued during hospitalization for NSTE-ACS because of the increased risk of MACE associated with their use	III: Harm	B
Beta-adrenergic blockers		
Initiate oral beta blockers within the first 24 h in the absence of HF, low-output state, risk for cardiogenic shock, or other contraindications to beta blockade	I	A

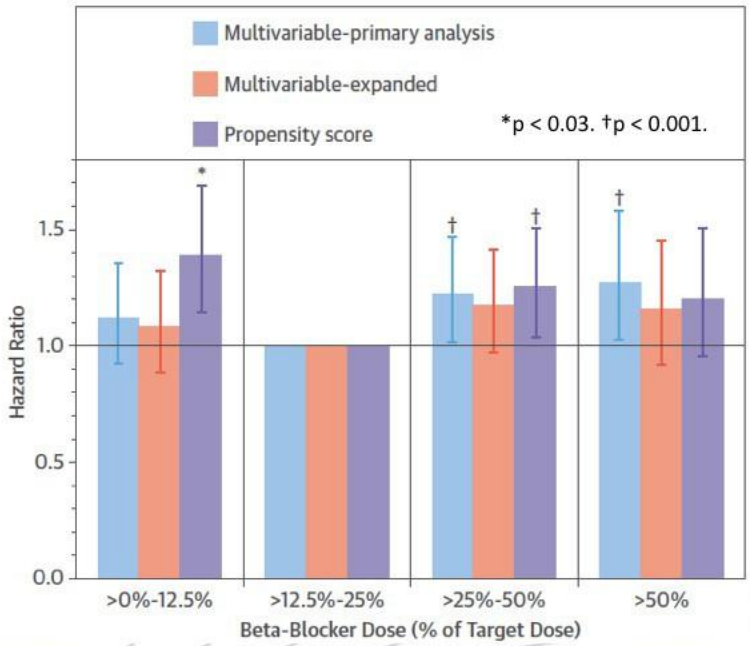
Beta-adrenergic blockers

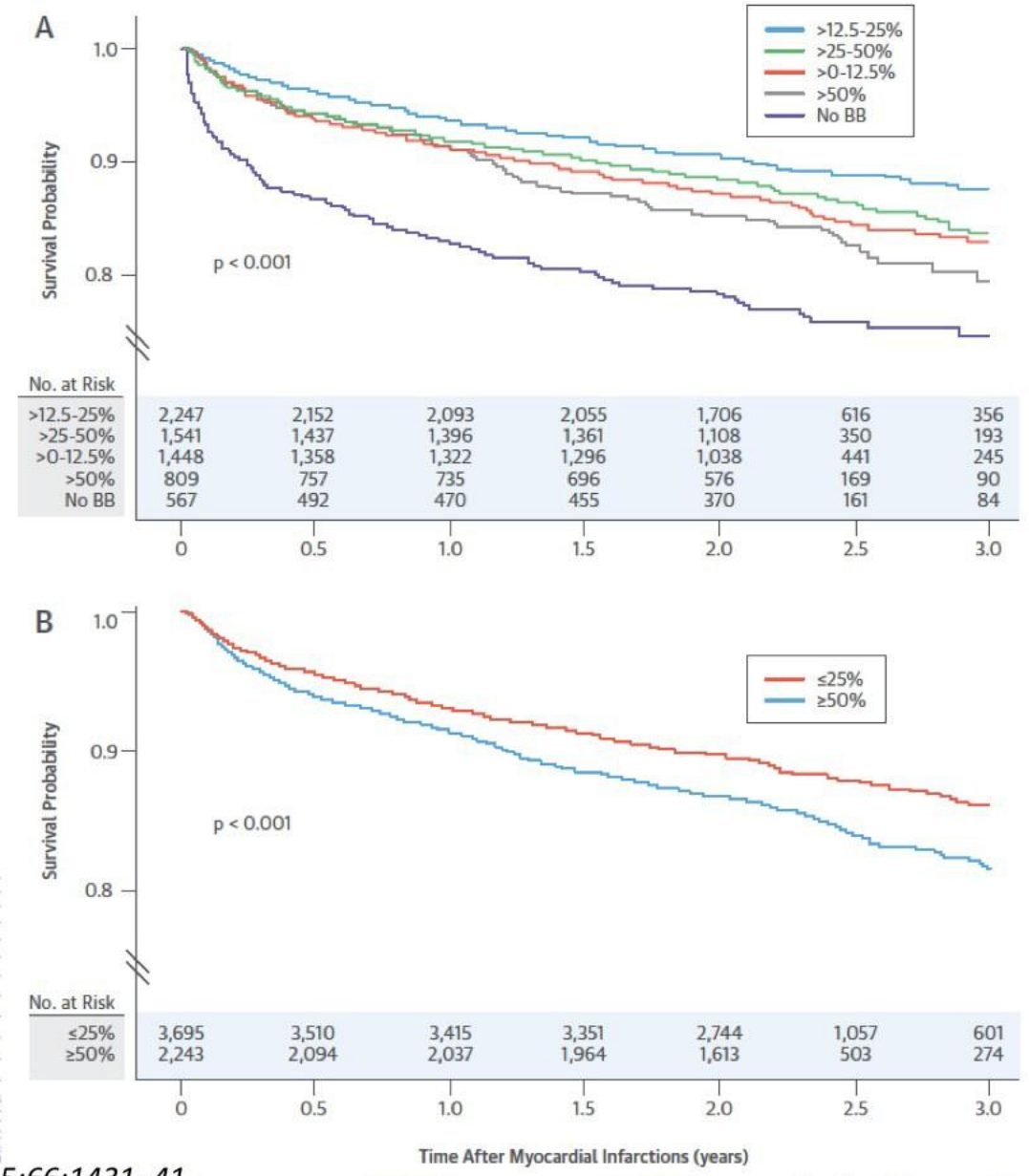
Initiate oral beta blockers within the first 24 h in the absence of HF, low-output state, risk for cardiogenic shock, or other contraindications to beta blockade	IA
Use of sustained-release metoprolol succinate, carvedilol, or bisoprolol is recommended for beta-blocker therapy with concomitant NSTE-ACS, *stabilized* HF, and reduced systolic function	IC
Re-evaluate to determine subsequent eligibility in patients with initial contraindications to beta blockers	IC
It is reasonable to continue beta-blocker therapy in patients with normal LV function with NSTE-ACS	IIaC
IV beta blockers are potentially harmful when risk factors for shock are present	III

Immediate-release nifedipine is contraindicated in the absence of a beta blocker	III: Harm	B
Cholesterol management		
Initiate or continue high-intensity statin therapy in patients with no contraindications	I	A
Obtain a fasting lipid profile, preferably within 24 h	IIa	C

Ezra A. Amsterdam EA, et al.
J Am Coll Cardiol, 2014;64(24):2645–87.

Liều dùng chẹn beta sau nhồi máu cơ tim

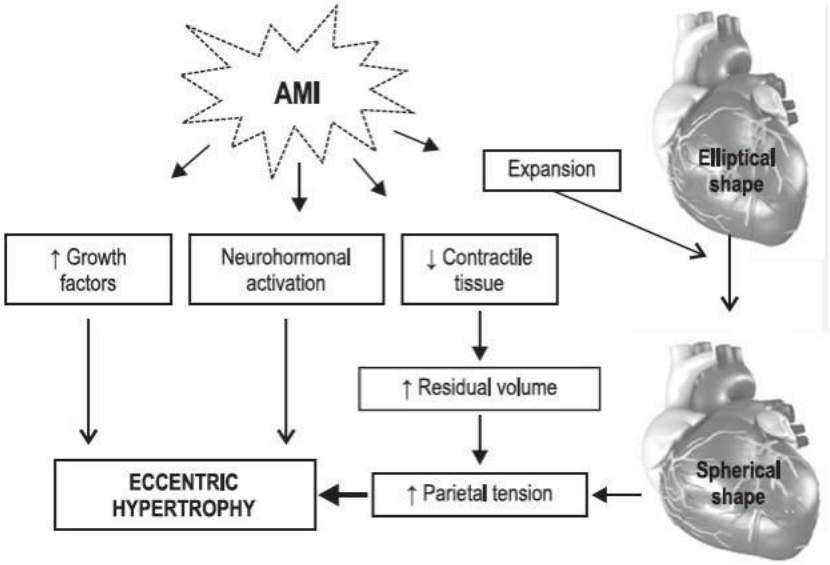


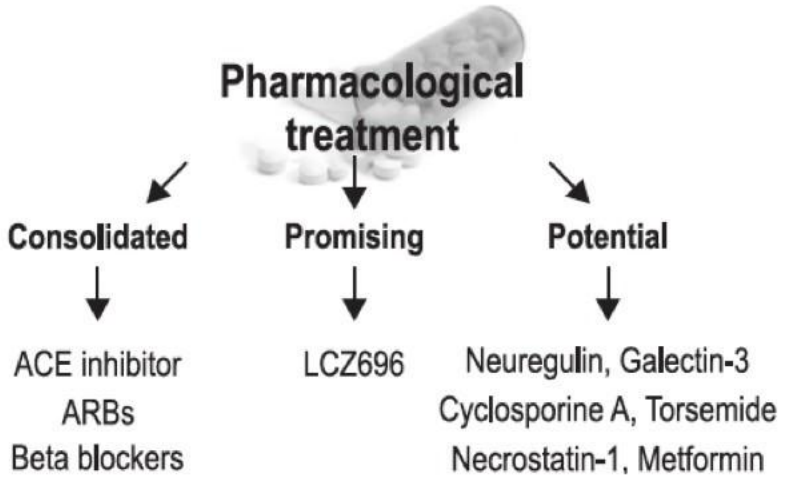


HỘI TIM MẠCH HỌC VIỆT NAM

Goldberger JJ, et al. J Am Coll Cardiol, 2015;66:1431–41.

Câu chuyện khác về tái cấu trúc sau NMCT



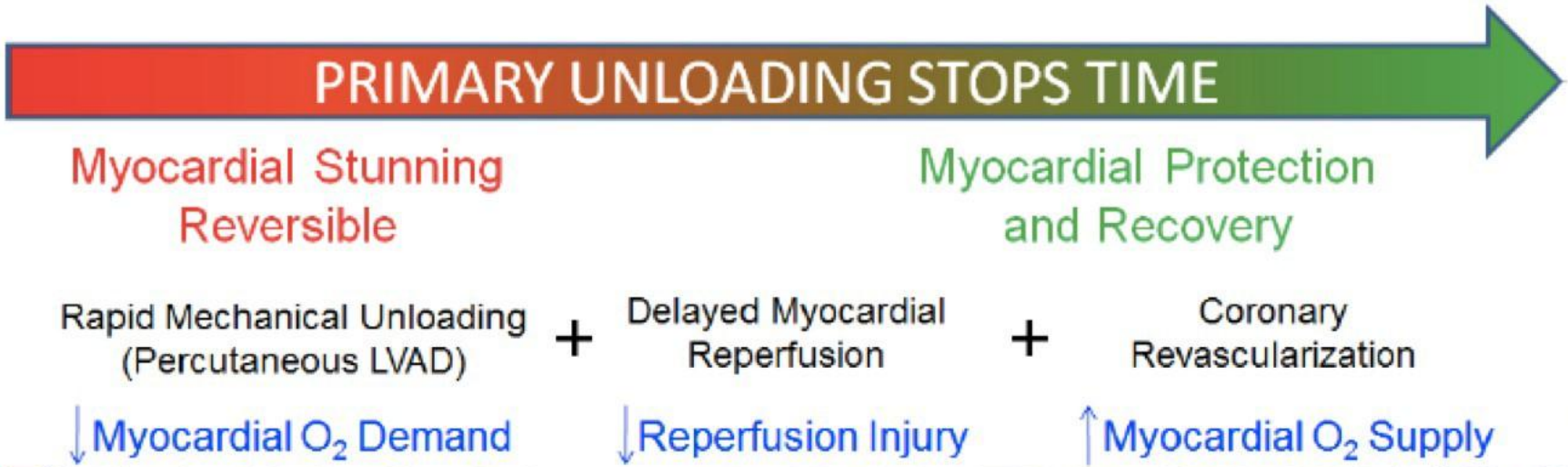


Mechanism	Main changes	
Cell death	↑ apoptosis, ↑necrosis ↓ autophagy	Progressive myocyte loss
Energy metabolism	β oxidation Triglyceride accumulation ↑ glycolysis Mitochondrial dysfunction Mitochondrial atrophy	Lipotoxicity ↓ energy ↑ oxidative stress
Oxidative stress	↑ NADPH oxidase ↑ catecholamine degradation ↑ xanthine oxidase Mitochondrial dysfunction ↓ antioxidant systems	Lipid peroxidation Protein oxidation DNA damage Cell dysfunction Fibroblast proliferation Metalloproteinase activation ↑ apoptosis ↑ signaling pathways to hypertrophy
Inflammation	innate response Adaptive response dysfunction	↑ inflammatory cytokines Macrophage, T cell and B cell dysfunction
Collagen	Fibroblast proliferation ↑ metalloproteinases	Degradation of normal collagen Fibrosis
Contractile proteins	β-myosin ↓ α-myosin ↑ troponin T type 2 ↓ troponin I phosphorylation	↓ contractility
Calcium transport	↓ L-type calcium channels ↓ ryanodine ↓ calsequestrin ↓ calmodulin ↓Phospholamban phosphorylation ↓ SERCA 2a	↓ Calcium in systole ↑ Calcium in diastole
Geometry	LV cavity ↓ wall thickness Elliptical shape → spherical shape	↑ parietal stress of the LV
Neurohormonal activation	↑ renin–angiotensin–aldosterone system ↑ Sympathetic	↑ cell death, ↑ oxidative stress, ↑ inflammation, ↑ metalloproteinases and fibroblasts, hypertrophy, vasoconstriction

LV: Left ventricle

Azevedo PS, et al. Arq Bras Cardiol, 2016;106(1):62-9.

Xu hương giảm tải thất trái và tái thông ĐMV



Kết luận

Xu thế mới chủ đạo trong xử trí hội chứng vành cấp nhằm ***giảm thiểu tử vong và biến cố tim mạch sớm/lâu dài bao gồm suy tim***

- Phát hiện sớm nhồi máu cơ tim để can thiệp hiệu quả sử dụng chỉ điểm sinh học có độ nhậy cao: ***phác đồ hs-cTn 0/1h hoặc CCT.***
- Lựa chọn chiến lược tái thông hiệu quả mạch vành bằng can thiệp sớm, can thiệp toàn diện, phối hợp tiêu sợi huyết-can thiệp
- Hạn chế các tác hại của bậc thang đông máu bằng điều trị sớm trước khi đến viện: *mon**APES***
- Ưu tiên ngăn ngừa tổn thương do tái tưới máu; giảm tải thất trái trong đó dùng chẹn beta sớm có vẻ có hiệu quả

Xin cảm ơn sự chú ý của các quý đại biểu!