



# KARDIJALNI TROPONIN

- teorija i klinička praksa -

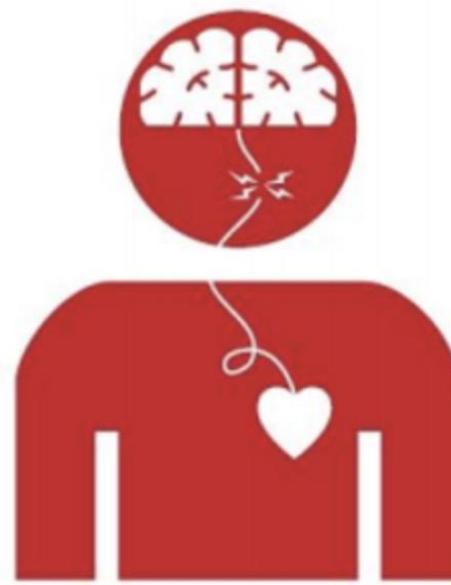
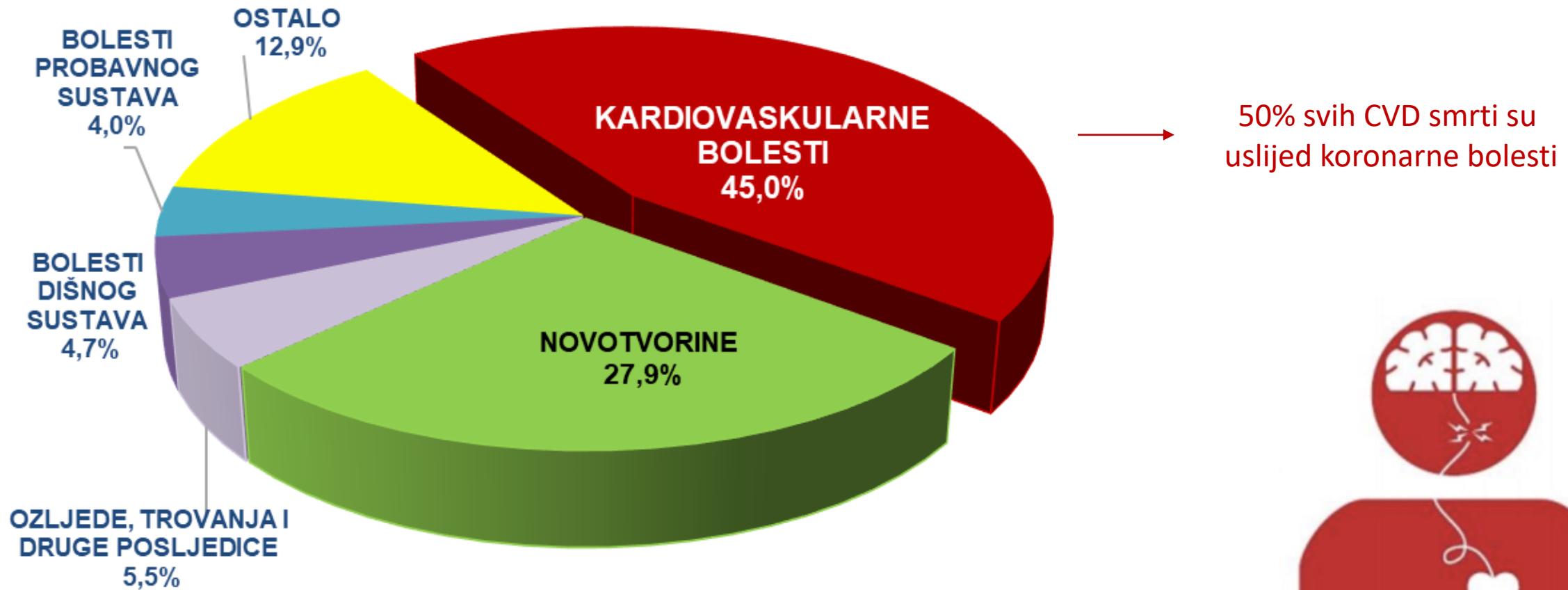
# Kardiovaskularne bolesti

ICD-10-CM

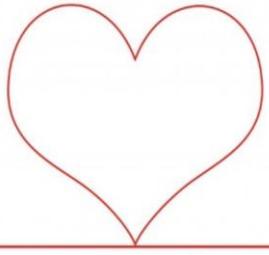
- **bolesti srca i krvožilnog sustava**
- prema Međunarodnoj klasifikaciji bolesti, povreda i uzroka smrti u tu skupinu pripadaju:
  - akutna reumatska groznica (I00-I02)
  - kronične reumatske srčane bolesti (I05-I09)
  - hipertenzivne bolesti (I10-I15)
  - ishemične (koronarna) bolesti srca (I20-I25)
  - plućna bolest srca i bolesti plućne cirkulacije (I26-I28)
  - ostali oblici srčane bolesti (I30-I52)
  - cerebrovaskularne bolesti (I60-I69)
  - bolesti arterija, arteriola i kapilara (I70-I79)
  - bolesti vena, limfnih žila i limfnih čvorova, nesvrstane drugamo (I80-I89)
  - ostale i nespecificirane bolesti cirkulacijskog sustava (I95-I99)

INTERNATIONAL  
CLASSIFICATION of  
DISEASES  
10<sup>th</sup> Revision  
Clinical Modification  
**2019**

# Kardiovaskularne bolesti



# AKUTNI KORONARNI SINDROM



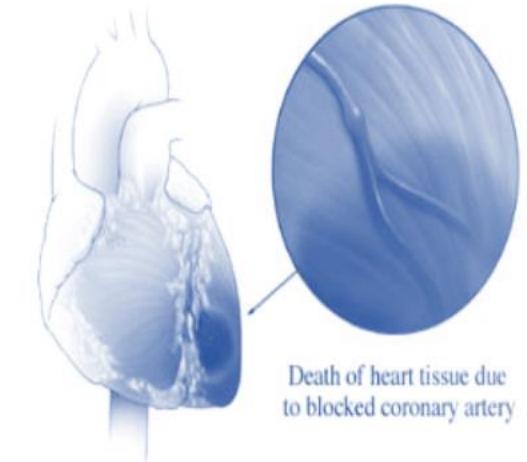
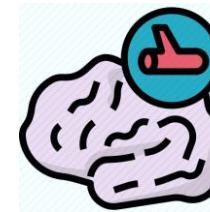
- ♥ **naglo smanjenje protoka krvi do srca**
- ♥ **nastaje zbog akutne opstrukcije koronarne arterije**



**angina**  
**nestabilna angina**  
**infarkt miokarda**

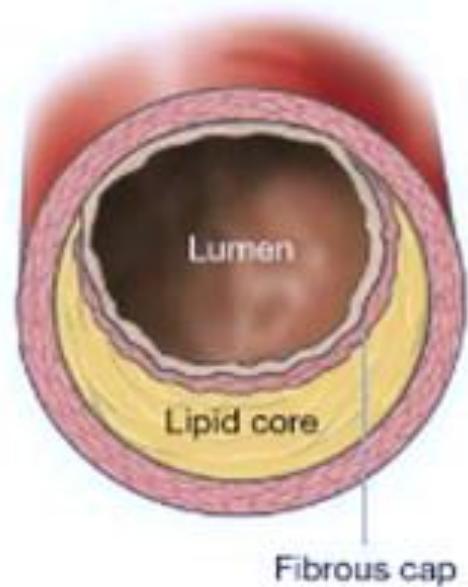
# AKUTNI INFARKT MIOKARDA

- neravnoteža između opskrbe i potrebe miokarda za kisikom
- ruptura aterosklerotskog plaka
- ischemija
- nekroza
- potpuna nekroza nastupa za 2-4 sata

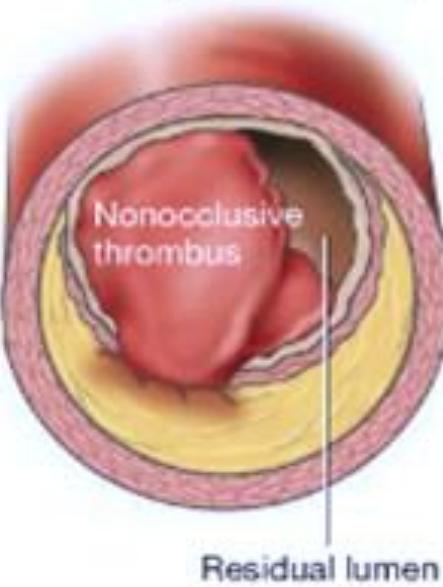


Death of heart tissue due  
to blocked coronary artery

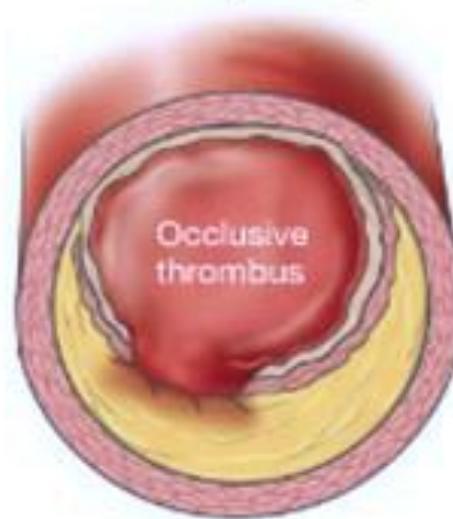
**Stable angina or asymptomatic**



**Unstable angina or non-ST segment elevation myocardial infarction (UA or NSTEMI)**



**ST segment elevation myocardial infarction (STEMI)**



# RAZLIČITI SIMPTOMI

- mučnina i povraćanje
- bolovi u vratu,  
čeljusti ili leđima
- bol u prsištu
- nedostatak dahaa



- mučnina i povraćanje
- bolovi u vratu,  
čeljusti ili gornjem  
dijelu leđa
- bol u prsištu (ali ne  
uvijek)
- nedostatak dahaa
- bol ili pritisak u  
gornjem abdomenu
- vrtoglavica
- ekstremni umor

# Third universal definition of myocardial infarction



dokaz nekroze miokarda i kliničkih pokazatelja ishemije

Porast i/ili pad srčanih biljega (poželjno cTn) uz barem jednu vrijednost iznad gornje 99.te percentile referentnog raspona i barem jedno od niže navedenog:

- simptomi ishemije
- promjene ST segmenta ili poremećaj provođenja
- pojava Q valova na EKG-u
- dokaz gubitka funkcionalnog miokarda slikovnim tehnikama
- dokaz intrakoronarnog tromba angiografijom ili autopsijom

alternativa?

CKMB masa iznad 99.-te percentile

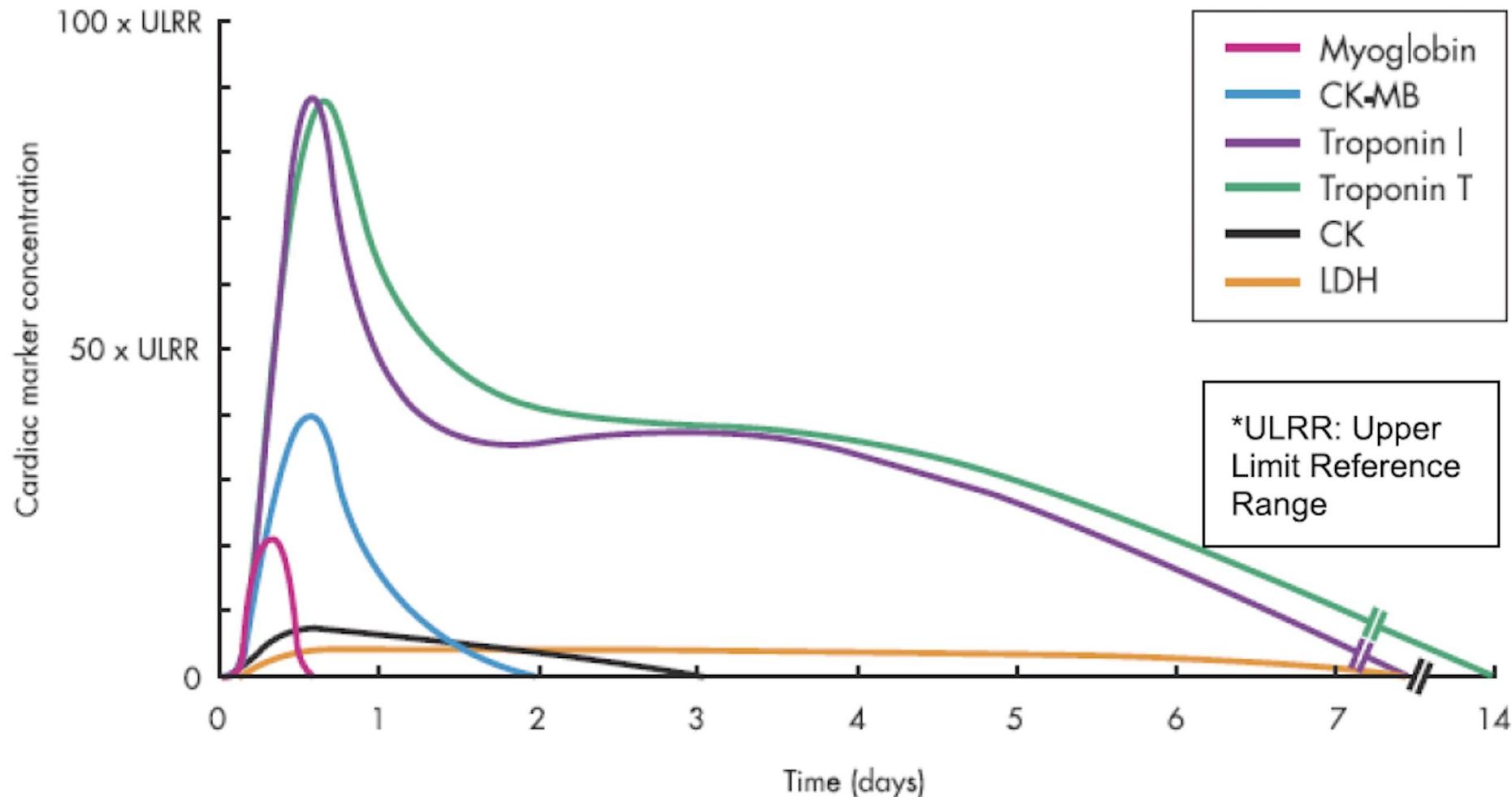
# Koji biljeg?

- Biljeg izbora je cTn (I ili T)
  - visoka specifičnost za tkivo miokarda
  - visoka dijagnostička osjetljivost  RuleOUT, NPV

	Najranije povećanje (sati)	Postizanje najveće vrijednosti (sati)	Vremenski period povećanih vrijednosti	Specifičnost (%)	Osjetljivost (%)
Troponin T	3-4	10-24	10-14 dana	80	>98
Troponin I	4-6	10-24	4-7 dana	95	>98
CK ukupni	4-8	24-36	36-48 sati	57-88	93-100
CK-MB	3-4	15-24	24-36 sati	93-100	94-100
Mioglobin	1-3	6-9	12-24 sati	70	75-95
BNP ili NT-proBNP	koristan biomarker pri diferencijalnoj dijagnozi srčane i plućne disfunkcije				

Legenda: CK: kreatin kinaza, CK-MB: srčani izoenzim kreatin kinaze, BNP: B-tip natrijuretski peptid, NT-proBNP: N-terminalni pro-B-tip natrijuretski peptid.

# drugi biljezi nisu potrebni



# 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Porast i/ili pad srčanih biljega (poželjno hs-cTn) uz barem jednu vrijednost iznad gornje 99.te percentile referentnog raspona i barem jedno od niže navedenog:

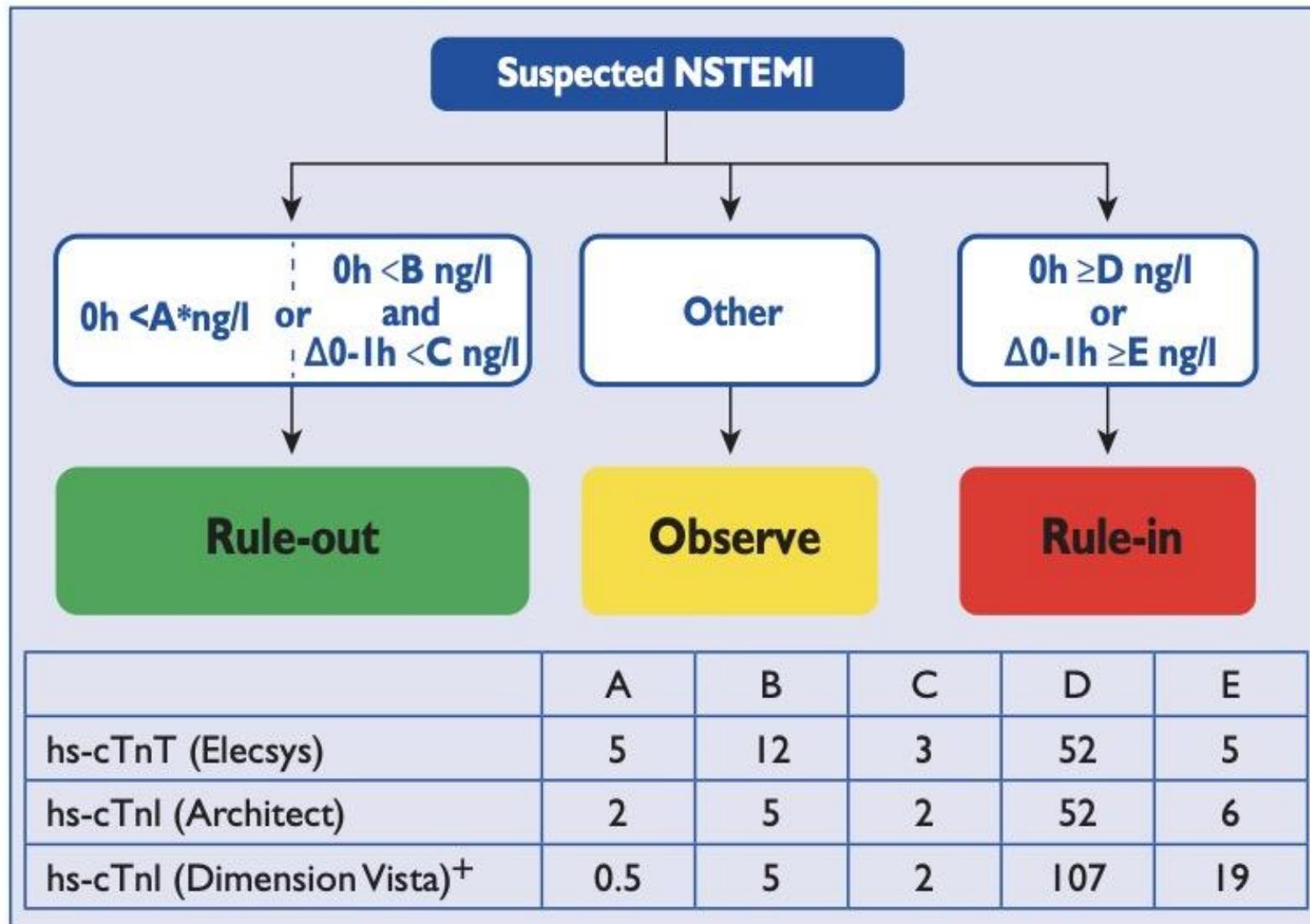
- simptomi ishemije
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alternativa?

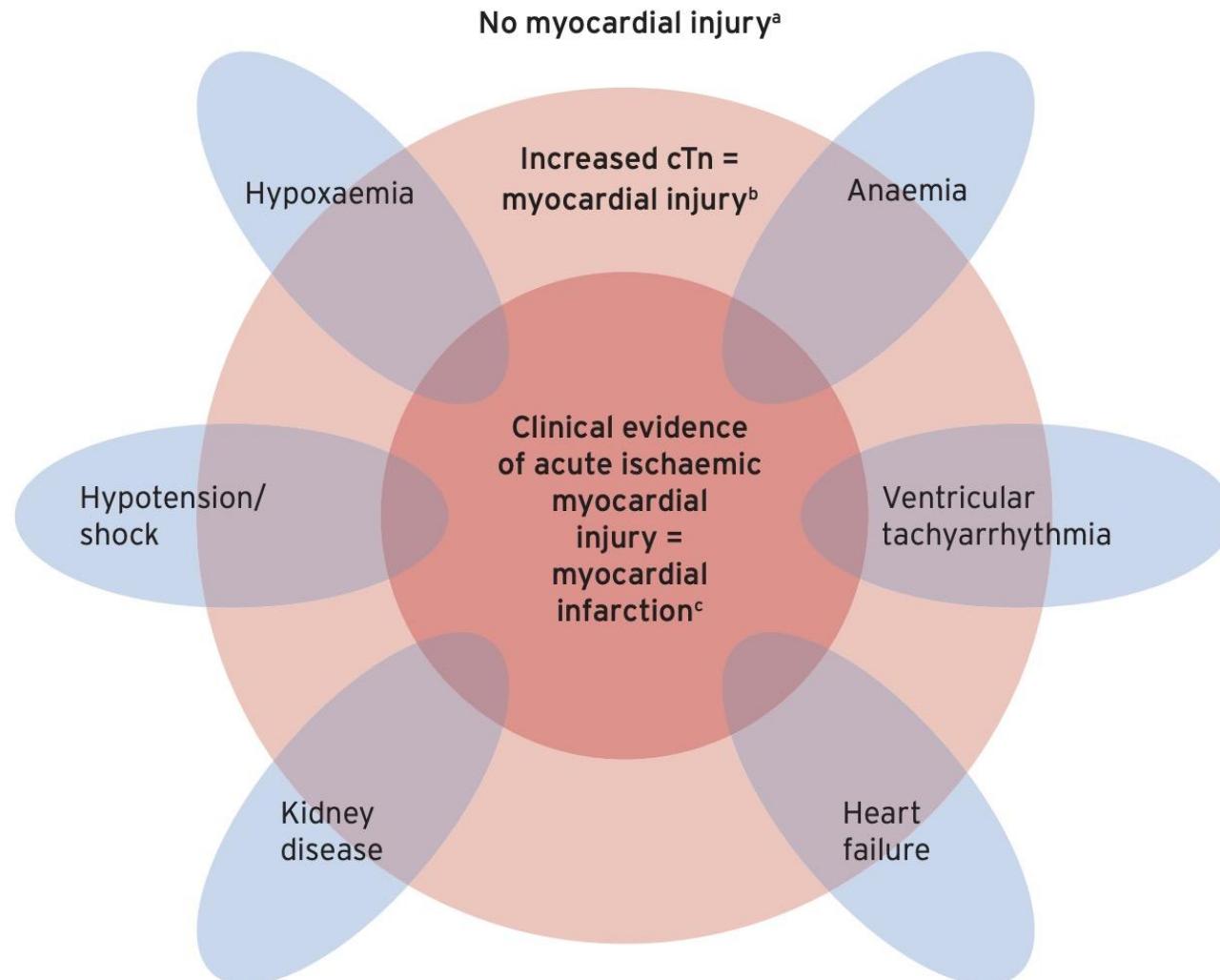
CKMB masa iznad 99.-te percentile  
kopeptin

otkrivanje reinfarkta

# Rule-out, rule-in algoritam



## **Fourth universal definition of myocardial infarction (2018)**



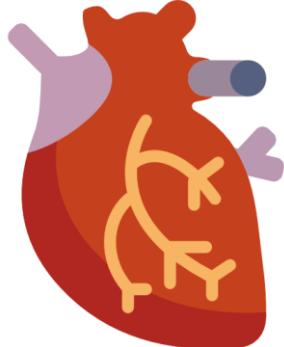
# DIFERENCIJALNA DIJAGNOZA

jedna povišena vrijednost cTn ne znači nužno AIM



## MOGUĆI UZROCI ↑ cTn

Kronična bubrežna bolest	Moždani udar
Hemodijaliza	Rabdomioliza
Tromboza	Ekstremni fizički napor
Trauma	Heterofilna At
Sepsa	

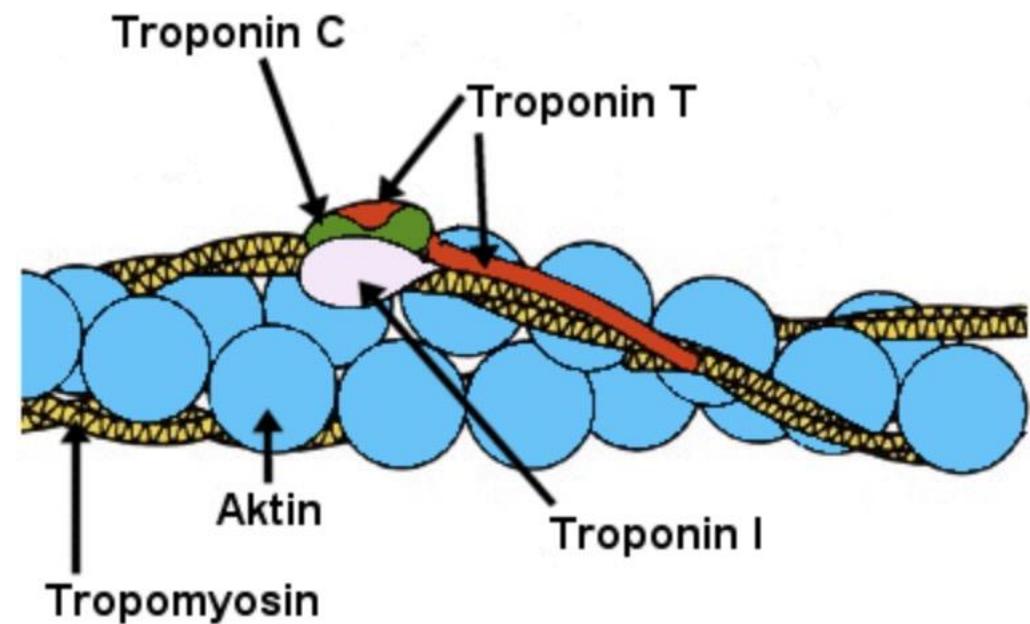


Što je hs-Tn?

Što je 99.-ta percentila referentnog raspona?

Što znači porast i pad?

Dva mjerena? U kojem intervalu?



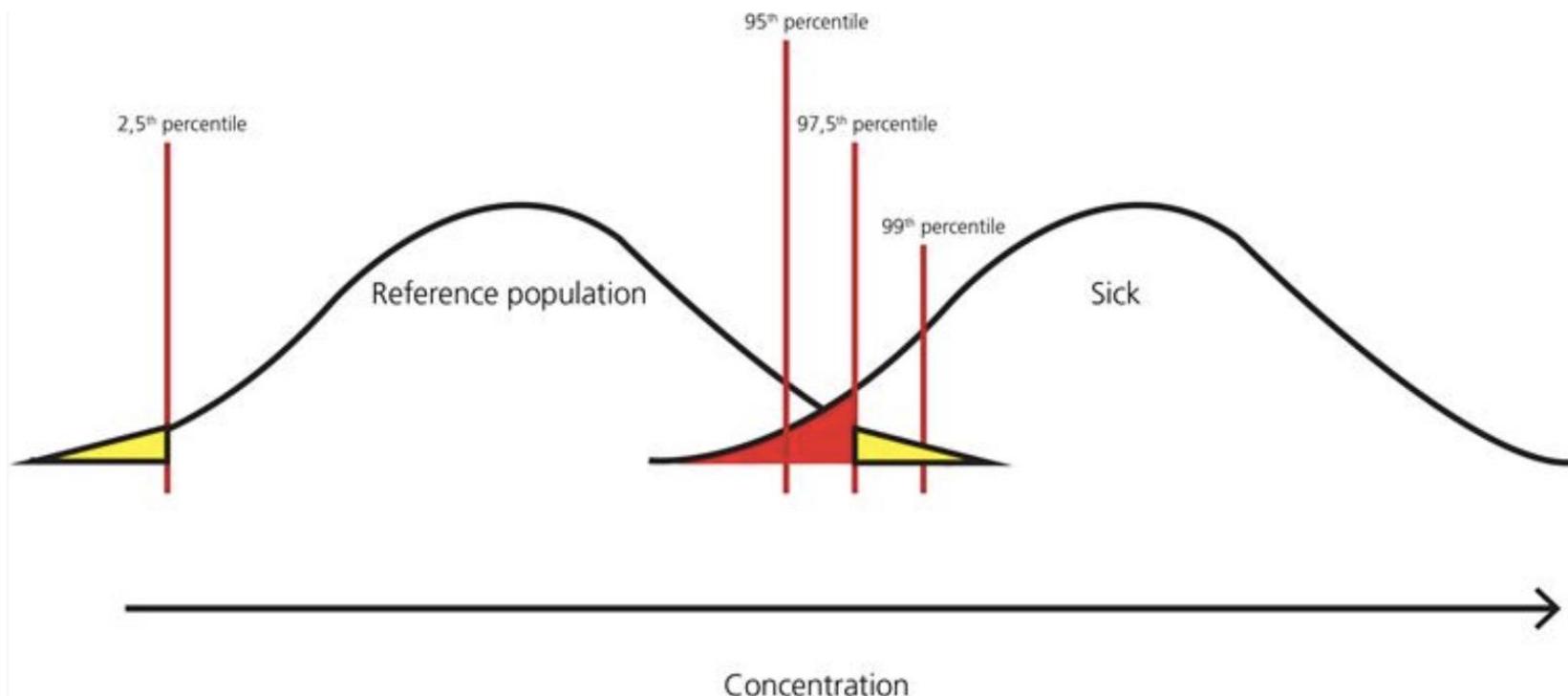
## Kako se definira high-sensitivity?

- analitički kriterij !!
- < 10% CV na 99.-toj percentili
- hs-test može izmjeriti koncentraciju u  $\geq 50\%$  referentne populacije iznad LoD
- osjetljiviji  $> 10x$  od konvencionalnih testova
- veća dijagnostička osjetljivost i niža specifičnost od konvencionalnih testova



# 99.-ta percentila?

- odnosi se na zdravu populaciju
- metoda mora imati zadovoljavajuću preciznost na 99.-toj percentili ( $CV \leq 10\%$ )
- kako ju odrediti?



# **Fourth universal definition of myocardial infarction (2018)**

- ne preporuča se izračunavanje 99.-te percentile prema dobnim skupinama
- preporuča se izražavanje cTn prema spolu

**Table 1. Scorecard designations of cTn assays.**

Acceptance designation	Total imprecision at the 99th percentile, CV%
Guideline acceptable	$\leq 10$
Clinically usable	>10 to $\leq 20$
Not acceptable	>20
Assay designation	Measurable normal values below the 99th percentile, %
Level 4 (third generation, hs)	$\geq 95$
Level 3 (second generation, hs)	75 to <95
Level 2 (first generation, hs)	50 to <75
Level 1 (contemporary)	<50

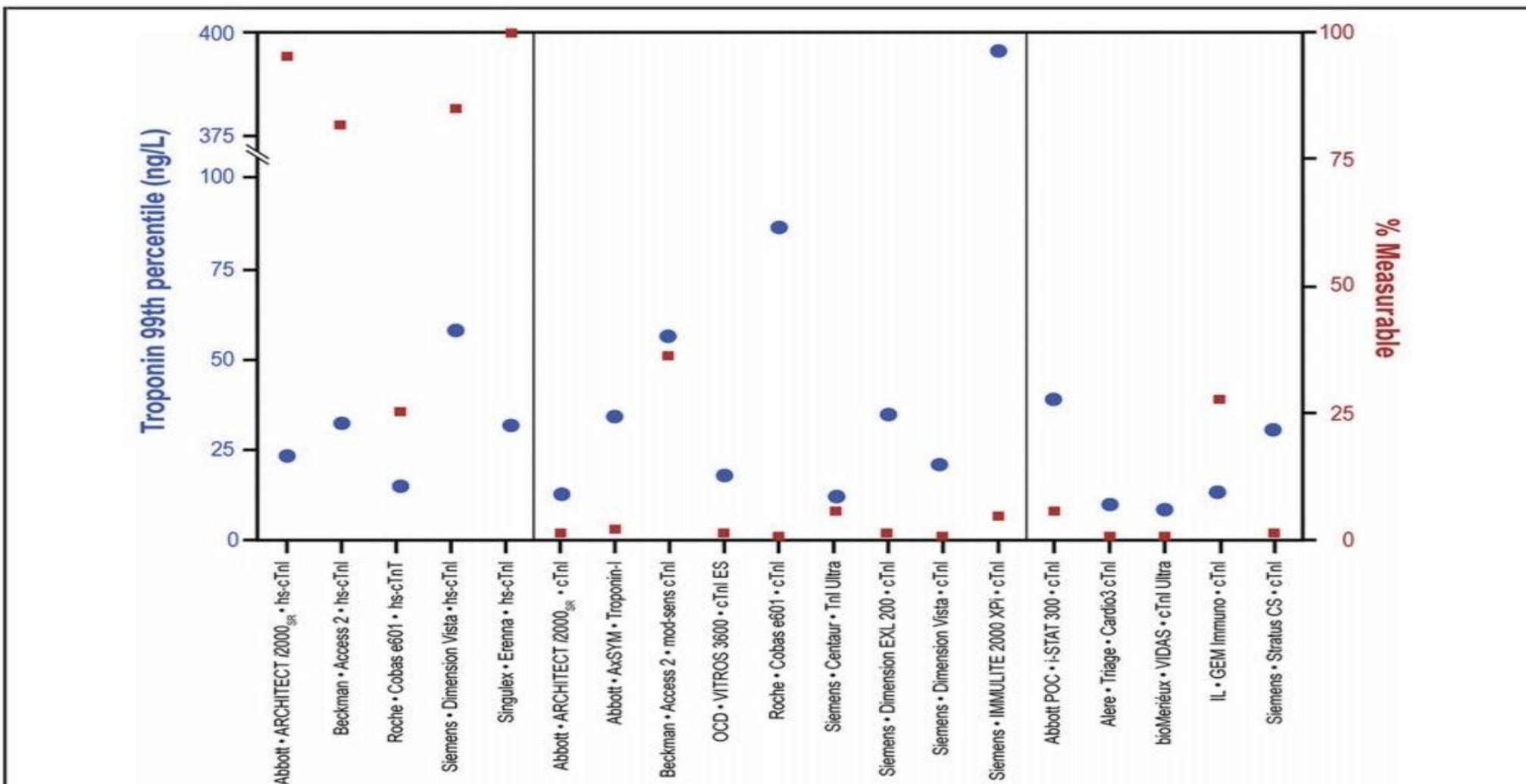
**Table 1.** Analytical characteristics of commercial and research contemporary, POC, and hs-cTnI and hs-cTnT assays.<sup>a</sup>

Company/platform/assay	LoD, µg/L	99th, µg/L	% CV at 99th	10% CV, µg/L	Epitopes/antibodies <sup>b</sup>	Detection tag
Contemporary assays						
Abbott ARCHITECT	<0.01	0.028	15	0.032	C: 87-91, 24-40; D: 41-49	Acridinium
Beckman Access 2	0.01	0.02	14	0.040	C: 41-49; D: 24-40	ALP
Beckman Coulter Dxl	0.01	0.03	14	0.040	C:41-49; D:28-80	ALP
Ortho-Clinical Diagnostics Vitros	0.012	0.034	10	0.034	C: 24-40, 41-49; D: 87-91	HRP
Siemens Centaur Ultra	0.006	0.04	10	0.030	C: 41-49, 87-91; D: 27-40	Acridinium
Siemens Dimension RxL	0.04	0.07	20	0.140	C: 27-32; D: 41-56	ALP
Siemens VISTA	0.015	0.045	10	0.040	C: 27-32; D: 41-56	Chemiluminescent
Tosoh AIA	0.06	<0.06	8.5	0.090	C: 41-49; D: 87-91	ALP
Roche 4th generation cTnT	0.01	0.01	18	0.03	C: 125-131; D: 136-147	Ruthenium
POC assays						
Abbott i-STAT	0.02	0.08	16	0.10	C: 41-49, 88-91; D: 28-39,62-78	ALP
Alere Triage	0.05	<0.05	NA	NA	C: NA; D: 27-40	Fluorophor
bioMérieux Vidas	0.01	0.01	27	0.11	C: 41-49, 22-29; D: 87-91, 7B9	ALP
LSI Medience PATHFAST	0.008	0.029	5.1	0.014	C: 41-49; D:71-116, 163-209	ALP
Radiometer AQT90 cTnI	0.0095	0.023	17	0.039	C: 41-49, 190-196; D: 137-149	Europium
Radiometer AQT90 cTnT	0.01	0.017	20	0.03	C: 125-131; D:136-147	Europium
Response Biomedical RAMP	0.03	<0.1	18	0.21	C: 85-92; D: 26-38	Fluorophor
Roche Cardiac Reader	<0.05	<0.05	NA	NA	C: 125-131; D:136-147	Gold particules
Siemens Stratus CS	0.03	0.07	10	0.06	C: 27-32; D: 41-56	ALP
Trinity Meritas	0.019	0.036	17	NA	C: 24-40; 41-49, D: 88-90, 137-148,190-196	Fluorophor
ET Health	0.1	0.2	NA	0.42	C: 87-91:D: 27-40	ALP
Nanomix	0.15	NA	NA	0.64	C: 87-91:D: 27-40	ALP
hs-Assays						
	ng/L	M/F, ng/L	% CV at 99th	10% CV, ng/L	Epitopes/antibodies	Detection tag
Abbott ARCHITECT hs-cTnI	1.2/1.9	34/16	5	3	C: 24-40; D: 41-49	Acridinium
Beckman Coulter Access hs-cTnI	2.5	52/23	<10	8	C: 41-49; D: 24-40	ALP
Ortho-Clinical Diagnostics hs-cTnI	1.0	19/16	<10	3	C:24-40, 41-49; D: 87-91	HRP
Roche E170 hs-cTnT	5	20/13	8	13	D: 125-131; C: 136-147	Ruthenium
Siemens Vista hs-cTnI	0.5	55/33	5	3	C: 30-35; D: 41-56,171-8	Luminescence
Singulex Errena hs-cTnI	0.09	36/30	5	0.9	C: 41-49; D: 27-41	Fluorescence

<sup>a</sup> Assays not designated as cTnT are cTnI.<sup>b</sup> C, capture antibody; D, detection antibody; NA, not available.

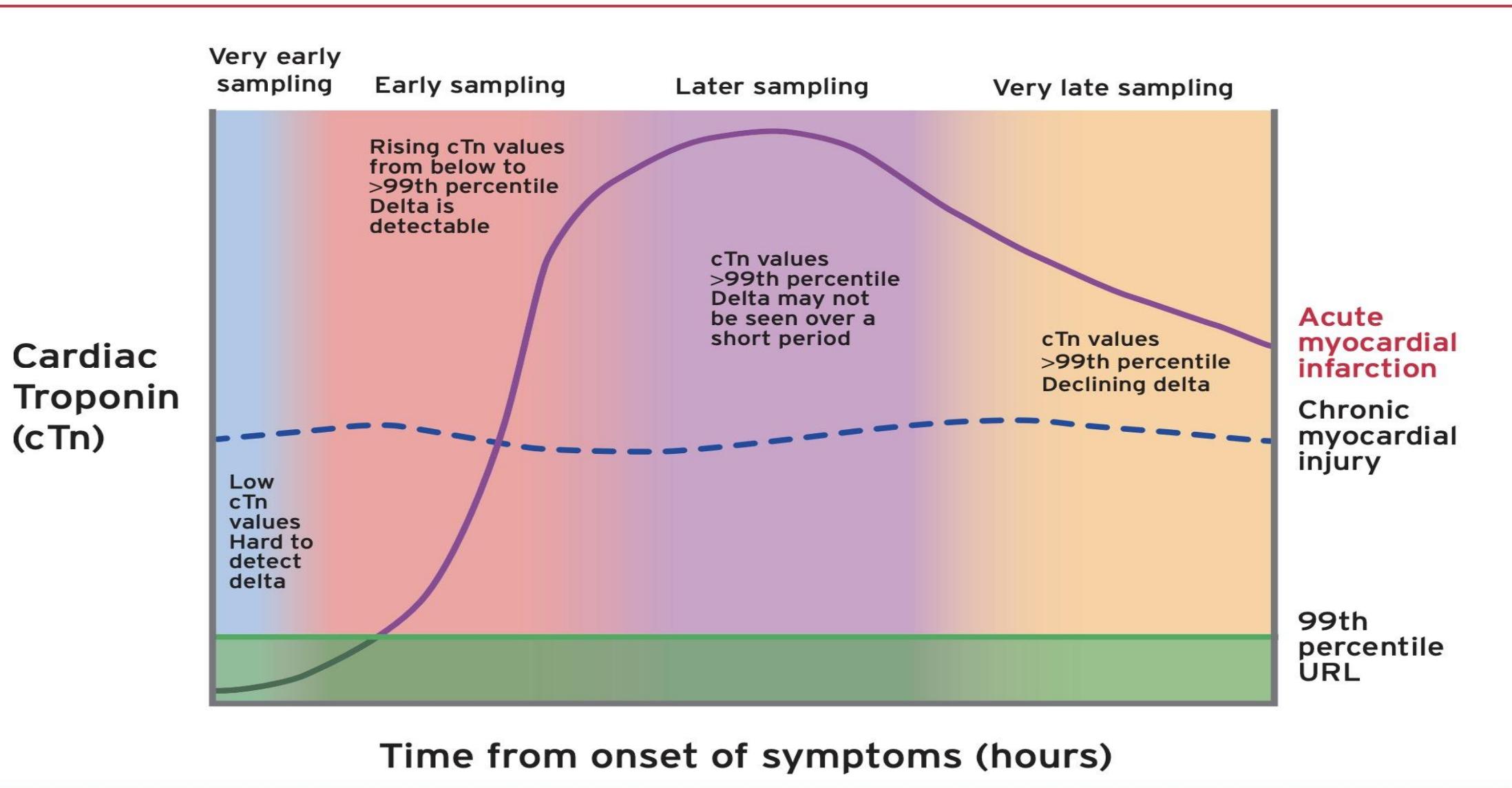
# Jedinice za cTn?      ng/L

laboratories [4]. In the same way the non-SI units for reporting of cTns, ng/mL is not recommended. In order to improve patient safety, we recommend that the reporting of cTns (I and T) is standardized in any specimen or instruments they are measured. We wish to express a strong recommendation for the reporting in whole numbers and for the use of nanogram per liter (ng/L) as the standard unit for reporting cTns, which is acceptable to the 'Système Internationale' (SI) of Measurement.



**Fig. 1.** Comparison of both 99th percentile values (circles) and percent measurable concentrations (boxes) in a presumably healthy population for 19 cardiac troponin assays designated by hs (left), sensitive-contemporary (middle), and POC (right). mod-sens, modified-sensitive [used with permission from Apple et al. (28)].

# Dinamika promjene koncentracije cTn



# PORAST I PAD?

## apsolutna ili relativna razlika?

- absolutna razlika (ng/L) hs-cTn!

## značajna razlika?

- 50-60% ako je početna vrijednost  $<$  99.-te percentile
- 20% za vrijednosti  $\geq$  99.-te percentile
- 10% za značajno povišene koncentracije pri primitku



HVALA NA PAŽNJI

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- Apple FS, Collinson PO, for the IFCC Task Force on Clinical Applications of Cardiac Biomarkers. Analytical characteristics of high-sensitivity cardiac troponin assays. *Clinical Chemistry* 2012; 58:1,54-61.
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- Dalal JJ, Ponde CK, et al. Time to shift from contemporary to high-sensitivity cardiac troponin in diagnosis of acute coronary syndromes. *Indian Heart Journal* 68 (2016); 851-855.
- Calderon JLM, Perez JMV, et al. Performance characteristics of loci method for measuring cardiac troponin I on the dimension EXL. *Practical Laboratory Medicine* 1 (2015);42-47.