Cardiaovascular biomarkers

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Worldwide CVD mortality rate

ESC European Society of Cardiology
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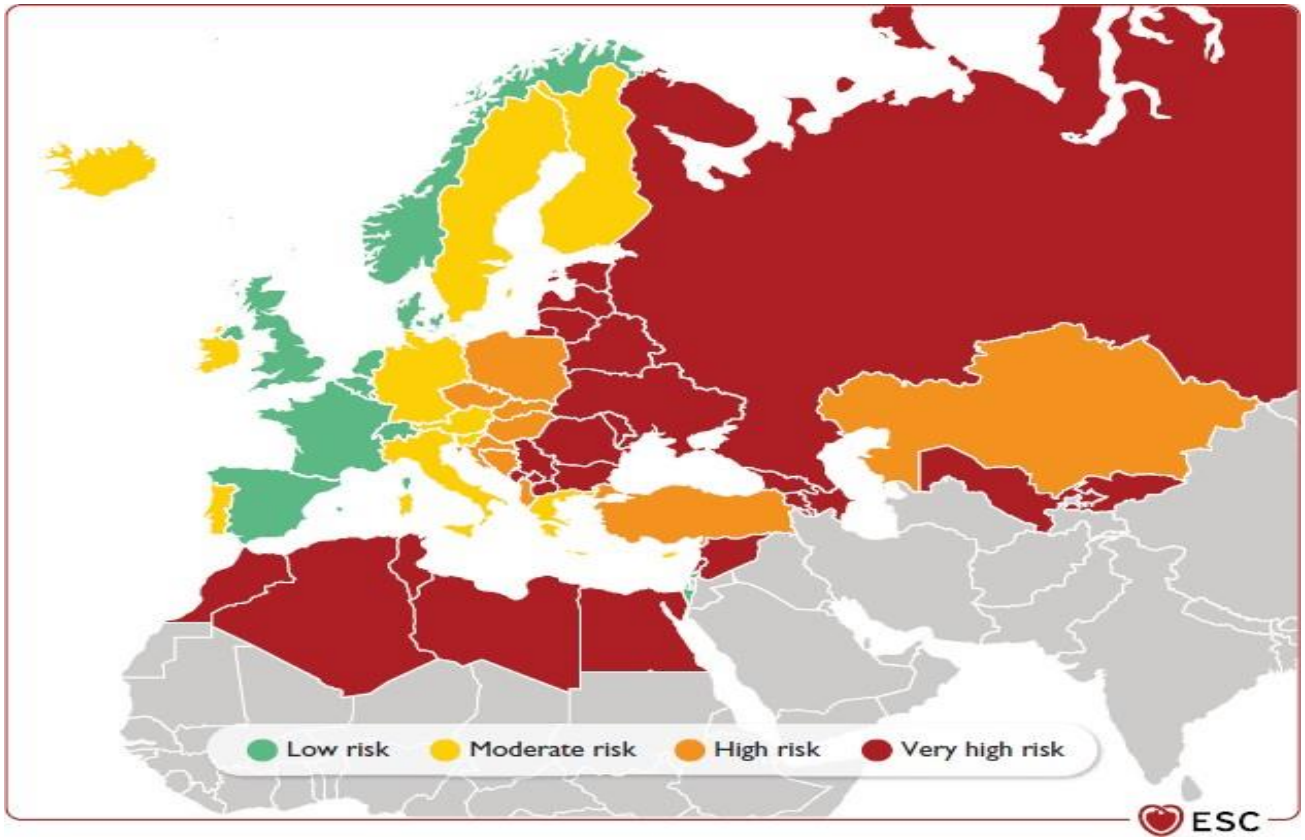
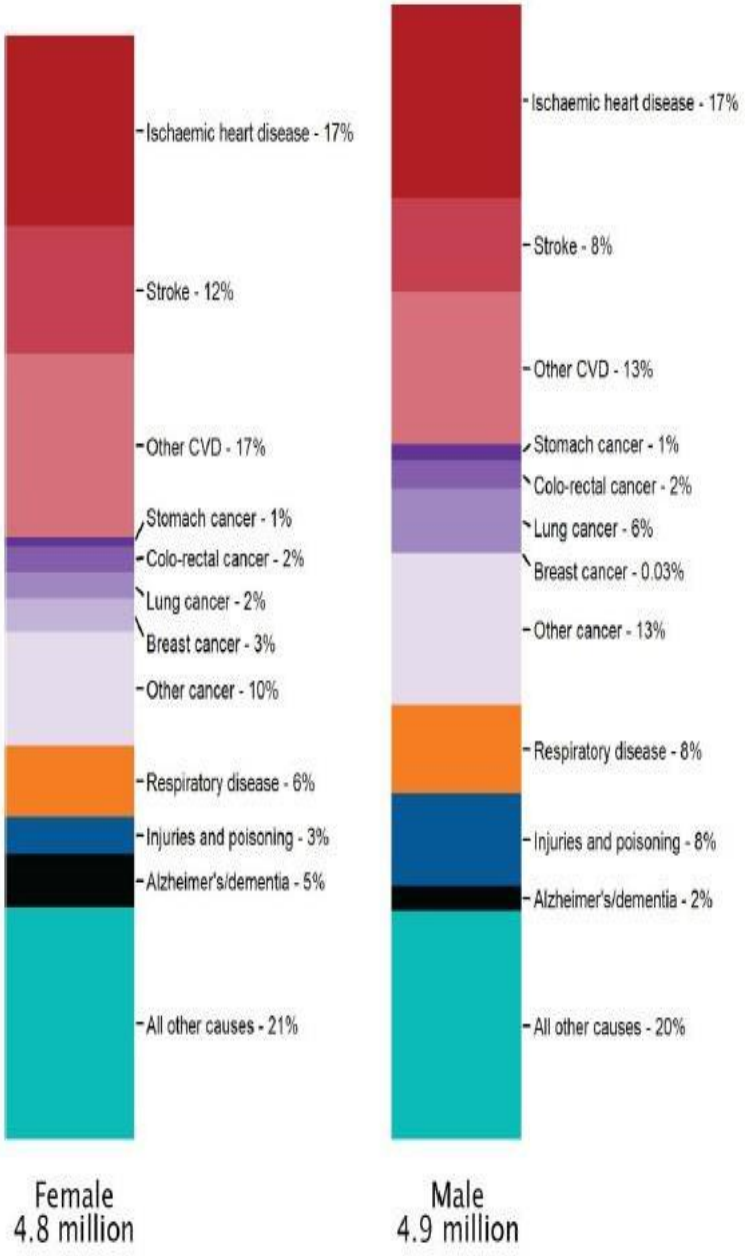
ESC GUIDELINES

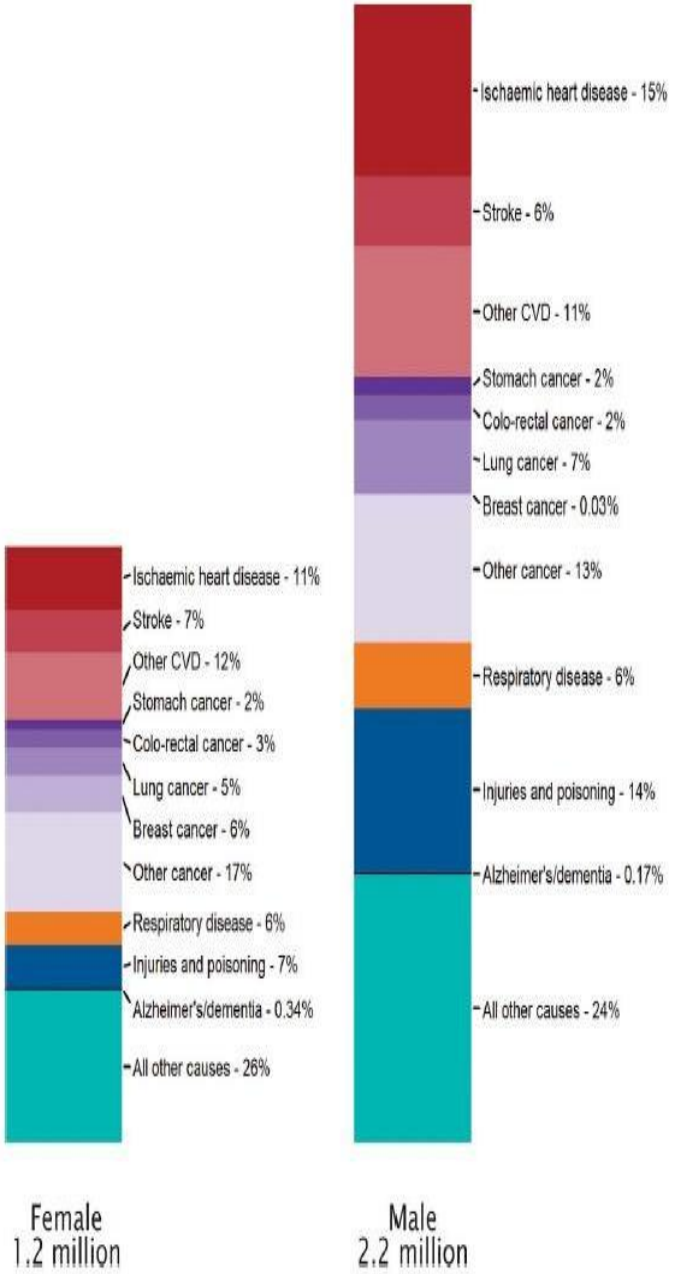
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice



ECDS 2021 – Europe Mortality data



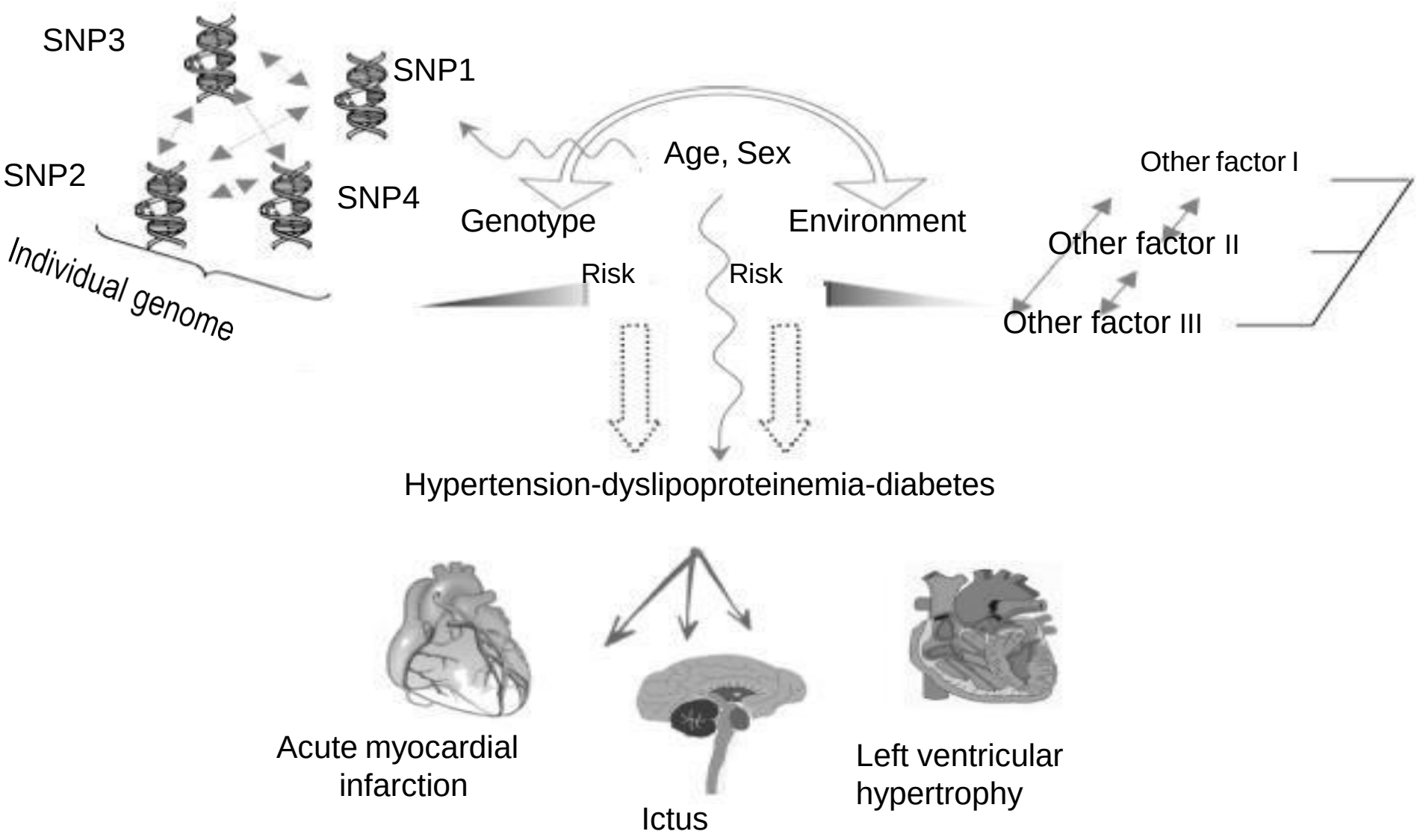
Premature mortality



Ischemia and cardiovascular diseases

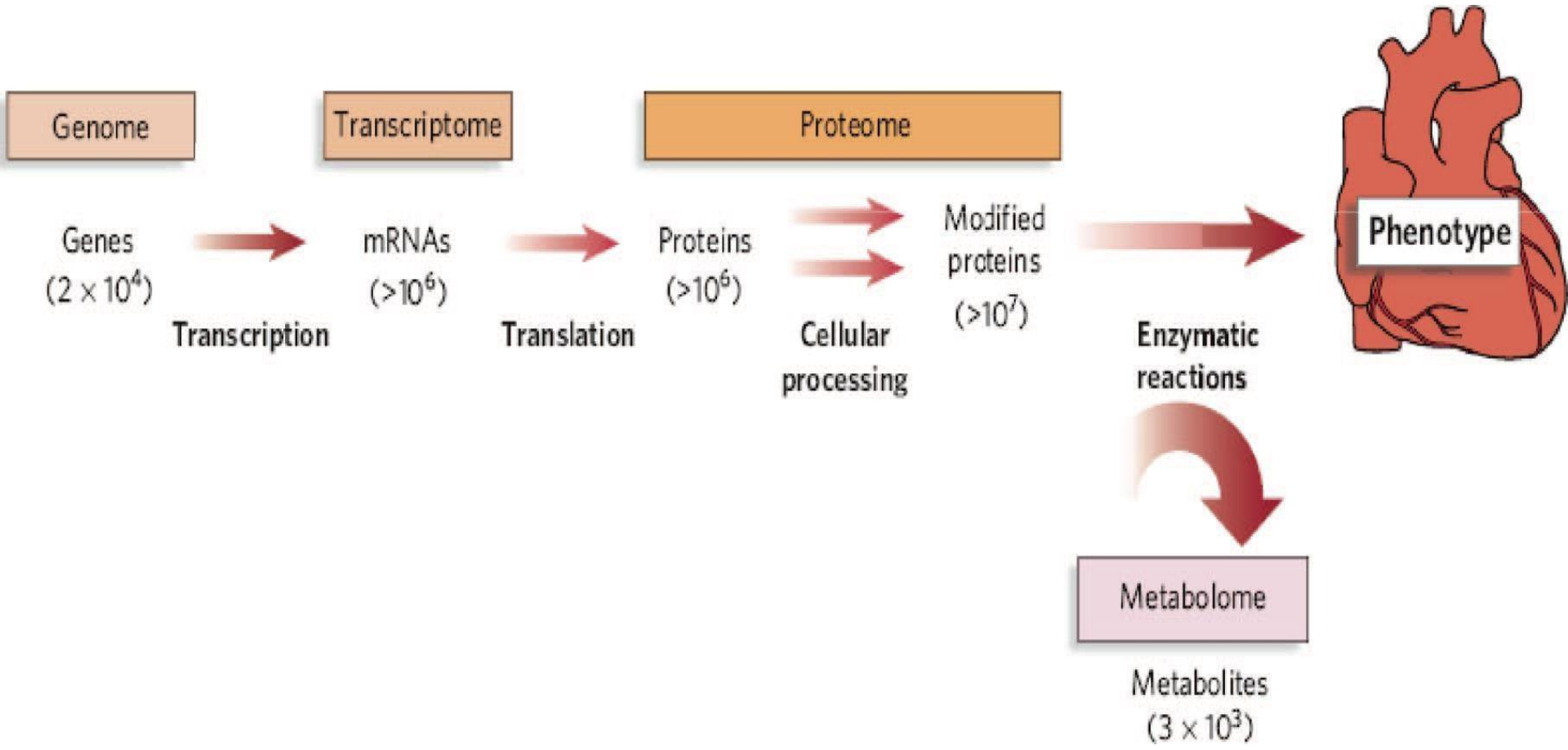
- Atherosclerosis
- Deep vein thrombosis
- Environmental factors (lifestyle, diet, alcohol)
- Risk factor – age, obesity, diabetes, lipid disorders
- Genetics

Interactions between genetic and risk factors



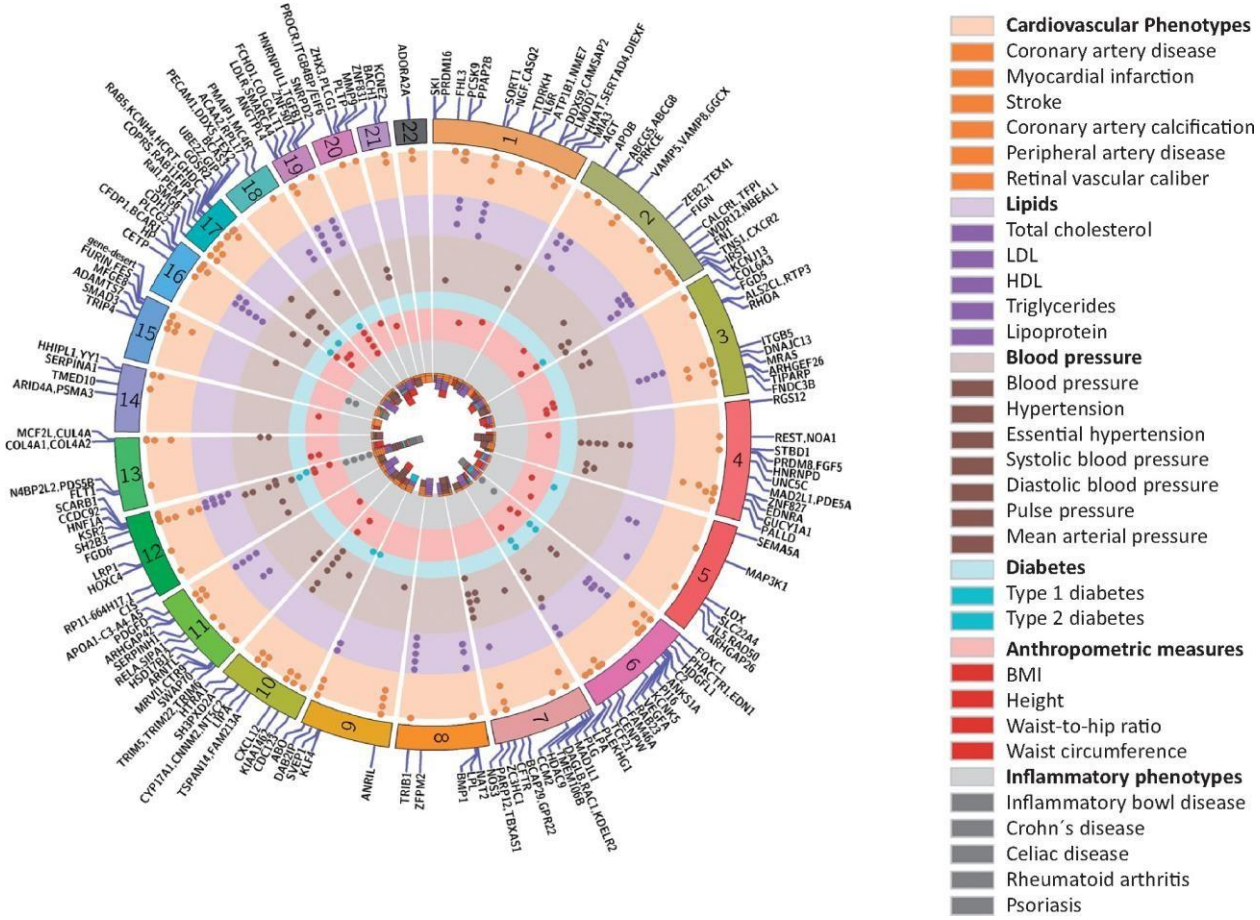
Visvikis Siest et al., Curr Opin Lipidol 2006

Complexity of cardiovascular diseases



Genetic aspects of cardiovascular diseases

Figure 3 Circosplot showing 163 risk loci for CAD under the chromosomes, where they are located.



Cardiovasc Res, Volume 114, Issue 9, 15 July 2018, Pages 1241–1257, https://doi.org/10.1093/cvr/cvy084

Mutations and polymorfisms involved in CVD

Protective

Chr	Gene	Protective alleles
1p13	*Rs599839 A>G Rs646776 T>C*	C/G haplotype
1q22	*E-selectin*	G2692A; C901T
1q31	*GLUL*	Rs10911021 T>C, TT allele
1q31	*IL-10*	G(-1082)A, GG genotype
1p34	*LRP 8*	TCCGC
2p21	*ABCG 5/8*	Rs41360247
3p25	*PPARγ2*	Pro12Ala homo
3p25	*PPARγ*	C161T
3q27	*Adiponectin*	Rs1501299 (G276T), TT allele
8q21	*FABP4*	Rs77878271
6p12.3	*PLA2G7*	R92H
6p25.3	*FXIII*	Val34Liu
7q21.3	*PON1/2*	Gln192Arg
7q32.3	*KLF14*	Rs4731702 T/T allele
7q36	*INSIG1*	Hap3 (T/G/A)
9q31.1	*ABCG1*	G1051A, r219K, KK allele
11q23.3	*APOC3*	R19X
13q34	*FVII*	R353Q; QQ allele
		A2 allele (without a 10 bp insertion)
16q13	*FKN*	T280M allele; Rs4329913; Rs7202364
16q24	*NADPH p22phox*	C242T
17p13.2	*GP1ba*	Thr/Th; TT haplotype
21q22.1	*MRPS6*	C699T (TT) or T1080C (CC)

Risk

Location/Chromosome	Gene (s)	SNPs	Risk Allele	Risk Allele Frequency
1p32.3	*PCSK9*	rs112065101	T/C	0.848
1p32.3	*PPAP2B*	rs9970807	C/T	0.915
1p13.3	*SORT1*	rs7528419	A/G	0.786
1q21	*CTSS*	rs6587520	T/C	0.480
1q21.3	*IL6R*	rs6689306	A/G	0.448
1q41	*MIA3*	rs67180937	G/T	0.663
2p24.1	*AK097927*	rs16986953	A/G	0.105
2p24.1	*APOB*	chr2:21378433:D	D/I	0.746
2p21	*ABCG5, ABCG8*	chr2:44074126:D	I/D	0.745
2p11.2	*VAMP5-VAMP8-GCX*	rs7568458	A/T	0.449
2q22.3	*ZEB2-ACO74093.1*	rs17678683	G/T	0.088
2q33.2	*WDR12*	chr2:203828796:I	I/D	0.108
3q22.3	*MRAS*	chr3:138099161:I	I/D	0.163
4q31.22-q31.23	*EDNRA*	rs4593108	C/G	0.795
4q32.1	*GUCY1A3*	rs72689147	G/T	0.817
4q12	*REST-NOA1*	rs17087335	T/G	0.210
5q31.1	*SLC22A4-SLC22A5*	rs273909	G/A	0.117
6p24.1	*ADTRP-C6orf105*	rs6903956	A/G	0.354
6p24.1	*PHACTR1*	rs9349379	G/A	0.432
6p21.31	*ANKS1A*	rs17609940	G/C	0.824
6p21.2	*KCNK5*	rs56336142	T/C	0.807
6q23.2	*TCF21*	rs12202017	A/G	0.700
6q25.3	*SLC22A3-LPAL2-LPA*	rs55730499	T/C	0.056
6q26	*PLG*	rs4252185	C/T	0.060
7p21.1	*HDAC9*	rs2107595	A/G	0.200
7q22.3	*BCAP29*	rs10953541	C/T	0.783
7q34	*ZC3HC1 (PARP12)*	rs11556924	C/T	0.687
7q36.1	*NOS3*	rs17087335	T/C	0.060
8p21.3	*LPL*	rs264	G/A	0.853
8q24.13	*TRIB1*	rs2954029	A/T	0.551
9p21.3	*CDKN2BAS*	rs2891168	G/A	0.489
9q34.2	*ABO*	rs2519093	T/C	0.191
10p11.23	*KIAA1462*	rs2487928	A/G	0.418
10q11.21	*CXCL12*	rs1870634	G/T	0.637
10q23.31	*LIPA*	rs1412444	T/C	0.369
10q24.32	*CYP17A1-CNNM2-NT5C2*	rs11191416	T/G	0.873

Location/Chromosome	Gene (s)	SNPs	Risk Allele	Risk Allele Frequency
10q26	*WDR11-FGFR2*	rs2257129	C/T	0.900
11q22.3	*PDGFD*	rs2128739	A/C	0.324
11q22	*RDX-FDX1*	rs10488763	T/A	0.180
11q23.3	*ZNF259-APOA5-APOA1*	rs964184	G/C	0.185
11p15.4	*SWAP70*	rs10840293	A/G	0.550
12q21.33	*ATP2B1*	rs2681472	G/A	0.201
12q24.12	*SH2B3*	rs3184504	T/C	0.422
12q24.22-q24.23	*KSR2*	rs1180803	G/T	0.360
13q12.3	*FLT1*	rs9319428	A/G	0.314
13q34	*COL4A1-COL4A2*	rs11838776	A/G	0.263
14q32	*HHIPL1*	rs10139550	G/C	0.423
15q25.1	*ADAMTS7*	rs4468572	C/T	0.586
15q26.1	*FURIN-FES*	rs17514846	A/C	0.440
15q22.33	*SMAD3*	rs56062135	C/T	0.790
15q26.1	*MFGE8-ABHD2*	rs8042271	G/A	0.900
17p13.3	*SMG6*	rs216172	C/G	0.350
17p11.2	*RAI1-PEMT-RASD1*	rs12936587	G/A	0.611
17q21.32	*UBE2Z*	rs46522	T/C	0.513
17q23.2	*BCAS3*	rs7212798	C/T	0.150
18q21.32	*PMAIP1-MC4R*	rs663129	A/G	0.260
19p13.2	*LDLR*	rs56289821	G/A	0.900
19q13.32	*APOE-APOC1*	rs4420638	G/A	0.166
19q13.11	*ZNF507-LOC400684*	rs12976411	T/A	0.090
21q22.11	*KCNE2*	rs28451064	A/G	0.121
22q11.23	*POM121L9P-ADORA2A*	rs180803	G/T	0.970

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Heart Failure

A huge burden to patients and society

Affects 1-3% of the general population, ~10% of elderly[1,2]

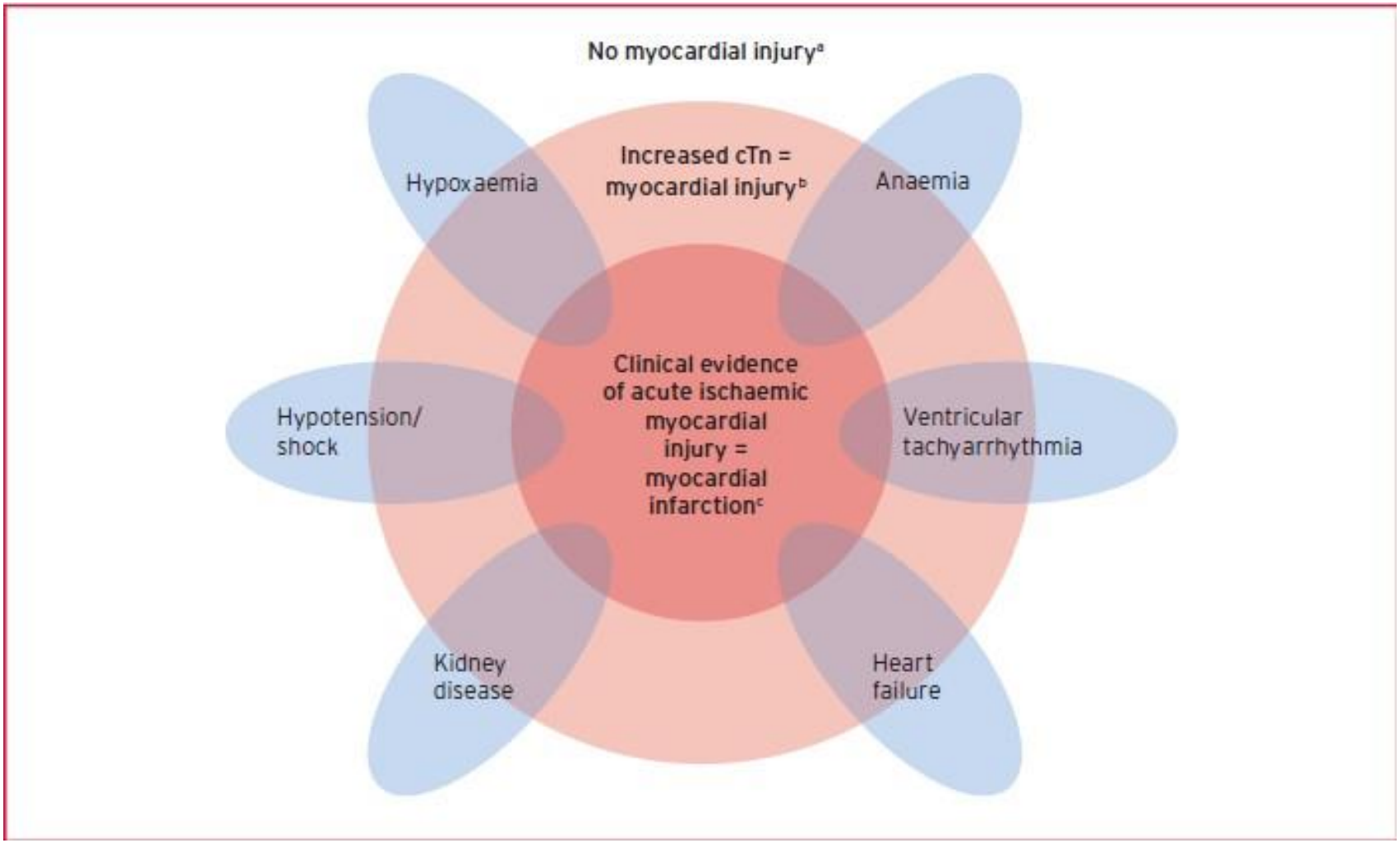
Survival similar to the most common forms of cancer [4]

Diagnosis is often difficult, and physician's indecision linked to worse outcomes[5]

HF is one of the most common causes of hospital admissions[3]

1.McMurray, J.J. et al. (2012). *Eur Heart J, 33*(14), 1787-847.
2.Mosterd, A. & Hoes, A.W. (2007). *Heart, 93*(9), 1137-46.
3.Adlbrecht, C. et al. (2011). Eur J Clin Invest, 41(3): 315-322
4.Smith, Koul, Kornhall et al (2012). Läkartidningen nr 41
5.Green, S. et al. (2008). Arch Int Medicine, 168(7), 741-748.

Myocardial injury



Acute myocardial infarction (AMI)

Time is life

Each year over 7 million people have an AMI worldwide[1]

AMI is a life-threatening condition

STEMI mortality[2]:
≈ **9 %** (1 year)

NSTEMI mortality[2]:
≈ **11.6 %** (1 year)

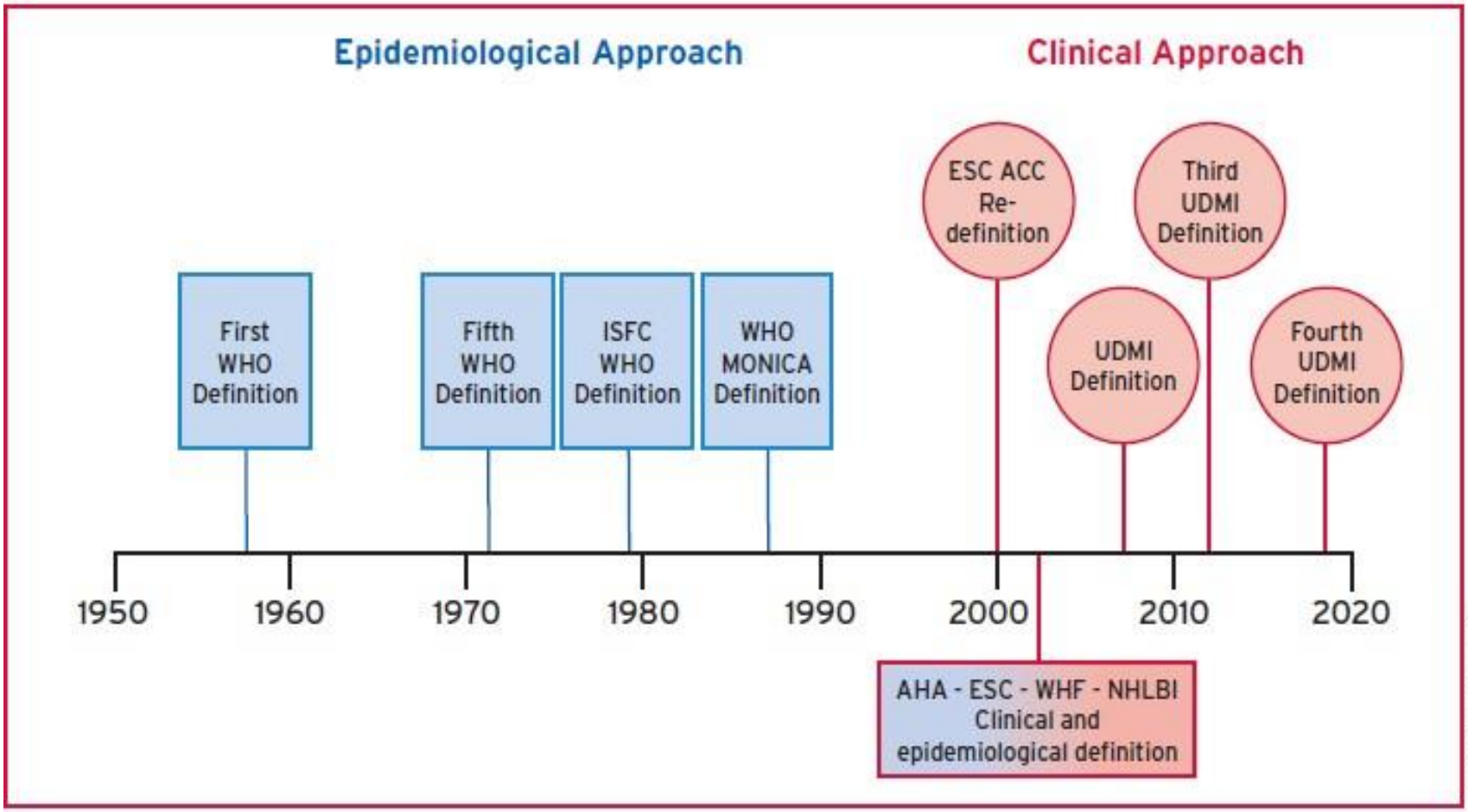
Every 30 minutes of delay between symptoms and treatment increases the relative risk of 1-year mortality by 7.5% in patients with AMI[3]

This is a race against the clock where every minute counts

There is a need for identifying low-risk patients to facilitate earlier discharge[4] and reduce unnecessary hospital admission[5]

1. White and Chew (2008). *Lancet* 372:570-54.
2. Montalescot G et al. (2007) *Eur Heart J* 28, 1409–17.
3. De Luca et al (2004). *Circulation* 109:1223-5.
4. Than M et al. (2011). *Lancet* 377:1077-84.
5. Hamilton AJ et al (2008). *Eur J Emerg Med* 15:9-15.

Acute myocardial infarction



ESC European Society of Cardiology
European Heart Journal (2018) 00, 1–33
doi:10.1093/eurheartj/ehy462

EXPERT CONSENSUS DOCUMENT

Fourth universal definition of myocardial infarction (2018)

Universal definitions of myocardial injury and myocardial infarction
Criteria for myocardial injury
The term myocardial injury should be used when there is evidence of elevated cardiac troponin values (cTn) with at least one value above the 99th percentile upper reference limit (URL). The myocardial injury is considered acute if there is a rise and/or fall of cTn values.

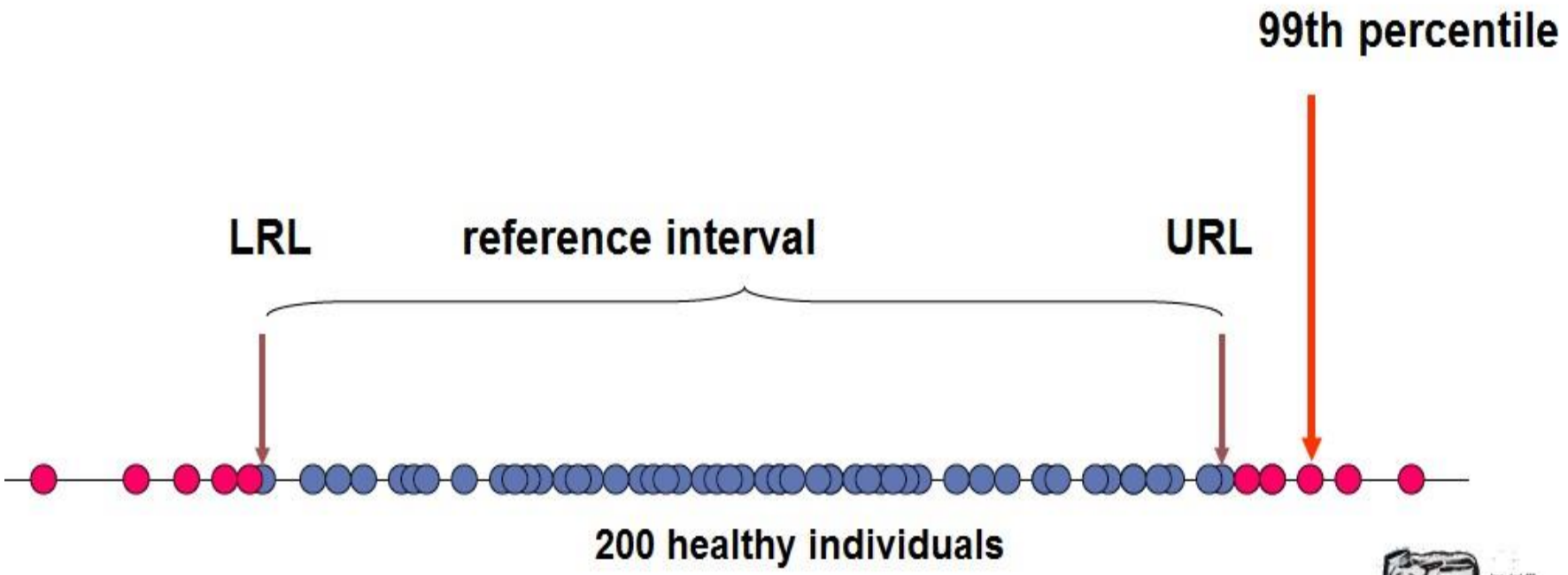
Clinical criteria for MI

The clinical definition of MI denotes the presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischaemia.

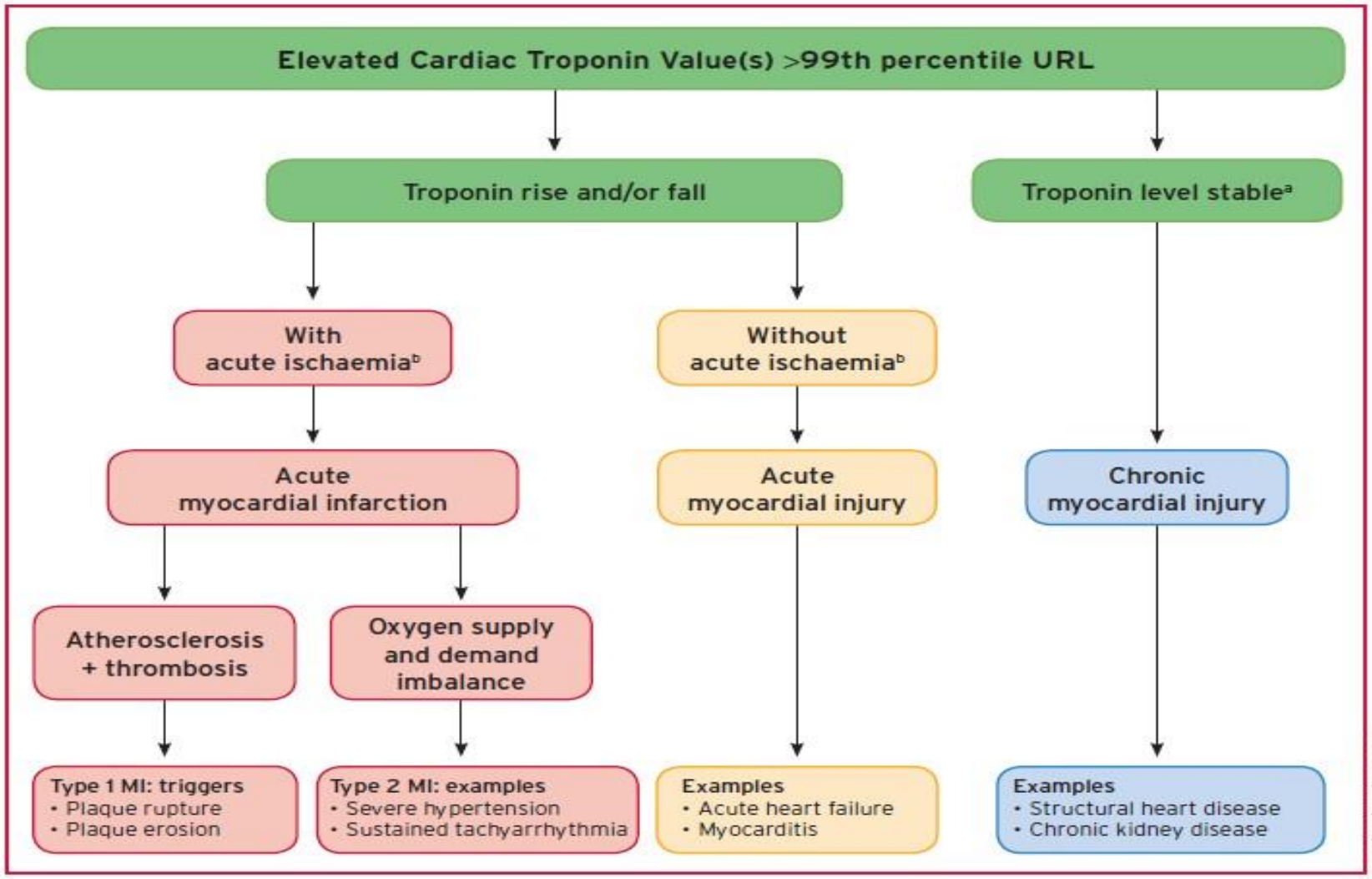
Cut off value vs reference limit

Upper reference limit - 97.5 th percentile

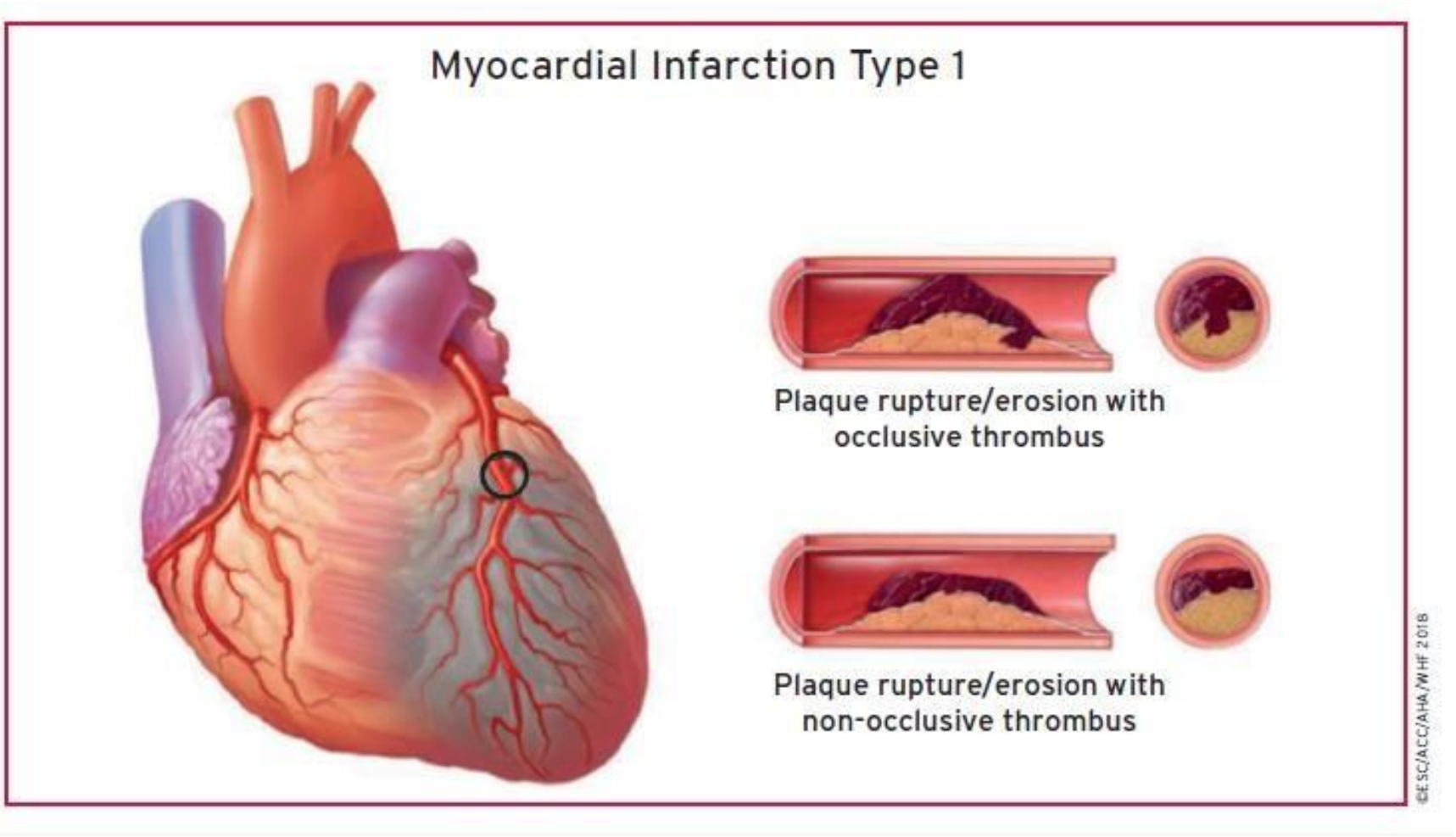
Cut off value - 99th percentile



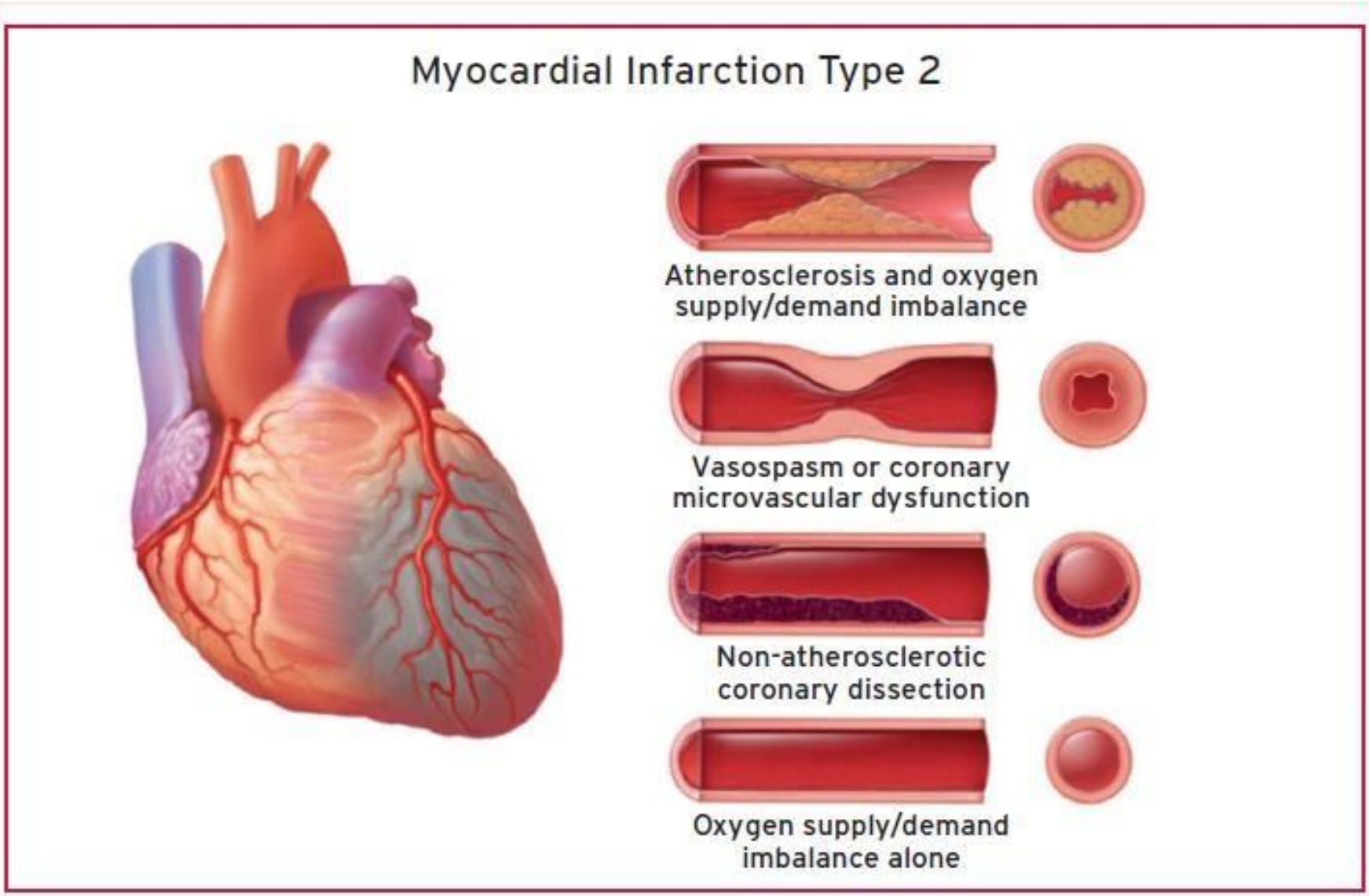
Model interpretation



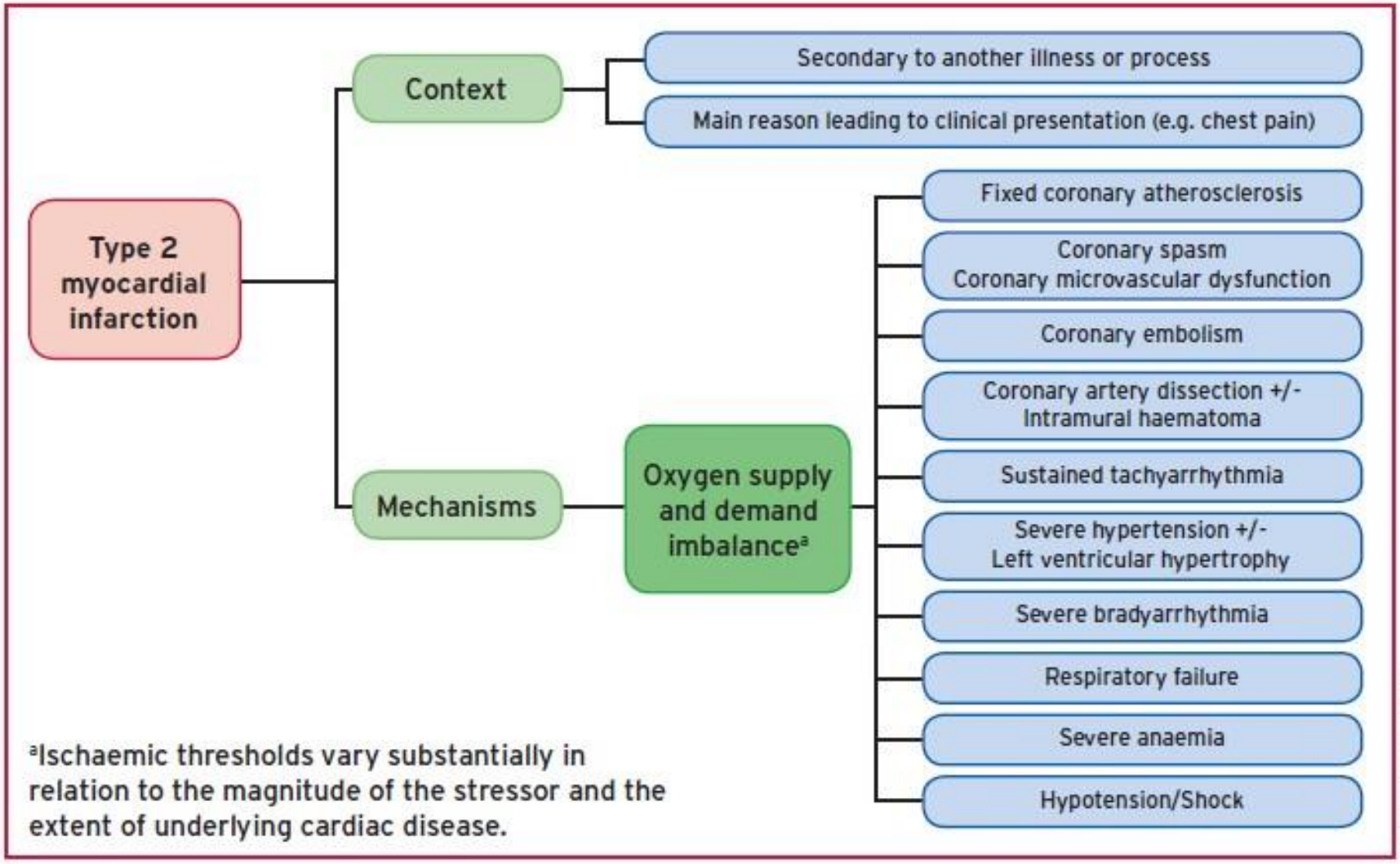
AMI type I


Myocardial Infarction Type 1
Plaque rupture/erosion with occlusive thrombus
Plaque rupture/erosion with non-occlusive thrombus
©ESC/ACC/AHA/WHF 2018

AMI type II


Myocardial Infarction Type 2
Atherosclerosis and oxygen supply/demand imbalance
Vasospasm or coronary microvascular dysfunction
Non-atherosclerotic coronary dissection
Oxygen supply/demand imbalance alone
©ESC/ACC/AHA/WHF 2018

AMI type II


Type 2 myocardial infarction
Context
Secondary to another illness or process
Main reason leading to clinical presentation (e.g. chest pain)
Mechanisms
Oxygen supply and demand imbalance[a]
Fixed coronary atherosclerosis
Coronary spasm
Coronary microvascular dysfunction
Coronary embolism
Coronary artery dissection +/-
Intramural haematoma
Sustained tachyarrhythmia
Severe hypertension +/-
Left ventricular hypertrophy
Severe bradyarrhythmia
Respiratory failure
Severe anaemia
Hypotension/Shock
[a]Ischaemic thresholds vary substantially in relation to the magnitude of the stressor and the extent of underlying cardiac disease.
©ESC/ACC/AHA/WHF 2018

Criteria for type 3 MI

Patients who suffer cardiac death, with symptoms suggestive of myocardial ischaemia accompanied by presumed new ischaemic ECG changes or ventricular fibrillation, but die before blood samples for biomarkers can be obtained, or before increases in cardiac biomarkers can be identified, or MI is detected by autopsy examination.

Criteria for cardiac procedural myocardial injury

Cardiac procedural myocardial injury is arbitrarily defined by increases of cTn values (> 99th percentile URL) in patients with normal baseline values (≤ 99th percentile URL) or a rise of cTn values > 20% of the baseline value when it is above the 99th percentile URL but it is stable or falling.

Criteria for PCI-related MI ≤ 48 h after the index procedure (type 4a MI)

Coronary intervention-related MI is arbitrarily defined by an elevation of cTn values more than five times the 99th percentile URL in patients with normal baseline values. In patients with elevated pre-procedure cTn in whom the cTn level are stable (≤ 20% variation) or falling, the post-procedure cTn must rise by > 20%. However, the absolute post-procedural value must still be at least five times the 99th percentile URL. In addition, one of the following elements is required:

- New ischaemic ECG changes;
- Development of new pathological Q waves;[a]
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;
- Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or a side branch occlusion/thrombus, disruption of collateral flow, or distal embolization.[b]

[a]Isolated development of new pathological Q waves meets the type 4a MI criteria if cTn values are elevated and rising but more than five times the 99th percentile URL.

[b]Post-mortem demonstration of a procedure-related thrombus in the culprit artery, or a macroscopically large circumscribed area of necrosis with or without intra-myocardial haemorrhage meets the type 4a MI criteria.

Diagnostic tests recommended in disgnostics

Natriuretic peptides (BNP, NT-proBNP, MR-proANP)	Admission, pre-discharge	Congestion	High negative predictive value	Recommended
Serum troponin	Admission	Myocardial injury	Exclusion of ACS	Recommended
Serum creatinine	Admission, during hospitalization,[a] pre-discharge	Renal dysfunction	None	Recommended for prognostic assessment
Serum electrolytes (sodium, potassium, chloride)	Admission, during hospitalization,[a] pre-discharge	Electrolyte disorders	None	Recommended for prognostic assessment and treatment
Iron status (transferrin, ferritin)	Pre-discharge	Iron depletion	None	Recommended for prognostic assessment and treatment
TSH	Admission	Hypo- hyperthyroidism	None	Recommended when hypo-hyperthyroidism is suspected
D-dimer	Admission	Pulmonary embolism	Useful to exclude pulmonary embolism	Recommended when pulmonary embolism is suspected
Procalcitonin	Admission	Pneumonia	Useful for diagnosis of pneumonia	May be done when pneumonia is suspected
Lactate	Admission, during hospitalization[a]	Lactic acidosis	Useful to assess perfusion status	Recommended when peripheral hypoperfusion is suspected

Laboratory markers of myocardial necrosis

- **Myoglobin**

❖Elevation **2 hours after onset . maximum after 6 - 9 hours and after 36 hours back in reference interval**

❖**False positive results – muscle injuries (manual resuscitation, impaired renal filtration)**

❖ **Important negative predictive value (between 2-12 hour) –**

(60% NPV 3 hrs after onset of ischemia , 90% NPV 4 hrs after) – **exclusion of acute coronary lesion**

Reference values

0 - 15 yrs: 15 - 50 µg/l,

Males: 15 - 150 years: 23 - 72 µg/l, Females: 15 - 150 yrs: 19 - 51 µg/l

Cardiac troponins

Absolutely Cardiospecific

Troponin T

❖Elevation of TnT in 4 – 6 hours, elevation during 10 days - 2 weeks .

Troponin I

❖ 6 hours after onset of ischemia with 7 – 10 days duration

Reference values and diagnostic cut offs are assay dependent

99. percentile

	Senzitivity	NPV	Specificity	PPV
cTnI	95	61	34	85
cTnT	78	83	71	65

Table 4 Conditions other than acute type 1 myocardial infarction associated with cardiomyocyte injury (= cardiac troponin elevation)

Tachyarrhythmias
Heart failure
Hypertensive emergencies
Critical illness (e.g. shock/sepsis/burns)
Myocarditis[a]
Takotsubo syndrome
Valvular heart disease (e.g. aortic stenosis)
Aortic dissection
Pulmonary embolism, pulmonary hypertension
Renal dysfunction and associated cardiac disease
Acute neurological event (e.g. stroke or subarachnoid haemorrhage)
Cardiac contusion or cardiac procedures (CABG, PCI, ablation, pacing, cardioversion, or endomyocardial biopsy)
Hypo- and hyperthyroidism
Infiltrative diseases (e.g. amyloidosis, haemochromatosis, sarcoidosis, scleroderma)
Myocardial drug toxicity or poisoning (e.g. doxorubicin, 5-fluorouracil, herceptin, snake venoms)
Extreme endurance efforts
Rhabdomyolysis

Bold = most frequent conditions.
CABG = coronary artery bypass graft(ing); PCI = percutaneous coronary intervention.
[a]Includes myocardial extension of endocarditis or pericarditis.

Troponins in other pathophysiological states

- 1. **CNS contusions and brain bleeding**
  – elevation of intracranial pressure → secretion of catecholamines →cardiomyocyte damage → cardiopulmonal dysfunction→ ↑cTn → ↑↑Cardiovascular mortality

- 2. **Malignant neoplasias** - anthracycline, cycofosfamide, trastuzumab (Herceptin), 5-fluorouracyl, doxorubicin – cardiotoxicity

- 3. **Extreme exercise** – Elevation of cTnI 2-4 hours after exercise

- 4. **Invazive and noninvazive therapeutical procedures**
  cathetrisation, use of defibrillators – short timed elevation of cTnI

- 5. **Cardiosurgery**

- (less invazive) –↑cTnI during three days post operation

- non extracorporal - ↑cTnI during three days post operation – long time - perioperative AIM
- Extracorporal - ↑cTnI during three days post operation

Troponins in other pathophysiological states

- 6. **Myocardial contusion** ¢TnI in 15 – 53% of cases (atrial disfunction, cardiogenic shock, arrhytmia), during 3-6 hours after contusion with prolonged elevation.
- 7. **Malignant tumours** – leukemias – ↑cTnI chemotherapy
- 8. **Myocarditis** – ↑cTnI in 40% viral myocarditis (no elevation in bacterial myocarditis), maximal concentrations in 1. - 2. week
- 9. **Perinatal period** – acute tocolysis, perinatal asphyxia
- 10. **Lung embolia** –↑cTnI in admission, maxima in 10 hours, elevation during 30-40 hrs, slower increase
- 11. **Burn trauma** – cTn elevated in large burns 30% of body, elevation after 6 hours with maxima after 12 hrs, continuous elevation – risk of toxemia

Troponins in other pathophysiological states

- 12. **Renal disease** – ↑↑cTnI in ESRD and after hemodialysis
- 13. **Sepsis, septic shock, multiorgan failures**– elevated cTnI – worse prognosis, ↑cTn
- 14. **Percutaneous coronary intervention (PCI)** – ↑cTnI in 5-73%, especially in patients with UAP
- 15. **Coronary artery bypass graft (CABG)**- ↑cTnI 2-6 hours after operation, max 18 – 48 hours, decrease in 3-6 days
- 16. **Heart failure** –↑cTnI in 11-60% , risk and morbidity stratification

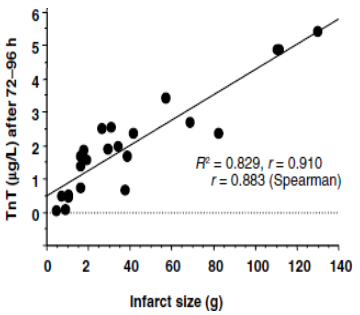
Summary of elevation Tn i various pathological states

pathology	Elevation of cTn (%)
Extracorporal cardiovascular operation	100 %
Burn trauma (more than 30%, 3-5. days)	100 %
Perinatal asphyxia	100%
Sepsis, hypovolemia, hypotension	100%
Radiofrequent ablation after 24 hrs	88%
Multiorgan failurewith renal failure	83%
Acute tocolysis 3. day	80%
Septic shock	75%
Cardiovascular operation without extracorporal (3.day)	75%
Subarachnoidal bleeding	60%
Chronic hemodialysis (>1 year)	60%
High dose chemotherapy (anthracyclines)	40%
Heart contusion	40%
Myocarditis (1.- 4. week)	35%
End stage of renal disease without hemodialysis	30%
Chronic hemodialysis(< 1 year)	30%
Defibrilator implantation (24 hours)	25%
Minimal invasive cardiovascular operation (1.-3. day)	20%
Stent (1.-3. day)	10%

Table 23 **Cancer drugs causing heart failure**

Cancer therapy	Indication
Anthracycline chemotherapy (doxorubicin, epirubicin, daunorubicin, idarubicin)	Breast cancer, lymphoma, acute leukaemia, sarcoma
HER2-targeted therapies (trastuzumab, pertuzumab, trastuzumab emtansine T-DM1, lapatinib, neratinib, tucatinib)	HER2+ breast cancer HER2+ gastric cancer
VEGF inhibitors TKIs (sunitinib, pazopanib, sorafenib, axitinib, tivozanib, cabozantinib, regorafenib, lenvatinib, vandetinib) and antibodies (bevacizumab, ramucirumab)	VEGF TKIs: renal cancer, hepatocellular cancer, thyroid cancer, colon cancer, sarcoma, GIST Antibodies: breast cancer, ovarian cancer, gastric cancer, gastro-oesophageal cancer, colon cancer
Multi-targeted kinase inhibitors: second and third generation BCR-ABL TKIs (ponatinib, nilotinib, dasatinib, bosutinib)	Chronic myeloid leukaemia
Proteasome inhibitors (carfilzomib, bortezomib, ixazomib) **Immunomodulatory drugs** (lenalidomide, pomalidomide)	Multiple myeloma
Combination RAF and MEK inhibitors (dabrafenib+trametinib, vemurafenib+cobimetinib, encorafenib+ binimetinib)	RAF mutant melanoma
Androgen deprivation therapies GnRH agonists (goserelin, leuprorelin) Antiandrogrens (abiraterone)	Prostate cancer, breast cancer
Immune checkpoint inhibitors: anti-programmed cell death 1 inhibitors (nivolumab, pembrolizumab) anti-cytotoxic T-lymphocyte-associated protein 4 inhibitor (ipilimumab) anti-programmed death-ligand 1 inhibitors (avelumab, atezolizumab, durvalumab)	Melanoma (metastatic and adjuvant) Metastatic renal cancer, non-small cell lung cancer, small cell lung cancer, refractory Hodgkin's lymphoma, metastatic triple negative breast cancer, metastatic urothelial cancer, liver cancer, MMR-deficient cancer

Cardiac Troponins



Advantages:

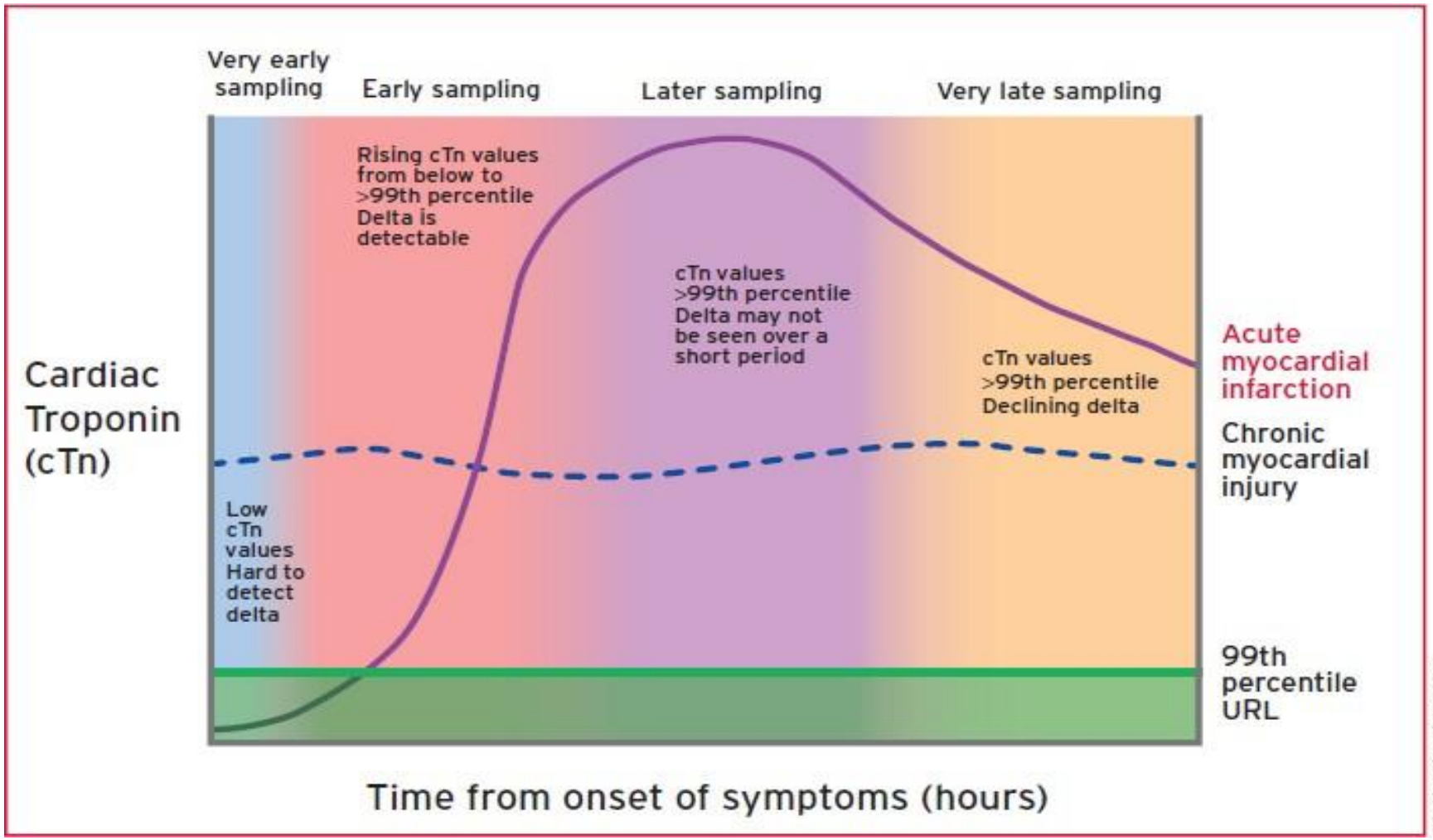
- Cardiospecifity
- High diagnostic sensitivity
- Elevation of concentration - result of myocardial necrosis
- Elevation of concentration correlated with large of myocardial necrosis
- Long time elevation of concentation
- Fast analytical methods
- Changes in concentrations are inevitable for changing medical therapy
- Evaluation of spontaneous and therapeutic thrombolysis
- Short and long time risk stratification

Cardiac troponins

Disadvantages

- **Relatively late elevation after the start of necrosis (3 hours)**
- **Analytical variability (different methods – different results)**
- **Biological variation – interindividual and intraindividual**
- **Values are population dependent**
- **Age related values**

Cardiac troponins



hs cTnI vs cTnI

hsCTn assays – detection of negative TnI values

hs cTnI	**conventional cTnI (POCT)**
Units **ng/l**	**µg/l**
Sex-specific cut off	**one cut off**
(156 ng/l F, 342 ng/l M)	(0,300 ug/l)
CV < 10 %	CV < 20 %

Practical case I

Conventional TnI vs hs CTn

- Woman 62 years, atypical chest pain, hypertension, smoker > 25 years, pain released into the left shoulder, at rest or in exercise during last 2 month

1. **Measured at admission in ED:**

ECG normal, cTnT (POCT) < 0,01 µg/l (cut off = 0,01 µg/l)

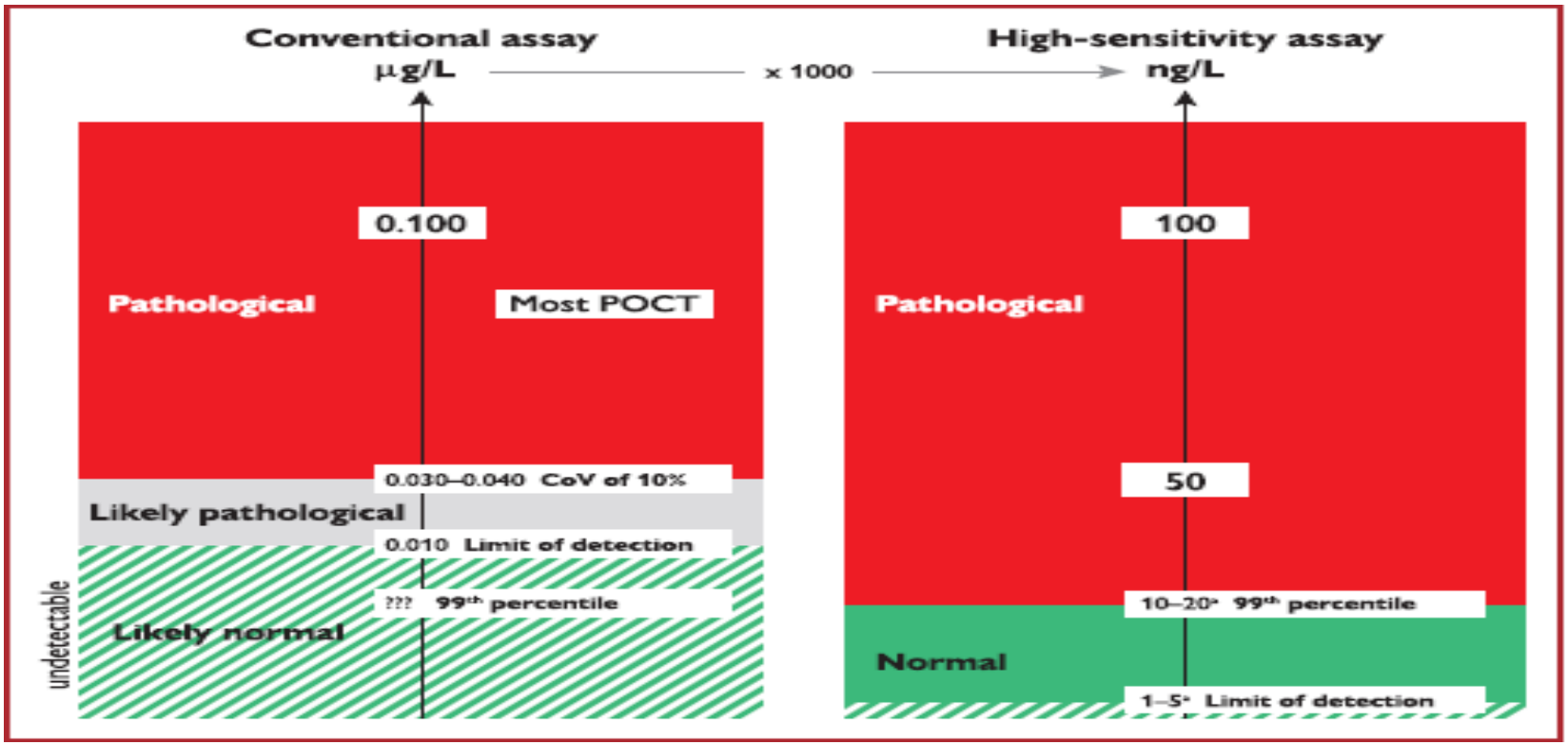
2. Measured in central laboratory (hs Tn)

hsCTnT (high sensitive) = 15 ng/l (cut off 10 ng/l) !!

Diagnosis – stable CAD

hsCTnI

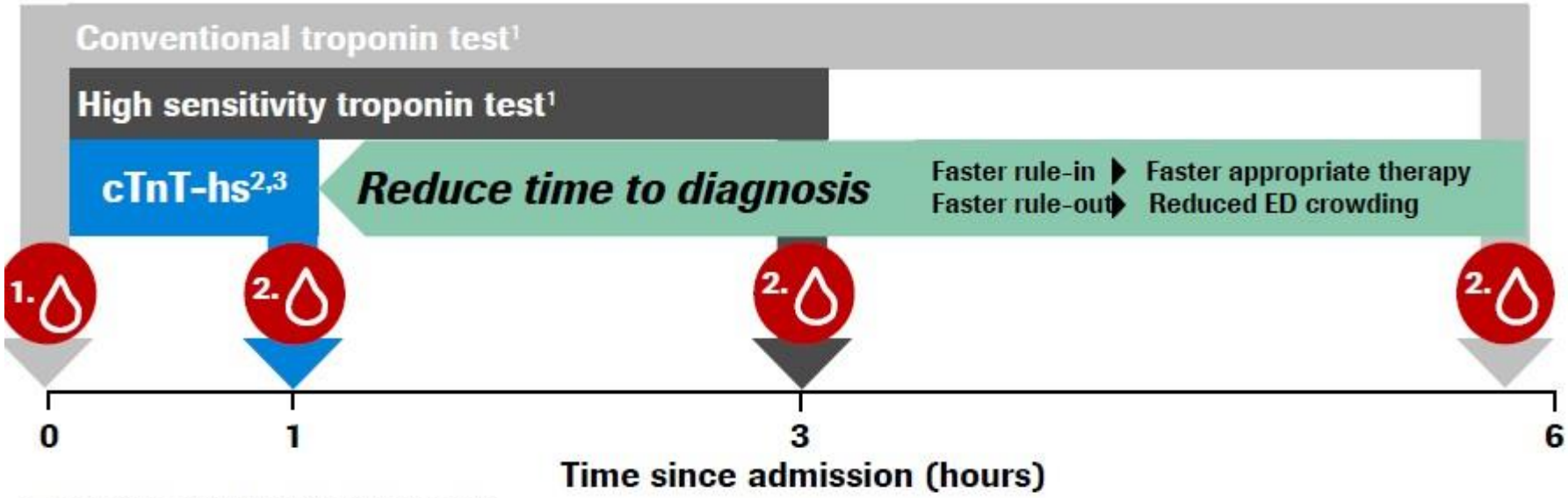
- cut off
- Diagnostic sensitivity
- Diagnostic specificity



Time is life

Is a safe AMI diagnosis possible in a shorter time?

- Serial blood samples at variable time intervals are required for the diagnosis of AMI and to differentiate acute from chronic cardiac disease[1]
- In conjunction with full clinical assessment including 12–lead ECG, the ESC guidelines recommend, a **6-9 hours** observation time with conventional cTn tests[1] or **T0/3-h or T0/1-h rule-in rule-out** protocol using high sensitivity Troponin[2]



1. Hamm C et al. (2011). *Eur Heart J* 32:2999–3054.
2. Roffi M et al. (2016). *Eur Heart J* 37:267-315
3. Mueller C et al. (2016). *Ann Emerg Med* in press (doi:10.1016/j.annemergmed.2015.11.013)

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

Delta troponin

Absolute or relative change of cTn value – clinically relevant change

Two serial measurements 0-3 or 6 hours after admission

1) Relative

$$\Delta = [(c_{max\ 3h\ or\ 6\ h}) - c_0)/c_0 \times 100] \ [\%]$$

2) Absolute

$$\Delta = c_{max\ 3h\ or\ 6\ h}) - c_0 \quad [ng/l]$$

Change of CTn concentration in 0,3 or 6 hours - 20% change of value is clinically relevant (NACB)

Practical cases of delta troponin (3 hours algorithm)

Na	149 []* mmol/l	137-146
K	4,9 [*] mmol/l	3,8-5,0
Cl	118 []* mmol/l	97-108
Ca total	2,32 [*] mmol/l	2,05-2,54
Ca++	1,49 []* mmol/l	1,13-1,32
Osmolality	321 []* mmol/kg	285-295
Osmolality calculated	319 []* mmol/kg	285-295
Glucose	9,0 []* mmol/l	3,3-5,8
ALT	1,25 []* ukat/l	0,17-0,78
Amylase	4,22 []* ukat/l	0,30-2,28
Bilirubin total	13,1 [*] umol/l	2,0-17,0
Bilirubin direct	4,0 [*] umol/l	0,0-5,1
Urea	11,8 []* mmol/l	2,8-8,0
S-CREA	81 []* umol/l	19-62

hs TnI + delta

hs Troponin I – 3 h.	**107,1 []* ng/l**	**cut-off AIM: M: 342; F: 156**	**0,0-33,6**
hs Troponin I – 0 h.	**569,8 []* ng/l**	**0,0-33,6**	
Absolute delta hs TnI	**-462,7 ng/l**		
Relative delta hs TnI	**-81,20 %**		
Myoglobin	**716,7 []* ug/l**	**23,0-72,0**	

Diagnosis ?

Practical cases of delta troponin (3 hours algorithm)

Na	132 *[] mmol/l	137-144
K	4,3 [*] mmol/l	3,9-5,3
Cl	102 [*] mmol/l	98-107
ALT	0,18 [*] ukat/l	0,10-0,63
GGT (GMT)	0,23 [*] ukat/l	0,15-0,92
Bilirubin total	24,6 []* umol/l	3,0-19,0
Urea	28,0 []* mmol/l	2,9-8,2

S-CREA		
Creatinin	174 []* umol/l	55-96
eGFR-krea-(CKD-EPI)	0,54 ml/s/1,73 m2	

hs TnI + delta hs		
Troponin I – 3 h.	**3,1 [*] ng/l**	**cut-off AIM: M: 342;F: 156 0,0-34,2**
hs Troponin I – 0 h.	**<2,0 ng/l**	**0,0-34,2**
Absolute delta hs	**no result**	
Relative delta hs TnI	**no result**	

CRP-HS	109,7 []* mg/l	0,0-5,0

Diagnosis ?

Practical cases of delta troponin (3 hours algorithm)

Na	137 [*] mmol/l	137-144
K	4,2 [*] mmol/l	3,9-5,3
Cl	92 *[] mmol/l	98-107
ALT	0,34 [*] ukat/l	0,10-0,63
GGT (GMT)	0,58 [*] ukat/l	0,15-0,92
Bilirubin total	6,1 [*] umol/l	3,0-19,0
Urea	23,6 []* mmol/l	2,9-8,2

S-CREA			
Creatinin	378 []* umol/l		42-80
eGFR-krea-(CKD-EPI)	0,16	ml/s/1,73 m2	

hs TnI + delta			
hs Troponin I – 3 h.	**116,8 []* ng/l**	**cut-off AIM: M: 342; F: 156**	**0,0-15,6**
hs Troponin I – 0 h.	**37,8 []* ng/l**		**0,0-15,6**
Absolute delta hs TnI	**79,0 ng/l**		
Relative delta hs TnI	**208,99 %**		

Diagnosis ?

Practical cases of delta troponin (3 hours algorithm)

Na	140	[*] mmol/l	137-144
K	4,8	[*] mmol/l	3,9-5,3
Cl	103	[*] mmol/l	98-107
Ca total	2,27	[*] mmol/l	2,05-2,40
Mg	0,74	[*] mmol/l	0,66-0,99
Mg++	0,43	*[] mmol/l	0,45-0,62
Osmolality	301	[*] mmol/kg	280-301
ALT	0,25	[*] ukat/l	0,10-0,63
GGT (GMT)	0,52	[*] ukat/l	0,15-0,92
Urea	7,7	[*] mmol/l	2,9-8,2

S-KREA

Creatinin	436	[]* umol/l	42-80
eGFR-krea-(CKD-EPI)	0,13 ml/s/1,73 m^2		

hs TnI + delta hs

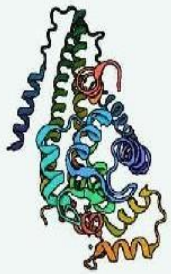
Troponin I 3 h.	**26,4 []* ng/l**	**cut-off AIM: M: 342; F: 156 0,0-15,6**
hs Troponin I – 0. h.	**24,6 []* ng/l**	
Absolute delta hs TnI	**1,8ng/l**	
Relative delta hs TnI	**7,32 %**	

Total protein	57,3 *[] g/l	62,0-77,0
CRP-HS	1,9 [*] mg/l	0,0-5,0

Diagnosis ?

Prognostic Role of Highly-Sensitive Cardiac Troponins in Women

Sex-specific cut-offs for increased CV risk

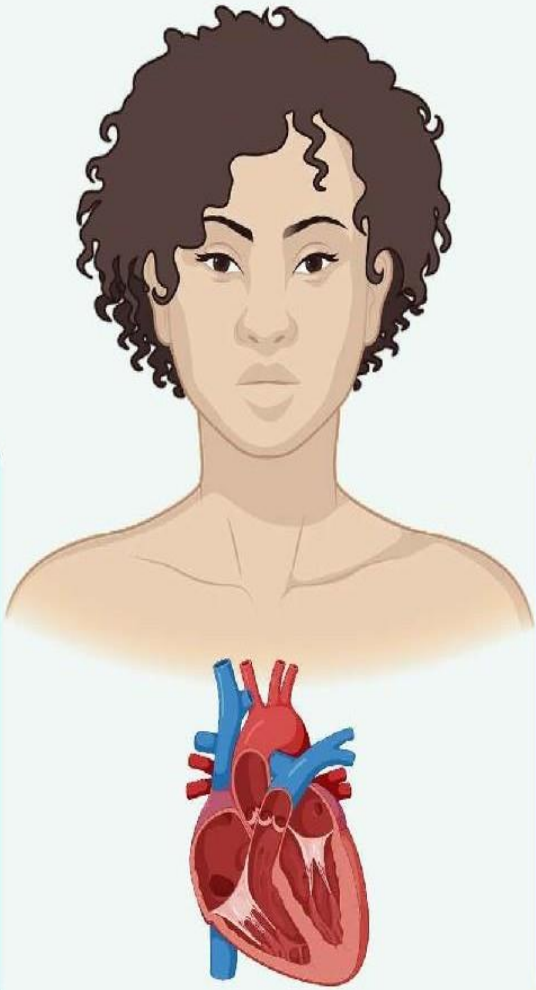


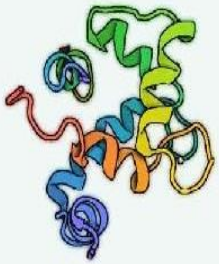
hs-TnT

High CV Risk ≥ 6 ng/L

CV events ≥ 6 ng/L

Heart Failure ≥ 5 ng/L





hs-TnI

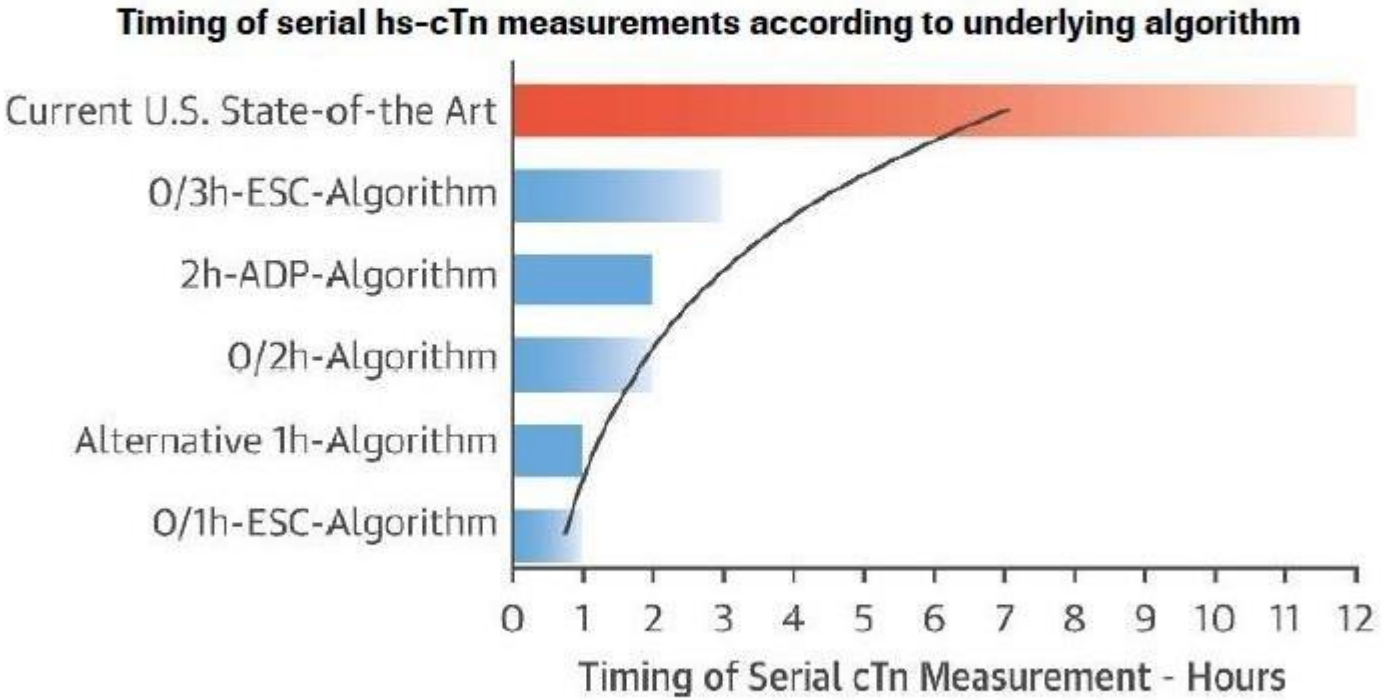
High CV risk ≥ 10 ng/L

CV events ≥ 5 ng/L

Heart Failure ≥ 5 ng/L

https://doi.org/10.3390/biom12101496

Diagnostic performance of Tn-based algorithms and their timing of blood resampling



ADP, accelerated diagnostic pathway; AMI, acute myocardial infarction; ESC, European Society of Cardiology; US, United States

Twerenbold et al. JACC,2017, 996-1012

Table 3 Clinical implications of high-sensitivity cardiac troponin assays

Compared with standard cardiac troponin assays, hs-cTn assays:
• Have higher NPV for AMI.
• Reduce the 'troponin-blind' interval leading to earlier detection of AMI.
• Result in ~4% absolute and ~20% relative increases in the detection of type 1 MI and a corresponding decrease in the diagnosis of unstable angina.
• Are associated with a 2-fold increase in the detection of type 2 MI.
Levels of hs-cTn should be interpreted as quantitative markers of cardiomyocyte damage (i.e. the higher the level, the greater the likelihood of MI):
• Elevations beyond 5-fold the upper reference limit have high (>90%) PPV for acute type 1 MI.
• Elevations up to 3-fold the upper reference limit have only limited (50–60%) PPV for AMI and may be associated with a broad spectrum of conditions.
• It is common to detect circulating levels of cardiac troponin in healthy individuals.
Rising and/or falling cardiac troponin levels differentiate acute (as in MI) from chronic cardiomyocyte damage (the more pronounced the change, the higher the likelihood of AMI).

AMI = acute myocardial infarction; hs-cTn = high-sensitivity cardiac troponin; MI = myocardial infarction; NPV = negative predictive value; PPV = positive predictive value.

ESC European Society of Cardiology

European Heart Journal (2021) **42**, 1289–1367
doi:10.1093/eurheartj/ehaa575

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Diagnosis

As an alternative to the ESC 0 h/1 h algorithm, it is recommended to use the ESC 0 h/2 h algorithm with blood sampling at 0 h and 2 h, if an hs-cTn test with a validated 0 h/2 h algorithm is available.

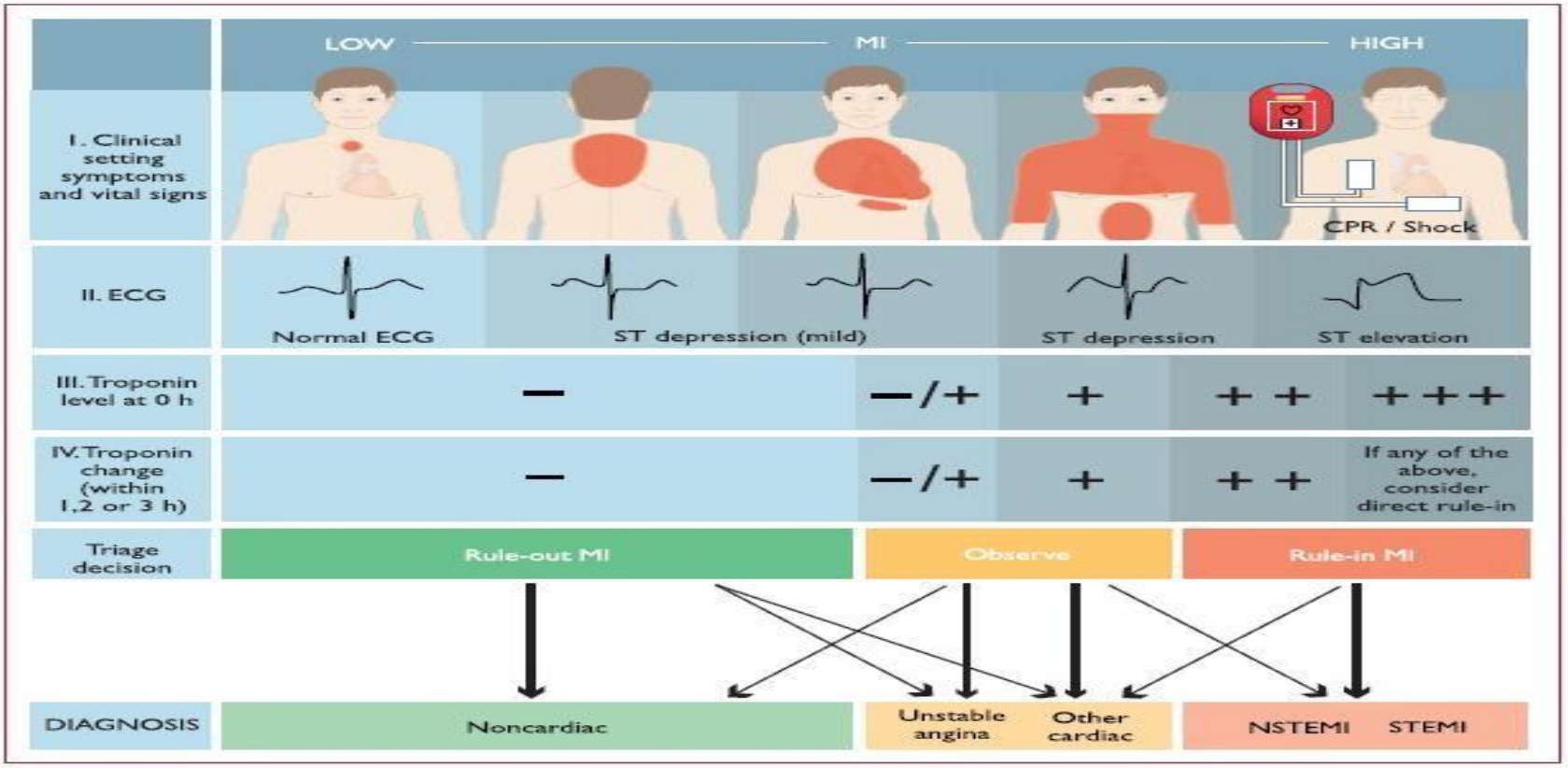
For diagnostic purposes, it is not recommended to routinely measure additional biomarkers such as CK, CK-MB, h-FABP, or copeptin, in addition to hs-cTn.

Risk stratification

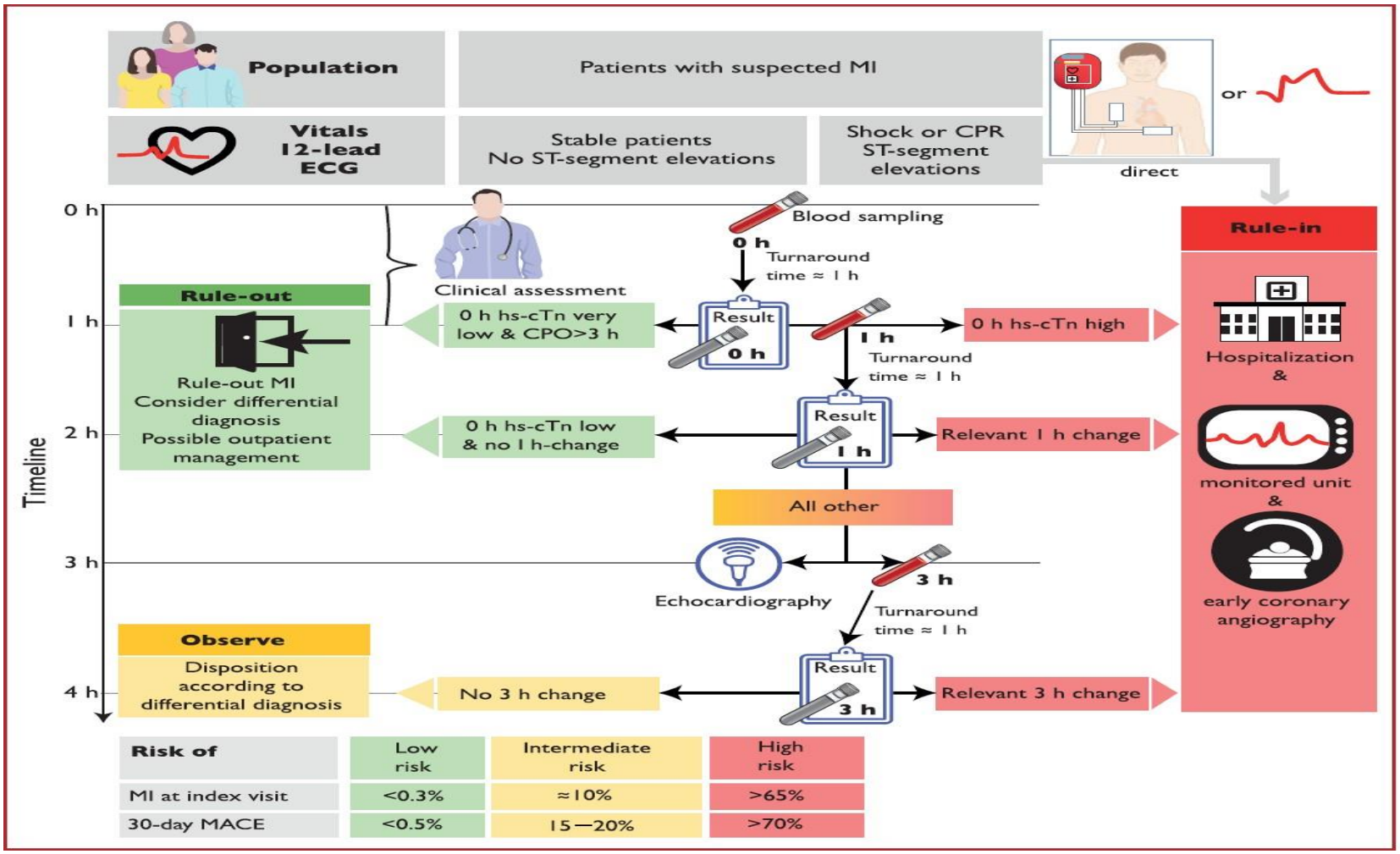
Measuring BNP or NT-proBNP plasma concentrations should be considered to gain prognostic information.

ESC
European Society of Cardiology
European Heart Journal (2020) **00**, 1–79
doi:10.1093/eurheartj/ehaa575

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

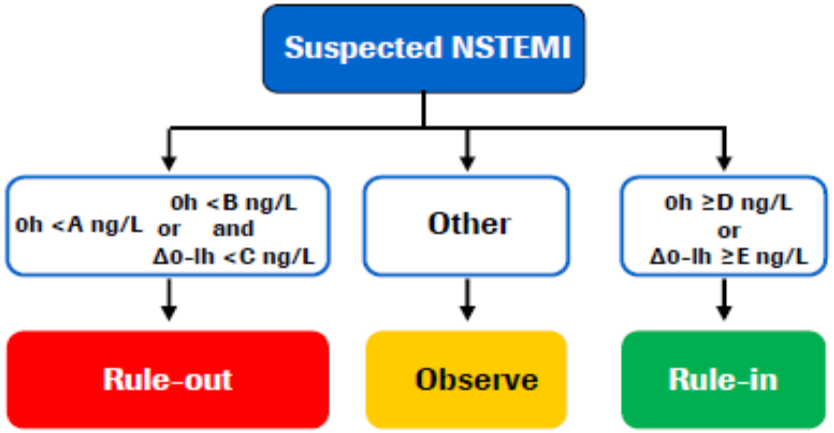


Strategy for laboratory test and sampling



The 0/1-h rule-in and rule-out algorithm

Cut-off levels within the 0/1-h algorithm are assay-specific[1]



	A	B	C	D	E
cTNT-hs (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)*	0.5	5	2	107	19

NSTEMI can be ruled out already at presentation, if hs-cTn level is very low and onset of chest pain >3h

*Prototype test not yet commercially available

Roffi M, et al. Eur Heart J 2016;37:267-315.

CTnI assay specific cut offs

Table 5 Assay specific cut-off levels in ng/l within the 0 h/1 h and 0 h/2 h algorithms

0 h/1 h algorithm	Very low	Low	No 1hΔ	High	1hΔ
hs-cTn T (Elecsys; Roche)	<5	<12	<3	≥52	≥5
hs-cTn I (Architect; Abbott)	<4	<5	<2	≥64	≥6
hs-cTn I (Centaur; Siemens)	<3	<6	<3	≥120	≥12
hs-cTn I (Access; Beckman Coulter)	<4	<5	<4	≥50	≥15
hs-cTn I (Clarity; Singulex)	<1	<2	<1	≥30	≥6
hs-cTn I (Vitros; Clinical Diagnostics)	<1	<2	<1	≥40	≥4
hs-cTn I (Pathfast; LSI Medience)	<3	<4	<3	≥90	≥20
hs-cTn I (TriageTrue; Quidel)	<4	<5	<3	≥60	≥8
0 h/2 h algorithm	**Very low**	**Low**	**No 2hΔ**	**High**	**2hΔ**
hs-cTn T (Elecsys; Roche)	<5	<14	<4	≥52	≥10
hs-cTn I (Architect; Abbott)	<4	<6	<2	≥64	≥15
hs-cTn I (Centaur; Siemens)	<3	<8	<7	≥120	≥20
hs-cTn I (Access; Beckman Coulter)	<4	<5	<5	≥50	≥20
hs-cTn I (Clarity; Singulex)	<1	TBD	TBD	≥30	TBD
hs-cTn I (Vitros; Clinical Diagnostics)	<1	TBD	TBD	≥40	TBD
hs-cTn I (Pathfast; LSI Medience)	<3	TBD	TBD	≥90	TBD
hs-cTn I (TriageTrue; Quidel)	<4	TBD	TBD	≥60	TBD

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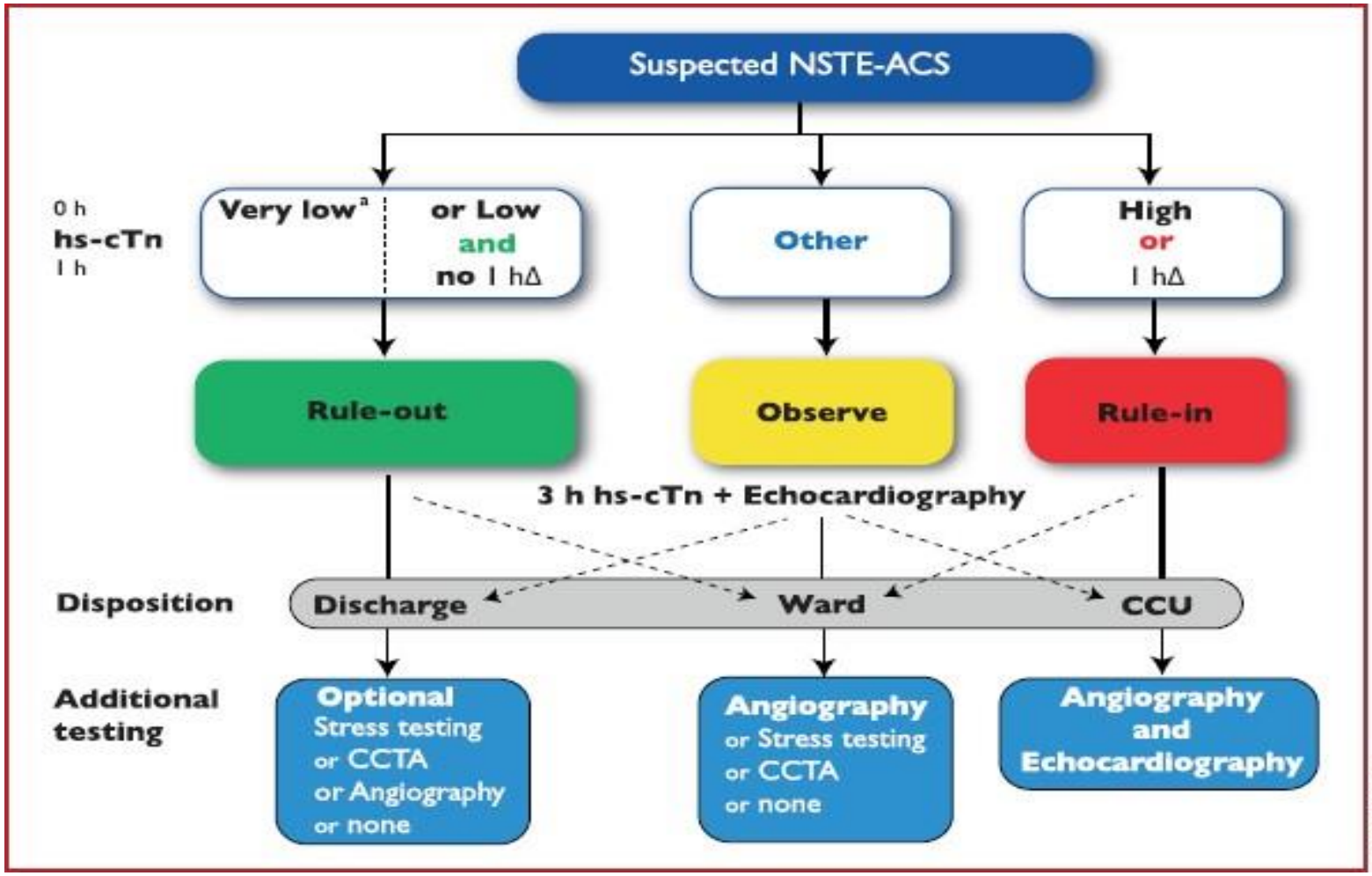
European Heart Journal (2020) 00, 1—79
doi:10.1093/eurheartj/ehaa575

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation



What to do in the observe zone?

- T0/1-h approach leaves up to **one third of patients** in observe zone (typically elderly men with **pre-existing CAD** and with shown increased **long term mortality)**
- In these patients, **clinical assessment, additional hs-cTn measurement at 3h and cardiac imaging** are integral for accurate diagnosis

- Up to one third of patients in observe zone are diagnosed with MI or UA. **Hs-cTn retesting at 3h should be performed to better differentiate acute cardiac disease** associated with dynamic hs-cTn course, from chronic cardiac disease reflected by stable hs-cTn course

Hs-cTn in patients with renal dysfunction

More frequently present in patients with atypical clinical presentation of MI

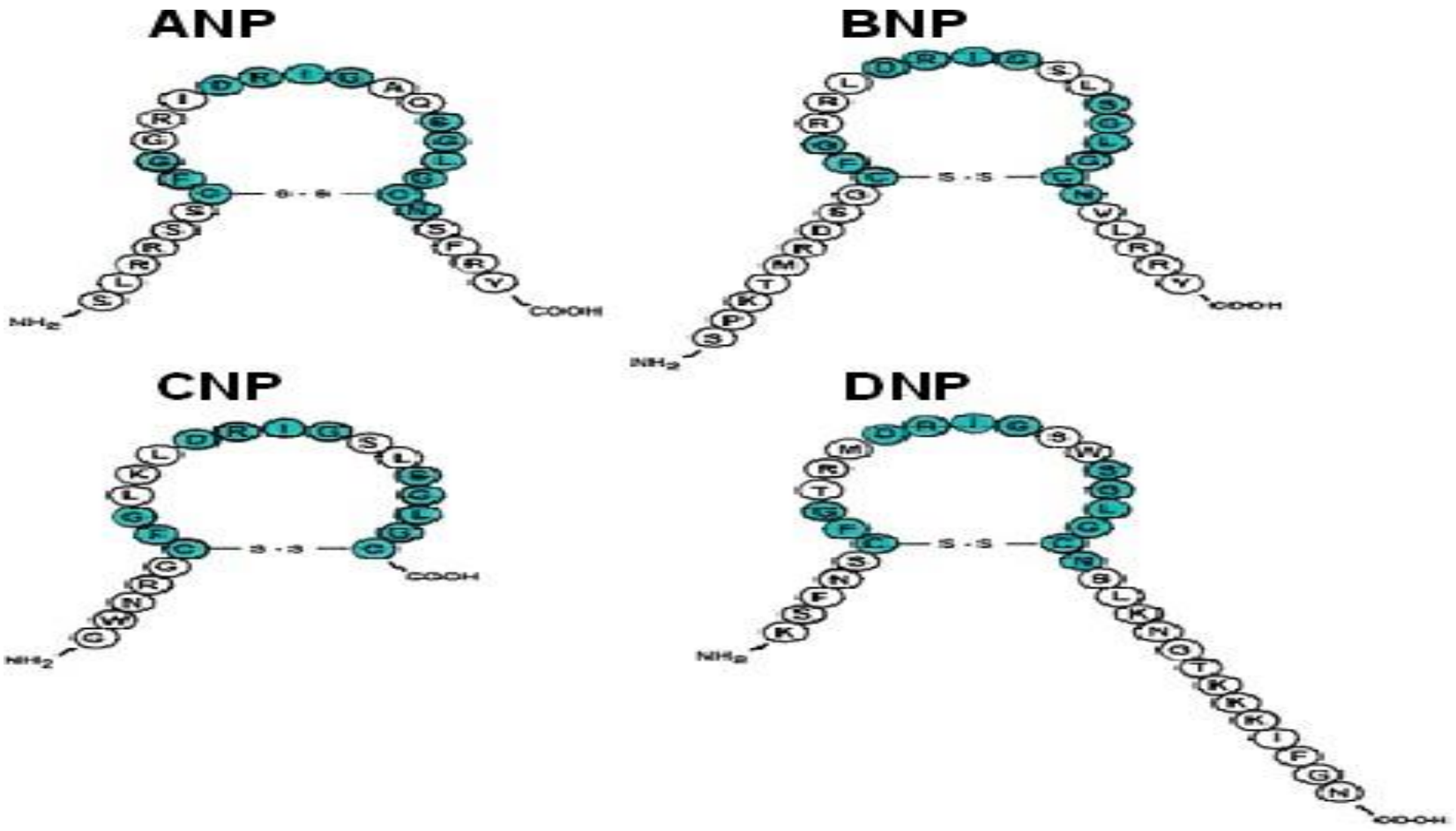
- Left ventricular hypertrophy is common in renal dysfunction, often **result in ECG changes that mimic or obscure MI**[1]

- **Baseline concentration** of cTn are **often chronically elevated** in patients with renal dysfunction even in conditions other than AMI and are associated with poor diagnosis

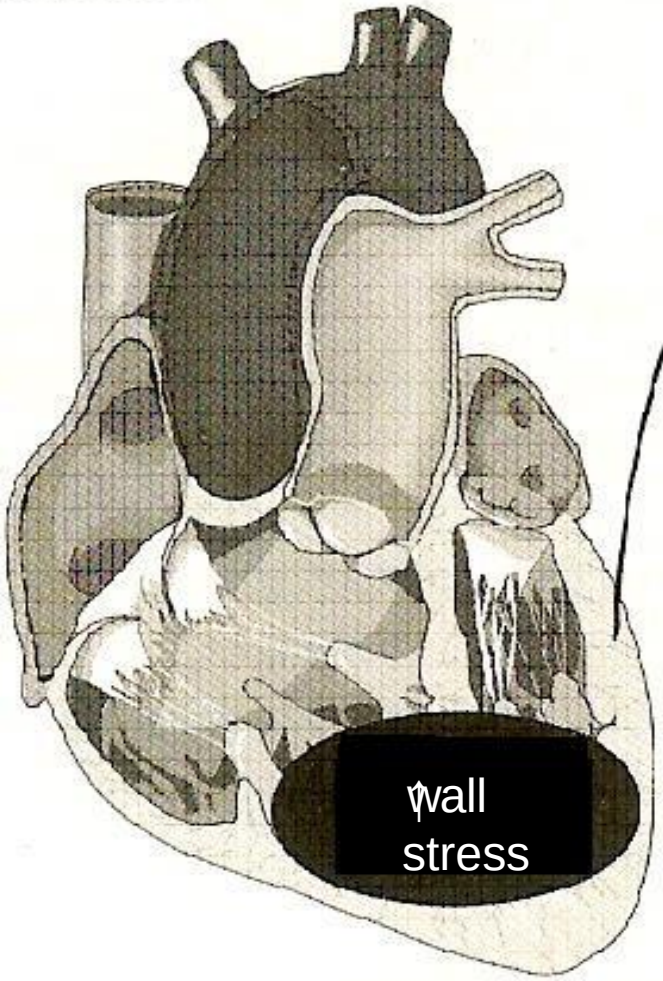
- A large study investigating 7 cTn assays showed that in patients with renal dysfunction and normal renal function, high diagnostic accuracy can be maintained using higher levels than the 99th percentiles (**≥29.5 ng/L with cTnT-hs**)[2]

[1]Twerenbold et al. JACC,2017, 996-1012
[2]Twerenbold et al. Circulation. 2015 9: 2041-50

Natriuretic peptides



Cleavage of NP

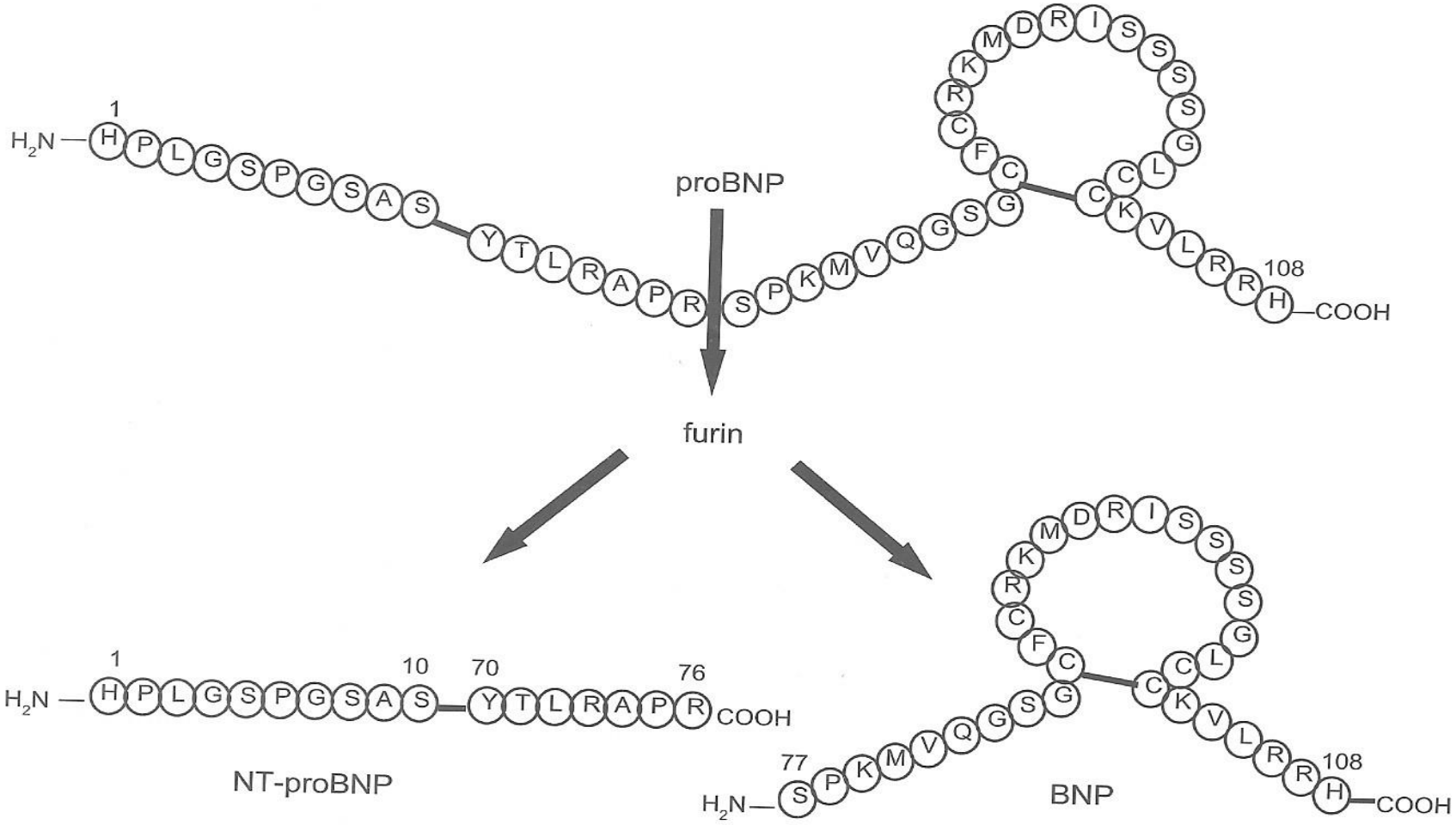


PreproBNP
(1-134)
26 AA signal peptide
ProBNP
(1-108)
N-terminal ProBNP (1-76)
BNP (77-108)
$t_{1/2}$ = 18 min

Natriuresis
↑ Diastolic relaxation

Vazodilatation
↓ RAAS

Natriuretic peptides



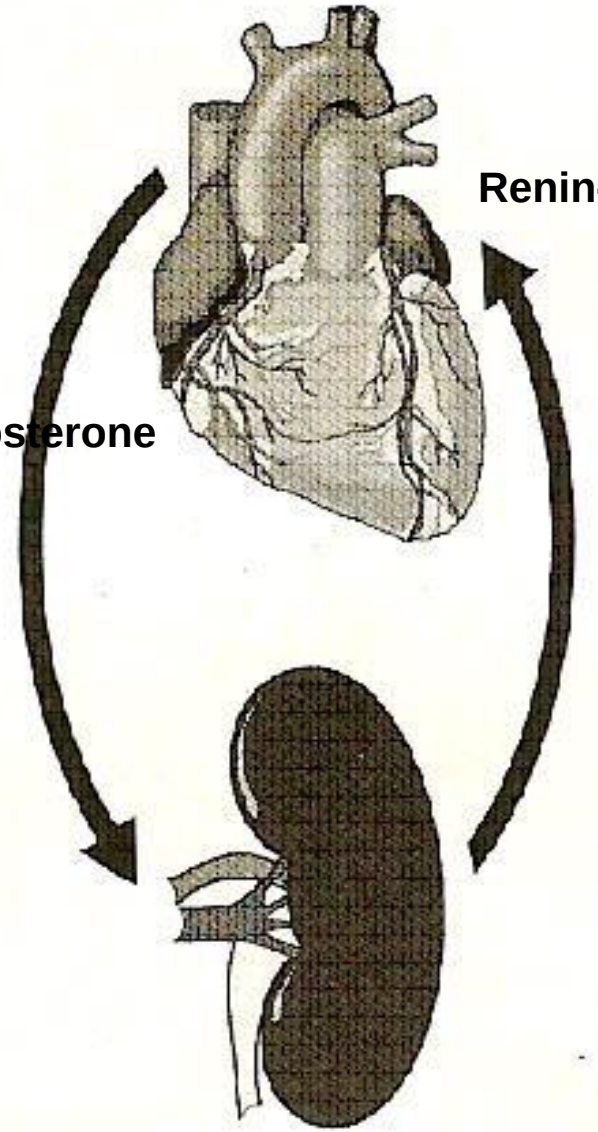
Nonactive fragment

Active peptide

Natriuretic peptides

Natriuretic peptides

Natriuresis
Diuresis
Vazodilatation
Inhibition of renine and aldosterone
Antifibrotic efect

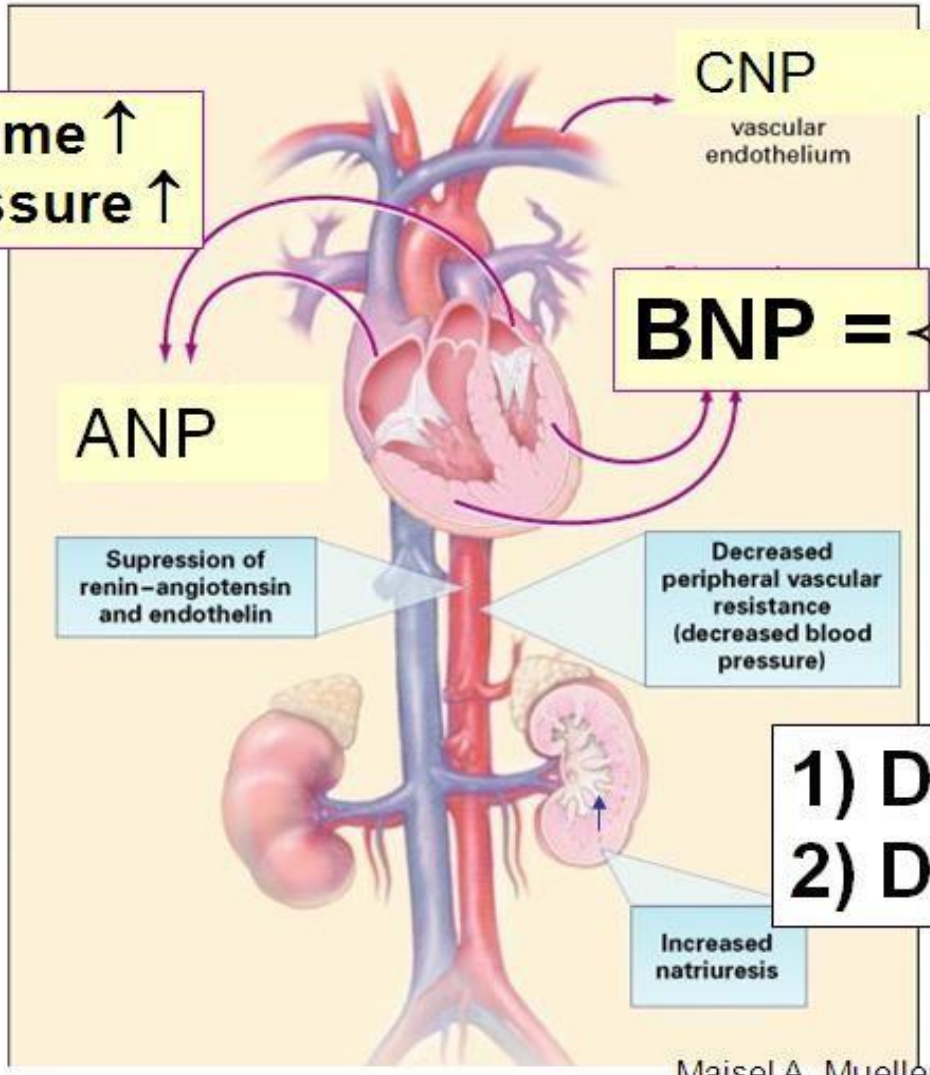


Renin-angiotensin-aldosterone system

Retention of natrium
Antidiuretic efects
Vasoconstriction
Fibrotization

FIGURE 2

NP: Marker of Cardiac Stress



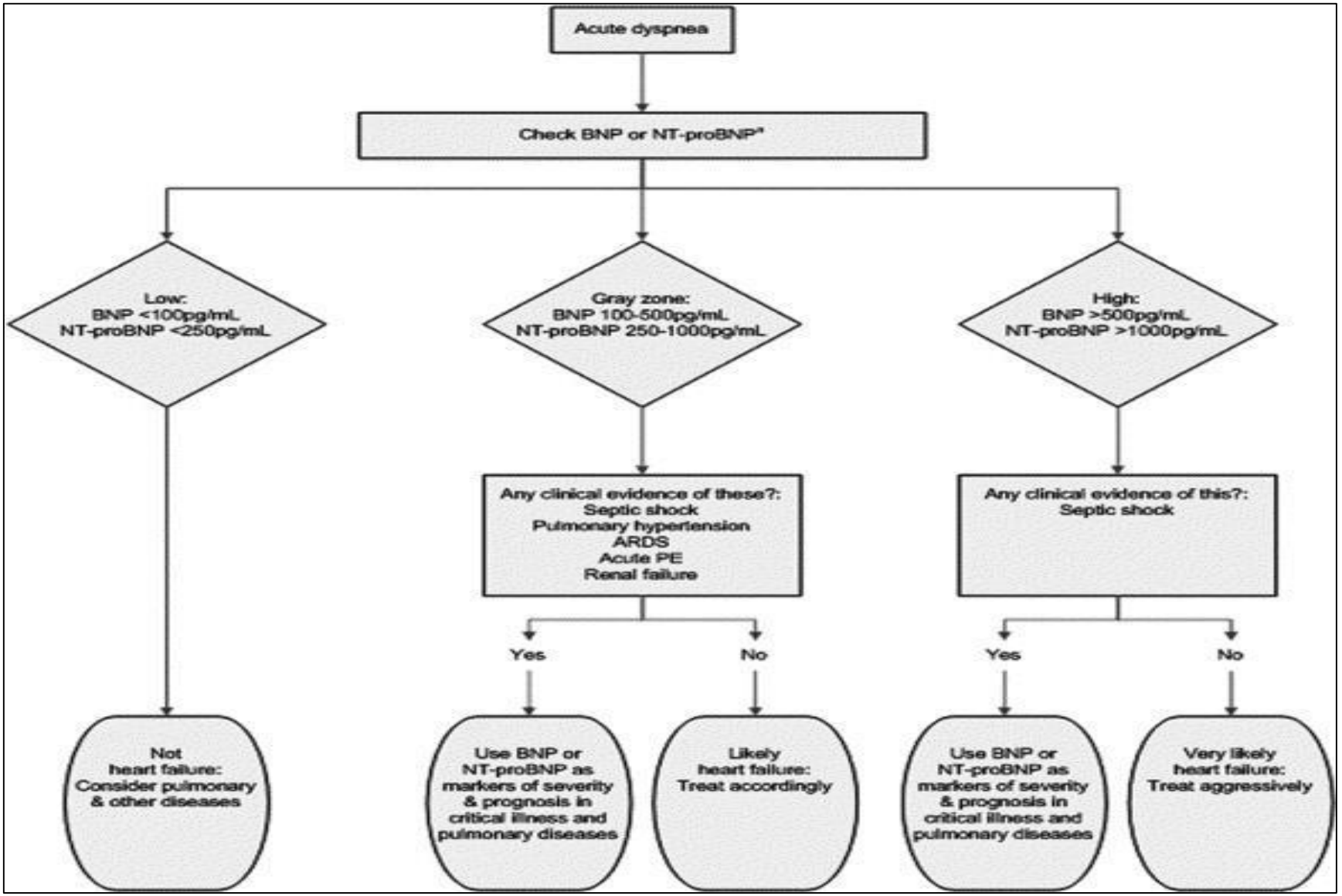
BNP =

- LV Syst. Dysfunction
- \+
- LV Diast. Dysfunction
- \+
- Valvul. Dysfunction
- \+
- RV Dysfunction

1) Diagnosis
2) Disease Severity

Maisel A, Mueller C, et al. Eur J Heart Fail 2008;10:824-39

Discrimination of cardiac and non-cardiac dyspnea



B-type natriuretic peptide: Issues for the intensivist and pulmonologist. Phua, Jason; Lim, Tow; Lee, Kang, Critical Care Medicine. 33(9):2094-2013, September 2005.

Diagnostic value of natriuretic peptides (NPs)

Cardiac vrs. Non-cardiac sources

Limitations of physical examination[1,2]

- HF symptoms are often non-specific
- This makes it hard to discriminate between HF and other conditions
- Symptoms are difficult to interpret in the obese, elderly and patients with chronic lung disease

Variable	Accuracy for HF[3]
History of HF	80
Dyspnea	54
Orthopnea	72
Rales	70
Third heart sound	66
Jugular vein distension	72
Edema	68
NT-proBNP [4]	83-95%

HF, heart failure; NP, natriuretic peptide

1. McMurray, J.J. et al. (2012). *Eur Heart J*, 33, 1787-1847.
2. Ponikowski, P. et al. (2016). *Eur J Heart Fail.*, 18:891-975.
3. Clerico, A. et al. (2015). *Clinica Chimica Acta*, 443: 17-24
4. Januzzi, J.L. et al. (2006). *Eur Heart J*, 27, 330-337.

Diagnostic use of natriuretic peptides

Concentration	Heart failure	Comments
Extremely elevated concentration (BNP > 500 ng/l, NTproBNP > 1000 ng/l)	Decompensated heat failure	
Grey zone (BNP 100 – 500 ng/l, NT-proBNP 250 – 1000 ng/l)	Ventricular dysfunction	
	Acute coronary syndrome	↑Cardiovascular mortality if levels remains elevated
	Unstable angina pectoris	
Mildly elevated or normal values (BNP <100 ng/l, NT-proBNP <250 ng/l)	Heart fibrosis	BNP secretion
	Cardiac arrhytmia	
	Myocardial hypoxia	↑BNP due to paracrine vascular regulation (protection against other ischemia)
	Endotelial dysfunction	Elevated sectretion of natriuretic peptides due to humoral factors (endothelin, TNF alfa, TGF beta)
	Stable angina pectoris	
	High atrial and ventricular volume	

ESC European Society of Cardiology
European Heart Journal (2019) **00**, 1–61
doi:10.1093/eurheartj/ehz405

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)

cTn – worse prognosis in acute PE
– high NPV in acute PE

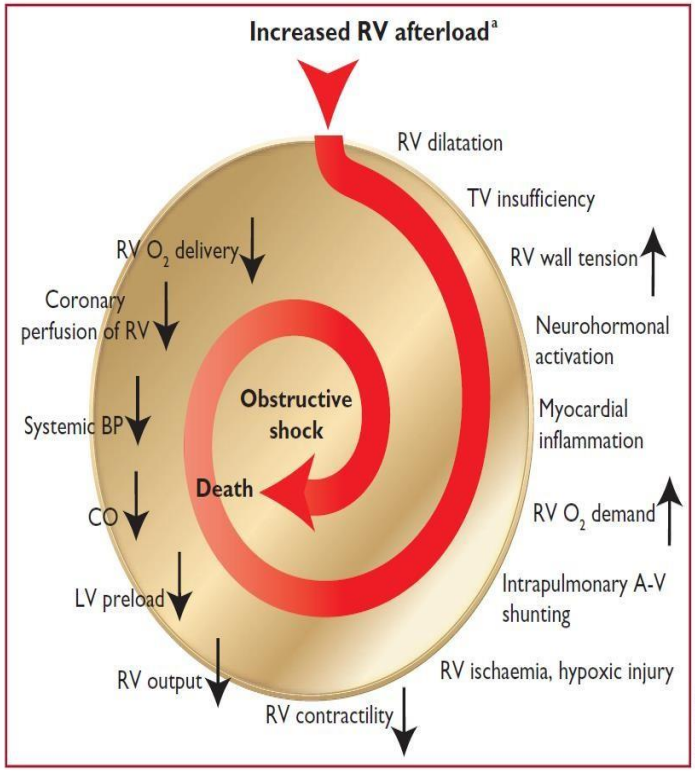
HFABP – prognostic factor in normotensive patients

BNP, NT-proBNP - markers of RV dysfunction
- high NPV

D-Dimers - high NPV

Additional biomarkers

Lactate, Vasopresin, Copeptin, GFR



International HF Guidelines

NP testing in HF – more than "just" HF diagnosis

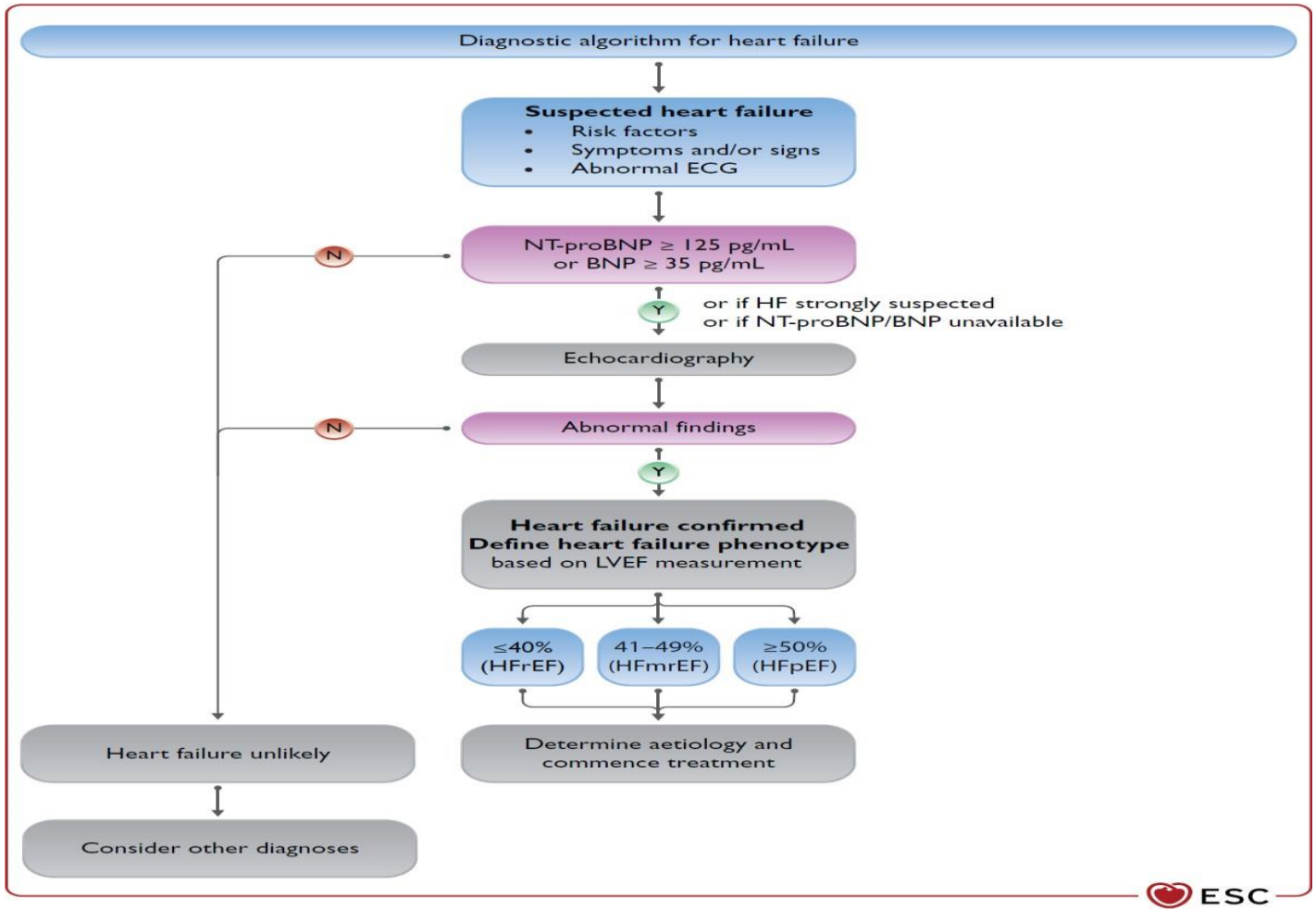
ESC[1]	• NP testing received the highest recommendation level for HF diagnosis in both acute and chronic setting as initial test before echo (Class I, LOE A) • Prognostic and discharge planning: SoC which include the pre-discharge of NP may be considered for prognostic information. • Follow-up and monitoring: benefit from regular monitoring of NP to ensure the safety and optimal dosing of medicines and detect the development of complications or disease progression
ACC /AHA[2]	• In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF (Class I, LOE A) • NPs testing in the setting of chronic ambulatory HF provides incremental diagnostic value to clinical judgment, especially when the etiology of dyspnea is unclear • In emergency settings, NP levels usually have higher sensitivity than specificity and may be more useful for ruling out than ruling in HF • Although lower values of natriuretic peptide biomarkers exclude the presence of HF, and higher values have reasonably high positive predictive value to diagnose HF, clinicians should be aware that elevated plasma levels for both natriuretic peptides have been associated with a wide variety of cardiac and noncardiac causes
NICE[3]	• NP testing should be used in the diagnosis of HF and referral to specialist or echocardiogram decision-making • Consider specialist monitoring of NPs in patients whom up titration is problematic or those who have been admitted to hospital
SIGN[4]	• Diagnostics consideration: NP levels should be measured to decide if Echo is needed or not in patients with suspected heart failure • NT-proBNP-guided treatment may be considered in patients with heart failure aged less than 75 years, especially in the presence of higher baseline NT-proBNP levels (>2,114 pg/ml)

ACC, American College of Cardiology; AHA, American Heart Association; ECS, European Society of Cardiology; HF, heart failure; MI, myocardial infarction; NICE, National Institute for Health and Clinical Excellence; NP, natriuretic peptide; LOE, level of evidence; SIGN - Scottish Intercollegiate Guidelines Network

1. Ponikowski, P. et al. (2016). Eur J Heart Fail., 18:891-975.
2. Yancy, C.W. et al. J Card Fail. 2017 :828-851.
3. NICE clinical guideline 108. Issue date: August 2010. Available at: www.nice.org.uk/guidance/CG108.
4. SIGN clinical guideline 147. Issue date: March 2016. Available at: http://www.sign.ac.uk/

ESC
European Society of Cardiology
European Heart Journal (2021) **42**, 3599—3726
doi:10.1093/eurheartj/ehab368

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure



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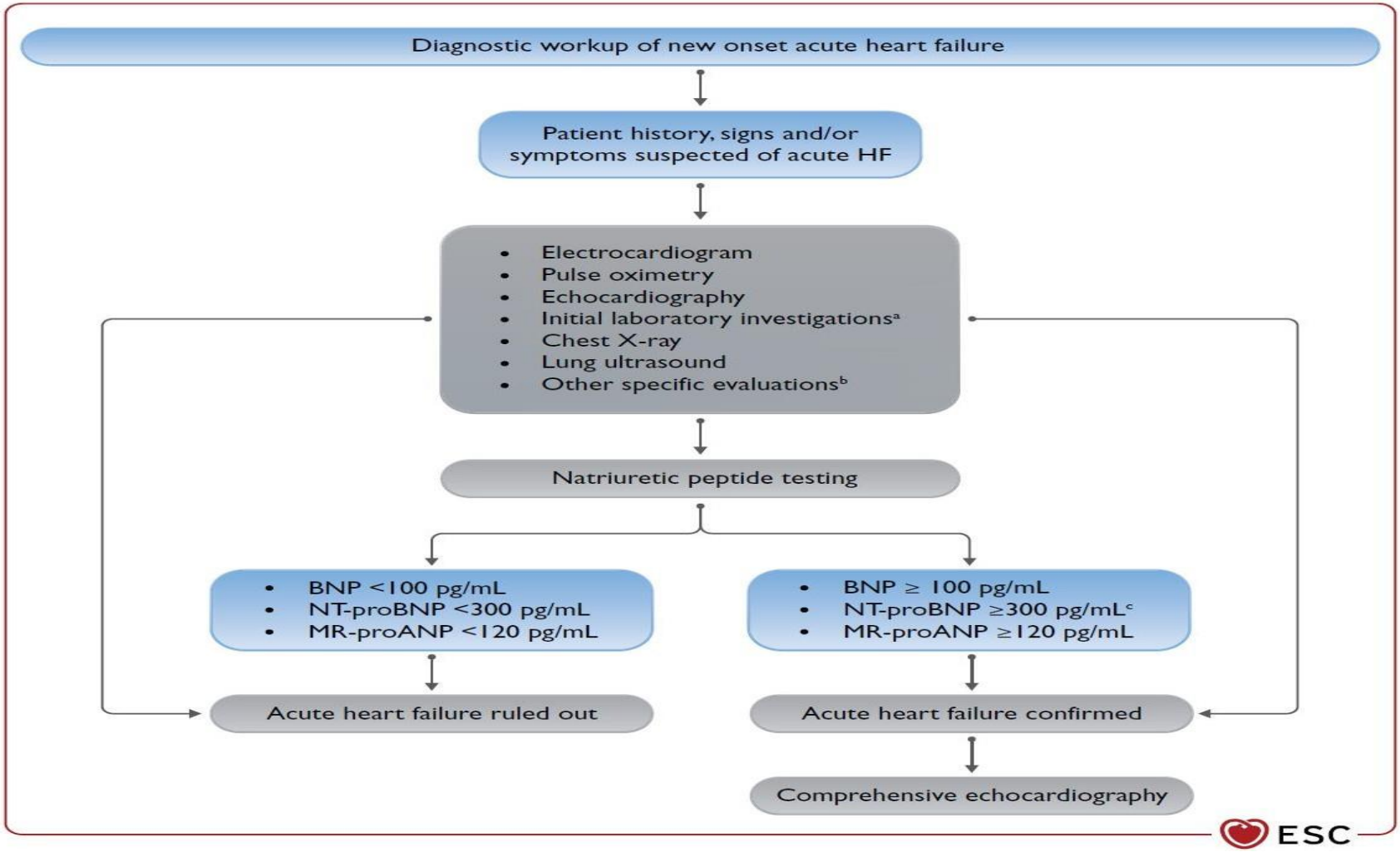


Natriuretic peptides

Table 7 Causes of elevated concentrations of natriuretic peptides[86-88]

Cardiac	Heart failure ACS Pulmonary embolism Myocarditis Left ventricular hypertrophy Hypertrophic or restrictive cardiomyopathy Valvular heart disease Congenital heart disease Atrial and ventricular tachyarrhythmias Heart contusion Cardioversion, ICD shock Surgical procedures involving the heart Pulmonary hypertension
Non-cardiac	Advanced age Ischaemic stroke Subarachnoid haemorrhage Renal dysfunction Liver dysfunction (mainly liver cirrhosis with ascites) Paraneoplastic syndrome COPD Severe infections (including pneumonia and sepsis) Severe burns Anaemia Severe metabolic and hormone abnormalities (e.g. thyrotoxicosis, diabetic ketosis)

ACS = acute coronary syndrome; COPD = chronic obstructive pulmonary disease; ICD = implantable cardioverter-defibrillator.

Diagnostic use of natriuretic peptides

1) Heart failure

AIM a ischemia
- ↑BNP maximum 24 hours after onset
- severe AIM second maximum after 5 days (ventricular remodelling)
- predictor mortality

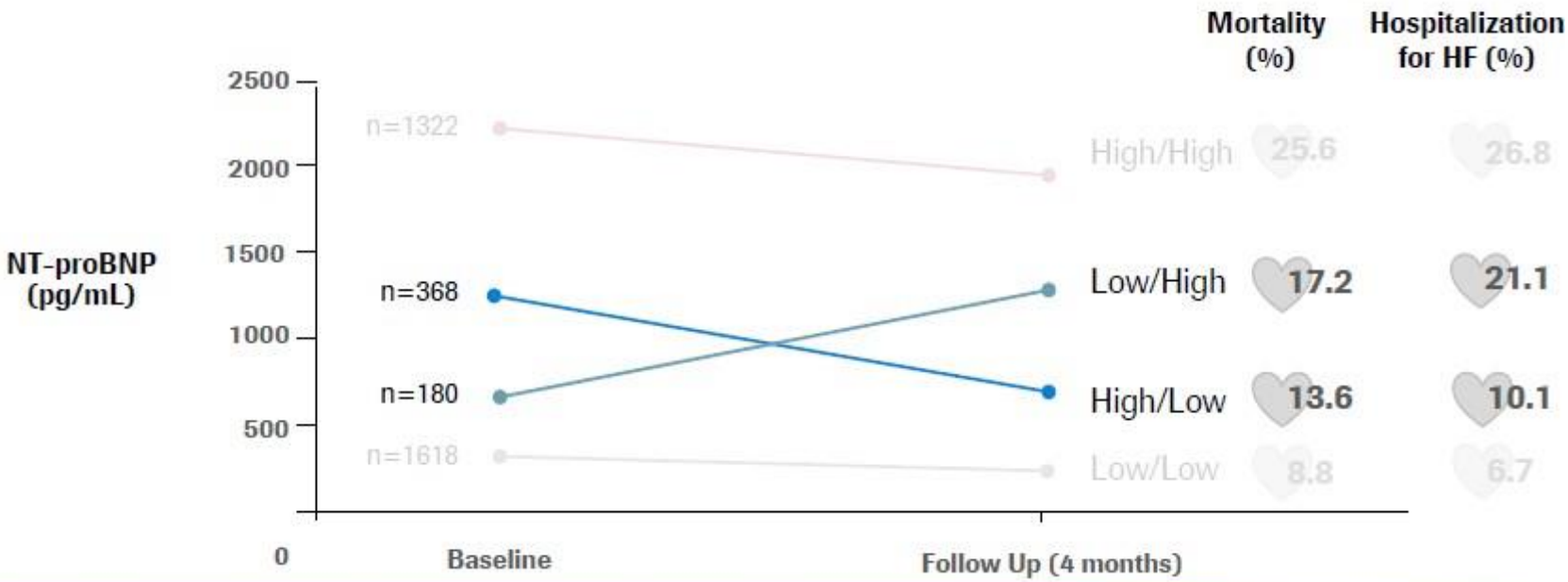
Left ventricular dysfunction
- low levels NP exclude LV dysfunction

Congenital and valvular heart diseases
- elevated levels and corelation with the severity

Acute and chronic heart failure
- prognosis and risk stratification
- prediction of mortality
- monitoring of disease progression

Chronic HF Monitoring

Serial testing provides more information than a single test[1,2,3,4]



- **Elevated NP values are powerfully predictive of adverse outcomes**[1,2,3,4]
- **Rising values identify a rising risk**[1,2,3,4]
- **Significant lowering of NP denotes improved outcomes**[1,2,3,4]

HF, heart failure; **NP**, natriuretic peptide

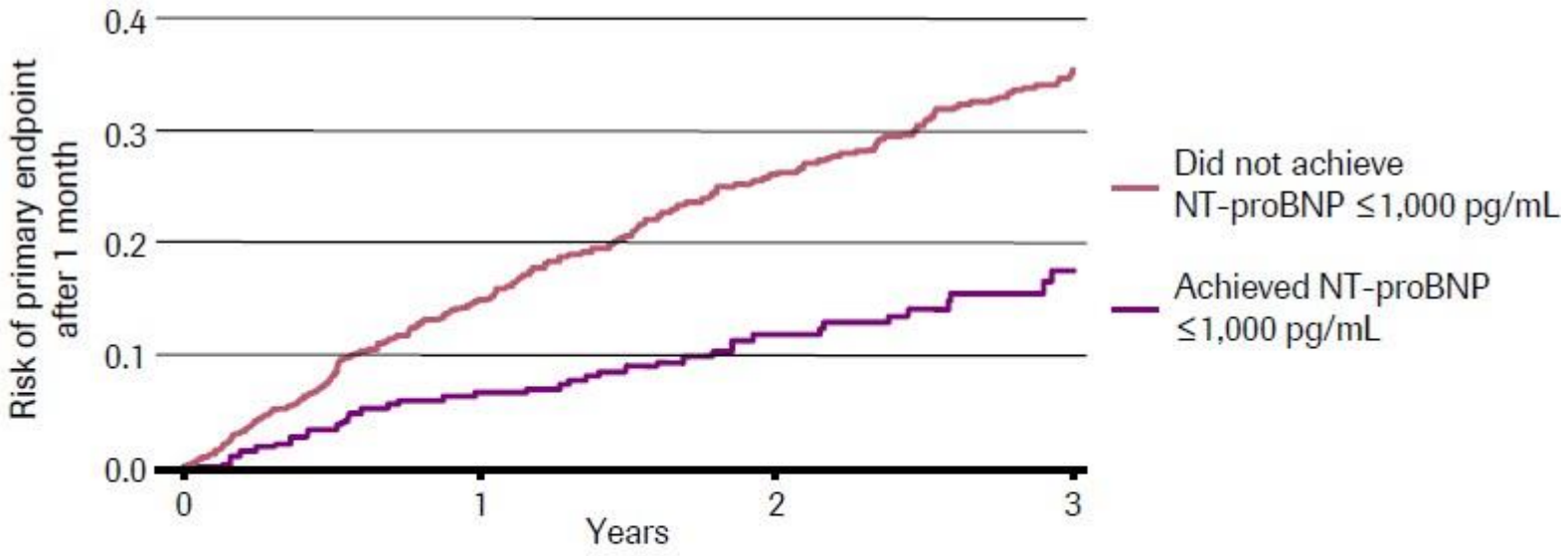
Graph Reproduced from adaptation by Januzzi, 2012, Figure 1 [5] from a study by Masson S, et al.[6]

1. Deberadinis. (2012). *Curr Opin Cardiol*, *27*(6): 661-668.
2. Chiong. (2010). *Heart Fail Rev*, *15*(4): 275-291.
3. McMurray. (2012). *Eur Heart J*, doi:10.1093/eurheart/ehs104
4. Weiner. (2012). *Eur J Heart Fail*, *15*(3), 342-351
5. Januzzi (2012) *Arch Cardiovasc Dis*. Jan;105(1):40-50
6. Masson et al. (2008) *J Am Coll Cardiol ;52:997—100*

Lower NT-proBNP is associated with better outcomes

At 3 years of follow-up, the risk was ~50% less in patients who achieved NT-proBNP ≤1,000 pg/mL

Risk of primary endpoint if NT-proBNP value of 1,000 pg/mL achieved or not achieved 1 month after randomization



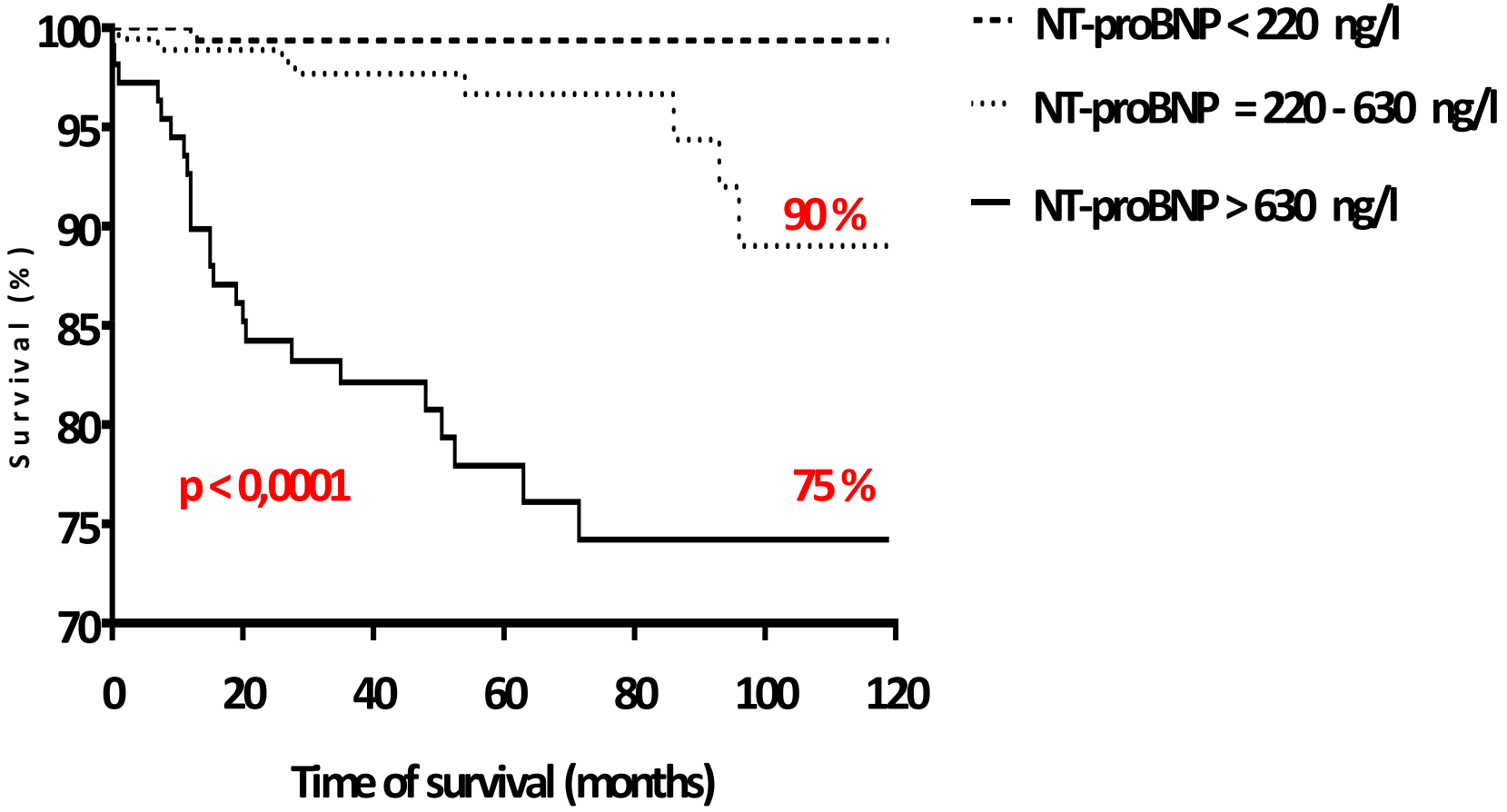
Primary endpoint: the first occurrence of CV death or HF hospitalization

CV, cardiovascular; HF, heart failure

Zile, M.R., et al. (2016). *J Am Coll Cardiol, 68(22):2425–2436*

Survival analysis

Adults with congenital heart diseases



Diagnostic use of natriuretic peptides

2) Renal dysfunction, transplantation

- impaired renal elimination NP
- ↑ANP – renal disease, ↑BNP – cardiological complication – cardiorenal syndrome
- hemodialysis – elimination of NP differed from membrane flux
- predictor clinical complications after transplantation (BNP >700 ng/l)

3) Subarachnoidal bleeding

- BNP predictor of hyponatremia
- Clinical complication – changes of values after admission
- elevations 4-12 day after admission – negativne prognosis

Diagnostic use of natriuretic peptides

4) Hypertension, diabetes, obesity

-hypertension – high concentrations NP → predictors of mortality

-DM II and obesity – ↓NP – complications of hypertension

-DM with microalbuminuria and nephropatia – ↑NP- predictors of mortality

5) Tumors

- ANP expresion in pancreatic carcinoma

-antiproliferative effect – decrease of tumour growth

6) Burns and other trauma

-correlation with severity

-prognostic factor

Practical cases

Na	142	[*] mmol/l	137-146
K	4.5	[*] mmol/l	3.8-5.0
Cl	109	[]* mmol/l	97-108
Ca	2.07	[*] mmol/l	2.05-2.54
Ca++	1.19	[*] mmol/l	1.13-1.32
Mg	0.86	[*] mmol/l	0.66-0.91
Mg++	0.57	[*] mmol/l	0.45-0.62
P	1.07	[*] mmol/l	0.65-1.61
Osm	298	[]* mmol/kg	285-295
P-Glu	8.0	[]* mmol/l	3.3-5.8
ALP	0.50	*[] ukat/l	0.66-2.20
AST	2.56	[]* ukat/l	0.16-0.72
ALT	3.04	[]* ukat/l	0.17-0.78
GGT	0.71	[*] ukat/l	0.14-0.84
AMS	6.24	[]* ukat/l	0.30-2.28
P-AMS	0.58	[*] ukat/l	0.22-0.88
TBil	12.3	[*] umol/l	2.0-17.0
DBil	6.2	[]* umol/l	0.0-5.1
UA	212	[*] umol/l	200-420
Urea	6.8	[*] mmol/l	2.8-8.0
S-Crea	78	[*] umol/l	55-96
eGFR	> 1.5	ml/s	
TG	0.37	*[] mmol/l	0.70-1.70
Chol	3.3	*[] mmol/l	3.4-5.0
TnI	0.057	[*] ug/l	0.000-0.300
Myo	618.7	[]* ug/l	23.0-72.0
CK-MB mass	7.90	[]* ug/l	0.00-7.20
ALB	31.1	*[] g/l	35.0-53.0
TP	50.3	*[] g/l	65.0-85.0
CRP-hS	30.8	[]* mg/l	0.0-5.0
PCT	1.91	[]* ug/l	0.00-0.50

Diagnosis ?

Practical cases

Na	142	[*] mmol/l	137-144
K	4.7	[*] mmol/l	3.9-5.3
Cl	106	[*] mmol/l	98-107
AST	0.28	[*] ukat/l	0.16-0.63
ALT	0.26	[*] ukat/l	0.10-0.63
TBil	15.7	[*] umol/l	3.0-19.0
Urea	10.0	[]* mmol/l	2.9-8.2
S-Crea	106	[]* umol/l	55-96
eGFR	1.02	ml/s	
TnI	0.011	[*] ug/l	0.000-0.300
NT-proBNP	1347.0	[]* ng/l	20.0-125.0
TP	63.3	[*] g/l	62.0-77.0
CRP-hS	195.9	[]* mg/l	0.0-5.0

Diagnosis ?

Practical cases

Na	137	[*]	mmol/l	137-146
K	4,2	[*]	mmol/l	3,8-5,0
Cl	109	[]*	mmol/l	97-108
Osm	290	[*]	mmol/kg	285-295
Urea	5,2	[*]	mmol/l	2,8-8,0
S-Creatinine	76	[*]	umol/l	55-96
eGFR	1,66		ml/s/1,73 m2	
hsTroponin I 3 h.	18281,2	[]*	ng/l	cut-off AIM: M: 342; Ž: 156
hsTroponin I 0 h.	26177,3	[]*	ng/l	0,0-34,2
Absolute delta hsTnI	-7896,1		ng/l	
Relative delta hsTnI	-30,2		%	
CRP-hS	78,1	[]*	mg/l	0,0-5,0

Diagnosis ?

Practical cases

Na	137	[*]	mmol/l	137-146
K	4,0	[*]	mmol/l	3,8-5,0
Cl	107	[*]	mmol/l	97-108
Ca++	1,40	[]*	mmol/l	1,13-1,32
Mg	0,77	[*]	mmol/l	0,66-0,91
Osm	289	[*]	mmol/kg	285-295
Osm Calc	284	*[]	mmol/kg	285-295
P-Glu	5,7	[*]	mmol/l	3,3-5,8
ALT	0,66	[*]	ukat/l	0,17-0,78
GMT	0,33	[*]	ukat/l	0,14-0,84
AMYL	1,07	[*]	ukat/l	0,30-2,28
TBil	9,8	[*]	umol/l	2,0-17,0
DBil	2,9	[*]	umol/l	0,0-5,1
Urea	4,6	[*]	mmol/l	2,8-8,0
S-Crea	66	[*]	umol/l	55-96
eGFR	1,98		ml/s/1,73 m2	
hscTnI	21,7	[*]	ng/l	cut-off AIM: M: 342; Ž: 156
hscTnI (init)	**not measured**			
Absolute delta hsTnI	**not calculated**			
Relative delta hsTnI	**not calculated**			
Myoglobin	374,9	[]*	ug/l	23,0-72,0
TP	61,1	*[]	g/l	65,0-85,0
CRP-hS	<0,5		mg/l	0,0-5,0
PCT	< 0,020		ug/l	0,00-0,50

Diagnosis ?

Practical cases

Na	145	[]* mmol/l		137-144
K	4,4	[*] mmol/l		3,9-5,3
Cl	105	[*] mmol/l		98-107
Urea	2,3	*[] mmol/l		2,9-8,2
S-Creatinine	74	[*] umol/l		42-80
eGFR	1,06	ml/s/1,73 m2		
hsTroponin I 3 h.	18,5	[]* ng/l	cut-off AIM: M: 342; Ž: 156	
hsTroponin I 0 h.	17,9	[]* ng/l		0,0-15,6
Absolute delta hsTroponin I	0,6	ng/l		
Relative delta hs Troponin I	3,4	%		
CRP-hS	52,0	[]* mg/l		0,0-5,0

Diagnosis ?

Practical cases

Na	141	[*]	mmol/l	137-146
K	4,8	[*]	mmol/l	3,6-5,9
Cl	107	[*]	mmol/l	95-110
P	1,26	[*]	mmol/l	1,16-1,90
Osm	291	[*]	mmol/kg	285-295
AST	2,24	[]*	ukat/l	0,20-0,63
ALT	0,55	[*]	ukat/l	0,25-0,60
Urea	4,0	[*]	mmol/l	1,8-6,7
S-Creat	66	[]*	umol/l	19-62

hscTnI	4,2	[*]	ng/l	cut-off AIM: M: 342; Ž: 156
hscTnI (init.)	**not measured**			
Absolute delta hscTnI	**not calculated**			
Relative delta hscTnI	**not calculated**			
Myoglobin	819,0	[]*	ug/l	15,0-50,0
NT-proBNP	119,4	[*]	ng/l	6,0-158,0
CK-MB mass	24,10	[]*	ug/l	0,00-7,20
CRP-hS	1,8	[*]	mg/l	0,0-5,0
ASLO	180	[*]	kU/l	0-200

Diagnosis ?

Practical cases

ALP	2,05	[*]	ukat/l	0,88-2,35
AST	0,44	[*]	ukat/l	0,16-0,63
ALT	0,53	[*]	ukat/l	0,10-0,63
GGT	0,68	[*]	ukat/l	0,15-0,92
Amy	0,45	[*]	ukat/l	0,40-2,51
TBil	10,4	[*]	umol/l	3,0-19,0
DBil	5,4	[]*	umol/l	0,0-2,0
hscTnI	199,5	[]*	ng/l	cut-off AIM: M: 342; Ž: 156
hscTnI (init.)	**not measured**			
Absolute delta hscTnI	**not calculated**			
Relative delta hscTnI	**not calculated**			
NT-proBNP	25034,0	[]*	ng/l	20,0-450,0

Diagnosis ?

Practical cases

Na	131	*[] mmol/l	137-144
K	6,0	[]* mmol/l	3,9-5,3
Cl	102	[*] mmol/l	98-107
Osm	310	[]* mmol/kg	280-301
ALP	4,28	[]* ukat/l	0,88-2,35
AST	0,45	[*] ukat/l	0,16-0,63
ALT	0,29	[*] ukat/l	0,10-0,63
GGT	7,64	[]* ukat/l	0,15-0,92
Urea	37,7	[]* mmol/l	2,9-8,2
S-Crea	505	[]* umol/l	42-80
eGFR	0,11	ml/s/1,73 m2	
NT-proBNP	29530,0	[]* ng/l	20,0-450,0
TP	58,0	*[] g/l	62,0-77,0
CRP-hS	159,8	[]* mg/l	0,0-5,0

Diagnosis ?

Practical cases

Na	139	[*]	mmol/l	137-144
K	3,7	*[]	mmol/l	3,9-5,3
Cl	95	*[]	mmol/l	98-107
ALP	1,28	[*]	ukat/l	0,88-2,35
AST	1,39	[]*	ukat/l	0,16-0,63
ALT	1,04	[]*	ukat/l	0,10-0,63
GMT	2,44	[]*	ukat/l	0,15-0,92
p-AMS	0,34	[*]	ukat/l	0,22-0,88
TBil	15,3	[*]	umol/l	3,0-19,0
DBil	7,4	[]*	umol/l	0,0-2,0
Urea	18,6	[]*	mmol/l	2,9-8,2
S-Crea	139	[]*	umol/l	42-80
eGFR	0,56		ml/s/1,73 m2	
hscTroponin I 3 h.	16,5	[]*	ng/l	cut-off AIM: M: 342; Ž: 156
hscTroponin I 0 h.	17,7	[]*	ng/l	0,0-15,6
Absolute delta hscTroponin I	-1,2		ng/l	
Relative delta hscTroponin I	-6,8		%	
NT-proBNP	1161,0	[]*	ng/l	20,0-125,0
Albumin	39,2	[*]	g/l	32,0-46,0
TP	64,7	[*]	g/l	62,0-77,0
CRP-hS	46,4	[]*	mg/l	0,0-5,0
TSH	1,207	[*]	mIU/l	0,350-4,800
FT4	22,11	[*]	pmol/l	10,00-24,00

Diagnosis ?

Practical cases

Na	137	[*] mmol/l	137-146
K	5.3	[]* mmol/l	3.8-5.0
Cl	99	[*] mmol/l	97-108
Ca	2.08	[*] mmol/l	2.05-2.54
Mg	0.82	[*] mmol/l	0.66-0.91
Osm	280	*[] mmol/kg	285-295
AST	0.61	[*] ukat/l	0.16-0.72
ALT	0.34	[*] ukat/l	0.17-0.78
TBil	4.5	[*] umol/l	2.0-17.0
DBil	2.5	[*] umol/l	0.0-5.1
Urea	5.4	[*] mmol/l	2.0-6.7
S-Crea	83	[]* umol/l	42-80
eGFR	1.16	ml/s	
cTnI	2.626	[]* ug/l	cut-off pro AIM 0,3000.000-0.0
TP	56.6	*[] g/l	65.0-85.0
CRP-hS	178.8	[]* mg/l	0.0-5.0
PCT	6.19	[]* ug/l	0.00-0.50

Diagnosis ?

Thank you for your attention