# *Troponinas cardíacas y síndrome coronario agudo*
# *20 años de retos técnicos y clínicos*

CLÍNICA CARDIO VID
Obra de la Congregación Mariana


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# Conflicto de intereses


- *Jefe de laboratorio clínico*
- *Usuario de Vitros 5600® OCD*
- *Conferencista de OCD*
- *Muchas diapositivas en inglés*

# *Enfermedad cardiovascular*

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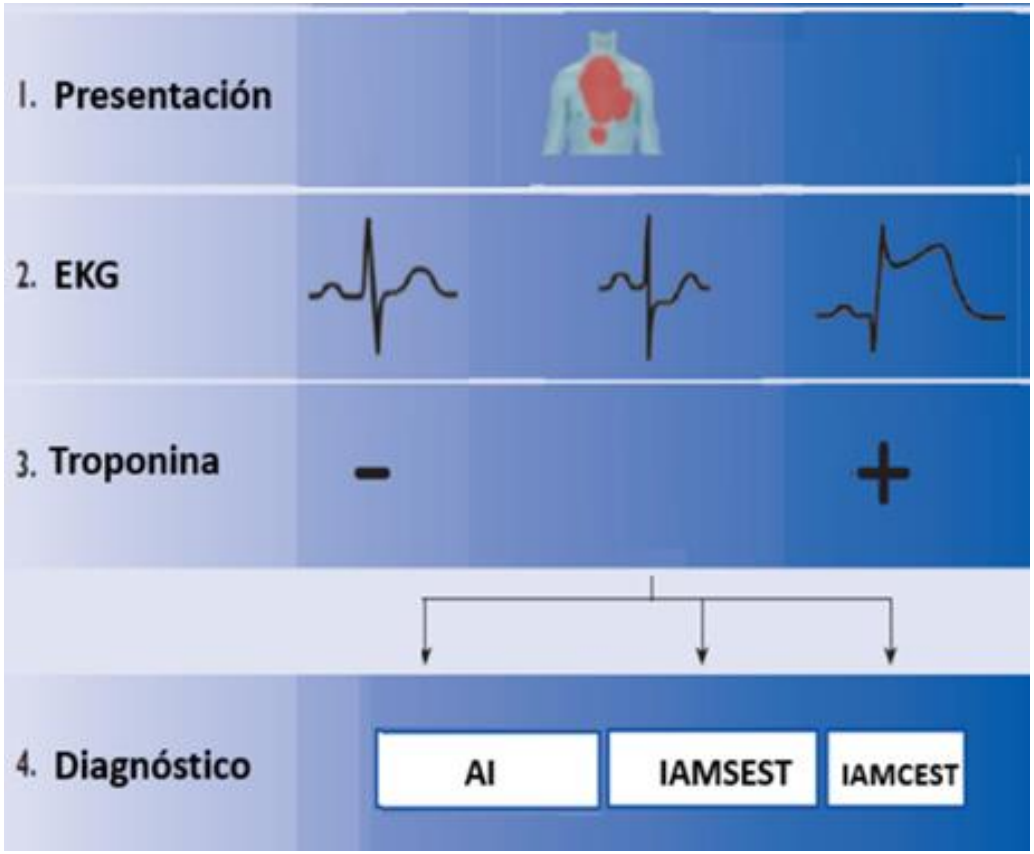
- *Principal causa de muerte*
- *36% de todas las causas en 2020*
- *73/100.000 en Medellín*
- *15% de todas las causas de muerte*
- *Letalidad ECV 50 al 54%*
- *IAM 66% sin atención hospitalaria*

Organización Mundial de la Salud

# Dolor torácico




- *20 – 30%  Urgencias*
- *Un tercio son SCA*
- *IAMCEST 16 – 60%*
- *Biomarcadores 40 – 70%*
- *2 – 8% Diagnóstico equivocado*
- *5% IAM egresan sin diagnóstico*
- *25% de estos mueren*

***Diagnóstico rápido y acertado***
***para estratificación e Intervención tempranas***

# *Evolución de los biomarcadores*

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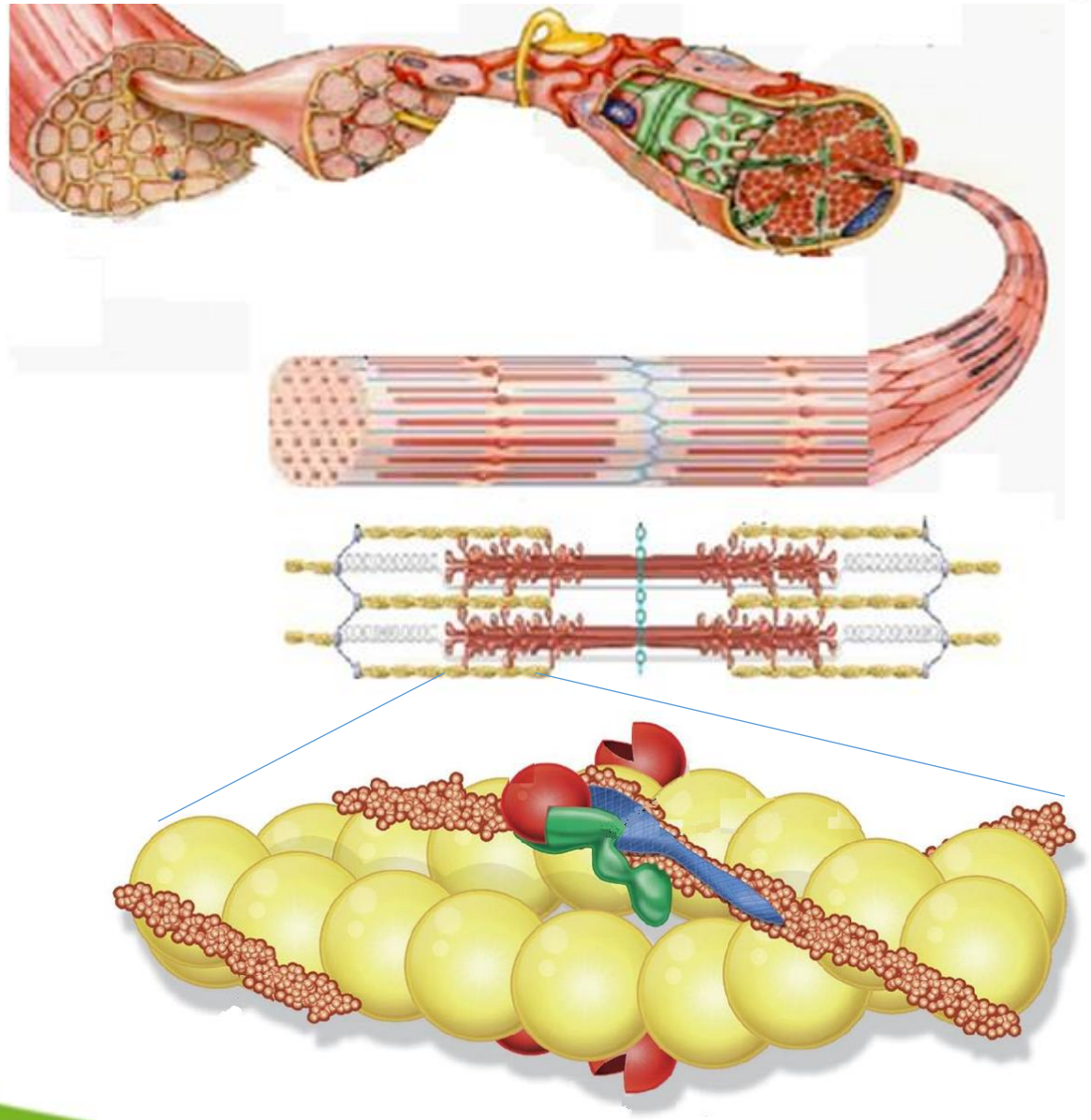
| | | |
|---|---|---|
| 1954 | Karmen | Primer reporte de elevación de **AST** en IAM |
| 1955 | Wroblewski | Uso de **DHL** en diagnóstico de IAM |
| 1960 | Dreyfus | Aplicación de **CK** |
| 1979 | Bruns/Vaidya | Introducción de las **isoenzimas CK** |
| 1987 | Cummins | Primer RIA para detectar **troponinas** cardiacas |
| 1996 | Dade Behring ® | Primera prueba comercial para troponinas |
| 1999 | NACB | Cualquier cantidad de necrosis debida a isquemia es IAM |
| 2000 | ESC/ACC | **Primera** definición universal (Eur Heart J, 2000;21:18) |
| 2000 | ESC/ACC | Marcador preferido para detectar necrosis cardiaca cTn, considerada positiva **al menos un valo**r por encima del LSR en **las primeras 24 horas** Recomendó p99 y CV<10% pero ninguna prueba lo cumplía en esos momentos |
| 2007 | ESC/ACC | **Segunda definición universal** Incorporó aumento o descenso (ALM 13:33 ref 4) pero no definió cuanto |
| 2011 | Sanger | Introducción del término **hs cTn** |
| 2012 | ESC/ACC | **Tercera** definición universal: muestras al **ingreso y 3 a 6 hora**s después, pero tampoco dijo cuanto era significativo |
| 2014 | AHA | Definió **delta significativo (>20%)**, muestras al ingreso y 3 a 6 horas después |
| 2015 | ESC | **hs cTn** con delta absoluto y específico para cada prueba. **0, 1 y 3 horas** |
| 2017 | FDA | 1ª cTn cuarta generación «hscTn» |



# Especificidad de las troponinas cardíacas

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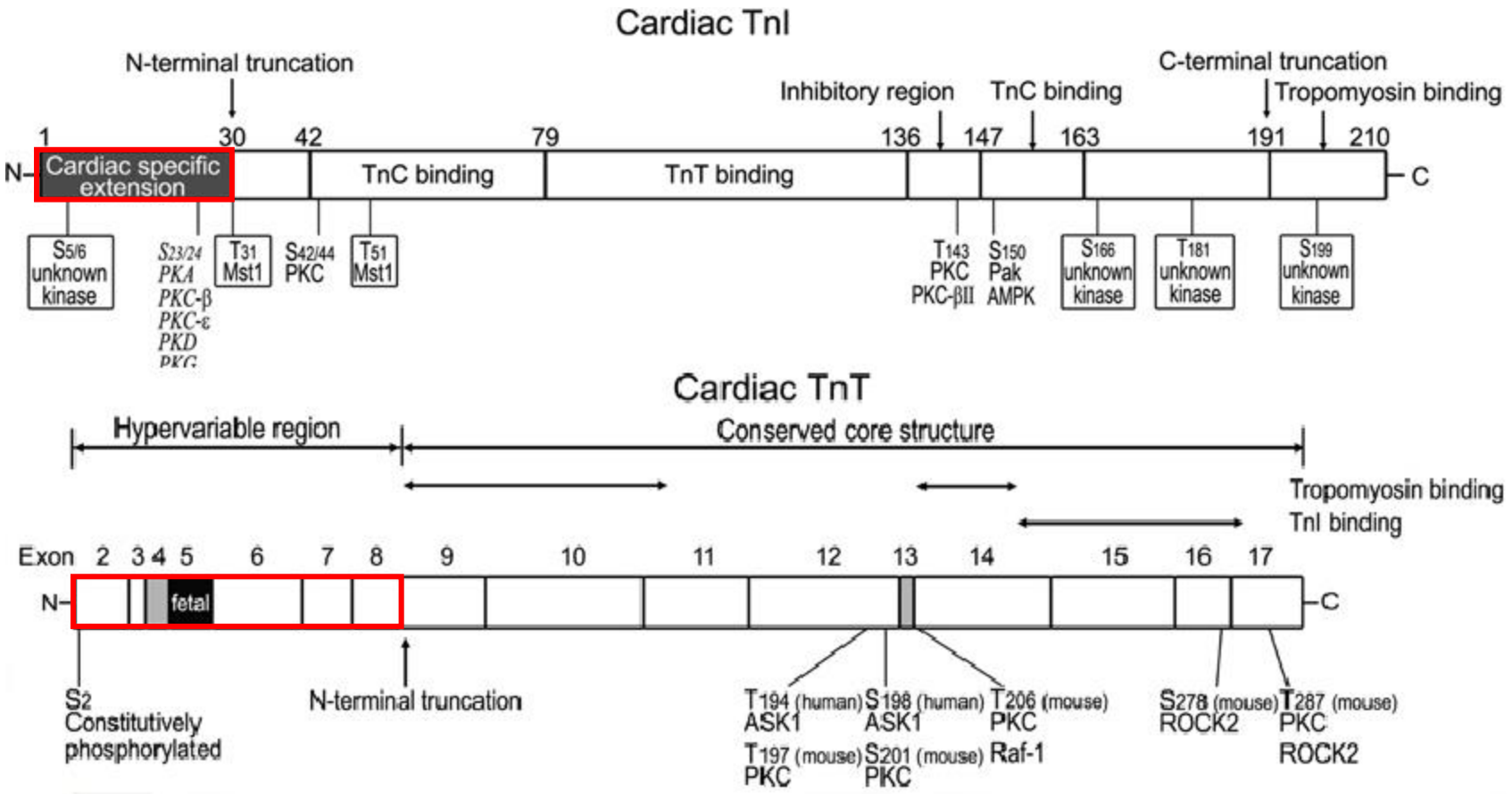
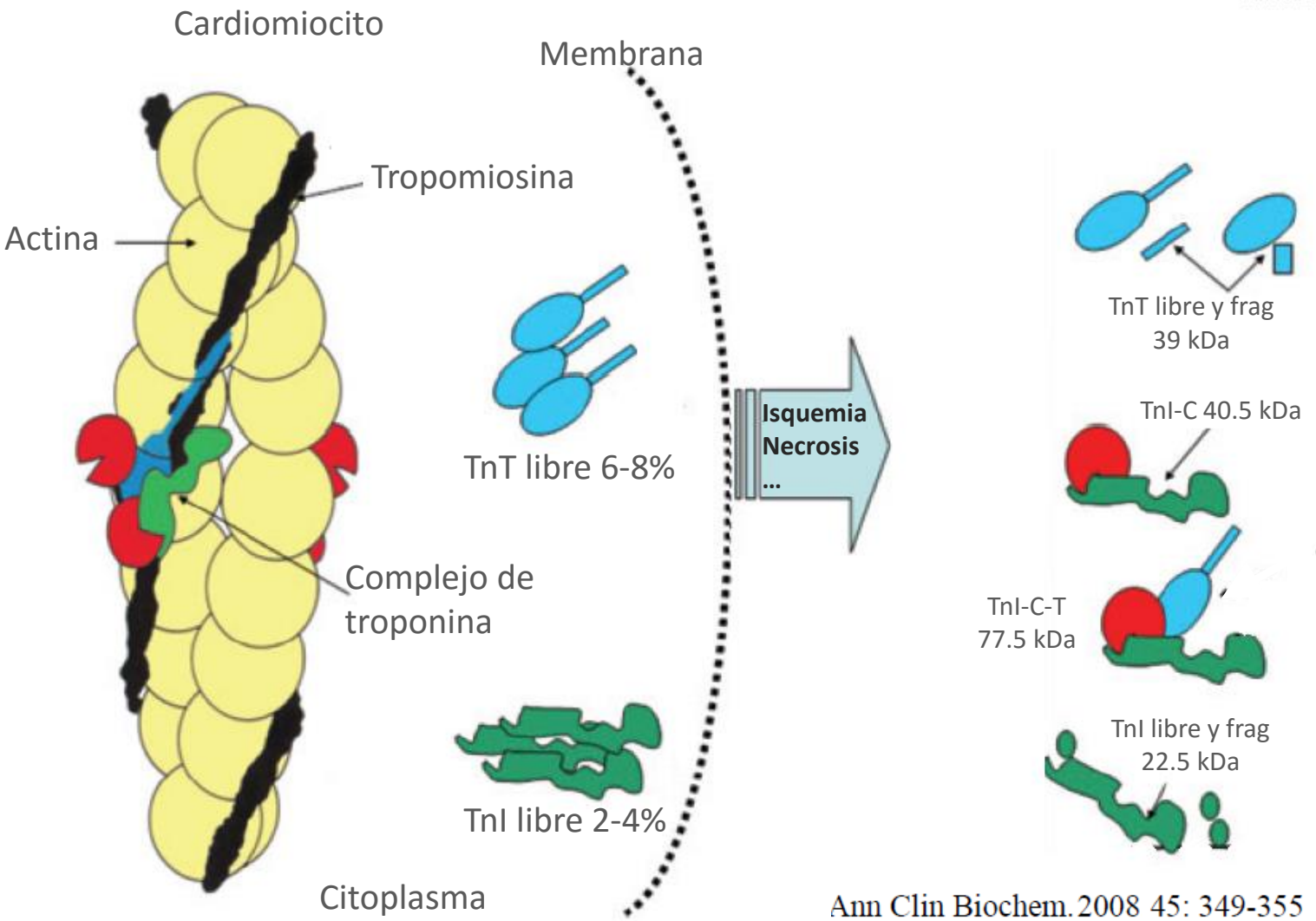


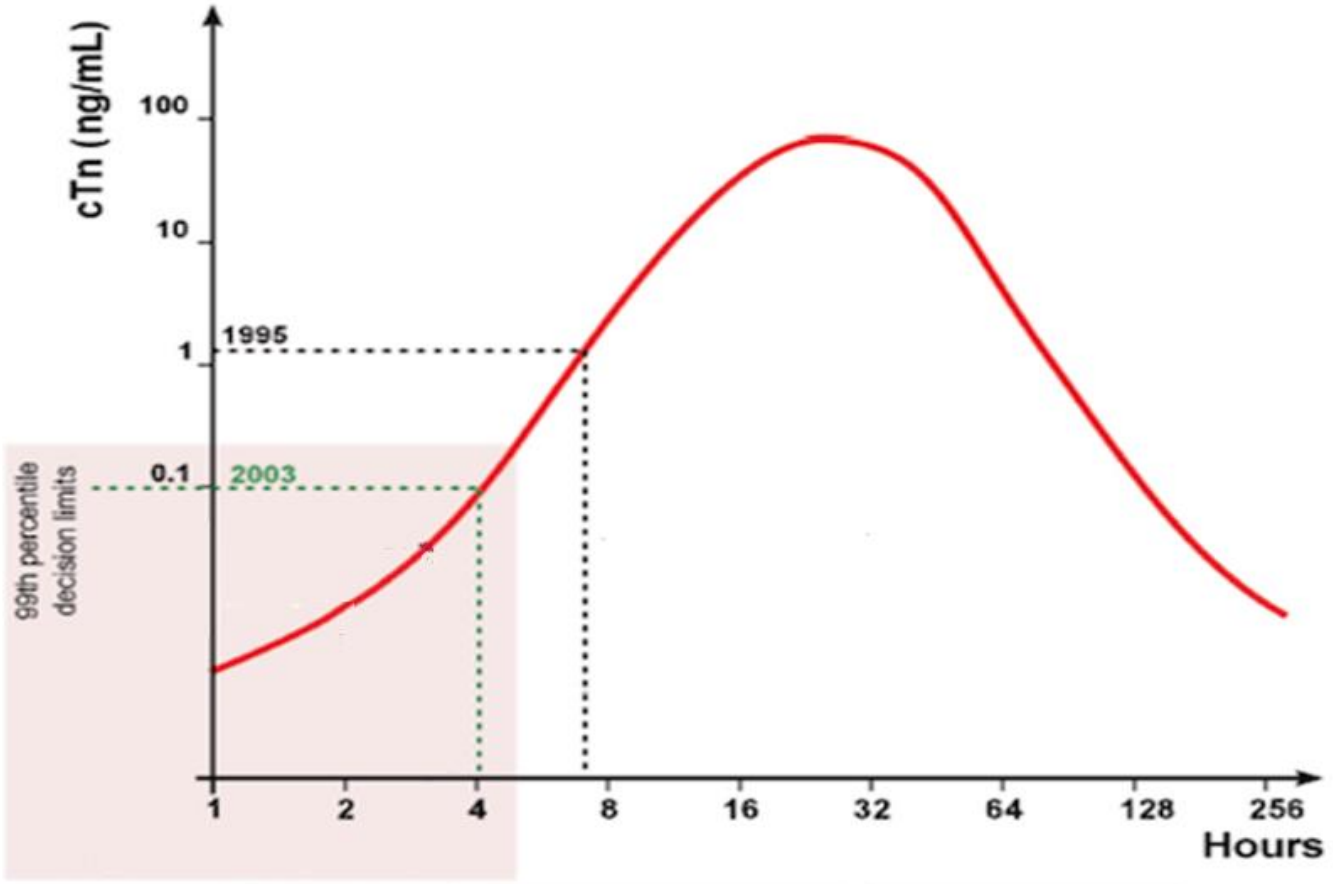

Sheng and Jin **Frontiers in Physiology** April 2014 5 6

Antioquia bilingüe

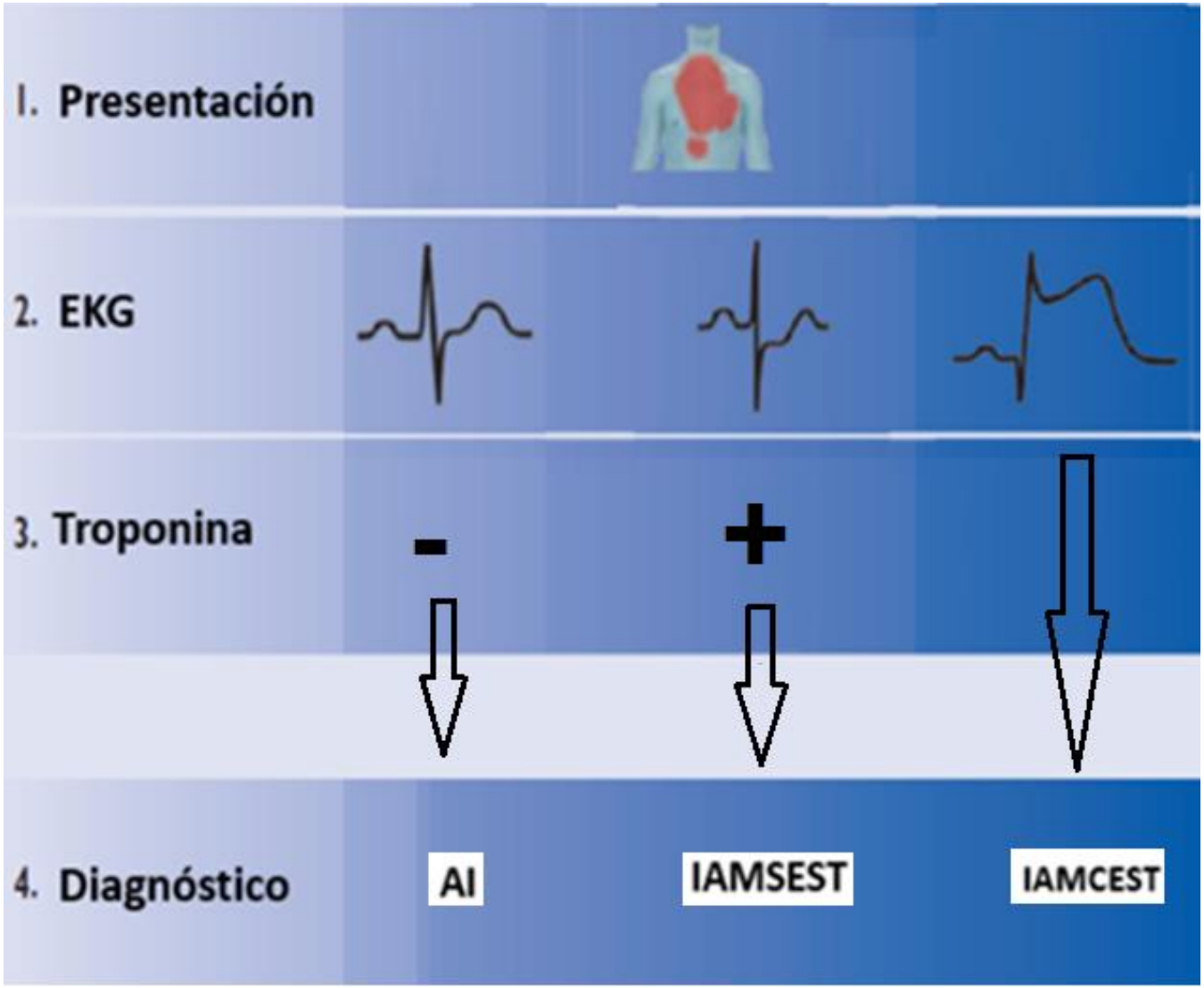
# Troponinas




Ann Clin Biochem. 2008 45: 349-355




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


1. Presentación
2. EKG
3. Troponina
-
+
4. Diagnóstico
AI
IAMSEST
IAMCEST

# *Clasificación de los pacientes con SCA de acuerdo con la tercera definición universal de infarto y con el uso de cTn de nuevas generaciones*

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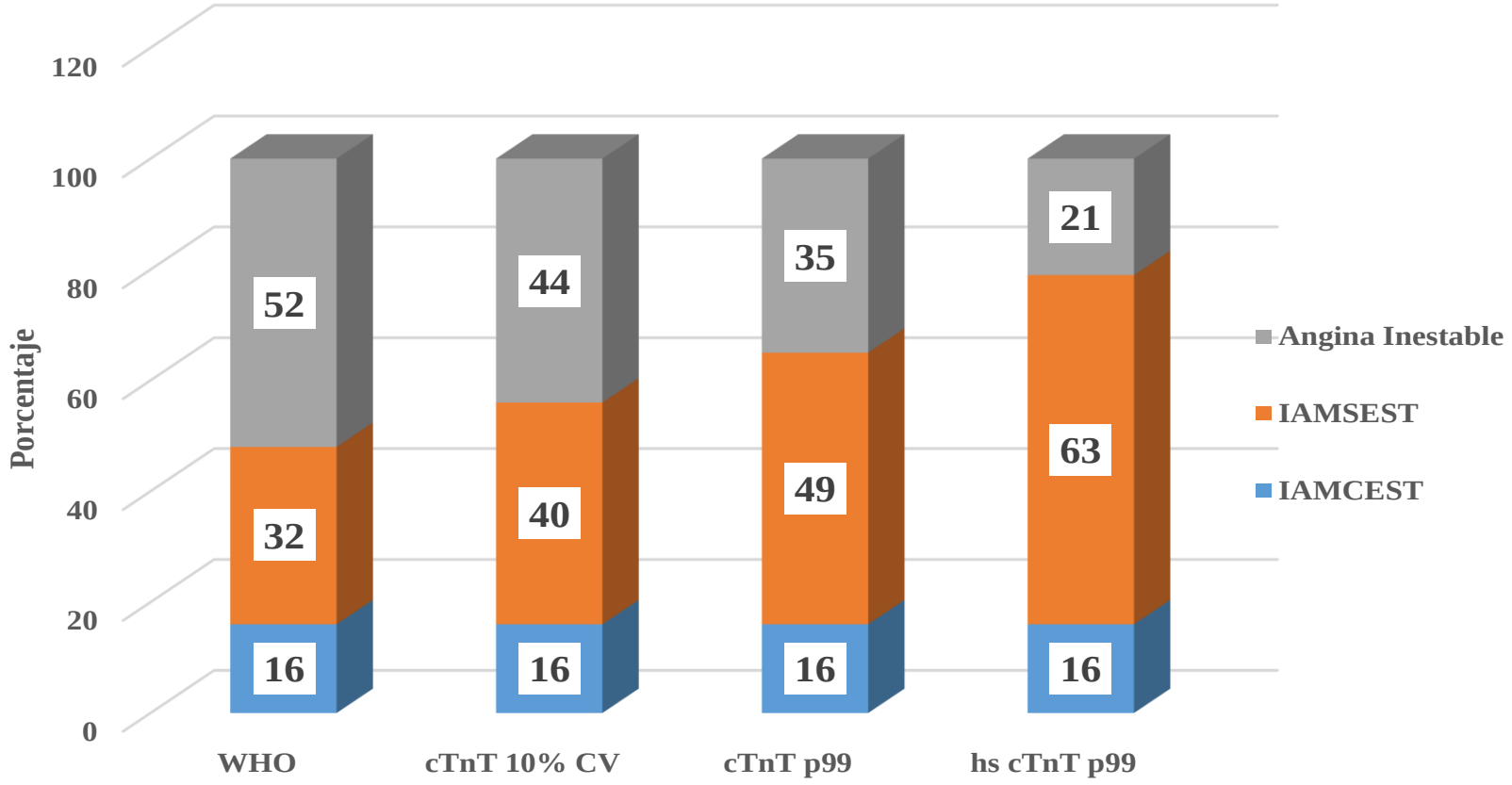


Muller y col Circ J 2013;(7):1657 (15)

# *Tercera definición universal de IAM*

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## 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.

Antioquia bilingüe

*Circulation*. 2012;126:2020-2035

# Tercera definición universal de IAM



elevations that tend not to change acutely. A list of such clinical circumstances associated with elevated values of cTn is presented in *Table 1*. The multifactorial contributions resulting in the myocardial injury should be described in the patient record.

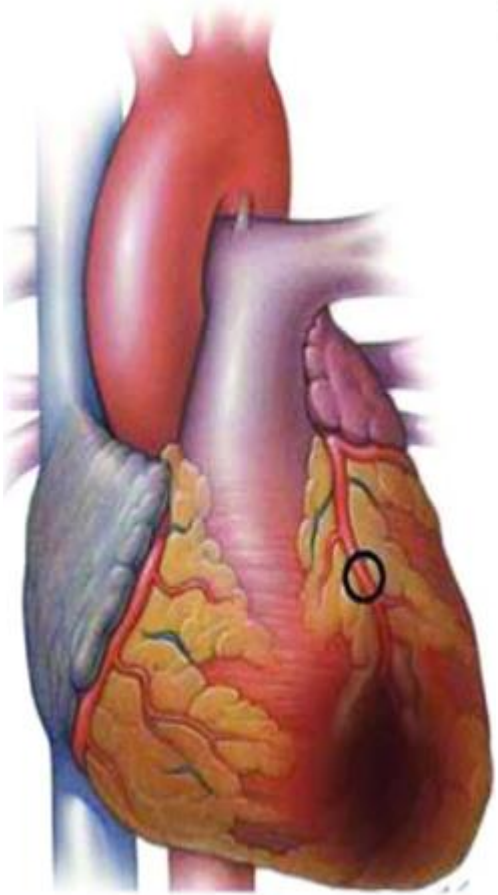
The preferred biomarker—overall and for each specific category of MI—is cTn (I or T), which has high myocardial tissue specificity as well as high clinical sensitivity. Detection of a rise and/or fall of the measurements is essential to the diagnosis of acute MI.[7] An increased cTn concentration is defined as a value exceeding the 99th percentile of a normal reference population [upper reference limit (URL)]. This discriminatory 99th percentile is designated as the decision level for the diagnosis of MI and must be determined for each specific assay with appropriate quality control in each laboratory.[8,9] The values for the 99th percentile URL defined by manufacturers, including those for many of the high-sensitivity assays in development, can be found in the package inserts for the assays or in recent publications.[10,11,12]

Values should be presented as nanograms per litre (ng/L) or picograms per millilitre (pg/mL) to make whole numbers. Criteria for the rise of cTn values are assay-dependent but can be defined from the precision profile of each individual assay, including high-sensitivity assays.[10,11] Optimal precision, as described by coefficient of variation (CV) at the 99th percentile URL for each assay, should be defined as ≤10%. Better precision (CV ≤10%) allows for more sensitive assays and facilitates the detection of changing values.[13] The use of assays that do not have optimal precision (CV >10% at the 99th percentile URL) makes determination of a significant change more difficult but does not cause false positive results. Assays with CV >20% at the 99th percentile URL should not be used.[13] It is acknowledged that pre-analytic and analytic problems can induce elevated and reduced values of cTn.[10,11]

Blood samples for the measurement of cTn should be drawn on first assessment and repeated 3–6 h later. Later samples are required if further ischaemic episodes occur, or when the timing of the initial symptoms is unclear.[14] To establish the diagnosis of MI, a rise and/or fall in values with at least one value above the decision level is required, coupled with a strong pre-test likelihood. The demonstration of a rising and/or falling pattern is needed to distinguish acute- from chronic elevations in cTn concentrations that are associated with structural heart disease.[10,11,15–19] For example, patients with renal failure or HF can have significant chronic elevations in cTn. These elevations can be marked, as seen in many patients with MI, but do not change acutely.[7] However, a rising or falling pattern is not absolutely necessary to make the diagnosis of MI if a patient with a high pre-test risk of

- Type 1: Spontaneous myocardial infarction
- Type 2: Myocardial infarction secondary to an ischaemic imbalance
- Type 3: Myocardial infarction resulting in death when biomarker values are unavailable
- Type 4a: Myocardial infarction related to percutaneous coronary intervention
- Type 4b: Myocardial infarction related to stent thrombosis
- Type 5: Myocardial infarction related to coronary artery bypass grafting

*Circulation*. 2012;126:2020-2035



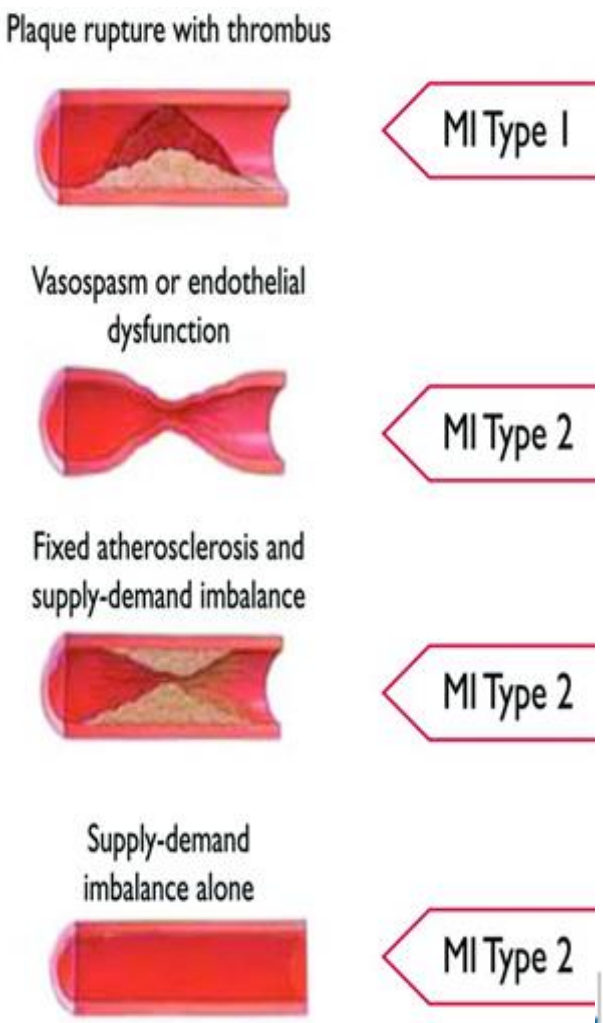


**Table 1. Elevations of Cardiac Troponin Values Because of Myocardial Injury**

| |
|---|
| **Injury related to primary myocardial ischaemia** |
| Plaque rupture<br>Intraluminal coronary artery thrombus formation |
| **Injury related to supply/demand imbalance of myocardial ischaemia** |
| Tachy-/brady-arrhythmias<br>Aortic dissection or severe aortic valve disease<br>Hypertrophic cardiomyopathy<br>Cardiogenic, hypovolaemic, or septic shock<br>Severe respiratory failure<br>Severe anaemia<br>Hypertension with or without LVH<br>Coronary spasm<br>Coronary embolism or vasculitis<br>Coronary endothelial dysfunction without significant CAD |
| **Injury not related to myocardial ischaemia** |
| Cardiac contusion, surgery, ablation, pacing, or defibrillator shocks<br>Rhabdomyolysis with cardiac involvement<br>Myocarditis<br>Cardiotoxic agents, e.g. anthracyclines, herceptin |
| **Multifactorial or indeterminate myocardial injury** |
| Heart failure<br>Stress (Takotsubo) cardiomyopathy<br>Severe pulmonary embolism or pulmonary hypertension<br>Sepsis and critically ill patients<br>Renal failure<br>Severe acute neurological diseases, e.g. stroke, subarachnoid haemorrhage<br>Infiltrative diseases, e.g. amyloidosis, sarcoidosis<br>Strenuous exercise |

*Circulation*. 2012;126:2020-2035

# *Troponinas elevadas*

*¡ Hemos reducido las posibilidades diagnósticas a 16…!*

ACUTE CORONARY SYNDROMES

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

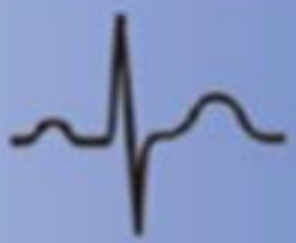
Allan S Jaffe *Heart* 2011;**97**:940–946.

Improvements in cardiac troponin (cTn) assays have outstripped the ability of clinicians to keep up with how to use them clinically. Marketing efforts and the lack of adequate quality control by some journals have made this situation still more difficult. Only recently have our professional organisations begun to provide educational guidance.

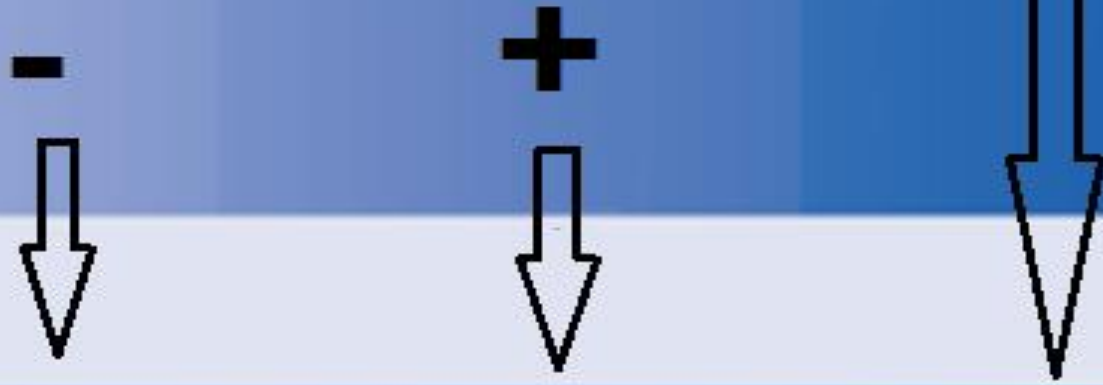
1. *Colaboración entre el Laboratorio y Urgencias*
2. *Entender algunos aspectos analíticos*
3. *Realizar el diagnóstico en el escenario clínico y la cTn*
4. *Confirmar y descartar IAM de formas diferentes*
5. *Usar el sentido común para interpretar elevaciones de cTn en pacientes críticamente enfermos*
6. *No dejarse intimidar por cTn elevada en IRC*
7. *Considerar el valor basal cTn para el diagnóstico en PCI*
8. *Evaluar múltiples parámetros para el diagnóstico de IAM post cirugía de puentes coronarios*
9. *No olvidar efectos de drogas citotóxicas*
10. *Tener precaución con las elevaciones de cTn post ejercicio*

1. Presentación

2. EKG



3. Troponina




4. Diagnóstico

AI

IAMSEST

IAMCEST

Baja---------- probabilidad----------Alta

1. Presentación

2. EKG

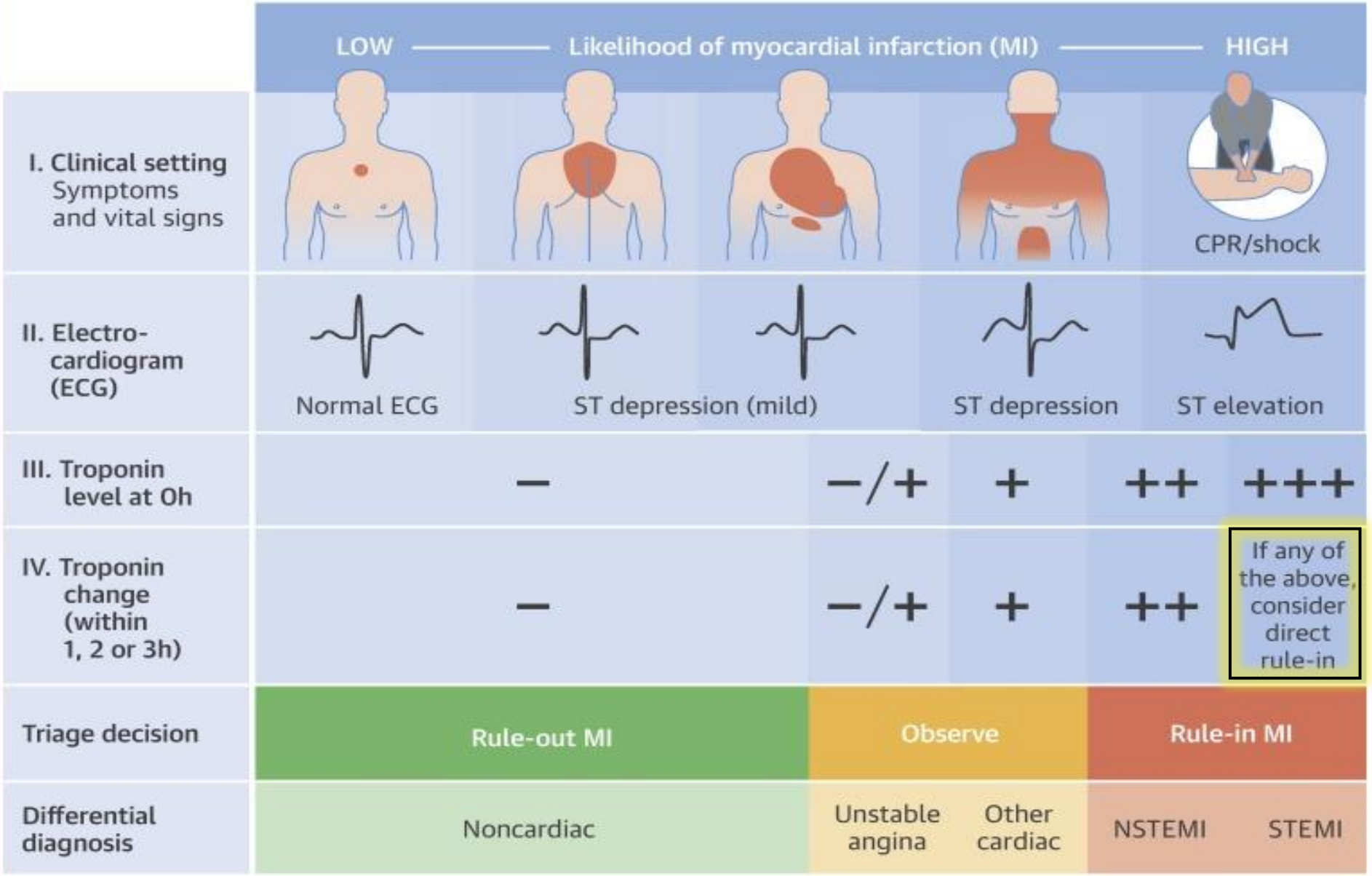
3. Troponina

\- + ++

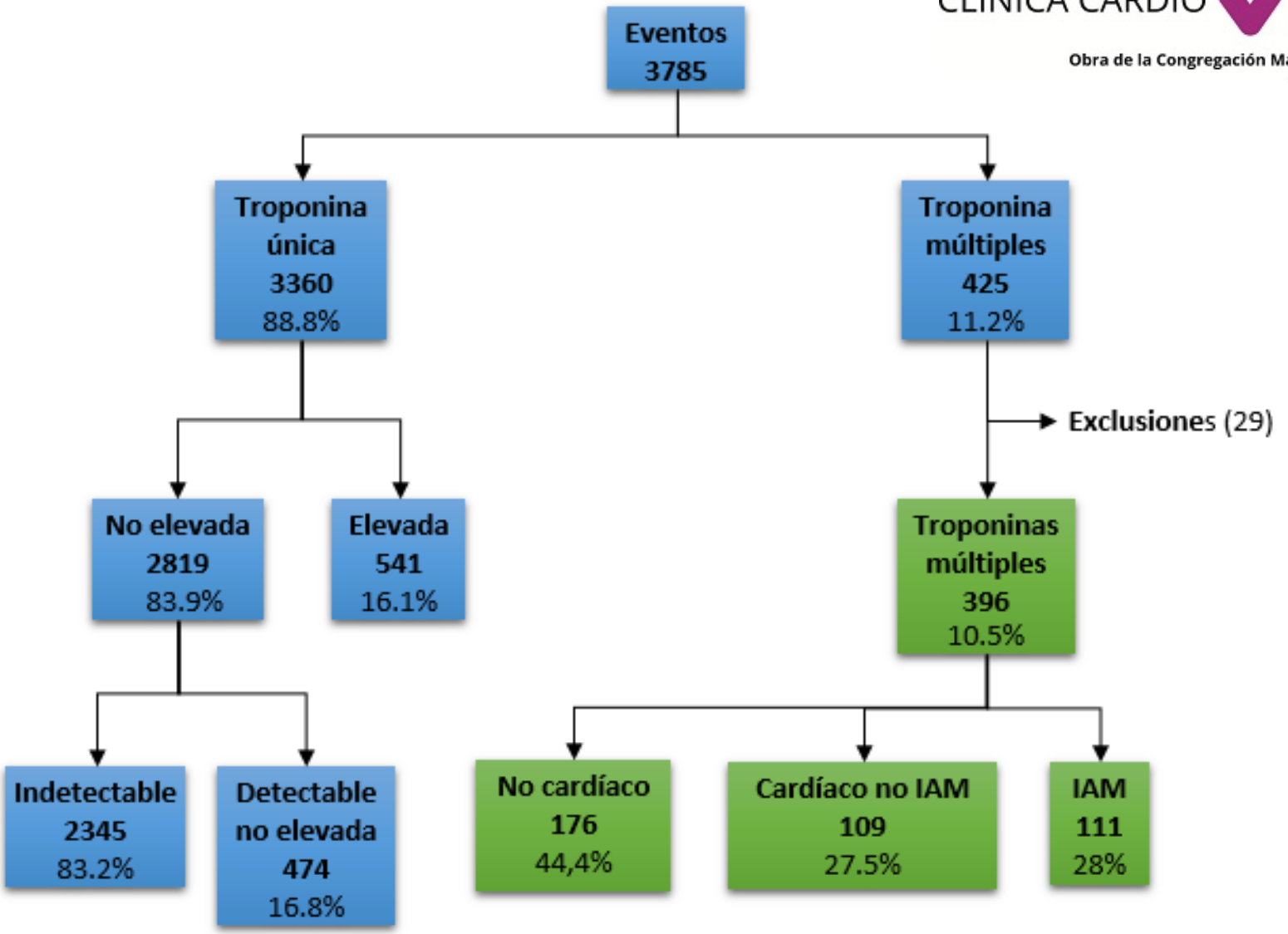
4. Diagnóstico

| No cardiaco | AI | Otro cardiaco | IAMSEST | IAMCEST |
|---|---|---|---|---|
| 50% | 10% | 15% | 15-20% | 5-15% |

# CENTRAL ILLUSTRATION: Patient Assessment With Suspected ACS




**Twerenbold, R. et al. J Am Coll Cardiol. 2017;70(8):996-1012.**


Eventos
3785
Troponina única
3360
88.8%
Troponina múltiples
425
11.2%
Exclusiones (29)
No elevada
2819
83.9%
Elevada
541
16.1%
Troponinas múltiples
396
10.5%
Indetectable
2345
83.2%
Detectable no elevada
474
16.8%
No cardíaco
176
44,4%
Cardíaco no IAM
109
27.5%
IAM
111
28%

# *Dolor torácico y cTn seriadas*

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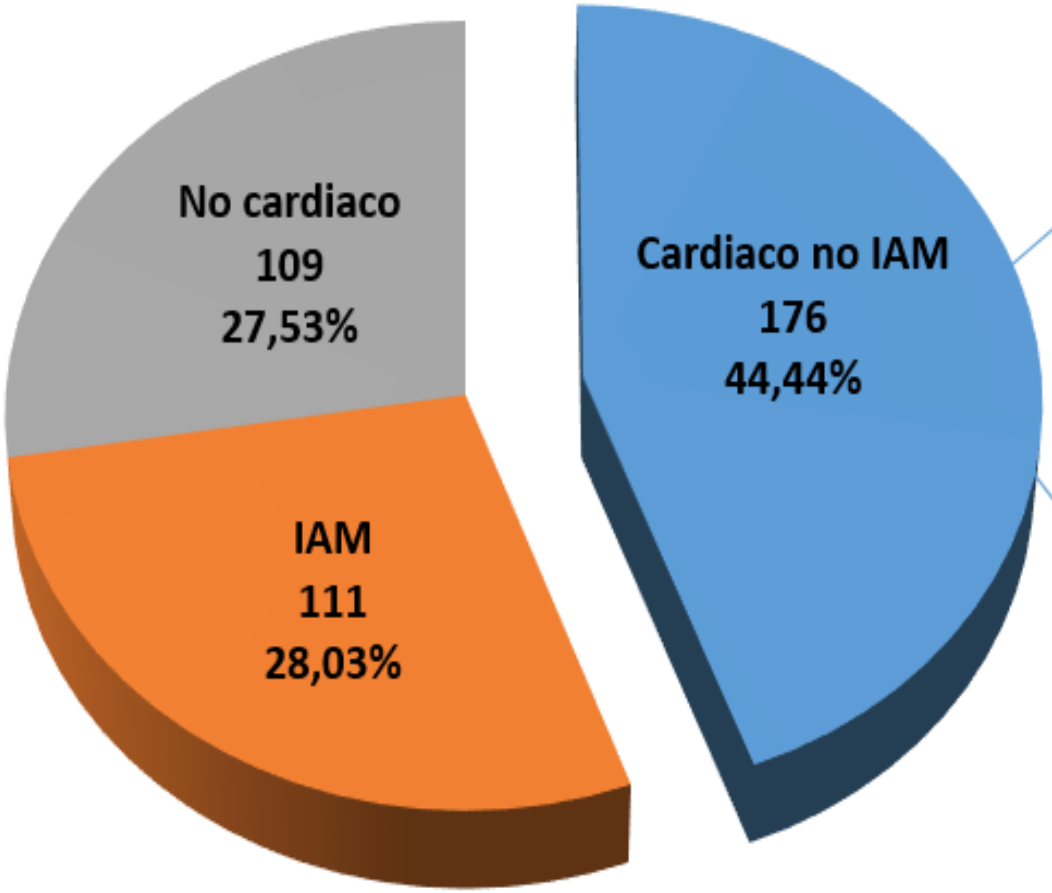
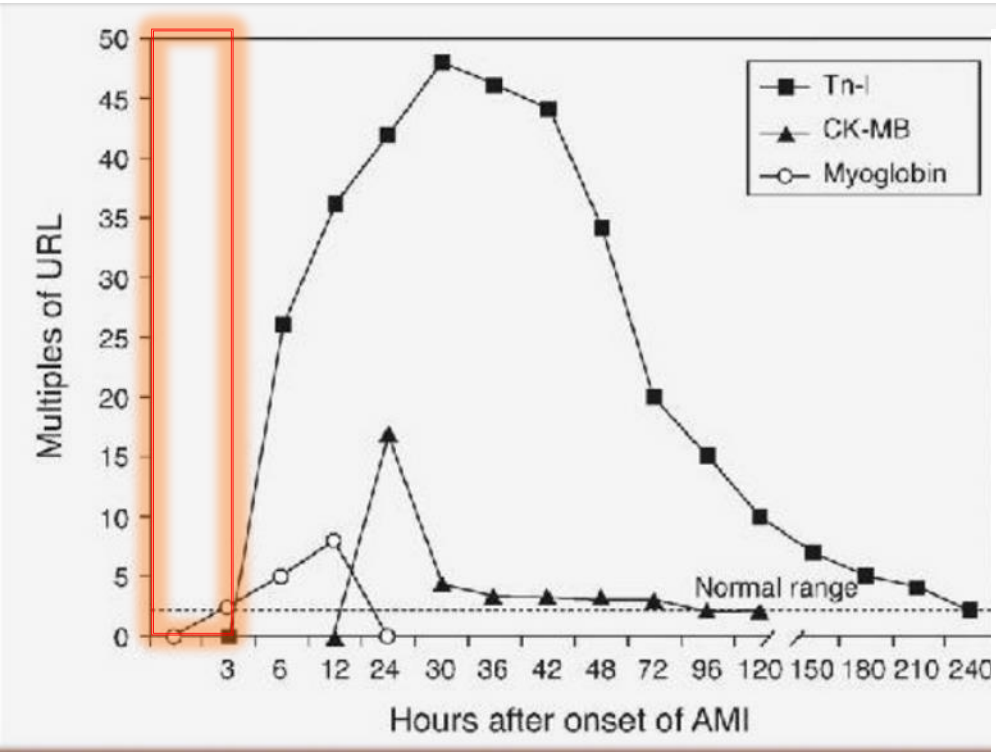
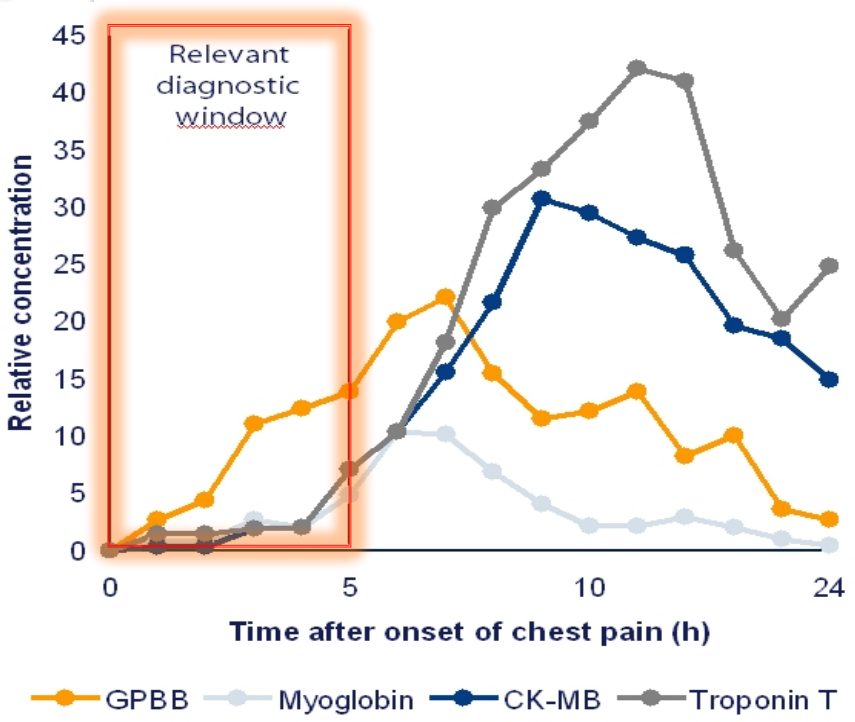
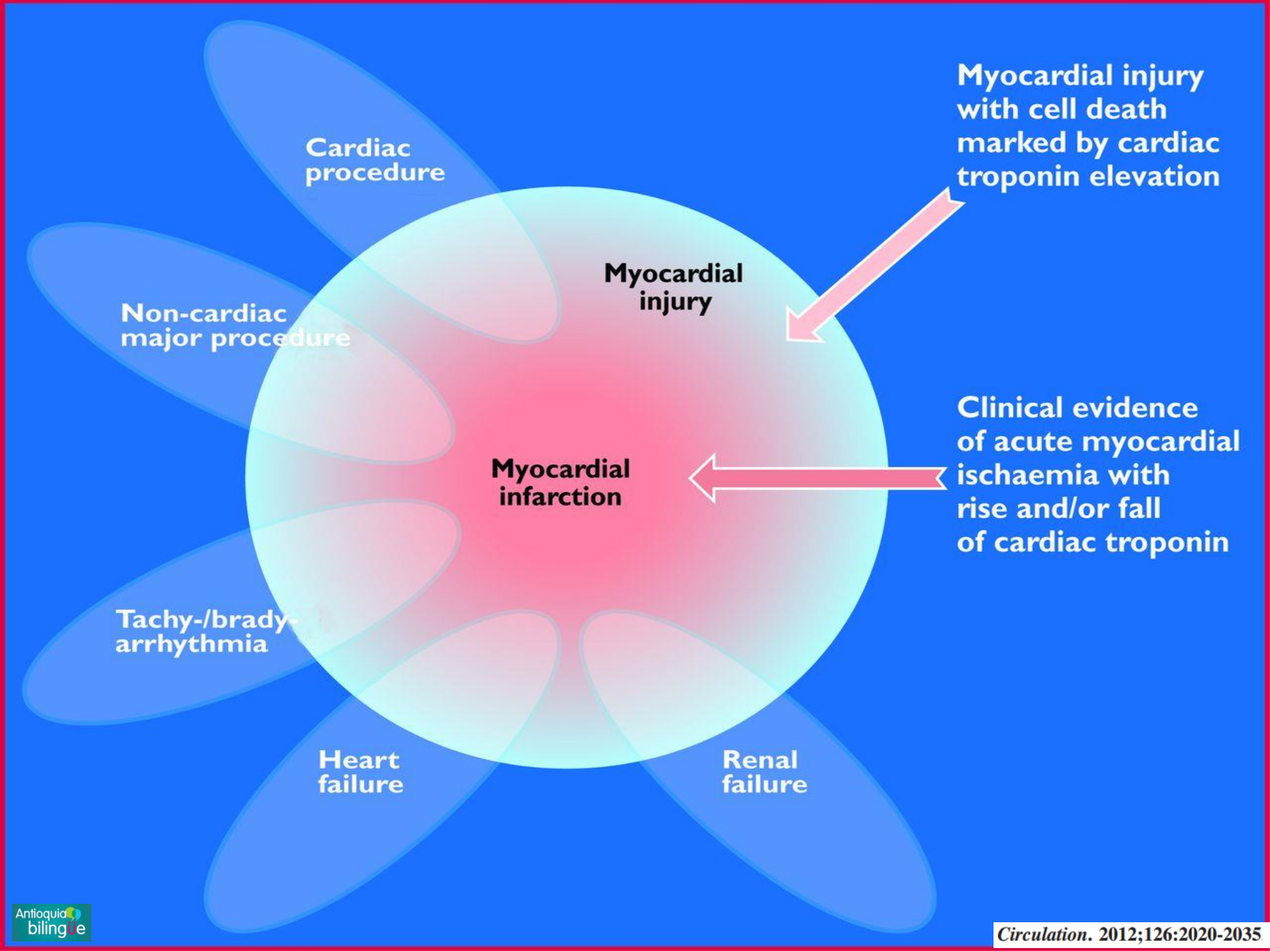



| Diagnóstico | n |
|---|---|
| Falla cardiaca | 39 |
| Crisis hipertensiva | 36 |
| Cardiomiopatia | 25 |
| Fibrilación / Aleteo auricular | 25 |
| Taquicardia supra y ventricular | 21 |
| Angina | 19 |
| Miopericarditis | 10 |
| Pericarditis | 1 |




*«El tiempo es miocardio…»*






*Circulation*. 2012;126:2020-2035


DAE

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# IMPLEMENTING HIGH-SENSITIVITY CARDIAC TROPONIN ASSAYS IN PRACTICE

## The 99th Percentile Value is Universally Endorsed as the Reference Cut-off to Aid in the Diagnosis of Acute Myocardial Infarction (AMI)[1]

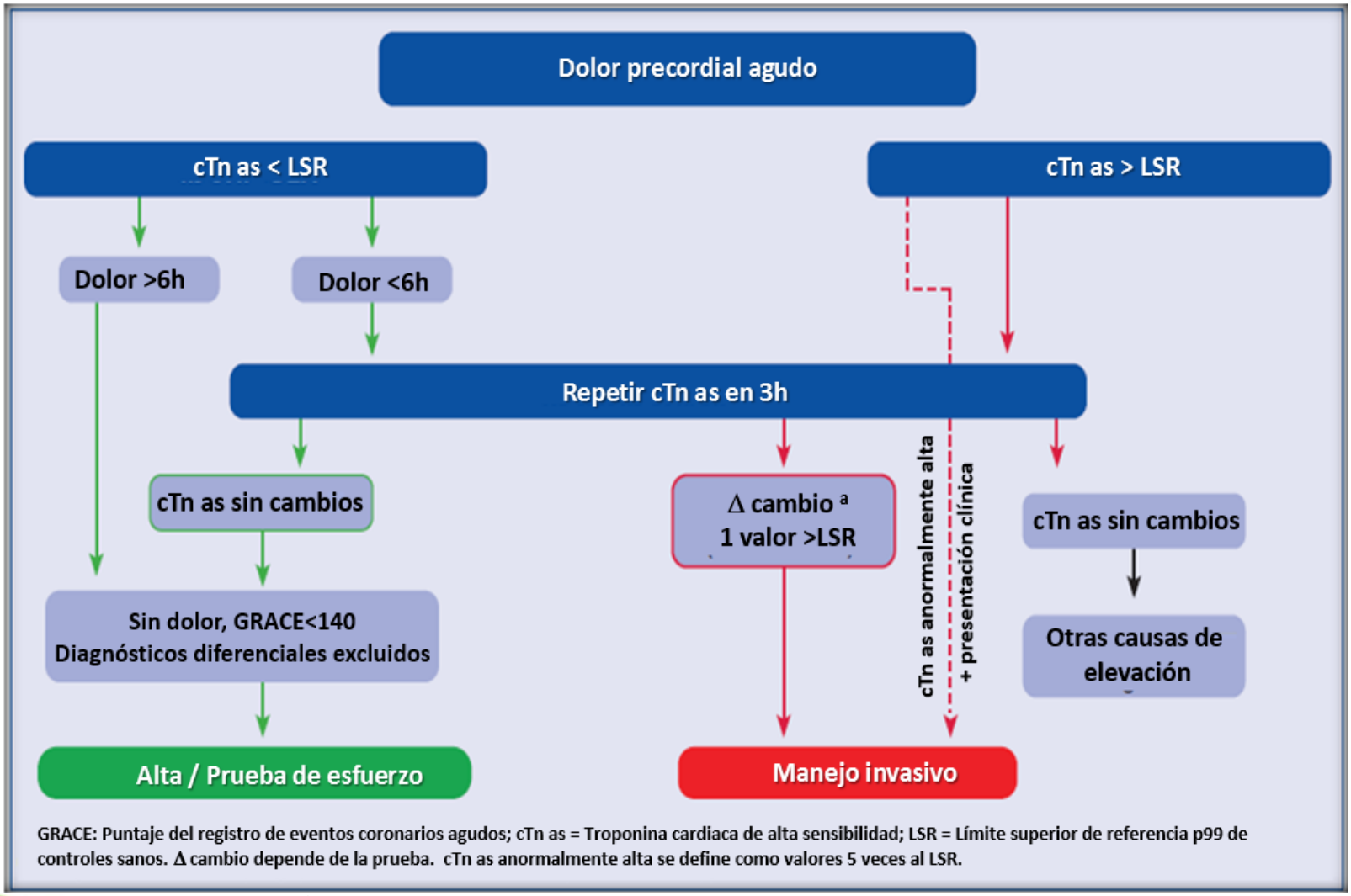
## Key Components to Implement High-Sensitivity Cardiac Troponin (hs-cTn) Assays In Practice

- 99th percentile should be determined in a healthy population[1,2]
- ✔ 99th percentile from either peer-reviewed literature or from manufacturers' product information are acceptable
- ✔ 99th percentile for hs-cTn assays should be measured with an analytical imprecision of ⩽ 10% (% CV; coefficient of variation)[1,2]
- hs-assays should measure cTn above the limit of detection in ⩾ 50% of healthy subjects[2,3,4]

Nuevo

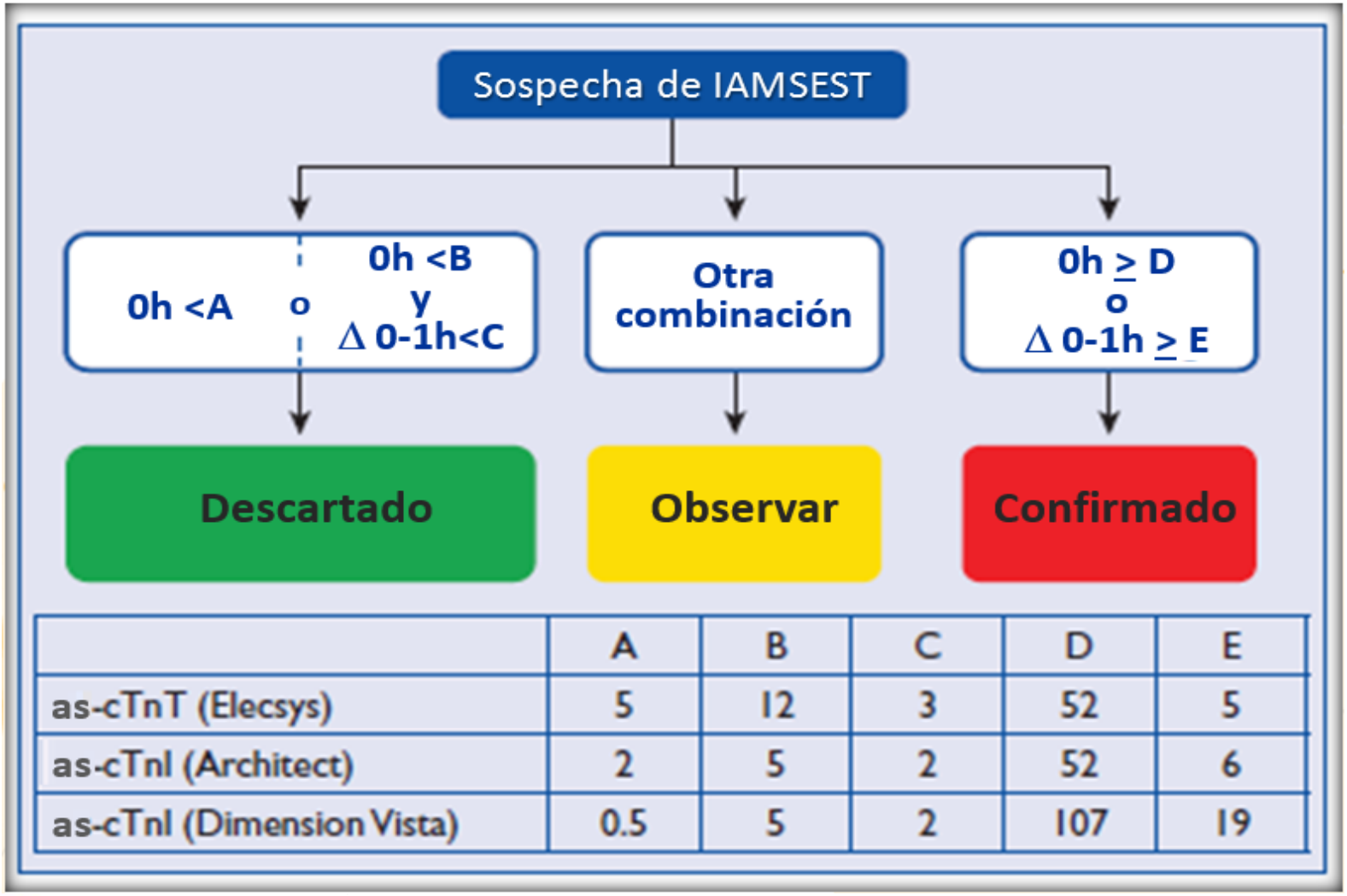
TASK FORCE ON CLINICAL APPLICATIONS OF CARDIAC BIO-MARKERS

ifcc
International Federation of Clinical Chemistry and Laboratory Medicine




GRACE: Puntaje del registro de eventos coronarios agudos; cTn as = Troponina cardiaca de alta sensibilidad; LSR = Límite superior de referencia p99 de controles sanos. Δ cambio depende de la prueba. cTn as anormalmente alta se define como valores 5 veces al LSR.

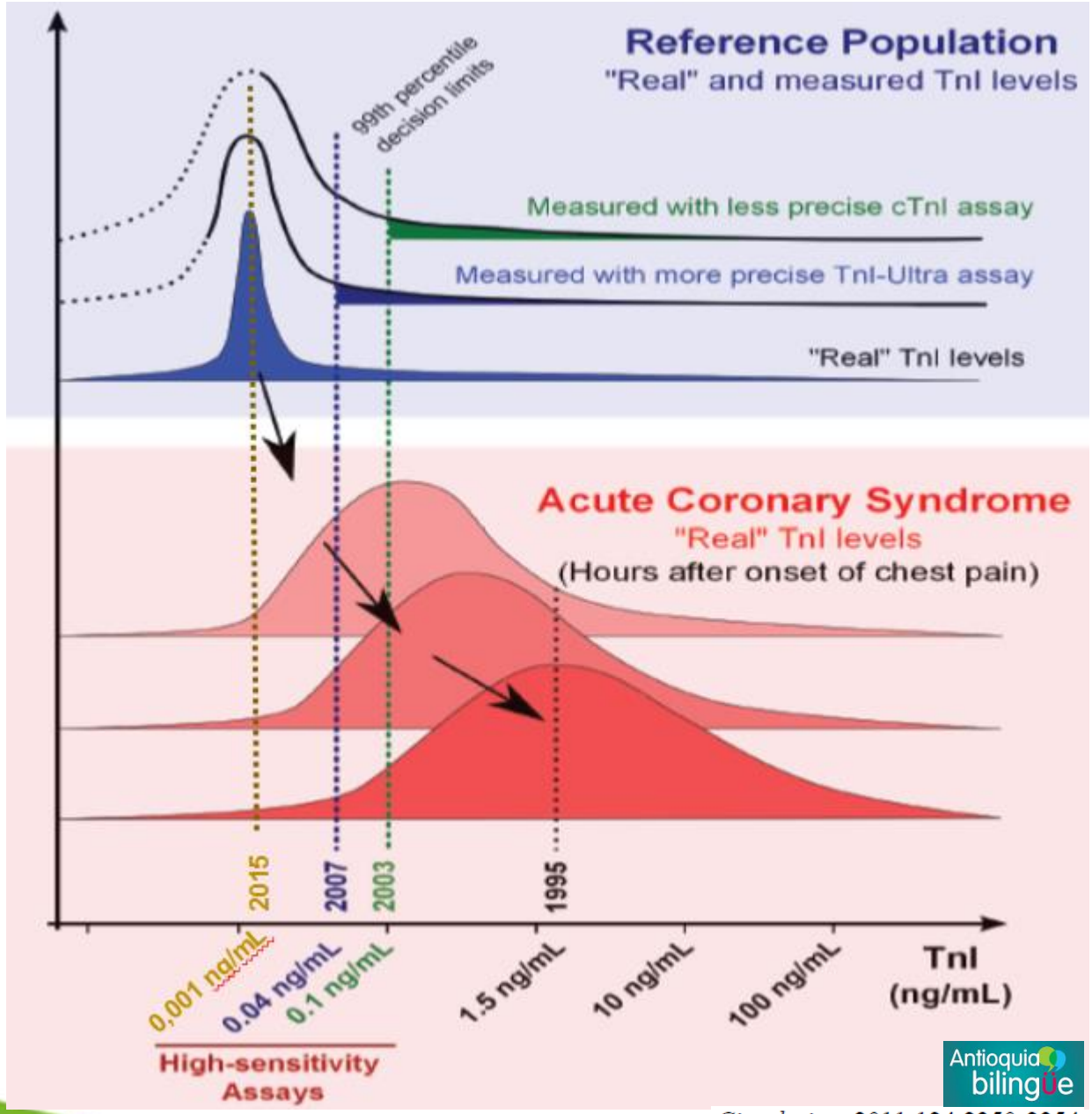
**ESC GUIDELINES** European Heart Journal August 29, 2015



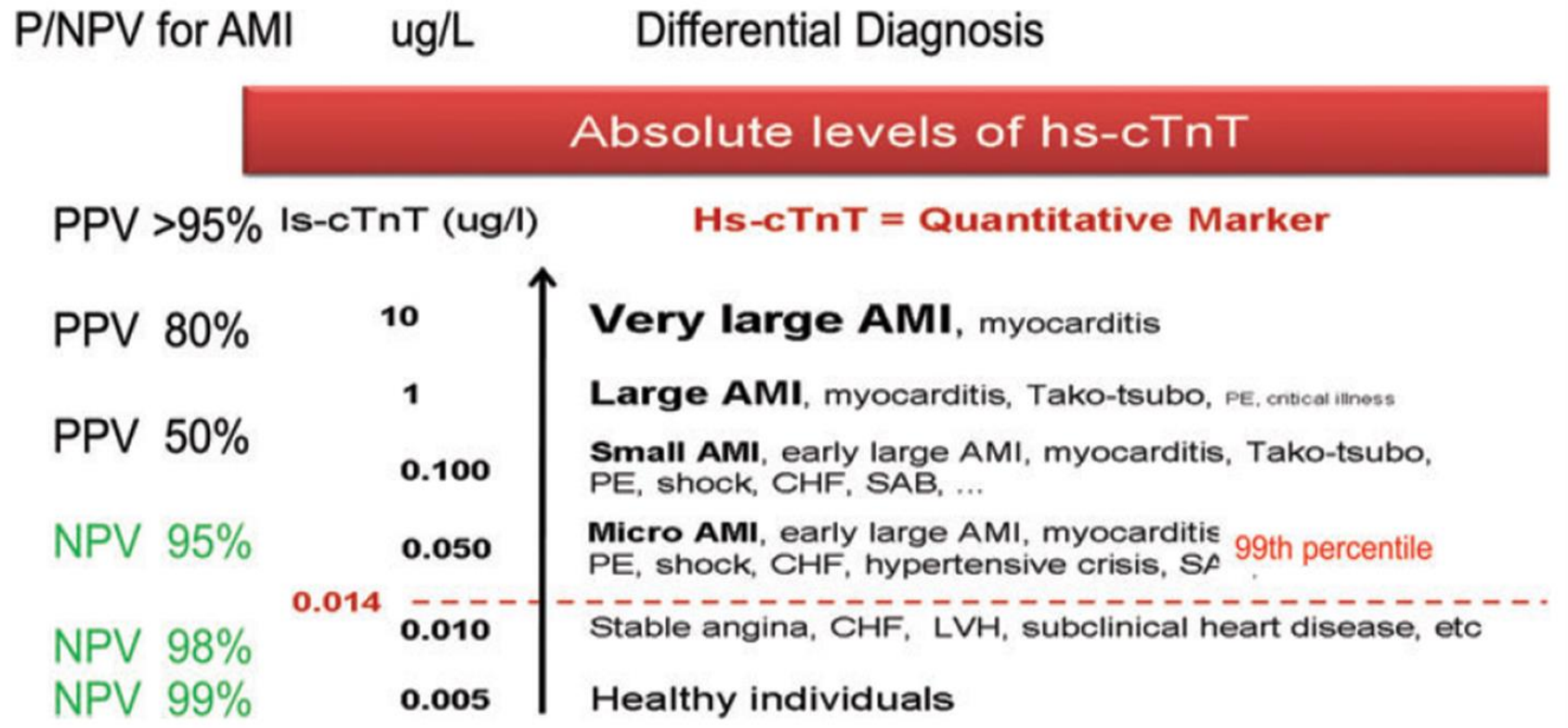

| | A | B | C | D | E |
|---|---|---|---|---|---|
| as-cTnT (Elecsys) | 5 | 12 | 3 | 52 | 5 |
| as-cTnI (Architect) | 2 | 5 | 2 | 52 | 6 |
| as-cTnI (Dimension Vista) | 0.5 | 5 | 2 | 107 | 19 |

**ESC GUIDELINES** European Heart Journal August 29, 2015


QUINO



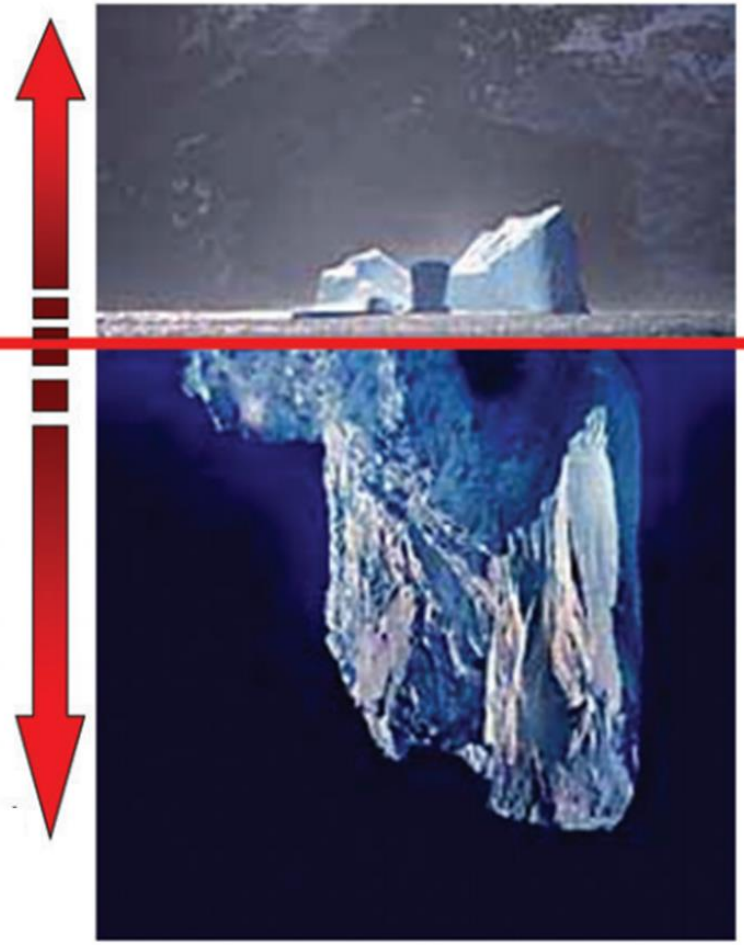

*Circulation.* 2011;124:2350-2354




European Heart Journal (2014) **35**, 552–556

# High sensitivity troponins – submerging evidence

- IAM
- Miocarditis
- Embolismo pulmonar
- Falla cardíaca aguda
- Enf renal terminal
- Taquicardia de reentrada NAV




- IAMNST pequeño
- IAM Tipo 2
- Quimiotóxicos
- Crisis hipertensiva
- Falla renal incipiente
- Taquicardias
- HTP crónica
- Falla cardíaca crónica
- EAC estable
- Isquemia ?
- Maratonistas
- Población general

European Heart Journal (2014) **35**, 268–270

# *Elevadas sin IAM*
# *Elevadas sin necrosis*
# *Detectables en sanos*

- *37% de pacientes con angina estable y placa lábil*
- *Hasta el 2% de la población normal en algunos estudios*
- *Detectable en 50 – 90 – 95% de sanos (por definición)*

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

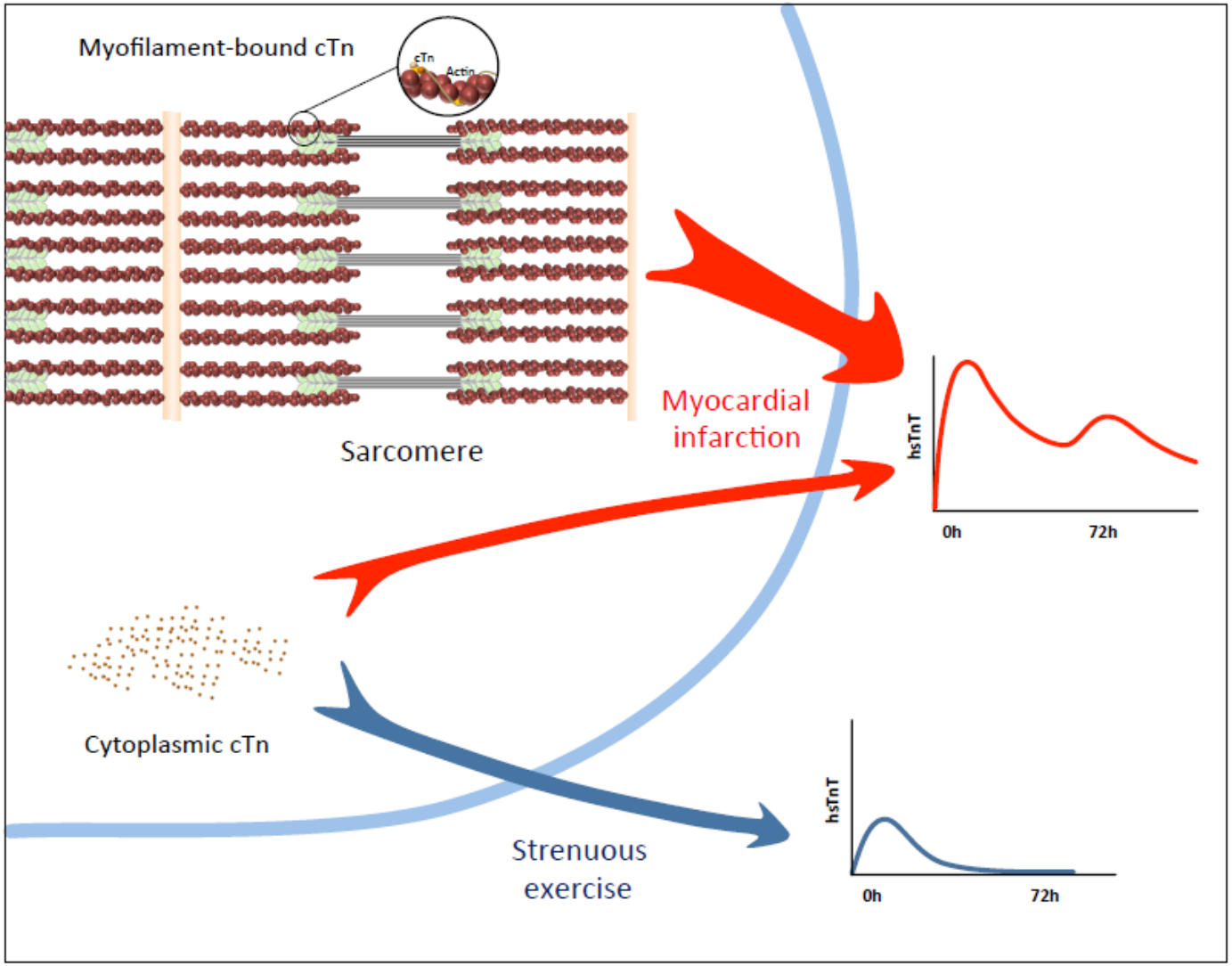
| | |
|---|---|
| Type 1 | Myocyte necrosis |
| Type 2 | Apoptosis |
| Type 3 | Normal myocyte turnover |
| Type 4 | Cellular release of proteolytic troponin degradation products |
| Type 5 | Increased cellular wall permeability |
| Type 6 | Formation and release of membranous blebs |

JACC Vol. 57, No. 24, 2011:2406–8

# Cardiac Biomarker Changes After Endurance Sports

Apr 14, 2016 Farbod Sedaghat-Hamedani, MD; Hugo A. Katus, MD, FACC; Benjamin Meder, MD





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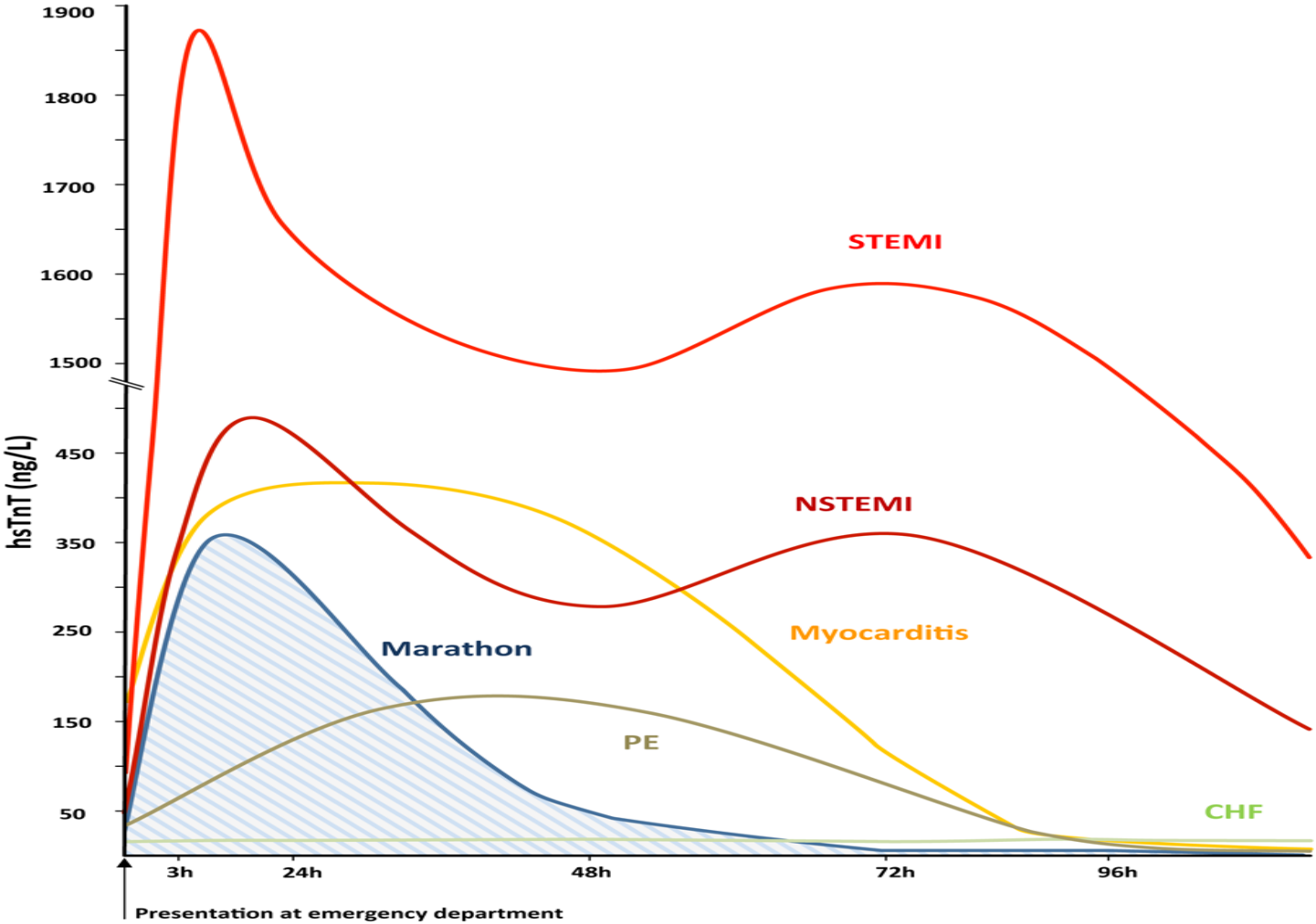

International Journal of Cardiology 195 (2015) 163–170

# Early rule-out and rule-in of myocardial infarction using sensitive cardiac Troponin I☆

Sophie Druey [a,c], Karin Wildi [a], Raphael Twerenbold [a], Cédric Jaeger [a], Tobias Reichlin [a], Philip Haaf [a],

### 2.3. Adjudicated final diagnosis

Adjudication of the final diagnosis was performed centrally at the laboratory for all patients using also levels of hs-cTnT in order to take advantage of the higher sensitivity and higher overall diagnostic accuracy offered by hs-cTn assays [11,15]. This allows the additional detection of small AMIs. Two independent cardiologists reviewed all available medical records pertaining to the patient from the time of ED presentation to a 90-day follow-up or longer (patient history, physical examination, results of laboratory testing, radiologic testing, ECG, echocardiography, cardiac exercise test, lesion severity and morphology in coronary angiography). In situations of disagreement about the diagnosis, cases were reviewed and adjudicated in conjunction with a third cardiologist.

# *Retos para el diagnóstico de IAM*

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Obra de la Congregación Mariana

- *Ventana diagnóstica*
- *cTn detectables, elevadas y positivas para IAM*
- *Arteriografía coronaria sin lesiones aparentes*
- *Otras causas de dolor con elevación cTn*

*Con las cTn actuales y una buena evaluación clínica; incluyendo pruebas de seguimiento, rara vez una cTn elevada corresponderá a un error técnico o falso positivo*

*Con un juicio clínico adecuado generalmente se logrará un diagnóstico acertado*

# *Conclusiones*

CLÍNICA CARDIO VID
Obra de la Congregación Mariana

- *Tener cTn detectables llegará a ser normal*
- *cTn elevadas*
  - *Casi siempre representará lesión miocárdica*
  - *Casi siempre implicará peor pronóstico*
  - ***Siempre requieren atención***
- *Aumento de la sensibilidad clínica (precisión analítica)*
  - *Acorta el tiempo de ventana*
  - *Acorta el intervalo entre mediciones*
  - *Aumenta el número de pacientes con cTn detectable o elevada*
  - *Requiere conocer la población de influencia y ajuste de protocolos*
  - *Requiere por lo menos tres horas de inicio del cuadro clínico*
  - *2ª conquista europea a América*
- *La mayoría de los pacientes sólo requerirán una medición*
- *El grupo de riesgo intermedio con cTn moderada o levemente elevadas necesita medición seriada*

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Q&A

By Fred S. Apple[1]

***David Morrow:*** *que el médico conozca las características de desempeño de la prueba que usa eso es más útil que contar con hs cTn*

***Consenso general:*** *que el médico tenga en consideración la probabilidad clínica de que se trate de un IAM y que conozca las características de desempeño de la prueba que usa… esa es la herramienta más útil con la que se puede contar*

El Doctor - Luke Fildes (1891)