Les nouveaux marqueurs cardiaques

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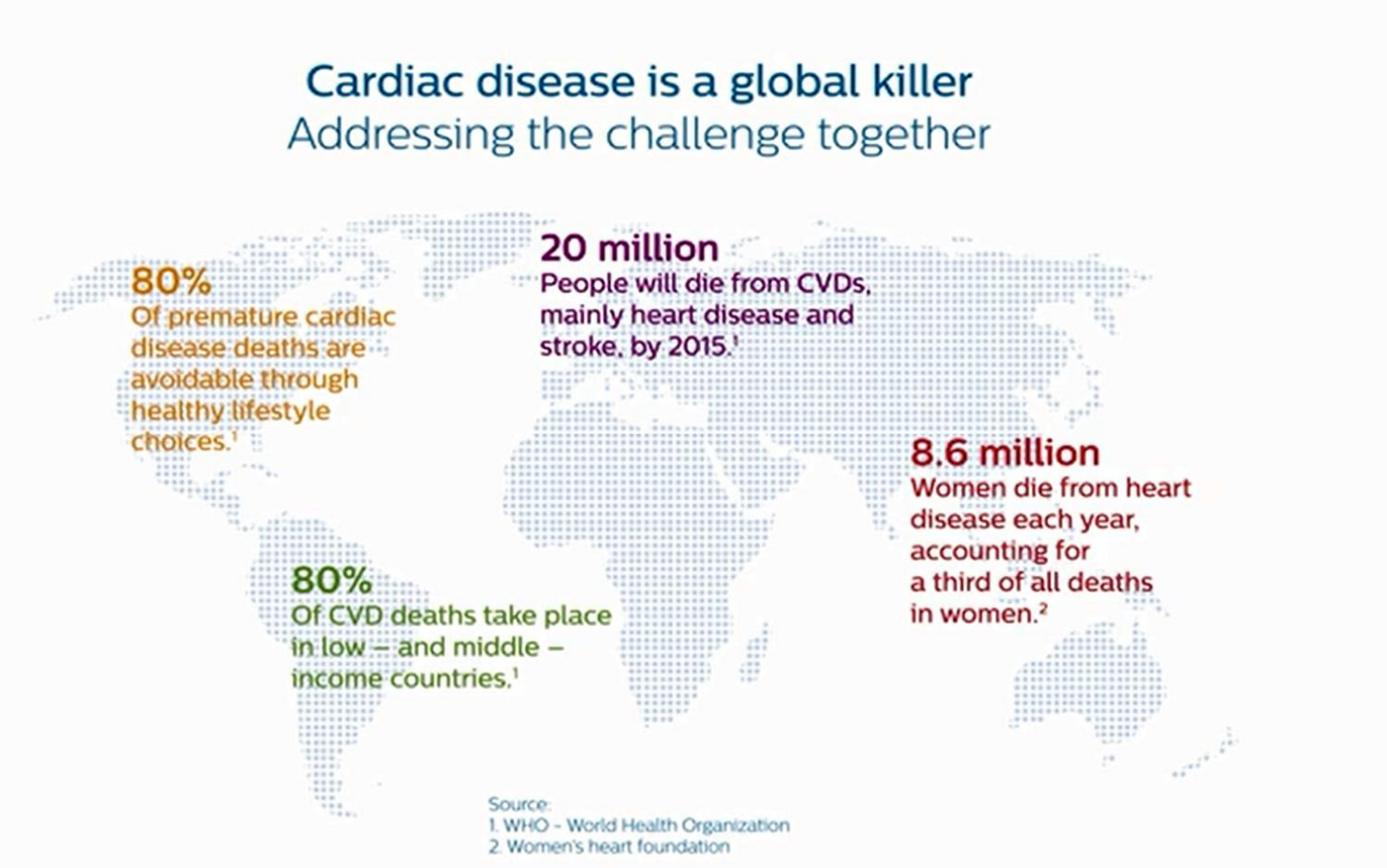
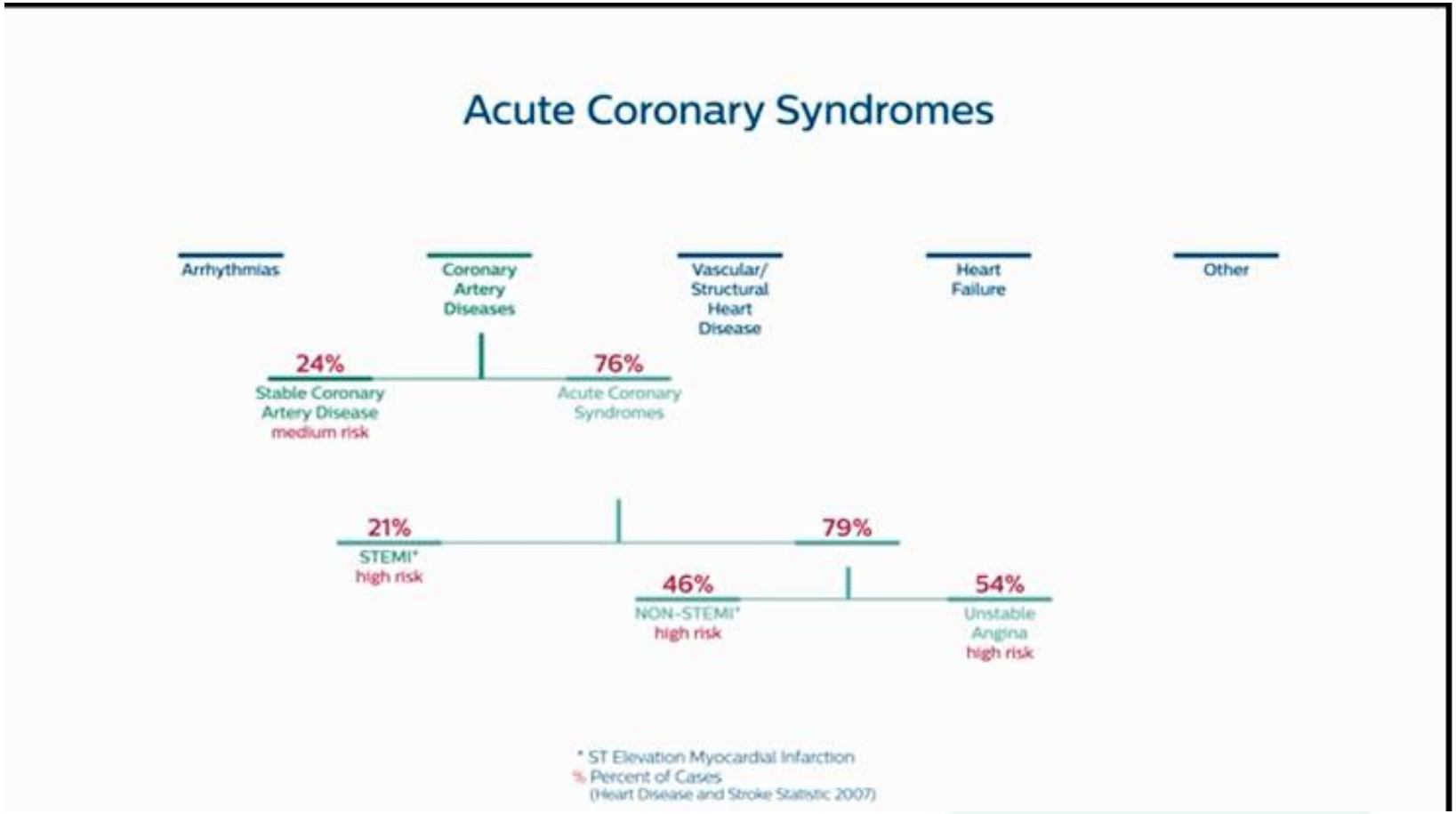
Corata 2016, Strasbourg

Introduction



Introduction



Biomarkers

- Significant impact in early detection of sub-clinical disease
- Diagnostic of acute or chronic syndromes
- Risk stratification
- Monitoring of disease or therapy

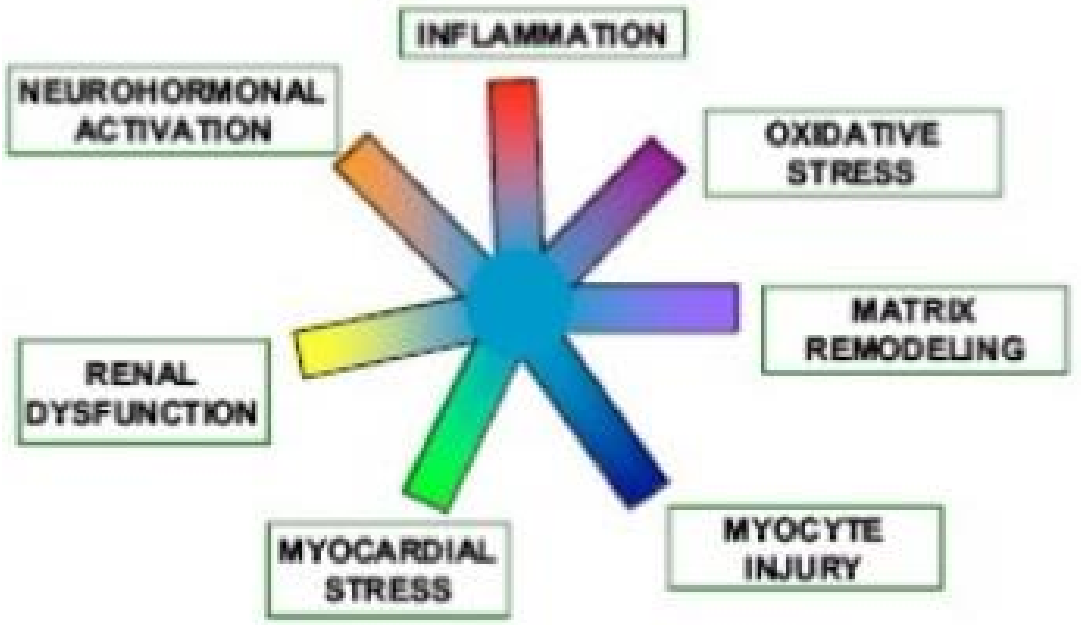
Biomarkers in cardiovascular medicine

Cardiac troponin I and T

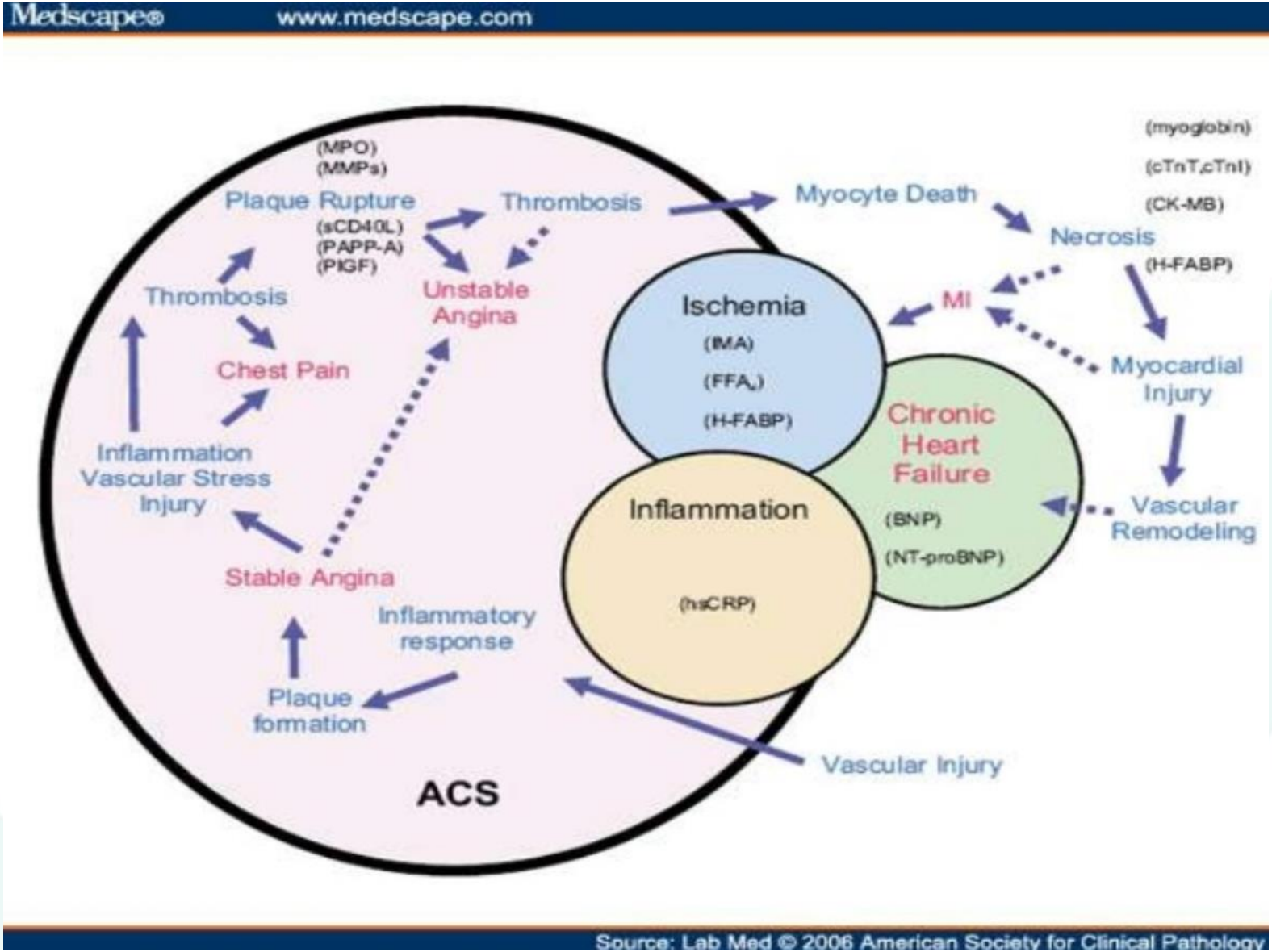
B-type natriuretic peptides (BNP and NT-proBNP)

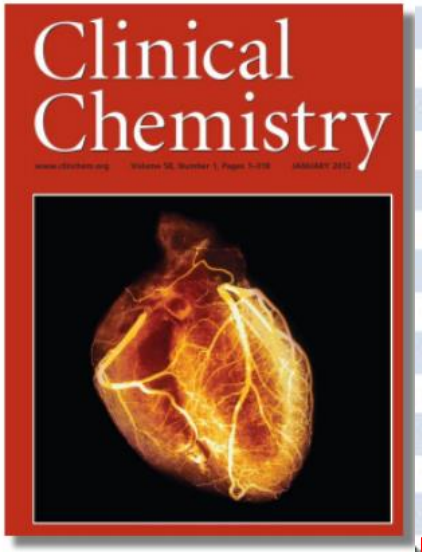
C-reactive protein(CRP)

Biomarkers in cardiovascular medicine



Biomarkers in cardiovascular medicine





Inflammation	Neurohormones
CRP	Norepinephrine
TNF-α	Renin
TWEAK (TNF-like weak inducer of apoptosis)	Angiotensin II
IL-1, −6, −10, and −18	Aldosterone
LP-PLA2 (lipoprotein-associated phospholipase A2)	Arginine vasopressin, copeptin
Soluble TNF receptors 1 and 2	Endothelin-1
YKL-40	Urocortin
IL-1 receptor antagonist	Chromogranin A and B
Midkine	MR-proADM
Leucine-rich 2-glycoprotein	**Myocyte injury and apoptosis**
PTX3	Troponins I and T
CA-125	Myosin light-chain kinase I
S100A8/A9 complex	Heart-type fatty-acid–binding protein
Osteoprotegerin	Creatine kinase MB fraction
Serine protease PR3	sFAS (soluble apoptosis-stimulating fragment)
Soluble endoglin	Heat shock protein 60
Adiponectin	sTRAIL (soluble TNF-related apoptosis-inducing ligand)
Oxidative stress	**Myocyte stress**
Oxidized LDLs	BNP, NT-proBNP, MR-proANP
MPO	sST2
Urinary biopyrrins	GDF-15
Urinary and plasma isoprostanes	**Extracardiac involvement**
Urinary 8-hydroxy-2′-deoxyguanosine	RDW
Plasma malondialdehyde	Cystatin-C, β-trace protein
Extracellular-matrix remodeling	NGAL, NAG [N-acetyl-β-(D)-glucosaminidase], KIM-1 (kidney injury molecule-1)
MMPs (MMP2, MMP3, MMP9)	β2-microglobulin
TIMP1	Urinary albumin-to-creatinine ratio
IL-6	Triiodothyronine
Collagen propeptides	
N-terminal collagen type III peptide	
Myostatin	
Syndecan-4	
Galectin-3	

Table 2. Clinical relevance of promising novel biomarkers.

Biomarker	Diagnosis	Prognosis	Therapy guidance	Cardiac production
NT-proBNP and BNP	++++	++++	++	Solely
MR-proANP	+++	++++	Likely similar to NT-proBNP/BNP	Solely
sST2	+	++++	?	Not exclusively
GDF-15	–	+++	?	Not exclusively
Highly sensitive troponins	+	++++	?	Solely
CRP	–	++	?	No
TNF-α	–	++	?	No
IL-6	–	++	?	No
PTX3	–	++	?	Unknown
MPO	–	++	?	Not exclusively
Gal-3	–	+++	?	Not exclusively
ET-1	–	++	?	Not exclusively
UCN-1	–	++	?	Not exclusively
Copeptin	–	++	?	No
MR-proADM	–	++++	?	No
RDW	–	++++	?	No
Cystatin C	–	++++	?	No
NGAL	–	++++	?	No
β-Trace protein	–	+++	?	No

Emerging Biomarkers in Heart Failure

Roland R.J. van Kimmenade[1] and James L. Januzzi, Jr.[2*]

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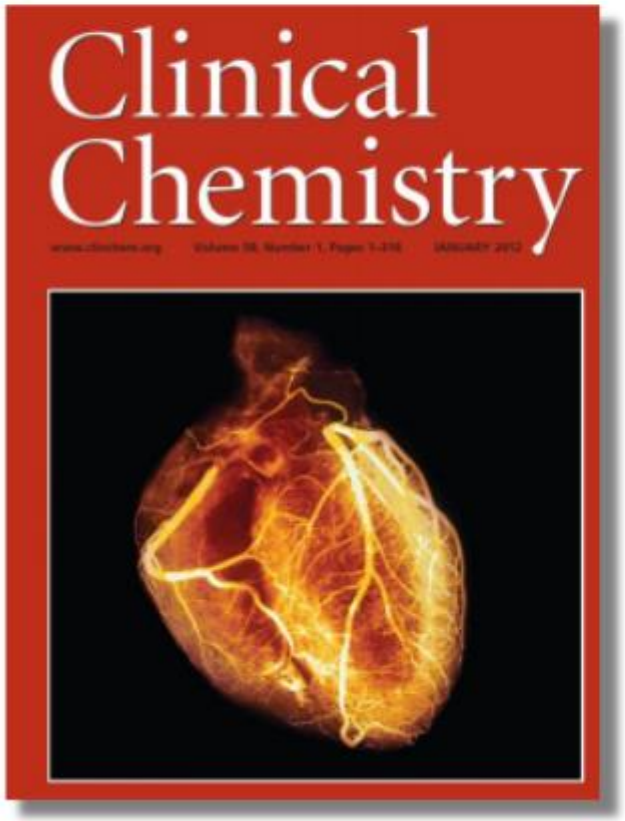


Novel markers should:

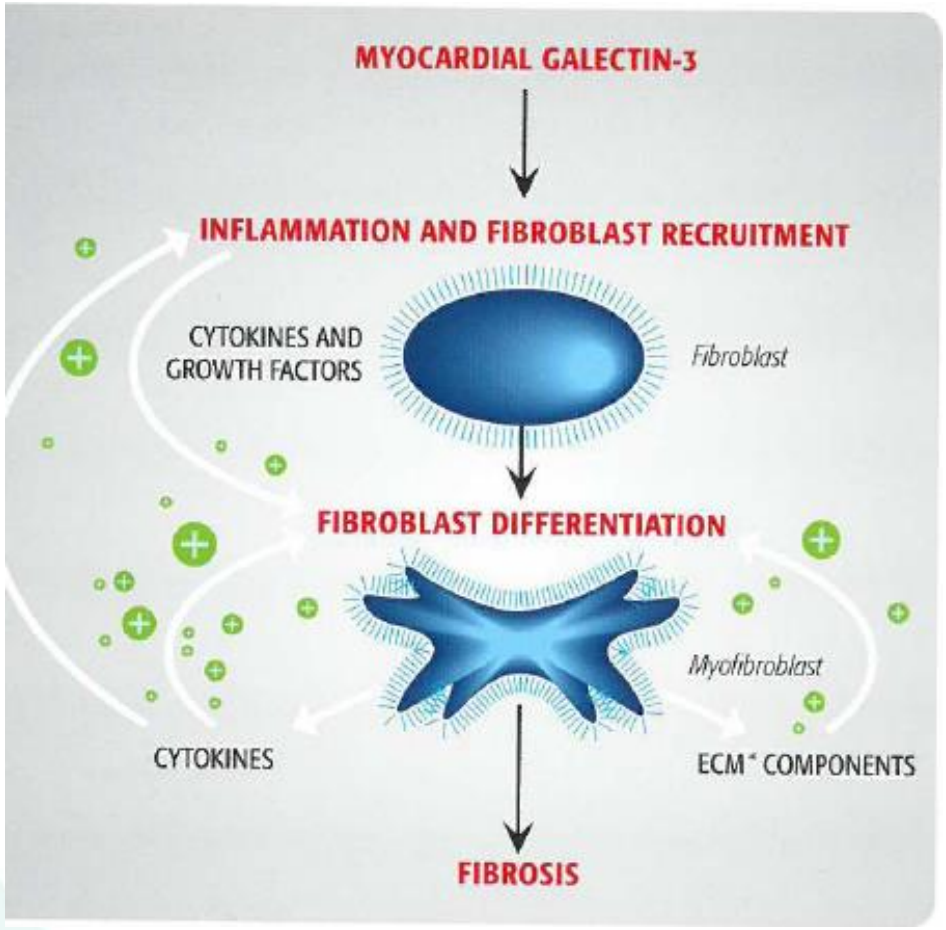
- **Be easy to measure and interpret**
- **Primarily reflect important processes involved in HF presence and progression**
- **Be independent of and additive to other biomarkers**
- **Add information about diagnosis or prognosis beyond that which is already known**
- **Should be useful for monitoring and treating**

Biomarkers in cardiovascular medicine

1. These new biomarkers can be useful for clinicians?
2. Can the clinicians easily measure the biomarker?
3. Does the biomarker add new information?
4. Will help the clinician manage patients?

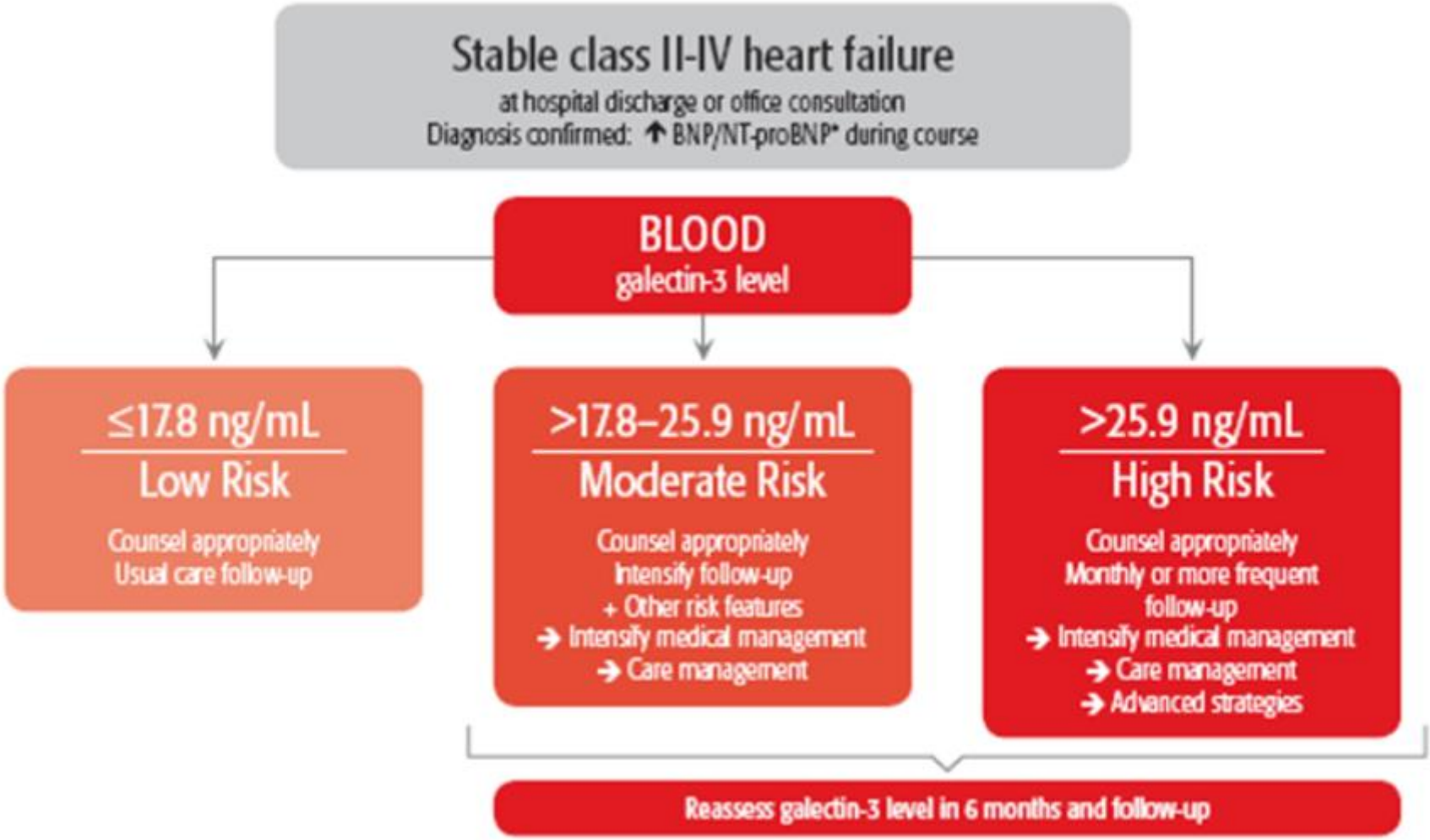
Galectin-3

Galectin-3



Galectin-3 is a beta-galactoside-binding lectin that appears to be a mediator of cardiac fibrosis in a number of recent experimental studies.

Galectin-3


Stable class II-IV heart failure
at hospital discharge or office consultation
Diagnosis confirmed: ↑ BNP/NT-proBNP* during course
BLOOD
galectin-3 level
≤17.8 ng/mL
Low Risk
Counsel appropriately
Usual care follow-up
>17.8–25.9 ng/mL
Moderate Risk
Counsel appropriately
Intensify follow-up
+ Other risk features
→ Intensify medical management
→ Care management
>25.9 ng/mL
High Risk
Counsel appropriately
Monthly or more frequent follow-up
→ Intensify medical management
→ Care management
→ Advanced strategies
Reassess galectin-3 level in 6 months and follow-up

Galectin-3

- After HF diagnosis
  - 60% men and 45% women die within 5y.

  (Ho JE et al, J Am Coll Cardiol 2012)
- Strategies to target patients with cardiac remodeling earlier
- Cardiac imaging is not recommended

Galectin-3

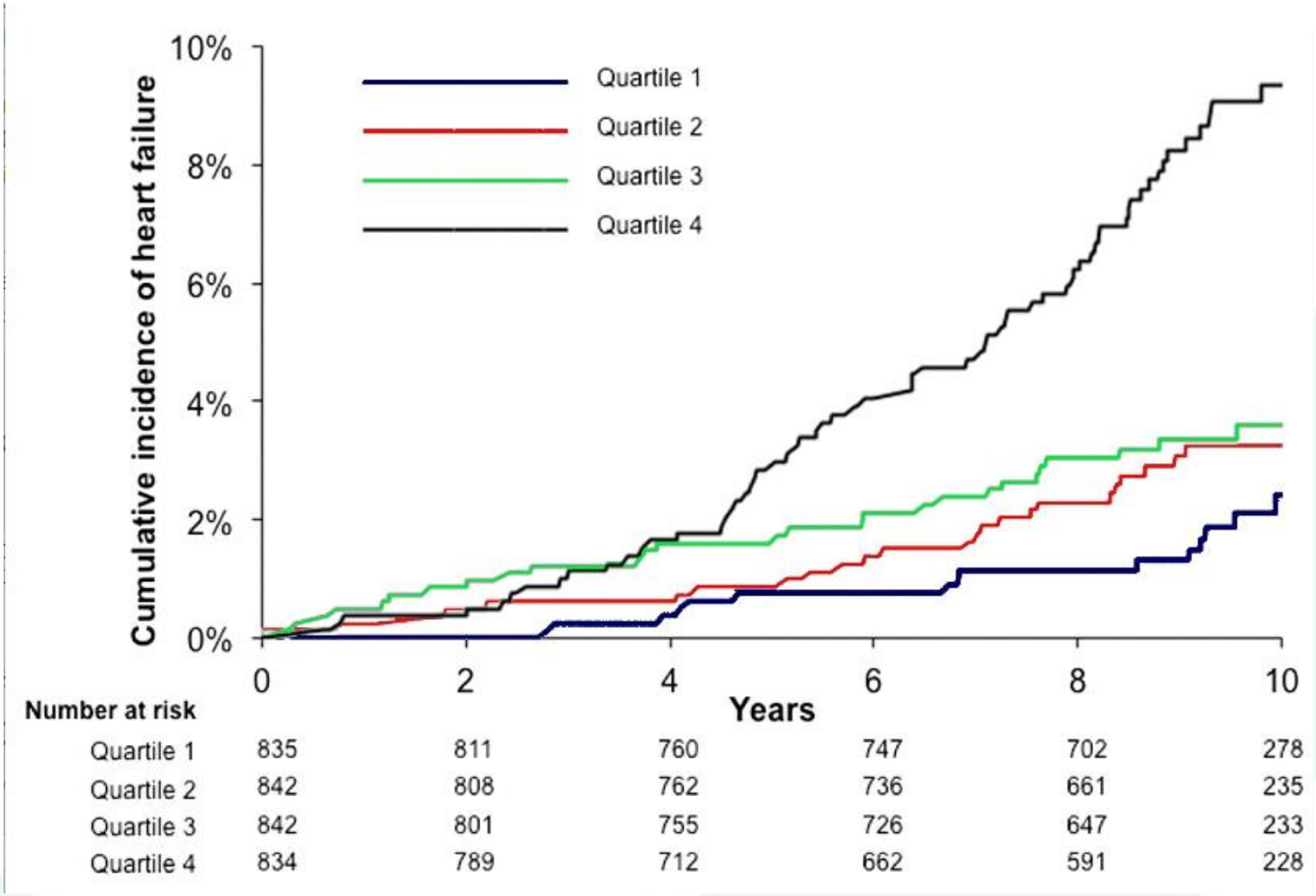
Clinical studies on the prognostic role

Study	Population	Outcome
HF-ACTION	CHF	Increased risk for all-cause and CV mortality and all-cause and HF-related hospitalization
COACH	CHF	Prognostic utility, stronger for HFpEF patients
DEAL-HF	CHF	Predictor of all-cause mortality, independent of natriuretic peptides
PRIDE	ADHF	Prognostic utility for 60 day mortality and death/recurrent HF
PROVE-IT TIMI 22	ACS	ACS patients with elevated Gal-3 were at higher risk for developing HF
PREVEND	Healthy	Elevated Gal-3 levels were associated with increased risk of long-term mortality
Framingham Offspring	Healthy	Elevated Gal-3 levels were associated with development of HF and long term mortality
CORONA	CHF	Predictive of long-term outcomes. Patients with low Gal-3 benefited more from statin therapy
CARE-HF	CHF	Elevated Gal-3 associated with death of HF hospitalization

Jennifer E. Ho, Galectin-3, a Marker of Cardiac Fibrosis, Predicts Incident Heart Failure in the Community, *Am Coll Cardiol*. October 02, 2012,60(14):1249-1256

Biomarkers in cardiovascular medicine

Framigham Study en 1941, prospective n=3353



Ho JE et al, J Am Coll Cardiol 2012

Galectine-3

- Higher circulating Gal-3 concentrations are associated with increased risk for new-onset HF and all-cause mortality in the community.

- Future potential clinical uses of Gal-3 measurement might include the identification of asymptomatic subjects with early evidence of cardiac fibrosis, in whom targeted therapies may be useful to delay the onset of HF.

- Animal data suggest that Gal-3 is a mediator of fibrosis, and directly targeting the Gal-3 pathway may represent a future preventive treatment strategy.

Copeptin

Copeptin

- Copeptin is the C-terminal fragment of the vasopressin precursor hormone and directly mirrors vasopressin production since it is stoichiometrically co-secreted.

- Physiological stress and shock hormone and released in response to low blood pressure,temperature,cytokines,endogenous stress, and hypoxemia.

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- Physiological stress and shock hormone
- Released in response to
  - Low blood pressure
  - Temperature
  - Cytokines
  - Endogenous stress
  - Hypoxemia

Copeptin

- Short halftime in vivo.
- The major advantage of copeptin compared to vasopressin is its longer half life in the circulation that makes it easier to measure.
- Combination of copeptin with troponin significantly improved the AMI diagnostic performance (ROC= 0.97).

Hochhlozer and al.American Heart Journal, 2010
Neuhold S et al. JACC2008;52:266

Copeptin

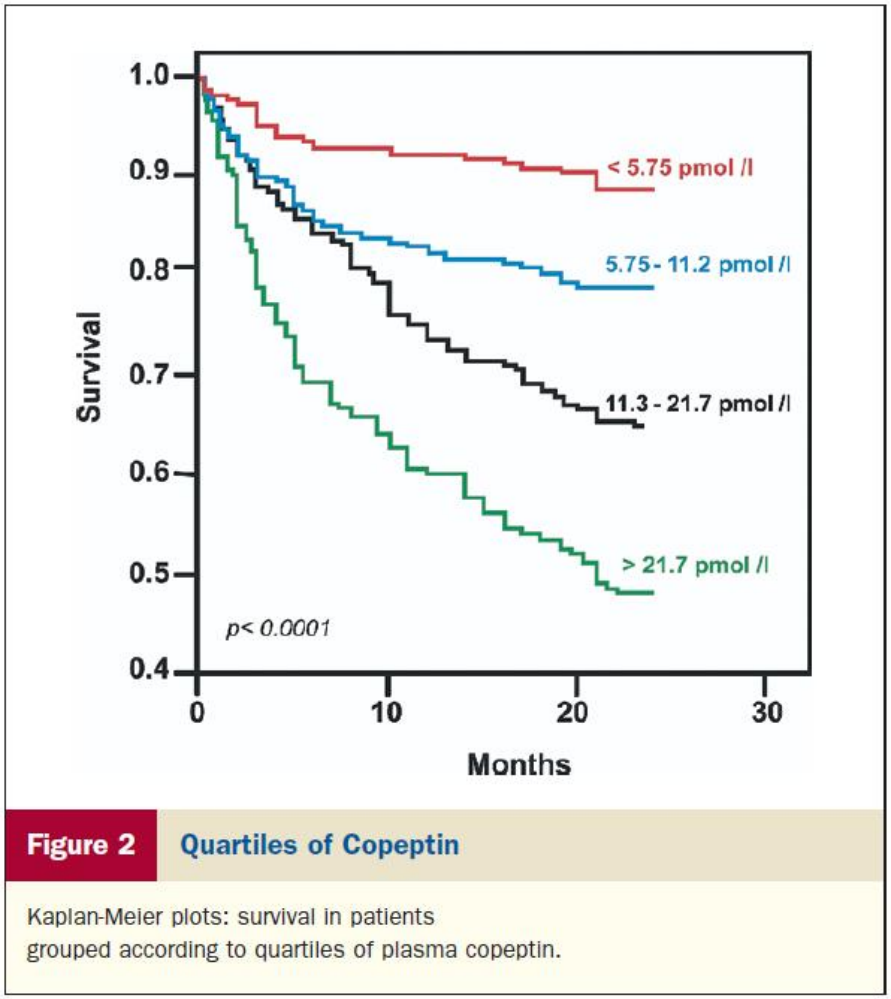


Figure 2 Quartiles of Copeptin

Kaplan-Meier plots: survival in patients grouped according to quartiles of plasma copeptin.

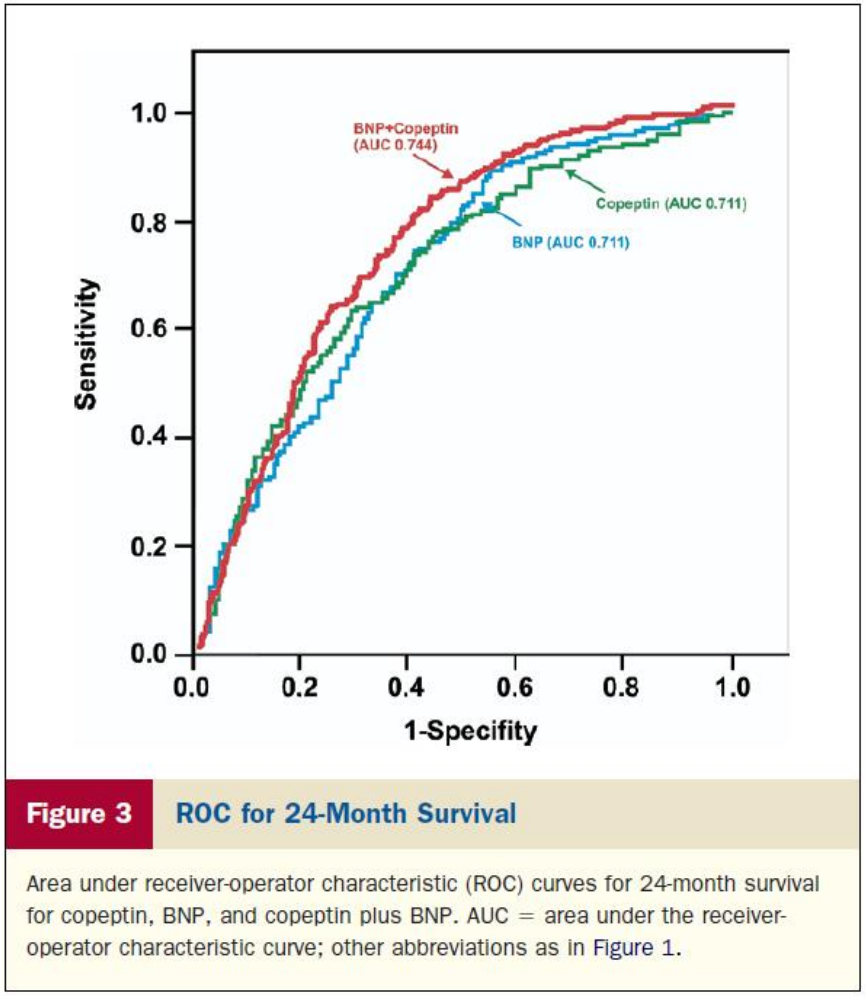


Figure 3 ROC for 24-Month Survival

Area under receiver-operator characteristic (ROC) curves for 24-month survival for copeptin, BNP, and copeptin plus BNP. AUC = area under the receiver-operator characteristic curve; other abbreviations as in Figure 1.

N=786 (NYHA) Neuhold S et al. JACC2008;52:266

GDF15

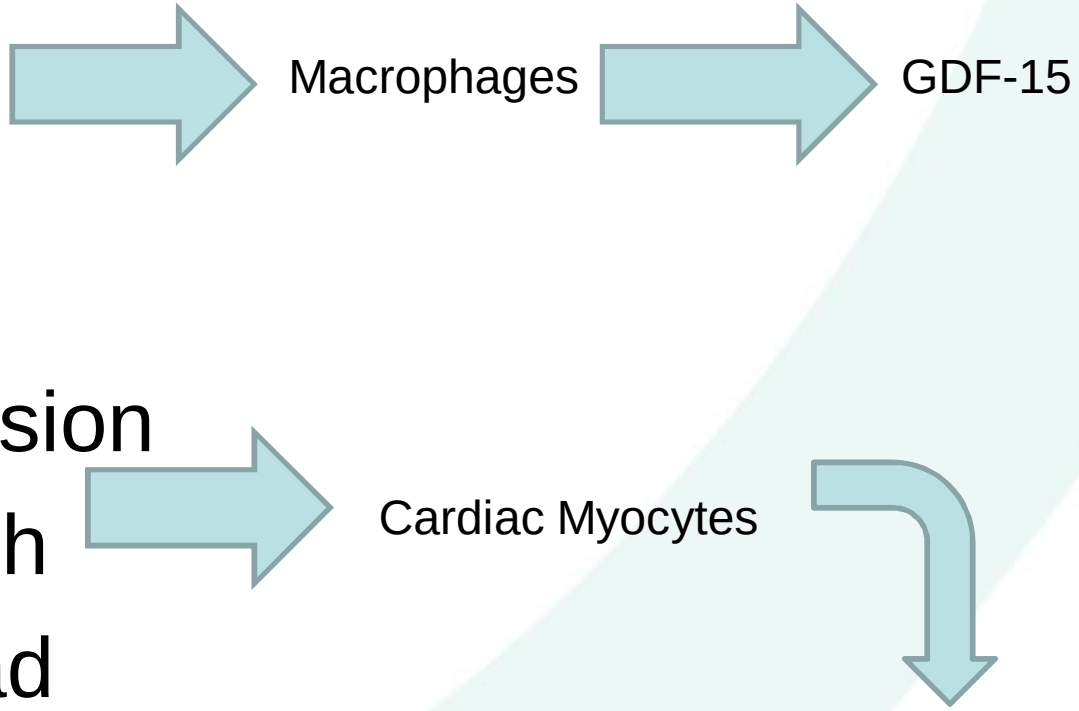
GDF-15

- A distinct up-regulation has been found in a wide range of cancers and in many tissues following injury, ischemia, and other forms of stress.
- Cardiomyocytes express and secrete GDF-15 in the setting of ischemia and reperfusion, suggesting that it might be a protective factor.

GDF-15

Growth differentiation factor 15 (GDF-15) is one of the more than 40 members of the transforming growth factor-ß superfamily

- Oxidative Stress
- Oxidized LDL
- Inflammatory Cytokines
- Ischemia/reperfusion
- Mechanical strech
- Pressure overload
- Heart failure



GDF-15

Higher GDF-15 levels

- Higher age
- Current smoking
- Physical activity
- Diabetes
- Acute or chronic inflammation
- Genetic factors
- Renal dysfunction
- Anemia and bleeding
- Vascular disease
- Heart failure
- Atrial fibrillation
- Cancer

GDF-15

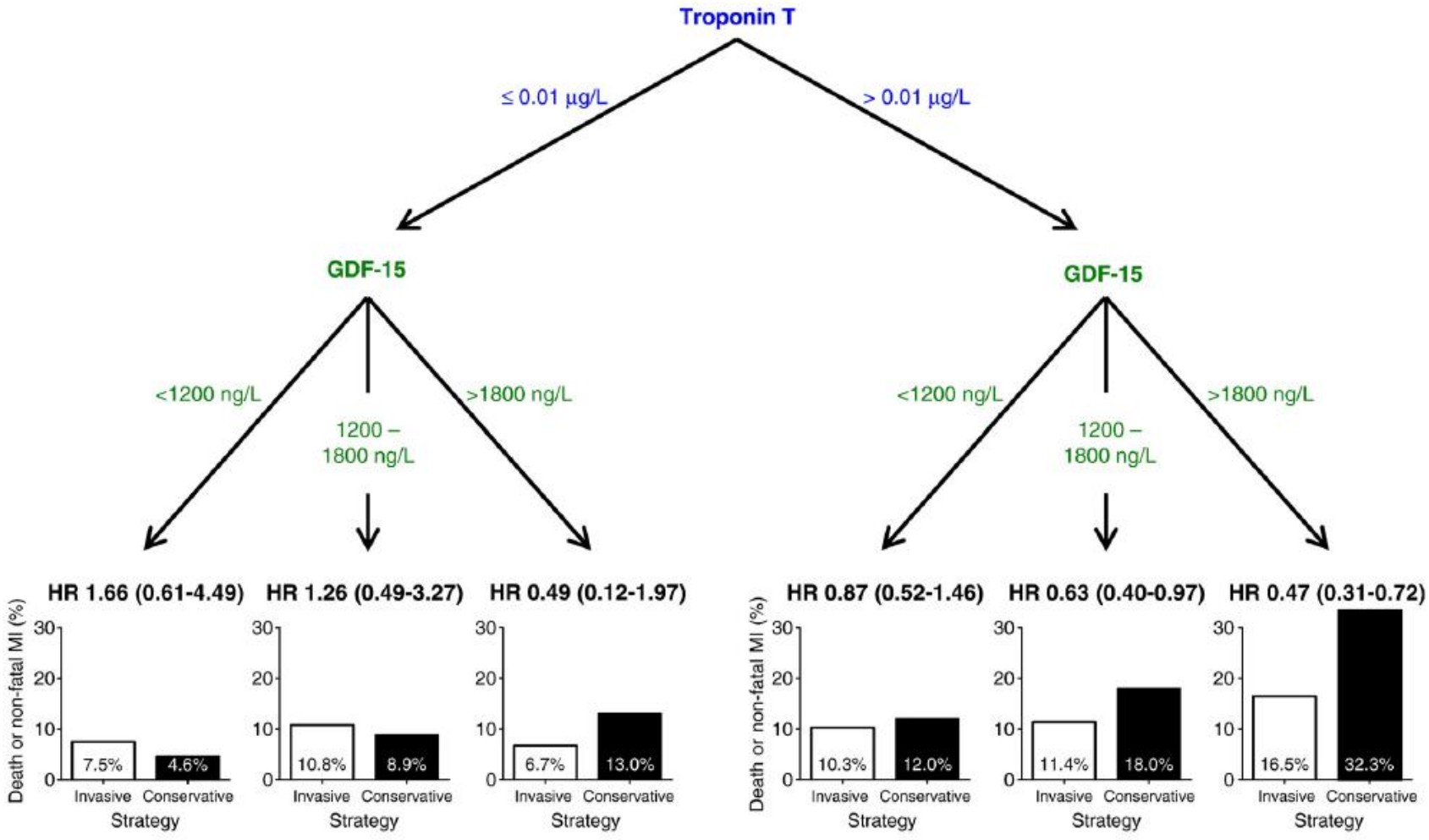
Disease/population/follow-up period	Sample size	Major findings
Acute myocardial infarction [AMI]	1142	GDF-15 is a prognostic marker of death and HF in patients with AMI Multimarker approach with GDF-15 and NT-pro-BNP is more informative than either marker alone and may be useful for risk stratification in AMI patients
Acute coronary syndrome [ACS] (PROVE IT-TIMI 22)	3501	GDF-15 is altered with recurrent events after ACS. GDF-15 may be used as a prognostic marker in ACS
Human model of acute muscle wasting following cardiac surgery	42	GDF-15 is a potential novel factor associated with muscle atrophy, which may become a therapeutic target in patients with ICU acquired paresis and other forms of acute muscle wasting
Non–ST-elevation ACS (FRISC-II) trial (2 years)	2079	GDF-15 is a potential tool for risk stratification and therapeutic decision making in patients with non-ST-elevation acute coronary syndrome
General adult population (Dallas Heart Study) (7.3 years follow up period)	3219	GDF-15 is independently marker for subclinical coronary atherosclerosis and mortality
Framingham Offspring cohort participants (9.5 years follow up period)	2614	Higher circulating GDF-15 was observed with incident renal outcomes and improves risk prediction of incident chronic kidney diseases (CKD)
Hypertensive left ventricular hypertrophy (H-LVH), hypertensive cardiomyopathy (HCM)	149	GDF-15 might be a useful biomarker for discriminating HCM from H-LVH

Ramu A.et al. Journal of Diabetes Research(2015)

GDF-15

Patients with stable ischemic heart disease (Heart and Soul study) (8.9 yrs follow-up period)	984	Higher GDF-15 level was observed with major cardiovascular (CV) events in patients with stable ischemic heart disease
Untreated hypertensive patients	299	Plasma GDF-15 level was increased with LVH in hypertensive patients
71-year-old men (ULSAM study)	940	In elderly men, GDF-15 improves progression of both cardiovascular, cancer mortality, and morbidity beyond established risk factors and biomarkers of cardiac, renal dysfunction, and inflammation
Heart failure (Val-HeFT study)	1734	Providing independent prognostic information in heart failure
Coronary artery diseases (CAD)	CAD (n = 348) and (n = 205) controls	Significant differences of GDF-15, IMA, and PAPP-A in patients with CAD. GDF-15 might be associated with severity of CAD
Coronary Artery Bypass Grafting with Cardiopulmonary Bypass	34 patients	GDF-15 levels were increased substantially and it is associated with the renal and cardiac biomarkers
Patients on maintenance hemodialysis	Hemodialysis (n = 87), and controls (n = 45)	Relation between GDF-15, mortality, and carotid artery thickening suggests that GDF-15 may be a novel marker of atherosclerosis, inflammation, and malnutrition in hemodialysis patients
ST segment elevation myocardial infarction (STEMI) (3 years)	Patients with STEMI (n = 216)	High GDF-15 level is a strong predictor of death and heart failure in patients with STEMI. Although patients with higher GDF-15 levels tend to have lower LV ejection fraction
Acute chest pain (APACE study)	646	GDF-15 is a better predictor of mortality than of nonfatal CV events

GDF-15



Hochholzer WD et al,Am Heart J 2010;160:583-94

GDF-15

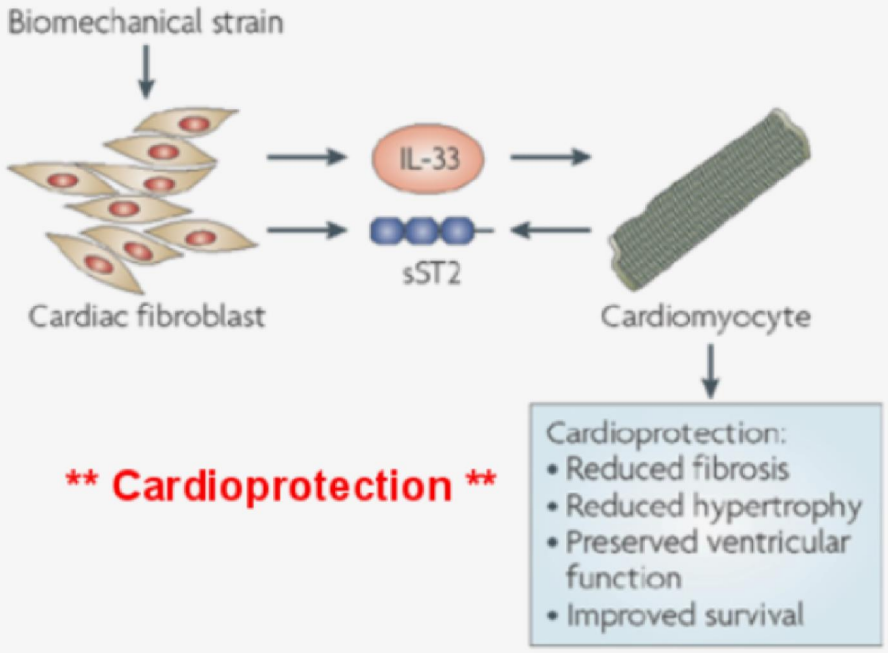
- GDF-15 could be a prognostic and diagnostic marker for the cardiovascular diseases.
- Proper reference ranges of GDF-15 need to be established to identify the disease severity and risk stratification of the diseases
- Questions
  - (1) Whether GDF-15 measurement can support therapeutic management?
  - (2) Can it be used for the routine clinical practice or clinical measurement?
  - (3) Whether GDF-15 level can give any diagnostic and prognostic information?
  - (4) Whether it can be used to take clinical decision for any particular diseases like B-type natriuretic peptide (BNP) for the heart failure and troponin for the acute coronary syndrome (ACS).
  - (5) GDF-15 can be used as a single marker or multi marker approach along with other individual marker.

ST2

ST2

ST2 and IL-33: Cardioprotective

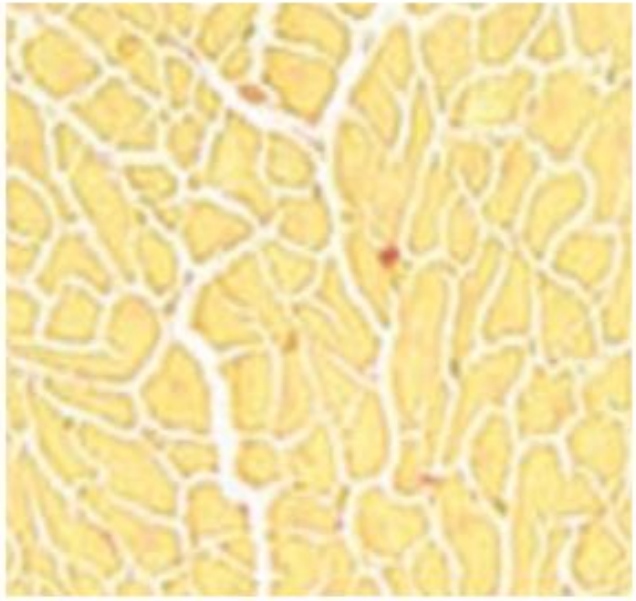
- ST2: member of the Interleukin-1 receptor family
- Exists in two main isoforms
  - ST2L
  - Circulating sST2
- IL-33 binding to ST2L triggers cardioprotective effects.



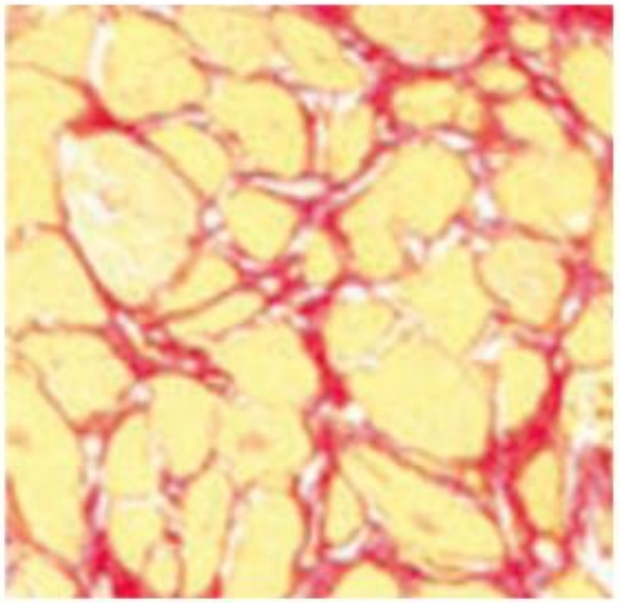
Kakkar et al. Nat Rev Drug Discov 2008

ST2 plays a role in reducing cardiomycyte hypertrophy and fibrosis

Intact sST2



sST2 knock out



ST2

- Is NOT a stretch marker
- Is NOT an inflammatory marker
- Is a marker of fibrosis and cardiac remodeling providing prognostic guidance
- Clinical use is not effected by typical confounders such as obesity and renal impairment!!!

ST2

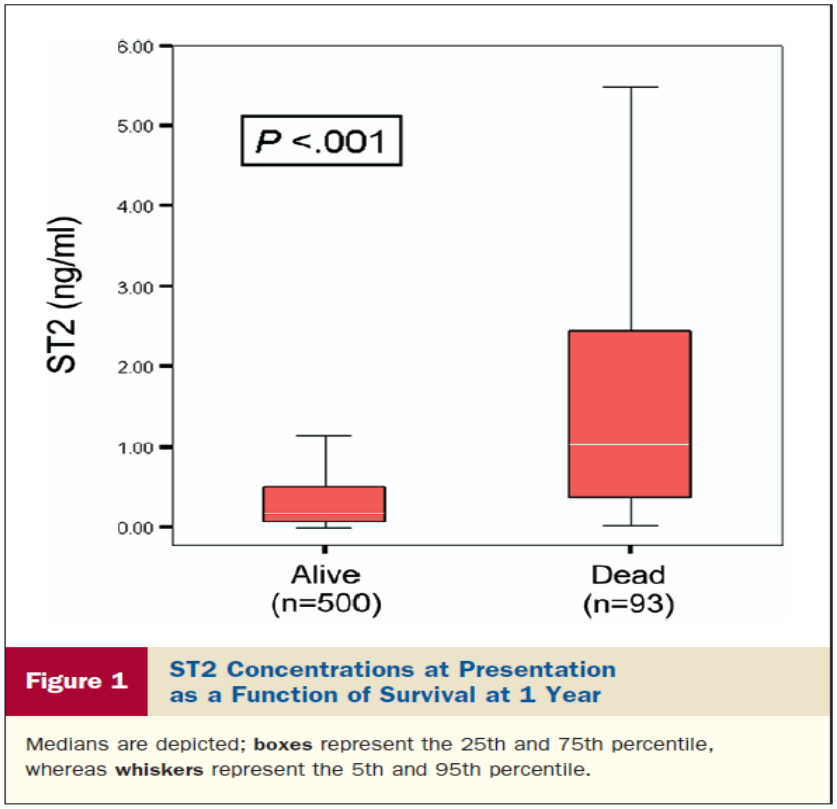


Figure 1 **ST2 Concentrations at Presentation as a Function of Survival at 1 Year**

Medians are depicted; **boxes** represent the 25th and 75th percentile, whereas **whiskers** represent the 5th and 95th percentile.

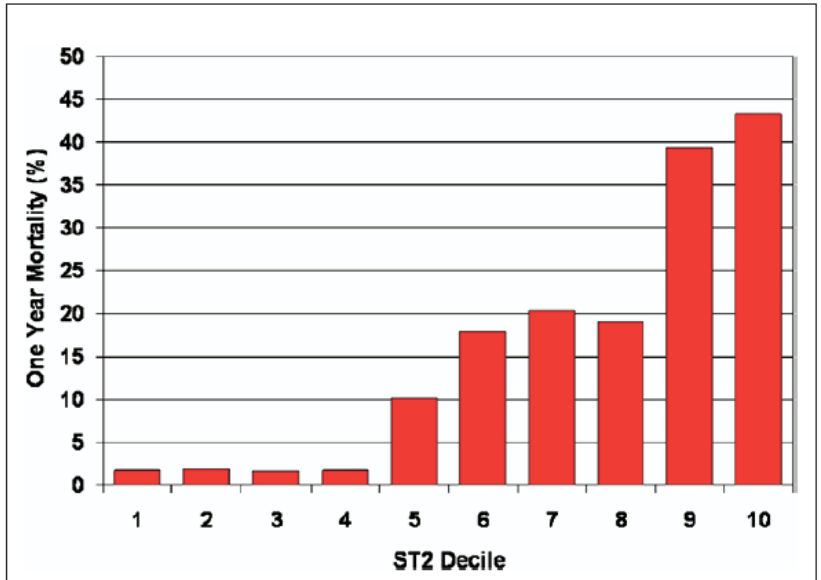


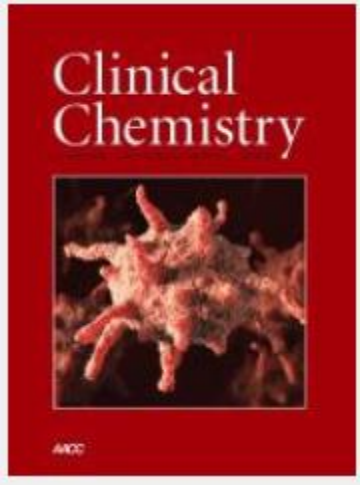
Figure 2 **Rates of Death at 1 Year as a Function of ST2 Decile in Dyspneic Patients**

Rates of death at 1 year as a function of ST2 concentrations in dyspneic patients.

Results From the PRIDE (Pro-Brain Natriuretic Peptide Investigation of Dyspnea in the Emergency Department) Study - Januzzi J. et al, JACC 2007

ST2

- Increased sST2 is an independent predictor of long-term all-cause mortality and provide complementary prognostic information to hs-cTnT and NT-proBNP

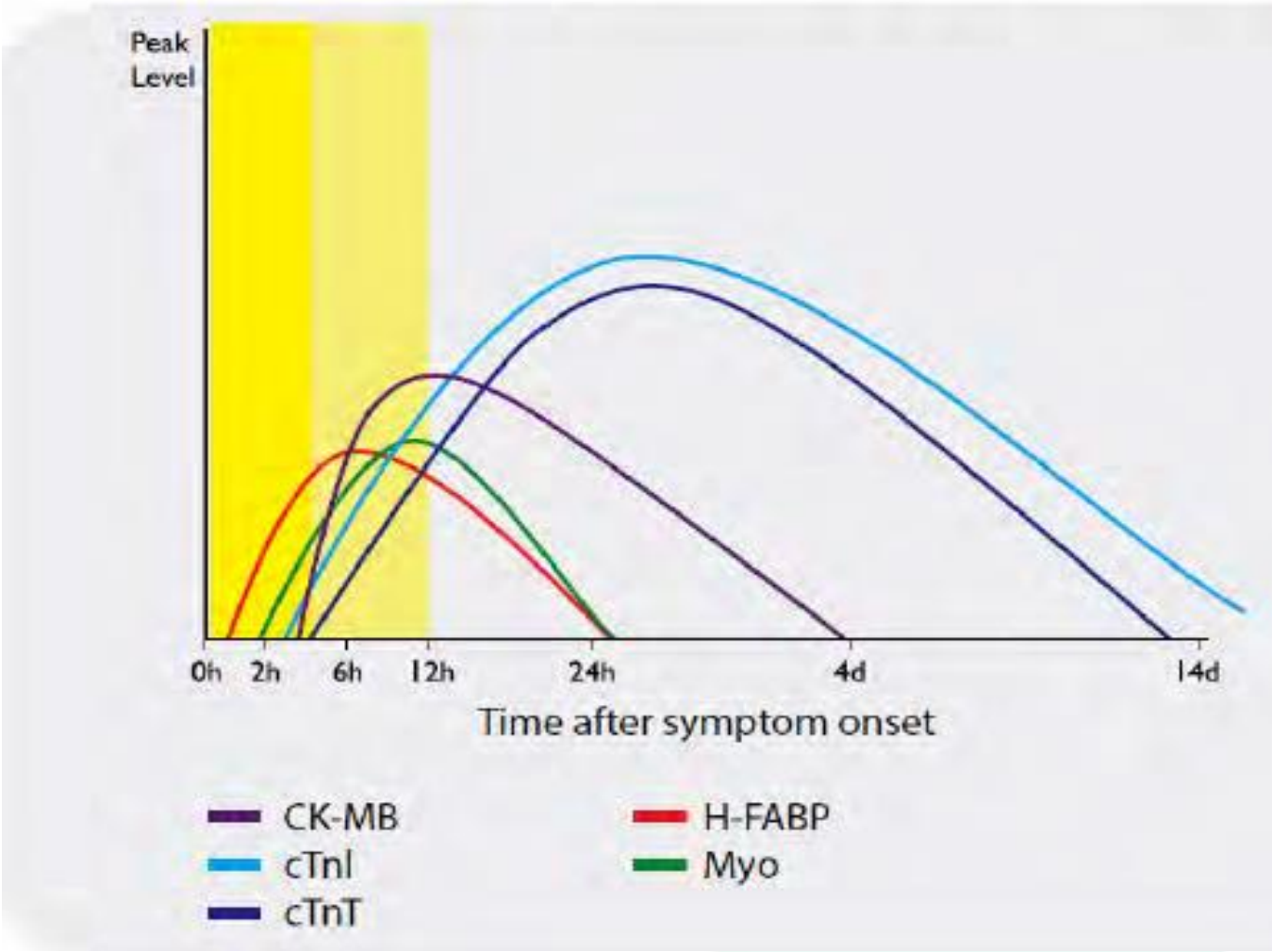


Dieplinger, Clin Chem 2013

H-FABP (heart-type fatty acid binding protein)

- ✓ Stable protein located in the cytoplasm
- ✓ Abundant in the heart (muscle, brain)
- ✓ Early rise marker of AMI (30 min following the onset of an ischemic episode)
- ✓ Combination with Tn improve the diagnostic sensitivity for AMI

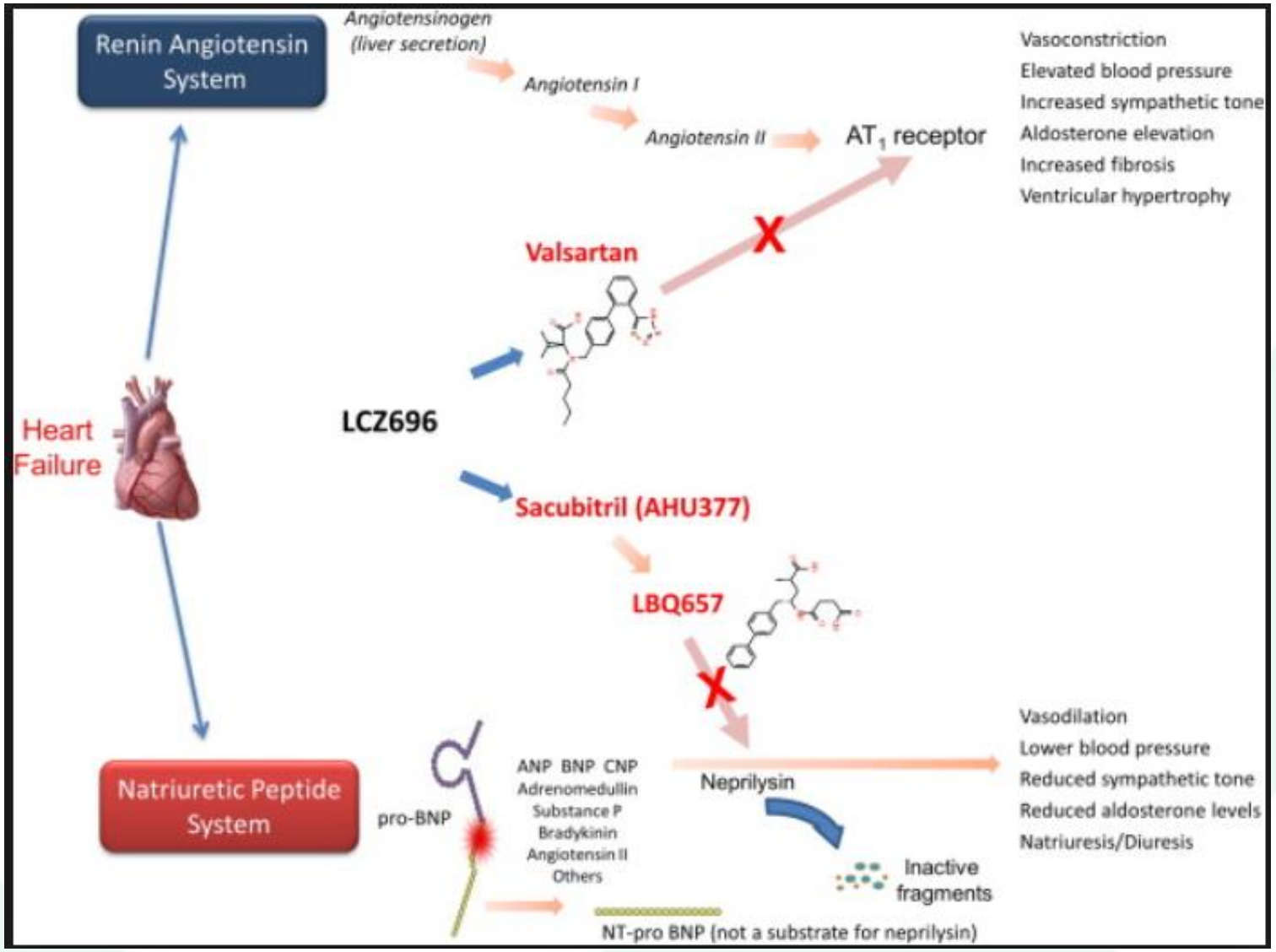
H-FABP (heart-type fatty acid binding protein)



H-FABP (heart-type fatty acid binding protein)

Entresto

Entresto


Renin Angiotensin System
Angiotensinogen (liver secretion)
Angiotensin I
Angiotensin II
AT1 receptor
Vasoconstriction
Elevated blood pressure
Increased sympathetic tone
Aldosterone elevation
Increased fibrosis
Ventricular hypertrophy
Valsartan
X
LCZ696
Heart Failure
Sacubitril (AHU377)
LBQ657
X
Natriuretic Peptide System
pro-BNP
ANP BNP CNP
Adrenomedullin
Substance P
Bradykinin
Angiotensin II
Others
Neprilysin
Inactive fragments
Vasodilation
Lower blood pressure
Reduced sympathetic tone
Reduced aldosterone levels
Natriuresis/Diuresis
NT-pro BNP (not a substrate for neprilysin)

BNP???

- Protease neprilysin is known to be responsible for the degradation of natriuretic peptides.
- Increase the circulating B-type natriuretic peptide (BNP) concentrations, making the results of BNP measurements diagnostically ambiguousé ..

Semenov et al., Different Susceptibility of B-Type Natriuretic Peptide (BNP) and BNP Precursor to Cleavage by Neprylisin,Clinical chemistry 2016, 62:4

Entresto

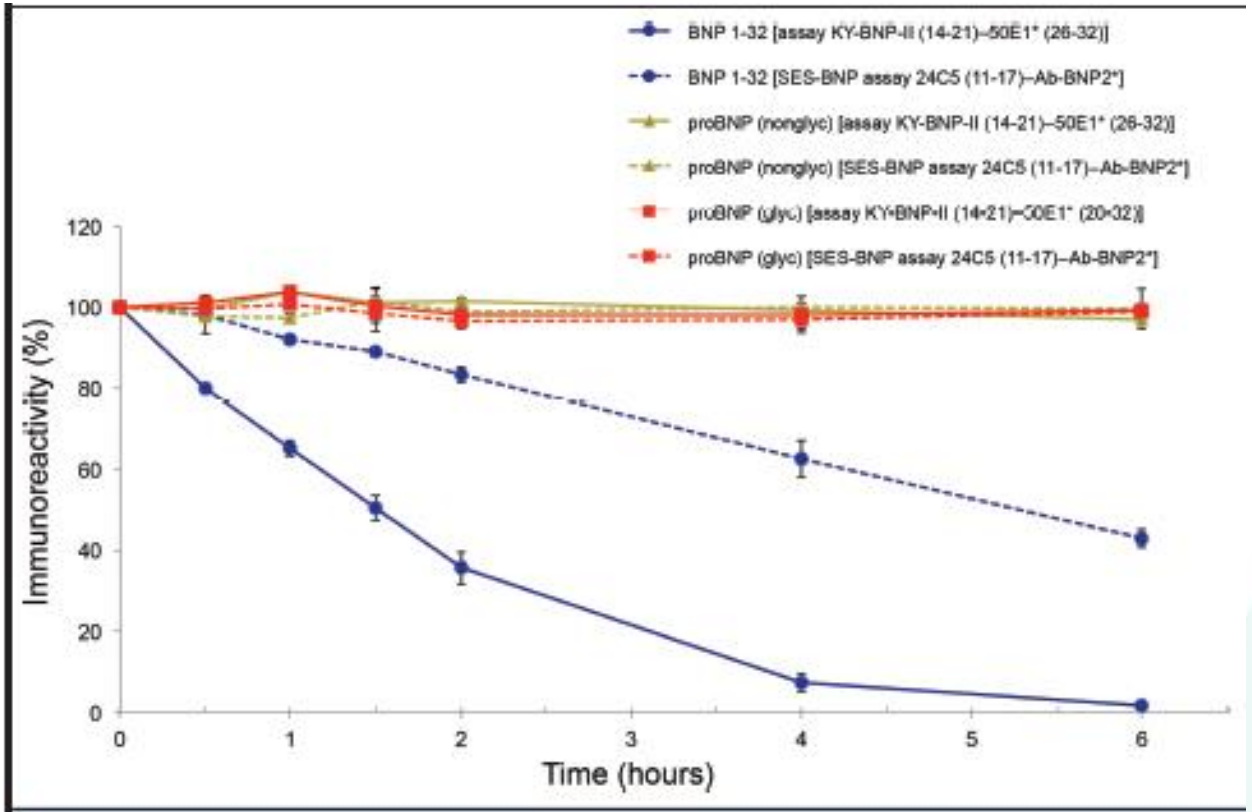


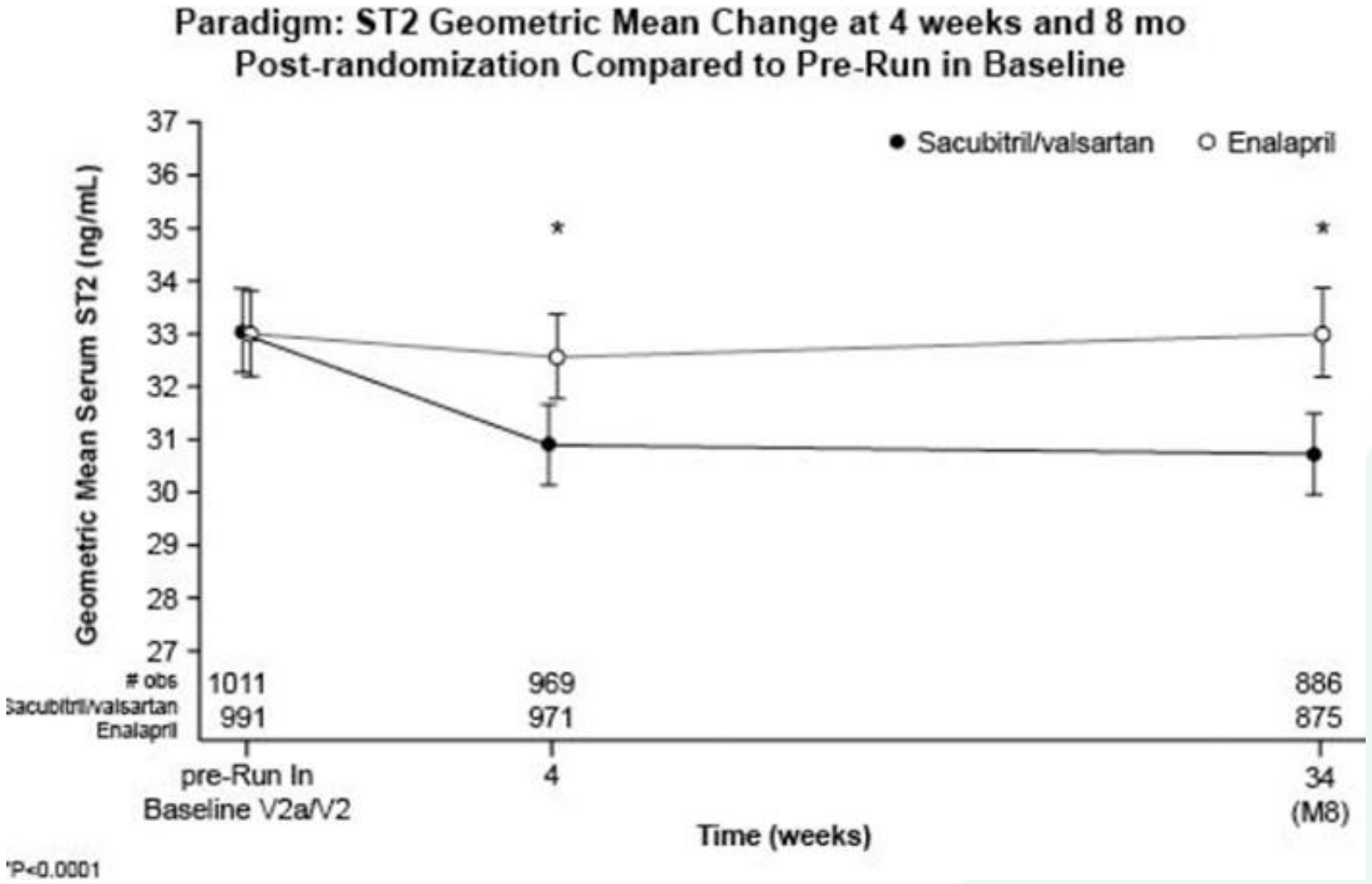
Fig. 1. Degradation of BNP 1–32, nonglycosylated (expressed in *E. coli*) and glycosylated (expressed in mammalian cells) proBNP 1–108 by the action of neprilysin.

The immunoreactivity of BNP, nonglycosylated and glycosylated proBNP was measured by the KY-BNP-II (14–21)–50E1 (26–32) assay and the SES-BNP assay (24C5 (11–17) Ab-BNP2).

The immunoreactivity was calculated as (immunoreactivity in neprilysin-treated sample/immunoreactivity in nontreated sample) × 100%. The data are presented as the mean (n = 3) (SD).

Semenov et al., Different Susceptibility of B-Type Natriuretic Peptide (BNP) and BNP Precursor to Cleavage by Neprylisin,Clinical chemistry 2016, 62:4

ST2



STOP GUIDE IT

Journal of Cardiac Failure 2016 22, S29-S30DOI: (10.1016/j.cardfail.2016.06.094

Troponins

Troponins

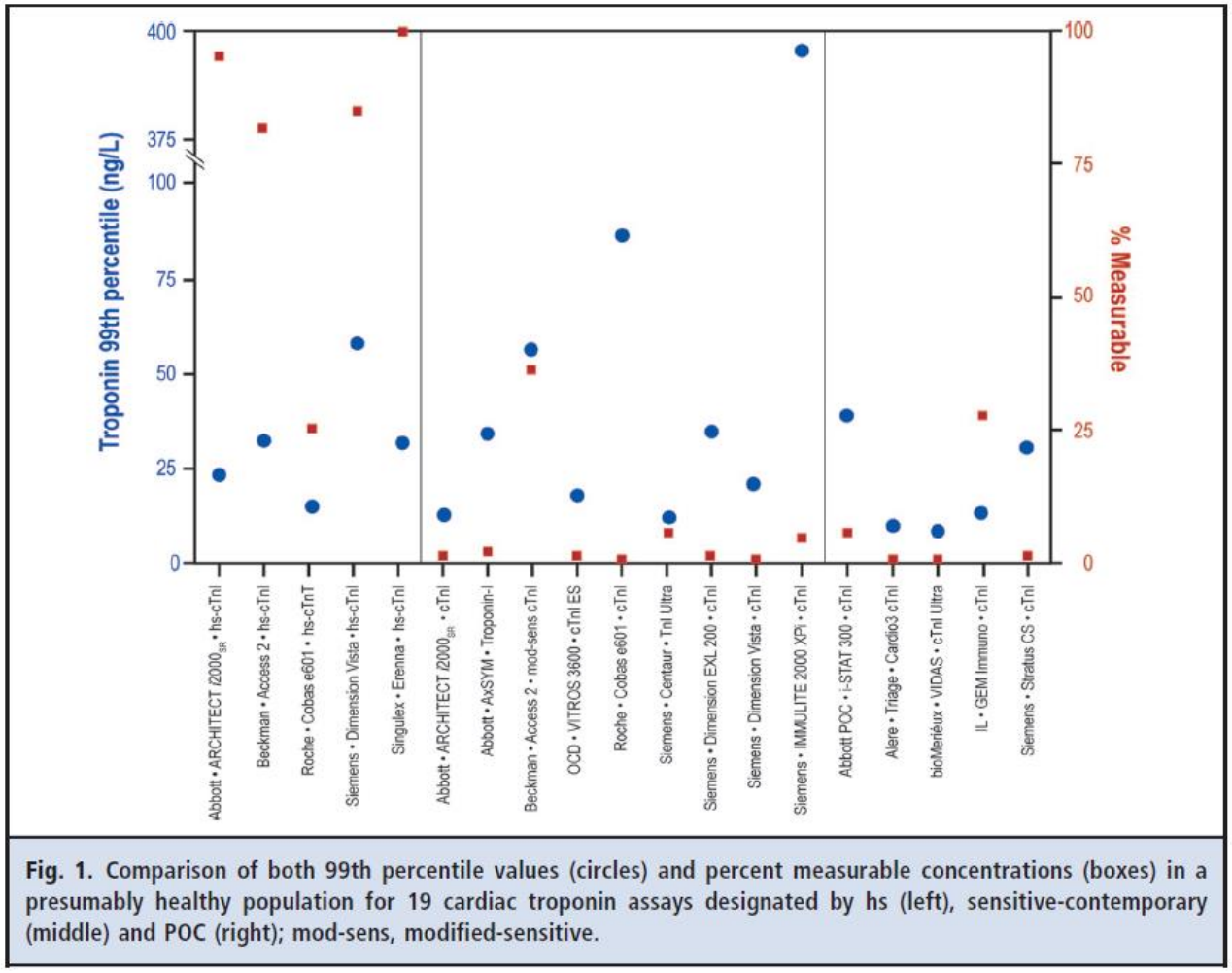


Fig. 1. Comparison of both 99th percentile values (circles) and percent measurable concentrations (boxes) in a presumably healthy population for 19 cardiac troponin assays designated by hs (left), sensitive-contemporary (middle) and POC (right); mod-sens, modified-sensitive.

Determination of 19 cardiac troponin I and T assay 99th percentile values from a common presumably healthy population. Apple FS, Ler R, Murakami MM. Clin Chem. 2012 Nov;58(11):1574-81

Troponins

Classification of Troponin assays

The 2 criteria of Fred Apple's scorecard

Scorecard designations of cTn assays	
Acceptance designation	**Total imprecision at the 99th percentile, CV%**
Guideline acceptable	≤10
Clinically usable	>10 to ≤20
Not acceptable	>20
Assay designation	**Measurable normal values below the 99th percentile, %**
Level 4 (third generation, hs)	≥95
Level 3 (first generation, hs)	75 to <95
Level 2 (first generation, hs)	50 to <75
Level 1 (contemporary)	<50

Precision (Guideline compliance) criteria

High Sensitivity criteria

High sensitive troponin I and T assays meet the follow 2 basic criteria:

- **CV** at the **99th percentile** value should be **≤10%**
- Concentrations below the 99th percentile should be detectable for at least **50%** (ideally ≥95%) of healthy individuals

Apple, F.S. (2009). A new season for cardiac troponin assays: It's time to keep a scorecard. *Clin Chem, 55,* 1303-6.

Troponins

- AMI
- Myocarditis
- Pulmonary embolism
- Acute heart failure
- ESRD
- AVNRT

cTnT 4th gen.

Troponins

- AMI
- Myocarditis
- Pulmonary embolism
- Acute heart failure
- ESRD
- AVNRT

cTnT 4th gen.

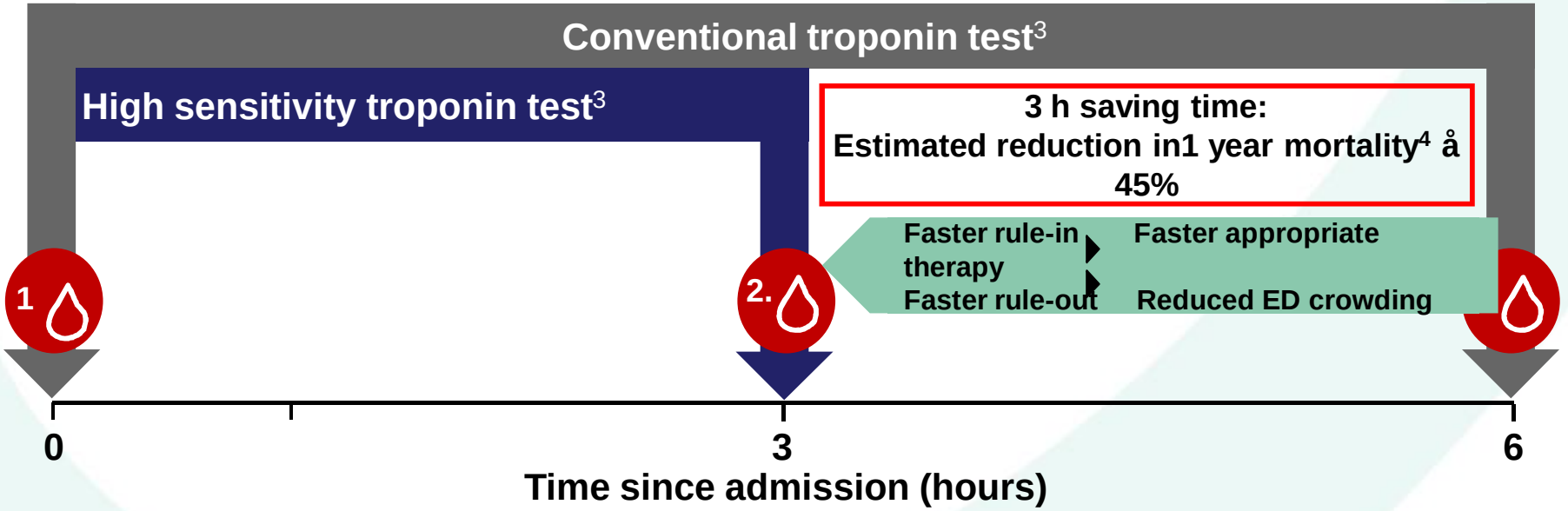
cTnT-hs

- Small NSTEMI or type II MI
- Myocardial injury
- Chemotoxic
- Hypertensive crisis
- Earlier stages of CKD
- Marathon run
- Chronic PAH
- Chronic heart failure
- Stable CAD
- Tachycardia
- Myocardial ischemia ?

Troponins

Is a safe AMI diagnosis possible in a shorter time?

- First studies demonstrate (2009-2010) that with cTnT-hs the time to diagnosis of NSTEMI was made **2h55 min** earlier with cTnT-hs than with cTnT Gen 4 [1,2]
- A rapid rule-out protocol (0 and 3h) has been recommended in 2011 by the ESC task force when hs cTn tests are available [3]



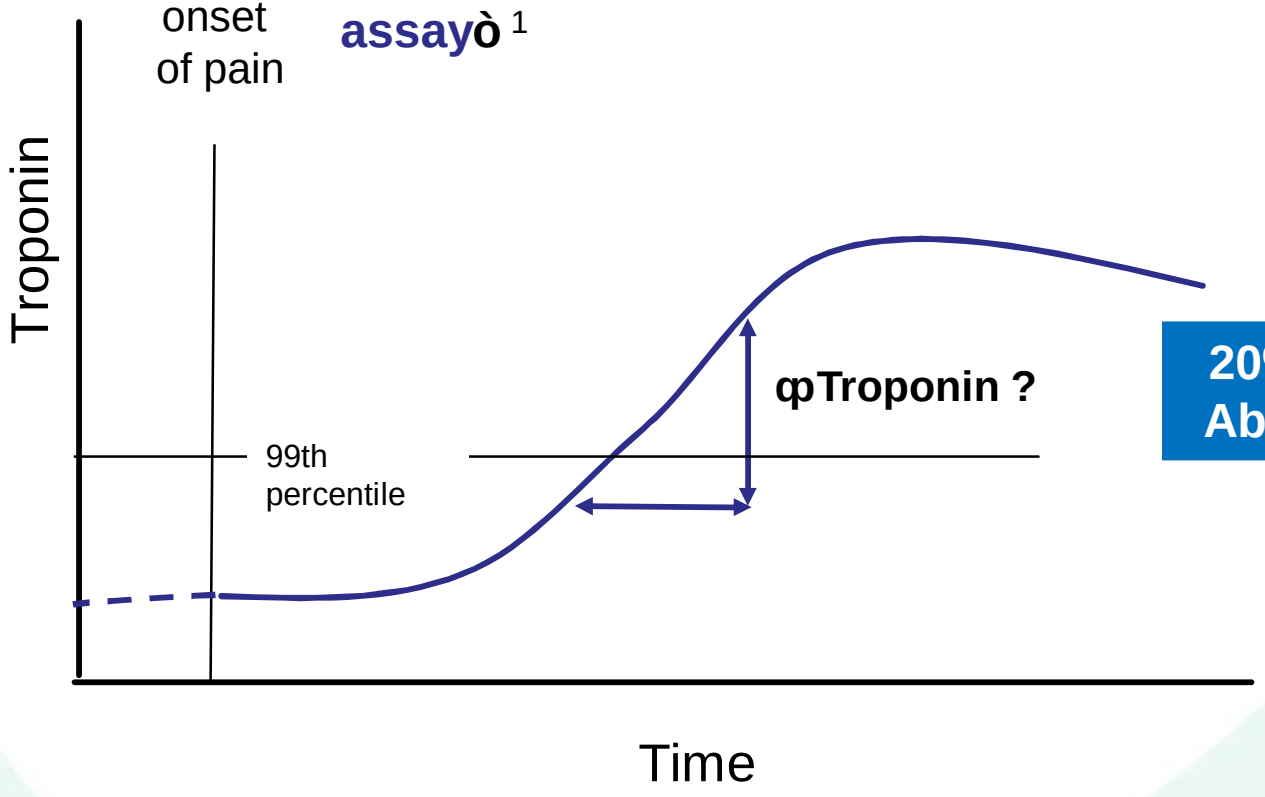
1. **Reichlin et al**. (2009). ***NEJM*** 361(9):858-67.
2. **Giannitsis et al**. (2010). ***Clin Chem*** 56 (2): 254-61.
3. **Hamm et al** (2011). ***Eur Heart J*** 32:2999–3054.
4. **De Luca et al** (2004). ***Circulation*** 109:1223-25.

cTn: Cardiac troponin; ECG: Electrocardiogram;
ED: Emergency department;
ESC: European Society of Cardiology

How to interpret the results?

Delta change from serial testing is essential

ñDelta change should be defined and validated for each assayò [1]



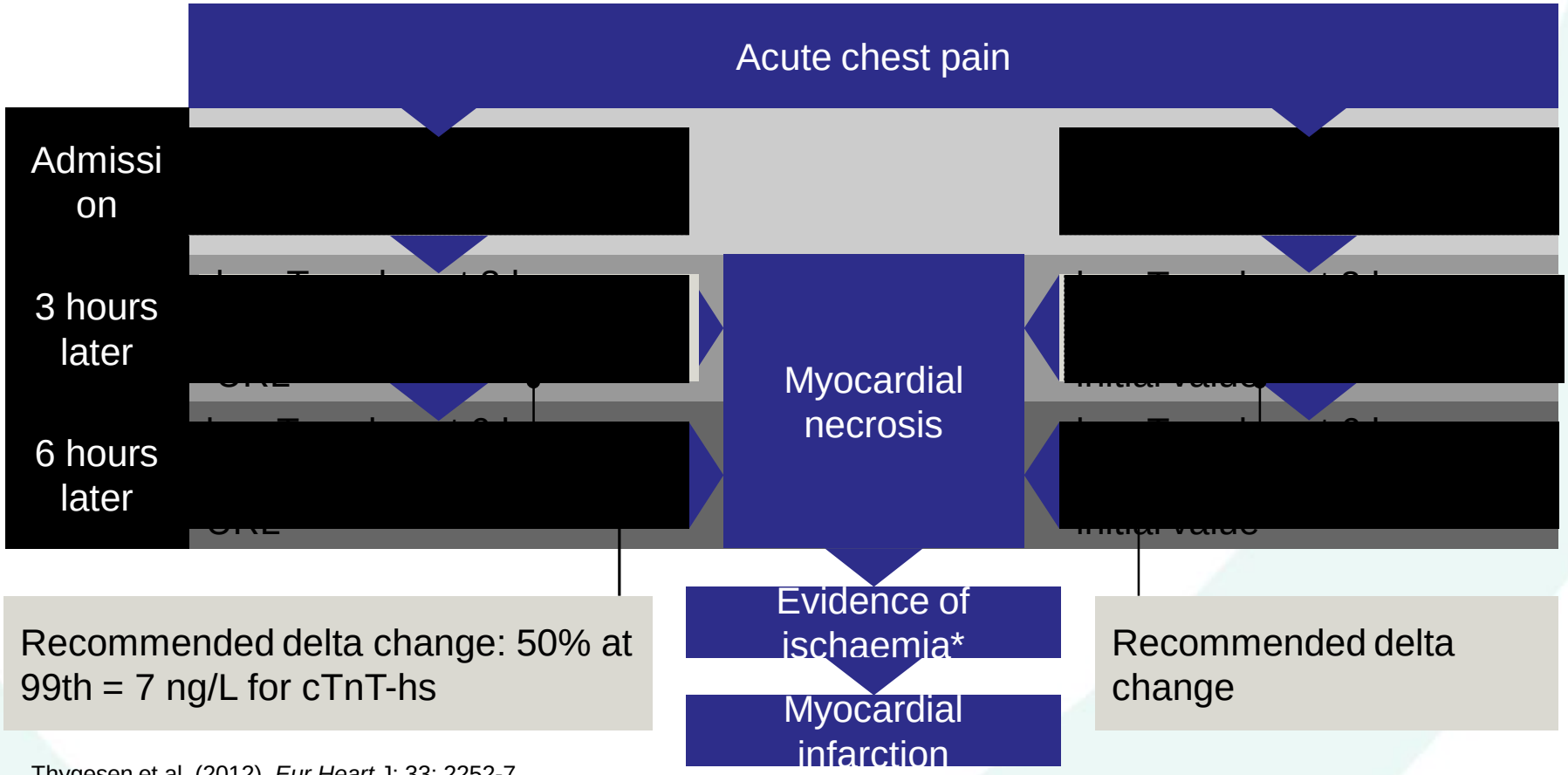
20% or 30% or 50% ?
Absolute or relative ?

1 Apple FS & Collinson PO for the IFCC Task Force on Clinical Applications of Cardiac Biomarkers. (2012) *Clin Chem* 58 (1):154ï 61.

ESC guideline recommendation on hs-cTn - 2012

Based on literature, which mainly has investigated cTnT-hs

ñOptimal change value will need to be established for each hs-cTn Assayò



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

Troponins

Is the safe diagnosis of AMI possible in a shorter time?

APACE trial[1] Advantageous Predictors of Acute Coronary Syndrome Evaluation

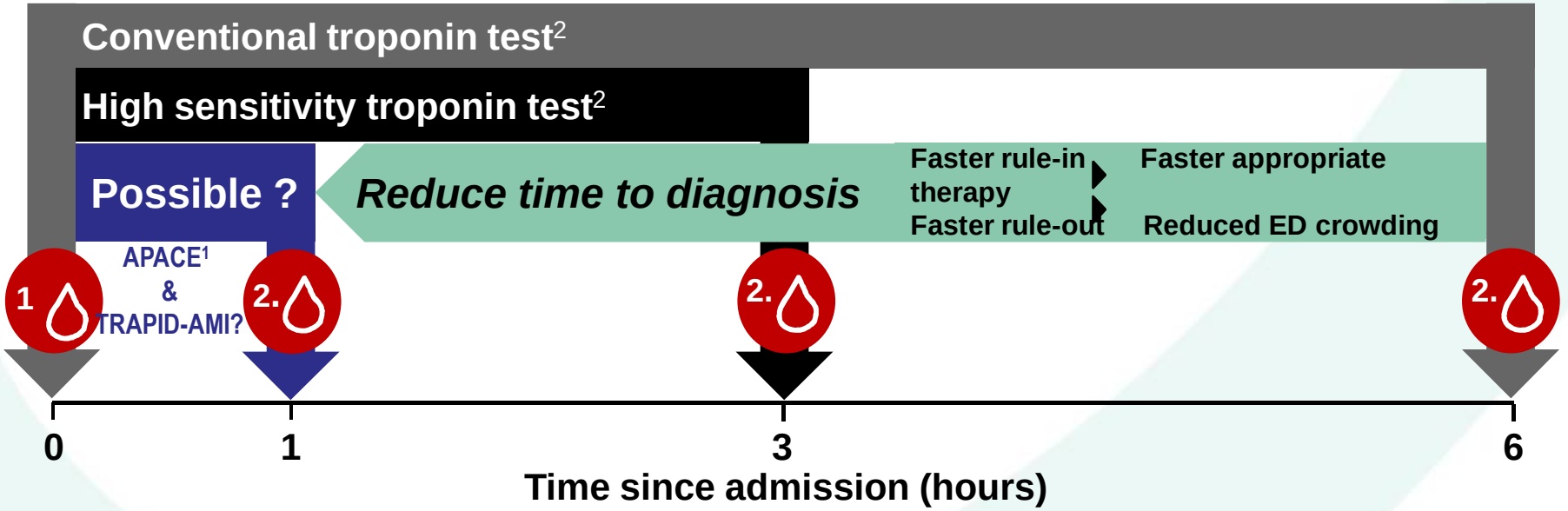
ORIGINAL INVESTIGATION

HEALTH CARE REFORM

One-Hour Rule-out and Rule-in of Acute Myocardial Infarction Using High-Sensitivity Cardiac Troponin T

Tobias Reichlin, MD; Christian Schnaller, PhD; Beatrice Drexler, MD; Raphael Twerenbold, MD; Miriam Reiter, MD; Christin Zellweger, MD; Berti Moehrin, MD; Ronny Ziller, MD; Rebeca Hoeller, MD; Maria Rubini Gimenez, MD; Philip Haaf, MD; Mihael Potocki, MD; Karin Wildi, MD; Cathrin Balmelli, MD; Michael Freese, RN; Claudia Stelzig, MSc; Heike Freidank, MD; Stefan Osswald, MD; Christian Mueller, MD, FESC

- pilot study (872 patients)
- <12 h from chest pain onset[1]



1. Reichlin et al. (2012). *Arch Intern Med* 172 (16):1211-8.
2. Hamm et al. (2011). *Eur Heart J* 32:2999ï 3054.

ESC 2015

Timing for measurements ?

1/ TAT

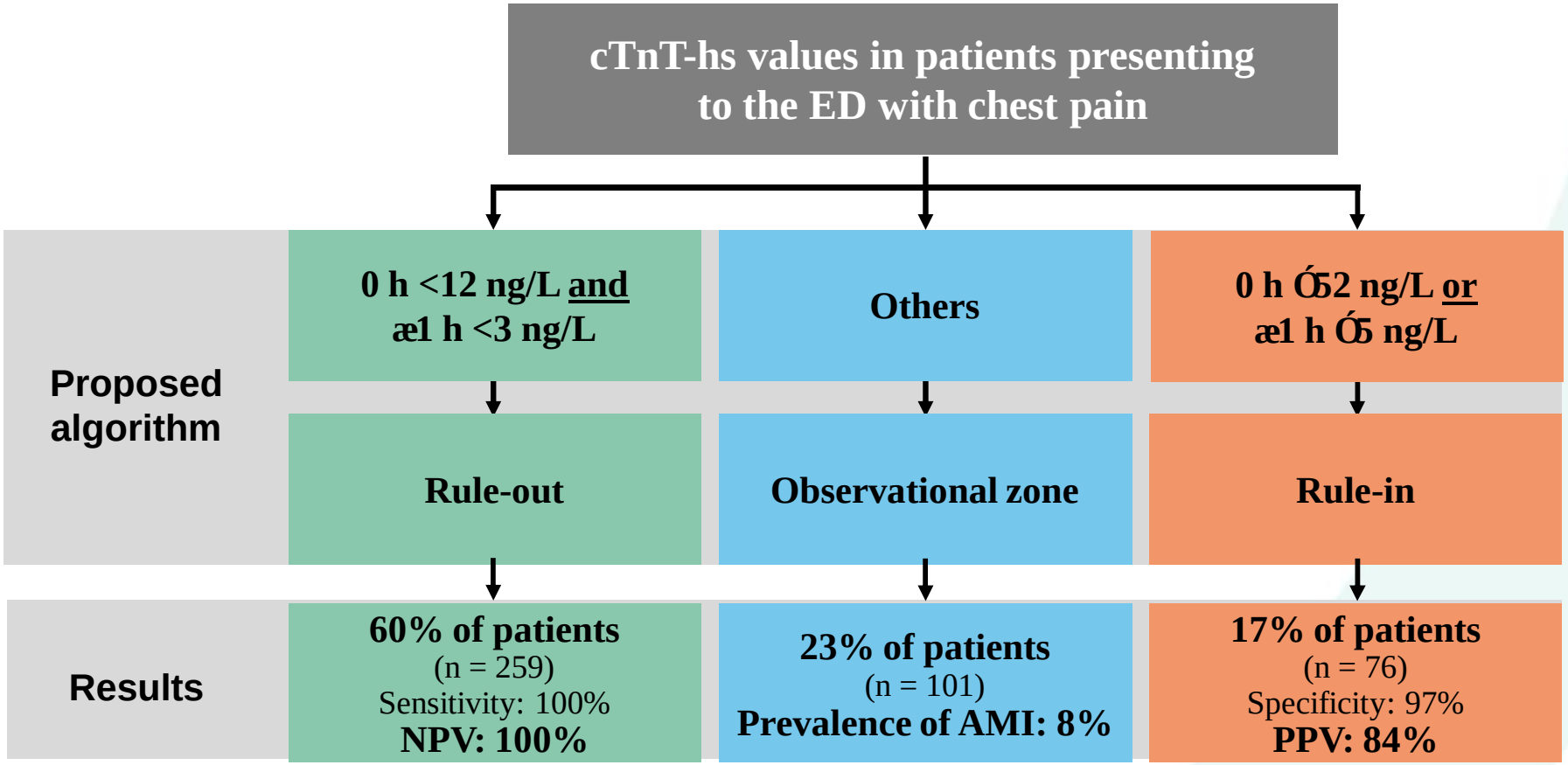
At present, measurements of troponins play a key role in the diagnosis of myocardial infarction. There is a consensus that a turnaround time (TAT) of 1 h or less should be achieved for cardiac marker assays. However, little is known about the real delays between the patient's arrival at the emergency department (ED) and the reporting of the test.

kinase (CK), its MB isoenzyme (CK-MB) and myoglobin. If the clinical presentation is compat with myocardial ischaemia, then a dynamic elevation of cardia ponin above the 99th percentile of healthy individuals indicates MI.[2] In patients with MI, levels of cardiac troponin rise rapidly (i.e. usually within 1 h if using high-sensitivity assays) after symptom onset and remain elevated for a variable period of time (usua y have led to a

2/ Algorithm

Performance of the 1-h algorithm for rapid AMI diagnosis
Reichlin T. et al., CMAJ. 2015

The APACE study: Algorithm and results



- **Very high NPV for a safe rule-out of 60 % patients within 1 hour** [1]
- **Definitive rule-in or rule-out of a total of 77 % of patients within 1 hour**[1]

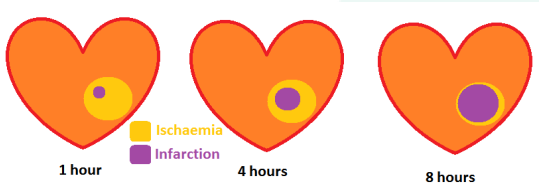
1. Reichlin et al (2012). *Arch Intern Med* 172 (16):1211-8.

0 h: Presentation to the ED; æ1 h: Absolute change of cTnT-hs within the first hour; AMI: Acute myocardial infarction; cTnT-hs: Cardiac Troponin T high-sensitive; ED: Emergency department; NPV: Negative predictive value; PPV: Positive predictive value

TnThs 1h-algorithm

1. Profit 1: Medical values for patients
   ➔***Time* is Life**

2. Profit 2: Medical values for the clinician
   ➔**Time is Myocardium**



3. Profit 3*:* Medical values for health care
   ➔**Time is Money**

Reichlin et al. (2012). *Arch Intern Med* 172 (16):1211-8.
Reichlin et al. (2015). *CMAJ* May 19;187 (8):E243-52.
De Luca *et al. (2004*). Circulation 109:1223-1225.
Hamm et al (2011).*Eur Heart J* 32:2999ï 3054.

Conclusions

- Many new biomarkers
- Selection based pragmatic criteria
- Good use of actual biomakers!

Annual meeting of the Royal Belgian Society of Laboratory Medicine and Joint meeting with the Belgian Bone club on Bone Turn-over and Bone Resorption Markers

Château du Val Saint Lambert
Esplanade du Val, 1
4100 Seraing
October 14th - 15th, 2016

Friday October 14th, 2016
Annual Meeting of the Belgian Society of Laboratory Medicine

Scientific Program:

13.00 : **Registration**
13.45 : **Welcome address**
Prof. Pieter Vermeersch, Chairman RBSLM

Part I: Plenary Sessions
13.50 : **Laudatio in honor of Prof. Camille Heusghem**
Prof. Em. Jean-Paul Chapelle, ULg
14.00 : **EFLM lecture: The pre-analytical Phase**
Prof. Ana Simundic, Chair EFLM WG-Preanalytical phase
14.40 : **The future of Laboratory Medicine: Linking genotypic and phenotypic information**
Prof. Elfride De Baere, UZ Gent
15.20 Lecture in honor of the retirement of Christel Van Campenhout:
Can quality be guaranteed for point-of-care testing?
Prof. Viviane Van Hoof, UZ Antwerpen

16.00 : **Coffee break and poster session**

Part II: Meet the expert session
Clinical chemistry
16.45 : **Novel cardiac markers** - *Pharm. Biol. Caroline Le Goff / Dr. Virginie D'Orio, CHU Liège*
17.25 : **How to measure renal function** - *Prof. Pierre Delanaye, CHU Liège*
18.05 : Selected oral presentations
Hematology
16.45 : **New anticoagulants: influence on routine coagulation testing and how to detect an overdose** - *Prof. F. Mullier CHU, UCL Namur*
17.25: **Use of Next Generation Sequencing for HLA typing** - *Dr. Barbara Cauwelier, AZ Sint-Jan Brugge-Oostende*
18.05: Selected oral presentations
Microbiology
16.45 : **Clinical and financial impact in routine microbiology** - *MSc. Jan-Willem Dik, UMC Groningen*
17.25 **The many faces of hantaviruses** - *Jan Clement, KULeuven*
18.05 : Selected oral presentations
Immunology
16.45 : **Anti-phospholipase A2 antibodies** - *Prof. Caroline Bonroy, UZ Gent*
17.25 : **Heavy-Lite** - *Pharm. Biol. Laurine Dierge, Zithaklinik Luxembourg*
18.05 : Selected oral presentation
18.45 : **Closing remarks**

18.50 -21.00 **Walking dinner**

Accreditation requested

Online registration required
or email
isabel.vandorpe@icloud.com

CHU de Liège

KBVLG
SRBML
RBSLM
Laboratory Medicine

Belgian Bone Club

Annual meeting of the Royal Belgian Society of Laboratory Medicine and Joint meeting with the Belgian Bone club on Bone Turn-over and Bone Resorption Markers

October 14th - 15th, 2016

Château du Val Saint Lambert
Esplanade du Val, 1
4100 Seraing

Saturday October 15th, 2016

Joint meeting of the Belgian Bone club on Bone turn-over and Bone resportion markers - Annual Meeting of the Belgian Society of Laboratory Medicine

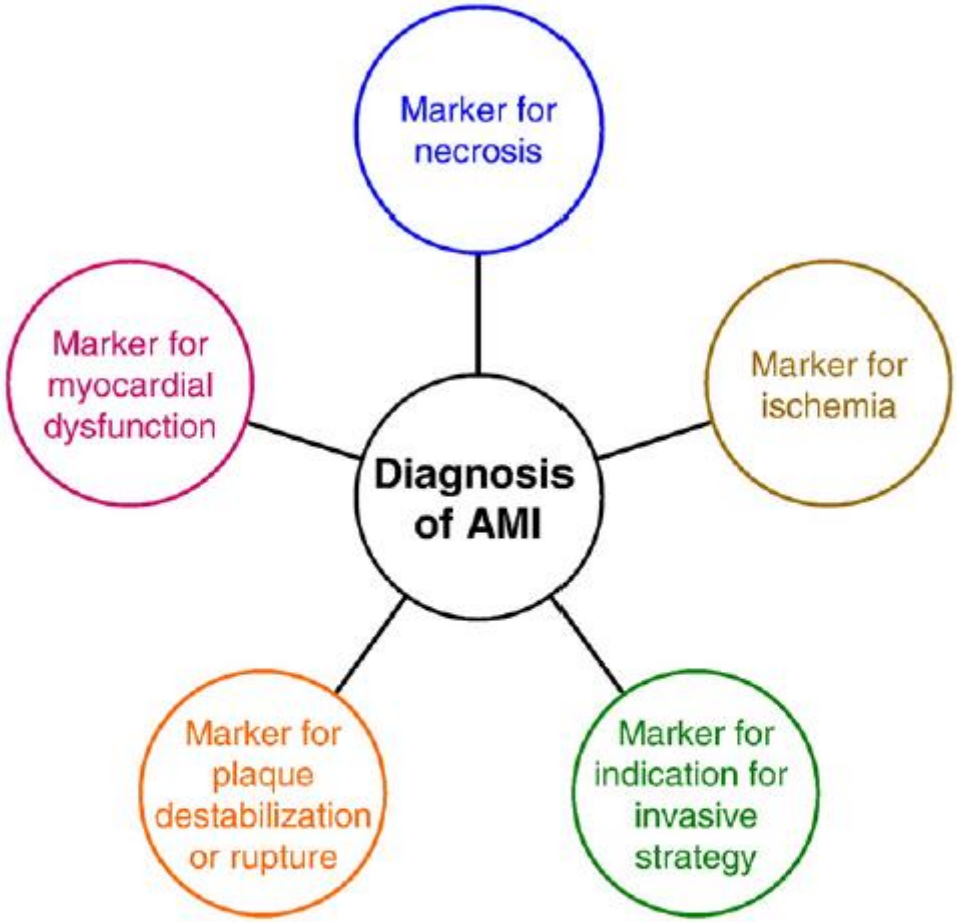
Scientific Program:
Chairmen: Prof. Jean-Jacques Body, ULB - Prof. Etienne Cavalier, ULg

08.30 :	**Registration**
08.55 :	**Welcome address** *Prof. Pieter Vermeersch, UZ Leuven*
09.00 :	**The goods and evils of bone turnover** *Prof. Pierre Bergmann, ULB*
09.20 :	**Biomarkers of BTR: methodological aspects** *Prof. Etienne Cavalier, ULg*
09.40 :	**Usefulness of BTR biomarkers in post-menopausal osteoporosis** *Prof. Stefan Goemare, UGent*
10.00 :	**Usefulness of BTR biomarkers in male osteoporosis** *Prof. Evelien Gielen, KUL*
10.20 :	**Bone and cartilage markers in rheumatology and corticosteroid induced osteoporosis** *Prof. Jean-Pierre De Vogelaere, UCL*
10.40-11.10 :	**Coffee break and poster session**
11.10 :	**Do BTR biomarkers add to the work up and follow up of bone metastasis?** *Prof. Jean-Jacques Body, ULB*
11.30 :	**Is there a place for BTR markers in renal osteodystrophy?** *Prof. Pierre Delanaye, ULg*
11.50 :	**General discussion and conclusions** *Prof. Jean-Jacques Body, ULB - Prof. Etienne Cavalier, ULg*
12.30:	**Closure**
12.30:	**Sandwich lunch - Walking buffet**

Accreditation requested

Online registration required

or email
isabel.vandorpe@icloud.com



Multimarker approach for diagnosing acute myocardial infarction. Diagram of possible ways how novel biomarkers can facilitate the diagnosis of AMI since they might cover different aspects of pathophysiologic processes associated with AMI and might help to guide therapy.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