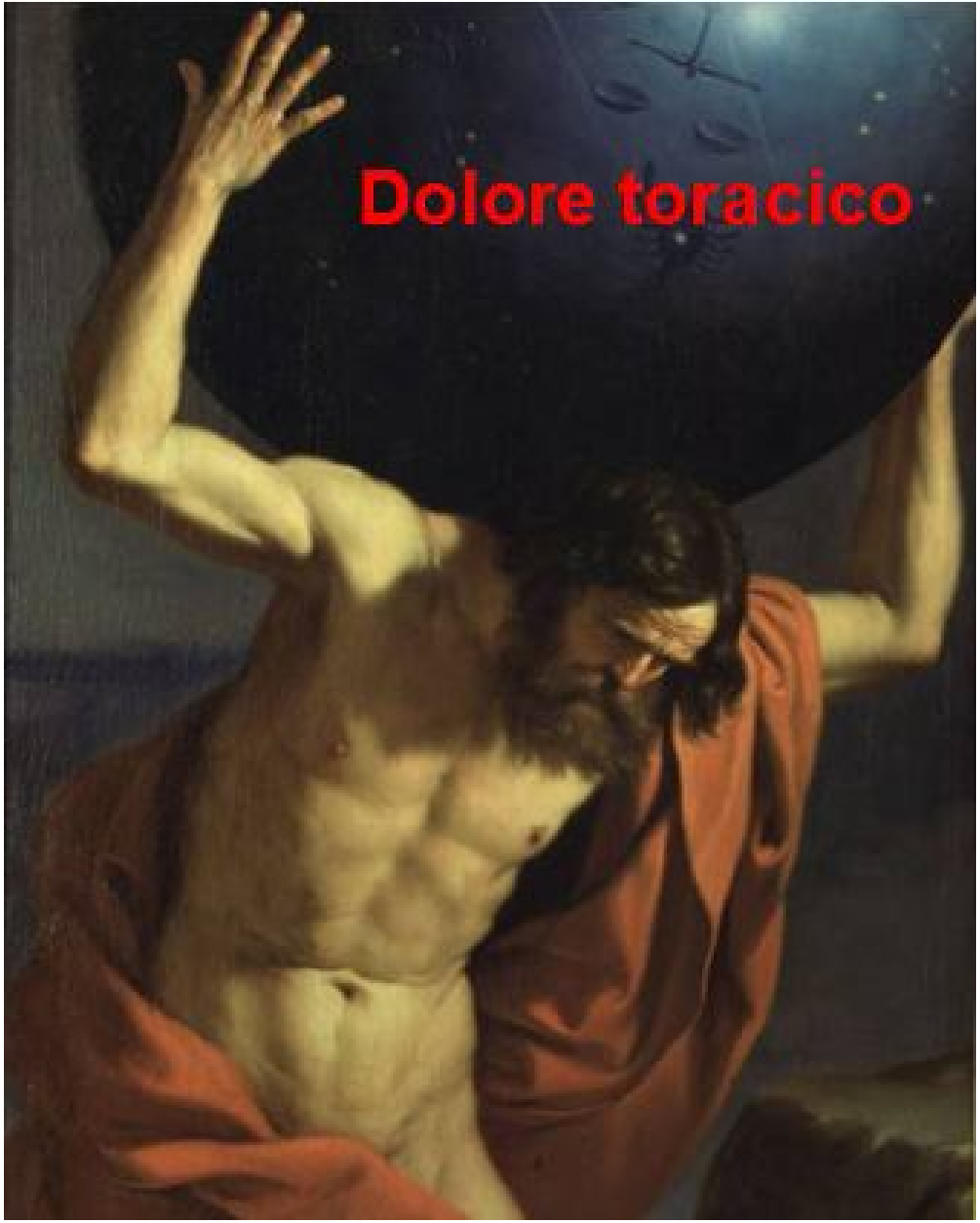
DOLORE TORACICO

La position paper SIMEU-ANMCO “in progress”

Dott. Nicola Binetti
PS ed Emergenza territoriale area Nord
AUSL Bologna

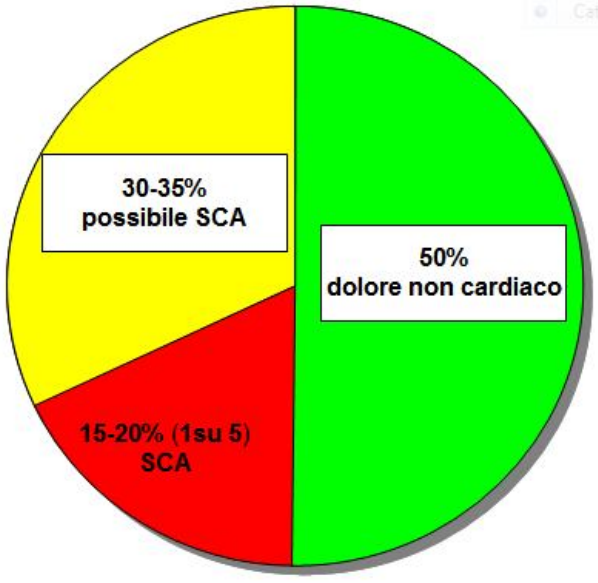


EPIDEMIOLOGIA

- circa il 5 (9*)% delle prestazioni di P

American College of Emergency Physicians

*Conti A, ***AHJ 2002***



Esigenza di:

>Avere un percorso comune.

>Centralità del paziente

Documento di Consenso

Percorso di valutazione del dolore toracico.
Valutazione dei requisiti di base per l'implementazione negli ospedali italiani

G Ital Cardiol 2009; 10 : 46-63

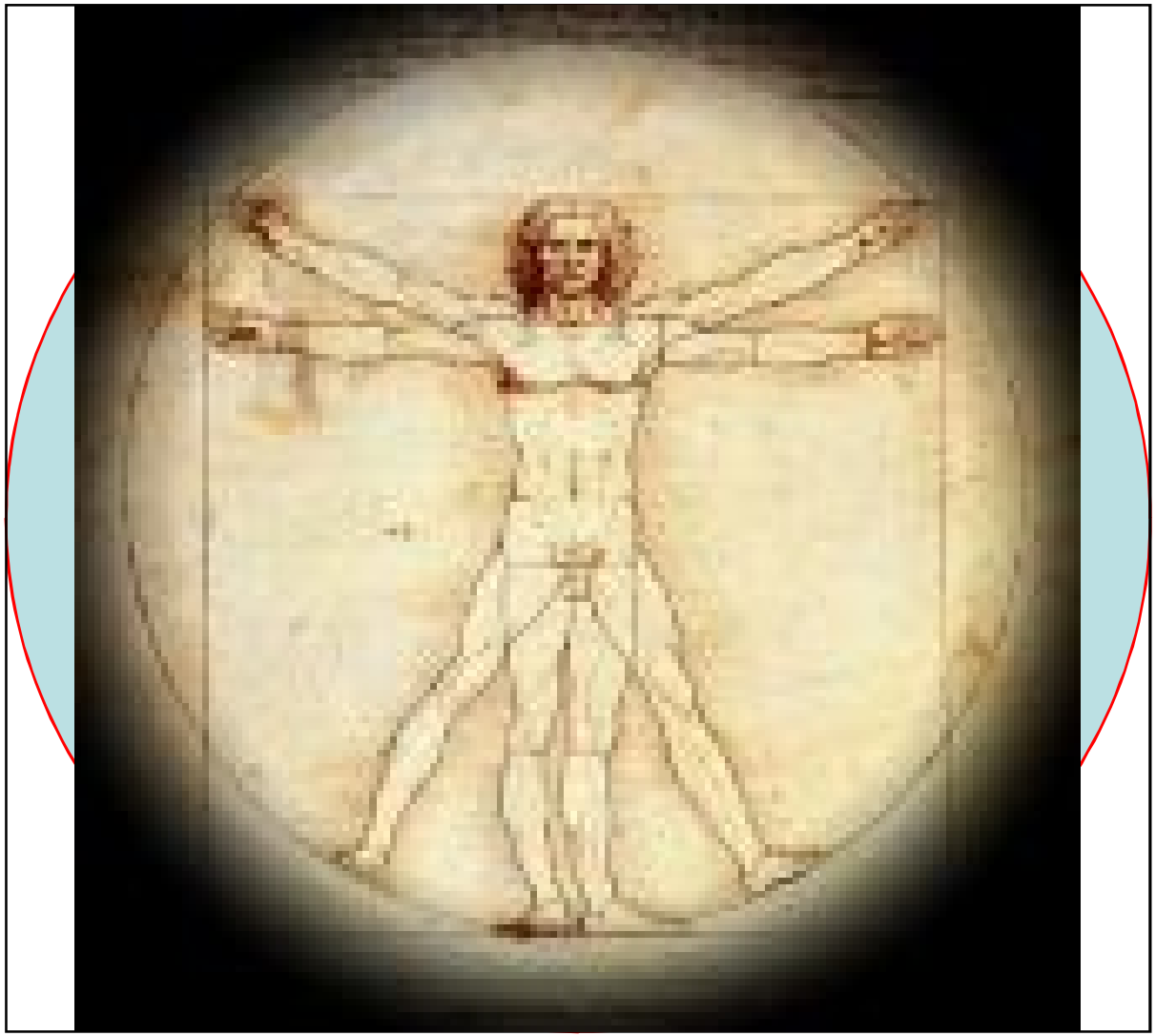
Ottani F, Binetti N, et al

DT: Probabilità che il sintomo sia di origine coronarica

anamnesi

ecg

Se diagnostico



troponina

esame obiettivo

Rischio di eventi maggiori

The diagnostic and therapeutic challenges arise especially when the ECG is normal or nearly normal,

ESC Guidelines for
the management of ACS in patients presenting without persistent ST-segment elevation
escardio.org 2011

Documento di Consenso

coordinatori: N. Binetti_M. Galvani

DT ANMCO SIMEU UPDATE

PUNTI in DISCUSSIONE:

- Uso della Tn di ultima generazione e timing dell'osservazione
- Rule in: come non sovrastimare
- Quali test in dimissione e rule out sicuro

Journal of the American College of Cardiology

Published by Elsevier Inc.

Vol. 54, No. 13, 2009

EDITORIAL COMMENT

Highly Sensitive Troponins

The Answer or Just More Questions?*

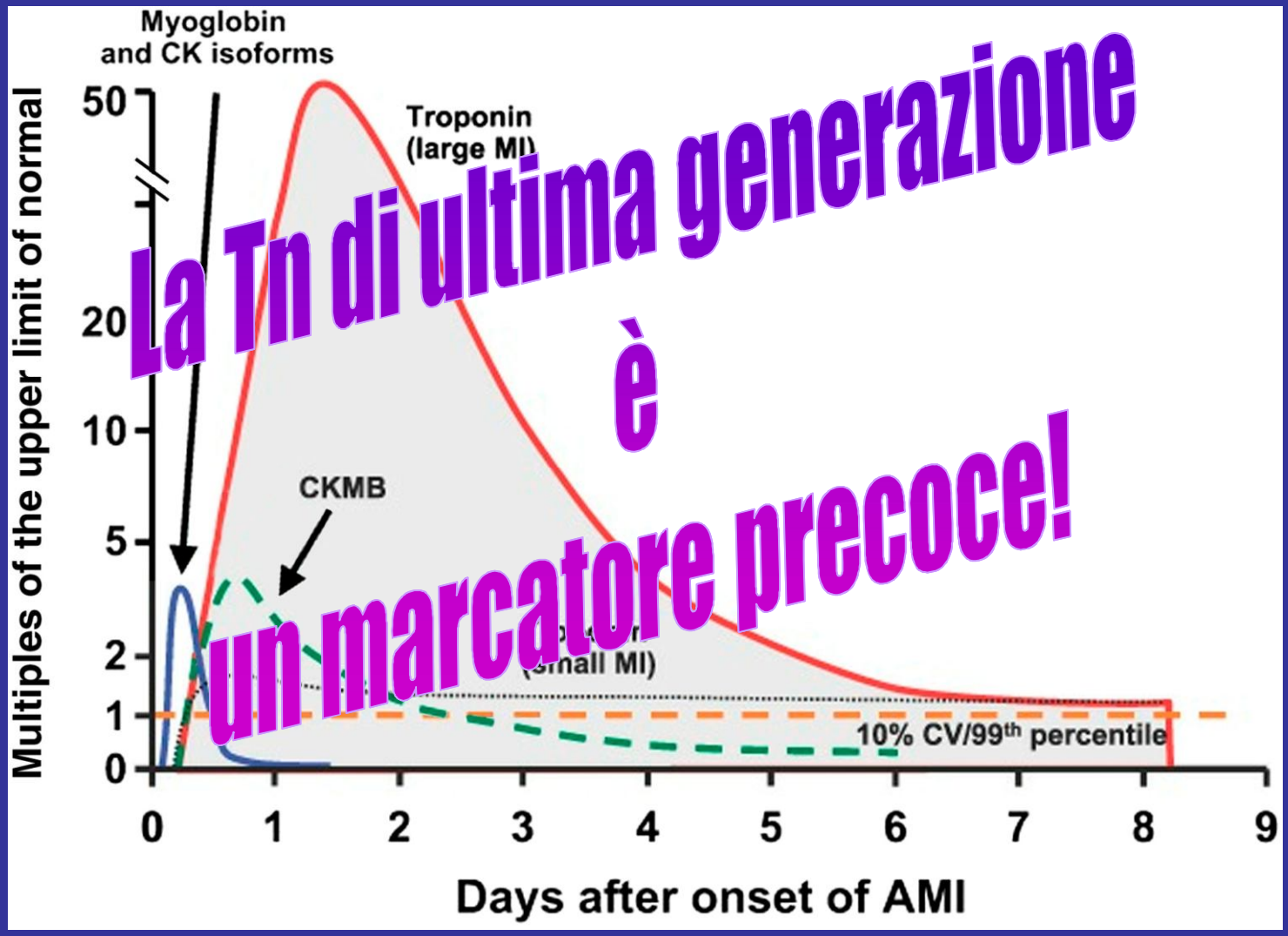
Judd E. Hollander, MD

Philadelphia, Pennsylvania

We will need to define the approach to management of this new class of troponin-positive patients.

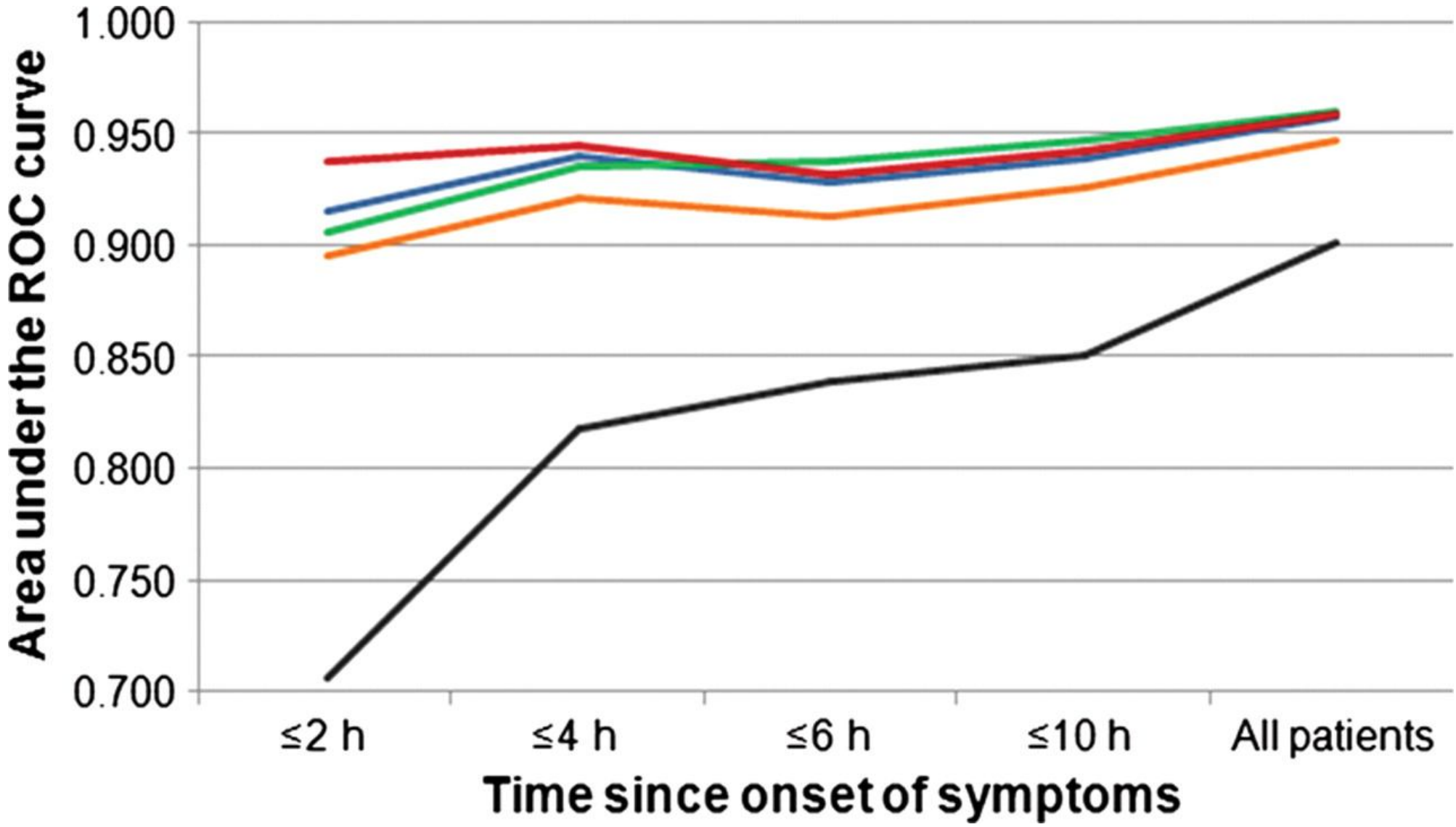
In 2006, the Institute of Medicine released a report detailing the crisis in emergency care (1). Our current approach to the care of patients with potential acute coronary syndromes (ACS) has contributed to this crisis. Physicians admit the majority of the 6 million patients that present to the emergency department (ED) with signs and symptoms of a possible ACS (2), yet a relatively small percentage actually turn out to have a cardiac etiology for their chest pain. The consequences of this practice have resulted in expenses exceeding $8 to $10 billion annually to rule out acute myocardial infarction (AMI) and ACS (3,4).

Timing of Release of Various Biomarkers After Acute Myocardial Infarction



Shapiro BP, Jaffe AS. Cardiac biomarkers. In: Murphy JG, Lloyd MA, editors. Mayo Clinic Cardiology: Concise Textbook. 3rd ed. Rochester, MN: Mayo Clinic Scientific Press and New York: Informa Healthcare USA, 2007:773–80. Anderson JL, et al. *J Am Coll Cardiol* 2007;50:e1–e157, Figure 5.

Diagnostic accuracy at presentation as quantified by the area under the receiver operating characteristic (ROC) curves for a contemporary cardiac troponin assay (black, fourth-generation cardiac troponin T) and four sensitive or high-sensitive cardiac troponin assays (red, Siemens cTnI Ultra; blue, Abbott cTnI Architect; green, Roche high-sensitivity cTnT; orange, Roche cTnI) in the diagnosis of acute myocardial infarction according to chest pain onset.



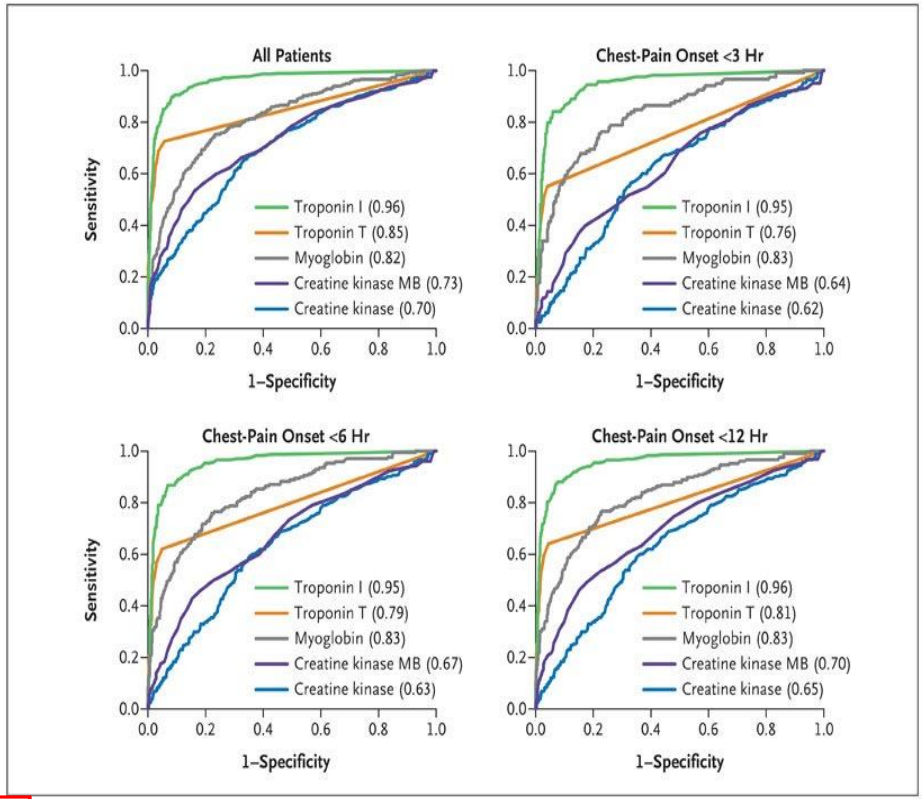
Twerenbold R et al. Eur Heart J 2012;eurheartj.ehr492

European Heart Journal

Diagnostic Accuracy
of Single Biomarker Testing
for Acute Myocardial Infarction

Troponine di ultima generazione: ricadute cliniche

- Aumentata sensibilità.
- **Dopo 3 ore dall'inizio del dolore, ha già raggiunto la massima potenzialità diagnostica**
- (dopo 6 ore il suo valore AUC aumenta solo marginalmente).



Keller T et al. N Engl J Med 2009;361:868-877

- **Marcatore precoce**
- **Alta sensibilità**
- **Specifico per danno miocardico, ma minor specificità per danno ischemico**

Clinical Update

High-sensitive troponin T measurements: what do we gain and what are the challenges?

Raphael Twerenbold[1], Allan Jaffe[2], Tobias Reichlin[1], Miriam Reiter[1], and Christian Mueller[1]*

[1]Department of Cardiology, University Hospital, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland; and [2]Cardiovascular Division, Gonda 5, Mayo Clinic and Medical School, Rochester, MA 55905, USA

Received 31 May 2011; revised 26 September 2011; accepted 15 December 2011

Gain:

sensitive and high-sensitive cardiac troponin assays

improve the early diagnosis of acute myocardial infarction

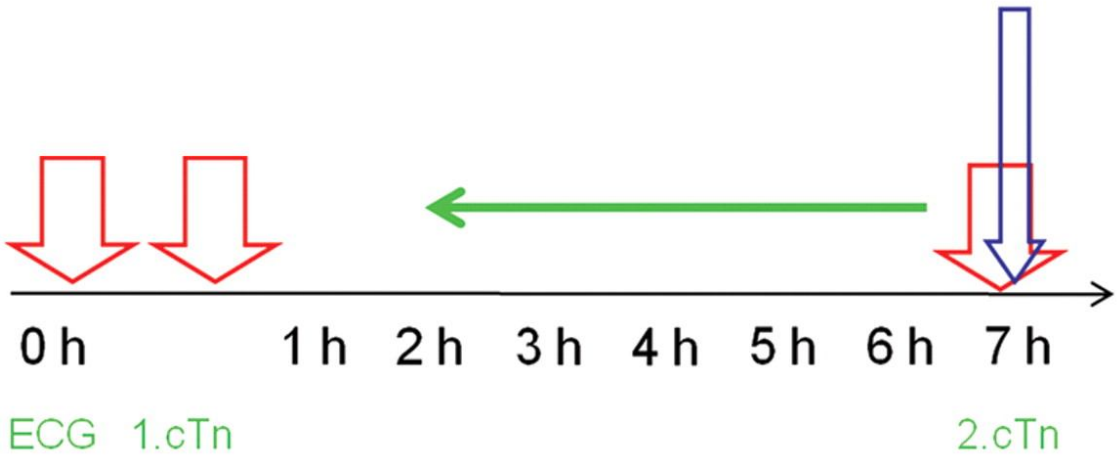
European Heart Journal

Rule-in of acute myocardial infarction can be at presentation (0 h) in patients with unequivocal ST-elevations, at 1 h in patients with elevations in cardiac troponin (cTn) in the measurement performed at presentation (turnaround time is around 1 h in most hospitals), and at 7 h if the first cardiac troponin is normal and the elevation in cardiac troponin becomes apparent only at the second measurement performed after 6 h.

Acute Chest Pain → AMI

2 Problems:

- **Rule-in**
- **Rule-out**



→ Delay in adequate therapy
→ Morbidity ↑ ('time is muscle')
→ Cost ↑
→ Patient: Anxiety…

Twerenbold R et al. Eur Heart J 2012;eurheartj.ehr492

European Heart Journal

La sfida:

•Rule out: alto valore predittivo negativo!!!! Ok
•(come dirimere la positività non SCA?)

•RULE_IN

Critical clinical concepts:

•L'IMA dovrebbe essere diagnosticato solo basandosi su **valori in aumento / diminuzione** * della Tn, partendo da un livello basale elevato e in un appropriato contesto clinico.

*processi acuti normalmente manifestano valori di Tn in aumento molto di più che quelli cronici (es IRC, CAD stabili, scompenso cardiaco, IVS severa, generalmente non mostrano un grande cambiamento dei valori di Tn, nei prelievi seriati)

ESC Guidelines for
the management of ACS in patients presenting without persistent ST-segment elevation
escardio.org 2011

Cause analitiche di incremento delle troponine cardiache

- Presenza di anticorpi eterofili nel campione
- Fattore reumatoide
- Presenza di coaguli di fibrina nel campione
- Campioni **francamente emolitici**, itterici o lipemici
- Presenza di mezzo di contrasto iodato
- Malfunzionamento strumentale

Recenti Prog Med 2010; 101: 423-428

Cause di aumento della concentrazione plasmatica della troponina non dovuto a SCA

Danno correlato ad ischemia miocardica secondaria (IM tipo 2)
•Tachi o bradiaritmia •Dissezione aortica e severa valvulopatia aortica •Ipo o ipertensione, cioè shock emorragico, emergenza ipertensiva •Scompenso cardiaco acuto e cronico, senza una significativa concomitante malattia delle coronarie •Cardiomiopatia ipertrofica •Vasculite, ad es., lupus eritematoso sistemico, sdr di Kawasaki •Disfunzione coronaria endoteliale senza significativa cardiopatia ischemica
Danno non correlato ad ischemia miocardica
•Contusione cardiaca •Incisioni cardiache prodotte da chirurgia •Terapia con radio frequenza o crioablazione •Rabdomiolisi con interessamento cardiaco •Miocardite •Agenti cardiotossici, ad es. antracicline, ercepetina, avvelenamenti da CO •Ustioni severe coinvolgenti > 30% della superficie cutanea
Gruppo indeterminato o multifattoriale
•Sindrome di Tako-Tsubo •Embolia polmonare severa o ipertensione polmonare di grado severo •Cardiomiopatia del periparto •Insufficienza Renale •Malattie neurologiche acute e gravi (ad es: stroke, trauma) •Malattie infiltrative (amiloidosi, sarcoidosi) •Sforzi fisici intensi •Sepsi •Insufficienza Respiratoria Acuta •Frequenti shock di defibrillazione

EUROPEAN SOCIETY OF CARDIOLOGY®
European Heart Journal (2010) **31**, 2197–2206
doi:10.1093/eurheartj/ehq251

Journal of the American College of Cardiology

Published by Elsevier Inc.

EDITORIAL COMMENT

Pathobiology of Troponin Elevations*

Do Elevations Occur With Myocardial Ischemia as Well as Necrosis?

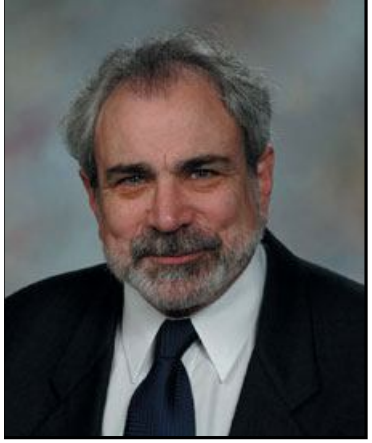
Harvey D. White, DSc

Auckland, New Zealand

JACC Vol. 57, No. 24, 2011
June 14, 2011:2406–8

Table 1 Pathobiological Classification of Types of Potential Mechanisms Causing Troponin Elevations

Type 1	Myocyte necrosis
Type 2	Apoptosis
Type 3	Normal myocyte turnover
Type 4	Cellular release of proteolytic troponin degradation products
Type 5	Increased cellular wall permeability
Type 6	Formation and release of membranous blebs



ACUTE CORONARY SYNDROMES

The 10 commandments of troponin, with special reference to high sensitivity assays

Allan S Jaffe

- Collaborazione PS e Laboratorio

- Capire alcuni problemi analitici
- **<u>Fare diagnosi di IMA con la tropo e la clinica</u>**
- **Escludere l'IMA (rule out) è diverso dal diagnosticarlo (rule in)**
- ***Usare il buon senso nell'interpretare aumenti della Tn nei pazienti critici***
- Tropo elevata e IRC: non farsi intimidire

- Troponina e PTCA: importanza del valore base
- IMA post BPAC: servono molti parametri per far diagnosi
- Non dimenticare la Cardiotossicità da farmaci come possibile causa di aumento della Tn
- **Tropo elevata post sforzo estremo: cautela**

Heart 2011;**97**:940–946.

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Vol. 50, No. 22, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.09.011

ESC/ACCF/AHA/WHF EXPERT CONSENSUS DOCUMENT

Universal Definition of Myocardial Infarction

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

European Heart Journal
doi:10.1093/eurheartj/ehs184

EXPERT CONSENSUS DOCUMENT

Third universal definition of myocardial infarction

Kristian Thygesen, Joseph S. Alpert, Allan S. Jaffe, Maarten L. Simoons, Bernard R. Chaitman and Harvey D. White: the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction

Definition of myocardial infarction

Criteria for acute myocardial infarction

The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for MI:

- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
  - Symptoms of ischaemia.
  - New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).
  - Development of pathological Q waves in the ECG.
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
  - Identification of an intracoronary thrombus by angiography or autopsy.

Non confondere

- Danno miocardico
- Danno ischemico

European Heart Journal
doi:10.1093/eurheartj/ehs184

Third universal definition of myocardial infarction

Kristian Thygesen, Joseph S. Alpert, Allan S. Jaffe, Maarten L. Simoons, Bernard R. Chaitman and Harvey D. White: the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction

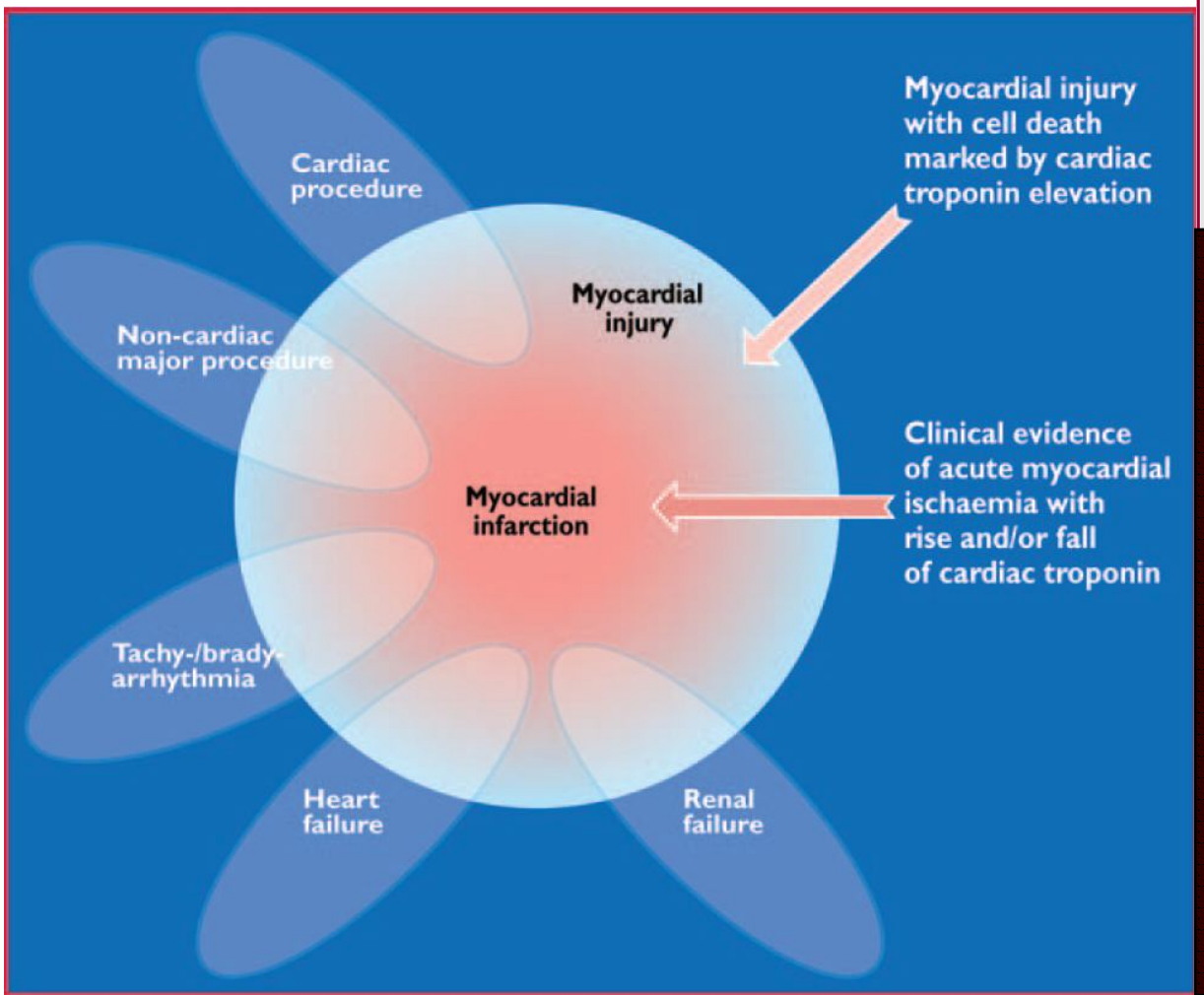
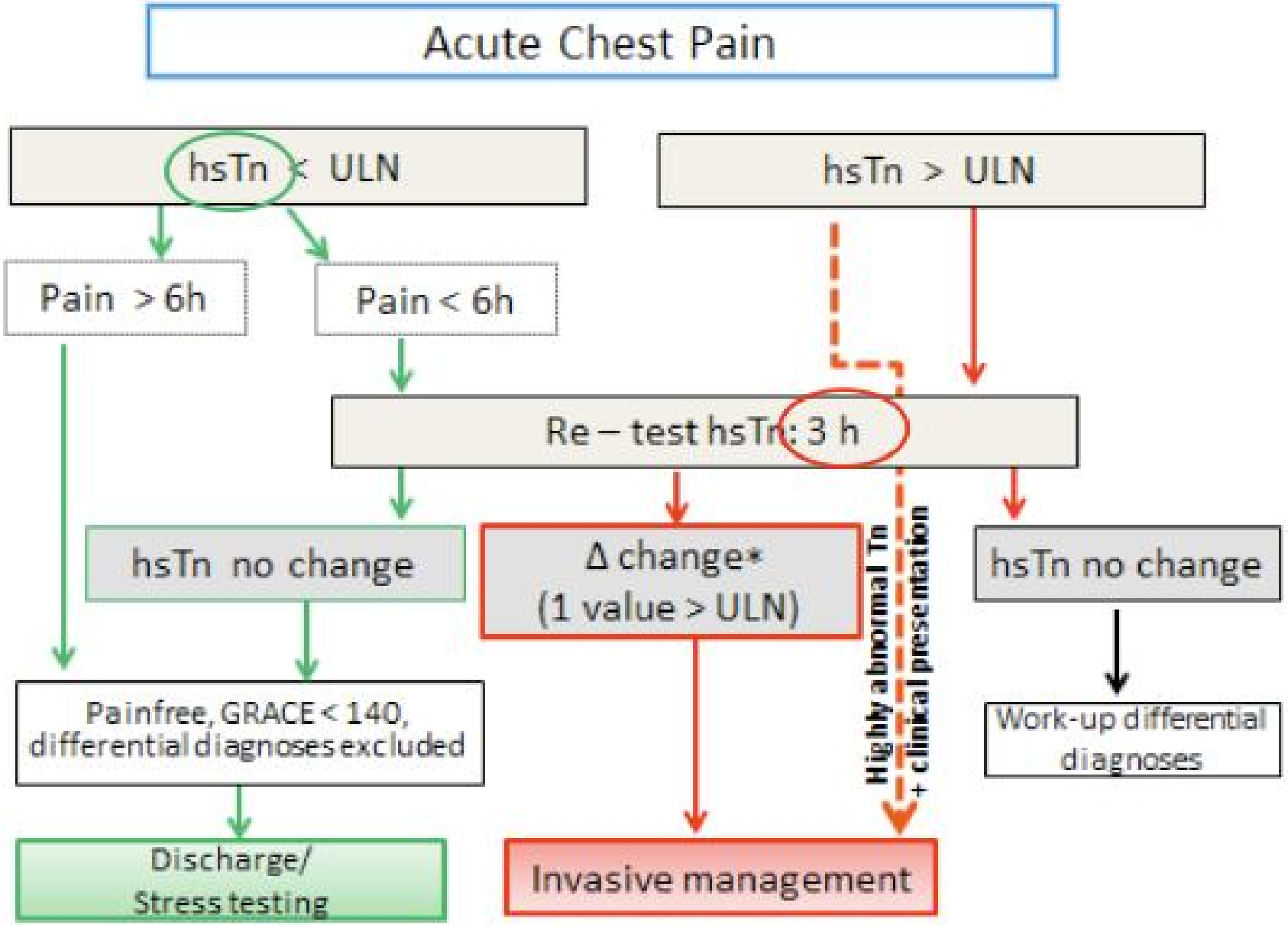


Table 1 Clinical classification of different types of myocardial infarction

Type 1
Spontaneous myocardial infarction related to ischaemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection

NSTEMI Guidelines 2011



*** Needs to be defined for each assay**

Hamm C, et al. ESC 2011

Migliorare la specificità: cinetica di incremento ?

La Definizione Universale di IMA prevedeva già una valutazione congiunta dei valori basali e dell'entità dell'incremento a 6 h, usando dei δ di incremento > 20%

EHJ 2007

Studi di riferimento con *δ di incremento*

- **20%**
  - Macrae AR, et al. Assessing the requirement for the 6-hour interval between specimens in the American Heart Association Classification of Myocardial Infarction in Epidemiology and Clinical Research Studies. *Clin Chem. 2006;52:812– 818.*
- **30%**
  - Apple FS, et al. Role of monitoring changes in sensitive cardiac troponin I assay results for early diagnosis of myocardial infarction and prediction of risk of adverse events. Clin Chem. 2009;55:930 –937
- **117 % - 243%**
  - Giannitsis E, et al. High sensitivity cardiac troponin T for early prediction of evolving non-Stsegment elevation myocardial infarction in patients with suspected acute coronary syndrome and negative troponin results on admission. *Clin Chem. 2010;56:642– 650.*
- **235%.**
  - Kavsak PA, Ko DT, Wang X, Macrae AR, Jaffe AS. 2007 Universal myocardial infarction definition change criteria for risk stratification by use of a high-sensitivity cardiac troponin I assay. *Clin Chem. 2010;56:* 487–489.

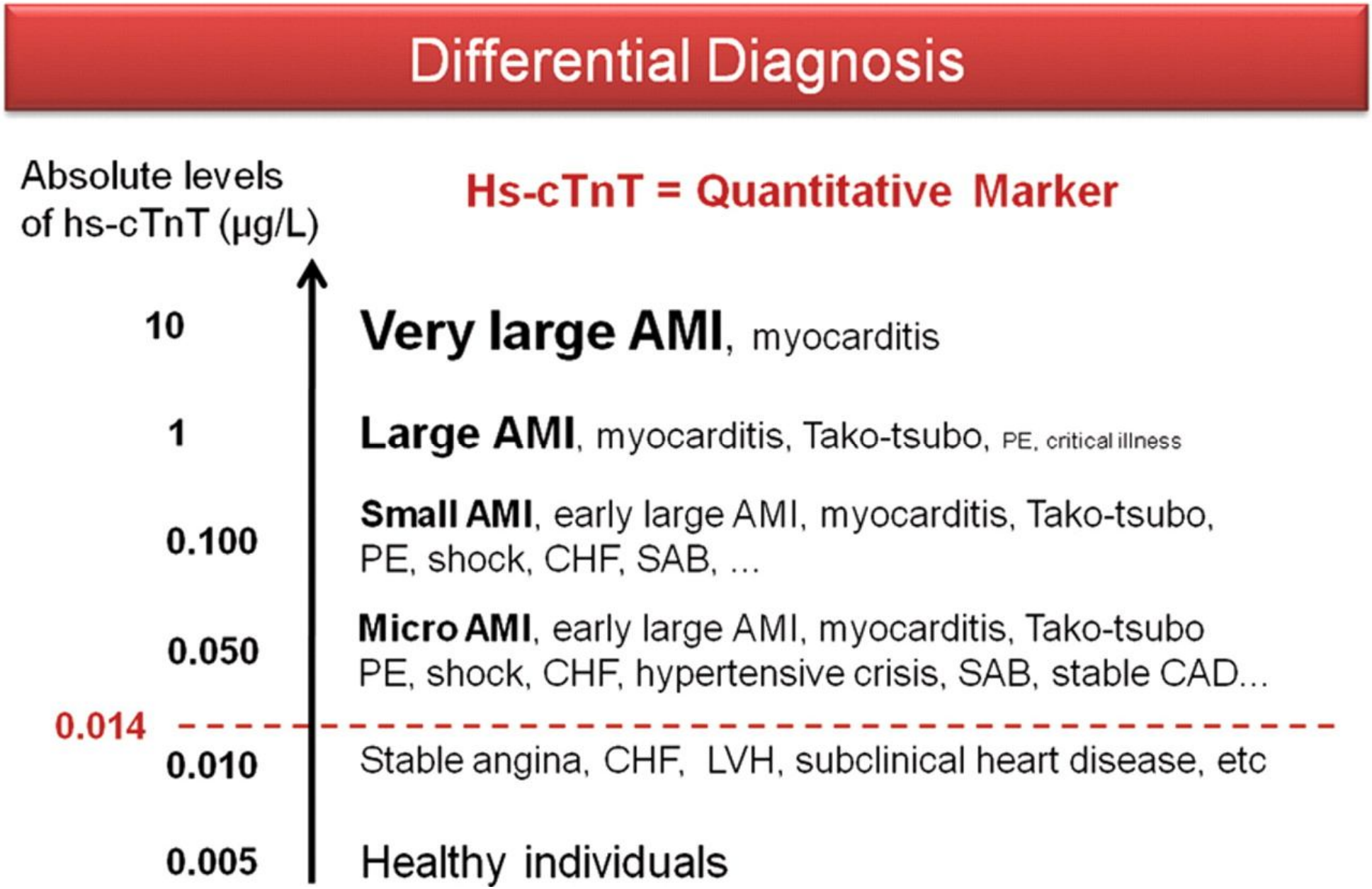
Utility of Absolute and Relative Changes in Cardiac Troponin Concentrations in the Early Diagnosis of Acute Myocardial Infarction

Tobias Reichlin, MD*; Affan Irfan, MD*; Raphael Twerenbold, MD; Miriam Reiter, MD; Willibald Hochholzer, MD; Hanna Burkhalter, MD; Stefano Bassetti, MD; Stephan Steuer, MD; Katrin Winkler, MD; Federico Peter, MD; Julia Meissner, MD; Philip Haaf, MD; Mihael Potocki, MD; Beatrice Drexler, MD; Stefan Osswald, MD; Christian Mueller, MD, FESC

1. **Early absolute cTn changes were superior to relative cTn changes in diagnosing AMI** among unselected patients with symptoms suggestive of AMI.
2. The ability of absolute cTn changes to diagnose AMI was similar for both assays.
3. The diagnostic superiority of absolute over relative cTn changes was **independent of the underlying cTn baseline** value and consistent in important subgroups of patients such as the elderly and patients with impaired renal function.
4. The **combination of baseline levels with absolute**, but not relative changes significantly improved the diagnostic accuracy provided by baseline cTn levels.
5. The optimal cut off values as derived by ROC curve analysis for the 2 hour absolute cTn changes were about **half the 99th percentile value** of their respective assay.

Circulation July 12, 2011

The differential diagnosis of high-sensitive cardiac troponin T (hs-cTnT) levels is highly dependent on the absolute level.



Twerenbold R et al. Eur Heart J 2012;eurheartj.ehr492

European Heart Journal

European Heart Journal Advance Access published June 21, 2012

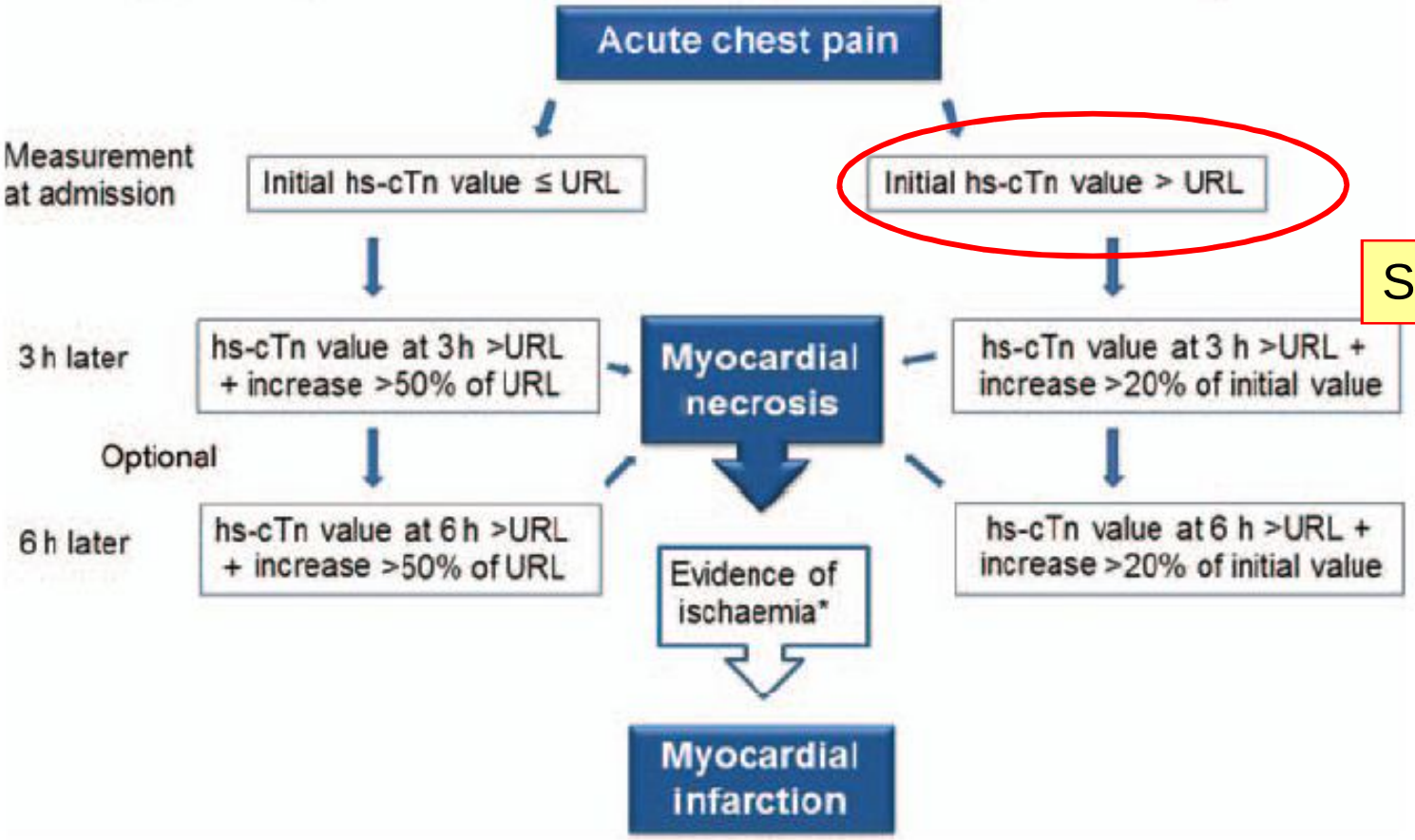
European Heart Journal
doi:10.1093/eurheartj/ehs154

CURRENT OPINION

How to use high-sensitivity cardiac troponins in acute cardiac care†

Kristian Thygesen*, Johannes Mair, Evangelos Giannitsis, Christian Mueller, Bertil Lindahl, Stefan Blankenberg, Kurt Huber, Mario Plebani, Luigi M. Biasucci, Marco Tubaro, Paul Collinson, Per Venge, Yonathan Hasin, Marcello Galvani, Wolfgang Koenig, Christian Hamm, Joseph S. Alpert, Hugo Katus, and Allan S. Jaffe, the Study Group on Biomarkers in Cardiology of the ESC Working Group on Acute Cardiac Care

Rapid early rule-in of AMI with high-sensitivity cardiac troponin



Sovrastima!!

AMI, acute myocardial infarction; hs-cTn, high-sensitivity cardiac troponin; URL, 99th percentile upper reference limit.
*Evidence of ischaemia by symptoms and/or new electrocardiogram changes and/or new imaging corroboration.

Uso della troponina T ad alta sensibilità nella diagnosi di SCA in presenza di Dolore Toracico ed ecg non diagnostico

Quadro clinico compatibile con ischemia miocardica

1° Prelievo TnT_tempo 0 (arrivo in PS)

< 14 ng/L

Ripetere dosaggio Tn dopo 3 e 6 ore per escludere SCA

Rule out

≥ 14 e < 53 ng/L

Garanzia di non sovrastima!!

≥ 53 ng/L

Ripetere dosaggio Tn dopo 3 ore

Ripetere dosaggio Tn dopo 3 ore

Variazione (in aumento o diminuzione) < 50%

Variazione (in > o <) ≥ 50%

Variazione (in > o <) < 20%

Variazione (in > o <) ≥ 20%

Aumentato rischio:
precisare contesto/ipotizzare diagnosi
Ripetere Tn alla 6 ora (e 12 ora se quadro non chiaro)

SCA nstemi

Modificato da:
D.White, Am Heart J 2010; 159: 933-936

La sfida

- Tn “positiva” fuori da un contesto clinico SCA:
  considera rischio globale del paziente (aritmia, scompenso ecc)

- Tn “positiva” ma di origine non chiara:

  a) possibile SCA (consulenza cardio/test diagnostico)

  b) esplora possibili fattori confondenti (laboratorio, età ecc)

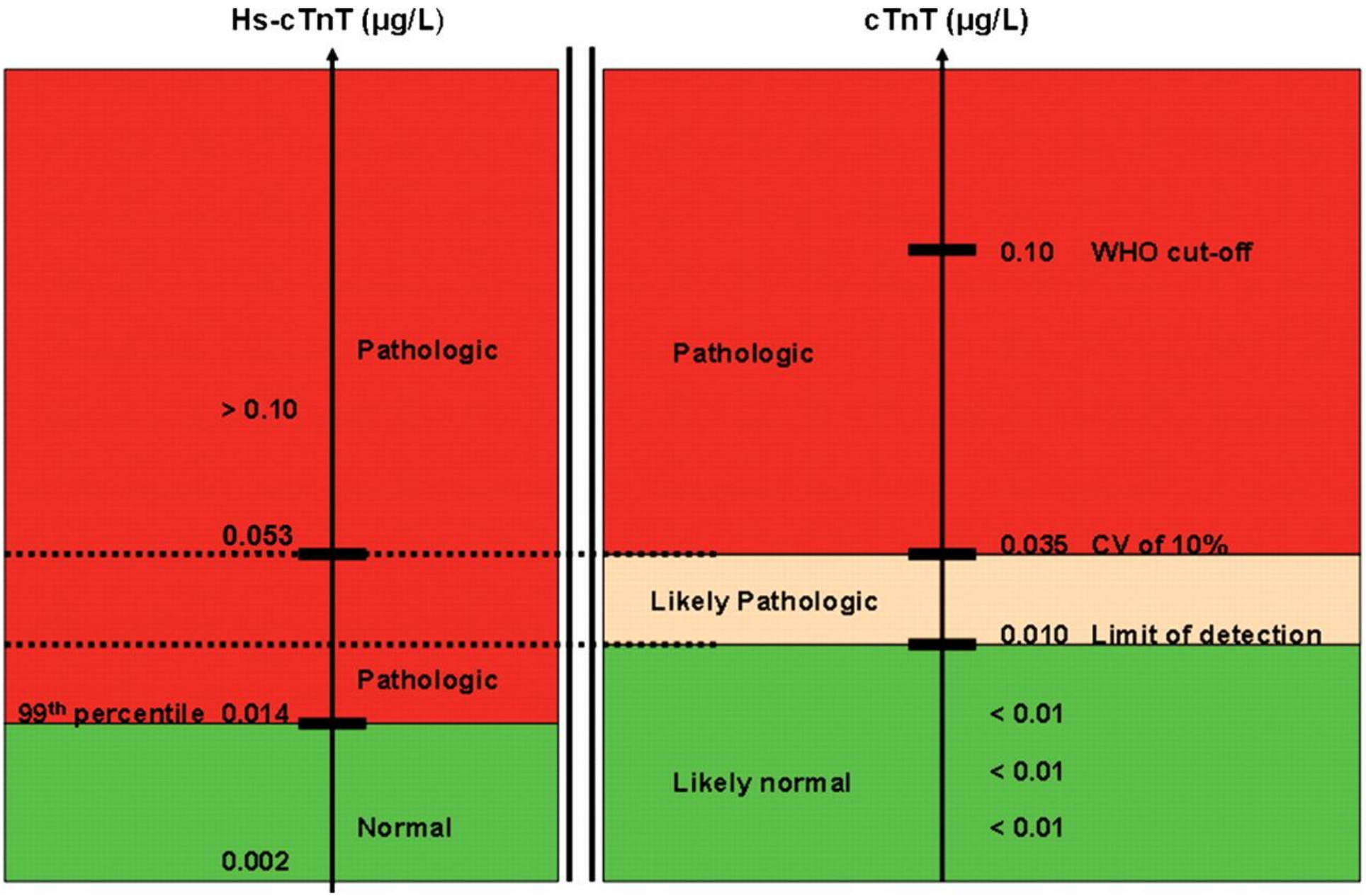
  c)non SCA valuta rischio globale del pz, per dimissione:
  Tn, rientra nel rischio globale: GRACE score

Quali test in dimissione? **CONDIVIDERE:**

- **Il paziente a Tn neg va studiato? E se si con quale test?**
- **Il paziente a Tn pos “non chiaro”, condividere come va studiato (?)**

Decidere per l’alto rischio
Dimettere il “basso rischio”!

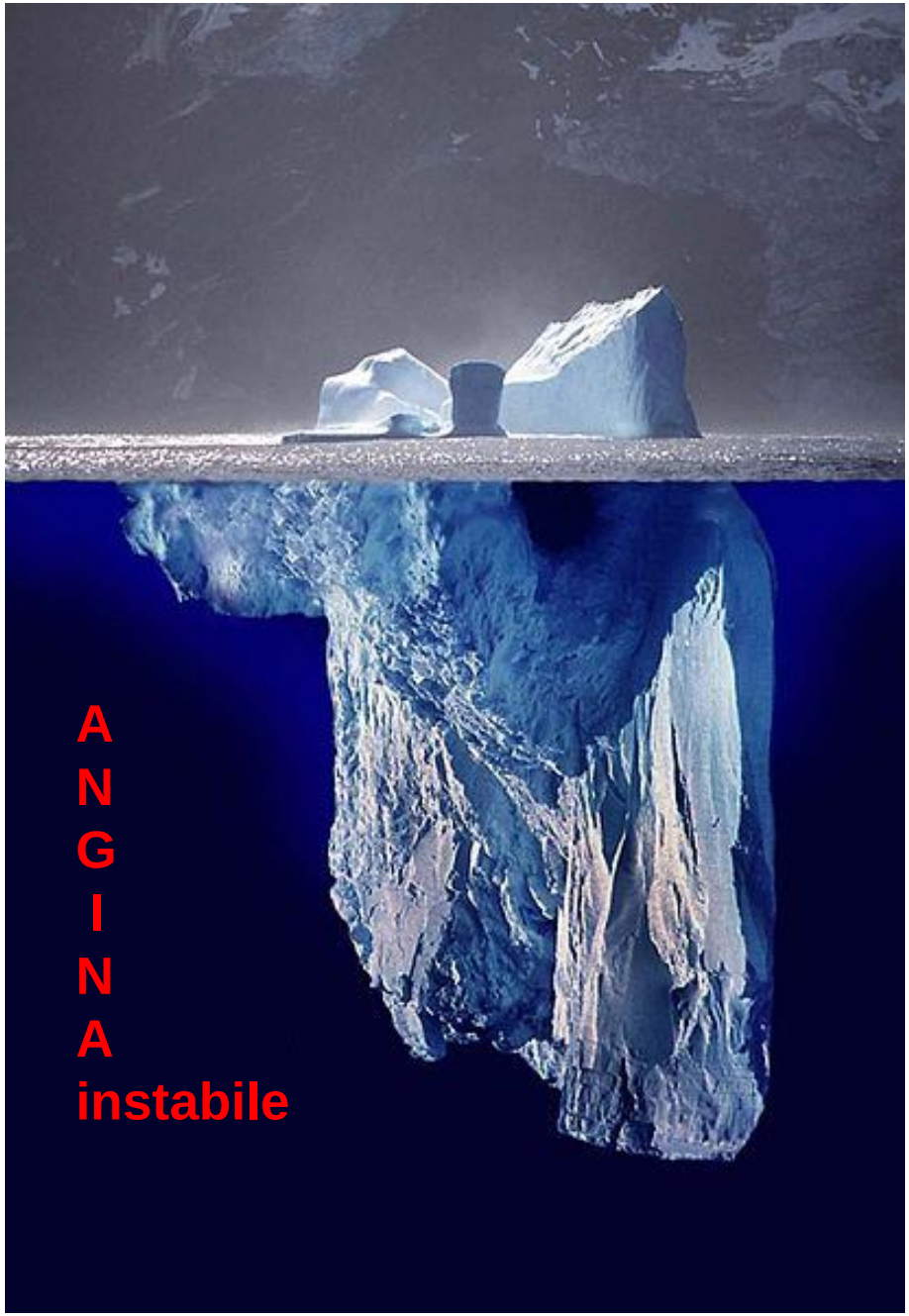
Interpretation of cardiac troponin concentrations in clinical practice, and changes offered by the consideration high-sensitive cardiac troponin.

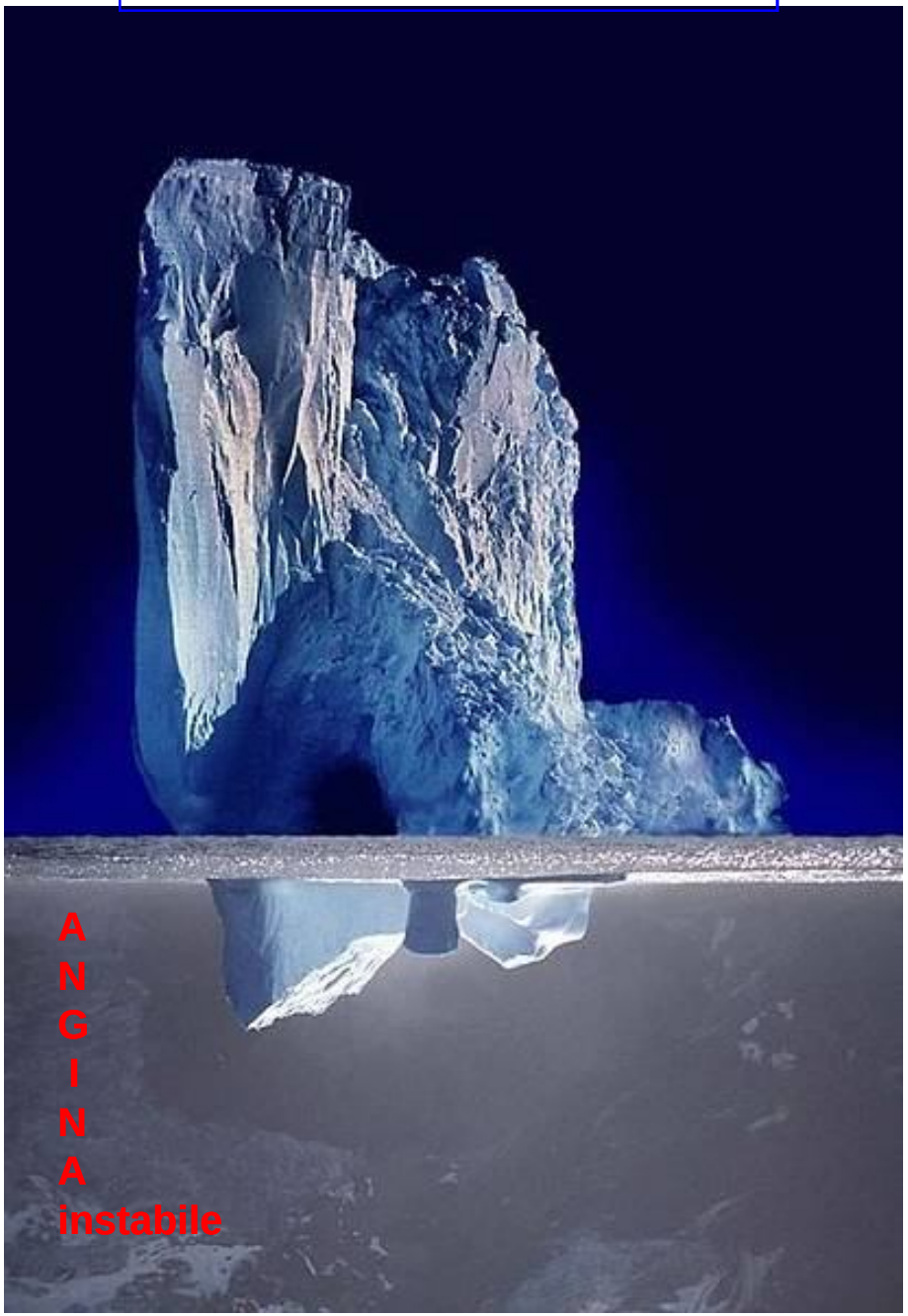


Twerenbold R et al. Eur Heart J 2012;eurheartj.ehr492

European Heart Journal

Tn di ultima generazione





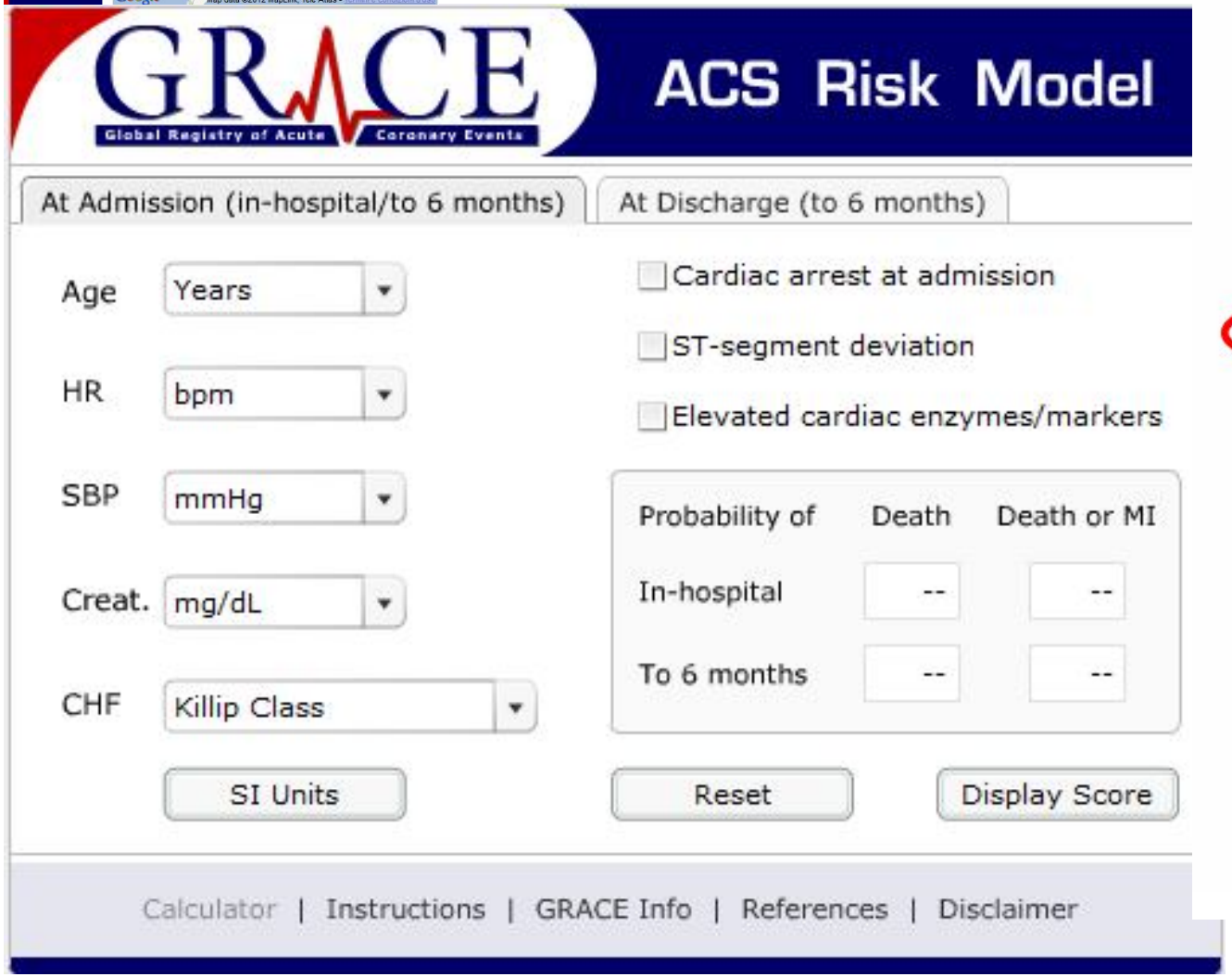
Valutazione probabilità/rischio: intimamente legati

“è un processo dinamico”

TIMI score

ANAMNESI	PUNTI
• Età > 65 anni	1
• > 3 fattori di rischio coronarico Familiarità, Ipertensione Ipercolesterolemia Diabete mellito Fumo attivo	1
• Coronaropatia nota (stenosi > 50%)	1
• Uso di ASA negli ultimi 7 gg	1
PRESENTAZIONE	
• Angina recente severa (< 24 h)	1
• Troponine positive	1
• ST sottolivell > 0,5 mm	1

http://www.outcomes-umassmed.org



Non STE-ACS: In-hospital Mortality

Risk Category (tertiles)	GRACE Risk Score	Probability of Death In-hospital (%)
Low	1-108	<1
Intermediate	109-140	1-3
High	141-372	>3

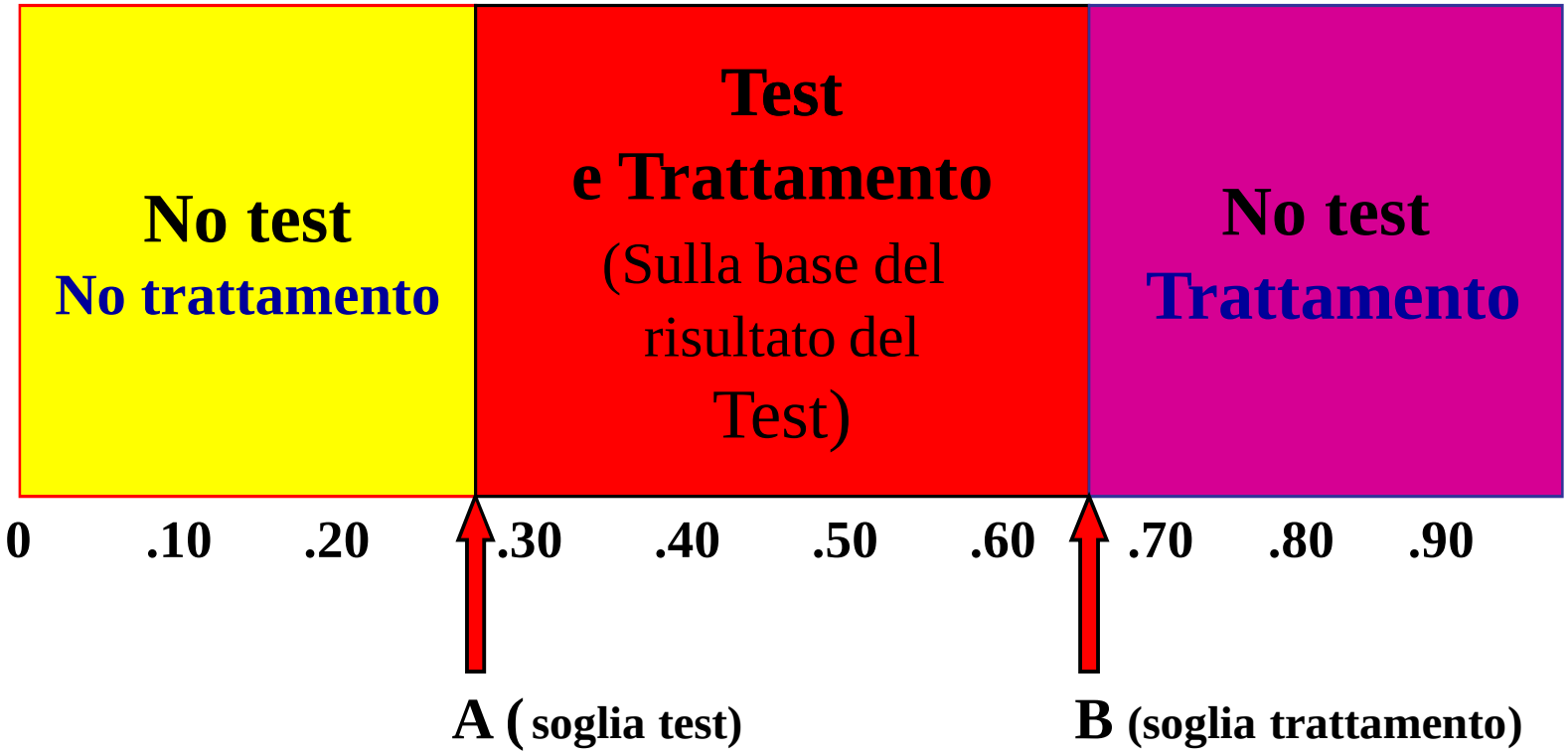
Non STE-ACS: Month Post-discharge Mortality

Risk Category (tertiles)	GRACE Risk Score	Probability of Death Discharge to 6 Months (%)
Low	1-88	<3
Intermediate	89-118	3-8
High	119-263	>8

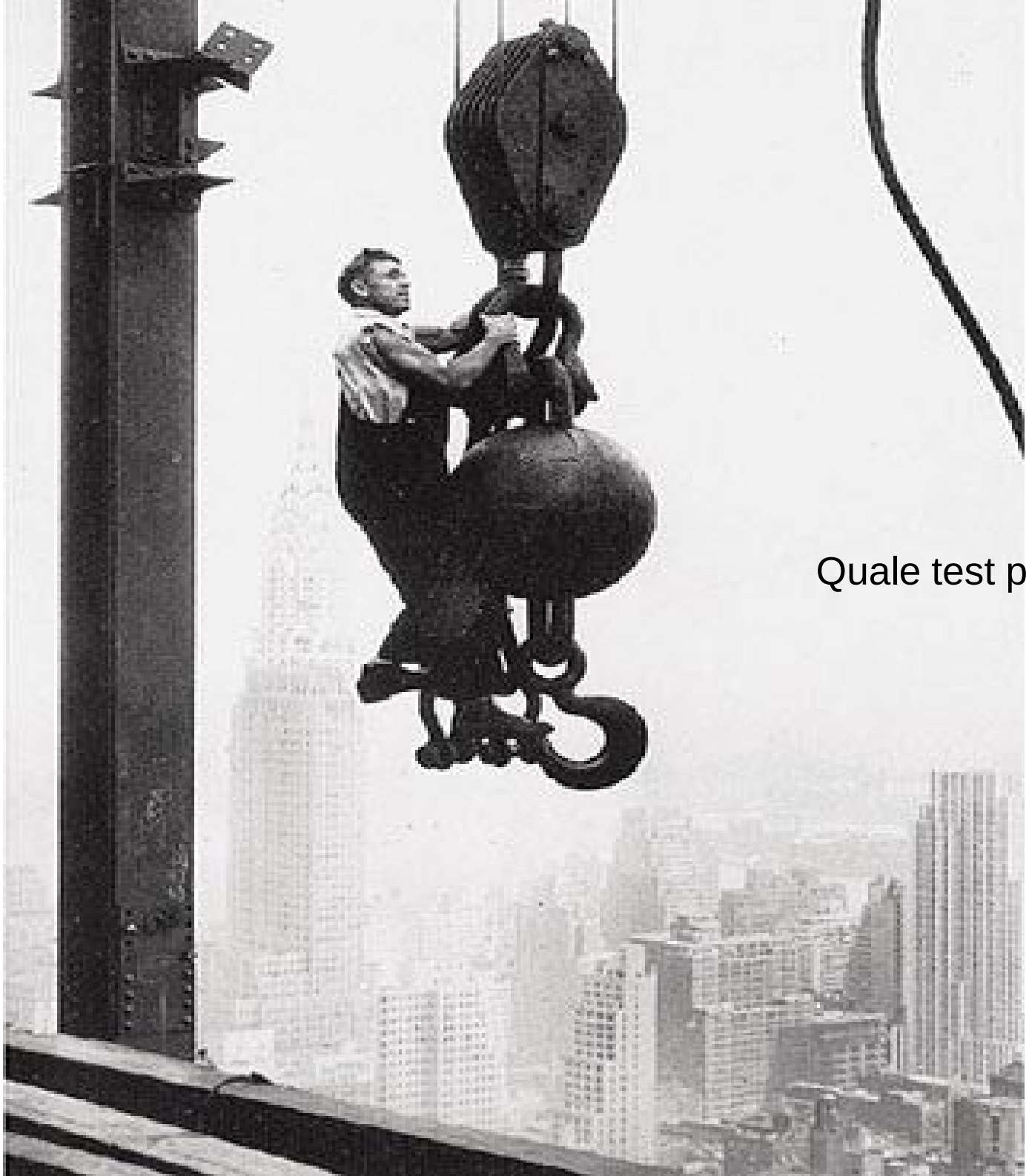
Eagle KA. JAMA 2004;291:2727-33.

(GRACE). BMJ 2006;333:1091.

Limiti test – treatment:
sono in funzione della probabilità di malattia



- Grimes & Schulz, Lancet 2005, April vol 365; 1500-5



Quale test provocativo?

quale test?

Gold Standard: angiografia

Invasiva	Alto costo	Alte dosi radiazioni	Angiografia (6)
Non invasiva	Costo molto alto	Molto alte dosi radiazioni	**MS-Angio-TC** (5)
Non invasiva	Alto costo	Medio-basse dosi radiazioni	**Stress-SPECT** (4)
Non invasiva	Basso costo	Nessuna radiazione	**Stress-Eco** (2,3)
Non invasiva	Costo molto basso	Nessuna radiazione	**ETT** (1)

Costi
Invasività
Radiazioni

(1) Circulation. 2000 Sep 19;102(12):1463-7
(2) Am J Med. 2001;111:18 –23.
(3) Eur Heart J. 2006 Oct;27(20):2448-58.
(4) NEJM vol 344,n°24 June 14, 2001
(5) Circulation 2007;115(13):1762-8
(6) J Am Coll Cardiol 2001;37:2042-9.

MSTC multi slice computer tomography
SPECT scintigrafia miocardica
ETT exercise tolerance test

Affidabilità diagnostica degli stress test: Test Ergometrico massimale

- Sensibilità 68-76%
  - Alta per coronaropatia della discendente anteriore, e malattia dei tre vasi
- Specificità 73-77%
  - Probabilmente più bassa nelle donne

In generale: sensibilità 68%, specificità 77%, 132 studi, 24.027 pazienti (1)

(1) NEJM vol 344,n°24 June 14, 2001.
Cardiol Clin 2005; 23:503-516
Am Heart J. 2005 May;149(5):894-901
Ann Emerg Med. 2006;47:427-435.

Affidabilità diagnostica degli stress test: Ecocardiografia

- Test ergometrico + Ecocardiografia (2)
  - Sensibilità 71-97%, Specificità 64-100%
- Dobutamina + Ecocardiografia
  - Sensibilità 76-89%, Specificità 70-95%
- Dipiridamolo (alte dosi) + Ecocardiografia
  - Sensibilità 74-83%, Specificity 80%

In generale: Sensibilità 76%, Specificità 88%, studi 10, 1.174 pazienti (1)

(1) NEJM vol 344,n°24 June 14, 2001, cumulativo

(2) Eur Heart J. 2006 Oct;27(20):2448-58. test ergometrico + eco

Affidabilità diagnostica degli stress test: Scintigrafia miocardica (SPECT)

- Test ergometrico + SPECT
  - Sensibilità 83-90%, Specificità 62-88%
- Dipiridamolo + SPECT
  - Sensibilità 82-89%, Specificità 75-78%
- Dobutamina + SPECT
  - Sensibilità 80-97%, Specificità 74-89%

In generale: Sensibilità 88%, Specificità 77%, 8 studi, 628 pazienti (1)

(1) NEJM vol 344,n°24 June 14, 2001.

NHS
National Institute for
Health and Clinical Excellence

http://guidance.nice.org.uk/CG95

Chest pain of recent onset:
Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin

Full Guideline

Final Draft - March 2010

National Clinical Guideline Centre for Acute and Chronic Conditions

ANGIO_TAC:

Difficile discernere nell'uso in DE.

NON VI SONO INFORMAZIONI PRECISE SU COME PROCEDERE.

Qual è il grado di stenosi su cui procedere?

Coles DR,.
Int J Cardiovasc Imaging. 2007;23 (5) :603-614.

Hoffmann U,
Circulation. 2006; 114 (21) :2251-2260.

Johnson TR,
AJR Am J Roentgenol. 2007; 188 (1) :76-82.

Rubinshtein R,
Circulation. 2007; 115 (13) :1762-1768.

TAC multislice (16-64).

1. In popolazioni ad **alta prevalenza di malattia coronarica**

BASSO VALORE PREDITTIVO NEG

2. In popolazioni a **bassa prevalenza**, **come nel caso del dolore toracico**,

BUON VALORE PREDITTIVO NEG ma anche FALSI POSITIVI

Per vincere la sfida:

- Mirare la richiesta della Tn (“al cuore Ramon”!!!!)
- Osservazione (OBI) e timing a t0, a 3 e a 6 ore
- Rule in: in base al risultato e al rischio del paziente
- Rule out basso rischio
- Mirare/concordare il test in base al paziente