

“Troponin: ‘leaks’, ‘bumps’
and ‘elevations’: is it an MI or
not an MI that is the
question?”.

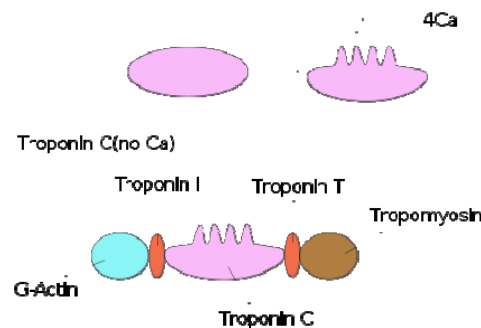
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Anesthesiology and Critical Care
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Conflicts of interest

- Baxter
- The Medicines Company

Outline

- Troponins have supplanted CK-MB
 - More sensitive, specific
 - Not perfect
- Do they provide **additive** information?
 - More than preoperative risk factors?
 - More than perioperative course?
 - The otherwise asymptomatic patient
- Costs?
 - Costs driven by interventions taken



Individual subunits serve different functions:

- [Troponin C](#) binds to calcium ions to produce a conformational change in TnI
- [Troponin T](#) binds to tropomyosin, interlocking them to form a troponin-tropomyosin complex
- [Troponin I](#) binds to actin in thin myofilaments to hold the troponin-tropomyosin complex in place

<http://en.wikipedia.org/wiki/Troponin>

Troponin reference ranges

Troponin I interpretative ranges:

- ≤ 0.03 ng/mL = no detectable cardiac injury
- $0.04 - 0.49$ ng/mL = cardiac muscle injury
- ≥ 0.5 ng/mL = myocardial infarction (96% sensitivity and 94% specificity)

Expert Consensus Document

Universal Definition of Myocardial Infarction

Kristian Thygesen; Joseph S. Alpert; Harvey D. White;
on behalf of the Joint ESC/ACCF/AHA/WHF Task Force
for the Redefinition of Myocardial Infarction

TASK FORCE MEMBERS

Chairpersons: Kristian Thygesen (Denmark)*, Joseph S. Alpert (USA)*, Harvey D. White (New Zealand)*
Biomarker Group: Allan S. Jaffe, Coordinator (USA), Fred S. Apple (USA), Marcello Galvani (Italy),
Hugo A. Katus (Germany), L. Kristin Newby (USA), Jan Ravkilde (Denmark) ECG Group: Bernard Chaitman, Co-ordinator
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Imaging Group: Richard Underwood, Coordinator (UK), Jeroen J. Bax (The Netherlands), George A. Beller (USA),
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Parkhomenko (Ukraine), Silvia G. Priori (Italy), Michal Tendera (Poland), Liisa-Maria Voipio-Pulkki (Finland)

Circulation. 2007 Nov 27;116(22):2634-53

When to draw troponins?

- Troponin levels should be drawn at the onset of symptoms and 6-9 hours later to evaluate the enzyme's rise and fall.
- Occasionally, the patient may require a blood sample 12-24 hours later if the initial troponin evaluation was normal and the clinical suspicion for cardiac ischemia was high.⁴

Circulation. 2007 Nov 27;116(22):2634-53

How to analyse troponins?

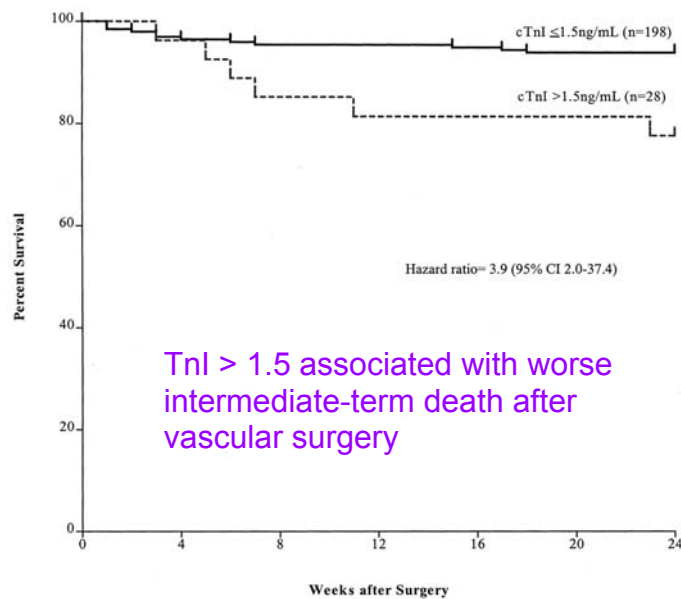
- An increased value for cardiac troponin is defined as a measurement > 99th percentile of a normal reference population (URL upper reference limit).
- Detection of a rise and/or fall of the measurements is essential to the diagnosis of acute myocardial infarction.⁶

Circulation. 2007 Nov 27;116(22):2634-53

Elevated troponin after vascular surgery associated with worse outcome

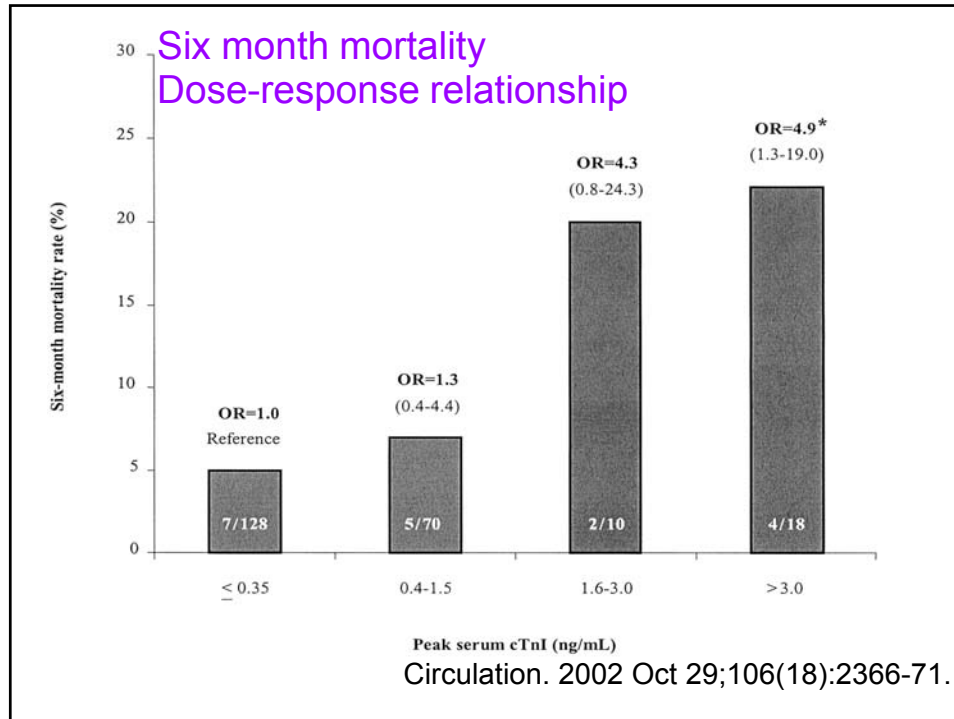
What time frame?

The otherwise stable/asymptomatic patient



TnI > 1.5 associated with worse intermediate-term death after vascular surgery

Circulation. 2002 Oct 29;106(18):2366-71.



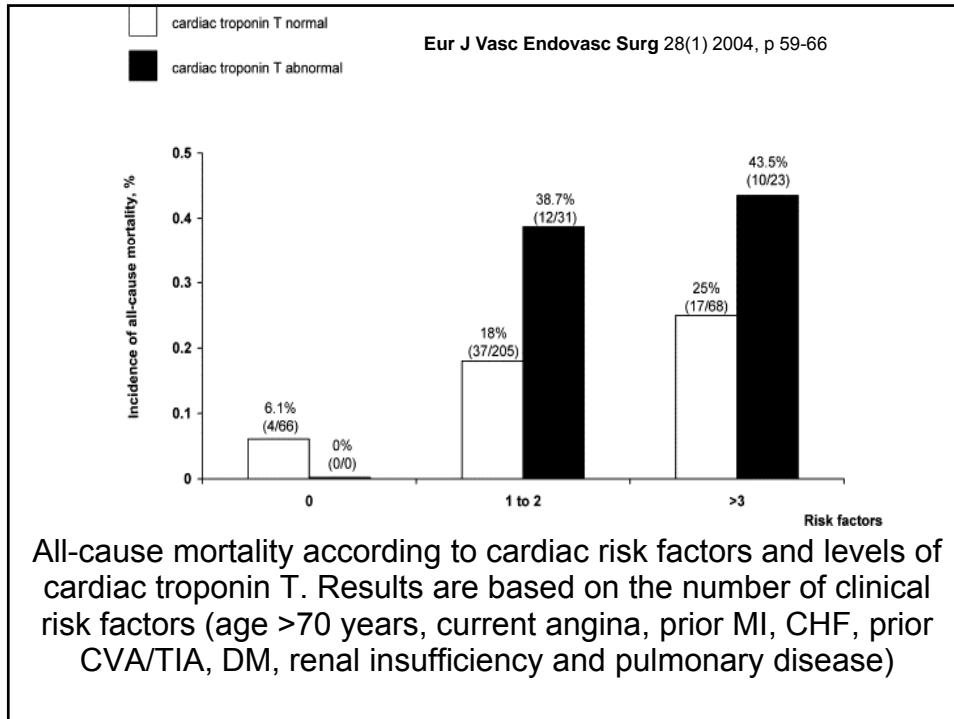
Long-term Prognostic Value of Asymptomatic Cardiac Troponin T Elevations in Patients After Major Vascular Surgery

M. D. Kertai,¹ E. Boersma,¹ J. Klein,² H. van Urk,³ J. J. Bax¹ and D. Poldermans^{3*}

Departments of ¹Cardiology, ²Anaesthesiology, and ³Vascular Surgery, Erasmus Medical Center, Rotterdam,
The Netherlands

An elevated cTnT was defined as serum
concentrations ≥ 0.1 ng/ml

Eur J Vasc Endovasc Surg 28(1) 2004, p 59-66



Perioperative asymptomatic cardiac damage after endovascular abdominal aneurysm repair is associated with poor long-term outcome

Tamara A. Winkel, MD,^a Olaf Schouten, MD,^a Jan-Peter van Kuijk, MD,^b Hence J. M. Verhagen, MD,^a Jeroen J. Bax, MD,^c and Don Poldermans, MD,^b *Rotterdam and Leiden, The Netherlands*

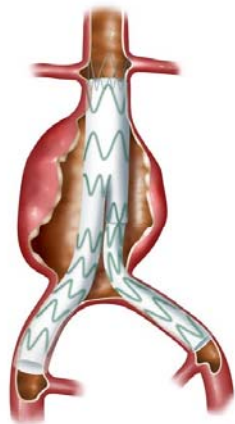
Elevated cardiac troponin T in ~10% of patients undergoing EVAR.

Routine testing done.

J Vasc Surg 2009;50:749-54

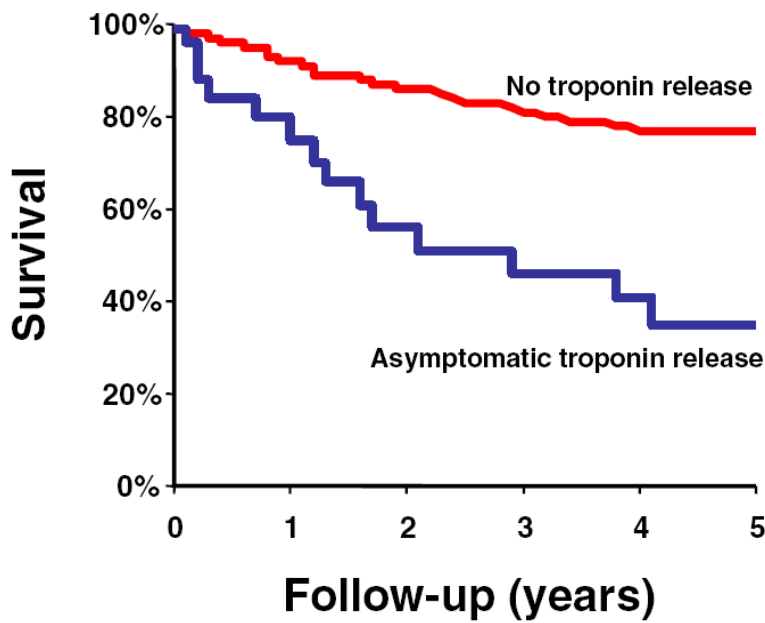
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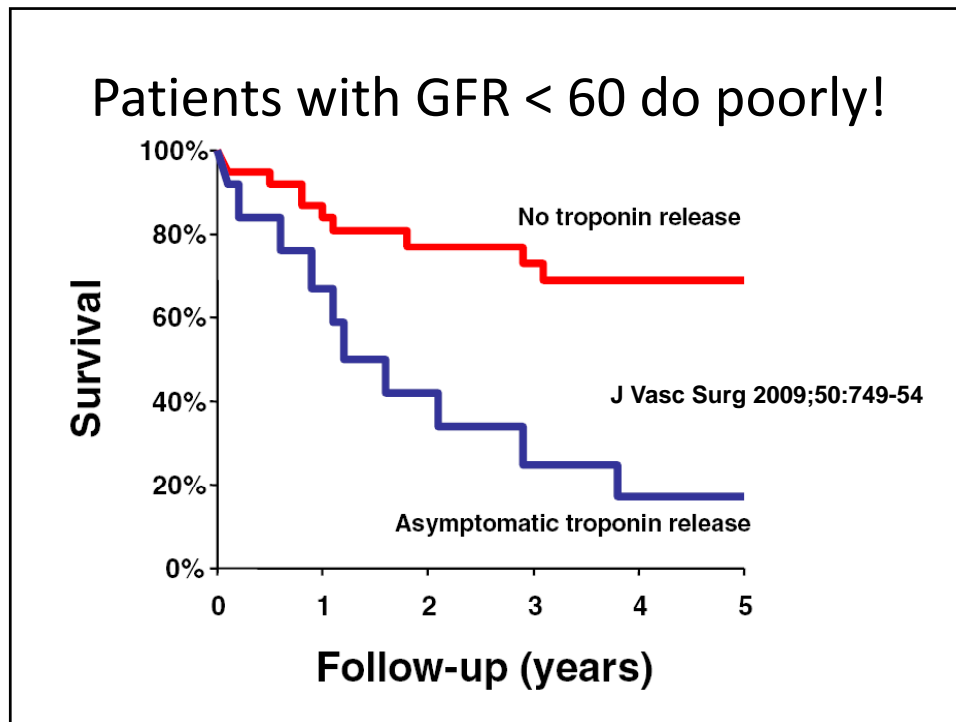


83% of troponin elevations were asymptomatic and without ECG changes!

J Vasc Surg 2009;50:749-54



J Vasc Surg 2009;50:749-54



Perioperative asymptomatic cardiac damage after endovascular abdominal aneurysm repair is associated with poor long-term outcome

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Table II. Multivariate Cox regression analysis for all-cause mortality^a

<i>Variable</i>	<i>HR</i>	<i>95% CI</i>	<i>P</i>
Peri-op troponin release	2.33	1.07-5.07	.03
Age, per year increase	1.05	1.01-1.10	.02
Ischemic heart disease	1.88	0.99-3.55	.05
GFR ^b <60 mL/min/1.73 m ²	1.81	0.92-3.56	.09
Statin use	0.47	0.25-0.90	.02

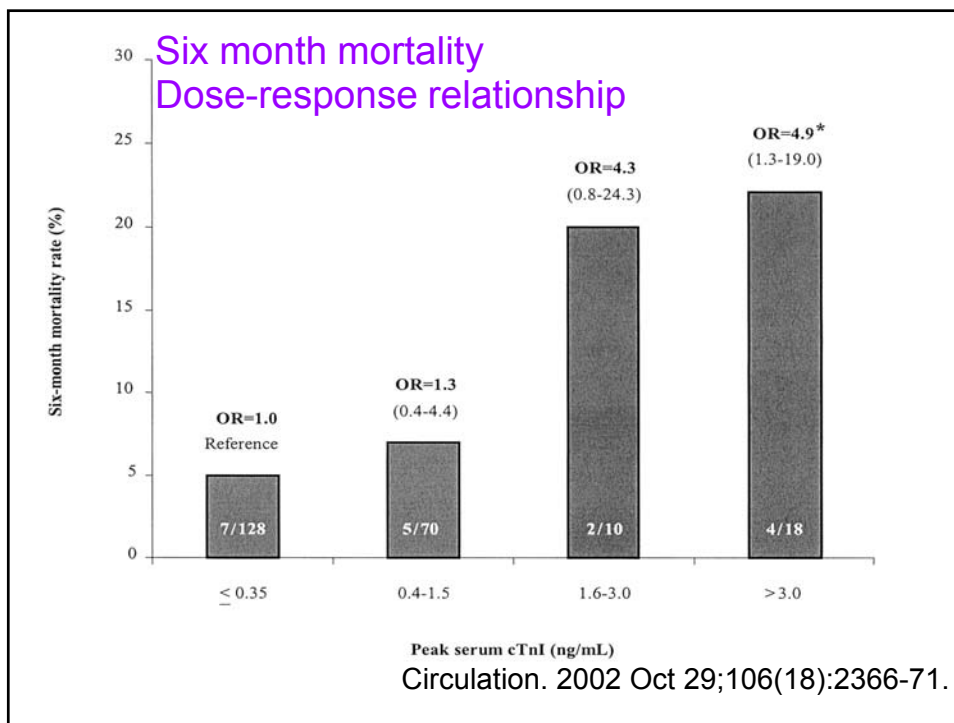
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No dose-response relationship reported

J Vasc Surg 2009;50:749-54



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Cardiac troponin I is reliable with immediate but not medium-term cardiac complications after abdominal aortic repair

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[Acta Anaesthesiol Scand](#). 2000 May;44(5):592-7.

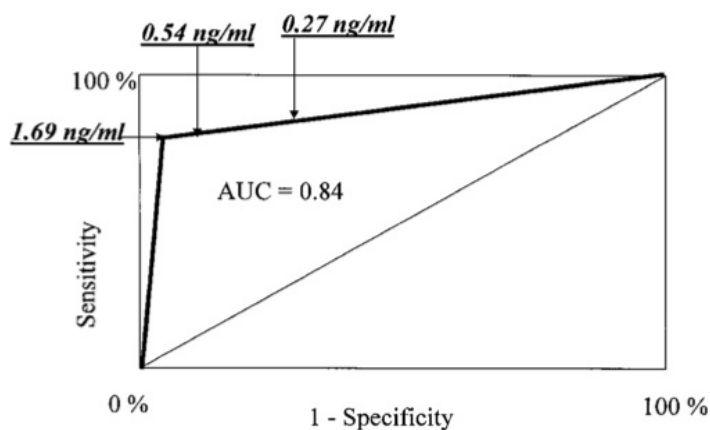


Fig. 2. ROC curve for postoperative cardiac complications.

[Acta Anaesthesiol Scand](#). 2000 May;44(5):592-7.

Troponin elevations in critical illness

Case study

- 48 yo BM
 - Obese
 - HTN
 - OSA
 - Cervical disc disease
- Acute diarrheal illness
 - Septic shock
 - No identifiable pathogen
- Troponin drawn



Cardiac cath

- Indications
 - Abnormal echo (EF 50%)
 - Mild troponin elevation
- Findings
 - EF 40-50%
 - Elevated LVEDP
 - 30-40% mid-LAD lesion

Was this an MI?

Table 2 Elevations of troponin in the absence of overt ischemic heart disease

Cardiac contusion, or other trauma including surgery, ablation, pacing, etc.
 Congestive heart failure—acute and chronic
 Aortic dissection
 Aortic valve disease
 Hypertrophic cardiomyopathy
 Tachy- or bradyarrhythmias, or heart block
 Apical ballooning syndrome
 Rhabdomyolysis with cardiac injury
 Pulmonary embolism, severe pulmonary hypertension
 Renal failure
 Acute neurological disease, including stroke or subarachnoid haemorrhage
 Infiltrative diseases, e.g. amyloidosis, haemochromatosis, sarcoidosis, and scleroderma
 Inflammatory diseases, e.g. myocarditis or myocardial extension of endo-/pericarditis
 Drug toxicity or toxins
 Critically ill patients, especially with respiratory failure or sepsis
 Burns, especially if affecting >30% of body surface area
 Extreme exertion

Circulation. 2007 Nov 27;116(22):2634-53

Troponin elevations in ICU

- Troponin elevation was adjudicated as:
 - MI in 53.1%
 - Sepsis in 18.4%
 - Renal failure in 12.2%
 - Other causes in 16.3%.
- Overall ICU mortality was 16.0%
 - 2.0% with no troponin elevation
 - 23.1% with MI
 - 39.1% with troponin elevation not due to MI.

J Crit Care. 2009 Sep 23

Troponin costs at Penn

- Troponin-I
- SerumHumanImmunoassay (bead-sandwich)
- \$22.80

Cost-effectiveness?

Intense Cardiac Troponin Surveillance for Long-Term Benefits Is Cost-Effective in Patients Undergoing Open Abdominal Aortic Surgery: A Decision Analysis Model

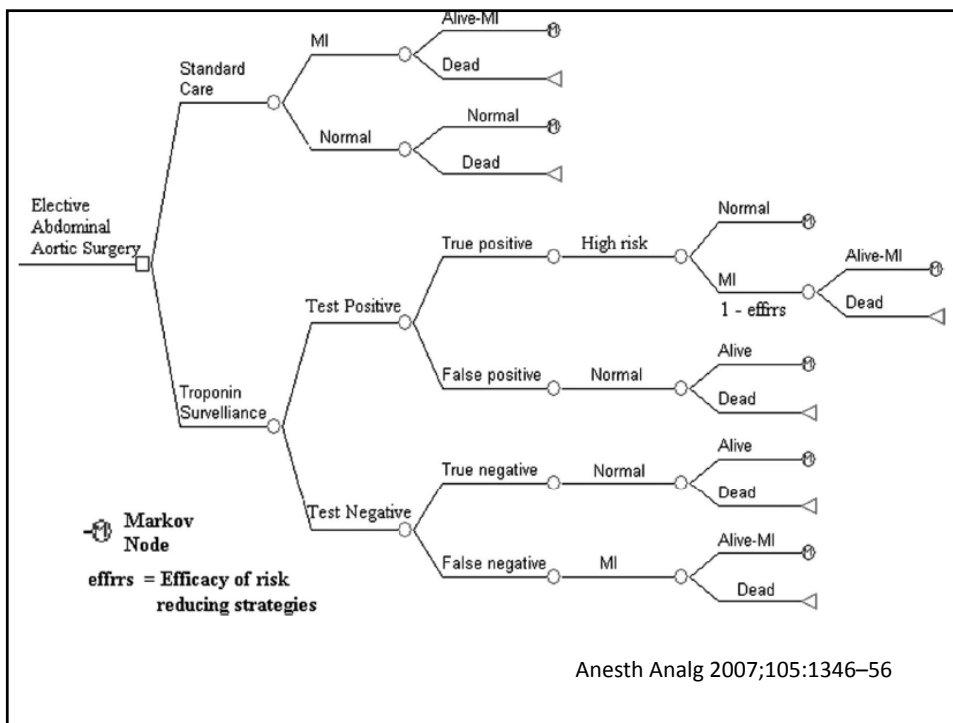
Srinivas Mantha, MD*

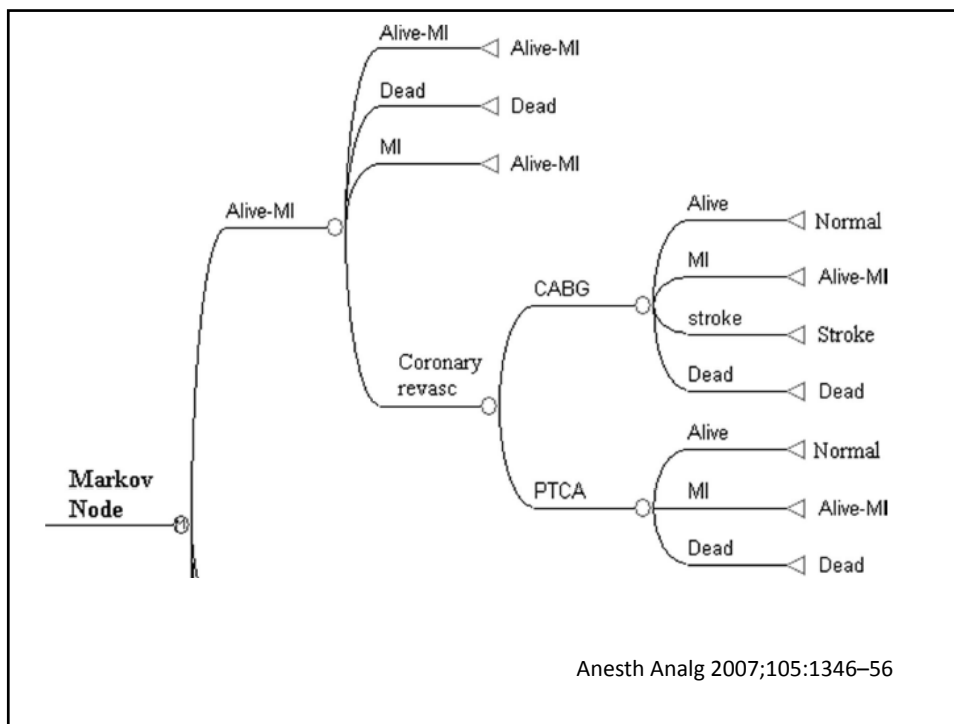
Joseph Foss, MD†

John E. Ellis, MD‡

Michael F. Roizen, MD†

Anesth Analg 2007;105:1346-56





Costs of interventions (Admit ICU, start β -blockade)

Table 2. Details of Interventions and Their Costs in Patients With Increased Cardiac Troponin I (cTnI)

Item component	Cost per day	Duration and time of intervention ^a	Total cost	References
DRG122 in the ICU ^b	\$2520	5 d (Day 1 to Day 5)	\$12,600	(33)
Esmolol (maximum dose 300 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	\$255.37	2 d (Day 1 to Day 2)	\$510.74	Red book ^c
Oral metoprolol 100 mg twice daily	\$2.08	2 d (Day 3 to Day 4)	\$4.16	Red book
Oral metoprolol 50 mg twice daily	\$1.04	7 d (Day 5 to Day 11)	\$7.28	Red book
Grand cost			\$13,145.46	

^aTime implies time from first increase in cTnI concentrations >1.5 ng/mL.

Anesth Analg 2007;105:1346-56

Cost-effectiveness

Table 3. Results of the Model With Baseline Values

Strategy	Direct medical costs	QALYs	ICER (cost/QALY)
Standard care	\$27,964	10.4577	
cTnI surveillance	\$29,639	10.5902	\$12,641

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year.

Anesth Analg 2007;105:1346-56

Cost-effectiveness

Table 3. R

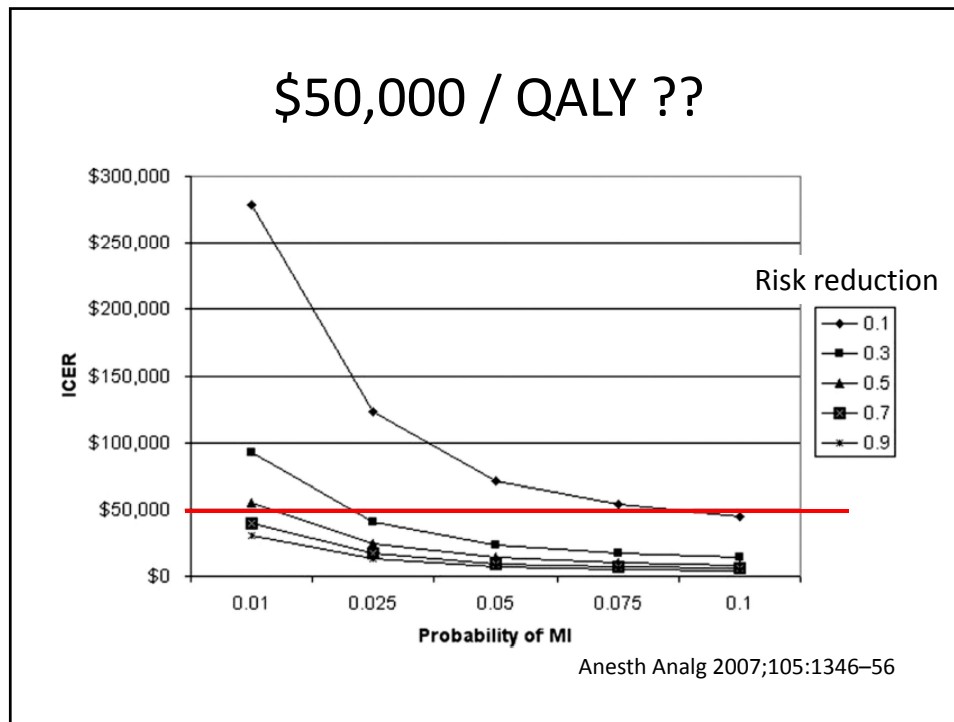
Strate	ICER (cost/QALY)	ICER (cost/QALY)
Standard		
cTnI surv		\$12,641

ICER = increm

year.

\$12,641

Anesth Analg 2007;105:1346-56



Troponins are cost-effective

- ...routine troponin surveillance on Days 0, 1, 2, and 3 is cost-effective in patients aged 65 yr and older with intermediate cardiac risk and who are undergoing AAA.
- The cost value of \$50,000 is comparable to the annual cost of renal dialysis and commonly funded interventions.

Anesth Analg 2007;105:1346-56

Role of ultrasensitive troponins

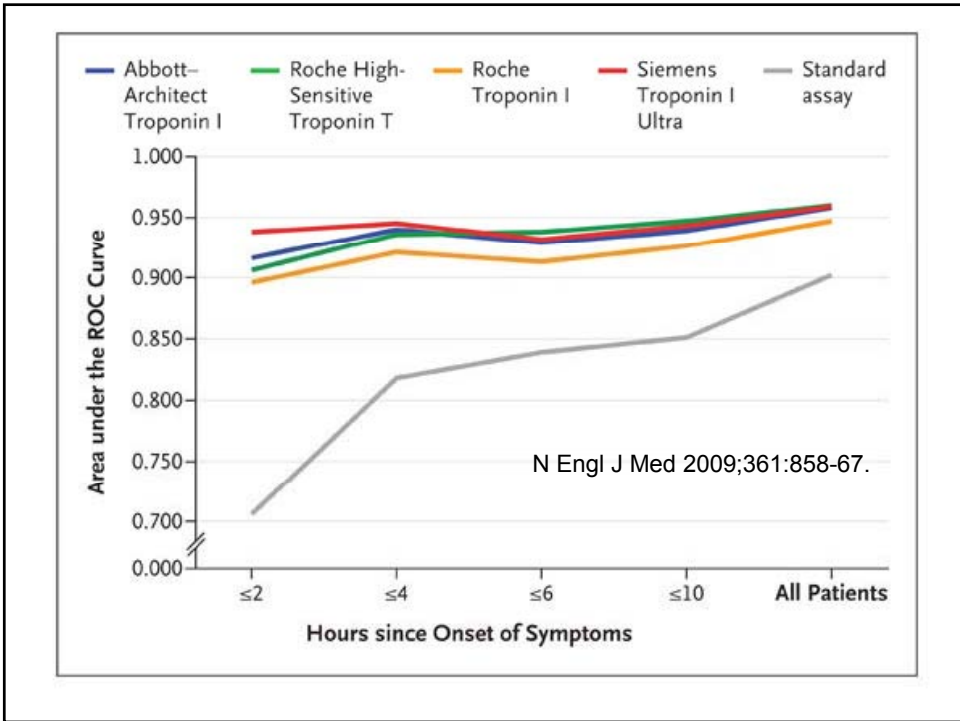
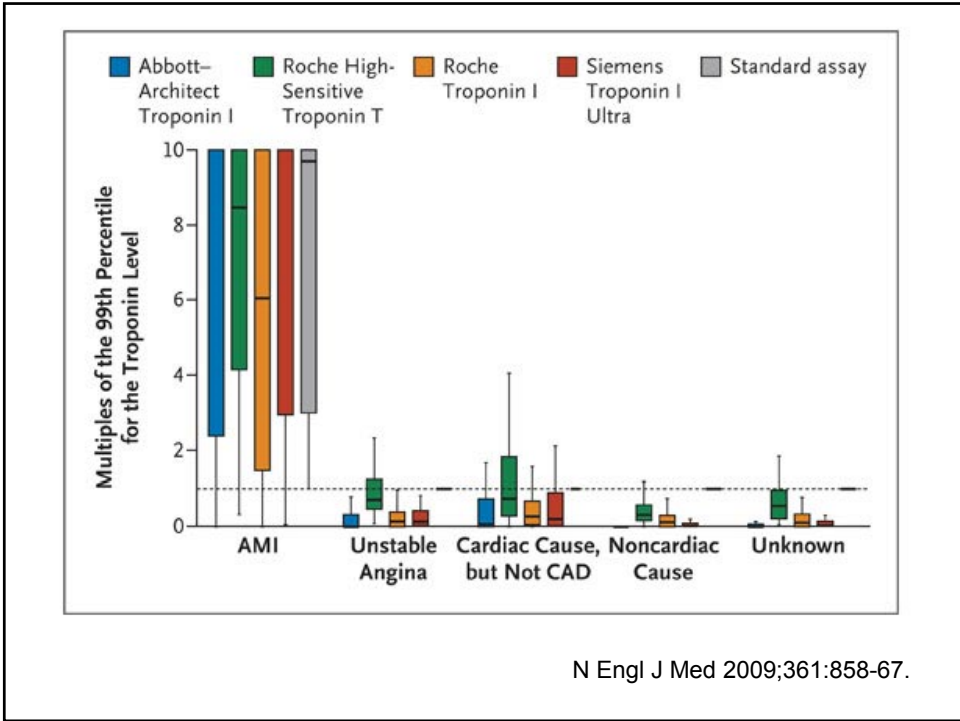
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Diagnosis of Myocardial Infarction with Sensitive Cardiac Troponin Assays

Tobias Reichlin, M.D., Willibald Hochholzer, M.D., Stefano Bassetti, M.D.,
Stephan Steuer, M.D., Claudia Stelzig, M.Sc., Sabine Hartwiger, M.D.,
Stefan Biedert, M.Sc., Nora Schaub, M.D., Christine Buerge, M.D.,
Mihael Potocki, M.D., Markus Noveanu, M.D., Tobias Breidhardt, M.D.,
Raphael Twerenbold, M.D., Katrin Winkler, M.D., Roland Bingisser, M.D.,
and Christian Mueller, M.D.

N Engl J Med 2009;361:858-67.



Conclusions

- Troponin elevations appear to predict MACE
 - In addition to preop risks and clinical course
 - Even in asymptomatic patients
- Cost-effectiveness analysis suggests benefit
 - Obtain routinely in high-risk patients?
 - **If** aggressive Rx can improve outcomes

Conclusions

- Beware elevations in critical illness
 - May not be MI, but still has poor prognosis
- New ultra-sensitive assays on the way
 - Earlier diagnosis and Rx