CardioTox 2019

Potential use of cardiac biomarkers in cardio-oncology

Antonio Buño Soto

Servicio Análisis Clínicos

Hospital Universitario La Paz – Madrid

21 de marzo de 2019

Role of Biomarkers

Curing Cancer, Saving the Heart: A Challenge That Cardioncology Should Not Miss

Daniela Cardinale[1] · Gina Biasillo[2] · Carlo Maria Cipolla

Curr Cardiol Rep (2016) 18: 51

D Cardinale said:

"The best treatment for chemotherapy-induced cardiotoxicity is its prevention in the first earliest stages"

start of chemotherapy

Individual predisposition: Genetics?

- CV factors control
- Limit AC dose
- AC continuous infusion
- AC analogues
- Liposomial AC
- Dexrazoxane
- Beta-blockers
- RAS inhibitors
- Statins

Primary prevention

Role of Biomarkers

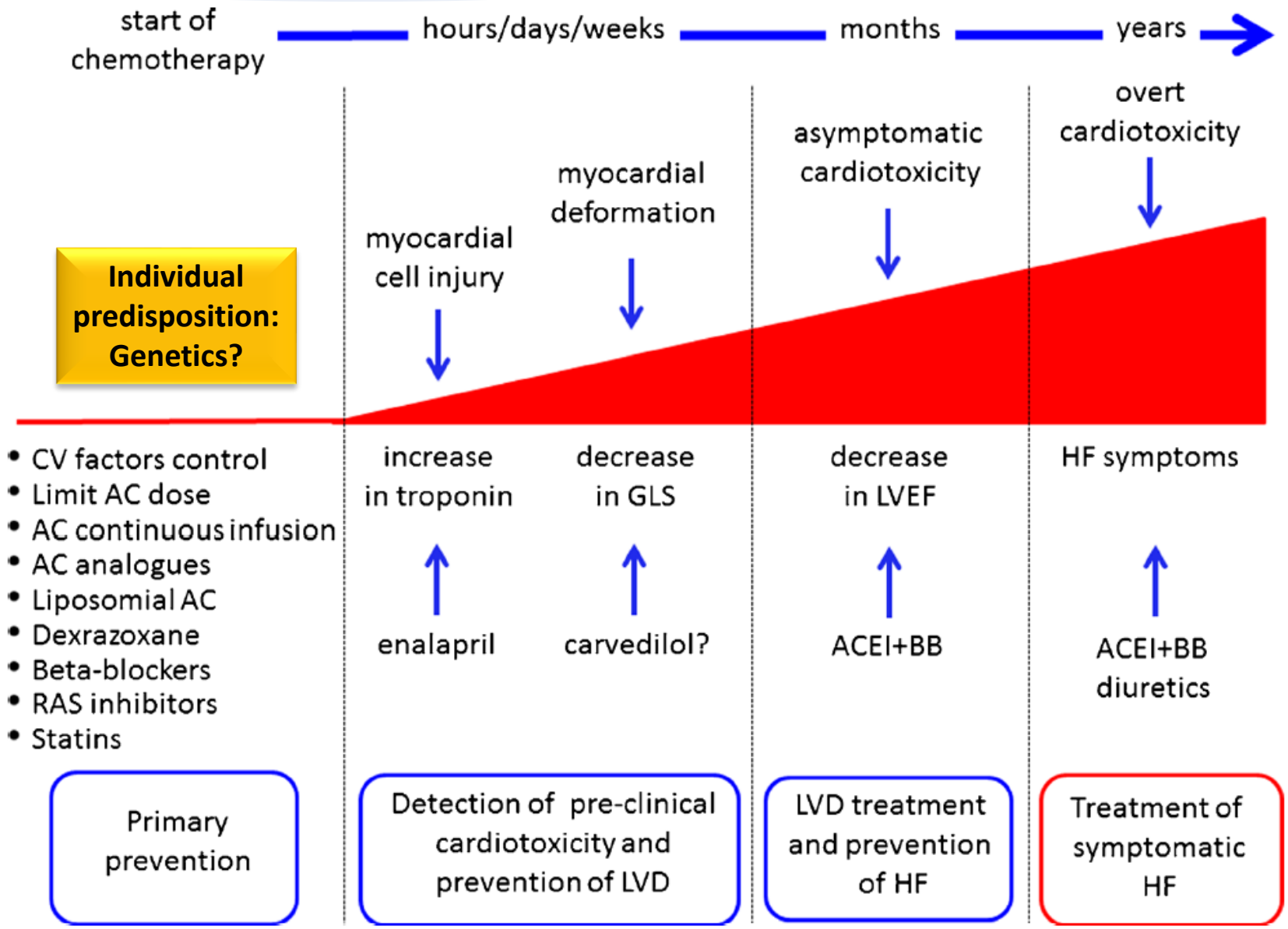
Curing Cancer, Saving the Heart: A Challenge That Cardioncology Should Not Miss

Daniela Cardinale[1] · Gina Biasillo[2] · Carlo Maria Cipolla

Curr Cardiol Rep (2016) 18: 51

D Cardinale said:

"The best treatment for chemotherapy-induced cardiotoxicity is its prevention in the first earliest stages"



Biomarkers

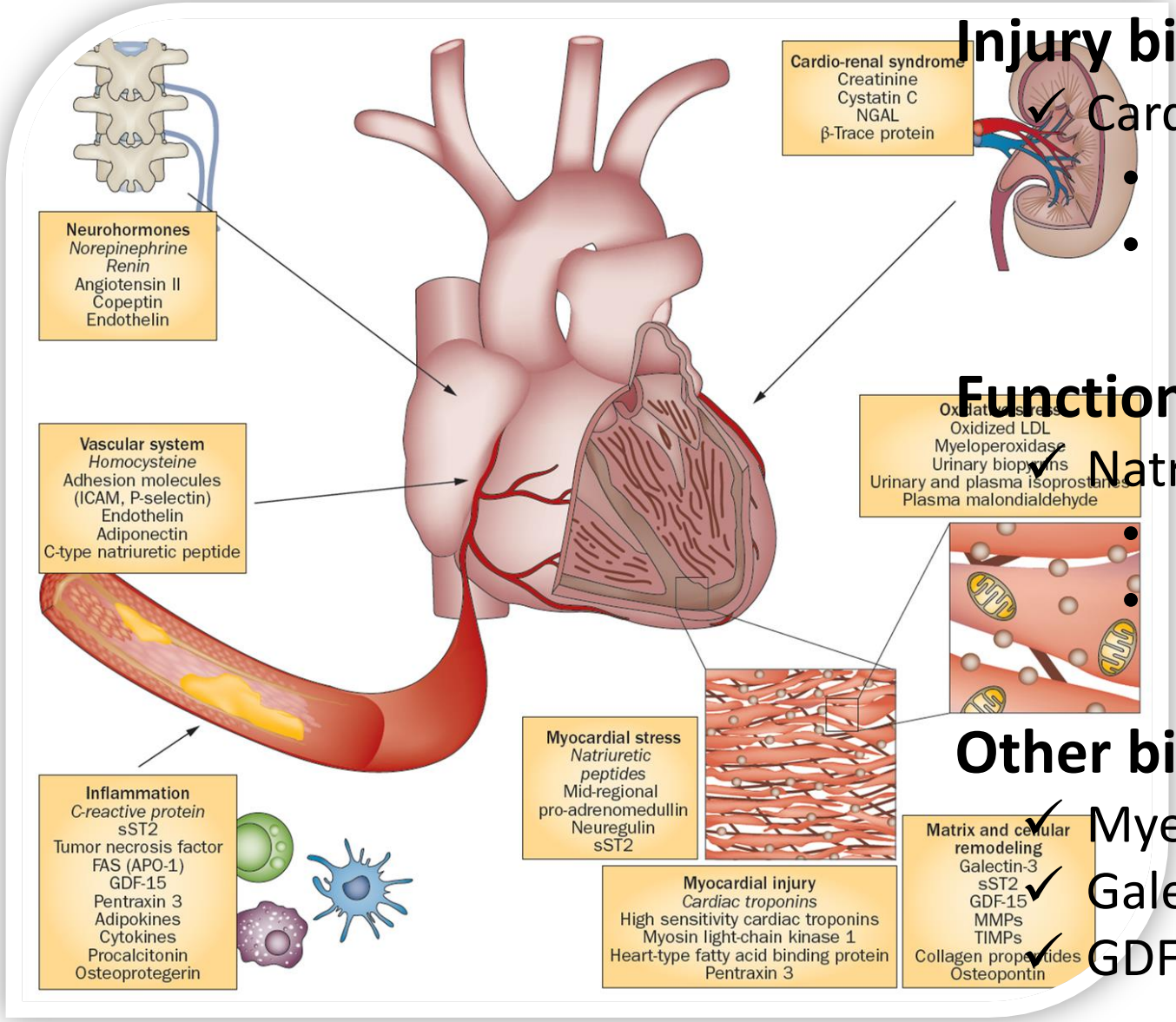
WHO definition

Any substance, structure, or process that can be measured in the body (or its products) that influences or predicts the incidence or outcome of disease → can include physiologic tests, clinical images, genetic variants, and biopsies of tissue specimens

Ideal biomarker in blood samples

- Sensitivity (baseline close to zero; rapid rise when illness)
- Specificity (exclusivity of a disease; rise in accordance to injury severity)
- Easy to measure (analytics and preanalytics)
- 24h available with short TAT
- Low individuality index
- Low biological variation
- Good balance cost / efectivity

Cardiac biomarkers and cardiotoxicity



Injury biomarkers

- ✓ Cardiac troponins
  - Conventional
  - High sensitivity

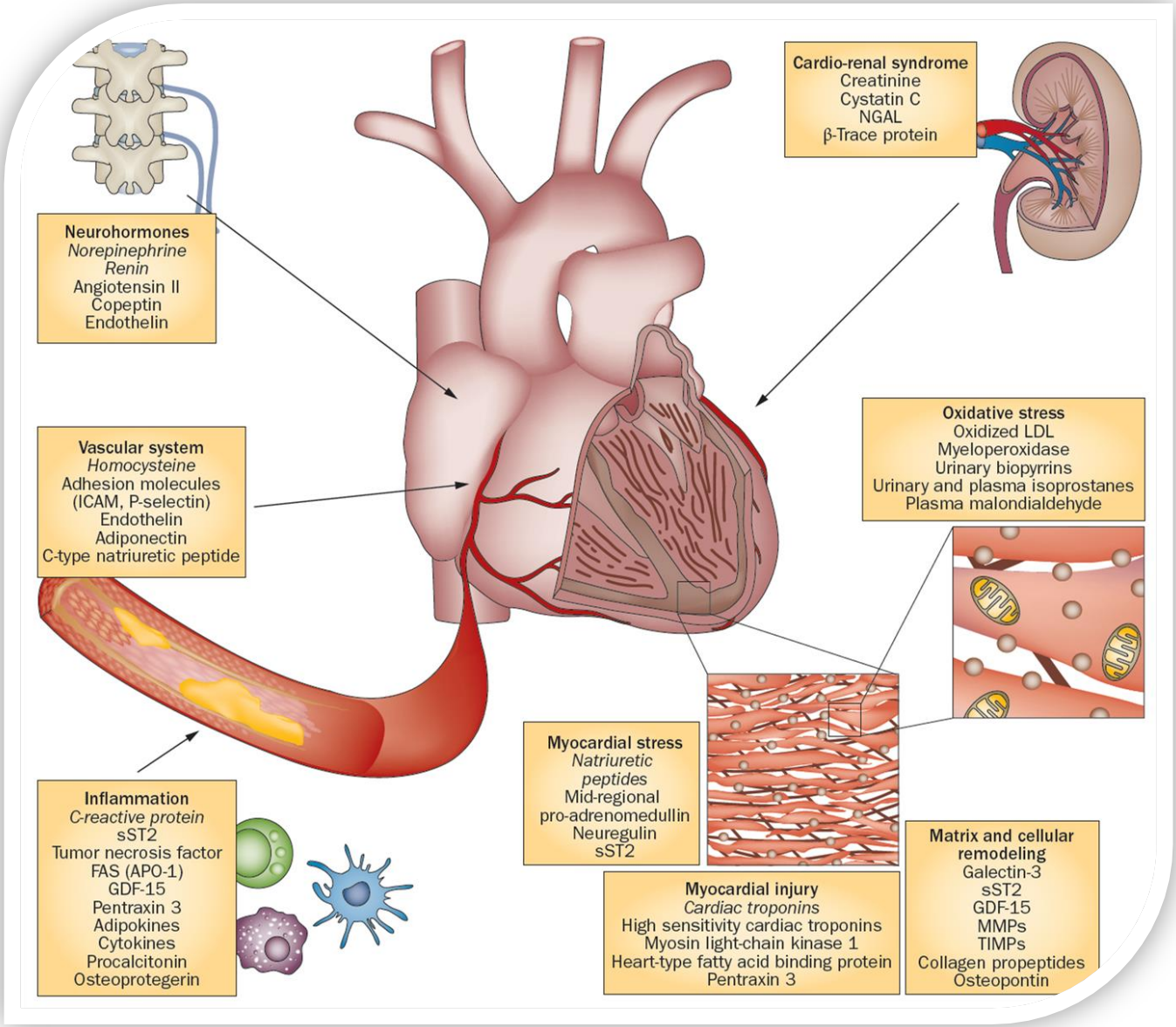
Function biomarkers

- ✓ Natriuretic peptides
  - NT-proBNP
  - BNP

Other biomarkers

- ✓ Myeloperoxidase
- ✓ Galectine 3
- ✓ GDF-15

Cardiac biomarkers and cardiotoxicity



Injury biomarkers

- ✓ Cardiac troponins
  - Conventional
  - High sensitivity

Function biomarkers

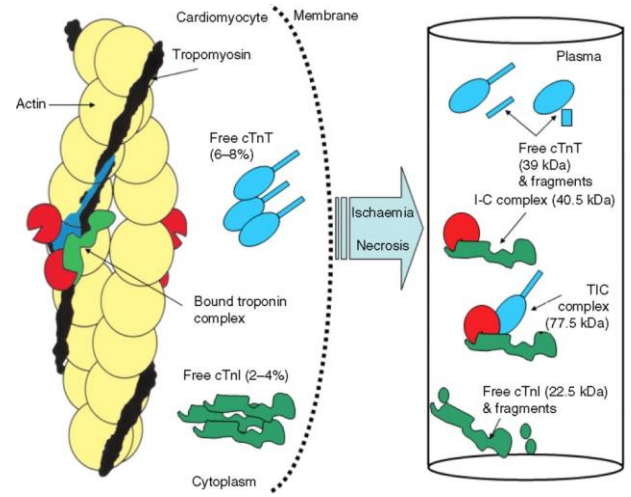
- ✓ Natriuretic peptides
  - NT-proBNP
  - BNP

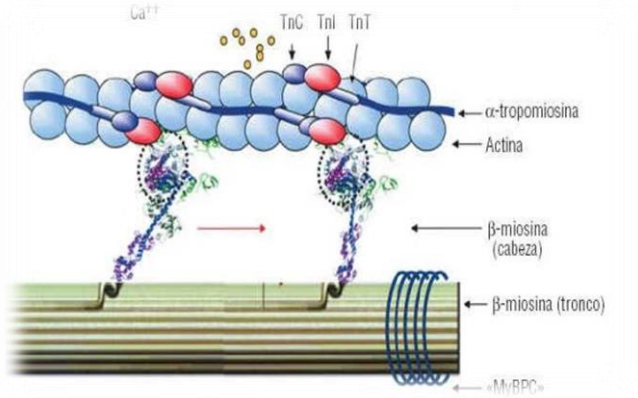
Other biomarkers

- ✓ Myeloperoxidase
- ✓ Galectine 3
- ✓ GDF-15

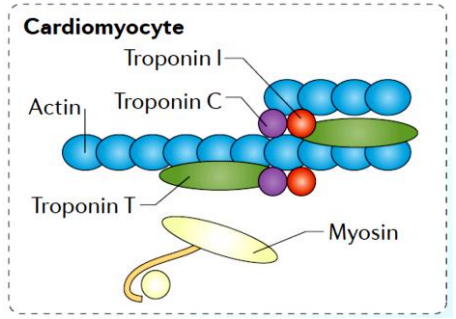
Troponina cardiaca

- Complejo troponina:
  - transmisión señal intracelular del Ca2+
  - interacción actina-miosina
- Presente en músculo estriado y cardiaco (no en liso)
- Hay isoformas específicas de músculo cardiaco (genes distintos)
- Un 7% TnT y 4% TnI disuelto citoplasma miocardiocito → liberación bifásica
- Rápida liberación
- cTnI libera 4-6h del daño → 7-10 días
- cTnT → 7- 14 días





Cardiac troponin

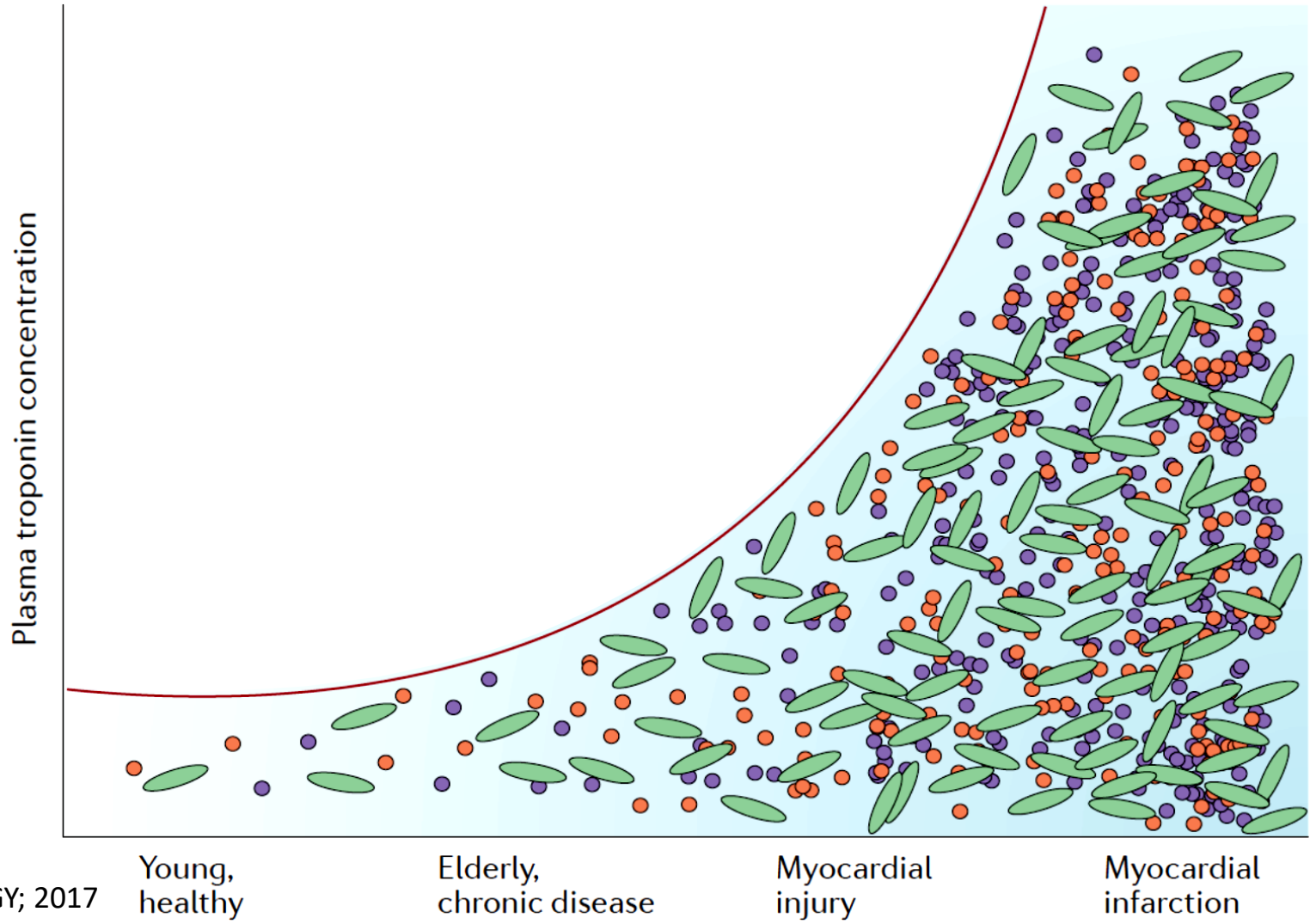


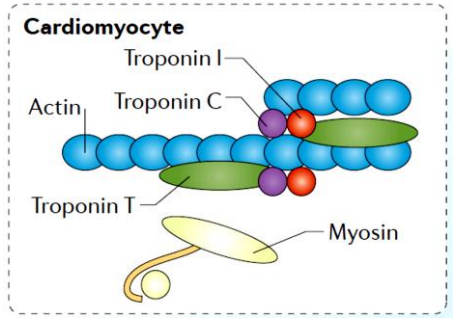
Analytical Methods (I or T)

- Conventional
- Improved sensitivity
- High sensitivity troponin
- New high sensitivity troponin

Cardiac troponin

High sensitivity troponin

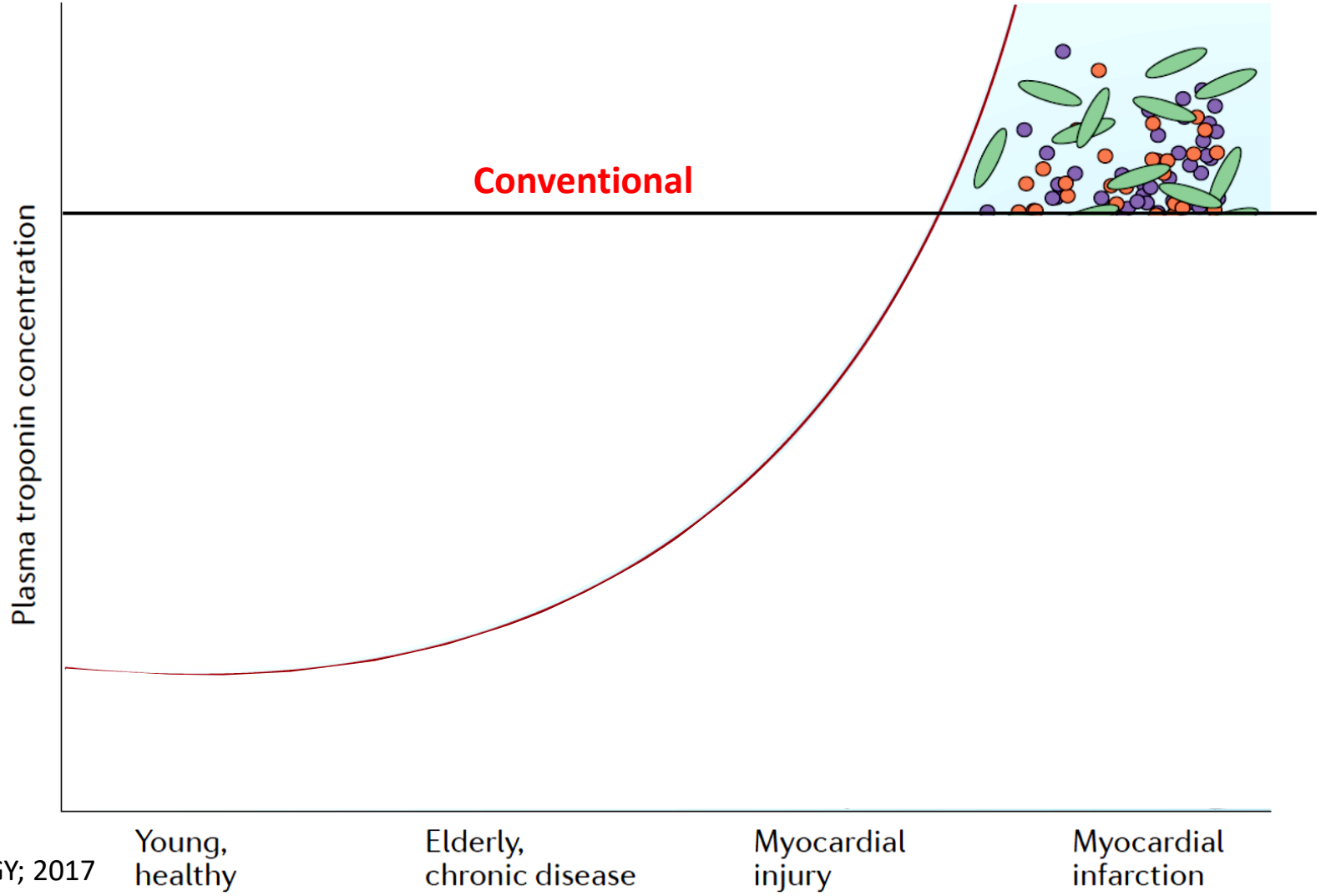


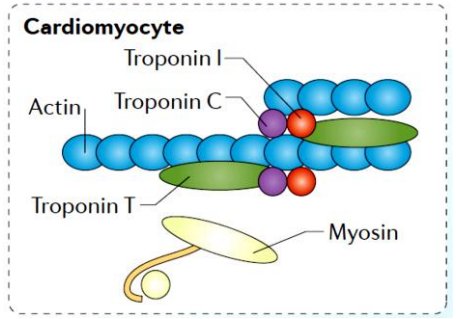


NATURE REVIEWS CARDIOLOGY; 2017

Cardiac troponin

Conventional troponin

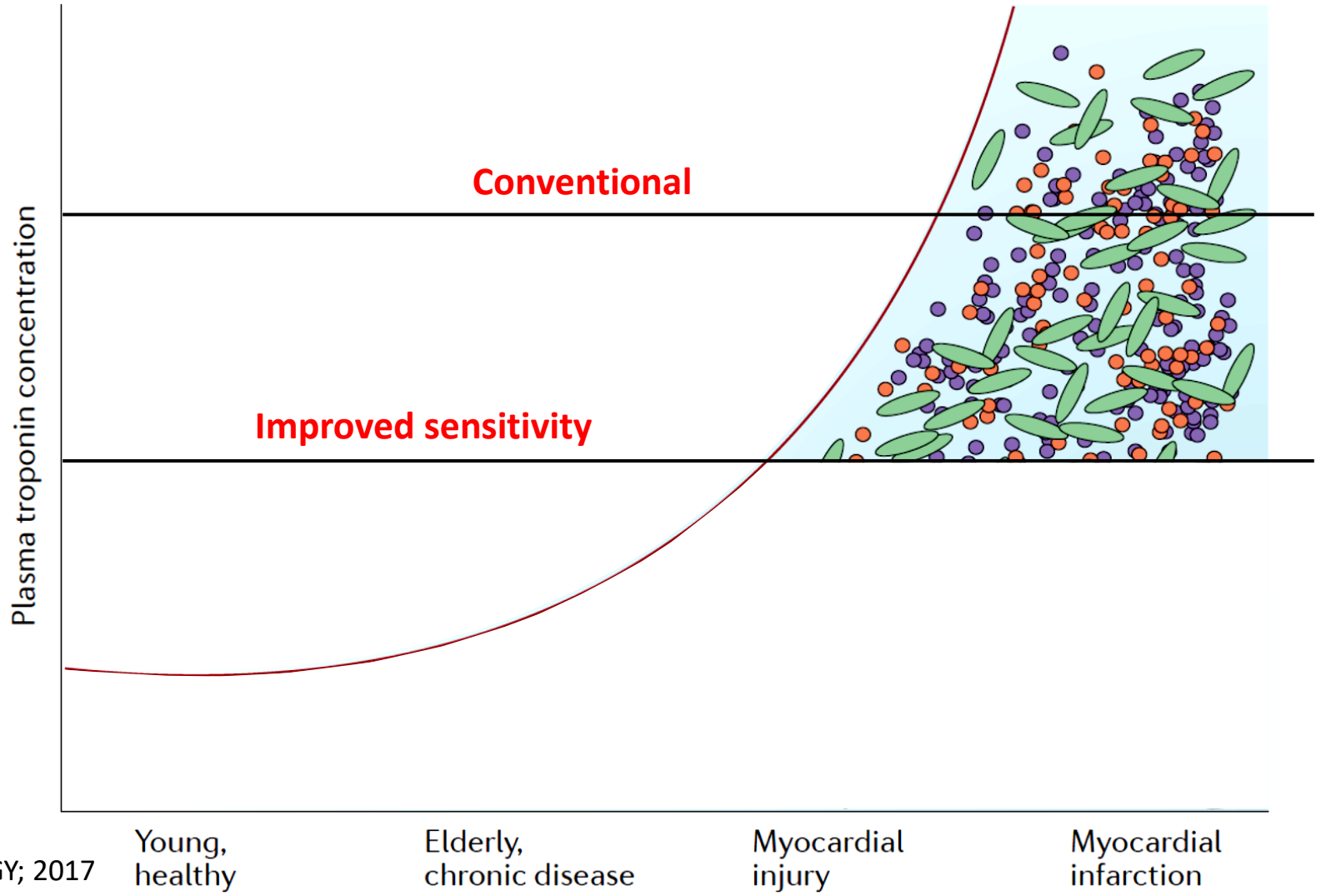


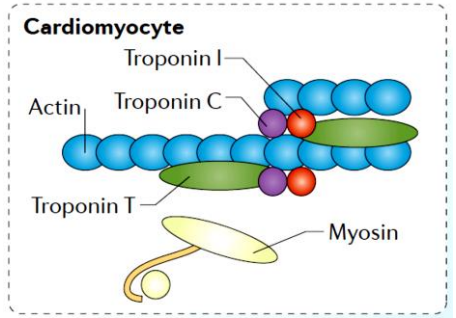


NATURE REVIEWS CARDIOLOGY; 2017

Cardiac troponin

Improved sensitivity troponin

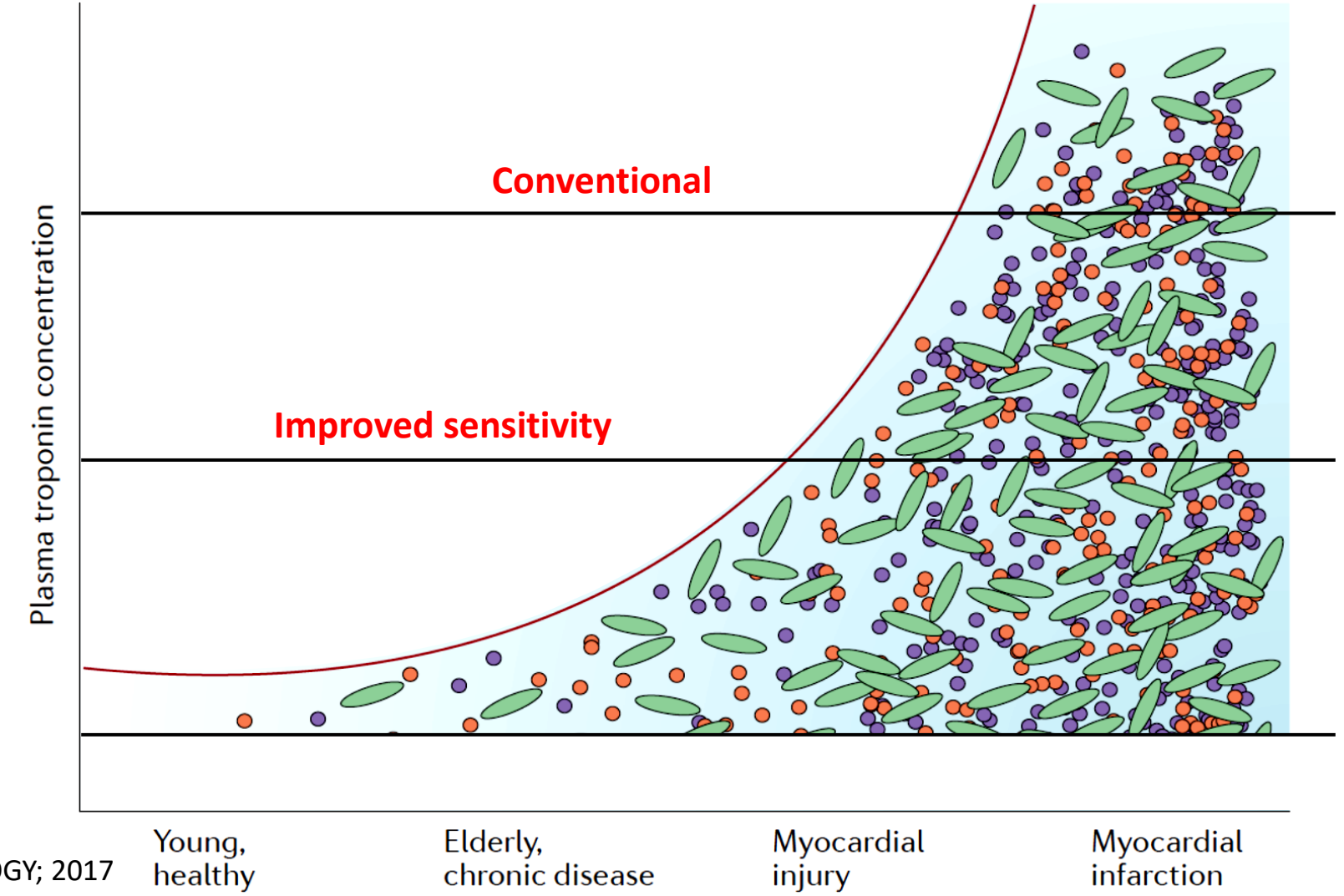


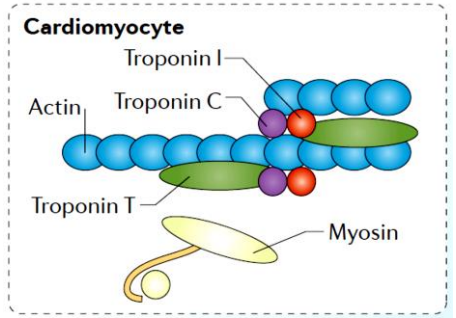


NATURE REVIEWS CARDIOLOGY; 2017

Cardiac troponin

High sensitivity troponin

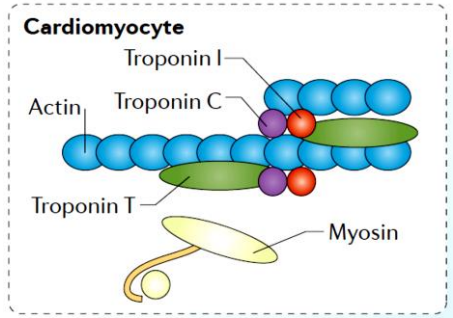


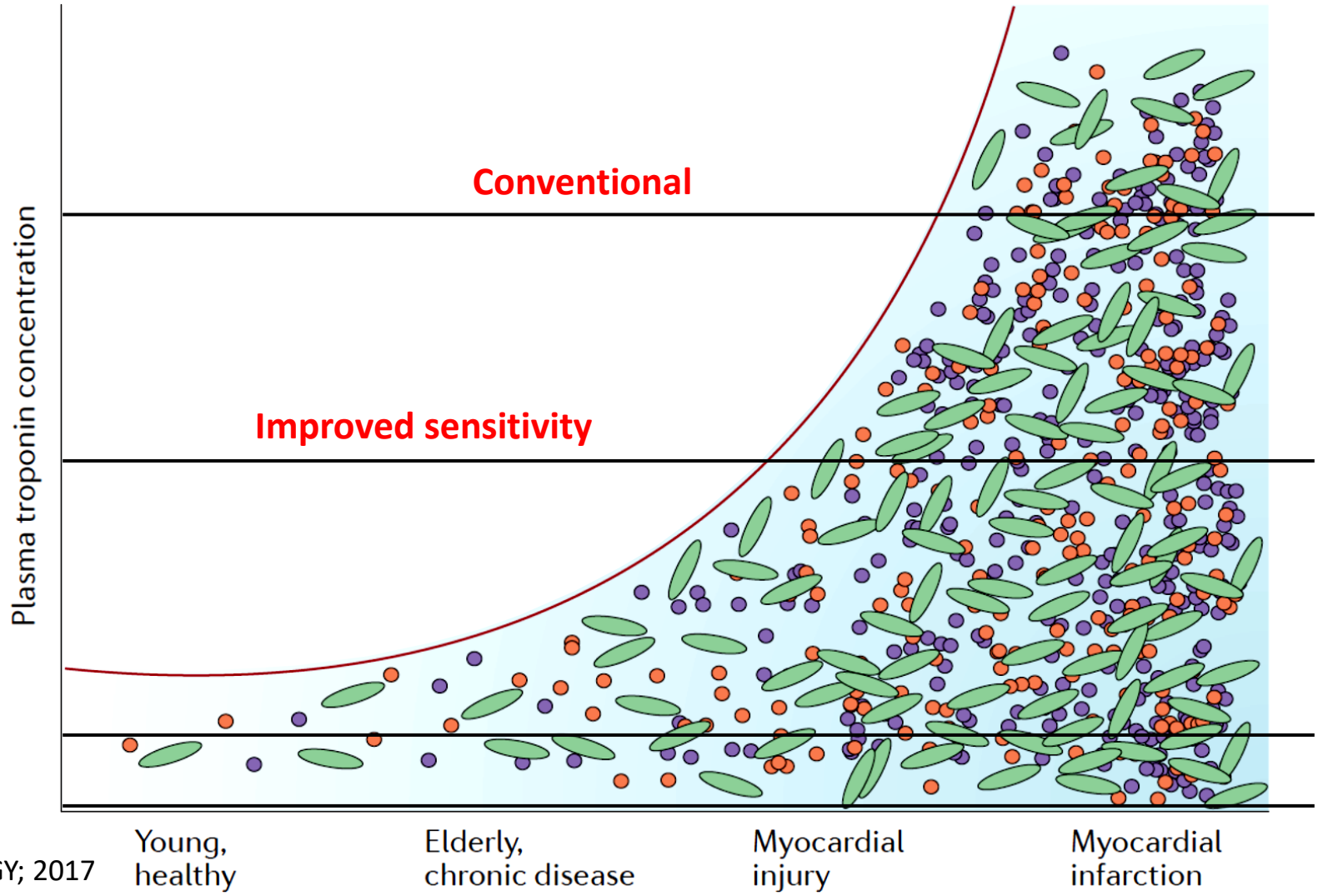


NATURE REVIEWS CARDIOLOGY; 2017

Cardiac troponin

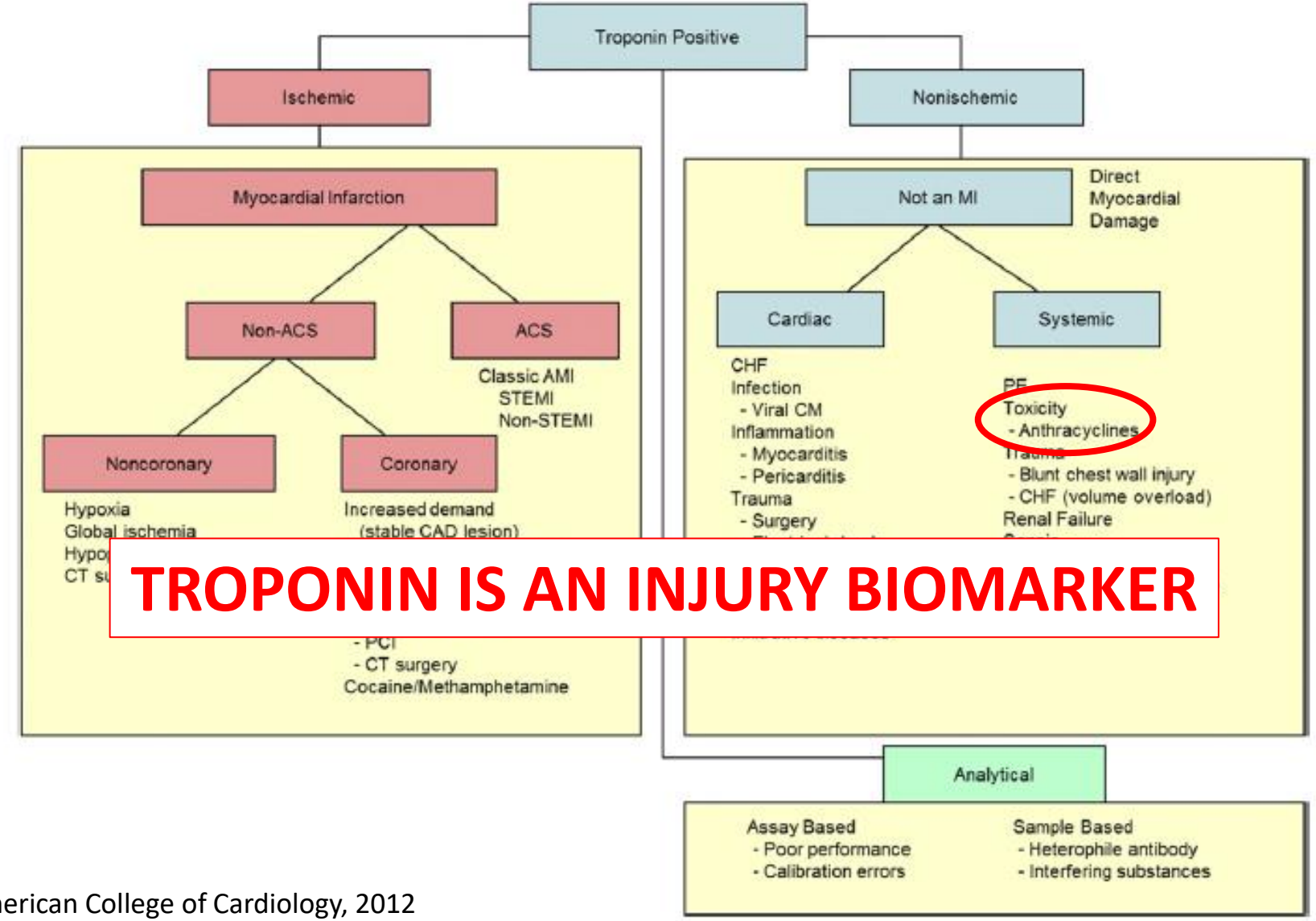
New high sensitivity troponin



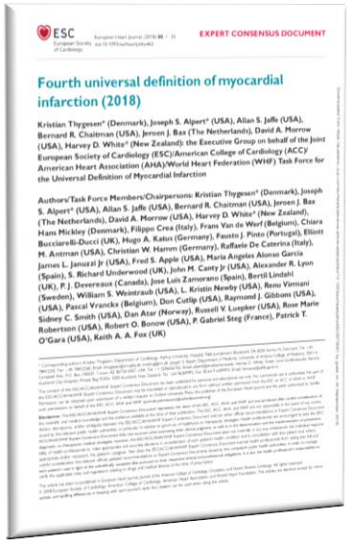


NATURE REVIEWS CARDIOLOGY; 2017

Cardiac troponin: causes of increase



TROPONIN IS AN INJURY BIOMARKER


ESC EXPERT CONSENSUS DOCUMENT

Fourth universal definition of myocardial infarction (2018)

2018

Journal of the American College of Cardiology, 2012

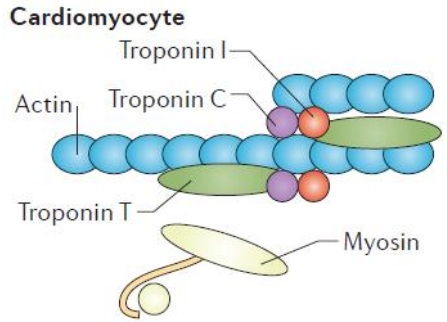
High sensitivity troponin

Clinical Chemistry 63:1
73-81 (2017)

Mini-Reviews

Cardiac Troponin Assays: Guide to Understanding Analytical Characteristics and Their Impact on Clinical Care

Fred S. Apple,[1*] Yader Sandoval,[2] Allan S. Jaffe,[3] and
Jordi Ordonez-Llanos,[4] for the IFCC Task Force on Clinical Applications of Cardiac Bio-Markers



- CV <10% at p99
- Measures troponin values in at least 50% of healthy individuals

Company/platform/assay hs-Assays	LoD, ng/L	99th, M/F, ng/L	% CV at 99th	10% CV, ng/L	% Normals Measurable >L0D
Abbott ARCHITECT hs-cTnI	1.2	34/16	5	3	83
Beckman Coulter Access hs-cTnI	2.5	52/23	<10	8	80
Ortho-Clinical Diagnostics hs-cTnI	1.0	19/16	<10	3	75
Singulex Errena hs-cTnI	0.09	36/30	5	0.9	100
Siemens Vista hs-cTnI	0.8	55/33	5	3	86

99th percentile

- Recommended as cut-off threshold for clinical use
- Imprecision (CV) below 10%
- Factors that influence:
  - Gender: men higher than women
  - Age: higher overall above 60y
- Very important, how to define healthy population
- Calculated according to guidelines

99th percentile

Table 2. Measurable values among hs-cardiac troponin assays using sex-specific cutoffs.

Manufacturer–analyzer–assay	No. of results	LoD, ng/L	99th percentile, ng/L	Excluded values above the 99th percentile, n	Measurable values ≥LoD–99th percentile	Proportion of undetectable values (<LOD)
Abbott ARCHITECT hs-cTnI	F: 252[a]	1.9	F: 16	F: 2	F: 67% (168/250)	F: 33% (82/250)
	M: 272		M: 34	M: 2	M: 80% (215/270)	M: 20% (55/270)
Beckman Access 2 hs-cTnI	F: 252	2.5	F: 9	F: 12	F: 73% (175/240)	F: 27% (65/240)
	M: 272		M: 11	M: 16	M: 87% (222/256)	M: 13% (34/256)
Roche Cobas e601 hs-cTnT	F: 252	5	F: 14	F: 1	F: 7% (17/251)	F: 93% (234/251)
	M: 272		M: 22	M: 2	M: 43% (115/270)	M: 57% (155/270)
Siemens Dimension Vista hs-cTnI	F: 239	0.5	F: 33	F: 5	F: 82% (191/234)	F: 18% (43/234)
	M: 264		M: 55	M: 3	M: 90% (234/261)	M: 10% (27/261)
Singulex Erenna hs-cTnI	F: 252	0.1	F: 15	F: 8	F: 100% (244/244)	F: 0% (0/0)
	M: 272		M: 27	M: 5	M: 100% (267/267)	M: 0% (0/0)

[a] F, female; M, male.

Apple FS, Sandoval Y, Jaffe A, Ordoñez-Llanos J. Clin Chem; 2017

What the guidelines say

JOURNAL OF CLINICAL ONCOLOGY

Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline

J Clin Oncol 34.

ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Serum cardiac biomarkers (troponins, natriuretic peptides)

- Useful in the surveillance and monitoring during and after treatment in patients at risk for cardiac dysfunction
- Use of BNP and NT-proBNP in asymptomatic patients with cancer remains largely investigational
- Need for additional studies to clarify the role of troponins and NPs assessment during cancer therapy

What the guidelines say

Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines†

Annals of Oncology 23 (Supplement 7): vii155–vii166, 2012

Serum cardiac biomarkers (troponins, natriuretic peptides)

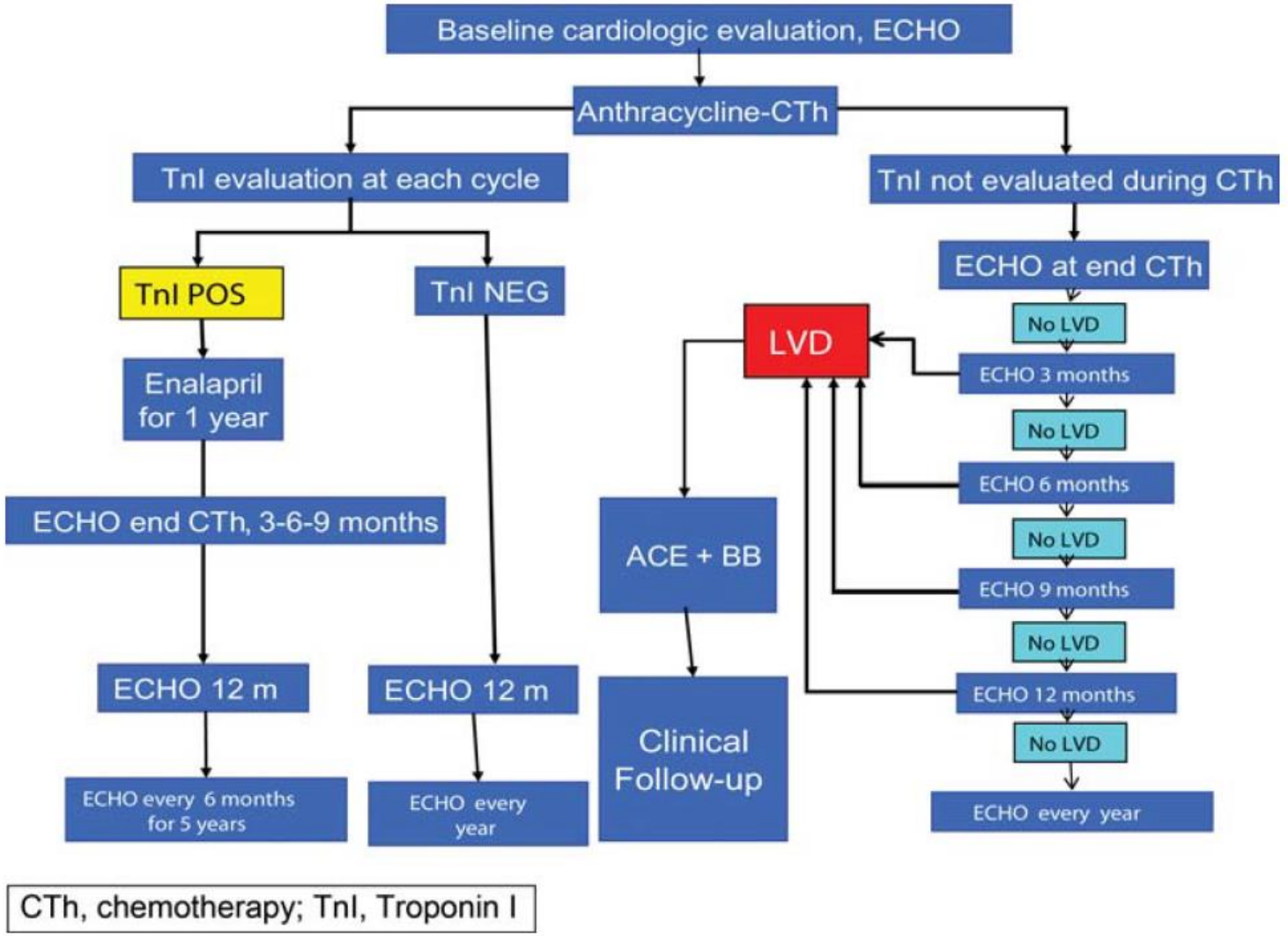
- CV evaluation before anticancer treatment
- CV monitoring during and after anticancer treatment
- Although it is not yet established whether their routine monitoring is useful in predicting cardiotoxicity, and this needs to be examined in prospective studies, there is a strong case to incorporate their use in the clinical trial setting

What the guidelines say

Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines†

Annals of Oncology 23 (Supplement 7): vii155–vii166, 2012

Algorithm for the management of cardiotoxicity in patients receiving anthracyclines



What the guidelines say

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

European Heart Journal (2016) **37**, 2768–2801

ESC
European Society of Cardiology

Table 6 Proposed diagnostic tools for the detection of cardiotoxicity

Technique	Currently available diagnostic criteria	Advantages	Major limitations
Cardiac biomarkers: **- Troponin I** **- High-sensitivity Troponin I** **- BNP** **- NT-proBNP**	• A rise identifies patients receiving anthracyclines who may benefit from ACE-Is. • Routine role of BNP and NT-proBNP in surveillance of high-risk patient needs futher investigation.	• Accuracy, reproducibility. • Wide availability. • High-sensitivity.	• Insufficient evidence to establish the significance of subtle rises. • Variations with different assays. • Role for routine surveillance not clearly established.

What the guidelines say

Long-term Cardiovascular Toxicity in Children, Adolescents, and Young Adults Who Receive Cancer Therapy: Pathophysiology, Course, Monitoring, Management, Prevention, and Research Directions
A Scientific Statement From the American Heart Association
(*Circulation*. 2013;128:1927-1995.)

American Heart Association®

Serum cardiac biomarkers (troponins, natriuretic peptides)

- Possible use for monitoring during and after anticancer treatment

What the guidelines say

Expert Consensus for Multimodality Imaging Evaluation of Adult Patients during and after Cancer Therapy: A Report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

(J Am Soc Echocardiogr 2014;27:911-39.)

ASE American Society of Echocardiography

EACVI European Association of Cardiovascular Imaging

Serum cardiac biomarkers (troponins, natriuretic peptides)

- Elevated troponins in patients receiving cardiotoxic chemotherapy may be a sensitive measurement for the early detection of toxicity
- Serum NPs, although likely reflective of elevated filling pressures, may be less consistent in the early identification of Cancer therapeutics–related cardiac dysfunction

What the guidelines say

Cardiovascular Disease in Survivors of Childhood Cancer: Insights Into Epidemiology, Pathophysiology, and Prevention

Saro H. Armenian, Gregory T. Armstrong, Gregory Aune, Eric J. Chow, Matthew J. Ehrhardt, Bonnie Ky, Javid Moslehi, Daniel A. Mulrooney, Paul C. Nathan, Thomas D. Ryan, Helena J. van der Pal, Elvira C. van Dalen, and Leontien C.M. Kremer

VOLUME 36 · NUMBER 21 · JULY 20, 2018

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

General recommendation

Survivors treated with anthracyclines and/or chest radiation and their providers should be aware of the risk of cardiomyopathy.

Who needs cardiomyopathy surveillance?
Anthracyclines

Cardiomyopathy surveillance *is recommended* for survivors treated with high dose (≥ 250 mg/m²) anthracyclines.

Cardiomyopathy surveillance *is reasonable* for survivors treated with moderate dose (≥ 100 to < 250 mg/m²) anthracyclines.

Cardiomyopathy surveillance *may be reasonable* for survivors treated with low dose (< 100 mg/m²) anthracyclines.

Who needs cardiomyopathy surveillance?
Chest radiation

Cardiomyopathy surveillance *is recommended* for survivors treated with high dose (≥ 35 Gy) chest radiation.

Cardiomyopathy surveillance *may be reasonable* for survivors treated with moderate dose (≥ 15 to < 35 Gy) chest radiation.

No recommendation can be formulated for cardiomyopathy surveillance for survivors treated with low dose (< 15 Gy) chest radiation with conventional fractionation.

Who needs cardiomyopathy surveillance?
Anthracyclines + chest radiation

Cardiomyopathy surveillance *is recommended* for survivors treated with moderate-high dose anthracyclines (≥ 100 mg/m²) and moderate-high dose chest radiation (≥ 15 Gy).

What surveillance modality should be used?

Echocardiography *is recommended* as the primary cardiomyopathy surveillance modality for assessment of left ventricular systolic function in survivors treated with anthracyclines and/or chest radiation.

Radionuclide angiography or cardiac magnetic resonance imaging *may be reasonable* for cardiomyopathy surveillance in at risk survivors for whom echocardiography is not technically feasible/optimal.

Assessment of cardiac blood biomarkers (eg, natriuretic peptides and troponins) *is not recommended* as the primary cardiomyopathy surveillance in at-risk survivors.

At what frequency should surveillance be performed for *high-risk* survivors?

Cardiomyopathy surveillance *is recommended* for *high-risk* survivors to begin no later than 2 years after completion of cardiotoxic therapy, repeated at 5 years after diagnosis, and continued every 5 years thereafter.

More frequent cardiomyopathy surveillance *is reasonable* for *high-risk* survivors.

Lifelong cardiomyopathy surveillance *may be reasonable* for *high-risk* survivors.

At what frequency should surveillance be performed for *moderate/low-risk* survivors?

Cardiomyopathy surveillance *is reasonable* for *moderate/low-risk* survivors to begin no later than 2 years after completion of cardiotoxic therapy, repeated at 5 years after diagnosis, and continue every 5 years thereafter.

More frequent cardiomyopathy surveillance *may be reasonable* for *moderate/low-risk* survivors.

Lifelong cardiomyopathy surveillance *may be reasonable* for *moderate/low-risk* survivors.

What surveillance modality should be used?

Echocardiography *is recommended* as the primary cardiomyopathy surveillance modality for assessment of left ventricular systolic function in survivors treated with anthracyclines and/or chest radiation.

Radionuclide angiography or cardiac magnetic resonance imaging *may be reasonable* for cardiomyopathy surveillance in at risk survivors for whom echocardiography is not technically feasible/optimal.

Assessment of cardiac blood biomarkers (eg, natriuretic peptides and troponins) *is not recommended* as the primary cardiomyopathy surveillance in at-risk survivors.

"… **cardiac blood biomarkers** … ***is not recommended*** for surveillance in survivors."

Role of cardiac biomarkers

Curr Probl Cancer 42 (2018) 375–385

Contents lists available at ScienceDirect

Curr Probl Cancer

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

The role of cardiac biomarkers in cardio-oncology

Elizabeth Riddell, MD, PharmD, Daniel Lenihan, MD*

Cardio-Oncology Center of Excellence, Cardiovascular Division, Washington University in St. Louis, St. Louis, MO

Troponin as a tool for detecting cardiotoxicity

Table 1
Selected clinical studies investigating troponin as a tool for detecting cardiotoxicity.

Reference	Patient population	Patient sample size	Chemotherapy regimen	Value cutoff for troponin	Timing of measurement	Results	
Ky et al[7]	HER2 + breast cancer	78	Doxorubicin, cyclophosphamide, paclitaxel, trastuzumab		-Biomarkers measured at baseline, 3, and 6 mo -LVEF was measured at baseline, 3, 6, 9, 12, and 15 mo	TnI and MPO rise at 3 mo was associated with subsequent cardiotoxicity	
Sawaya et al[19]	HER2 + breast cancer	81	Anthracycline, paclitaxel, trastuzumab	≥30 pg/mL	Measurements were made at baseline, 3, 6, 9, 12, and 15 mo	Elevated TnI at 3 mo was predictive of subsequent cardiotoxicity	
Onitilo et al[15]	HER2 + breast cancer	54	Trastuzumab adjuvant	≥0.01 ng/mL	-Biomarkers measured at baseline, then every 3 wk up to 1 y -LVEF was measured every 3-4 mo	-Only hs-CRP was associated with a clinically significant decline in LVEF -Troponin was not	
Morris et al[16]	HER2 + breast cancer	95	Doxorubicin, cyclophosphamide, paclitaxel, trastuzumab	>0.04 ng/mL (DF/HCC) >0.06 ng/mL (MSKCC)	-Biomarkers measured every 2 wk during chemo and at 6, 9, and 18 mo -LVEF measured at 0, 6, 9, and 18 mo	-TnI rise (peak ~14 wk) preceded max decline in LVEF but did not predict or relate to max LVEF decline -CRP did not correlate with LVEF	
Cardinale et al[18]	Breast cancer	251	Anthracycline, cyclophosphamide, paclitaxel, trastuzumab	>0.08 ng/mL	-TnI was measured before and after each cycle -LVEF was measured at baseline, every 3 mo during therapy, and every 6 mo after	-TnI independently predicted cardiotoxicity and LVEF recovery	
Feola et al[14]	Breast cancer	53	Cyclophosphamide, epirubicin Fluorouracil ± locoregional XRT	>0.03 ng/mL	-Biomarkers and MUGA were assessed at baseline, 1 mo, 1 y, and 2 y	-Troponin level did not correlate with LV dysfunction	

Troponin as a tool for detecting cardiotoxicity

Table 1
Selected clinical studies investigating troponin as a tool for detecting cardiotoxicity.

Reference	Patient population	Patient sample size	Chemotherapy regimen	Value cutoff for troponin	Timing of measurement	Results	
Cardinale et al[11]	Advanced or primary resistant breast CA (326), high grade NHL (264), myeloma (44), poor prognosis Hodgkin's disease (30), relapsed or refractory ovarian CA (16), SCLC (10), germ-cell tumors (8), and Ewing's sarcoma (5)	703	High-dose chemotherapy (Some regimens did not contain an anthracycline)	≥0.08 ng/mL	-Troponin was measured soon after chemo administration and 1 mo after -LVEF by TTE was evaluated at baseline, 1, 3, 6, and 12 mo after treatment	-A persistent TnI increase was associated with a greater incidence of cardiac events PPV was 84% for patients was persistent troponin elevation and NPV was 99% for patients without troponin elevation	
Cardinale et al[10]	High risk breast cancer	211	Epirubicin, Taxotere, ifosfamide, Carboplatin, Etoposide, Cyclophosphamide (Some regimens did not contain an anthracycline)	≥0.05 ng/mL	- TnI was measured before, immediately after, and then 12, 24, 36, and 72 h after every single cycle of chemo	-Positive TnI was associated with a reduction in LVEF during 12 mo of follow-up.	
Kremer et al[12]	Various malignancies (pediatric); 16 with solid tumor and 22 with leukemia or lymphoma	38	Anthracyclines (33) or mitoxantrone (5)	>0.01 ng/mL	-TnT was measured prior to each chemo cycle, 4-6 h after each chemo cycle and 24 h after each chemo cycle. -Measurement of LV shortening fraction was measured using M-mode echo before, during, and after chemo	-TnT measured in the first 24 hours after administration of chemotherapy did not predict cardiotoxicity or cardiac dysfunction	
Cardinale et al[9]	Breast Cancer, ovarian cancer, SCLC, Hodgkin's lymphoma, NHL	204	Various regimens with epirubicin, etoposide, taxotere, carboplatin, and cyclophosphamide	>0.5 ng/mL	TnI was measured before, immediately after, and then 12, 24, 36, and 72 h after every single cycle of chemo -TTEs were performed at baseline, 1, 2, 3, 4, and 7 mo after chemo	-TnI elevation predicted future decline in LVEF	

Natriuretic peptides for the monitoring of cardiotoxicity

Table 2
Selected studies investigating natriuretic peptides (NPs) for the monitoring of cardiotoxicity.

Reference	Patient population	Patient sample size	Chemotherapy regimen	Normal reference value	Timing of measurement	Results	
De Iuliis et al[27]	Breast CA	100	Anthracyclines, Taxanes, trastuzumab	Not defined	NT-pro BNP and LVEF were measured at baseline, 3, 6, and 12 mo	-Significant increase in NT-proBNP ($P > 0.0001$) was seen before LVEF decrease became evident -There was a correlation between increased NT-proBNP after chemo and predicted 1 year mortality	
Lenihan, D et al[25]	Sarcoma, lymphoma, breast cancer	109	Anthracyclines	BNP > 100 pg/mL	Pre- and postcycle	-BNP was superior for the detection of cardiac events than LVEF	
Skovgaard et al[26]	Breast CA, hematologic malignancies, uterine/ovarian CA	333	Anthracyclines	BNP < 100 pg/mL	No standard intervals for measurement	-BNP and LVEF independently predicted hospitalization for CHF -Only BNP showed prognostic value in predicting mortality	
Daugaard et al[28]	Various advanced cancers (malignant disease)	107	Anthracyclines	Not defined	No standard intervals for measurement but started after ½ cumulative dose of anthracycline was administered	-Neither baseline levels of BNP or change in level of BNP during therapy were predictive of change in LVEF -BNP cannot replace measurement of LVEF	
Sandri et al[24]	Various aggressive malignancies	52	High-dose chemo-based on study institution protocol	NT-pro BNP cutoff values differed based on age and gender. >153 ng/mL for women < 50 y; >88 ng/mL for men <50 y; 334 ng/mL for women >50 y; 227 ng/L for men >50 y	-NT-pro BNP levels were drawn at baseline (before each treatment), at the end of chemo infusion, and 12, 24, 36, and 72 h after the end of each chemo cycle -TTE was performed at baseline and at 4 and 12 mo after treatment	-Persistent increase in NT-proBNP was associated with development of cardiac dysfunction	
Suzuki et al[23]	Hematologic malignancies	27	Anthracyclines	BNP < 19 pg/mL	BNP levels were drawn at baseline and after chemo administration	-Concentrations of BNP increased after treatment -Persistent elevations in BNP were associated with poor prognosis	

Role of cardiac biomarkers

Curr Probl Cancer 42 (2018) 375–385

Contents lists available at ScienceDirect

Curr Probl Cancer

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

The role of cardiac biomarkers in cardio-oncology

Elizabeth Riddell, MD, PharmD, Daniel Lenihan, MD*

Cardio-Oncology Center of Excellence, Cardiovascular Division, Washington University in St. Louis, St. Louis, MO

"Current clinical research in cardio-oncology has not firmly established these biomarkers as effective screening tools for cardiotoxicity in a broad range of populations or cancer therapeutics but the future is bright for these markers as indicators of cardiac risk as well as tools to ensure cardiac safety".

Potential explanations

- The timing of serum troponin collection
- Studies with chemotherapy regimens that are now out of date
- Different methods for troponin measurement
- Several cut-offs used to consider a test as positive
- Percentage of cardiac injury of chemotherapy agents is variable

Potential explanations

Prognostic Value of Troponin I in Cardiac Risk Stratification of Cancer Patients Undergoing High-Dose Chemotherapy

Daniela Cardinale, MD; Maria T. Sandri, MD; Alessandro Colombo, MD; Nicola Colombo, MD; Marina Boeri, MD; Giuseppina Lamantia, MD; Maurizio Civelli, MD; Fedro Peccatori, MD; Giovanni Martinelli, MD; Cesare Fiorentini, MD; Carlo M. Cipolla, MD

(*Circulation*. 2004;109:2749-2754.)

- 703 pacientes con cáncer y QT a altas dosis sin cardiopatía previa
- Troponina medida por método convencional. Cut-off 0,08 ng/mL
- Medición de TnI basal y al mes del tto (inmediatamente después, 12, 24, 36, 72h)

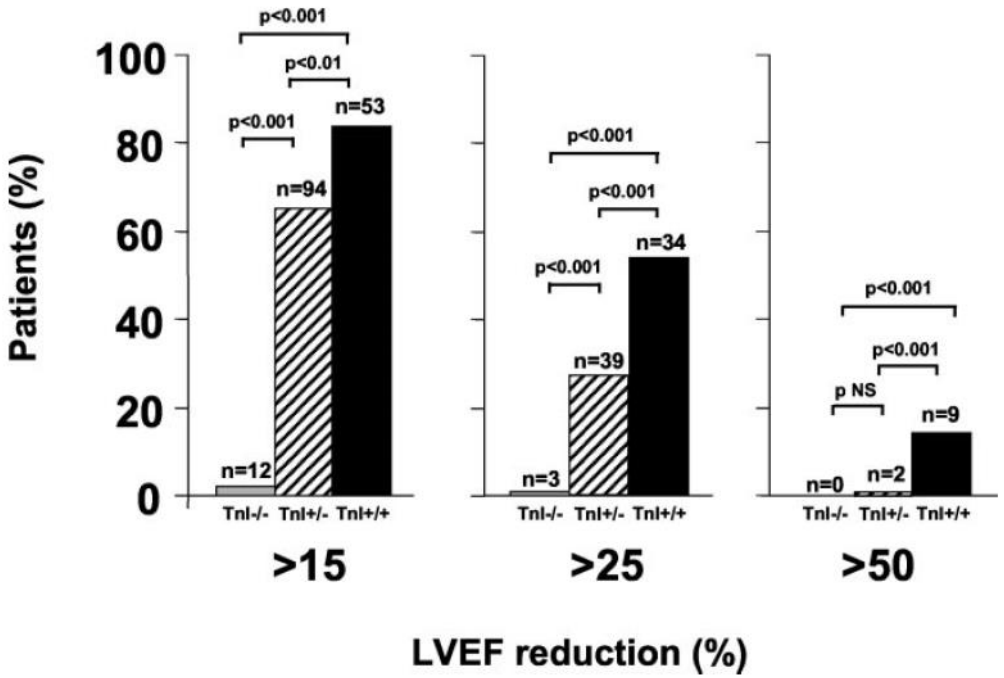
  Considera el valor más alto:

  - Al terminar 33%; tras 12h 22%; tras 24h 8%; tras 36h 24%; tras 72h 13%

Potential explanations

Prognostic Value of Troponin I in Cardiac Risk Stratification of Cancer Patients Undergoing High-Dose Chemotherapy

Daniela Cardinale, MD; Maria T. Sandri, MD; Alessandro Colombo, MD; Nicola Colombo, MD; Marina Boeri, MD; Giuseppina Lamantia, MD; Maurizio Civelli, MD; Fedro Peccatori, MD; Giovanni Martinelli, MD; Cesare Fiorentini, MD; Carlo M. Cipolla, MD



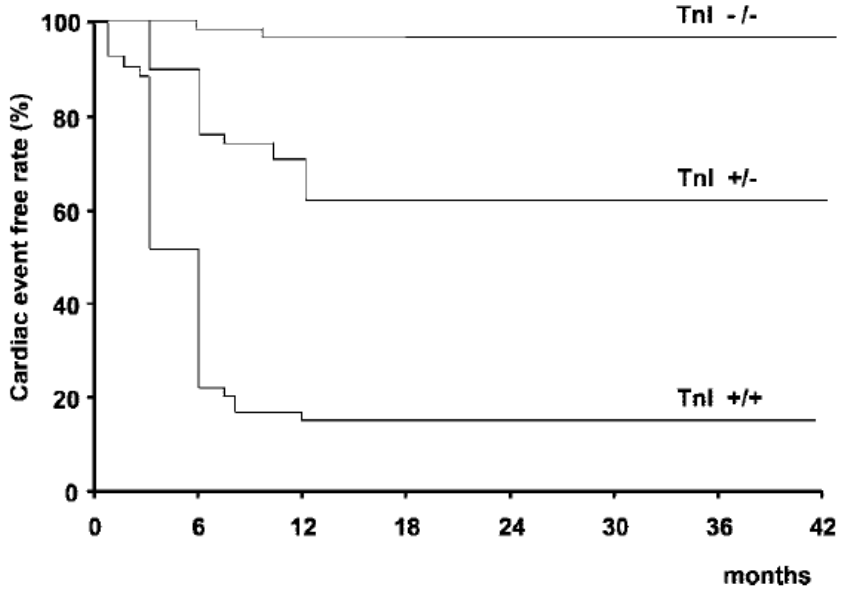


Figure 3. Cumulative cardiac events rate in 3 study groups. $P<0.001$ for $TnI^{+/+}$ vs $TnI^{-/-}$ and $TnI^{+/-}$, and for $TnI^{+/-}$ vs $TnI^{-/-}$.

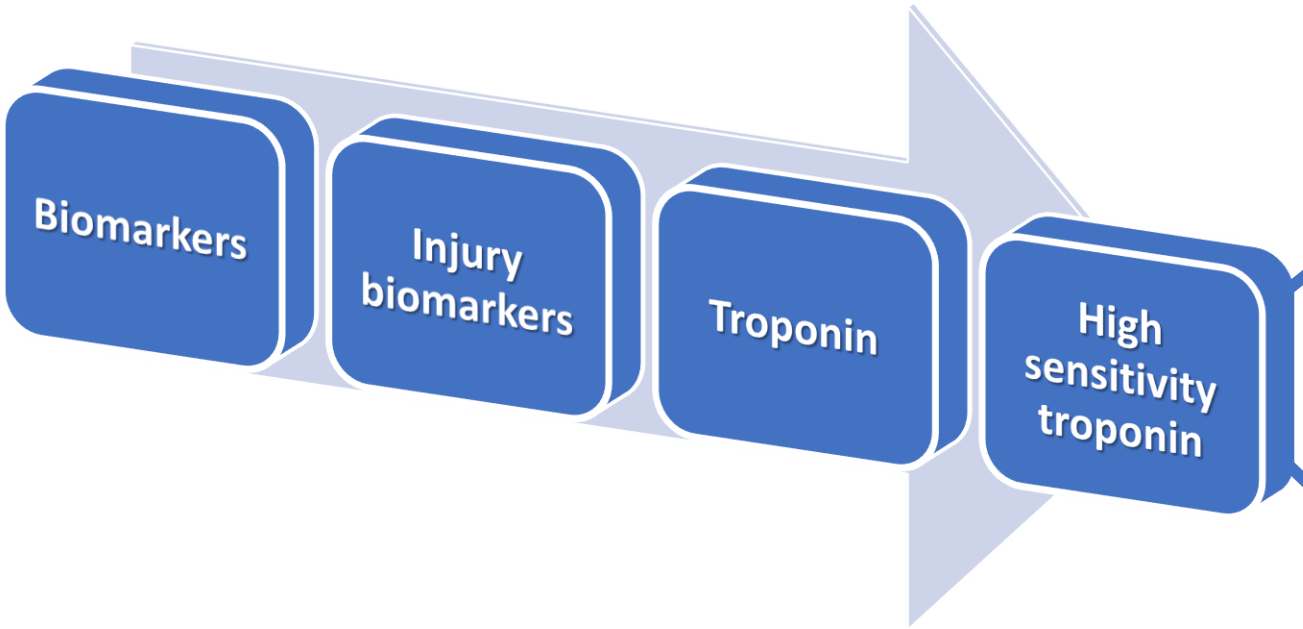
Advantages of cardiac biomarkers

- “Easy to use” - availability
- Minimally invasive
- Costs less than echocardiogram and than a nuclear LVEF assessment
- Without direct damage for patient
- Interpretation of results doesn't depend on the experience of an operator
- Early detection of potential cardiotoxicity
- Potential high negative predictive value → allows identification of low-risk patients who will not require further cardiac monitoring
- TnI-positive patients require more strict surveillance

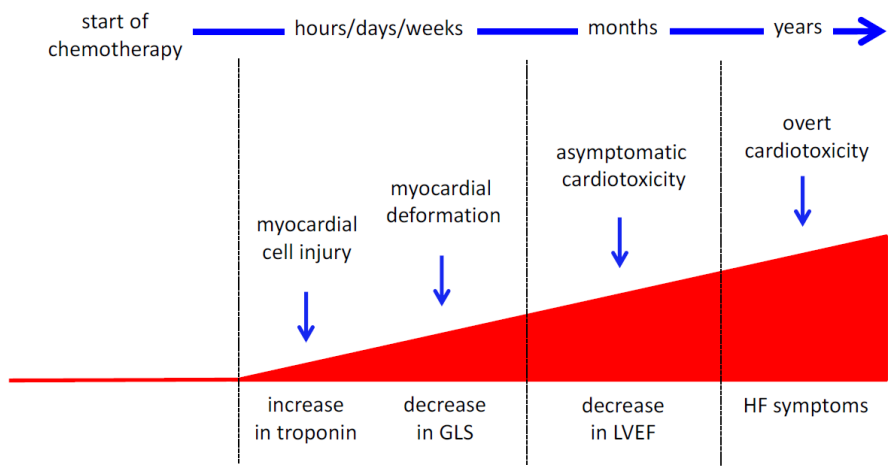
Possible utilities of cardiac biomarkers

- Identify patients at risk **before** cancer therapy (chemo or radio): unknown cardiac diseases vs cancer damage?
- Identify patients that develop myocardial injury **during** cancer therapies (surveillance and monitoring)
- **Monitoring** of the cardioprotective **effect** preventive treatments (dexrazoxane, nebivolol, valsartan, …)
- Long term **follow up** of patients after cancer treatment: “personalization” of the frequency of cardiac function monitoring
- **Prognostic** value → prediction of future LVD severity

Proposal of a biomarker algorithm

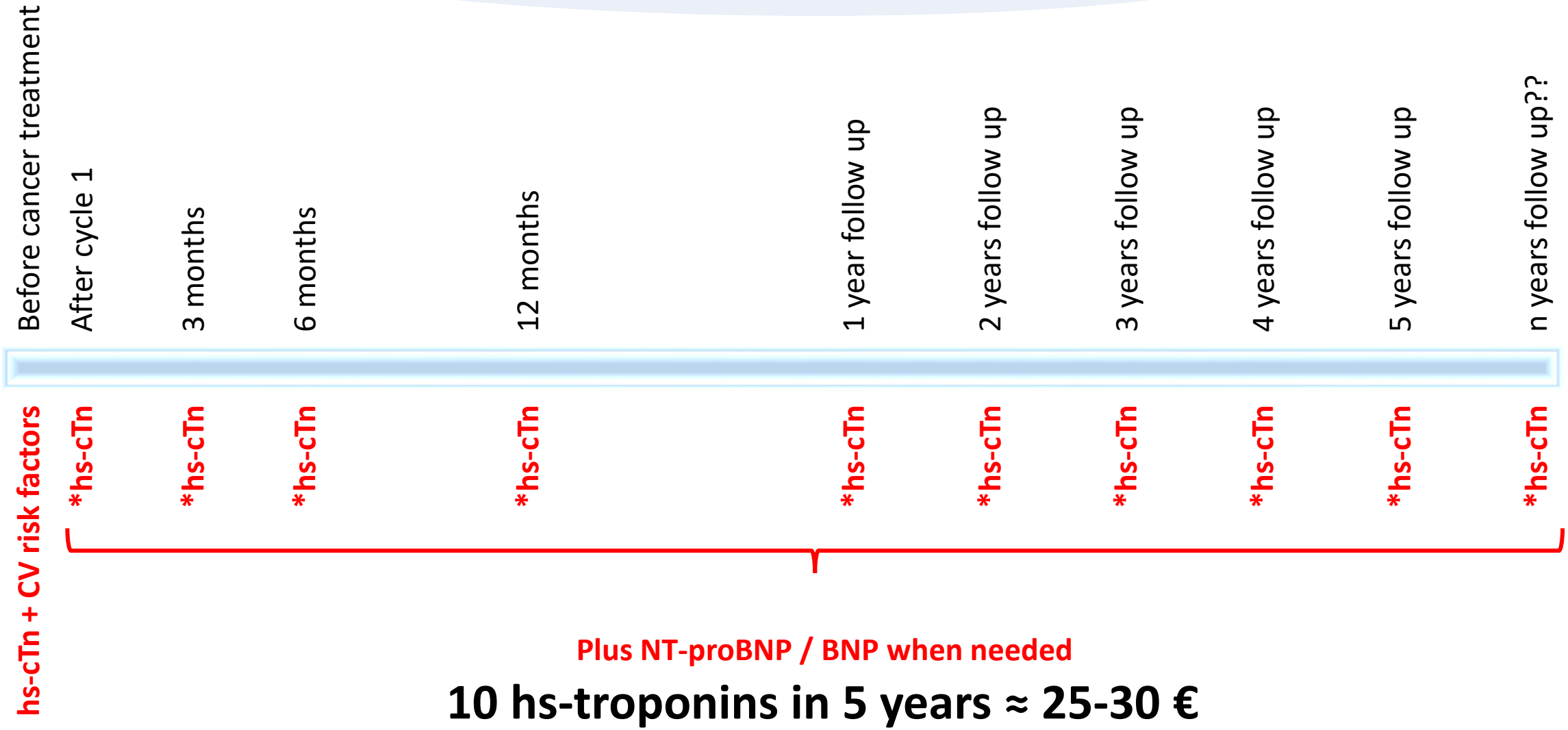


Early detection



High negative predictive value

Proposal of how to use a biomarker



Plus NT-proBNP / BNP when needed

10 hs-troponins in 5 years ≈ 25-30 €

*** High sensitivity troponin is better than conventional, but conventional is better than nothing.**

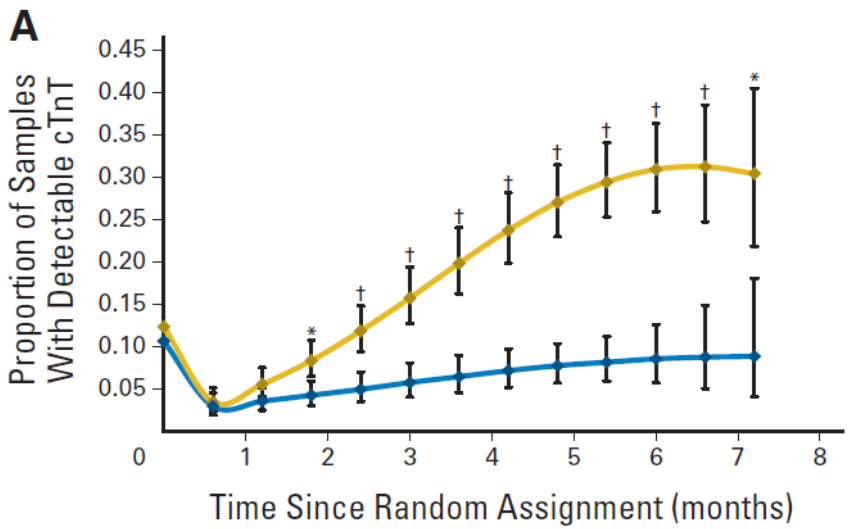
Cardiotoxicidad en la infancia

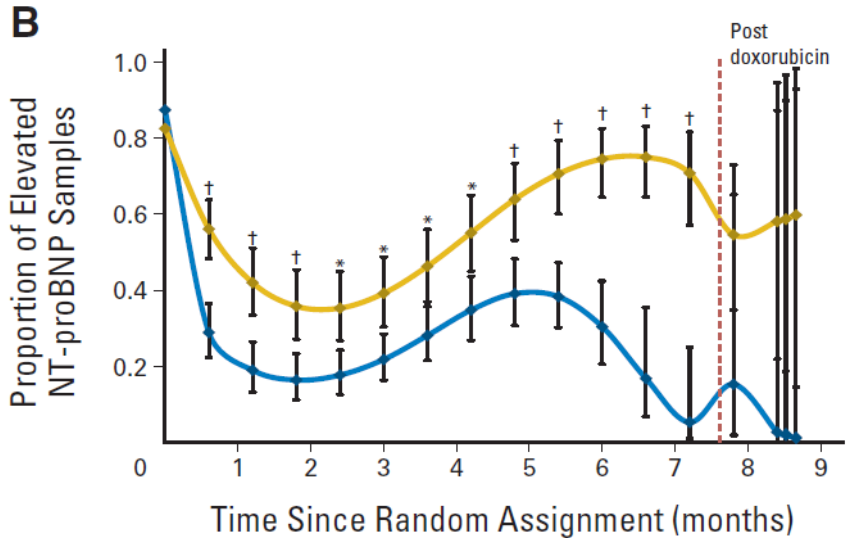
VOLUME 30 · NUMBER 10 · APRIL 1 2012

JOURNAL OF CLINICAL ONCOLOGY

Changes in Cardiac Biomarkers During Doxorubicin Treatment of Pediatric Patients With High-Risk Acute Lymphoblastic Leukemia: Associations With Long-Term Echocardiographic Outcomes

- Doxorrubicina (n: 100/75) vs doxorrubicina y dexrazoxano (n: 105/81)
- cTnT (cualquier valor medible) y NT-proBNP (>150 pg/mL en <1a y >100 pg/mL en >1a)
- Clara asociación entre % de aumento de BM y hallazgos ecocardiográficos





Cardiotoxicidad en la infancia

Skitch *et al. BMC Cancer* (2017) 17:519
DOI 10.1186/s12885-017-3505-0

Novel approaches to the prediction, diagnosis and treatment of cardiac late effects in survivors of childhood cancer: a multi-centre observational study

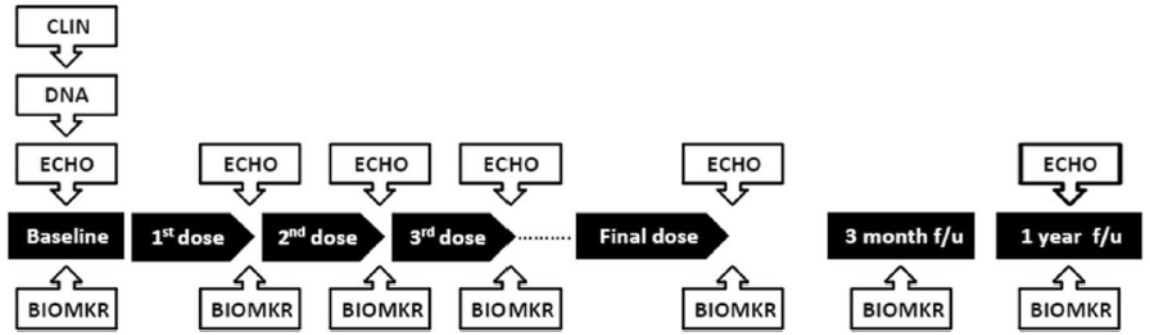


Fig. 1 Data and specimen acquisition from the Acute Cohort. BIOMKR: Serum for biomarkers, ECHO: Echocardiogram, DNA: Blood or saliva for DNA, CLIN: Gather baseline clinical data

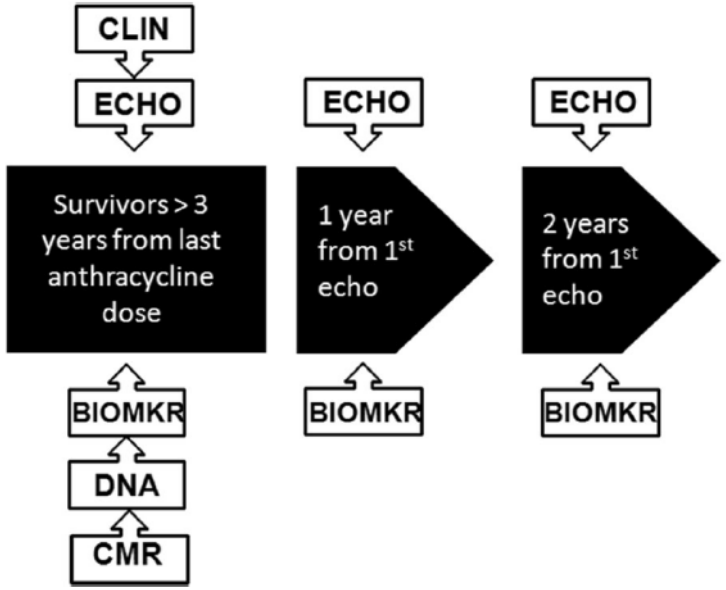
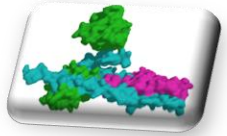


Fig. 2 Data and specimen acquisition from the Survivor Cohort. BIOMKR: Serum for biomarkers, ECHO: Echocardiogram, DNA: Blood for DNA, CMR: Cardiac Magnetic Resonance, CLIN: Gather baseline clinical data

Take home messages

- Biomarkers has the potential to anticipate other diagnostics techniques (cell injury level)



- High sensitivity troponin (not conventional) is the preferable biomarker but we need to learn how to use it

- Results with natriuretic peptides are controversial

- Other biomarkers are less practicable and results are inconclusive
- Possible roles:
  a) Identify patients at risk before and during cancer therapy
  b) Monitoring cancer treatment or cardioprotective treatments
  c) Surveillance after treatment
  d) Prognostic value

- But … there are many questions to be solved with future investigations


tusind tak
谢谢
dakujem vám
ありがとう
ngiyabonga
dziękuję
merci
suksema
danke
thank
you
baie dankie
धन्यवाद
molte grazie
gracias
takk
obrigada
obrigado
teşekkür ederim
شكرا
gràcies
tänan
dank u
tạ ơn
tack så mycket
teşekkür ederim
mahalo