ЗИМНО УЧИЛИЩЕ ПО

КАРДИОЛОГИЯ

ВИСОКО-ЧУВСТВИТЕЛЕН ТРОПОНИН – НОВАТА ПАРАДИГМА В ДИАГНОСТИКАТА НА ОСТЪР КОРОНАРЕН СИНДРОМ

Д-р Веселина Колева

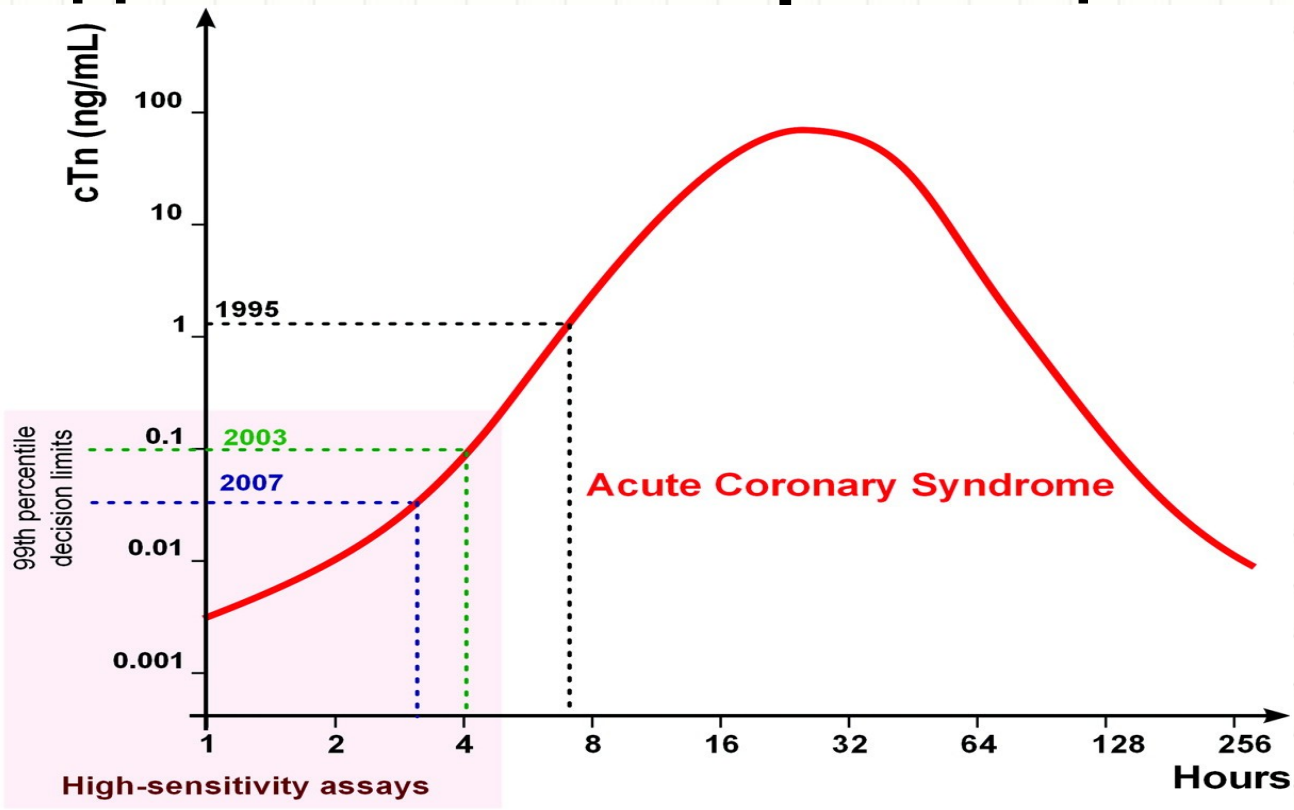
Токуда Болница София

Банско, 20 март 2014

АКЦЕНТИ

- Еволюция в тестовете за тропонини
- Аналитична характеристика на hsTn
- Клинична интерпретация
- Изводи за практиката

Еволюция в методологията за измерване на сърдечни тропонини и тяхната диагностична отрязваща стойност

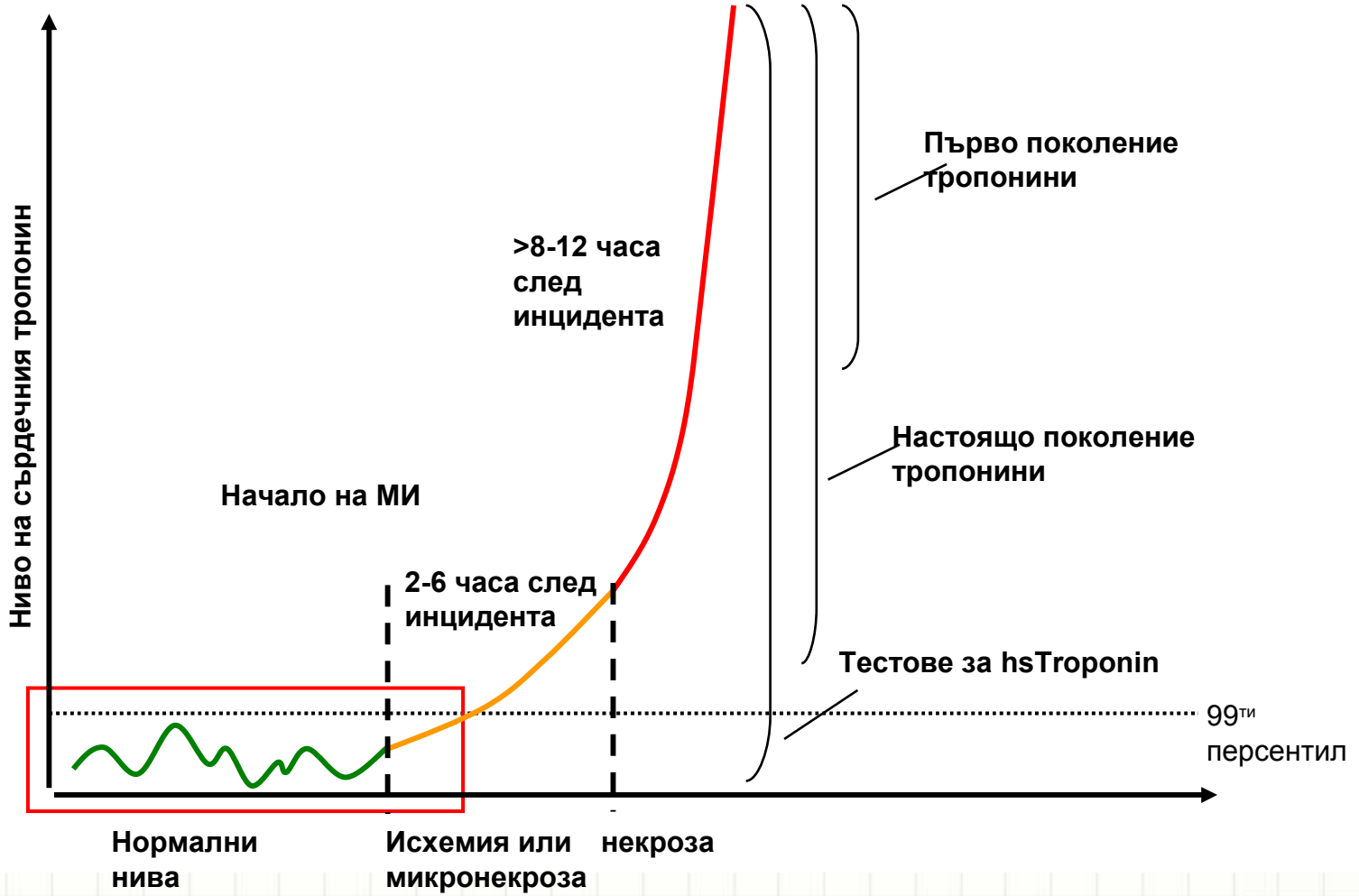


cTn Assay	Diagnostic cutoff	Implementation
TnI	≥ 1.5 ng/mL	1995
cTnI	> 0.10 ng/mL	2003
TnI-Ultra	> 0.04 ng/mL	2007

American Heart Association
Learn and Live

Mahajan V, Jarolim P. Circulation 2011;124:2350-2354

Граници на откриване за различните поколения методи за тропонини



Hochholzer, Am Heart J, 2010
F. Apple, AACC Webinar, Jan 2012

Нови Препоръки на ESC 2012 – Актуализирани от 2007

European Heart Journal
doi:10.1093/eurheartj/ehs184

EXPERT CONSENSUS DOCUMENT

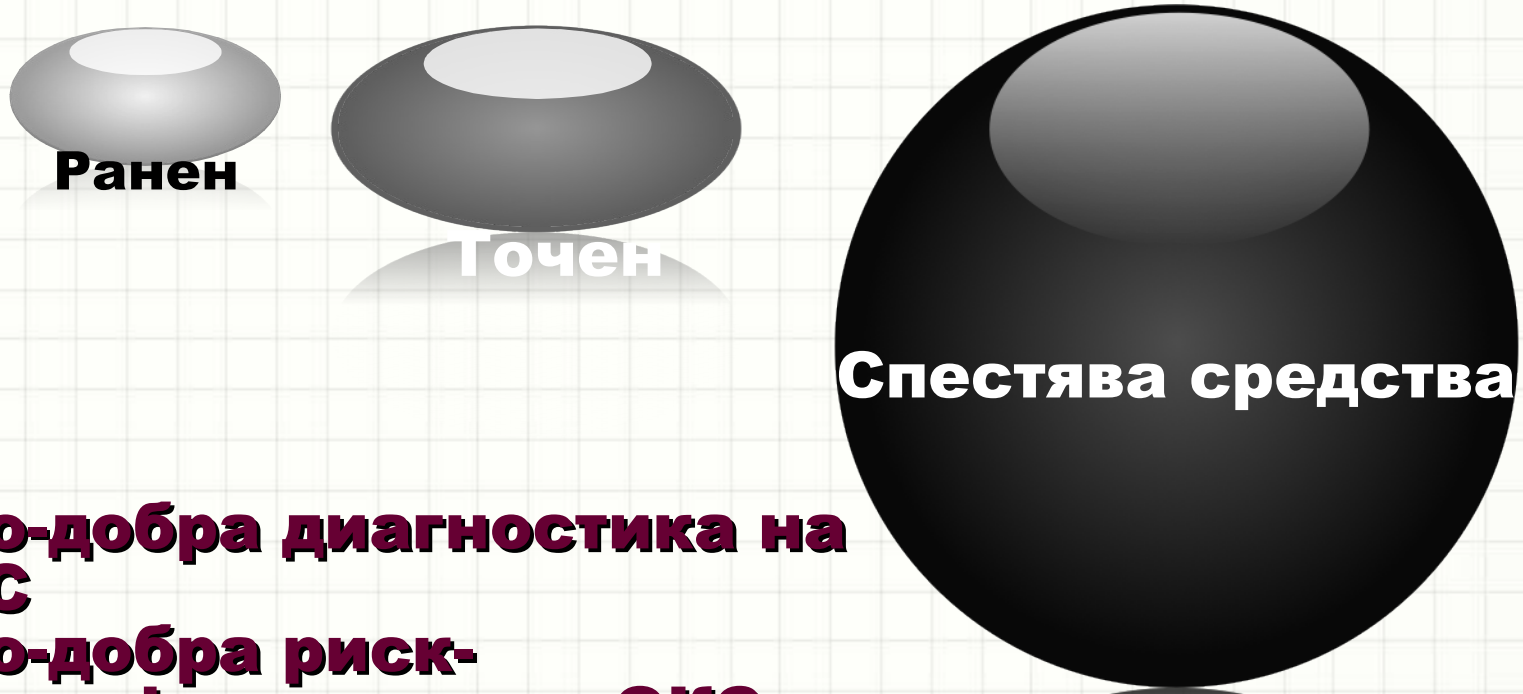
Third universal definition of myocardial infarction

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

Authors/Task Force Members Chairpersons: Kristian Thygesen(Denmark)*, Joseph S. Alpert, (USA)*, Harvey D. White, (New Zealand)*, Biomarker Subcommittee: Allan S. Jaffe (USA), Hugo A. Katus (Germany), Fred S. Apple (USA), Bertil Lindahl (Sweden), David A. Morrow (USA), ECG Subcommittee: Bernard R. Chaitman (USA), Peter M. Clemmensen (Denmark), Per Johanson (Sweden), Hanoch Hod (Israel), Imaging Subcommittee: Richard Underwood (UK), Jeroen J. Bax (The Netherlands), Robert O. Bonow (USA), Fausto Pinto (Portugal), Raymond J. Gibbons (USA), Classification Subcommittee: Keith A. Fox (UK), Dan Atar (Norway), L. Kristin Newby (USA), Marcello Galvani (Italy), Christian W. Hamm (Germany), Intervention Subcommittee: Barry F. Uretsky (USA), Ph. Gabriel Steg (France), William Wijns (Belgium), Jean-Pierre Bassand (France), Phillippe Menasché (France), Jan Ravkilde (Denmark), Trials & Registries Subcommittee: E. Magnus Ohman (USA), Elliott M. Antman (USA), Lars C. Wallentin (Sweden), Paul W. Armstrong (Canada), Maarten L. Simoons (The Netherlands), Heart Failure Subcommittee: James L. Januzzi (USA), Markku S. Nieminen (Finland), Mihai Gheorghiade (USA), Gerasimos Filippatos (Greece), Epidemiology Subcommittee: Russell V. Luepker (USA), Stephen P. Fortmann (USA), Wayne D. Rosamond (USA), Dan Levy (USA), David Wood (UK), Global Perspective Subcommittee: Sidney C. Smith (USA), Dayi Hu (China), José-Luis Lopez-Sendon (Spain), Rose Marie Robertson (USA), Douglas Weaver (USA), Michal Tendera (Poland), Alfred A. Bove (USA), Alexander N. Parkhomenko (Ukraine), Elena J. Vasilieva (Russia), Shanti Mendis (Switzerland).

Thygesen et al. *Eur Heart J*. 2012;33:2551-67.

Защо високо-чувствителен тропонин



- **По-добра диагностика на ОКС**
- **По-добра риск-стратификация при ОКС**
- **По-добра риск-стратификация при не-ОКС**
- **Мониториране на кардиотоксична терапия, напр.. herceptin?**

Лабораторията в помощ на клиниката

Какво означава hsTn

Analytical Characteristics of High-Sensitivity Cardiac Troponin Assays

Fred S. Apple[1,2*] and Paul O. Collinson,[3]
for the IFCC Task Force on Clinical Applications of Cardiac Biomarkers[†]

1. Касае се за подобрена чувствителност
2. Общата грешка при 99я персентил да е ≤10% CV
3. концентрация > LoD при 50% и повече от здравите индивиди

Reference: Apple, F.S., et al. Clin Chem, 2012; 58(1) :54–61

Препоръчителни мерни единици

1

- ng/L или pg/ml

2

- Изразяване на резултата като цяло число

3

- Пример :
- 0.03 граница е в **ng/ml** = 0.03 **µg/l**
- = 30 **ng/l** = 30 **pg/ml**

Значение на чувствителността и специфичността

Table 2 Classification of High-Sensitivity Cardiac Troponin Assays*

Category	Description
First Generation	Able to measure cTn in 50%–75% of a reference population
Second Generation	Able to measure cTn in 75%–95% of a reference population
Third Generation	Able to measure cTn in more than 95% of a reference population.

*Adapted from Apple and Collinson (3).

J Am Coll Cardiol. 2013;61(17):1753-1758. doi:10.1016/j.jacc.2012.09.069

Сравнение: ARCHITECT TnI & hsTnI

	ARCHITECT TnI*		ARCHITECT hsTnI**	
	µg/L (ng/mL)	ng/L (pg/mL)	µg/L (ng/mL)	ng/L (pg/mL)
LoD	0.010	10	0.002	1.9
10% CV	0.032	32	0.005	4.7
99th Percentile (overall)	0.028	28	0.026	26.2
99th Percentile (males)	0.033	33	0.034	34.2
99th Percentile (females)	0.013	13	0.016	15.6
% Detectable above LoD	**<50% of normals**		**>50% of normals**	

- ~7x подобрение в точността без значима промяна в 99я персентил
- Повишен е % на откриваеми стойности сред кардио-здрави или “нормални” индивиди

*Representative data from ARCHITECT TnI Package Insert 840653_R08. **Representative data from ARCHITECT hsTnI Package Insert G1-0139/R02.

Сравнение: TnT4G и hsTnT

		TnT 4th generation	TnT-hs
LoD		Analytical sens 0.01 ng/ml	0.003 ng/ml
range		0.01 - 25 ng/ml	0.003 -10 ng/ml
99th percentile		< 0.01 ng/ml	< 0.014 ng/ml
LoQ (10% CV)		0.03 ng/ml	0.013 ng/ml

Сравнение между тестове за високочувствителен тропонин

ARTICLE IN PRESS

CLB-08561; No. of pages: 6; 4C:

Clinical Biochemistry xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Comparison of high sensitivity troponin T and I assays in the diagnosis of non-ST elevation acute myocardial infarction in emergency patients with chest pain ☆,☆☆

Louise Cullen [a,b,*,1], Sally Aldous [c,1], Martin Than [c], Jaimi H. Greenslade [a,b,d], Jillian R. Tate [a], Peter M. George [c], Christopher J. Hammett [a,d], A. Mark Richards [e,f], Jacobus P.J. Ungerer [a], Richard W. Troughton [e], Anthony F.T. Brown [a,d], Dylan F. Flaws [d], Arvin Lamanna [a,d], Christopher J. Pemberton [e], Christopher Florkowski [c], Carel J. Pretorius [a], Kevin Chu [a,d], William A. Parsonage [a,d]

[a] Royal Brisbane and Women's Hospital, Herston, QLD, Australia
[b] Queensland University of Technology, Brisbane, QLD, Australia
[c] Christchurch Hospital, Christchurch, New Zealand
[d] The University of Queensland, Brisbane, QLD, Australia
[e] Christchurch Heart Institute, University of Otago, Christchurch, New Zealand
[f] Cardiovascular Research Institute, National University Heart Centre, Singapore

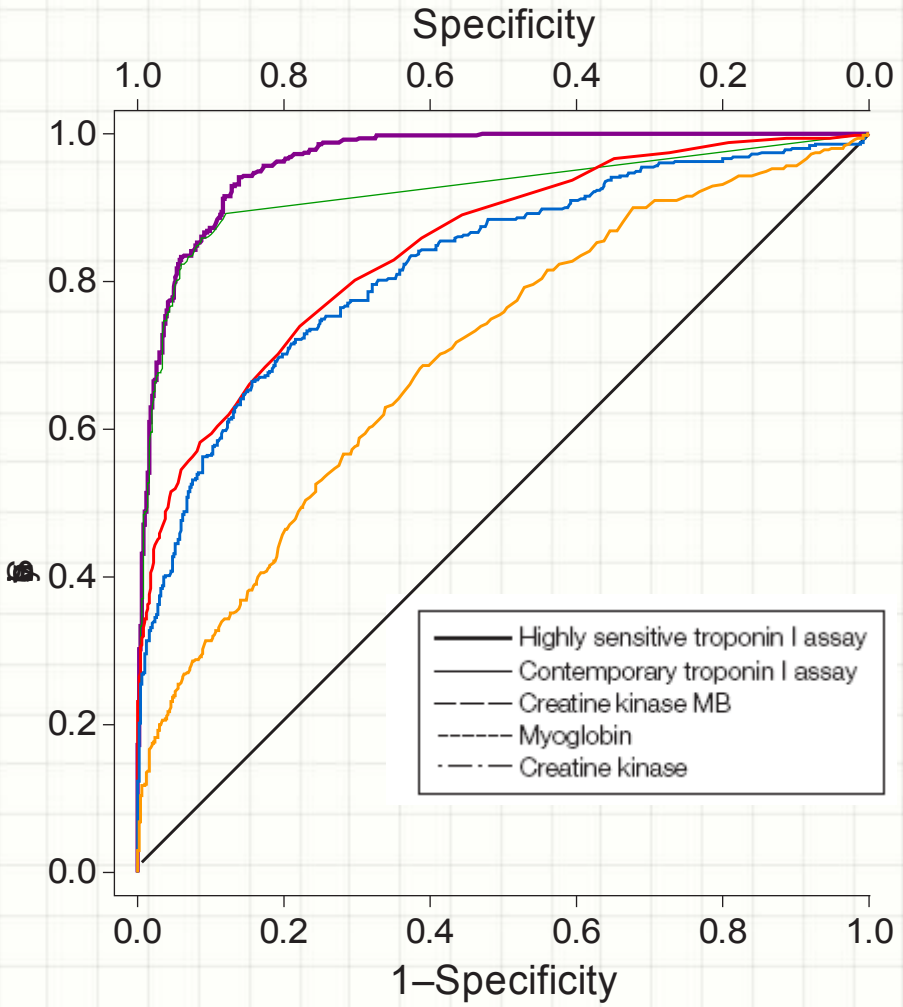
Публикувана on line 05.12.2013

Сравнение на hsTnI спрямо hsTnT

	Hs-cTnT	Hs-cTnI
Sensitivity	**94.1** (90.0-96.6)	**95.6** (91.8-97.7)
NPV	**98.9** (98.1-99.4)	**99.3** (98.7-99.6)
Specificity	**79.0** (76.8-81.1)	**92.5** (90.9-93.7)
PPV	**40.1** (35.8-44.5)	**65.4** (59.9-70.6)

Cullen et. al. JACC 2013

hsTnI спрямо TnI и други биомаркери на некроза



JAMA. 2011;306(24):2684-2693

Chest pain cohort Figure, n=1578):
AUC for hsTnI: 0.962
AUC for cTnI: 0.921

Early Presenters:
Chest pain <2h (n=407):
AUC for hsTnI: 0.970
AUC for cTnI: 0.888

Assay	AUC
hsTnI	0.96
cTnI	0.92
CK-MB	0.85
Myo	0.83
CK	0.71

Преданалитични акценти

"The Impact of Hemolysis on Ortho-clinical Diagnostic's ECI and Roche's Elecsys Immuoassay Systems." JA Snyder et al. Clin Chim Acta. 2004;348:181-7.

"The Effect of Sample Hemolysis on Cardiac Troponin I and T Assays." R Bais. Clin Chem. 2010;56:1357-9.

"The Effect of Hemolysis on Current Troponin Assays- A Confounding Preanalytical Variable?" C Florkowski et al. Clin Chem. 2010;56:1195-7.

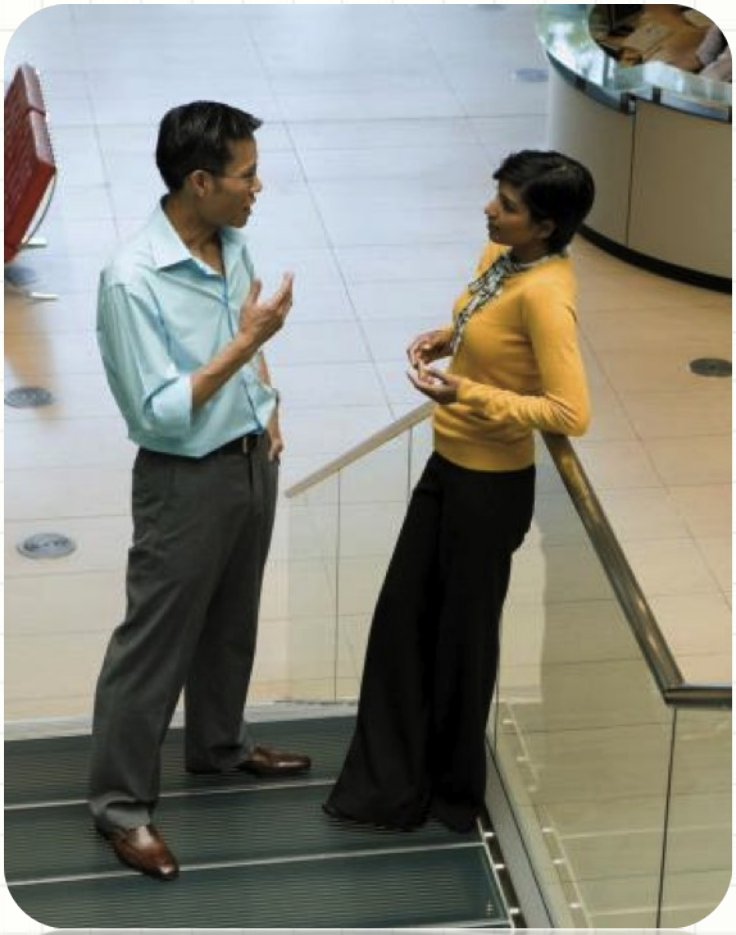
	Recovery (%) при различни конц.на Хб		
Хемолиза (Hb в плазмата mg/L)	Abbott TnI (0.032 ng/mL)	Roche hsTnT (19 pg/mL)	Vitros esTnI (0.050 ng/mL)
12	100.0	100.0	100.0
43	90.6	99.6	**162.0**
77	93.8	99.8	**238.0**
132	81.3	**84.3**	**348.0**
235	84.4	**59.5**	**510.0**
392	90.6	**50.2**	**676.0**

- Серум или плазма?
- Интерференция на хемолизата

Florkowski, *Clin Chem*. 2010;56:1195-7

Опорни точки

- Избор на референтна популация
- Полово зависима ГГН
- Възрастово зависима ГГН
- Биологична вариация



„Нормална популация“

- Все още е дискутабилно определението, въпреки че някои препоръки са направени
- Две популации с по-млади (<30 год) и по-стари (>30 год, със средна възраст от 60-65 years)
- Включващи критерии
  - Да няма известно заболяване
  - Да не приемат медикаменти за сърдечни заболявания, напр хипертония, дислипидемия
  - Резултат от изследване на натриуретичен пептид под границата за изключващ критерий поради камерна дисфункция
- Равно разпределени според пол и смес от различни раси и етноси
- 300-500 индивида

Apple et al. *Clin Chem*. 2012;58:54-61.

Определяне на 99я персентил с различни методи за High Sensitive Troponin

Скоро публикувано проучване изследва една и съща популация с 5 “high sensitive” метода

Метод	N	Мерими стойности, >LoD, %	99th (90%CI) ng/L	Мъже 99th ng/L	Жени 99th ng/L
Abbott: ARCHITECT STAT hs-cTnI	524	96	23 (16-63)	36	15
Beckman: Access 2 hs-cTnI	524	80	32 (22-69)	52	23
Roche: Cobas e601 hs-cTnT	523	25	15 (13-21)	20	13
Siemens: Dimension Vista hs-cTnI	503	86	58 (34-125)	81	42
Singulex: Erenna hs-cTnI	522	100	31 (21-47)	36	30

Apple et al. *Clin Chem*. 2012;58:1574-81.

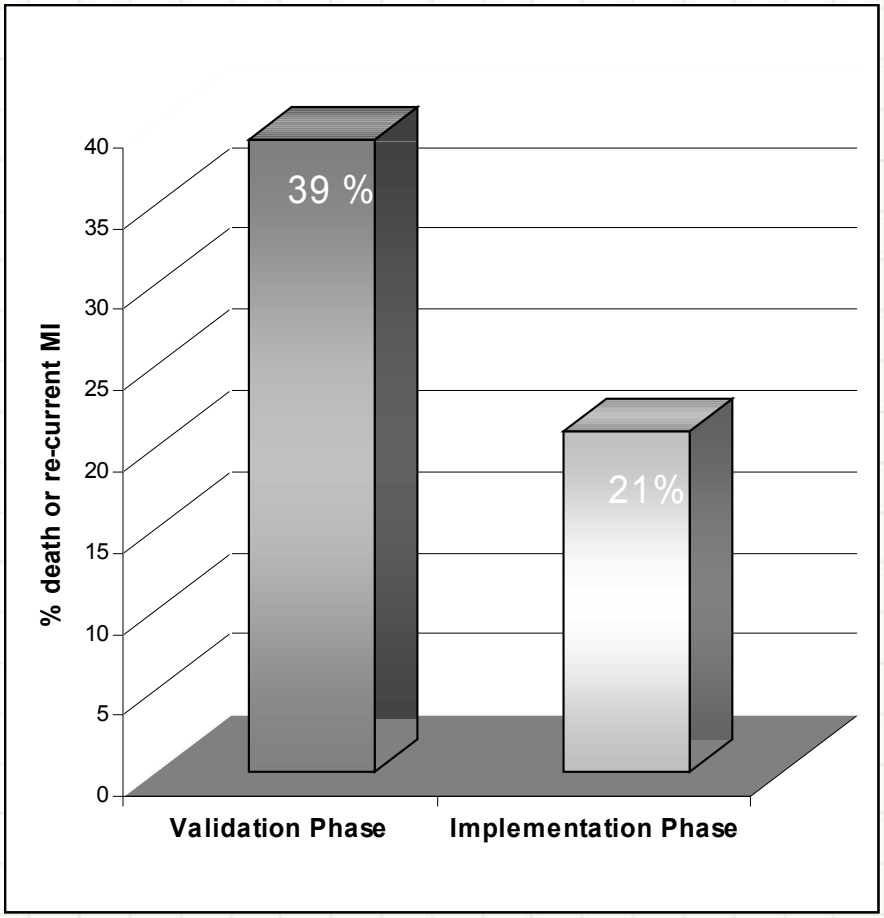
Стойности на 99я персентил сред здрава популация, измерени с високо-чувствителни и настоящи, cTnI и cTnT тестове.

Производител/анализатор/тест	LoD ng/L	Measureable Values >LoD, %	99я персентил Обща популация (90% CI), ng/L	Мъже 99я персент ng/L	Жени 99я персент ng/L
High sensitivity					
Abbott • ARCHITECT i2000$_{SR}$ STAT • hs-cTnI	1.2	96	23 (16-63)	36	15
Beckman • Access 2 • hsTnI**	2.5	80	32 (22-69)	52	23
Roche • Cobas e601 • hs-cTnT	5	25	15 (13-28)	20	13
Siemens • Dimension Vista • hsTnI**	0.5	86	58 (34-125)	81	42
Singulex • Erenna • hsTnI**	0.09	100	40 (25-215)	36	30
Sensitive contemporary					
Abbott • ARCHITECT i2000$_{SR}$ STAT• cTnI	9	2	13 (<9-23)	20	<9
Abbott AxSYM *ADV* Troponin-I	20	3	34 (22-39)	38	29
Beckman • Access 2 • modified-sensitive cTnI	2.5	35	56 (27-100)	48	85
OCD • Vitr os 3600 • cTnI ES	12	2	19 (12-22)	21	15
Roche • Cobas e 601 • cTnI	160	1	184 (<160-706)	300	60
Siemens • Centaur • Tnl U tra	6	6	12 (10-16)	14	11
Siemens • Dimension EXL 200 • cTnI	17	2	34 (17-44)	39	22
Siemens • Dimension Vista • cTnI	15	1	21 (<15-39)	30	<15
Siemens • Immulite 2000 XPi • cTnI	100	5	392 (190-520)	394	451

Apple, F.S., et al. Clin Chem, 2012; 58(11): 1574-1581.

Полза от възприемането на 99я персентил като ULN Cutoff

- ✓ Възможност за идентифициране на повече пациенти с повишен риск



Понижаването на диагностичния праг от 0.2 ng/mL до 0.05 ng/mL се асоциира с 46% намаление на риска от смърт и рецидив на МИ.

Mills et al. *JAMA*. 2011;305:1210-6.

Клинично значима промяна

- При изходно негативен маркер
- При изходно позитивен маркер
- За отдиференциране на остра от хронична увреда
- За откриване на реинфаркт

JAMA Article 2011

Serial Changes in Highly Sensitive Troponin I Assay and Early Diagnosis of Myocardial Infarction

Till Keller, MD
Tanja Zeller, PhD
Francisco Ojeda, PhD
Stergios Tzikas, MD
Lars Lillpopp
Christoph Sinning, MD
Philipp Wild, MD
Sabine Genth-Zotz, MD
Ascan Warnholtz, MD
Evangelos Giannitsis, MD
Martin Möckel, MD
Christoph Bickel, MD
Dirk Peetz, MD
Karl Lackner, MD
Stephan Baldus, MD
Thomas Münzel, MD
Stefan Blankenberg, MD

Context Introduction of highly sensitive troponin assays into clinical practice has substantially improved the evaluation of patients with chest pain.

Objective To evaluate the diagnostic performance of a highly sensitive troponin I (hsTnI) assay compared with a contemporary troponin I (cTnI) assay and their serial changes in the diagnosis of acute myocardial infarction (AMI).

Design, Setting, and Patients A total of 1818 patients with suspected acute coronary syndrome were consecutively enrolled at the chest pain units of the University Heart Center Hamburg, the University Medical Center Mainz, and the Federal Armed Forces Hospital Koblenz, all in Germany, from 2007 to 2008. Twelve biomarkers including hsTnI (level of detection, 3.4 pg/mL) and cTnI (level of detection, 10 pg/mL) were measured on admission and after 3 and 6 hours.

Main Outcome Measures Diagnostic performance for AMI of baseline and serial changes in hsTnI and cTnI results at 3 hours after admission to the emergency department.

Results Of the 1818 patients, 413 (22.7%) were diagnosed as having AMI. For discrimination of AMI, the area under the receiver operating characteristic (ROC) curve was 0.96 (95% CI, 0.95-0.97) for hsTnI on admission and 0.92 (95% CI, 0.90-0.94) for cTnI on admission. Both were superior to the other evaluated diagnostic biomarkers. The use of hsTnI at admission (with the diagnostic cutoff value at the 99th percentile of 30 pg/mL) had a sensitivity of 82.3% and a negative predictive value (for ruling out AMI) of 94.7%. The use of cTnI (with the diagnostic cutoff value at the 99th percentile of 32 pg/mL) at admission had a sensitivity of 79.4% and a negative predictive value of 94.0%. Using levels obtained at 3 hours after admission, the sensitivity was 98.2% and the negative predictive value was 99.4% for both hsTnI and cTnI assays. Combining the 99th percentile cutoff at admission with the serial change in troponin concentration within 3 hours, the positive predictive value (for ruling in AMI) for hsTnI increased from 75.1% at admission to 95.8% after 3 hours, and for cTnI increased from 80.9% at admission to 96.1% after 3 hours.

Conclusions Among patients with suspected acute coronary syndrome, hsTnI or cTnI determination 3 hours after admission may facilitate early rule-out of AMI. A serial change in hsTnI or cTnI levels from admission (using the 99th percentile diagnostic cutoff value) to 3 hours after admission may facilitate an early diagnosis of AMI.

JAMA. 2011;306(24):2684-2693 www.jama.com

ACUTE CHEST PAIN IS ONE OF the most common reasons patients seek care in an emergency department.[1] Early identification of individuals at high and intermediate risk for myocardial ischemia is crucial because they benefit the most from early and aggressive treatment.[2]

Включени пациенти 1818

Не-коронарна гръдна болка: 1165

Нестабилна Ангина пекторис: 240

ОМИ: 413

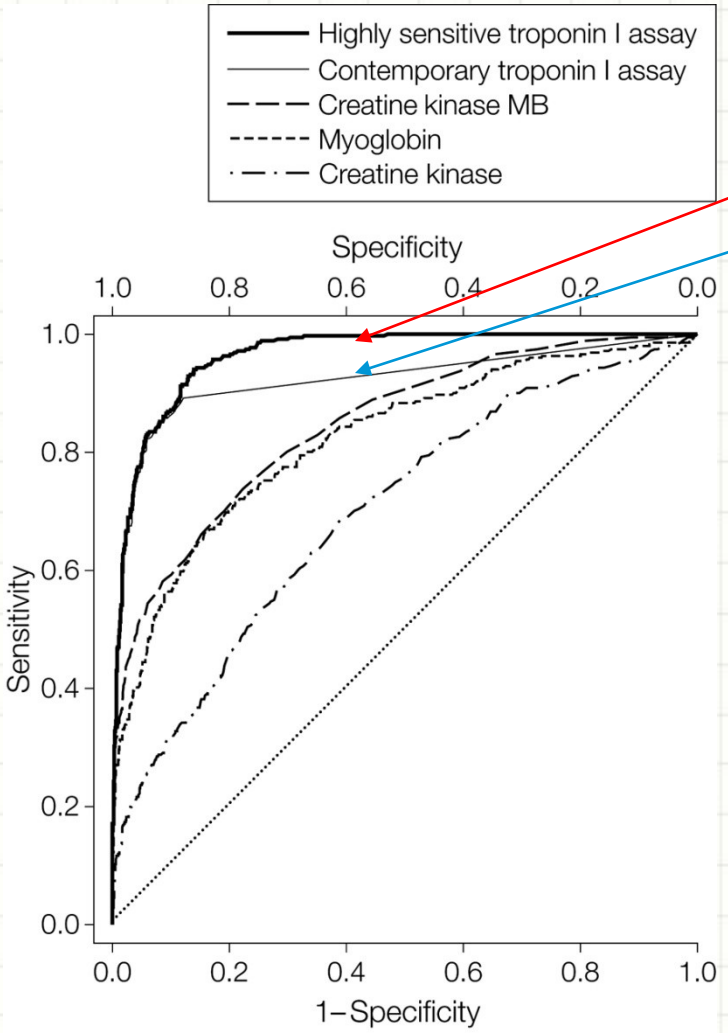
STEMI: 56

NSTEMI: 357

hsTroponin
NPV след 3 ч
PPV след 3 h
TnI динамика %
Други маркери

Keller, T. et al. *JAMA* 2011;306:2684-2693

ROC криви за диагностика на МИ с тестове за тропонин и маркери на некроза при постъпване в спешно отделение



Assay	AUC
hsTnI	0.96
cTnI	0.92
CK-MB	0.85
Myo	0.83
CK	0.71

- The difference in the diagnostic performance between hsTnI and cTnI was apparent in the first hours after chest pain onset. In the subgroup of patients (n=407) with onset of <2 hours, hsTnI had an AUC of 0.970 whereas cTnI had an AUC of 0.888.
- The AUC was also calculated for the combination of baseline Tn and 3 hour delta. hsTnI AUC changed from 0.96 to 0.99 and cTnI from 0.92 to 0.98. There was no statistical difference between the hsTnI and cTnI AUC with the combination.

Keller, T. et al. *JAMA* 2011;306:2684-2693

hsTnI - Rule Out значение

cTnI и hsTnI при постъпване и след 3 часа

hsTnI,% (95%CI)

	При постъпване		След 3 часа	
	LoD	**99th Percentile**	**LoD**	**99th Percentile**
Чувствителност	100.0 (98.0-100.0)	82.3 (77.3-86.5)	100.0 (98.0-100.0)	98.2 (95.9-99.4)
Специфичност	35.3 (32.3-38.4)	92.1 (90.3-93.7)	1.9 (1.2-3.0)	90.4 (88.4-92.2)
Positive predictive Value (PPV)	30.8 (27.8-33.9)	75.1 (69.9-79.8)	22.7 (20.4-25.2)	74.7 (69.9-79.0)
Negative predictive value (NPV)	100.0 (98.4-100.0)	94.7 (93.1-96.1)	100.0 (75.1-100.0)	99.4 (98.7-99.8)
Брой пол/ общ брой*	915/1260	309/1260	1241/1260	371/1260

*брой пациенти, отговарящи на критерии за положителен тест/ общ брой пациенти .

Keller, T., et al.JAMA , 2011; 306 (24): 2684-2693.

Отхвърляне на ОМИ чрез LoD

ARTICLE IN PRESS

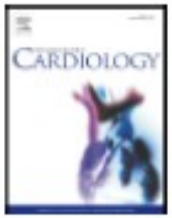
IJCA-16469; No of Pages 6

International Journal of Cardiology xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

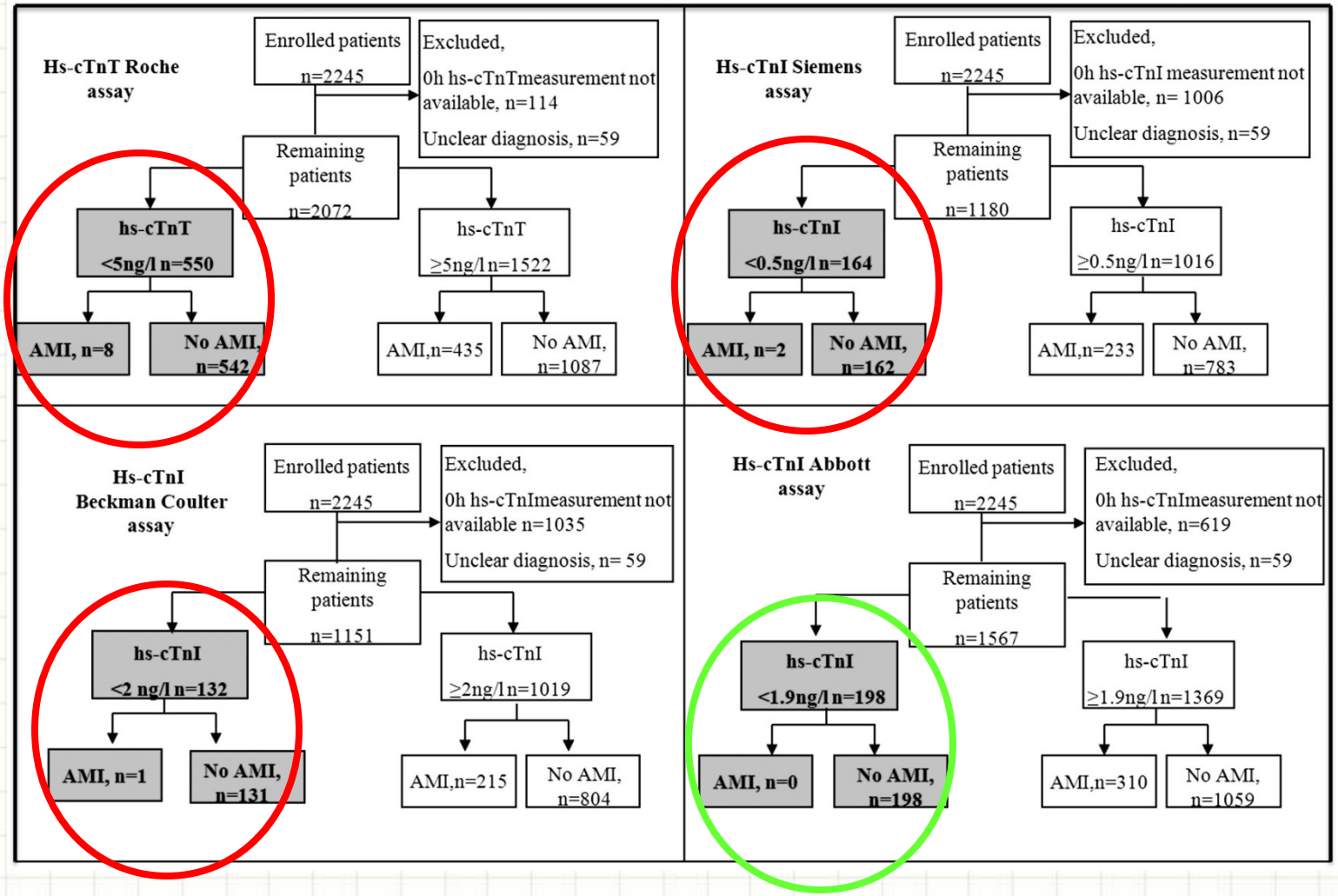


Rapid rule out of acute myocardial infarction using undetectable levels of high-sensitivity cardiac troponin ☆

Maria Rubini Giménez [a,1], Rebeca Hoeller [a,1], Tobias Reichlin [a,h], Christa Zellweger [a], Raphael Twerenbold [a,b,c], Miriam Reiter [a], Berit Moehring [a], Karin Wildi [a], Tamina Mosimann [a], Mira Mueller [a], Bernadette Meller [a], Thomas Hochgruber [a], Ronny Ziller [a], Seoung Mann Sou [a], Karsten Murray [a], Konstantin Sakarikos [a], Susanne Ernst [d], Joaquim Gea [e], Isabel Campodarve [f], Carles Vilaplana [g], Philip Haaf [a,b], Stephan Steuer [i], Jan Minners [a], Stefan Osswald [a], Christian Mueller [a,*]

[a] Department of Cardiology, University Hospital Basel, Switzerland
[b] Department of Internal Medicine, University Hospital, Basel, Switzerland
[c] Universitaeres Herz-Zentrum Bad Krozingen, Germany
[d] Emergency Department, KantonsspitalOlten, Switzerland
[e] Pneumology Department, Parc de Salut Mar – IMIM – UPF. CIBERES (ISC iii), Barcelona, Spain
[f] Emergency Department, Parc de Salut Mar, Barcelona, Spain
[g] Laboratory Services, Parc de Salut Mar, Barcelona, Spain
[h] Cardiovascular Division, Department of Medicine Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA
[i] Emergency Department, Spital Lachen, Switzerland

Отхвърляне на ОКС чрез LoD



Gimenez et al, Int J Card 2013;168(4): 3896–3901

Rule out чрез стойност на 2я час

Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation
Published by Elsevier Inc.

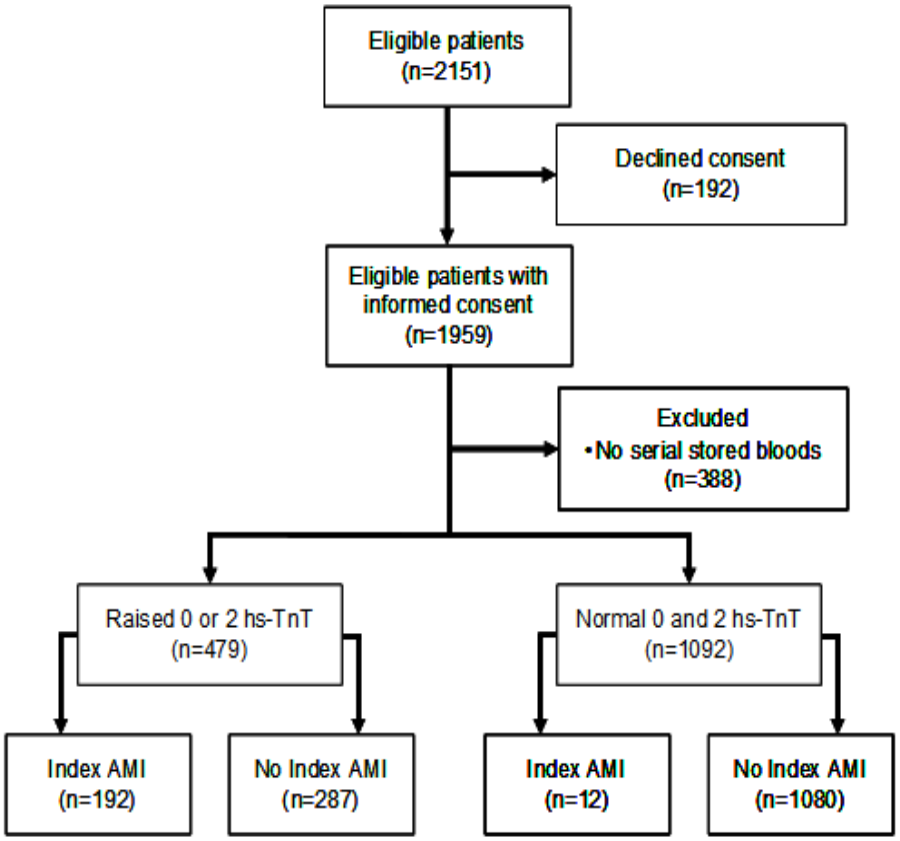
Vol. 62, No. 14, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.02.078

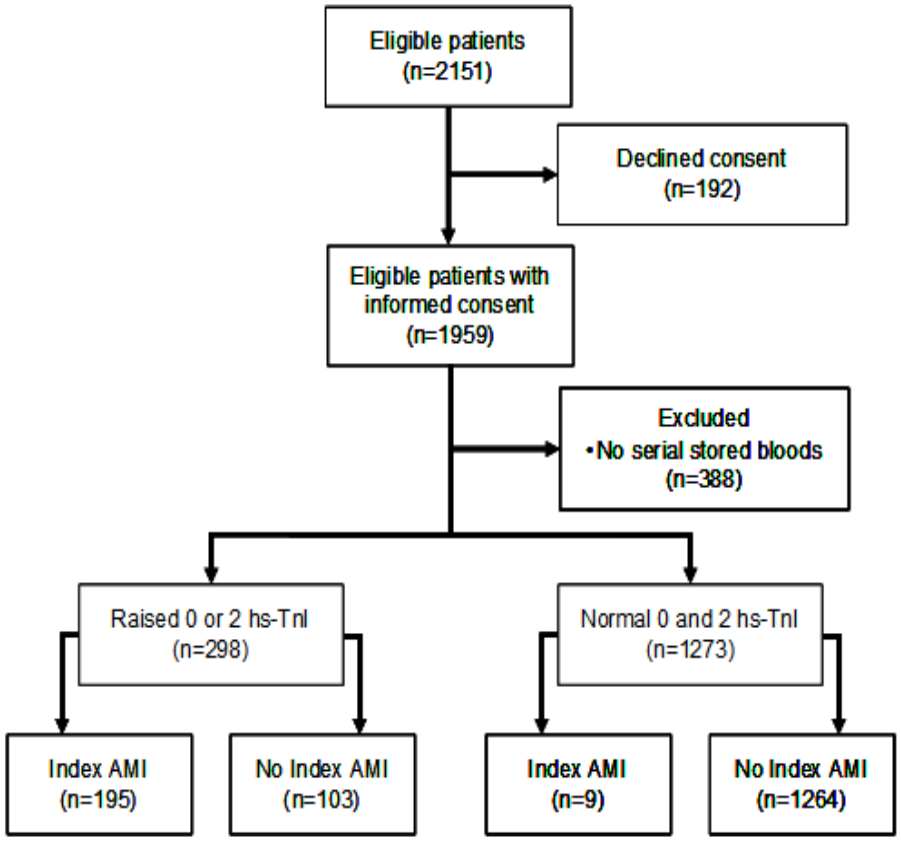
Validation of High-Sensitivity Troponin I in a 2-Hour Diagnostic Strategy to Assess 30-Day Outcomes in Emergency Department Patients With Possible Acute Coronary Syndrome

Louise Cullen, MB, BS,*† Christian Mueller, MD,‡ William A. Parsonage, DM,*§
Karin Wildi, MD,‡ Jaimi H. Greenslade, PhD,*†§ Raphael Twerenbold, MD,‡
Sally Aldous, MB, ChB, MD,‖ Bernadette Meller, MD,‡ Jillian R. Tate, MSc,*
Tobias Reichlin, MD,‡¶ Christopher J. Hammett, MB, ChB, MD,* Christa Zellweger, MD,‡
Jacobus P. J. Ungerer, MMed, MB, ChB,* Maria Rubini Gimenez, MD,‡
Richard Troughton, MB, ChB, PhD,# Karsten Murray, MD,‡ Anthony F. T. Brown, MB, ChB,*§
Mira Mueller, MD,‡ Peter George, MB, BS,‖ Tamina Mosimann, MD,‡ Dylan F. Flaws, BA, MSc,§
Miriam Reiter, MD,‡ Arvin Lamanna, MB, BS,* Philip Haaf, MD,‡ Christopher J. Pemberton, PhD,#
A. Mark Richards, PhD, MD,# Kevin Chu, MB, BS, MS,*§ Christopher M. Reid, PhD,**
William Frank Peacock, MD,†† Allan S. Jaffe, MD,‡‡ Christopher Florkowski, MB, BS,‖
Joanne M. Deely, PhD,§§ Martin Than, MB, BS‖

Herston, Brisbane, and Melbourne, VIC, Australia; Basel, Switzerland; Christchurch, New Zealand; Boston, Massachusetts; Houston, Texas; and Rochester, Minnesota

Ruling out посредством 99я персентил hsTnT срещу hsTnI





Cullen et. Al, Clin Biochem, 2013

Употреба на сърдечни тропонини за ранна Rule-in и Rule-out диагностика на МИ

- Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. C Hamm et al. Eur Heart J. 2011;32:2999-3054.
- Third universal definition of myocardial infarction. K Thygesen et al. Eur Heart J. 2012;33:2551-67.
- How to use high-sensitivity cardiac troponins in acute cardiac care. K. Thygesen et al. Eur Heart J. 2012;33:2252-7.

Препоръки за алгоритъм

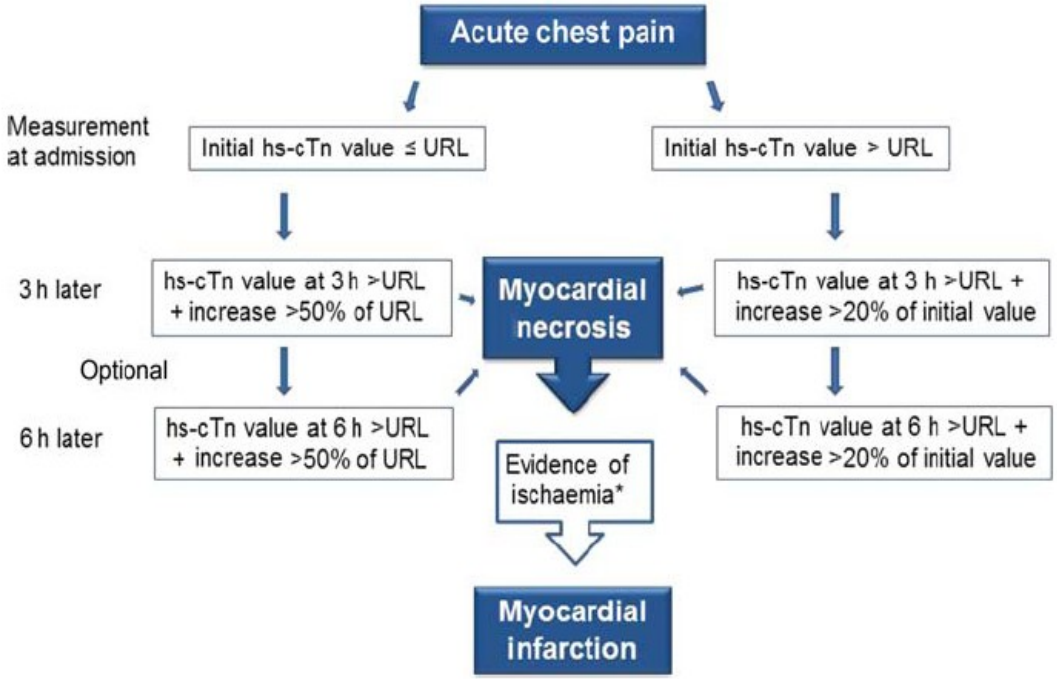


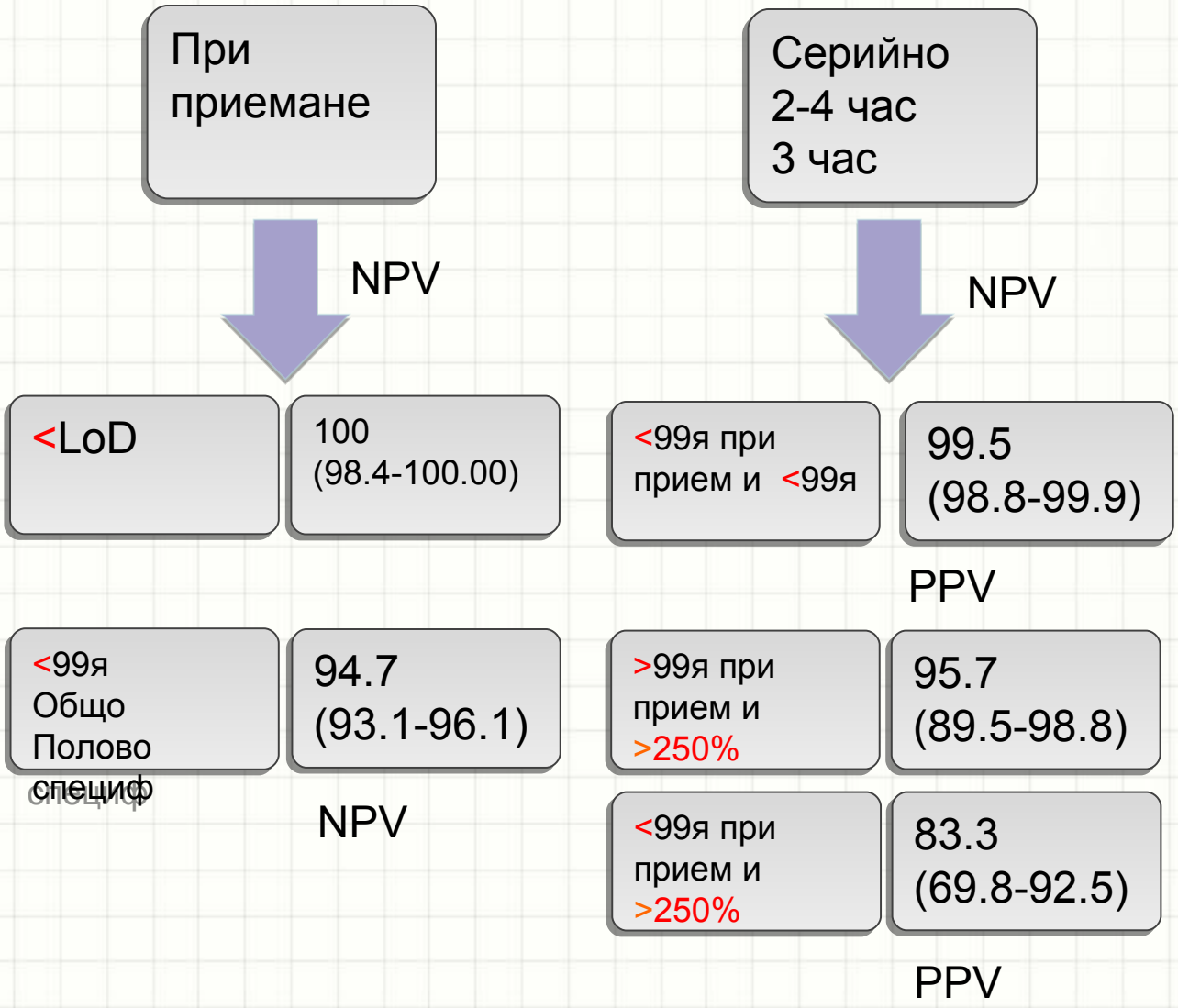
Figure 1 Template for rapid early rule-in of acute myocardial infarction with high-sensitivity cardiac troponin displaying an algorithm for clinical use of high-sensitivity cardiac troponin testing based on current knowledge. It should be noted that the stated algorithm may vary according to the troponin assay evaluated. This approach optimizes sensitivity for acute myocardial infarction diagnosis, but clinicians may also wish to choose more stringent metrics to improve specificity (see text).
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.

Thygesen et al. *Eur Heart J.* 2012;33:2252-7.

Rule in диагностика на ОМИ

Delta Change				
High Sensitive Troponin I 99th percentile at 29 pg/mL	**Sensitivity (CI)**	**Specificity (CI)**	**PPV (CI)**	**NPV (CI)**
On admission > 99th percentile	82.6 (77.7,86.9)	91.8 (89.9,93.5)	**74.4 (69.2,79.2)**	94.8 (93.2,96.1)
After 3 hours > 99th percentile	98.6 (96.4,99.6)	90.0 (87.9,91.8)	**73.9 (69.2,78.3)**	**99.5 (98.8,99.9)**
On admission or after 3 hours > 99th percentile AND				
Change ≥20%	60.6 (54.7-66.4)	96.7 (95.4-97.8)	84.2 (78.5-89.0)	89.5 (87.5-91.3)
Change ≥30%	56.0 (50.0-61.9)	97.9 (96.7-98.7)	88.3 (82.6-92.6)	88.5 (86.5-90.4)
Change ≥50%	50.4 (44.4-56.3)	99.0 (98.1-99.5)	93.4 (88.2-96.8)	87.4 (85.3-89.3)
Change ≥75%	44.7 (38.8-50.7)	99.1 (98.3-99.6)	93.3 (87.7-96.9)	86.1 (84.0-88.1)
Change ≥100%	41.8 (36.0-47.8)	99.3 (98.5-99.7)	94.4 (88.8-97.7)	85.6 (83.4-87.5)
Change ≥150%	37.2 (31.6-43.2)	99.3 (98.5-99.7)	93.8 (87.5-97.5)	84.6 (82.4-86.6)
Change ≥200%	34.8 (29.2-40.6)	99.5 (98.8-99.8)	95.1 (89.0-98.4)	84.1 (81.9-86.2)
Change ≥250%	**33.0 (27.5-38.8)**	**99.6 (99.0-99.9)**	**95.9 (89.8-98.9)**	**83.7 (81.5-85.8)**
Change ≥266%*	33.0 (27.5-38.8)	99.6 (99.0-99.9)	95.9 (89.8-98.9)	83.7 (81.5-85.8)

Обобщен алгоритъм



Повишение на cTn без ОКС - кардиогенни причини

- Застойна сърдечна недостатъчност
- Аритмии, сърдечен блок
- Сърдечна контузия, аблация, пейсмейкър, кардиоверсия, биопсия
- Кардиомиопатия
- Възпаление – напр. миокардит, ендокардит
- Рабдомиолиза със сърдечна увреда
- Инфилтративни заболявания, напр.амилоидоза, хемохроматоза, саркоидоза, склеродермия
- Лекарствена токсичност, напр. адриамицин, херцептин, клозапин
- Аортна дисекация, аортно клапно заболяване

Повишение на cTn без ОКС не - кардиогенни причини

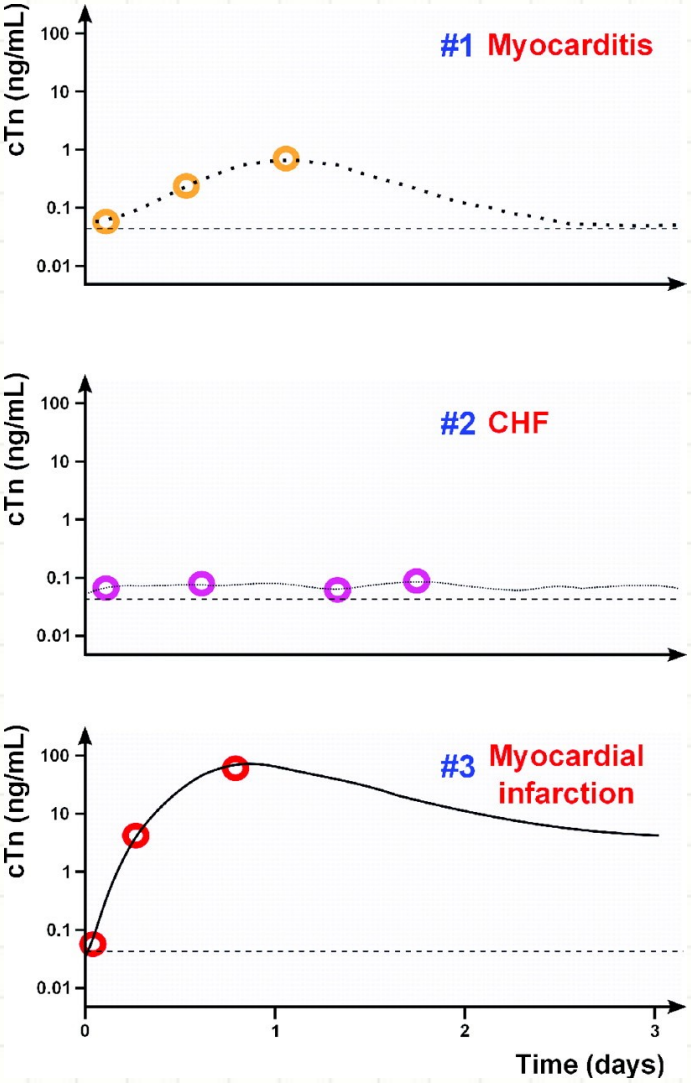
- Остра или хронична бъбречна недостатъчност
- Остро неврологично заболяване, вкл.инсулт или субарахноидален кръвоизлив
- БТЕ, тежка пулмонална хипертония
- Обострена ХОББ
- Хипотиреоидизъм
- Феохромоцитом
- Изгаряне >30% от телесната повърхност
- Пациенти с дихателна недостатъчност или сепсис
- Ухапване от змия

Кинетика в стойностите на тропонин

1. Миокардит

2. Хронична сърдечна недостатъчност

3. Миокарден инфаркт



Mahajan V S , and Jarolim P *Circulation*. 2011;124:2350-2354

American Heart Association

European Heart Journal Advance Access published October 8, 2013

European Heart Journal
doi:10.1093/eurheartj/eht406

CLINICAL RESEARCH
Prevention and epidemiology

High population prevalence of cardiac troponin I measured by a high-sensitivity assay and cardiovascular risk estimation: the MORGAM Biomarker Project Scottish Cohort

Tanja Zeller[1], Hugh Tunstall-Pedoe[2]*, Olli Saarela[3,4], Francisco Ojeda[1], Renate B. Schnabel[1], Tarja Tuovinen[4], Mark Woodward[2,5,6], Allan Struthers[7], Maria Hughes[8], Frank Kee[8], Veikko Salomaa[4], Kari Kuulasmaa[4], and Stefan Blankenberg[1]*, for the MORGAM Investigators

[1]Clinic for General and Interventional Cardiology, University Heart Centre Hamburg, Hamburg, Germany; [2]Cardiovascular Epidemiology Unit, Institute of Cardiovascular Research, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, UK; [3]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, QC, Canada H3A 1A2; [4]National Institute for Health and Welfare, Helsinki, Finland; [5]Department of Epidemiology, Johns Hopkins University, Baltimore, MD, USA; [6]George Institute, University of Sydney, Sydney, Australia; [7]Centre for Cardiovascular and Lung Biology, University of Dundee, Dundee, UK; and [8]UK Clinical Research Collaboration Centre of Excellence for Public Health, Queens University of Belfast, Northern Ireland

Received 3 November 2012; revised 30 August 2013; accepted 10 September 2013

Високо-чувствителен тропонин и сърдечно-съдов риск

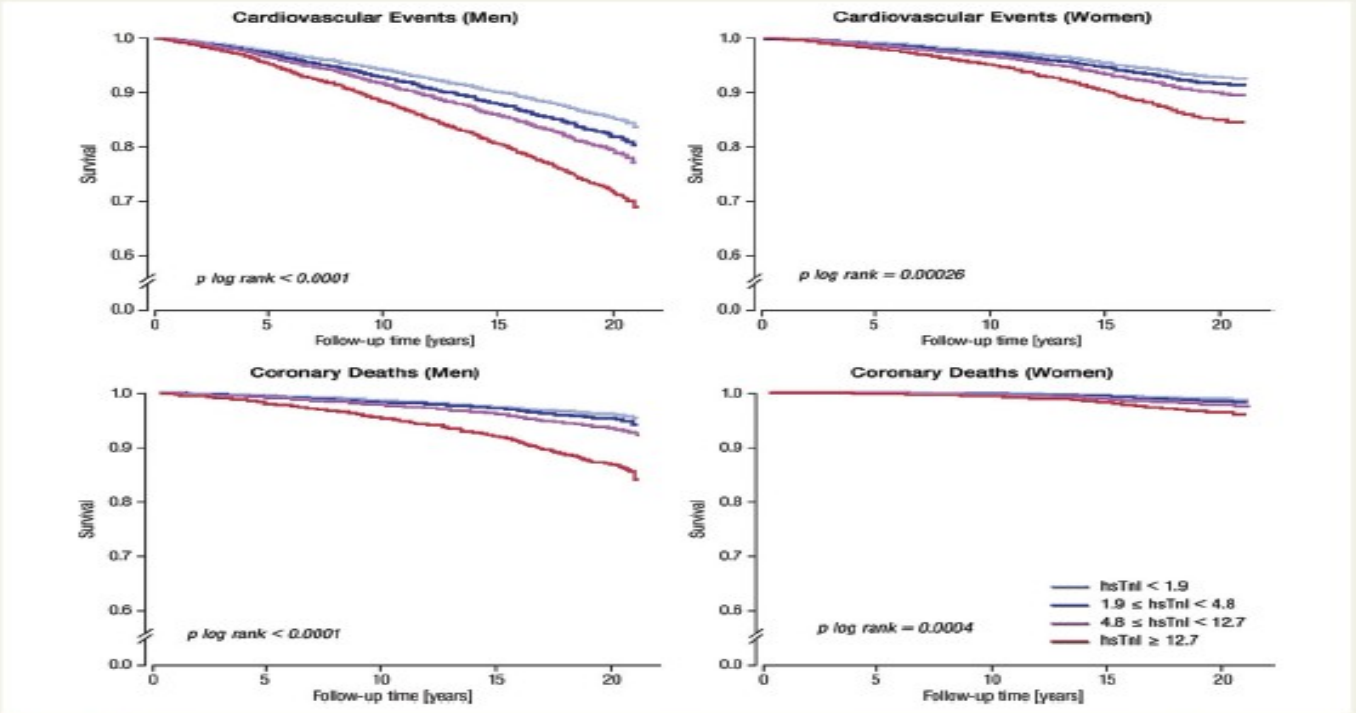


Figure 1 Survival curves assessing the time to event across troponin I categories measured by a high-sensitivity assay (hsTnI). Cox model based survival curves adjusted for age, cohort and all risk factors in the ASSIGN score.[20] P-values are for the comparison of the highest and lowest hsTnI categories. Total number of individuals at risk when the follow-up started was 7598 men and 7742 women. At year 10 there were 6399 and 6856 men and 7075 and 7331 women in the at risk population for cardiovascular events and coronary death, respectively. At year 20 the size of the population at risk were 1154 and 1358 men and 1413 and 1514 women.

hsTnI е независим предиктор за сърдечно-съдов инцидент и допринася за идентифицирането на рискови пациенти

Още кога hsTnI има значение?

ARTICLE IN PRESS

Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. xx, No. x, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.12.026

Prognostic Value of Cardiac Troponin I Measured With a Highly Sensitive Assay in Patients With Stable Coronary Artery Disease

Torbjørn Omland, MD, PHD, MPH,*‡ Marc A. Pfeffer, MD, PHD,‖¶ Scott D. Solomon, MD,‖¶
James A. de Lemos, MD,# Helge Røsjø, MD, PHD,*‡ Jūratė Šaltytė Benth, PHD,†§
Aldo Maggioni, MD,** Michael J. Domanski, MD,†† Jean L. Rouleau, MD,‡‡§§
Marc S. Sabatine, MD, MPH,‖¶ Eugene Braunwald, MD,‖¶ for the PEACE Investigators

Lørenskog and Oslo, Norway; Boston, Massachusetts; Dallas, Texas; Florence, Italy; New York, New York; Montreal, Quebec, Canada

J Am Coll Cardiol. 2013;61(12):1240-1249. doi:10.1016/j.jacc.2012.12.026

Прогноза за СС смърт и СН

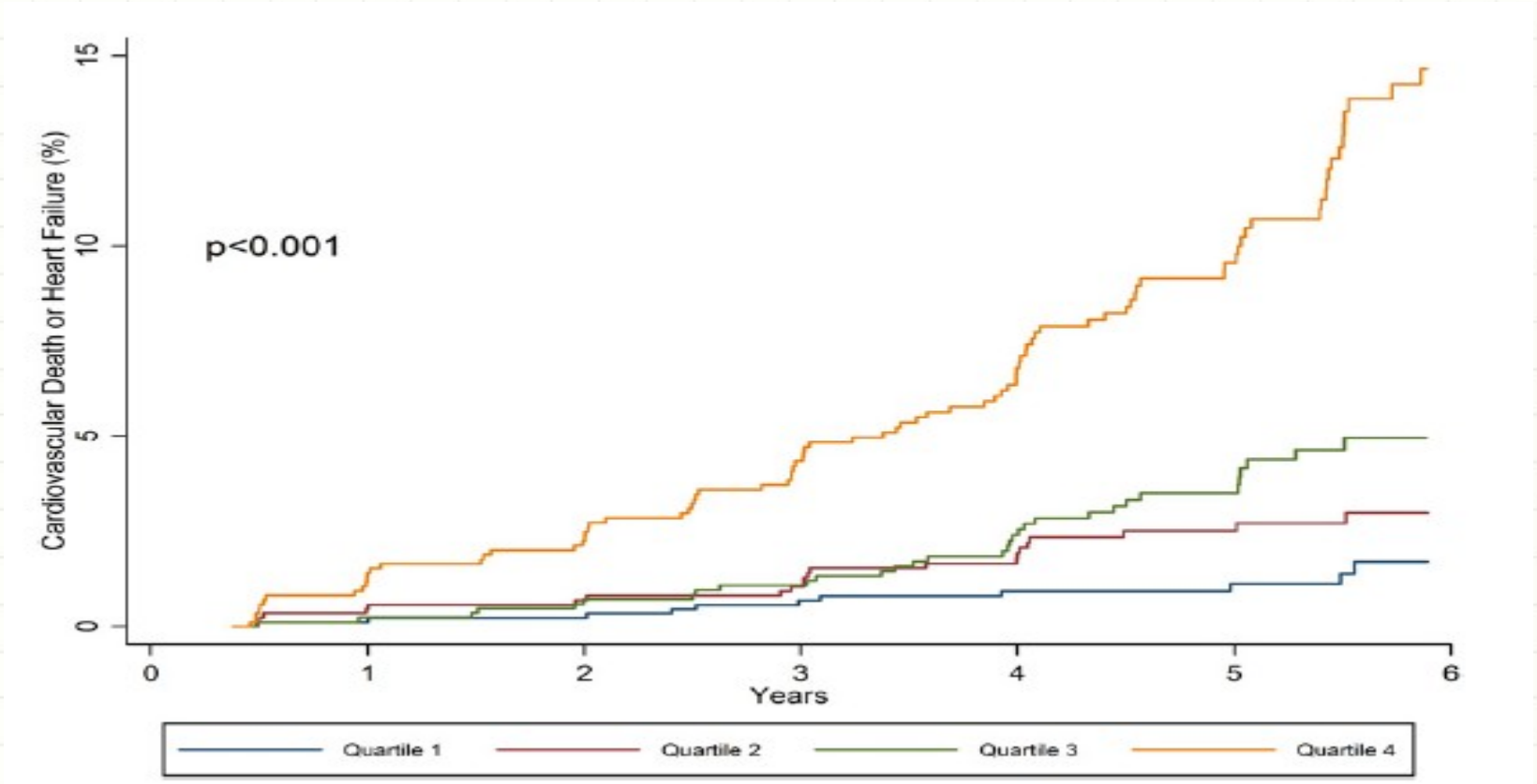


Figure 2 **Risk for Cardiovascular Death or Heart Failure by Baseline hs-TnI Level**

Cumulative incidence of the composite endpoint of cardiovascular death or hospitalization for heart failure by baseline concentrations of high-sensitivity cardiac troponin I (hs-TnI). There was a strong and graded association between increasing quartiles of cardiac troponin I and the risk for cardiovascular death or hospitalization for heart failure.

Omland et. al. Troponin in Stable CAD, JACC 2013

Прогноза при МИ

Table 4 Final Multivariate Cox Regression Models for Myocardial Infarction

	Fourth Quartile for hs-TnI and hs-TnT		Continuous hs-TnI and hs-TnT	
Variable	HR (95% CI)	p	HR (95% CI)	p
hs-TnI	1.44 (1.03–2.01)	0.031	1.21 (1.04–1.41)*	0.013
hs-TnT	0.93 (0.65–1.31)	0.67	0.97 (0.84–1.13)*	0.714
Age	1.01 (0.99–1.03)	0.25	1.01 (0.99–1.03)	0.262
LVEF < 50%	1.22 (0.89–1.66)	0.21	1.21 (0.89–1.65)	0.232
Current smoking	1.73 (1.22–2.46)	0.002	1.71 (1.21–2.43)	0.003
History of hypertension	1.19 (0.89–1.58)	0.24	1.19 (0.90–1.59)	0.227
History of diabetes mellitus	1.70 (1.21–2.37)	0.002	1.70 (1.22–2.38)	0.002
History of CABG	1.59 (1.17–2.17)	0.003	1.55 (1.14–2.12)	0.006
ln NT-proBNP	1.06 (0.90–1.25)	0.46	1.05 (0.89–1.23)	0.580
ln CRP	1.16 (1.01–1.34)	0.039	1.16 (1.00–1.34)	0.043

Omland et. al. Troponin in Stable CAD, JACC 2013

Проблеми за бъдещо решение

- Необходимо е да се разработи универсална номенклатура на тестовете за високо-чувствителен тропонин.
- Има нужда от унифицирани критерии за избор на референтна популация.
- Критериите за delta чек, разграничаващи остра от хронична сърдечна увреда все още са неясни и метод-специфични.
- Разграничаването между тип 1 и тип 2 ОМИ е предизвикателство и повече ОМИ от тип 2 ще бъдат откривани с помощта на тестовете за hsTn.
- С използването на тестове за hs-cTn стават все по-значими факторите, влияещи на аналитичната точност на методите за тропонин (включително как взимаме пробите).
- Все още не са ясно дефинирани времевите интервали за отхвърляне на ОМИ; разработват се нови алгоритми за това.

- Увеличен hs-cTn, независимо от причината, има важно прогностично значение и служи за допълнителна оценка; много случаи на хронично повишени стойности могат да бъдат анализирани при амбулаторни пациенти.
- Hs-cTn може да се използва за стратифициране на риска при пациенти с кардиоваскуларни заболявания, различни от ОКС.

Korley and Jaffe, JACC 2013;61(17):1753-1758

БЛАГОДАРЯ ЗА ВНИМАНИЕТО

Д-р Веселина Колева
Токуда Болница София