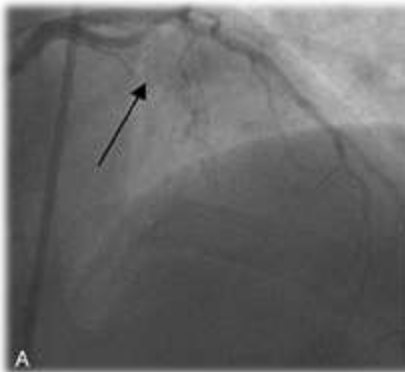
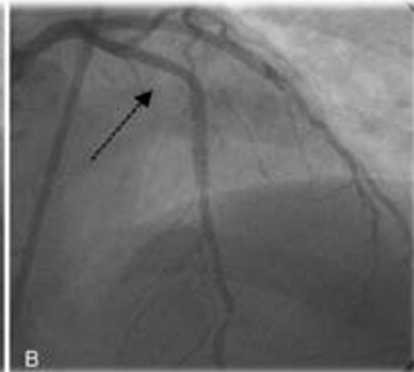


'A second fast strong blow is, usually, the final blow'

Mohammed Ali (1942- 2016)



Ischemia



Reperfusion

A double injury process

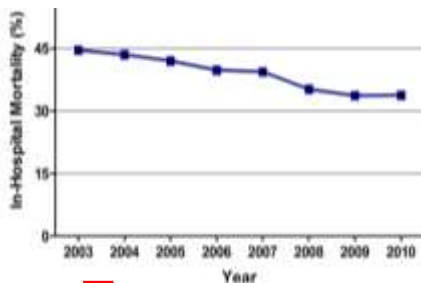
N-acetylcysteine for myocardial salvage in STEMI

The NACIAM trial

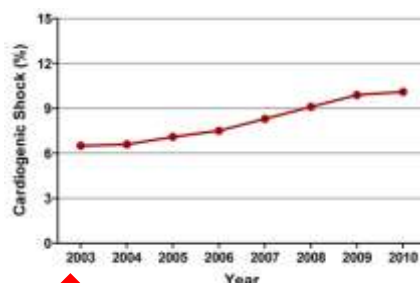
By

Ahmed Bendary (MD)

Cardiology department
Benha University



Mortality



Heart failure

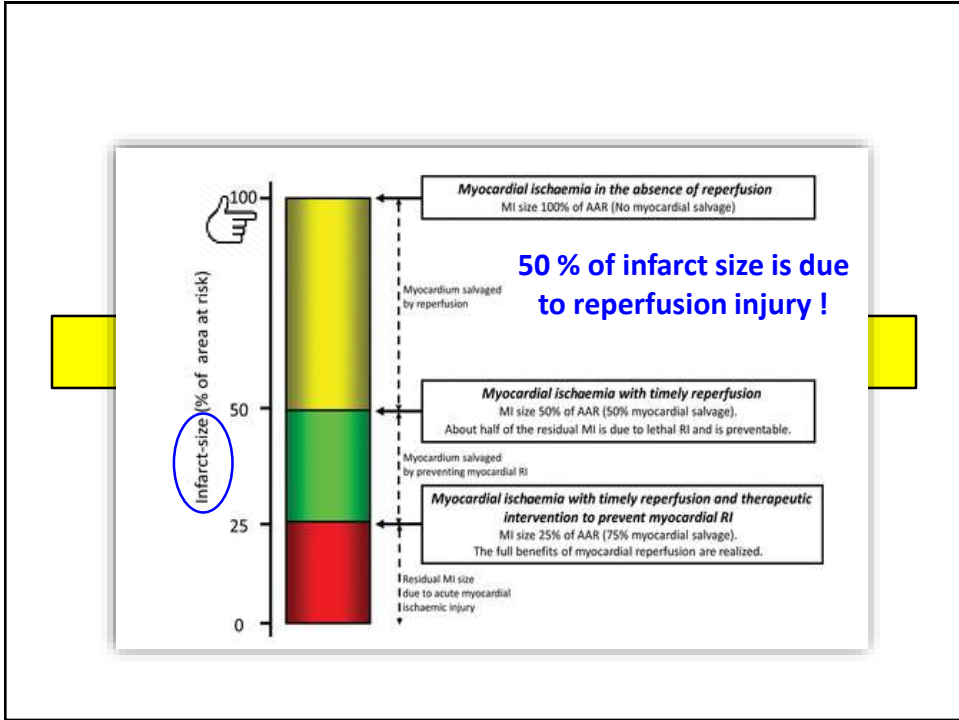


ORIGINAL RESEARCH



Infarct Size, Shock, and Heart Failure: Does Reperfusion Strategy Matter in Early Presenting Patients With ST-Segment Elevation Myocardial Infarction?

Jay Shrivastava, MD; Yinggan Zheng, MA, MEd; Nasta Dhanraj Maleki, MD; Kurt Huber, MD; Signun Hakvonen, MD; Patrick Goldstein, MD; Anthony K. Denstchick, MD; Robert Wilcox, MD; Franz Van de Werf, MD, PhD; Paul W. Armstrong, MD



Acute ischemia is unpredictable

BUT

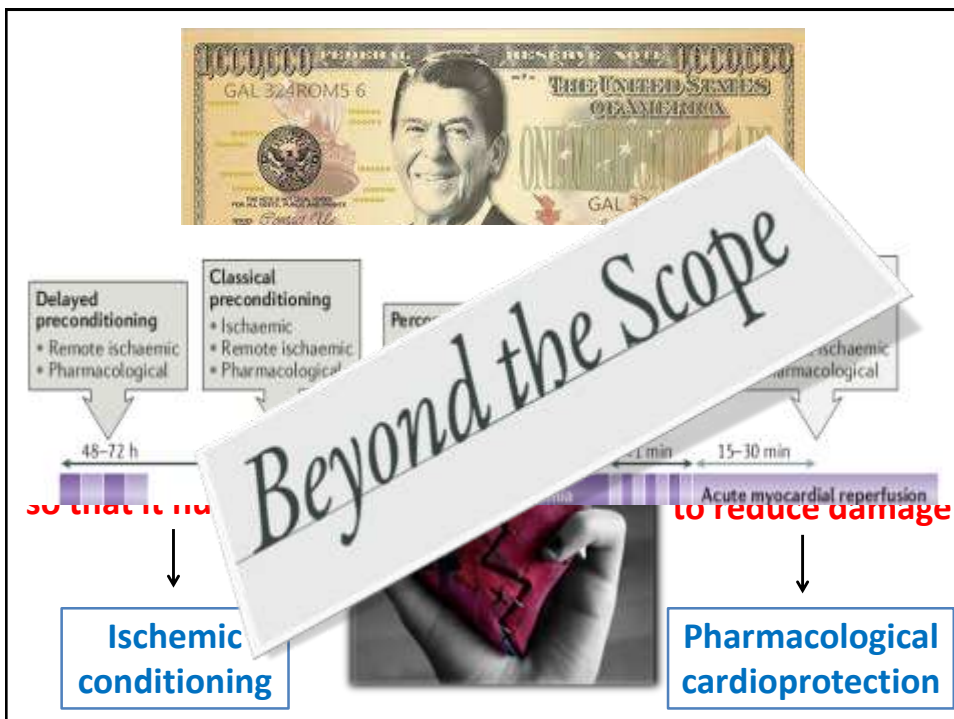
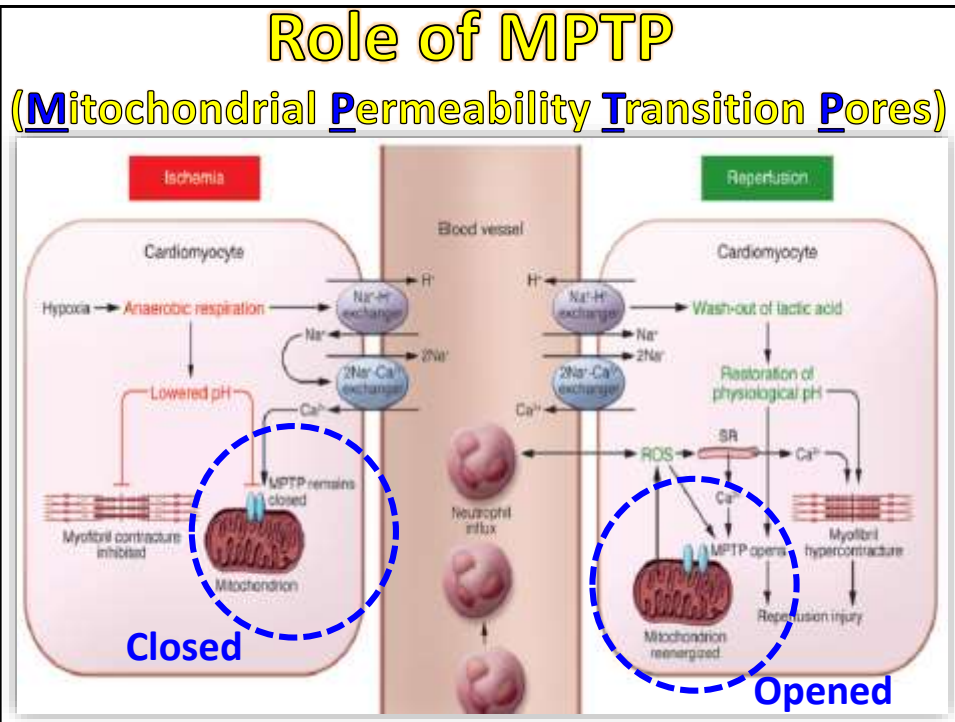
What we miss is really important

Tempo and momentum of reperfusion could be timely controlled



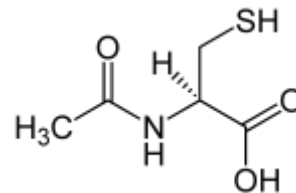
1 O'Clock







N-acetylcysteine



- N-acetyl derivative of amino acid L-cysteine.
- Precursor of the anti-oxidant 'Glutathione'.

Circulation

ARTICLES

N-Acetylcysteine in Combination With Nitroglycerin and Streptokinase for the Treatment of Evolving Acute Myocardial Infarction
Safety and Biochemical Effects


Margaret A. Anstall, Jialu Yang, Irene Stafford, W. Henry Betts, John D. Horowitz

1995

https://doi.org/10.1161/01.CIR.92.10.2855
Circulation. 1995;92:2855-2862
Originally published November 15, 1995


Conclusions NAC in combination with NTG and streptokinase appeared to be safe for the treatment of evolving AMI and was associated with significantly less oxidative stress, a trend toward more rapid reperfusion, and better preservation of left ventricular function.

- Primitive.
- Small number (27).
- Used ST resolution & Echo only for assessment of infarct size.

 **Journal of the American College of Cardiology** 
Volume 39, Issue 9, 1 May 2002, Pages 1422-1428

Review article

N-acetylcysteine in acute cardiology: 10 years later: What do we know and what would we like to know?!

Jan Sochman, MD, PhD[†]  

[†] Institute for Clinical and Experimental Medicine, Prague, Czech Republic

2002

Question formulation **????????????????**

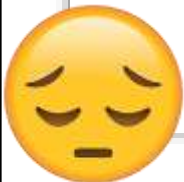
It is therefore logical to formulate what we want to learn: Is NAC clearly a beneficial agent reducing reperfusion injury in the treatment of acute MI as practiced today? To be able to answer this question, a large randomized multicentric study of the scope of GISSI, ISIS or GUSTO would be required.

CLINICAL RESEARCH **Interventional Cardiology**

Impact of High-Dose N-Acetylcysteine Versus Placebo on Contrast-Induced Nephropathy and Myocardial Reperfusion Injury in Unselected Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention **JACC, 2010**

The LIPSIA-N-ACC (Prospective, Single-Blind, Placebo-Controlled, Randomized Leipzig Immediate Percutaneous Coronary Intervention Acute Myocardial Infarction N-ACC) Trial

Conclusions High-dose intravenous N-acetylcysteine reduces oxidative stress. However, it does not provide an additional clinical benefit to placebo with respect to CIN and myocardial reperfusion injury in nonselected patients undergoing angioplasty with moderate doses of contrast medium and optimal hydration. (Myocardial Salvage and Contrast Dye Induced Nephropathy Reduction by N-Acetylcysteine [LIPSIA-N-ACC]; NCT00463749) (J Am Coll Cardiol 2010;55:2201-9) © 2010 by the American College of Cardiology Foundation



2011






The early use of N-acetylcysteine (NAC) with Glyceryl Trinitrate (GTN) in STEMI
 NACIAM Trial: A pilot study

2014
2015
2016

ESC CONGRESS ROME 2016

Objective

To assess the efficacy of adding high dose intravenous NAC to low dose intravenous GTN, in acute STEMI patients undergoing PCI

Endpoints

Efficacy

- Myocardial infarct size on early cardiac MRI (**Primary Endpoint**)
- Myocardial salvage (MRI)
- Left ventricular ejection fraction (MRI)
- Creatine kinase kinetics

Safety

- Acute adverse events
- 2 year outcomes

Study design

- Randomised, double-blind, placebo-controlled multicentre trial
- Conducted in three South Australian tertiary hospitals
- **Study entry:** March 2010 and March 2013
- **Follow up:** 2 Years (March 2015)



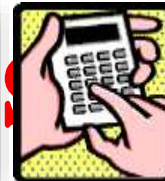
Sample size calculation

Sample size calculation (Powered for infarct size)



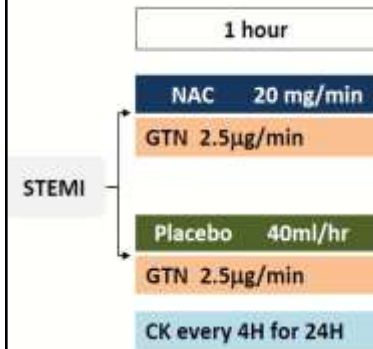
Assuming mean infarct size for placebo of $13 \pm 3\%$

- **Sample size:** 36 patients/group for a 2% absolute difference

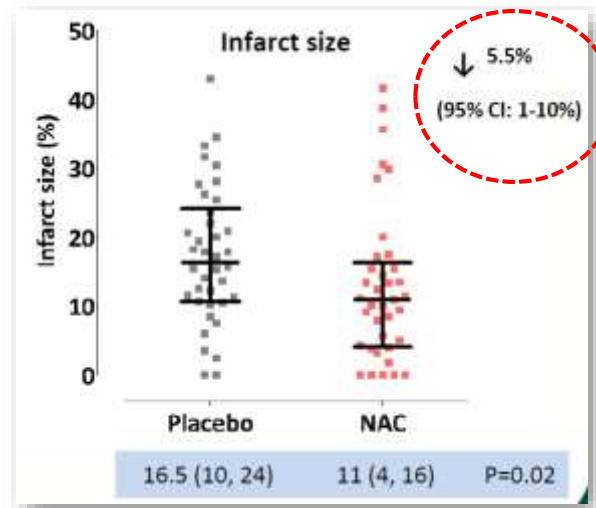


Recruitment target: ~50 patients per group (Assumed ~ 30% dropouts)

Study timeline



Main results



5.5% ABSOLUTE RISK REDUCTION IN INFARCT SIZE

Main results

Other MRI parameters...

	Placebo (38)	NAC (37)	P
Anterior Infarct	39%	35%	0.81
Microvascular obstruction	1.1 ± 1.8	0.95 ± 1.8	0.66
Myocardial Salvage	27% (14%, 41%)	60% (37%, 79%)	0.001
Transmural infarct	79%	54%	0.02
Infarct size at late MRI	10% (7%, 15%)	5% (1%, 12%)	0.02

Main results

Safety

	Placebo(59)	NAC(53)	P value
Acute adverse events			
Deaths	4%	0	0.49
Hypotension	27%	26%	1.00
Bleeding	7%	6%	1.00
Renal dysfunction	9%	6%	0.72
2 Year Outcomes			
Death or Cardiac readmission	27%	6%	0.02



Limitations

- **Dose response characteristics** – need further evaluation
- **Magnitude of effect** – wide confidence intervals
- **Mechanism of effect** – further investigation
- **Impact on clinical outcomes** – requires larger study

Study conclusion

Addition of intravenous NAC to intravenous GTN:

- Reduces infarct size
- Increases myocardial salvage
- Larger effect with shorter duration of ischaemia
- Safe



THE

TAKE-HOME MESSAGE

In re-perfused STEMI, the image may be so beautiful ...

thank you!



But always look twice ...

And take care of the ugly side of reperfusion