ACC Middle East Conference 2018

In partnership with:

جمعية القلب السعودية
Saudi Heart Association

Rapid assessment algorithms using hs-cTnT; ensuring timely reperfusion including pharmacoinvasive strategies

Nasser A Mahdi, MD, FACC
King Faisal Specialist Hospital & Research Center

Rapid assessment algorithms using hs-cTnT

- About 20 million patients present with symptoms suggestive of myocardial infarction (MI) to ED
- Demographics, traditional risk factors, chest pain characteristics, and physical examination can assist but are insufficient who does and does not have MI
- The early diagnosis of MI is crucial for the early initiation of evidence-based treatment
- 20% of AMI & 40% of UA have normal EKG in emergency room
- Only about one in four of those with significant ST depression prove to have ACS

MI with Non-diagnostic EKG

EKG often does not detect:-

- Transient myocardial ischemia.
- Ischemia in patients with prior MI.
- Vein graft occlusion.

MI with Non-diagnostic EKG

- Ronan 1989 (AJC), Slaler 1987 (AJC) 3 – 10%
- Singer 1997 (Ann Emerg Med) 17%
- Forest 2004 (Ann Emerg Med) 2%
- Chase M 2006 (Acta Emerg Med) 2.8%
- Samuel D 2009 (Acta Emerg Med) 7%

Myocardial Necrosis Markers
Troponins

- Troponin T exhibits a dual release initially of the cytoplasmic component and later of the bound component.
- Troponin I is extremely specific for the cardiac muscle and has not been isolated from the skeletal muscle.
- This absolute specificity makes it an ideal marker of myocardial injury.
- They are released into the circulation 6-8 h after myocardial injury, peak at 12-24 h and remain elevated for 7 – 10 days. Only disadvantage of cTn is the late clearance that makes it difficult to identify a recurrent myocardial infarction.

MI with Non-diagnostic EKG

- EKG should be obtained within 10 minutes of arrival of patient in ED.
- EKG should be repeated at 20 – 30 minute intervals for any patient with ongoing chest pain in high suspicion case.
- Serial EKG equally specific (95%) but more sensitive than an initial single EKG for detecting acute MI (68 Vs 55%).

- If the standard leads are inconclusive, additional leads to be obtained. V3R, V4R, V6,7,8, 9, high lateral leads.
- Computer assisted ST-T monitoring.

Sensitive & High Sensitivity Cardiac Troponin Assays

- Detection of cTn in
- ~ 20 -50% of healthy individuals (sensitive)
- ~ 50-70% of healthy individuals (high sensitivity)
- Normal = the 99th percentile

- cTn value above the 99 percentile of a normal reference population is a ‘condition sine que non’ for diagnosis of AMI

Clinical implications of high-sensitivity cardiac troponin assays

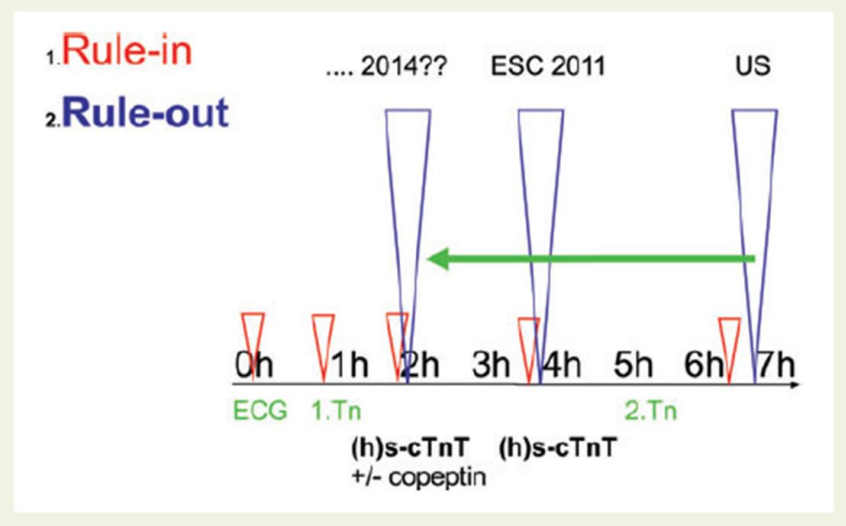
Compared with standard cardiac Troponin assays, high sensitivity assays:

- Have higher negative predictive value for acute MI.
- Reduce the “troponin-blind” interval leading to earlier detection of acute MI.
- Result in a ~4% absolute and ~20% relative increases in the detection of type I MI and a corresponding decrease in the diagnosis of unstable angina.
- Are associated with a 2-fold increase in the detection of type 2 MI.

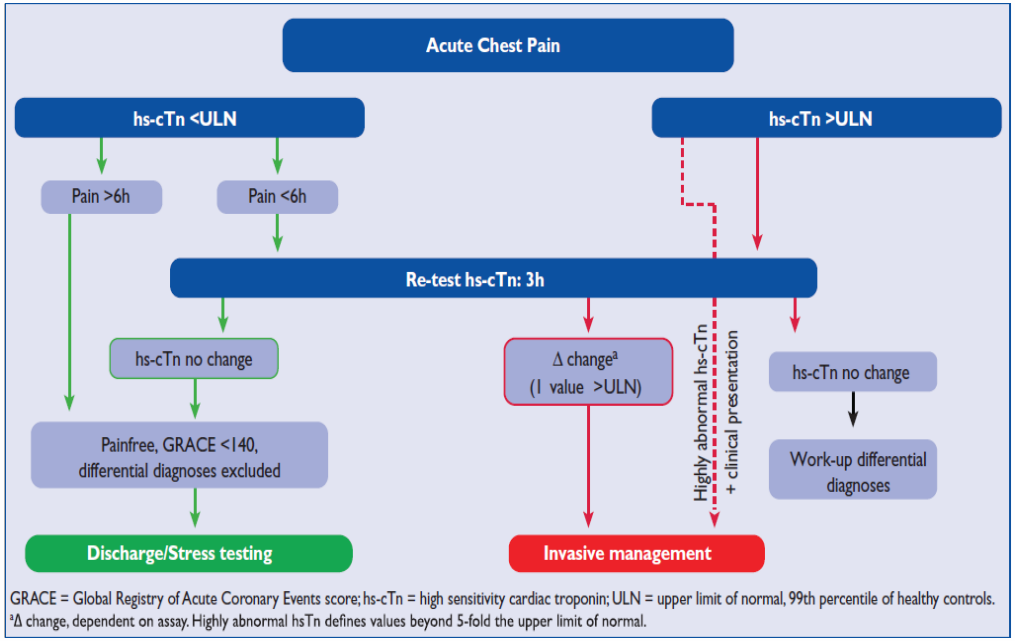
Rapid Rule-out & Rule-in Protocol

- Excellent performance of 2 hrs rule-out protocol that combines hs-cTn value with clinical information.
- Also 1 hr rule-out & rule-in protocol based on hs-cTnT values.
- There is immense diagnostic value of interpreting hs-cTn concentration as quantitative value.

The use of sensitive or high-sensitivity cardiac troponin [(h)s-cTn] allows more rapid rule-out and more rapid rule-in.

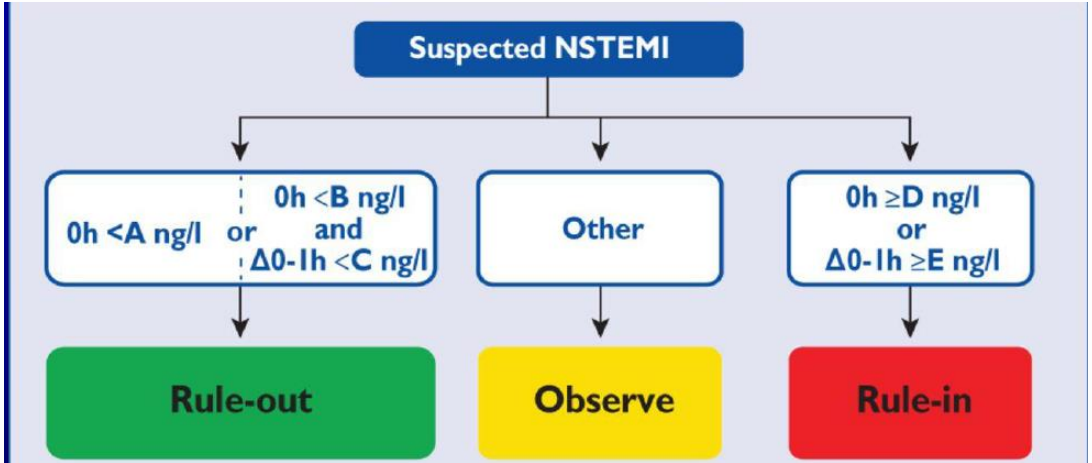


0 h / 3 h rule-out algorithm of non-ST elevation acute coronary syndrome using high-sensitivity cardiac troponin assays

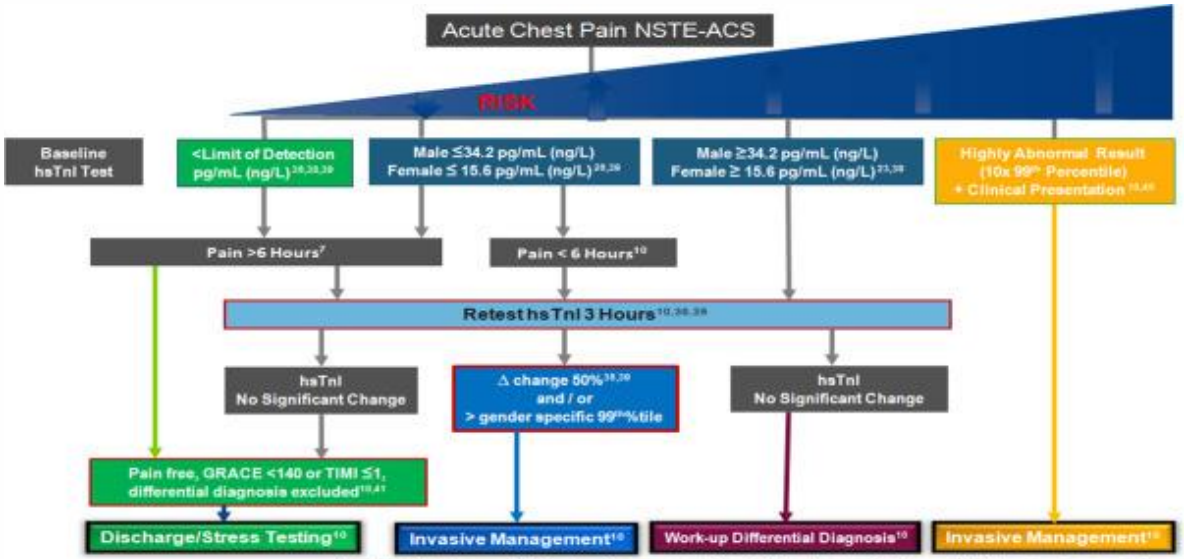


GRACE = Global Registry of Acute Coronary Events score; hs-cTn = high sensitivity cardiac troponin; ULN = upper limit of normal, 99th percentile of healthy controls.
[a]Δ change, dependent on assay. Highly abnormal hsTn defines values beyond 5-fold the upper limit of normal.

0 h / 1 h rule-out algorithm of non-ST elevation acute coronary syndrome using high-sensitivity cardiac troponin assays

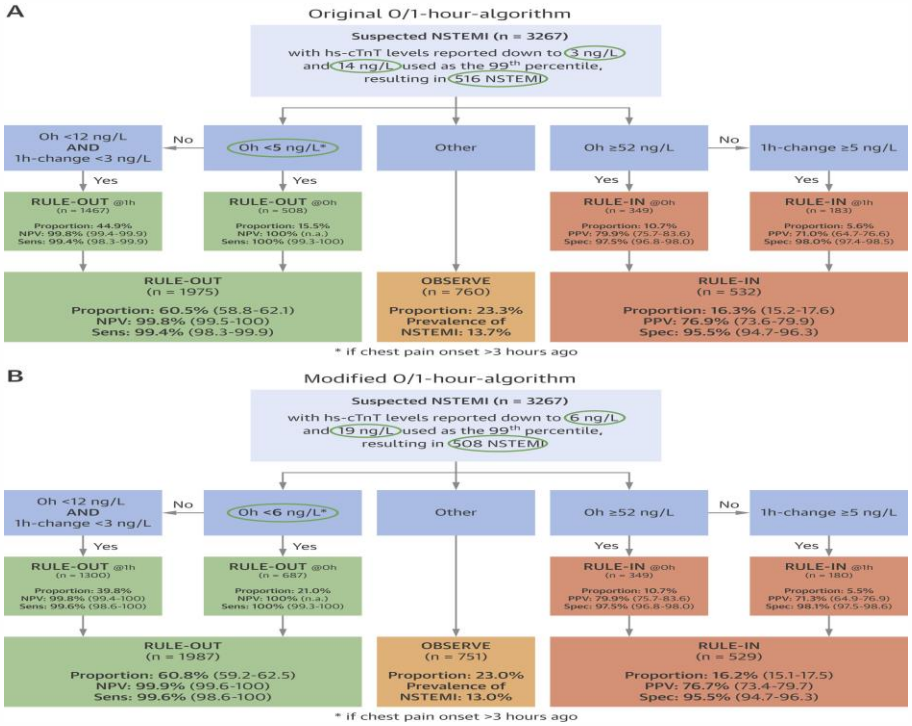


	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)	0.5	5	2	107	19



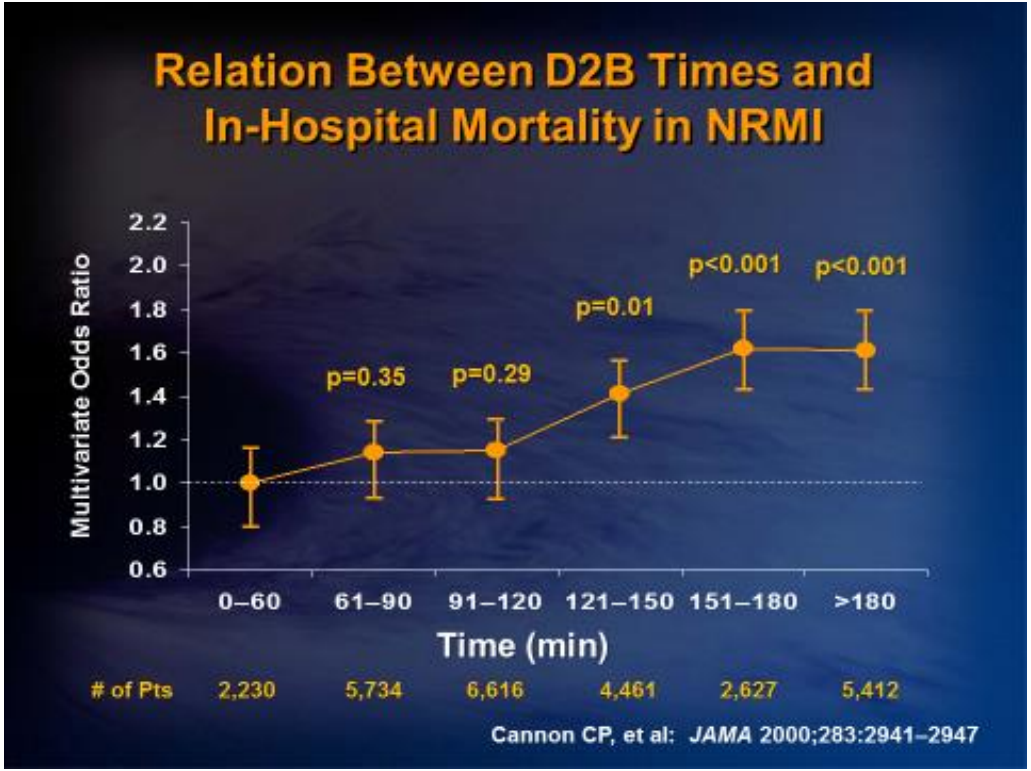
*Each institution must determine the appropriate delta for their patients, while this may be a good starting point for evaluation purposes

hsTnI= Abbott *STAT* high sensitive troponin I, GRACE=global registry of acute coronary events, TIMI=thrombolysis UA/NSTEMI, NSTE-ACS = Non ST Elevation Acute Coronary Syndrome


A
Original 0/1-hour-algorithm
Suspected NSTEMI (n = 3267)
with hs-cTnT levels reported down to 3 ng/L
and 14 ng/L used as the 99th percentile,
resulting in 516 NSTEMI
0h <12 ng/L AND 1h-change <3 ng/L
No
0h <5 ng/L*
Other
0h ≥52 ng/L
No
1h-change ≥5 ng/L
Yes
Yes
Yes
Yes
RULE-OUT @1h (n = 1467)
Proportion: 44.9%
NPV: 99.8% (99.4-99.9)
Sens: 99.4% (98.3-99.9)
RULE-OUT @0h (n = 508)
Proportion: 15.5%
NPV: 100% (n.a.)
Sens: 100% (99.3-100)
RULE-IN @0h (n = 349)
Proportion: 10.7%
PPV: 79.9% (75.7-83.6)
Spec: 97.5% (96.8-98.0)
RULE-IN @1h (n = 183)
Proportion: 5.6%
PPV: 71.0% (64.7-76.6)
Spec: 98.0% (97.4-98.5)
RULE-OUT
(n = 1975)
Proportion: 60.5% (58.8-62.1)
NPV: 99.8% (99.5-100)
Sens: 99.4% (98.3-99.9)
OBSERVE
(n = 760)
Proportion: 23.3%
Prevalence of NSTEMI: 13.7%
RULE-IN
(n = 532)
Proportion: 16.3% (15.2-17.6)
PPV: 76.9% (73.6-79.9)
Spec: 95.5% (94.7-96.3)
* if chest pain onset >3 hours ago
B
Modified 0/1-hour-algorithm
Suspected NSTEMI (n = 3267)
with hs-cTnT levels reported down to 6 ng/L
and 19 ng/L used as the 99th percentile,
resulting in 508 NSTEMI
0h <12 ng/L AND 1h-change <3 ng/L
No
0h <6 ng/L*
Other
0h ≥52 ng/L
No
1h-change ≥5 ng/L
Yes
Yes
Yes
Yes
RULE-OUT @1h (n = 1300)
Proportion: 39.8%
NPV: 99.8% (99.4-100)
Sens: 99.6% (98.6-100)
RULE-OUT @0h (n = 687)
Proportion: 21.0%
NPV: 100% (n.a.)
Sens: 100% (99.3-100)
RULE-IN @0h (n = 349)
Proportion: 10.7%
PPV: 79.9% (75.7-83.6)
Spec: 97.5% (96.8-98.0)
RULE-IN @1h (n = 180)
Proportion: 5.5%
PPV: 71.3% (64.9-76.9)
Spec: 98.1% (97.5-98.6)
RULE-OUT
(n = 1987)
Proportion: 60.8% (59.2-62.5)
NPV: 99.9% (99.6-100)
Sens: 99.6% (98.6-100)
OBSERVE
(n = 751)
Proportion: 23.0%
Prevalence of NSTEMI: 13.0%
RULE-IN
(n = 529)
Proportion: 16.2% (15.1-17.5)
PPV: 76.7% (73.4-79.7)
Spec: 95.5% (94.7-96.3)
* if chest pain onset >3 hours ago

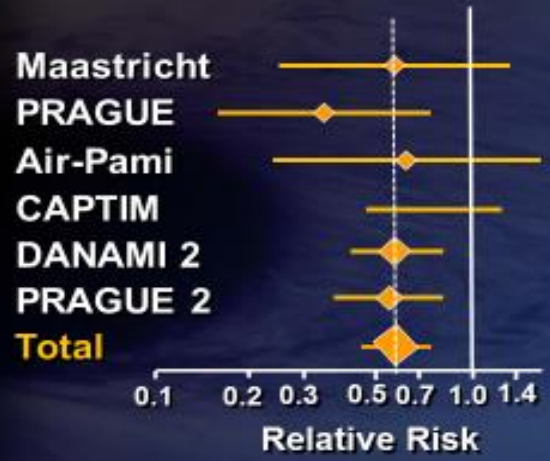
Current Guidelines for STEMI Patients With Expected Delays to PCI

Fibrinolysis Recommended if:	ACC/AHA	ESC
First Medical Contact (Door) to balloon	> 90 minutes	> 120 minutes


Relation Between D2B Times and In-Hospital Mortality in NRMI
Multivariate Odds Ratio
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
p=0.35
p=0.29
p=0.01
p<0.001
p<0.001
0–60
61–90
91–120
121–150
151–180
>180
Time (min)
# of Pts
2,230
5,734
6,616
4,461
2,627
5,412
Cannon CP, et al: JAMA 2000;283:2941–2947

Transfer for Primary PCI vs Lysis

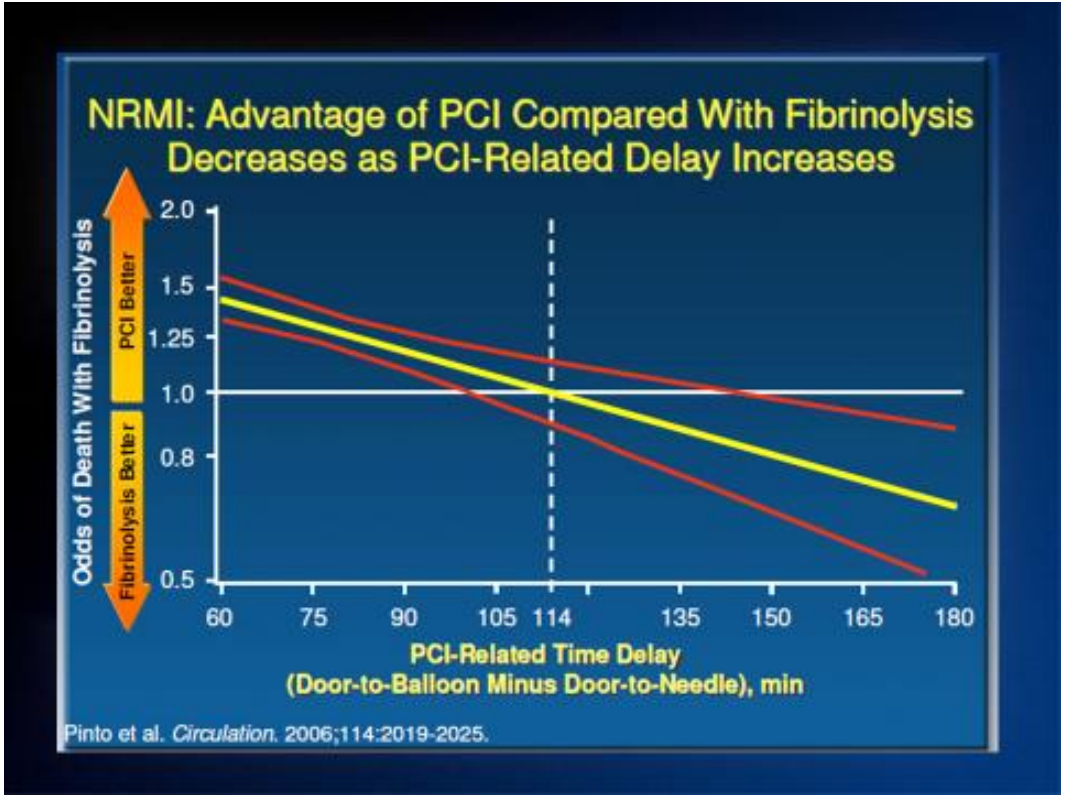
Death, Re-MI, Stroke



	PCI	Lysis
Maastricht	8/75	14/75
PRAGUE	8/101	23/99
Air-Pami	6/71	9/66
CAPTIM	26/421	34/419
DANAMI 2	63/790	107/782
PRAGUE 2	36/429	64/421
Total	147/1887	251/1863

OR: 0.58 p<0.001

Dalby M et al: Circ; 2003; 108: 1809


NRMI: Advantage of PCI Compared With Fibrinolysis Decreases as PCI-Related Delay Increases
Odds of Death With Fibrinolysis
PCI Better
Fibrinolysis Better
2.0
1.5
1.25
1.0
0.8
0.5
60
75
90
105
114
135
150
165
180
PCI-Related Time Delay
(Door-to-Balloon Minus Door-to-Needle), min
Pinto et al. Circulation. 2006;114:2019-2025.

Reperfusion Options for Transfer Patients with Expected Delays

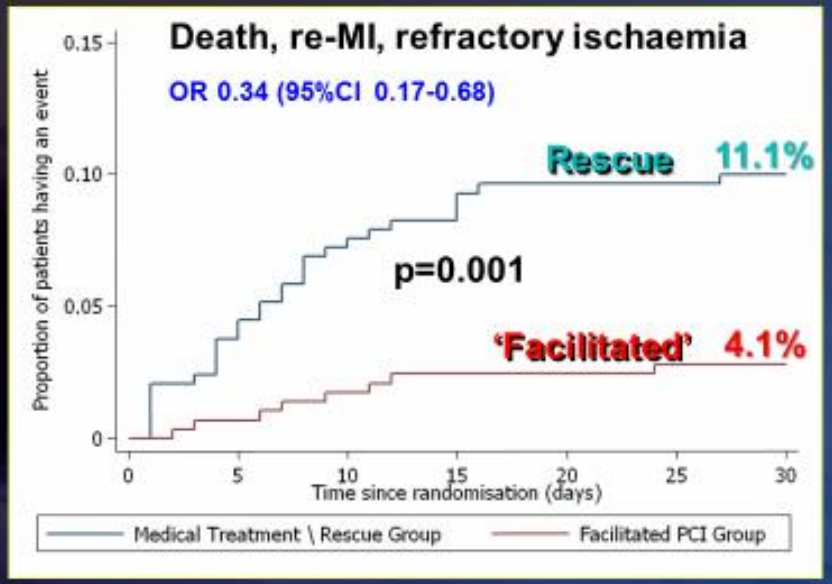
- Primary PCI (no matter how long it takes)
- Lysis; ischemia-guided transfer for rescue PCI
- Lysis with transfer for immediate ("early" PCI):
  Pharmaco-invasive strategy

Facilitated or Pharmaco-invasive

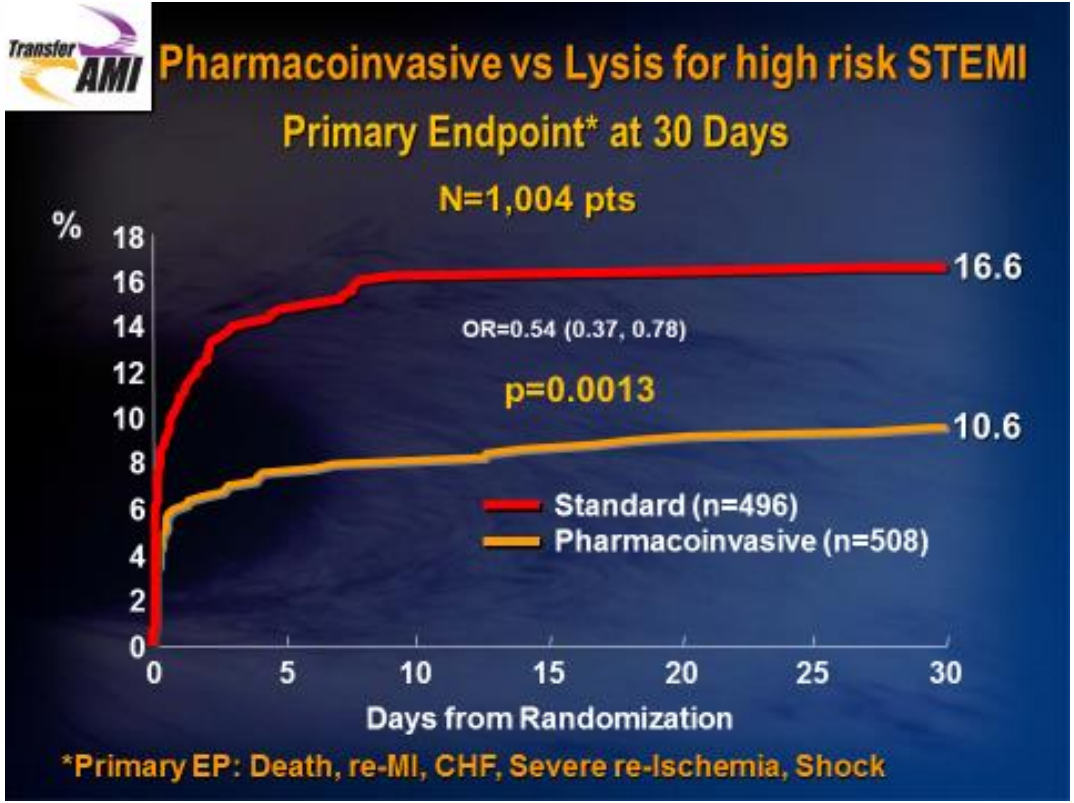
- AMICO Registry
- CARESS-in-AMI
- TRANSFER-AMI
- NOR-DISTEMI

CARESS IN AMI

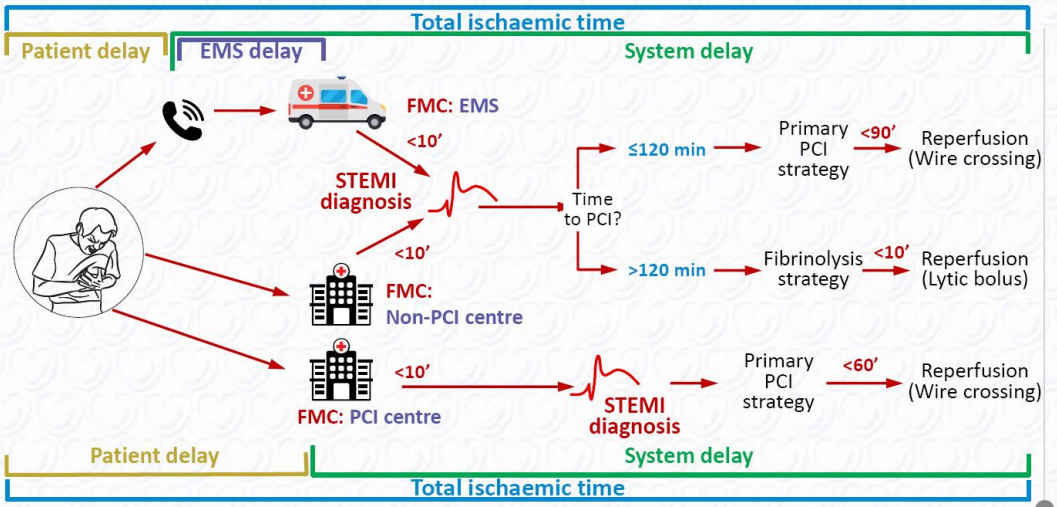
Primary Outcome at 30 days



DiMario C: Lancet 2008; 371:559-568


Transfer AMI
Pharmacoinvasive vs Lysis for high risk STEMI
Primary Endpoint* at 30 Days
N=1,004 pts
%
18
16
14
12
10
8
6
4
2
0
16.6
OR=0.54 (0.37, 0.78)
p=0.0013
10.6
Standard (n=496)
Pharmacoinvasive (n=508)
0
5
10
15
20
25
30
Days from Randomization
*Primary EP: Death, re-MI, CHF, Severe re-Ischemia, Shock

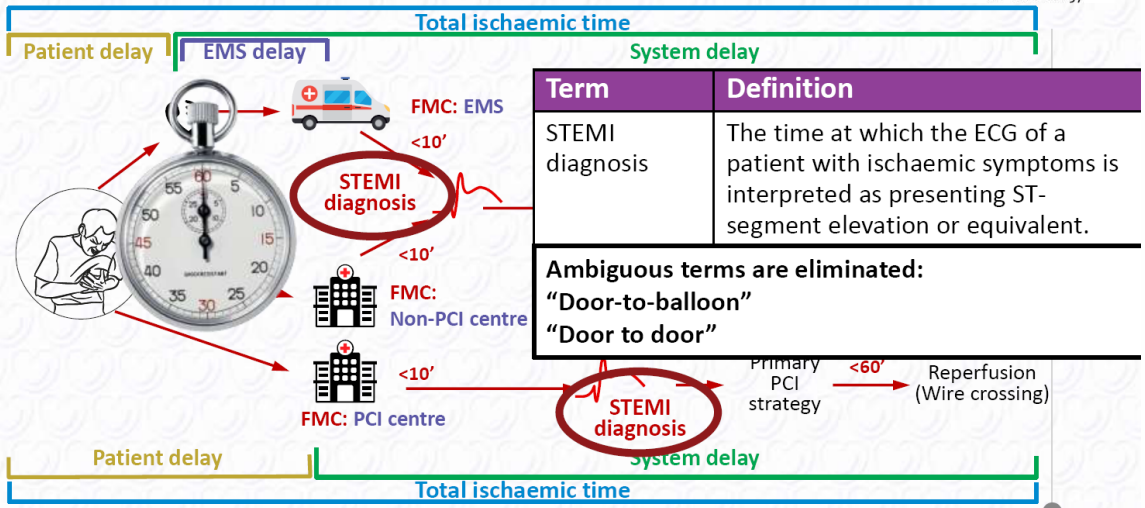
Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection



www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection

ESC European Society of Cardiology



Term	Definition
STEMI diagnosis	The time at which the ECG of a patient with ischaemic symptoms is interpreted as presenting ST-segment elevation or equivalent.

Ambiguous terms are eliminated:
"Door-to-balloon"
"Door to door"

www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Summary of important time targets

ESC European Society of Cardiology

Intervals	Time targets
Maximum time from FMC to ECG and diagnosis.	≤10 min
Maximum expected delay from STEMI diagnosis to primary PCI (wire crossing) to choose primary PCI strategy over fibrinolysis (if this target time cannot be met, consider fibrinolysis).	≤120 min
Maximum time from STEMI diagnosis to wire crossing in patients presenting at primary PCI hospitals.	≤60 min
Maximum time from STEMI diagnosis to wire crossing in transferred patients.	≤90 min

Summary of important time targets
(continued)

ESC European Society of Cardiology

Intervals	Time targets
Maximum time from STEMI diagnosis to bolus or infusion start of fibrinolysis in patients unable to meet primary PCI target times.	≤10 min
Time delay from start of fibrinolysis to evaluation of its efficacy (success or failure).	60-90 min
Time delay from start of fibrinolysis to angiography (if fibrinolysis is successful).	2-24 hours

Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection

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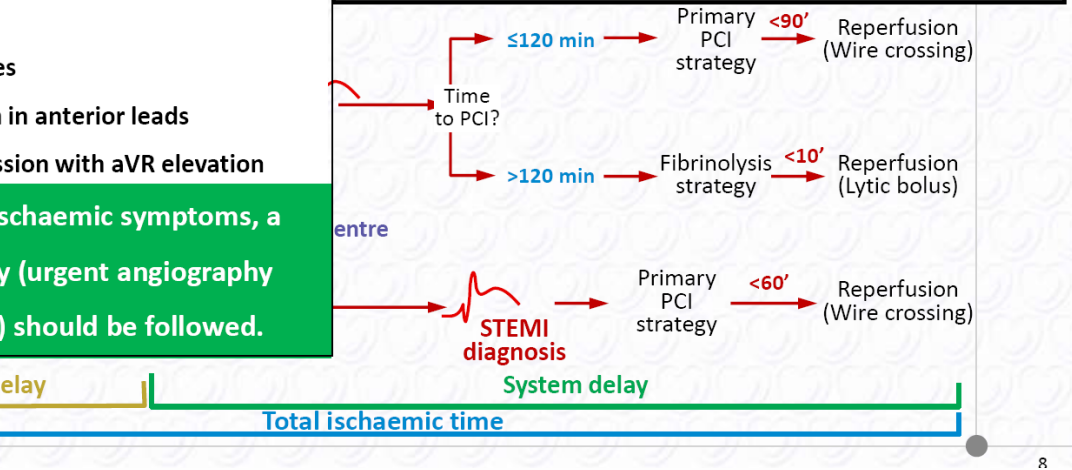
Atypical ECG presentations

- Bundle branch block
- Ventricular pacing
- Hyper-acute T waves
- Isolated depression in anterior leads
- Universal ST depression with aVR elevation

In the presence of ischaemic symptoms, a primary PCI strategy (urgent angiography and PCI if indicated) should be followed.

Left and right bundle branch block are considered equal for recommending urgent angiography if ischaemic symptoms.



Reperfusion strategies in the infarct-related artery according to time from symptoms onset

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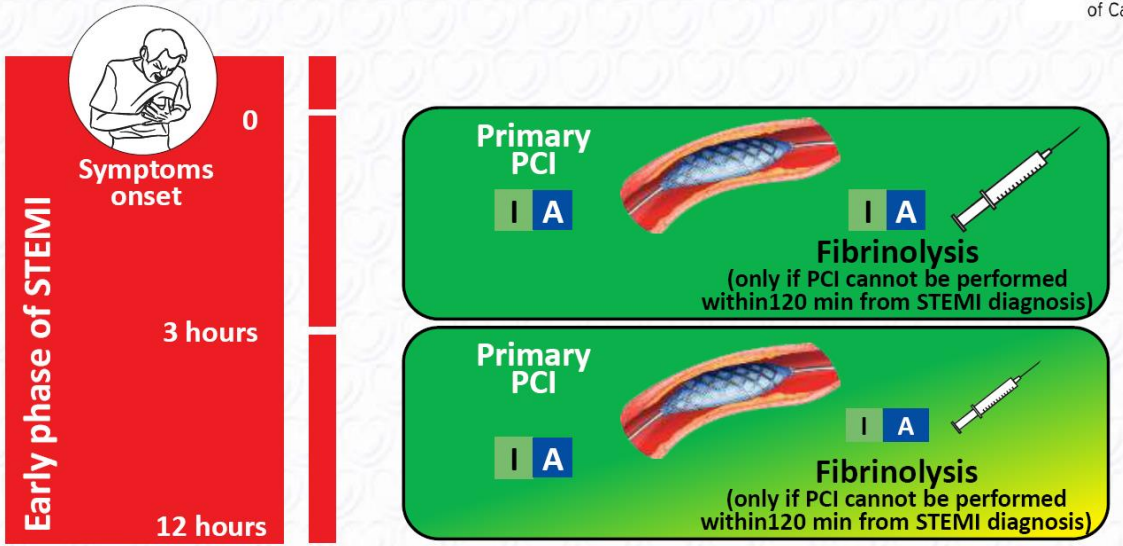

Reperfusion strategies in the infarct-related artery according to time from symptoms onset *(continued)*

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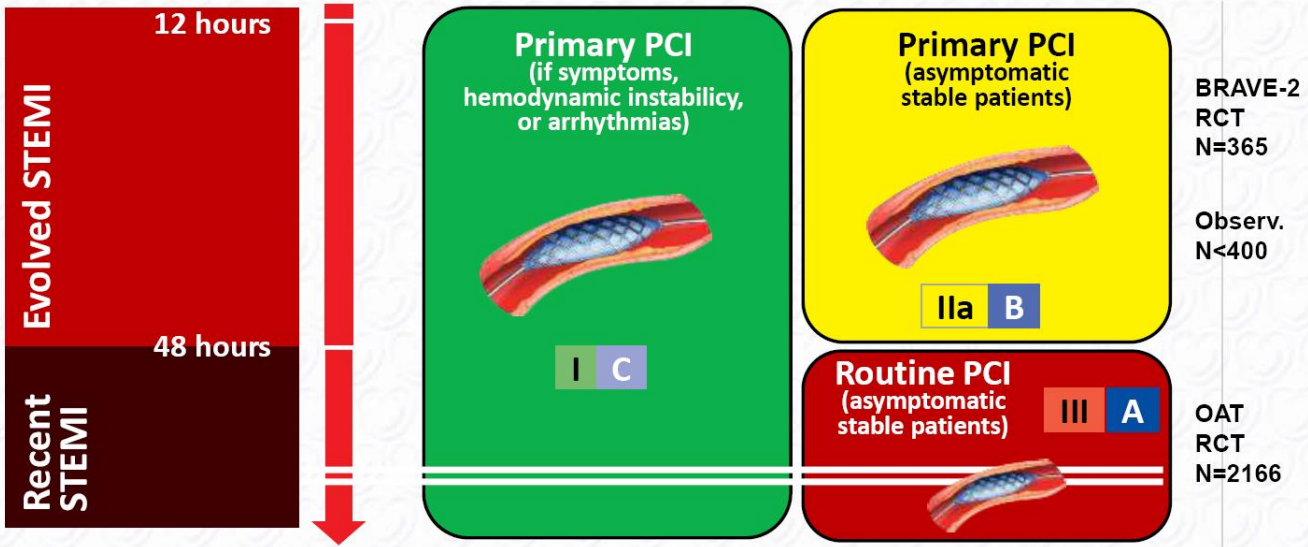

Fibrinolytic therapy

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Recommendations	Class	Level
When fibrinolysis is the reperfusion strategy, it is recommended to initiate this treatment as soon as possible after STEMI diagnosis, preferably in the prehospital setting.	I	A
A fibrin-specific agent (i.e. tenecteplase, alteplase, reteplase) is recommended.	I	B
A half-dose of tenecteplase should be considered in patients ≥75 years of age.	IIa	B
Antiplatelet co-therapy with fibrinolysis		
Oral or i.v. aspirin is indicated.	I	B
Clopidogrel is indicated in addition to aspirin.	I	A
DAPT (in the form of aspirin plus a $P2Y_{12}$ inhibitor) is indicated for up to 1 year in patients undergoing fibrinolysis and subsequent PCI.	I	C

NEW*

*STREAM study: 3/37 pts in this age group had ICH → protocol amendment → 0/97 pts with half dose

Fibrinolytic therapy *(continued)*

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Recommendations	Class	Level
Interventions following fibrinolysis		
Emergency angiography and PCI if indicated is recommended in patients with heart failure/shock.	I	A
Rescue PCI is indicated immediately when fibrinolysis has failed (< 50% ST-segment resolution at 60-90 min) or at any time in the presence of haemodynamic or electrical instability, or worsening ischaemia.	I	A
Angiography and PCI of the IRA, if indicated, is recommended between2 and 24 hours after successful fibrinolysis.	I	A
Emergency angiography and PCI if needed is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.	I	B

What is new in 2017 Guidelines on AMI-STEMI

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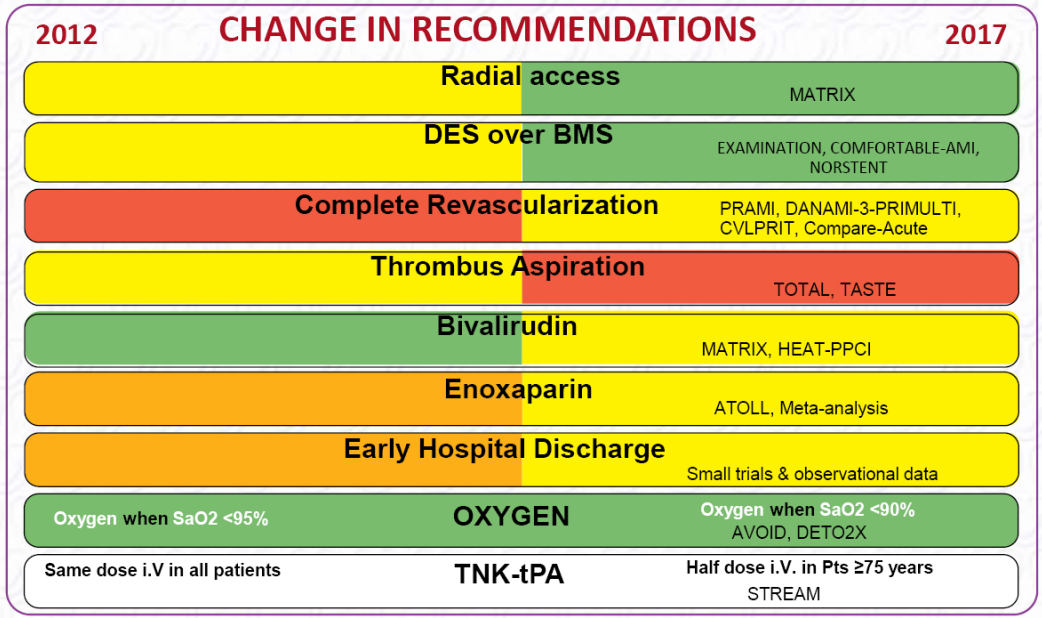

What is new in 2017 Guidelines on AMI-STEMI

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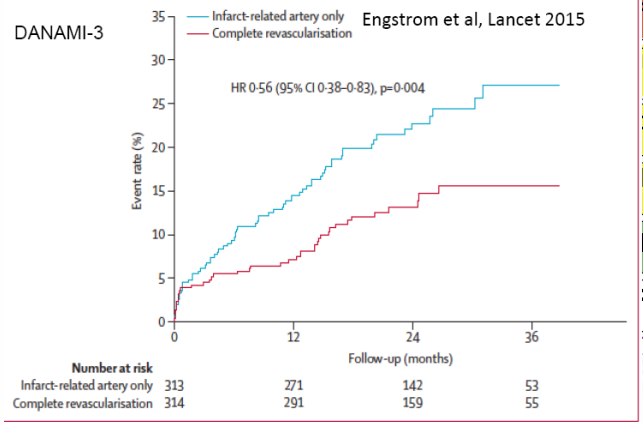
CHANGE IN RECOMMENDATIONS

2012	2017
Radial access	MATRIX
DES over BMS	EXAMINATION, COMFORTABLE-AMI, NORSTENT
Complete Revascularization	PRAMI, DANAMI-3-PRIMULTI, CVLPRIT, Compare-Acute
…spiration	TOTAL, TASTE
…din	MATRIX, HEAT-PPCI
…parin	ATOLL, Meta-analysis
Discharge	Small trials & observational data
…EN	Oxygen when SaO2 <90% AVOID, DETO2X
…PA	Half dose i.V. in Pts ≥75 years STREAM

DANAMI-3



…nt of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

What is new in 2017 Guidelines on AMI-STEMI

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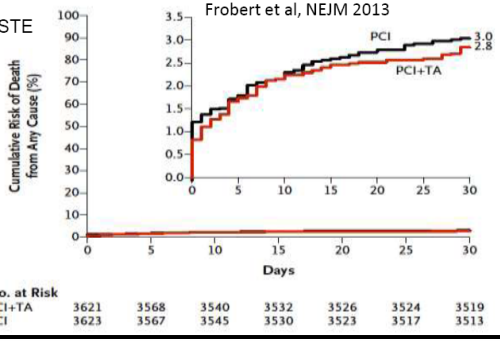
CHANGE IN RECOMMENDATIONS

2012	2017
Radial access	MATRIX
DES over BMS	EXAMINATION, COMFORTABLE-AMI, NORSTENT
Complete Revascularization	PRAMI, DANAMI-3-PRIMULTI, CVLPRIT, Compare-Acute
Thrombus Aspiration	TOTAL, TASTE
valirudin	
oxaparin	
pital Discharge	
XYGEN	
NK-tPA	

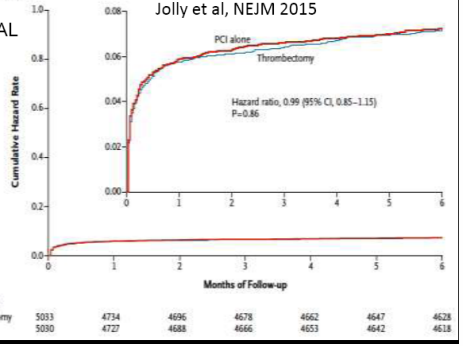
TASTE

Frobert et al, NEJM 2013



TOTAL

Jolly et al, NEJM 2015



nagement of AMI-STEMI (Eu

Thank You