New Cardiac Biomarkers

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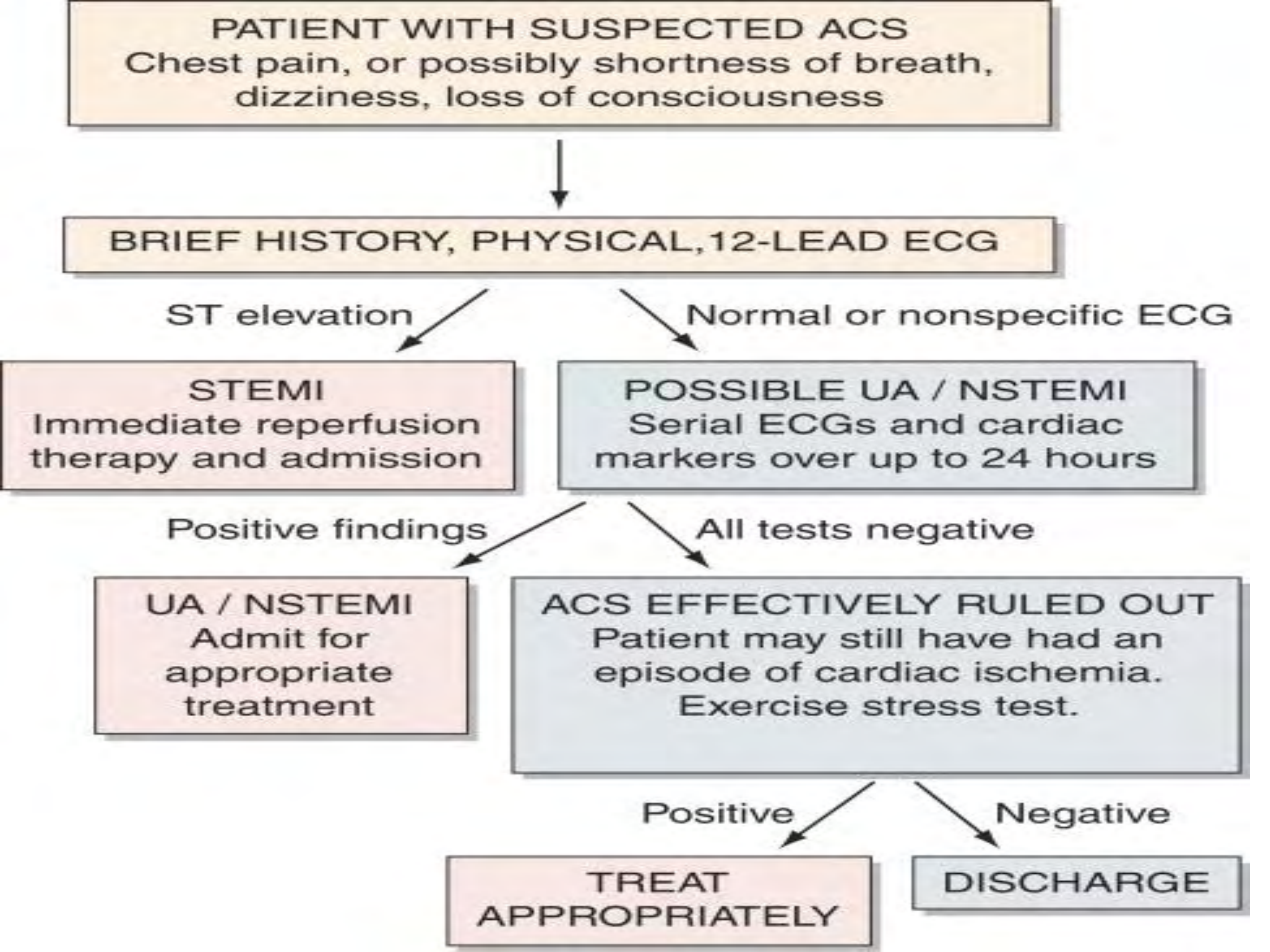
WHO classification of MI

2/3 these criteria:

- ✓Ischemic symptoms
- ✓EKG changes.
- ✓Increased serum markers.


PATIENT WITH SUSPECTED ACS
Chest pain, or possibly shortness of breath, dizziness, loss of consciousness
BRIEF HISTORY, PHYSICAL, 12-LEAD ECG
ST elevation
Normal or nonspecific ECG
STEMI
Immediate reperfusion therapy and admission
POSSIBLE UA / NSTEMI
Serial ECGs and cardiac markers over up to 24 hours
Positive findings
All tests negative
UA / NSTEMI
Admit for appropriate treatment
ACS EFFECTIVELY RULED OUT
Patient may still have had an episode of cardiac ischemia.
Exercise stress test.
Positive
Negative
TREAT APPROPRIATELY
DISCHARGE

Cardiac Biomarkers

- Cardiac biomarkers are substances that are released into the blood when the heart is damaged. **Measurement of these biomarkers is used to help diagnose, evaluate, and monitor patients with suspected acute coronary syndrome (ACS)**
- The symptoms of ACS include chest pain, pressure, nausea, and/or shortness of breath. These symptoms are associated with heart attacks and angina, but they may also be seen with non-heart-related conditions. Increases in one or more cardiac biomarkers can identify patients with ACS, allowing rapid diagnosis and appropriate treatment of their condition.

Cardiac Biomarkers

- Cardiac biomarker tests must **be available to the doctor 24 hours a day, 7 days a week with a rapid turn-around-time**. Some of the tests may be performed at the point of care (POC) – in the Emergency Room or at the patient's bedside.
- Serial testing of one or more cardiac biomarkers is often done to ensure that a rise in their blood levels is not missed and to **estimate the severity of a heart attack.**

Cardiac Biomarkers

- Note: Cardiac biomarkers are not the same tests as those that are used to screen the general healthy population for their risk of developing heart disease. Those can be found under **Cardiac Risk Assessment**

Cardiac Biomarkers

- **Current cardiac biomarker tests** used to help diagnose, evaluate, and monitor patients suspected of having Acute Coronary Syndrome (ACS):
- **CK and CK-MB**
- **Troponin**
- **Myoglobin**

Cardiac Biomarkers

- **Additional biomarker tests** that may be used to evaluate risk of future cardiac events (prognosis):
- **BNP (or NT-proBNP)**
- **hs-CRP**

Cardiac Biomarkers

- **Phased out biomarkers**—the tests below are not specific for damage to the heart and are no longer recommended for evaluating patients with suspected ACS:
- **AST**
- **LDH**

Cardiac Biomarkers

- **More general tests** frequently ordered along with cardiac biomarkers:
- **Blood gases**
- **CMP**
- **BMP**
- **Electrolytes**
- **CBC**

Ischemia modified albumin (IMA)

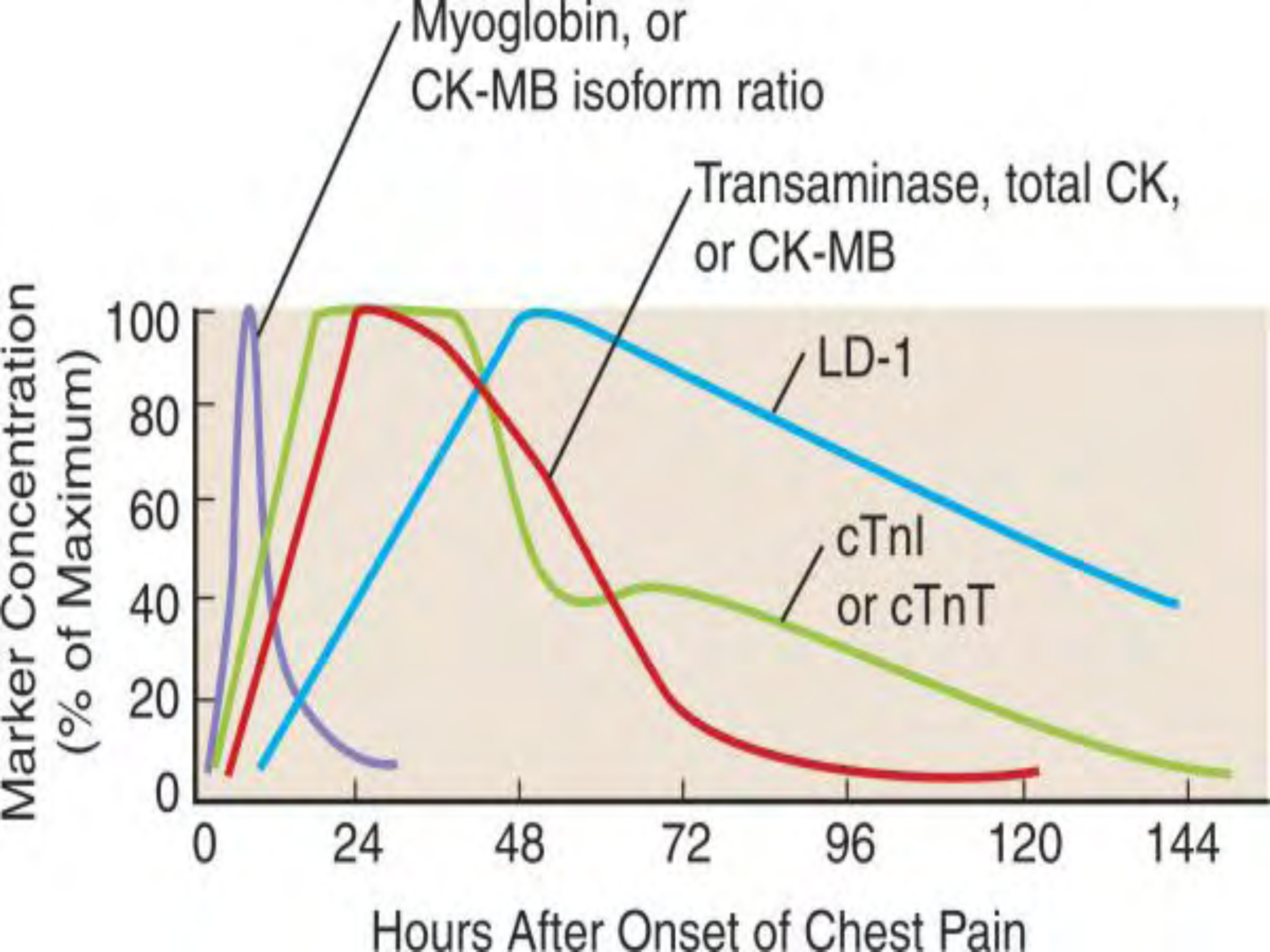
- Ischemia modified albumin (IMA) – This test has received FDA approval for use with troponin and an electrocardiogram. It is not widely available but may become useful some day for identifying patients at higher risk of heart attack

Non-laboratory Tests

- These tests allow doctors to look at the size, shape, and function of the heart as it is beating. They can be used to detect changes to the rhythm of the heart as well as to detect and evaluate damaged tissues and blocked arteries.
- **EKG (ECG, electrocardiogram)**
- **Nuclear scan**
- **Coronary angiography (or arteriography)**
- **ECG (echocardiogram)**
- **Stress testing**
- **Chest X-ray**

Timing Summary

TEST	ONSET	PEAK	DURATION
CK/CK-MB	3-12 hours	18-24 hours	36-48 hours
Troponins	3-12 hours	18-24 hours	Up to 10 days
Myoglobin	1-4 hours	6-7 hours	24 hours
LDH	6-12 hours	24-48 hours	6-8 days


Myoglobin, or
CK-MB isoform ratio
Transaminase, total CK,
or CK-MB
LD-1
cTnI
or cTnT
Marker Concentration
(% of Maximum)
100
80
60
40
20
0
0
24
48
72
96
120
144
Hours After Onset of Chest Pain

Expand Table Commonly Used Cardiac Biomarker Tests

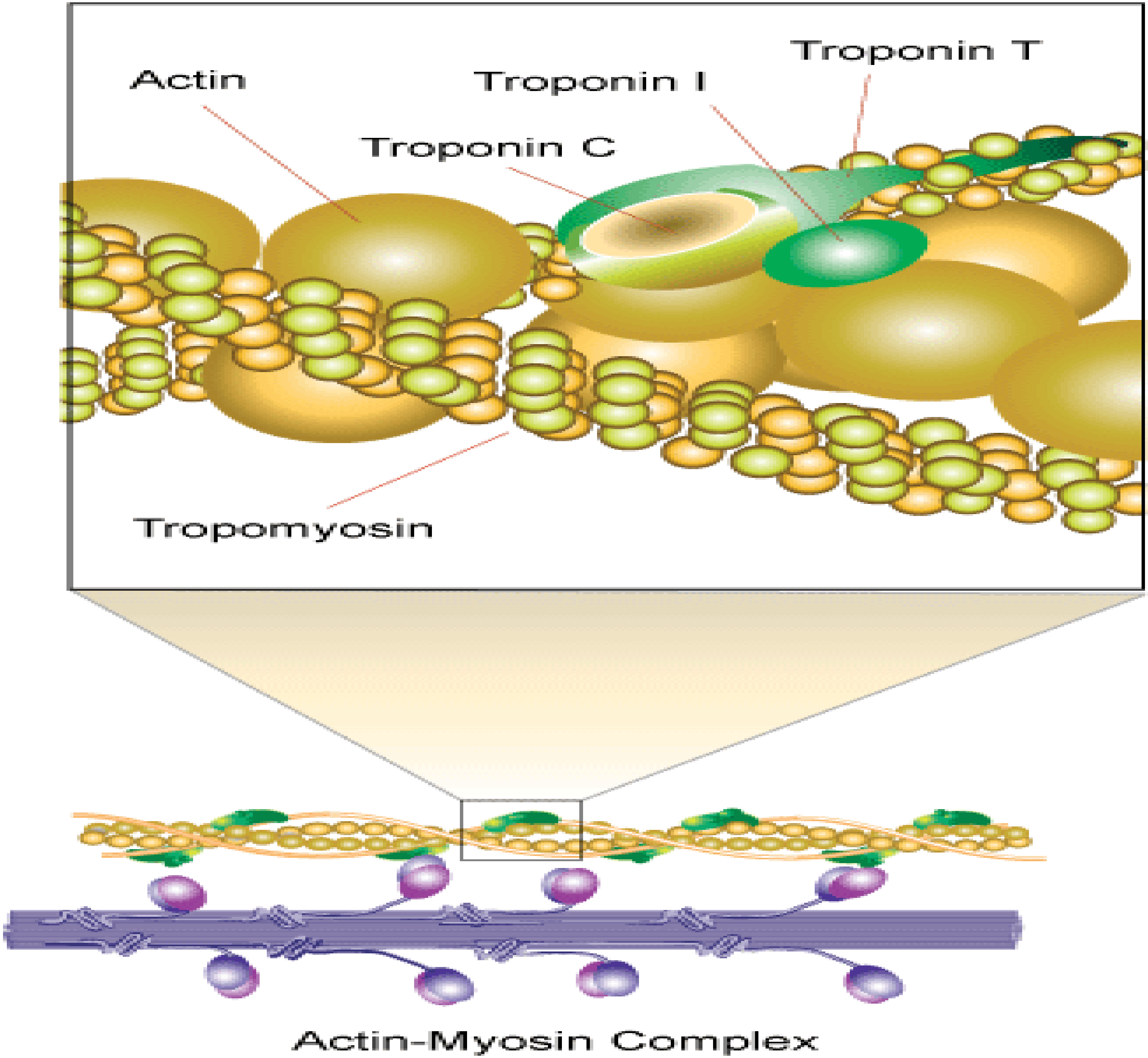
MARKER	WHAT IT IS	TISSUE SOURCE	REASON FOR INCREASE	TIME TO INCREASE	TIME BACK TO NORMAL	WHEN/HOW USED
CK	Enzyme - three different isoenzymes exist	Heart, brain, and skeletal muscle	Injury to muscle and/or heart cells	4 to 6 hours after injury, peaks in 18 to 24 hours	48 to 72 hours, unless due to continuing injury	Performed in combination with CK-MB
CK-MB	Heart-related isoenzymes of CK	Heart primarily, but also in skeletal muscle	Injury to heart and/or muscle cells	4 to 6 hours after heart attack, peaks in 12 to 20 hours	24 to 48 hours, unless new or continuing damage	Less specific than troponin, may be ordered when troponin is not available
Myoglobin	Oxygen-storing protein	Heart and other muscle cells	Injury to muscle and/or heart cells	2 to 3 hours after injury, peaks in 8 to 12 hours	Within one day after injury	Sometimes performed with troponin to provide early diagnosis
Cardiac Troponin	Regulatory protein complex. Two cardiac-specific isoforms: T and I	Heart	Injury to heart	4 to 8 hours	Remains elevated for 7 to 14 days	Diagnose heart attack, assess degree of damage

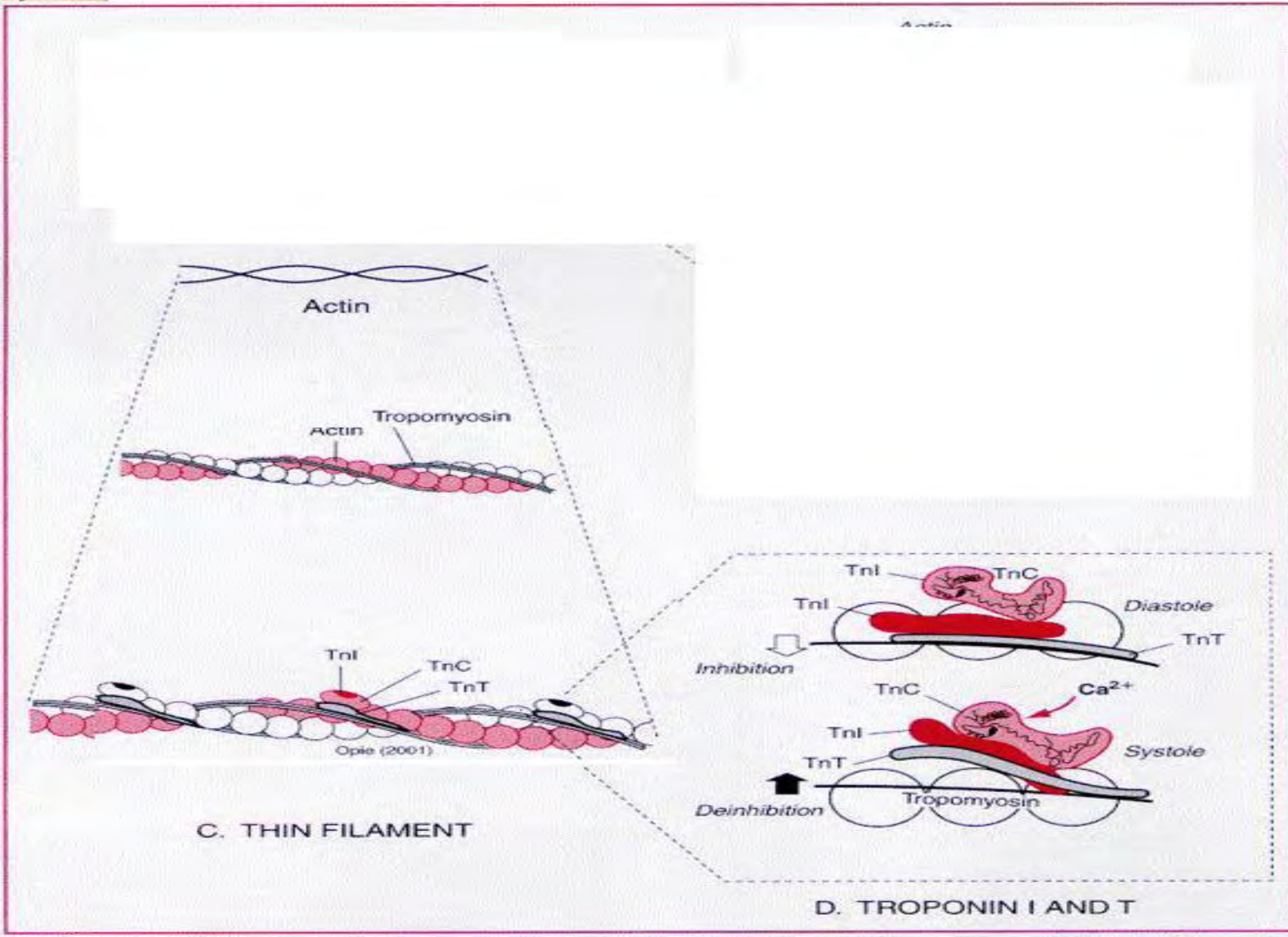
Expand Table Biomarker Tests User for Prognosis

BIOMARKER	WHAT IT IS	REASON FOR INCREASE	WHEN/HOW USED
hs-CRP	Protein	Inflammation	May help determine risk of future cardiac events in patients who have had a heart attack
BNP and NT-proBNP	Hormone	Heart failure	Help diagnose and evaluate heart failure, prognosis and to monitor therapy

Troponin

- The troponins are a family of proteins found in skeletal and heart muscle fibers. The **three different types of troponin are called troponin C (TnC), troponin T (TnT), and troponin I (TnI).**
- Together, these three proteins regulate muscular contraction.
- **Two of the proteins, TnI and TnT,** occur in a form that is **found only in the heart**


Troponin T
Actin
Troponin I
Troponin C
Tropomyosin
Actin-Myosin Complex



Actin
Actin
Tropomyosin
TnI
TnC
TnT
Opie (2001)
C. THIN FILAMENT
TnI
TnC
TnI
Diastole
TnT
Inhibition
TnC
Ca2+
TnI
TnT
Systole
Deinhibition
Tropomyosin
D. TROPONIN I AND T

Troponin T & I

- Require myocardial necrosis for release from sarcomere.
- **Early rise (4-12 hours after symptom).**
- **Peak 12-24 hours.**
- **Continuous release up to 10-14 days 2nd to constant release/necrotic sarcomeres.**
- Unclear excretion pathway.

Troponin

- These cardiac-specific troponins, called cTnI and cTnT, are normally **present in very small quantities in the blood**.
- When there is damage to heart muscle cells, **cardiac troponins I and T are released into the circulation. The more damage there is, the greater the concentration of cardiac troponins I and T in the blood**.
- When a patient has **a heart attack**, levels of troponins can become elevated in the blood within **3 or 4 hours after injury and may remain elevated for 10 to 14 days.**

Troponin

- usually a laboratory will offer one test or the other. Troponins are sometimes ordered along with other **cardiac biomarkers**, such as **CK–MB** **or** **myoglobin**.
- However, troponins are the **preferred tests** for a suspected heart attack because they are **more specific** for heart injury than other tests (which may become positive in skeletal muscle injury) and **remain elevated for a longer period of time**.

Troponin

- The troponin test is used to help diagnose a heart attack, to detect and **evaluate mild to severe heart injury, and to distinguish chest pain that may be due to other causes**.
- In patients who experience heart-related chest pain, discomfort, or other symptoms and do not seek medical attention for a day or more, the troponin test will still be positive if the symptoms are due to heart damage.

Troponin

- **When is it ordered?**

- The troponin test will usually be ordered when a patient with a suspected **heart attack** first comes into the emergency room and then may be **repeated at 6 and 12 hours later**.
- It is sometimes ordered along with other tests such as **CK**, **CK–MB**, or myoglobin.
- **Typically, 2 or 3 troponin tests are done over a 12- to 16-hour period**

Troponin

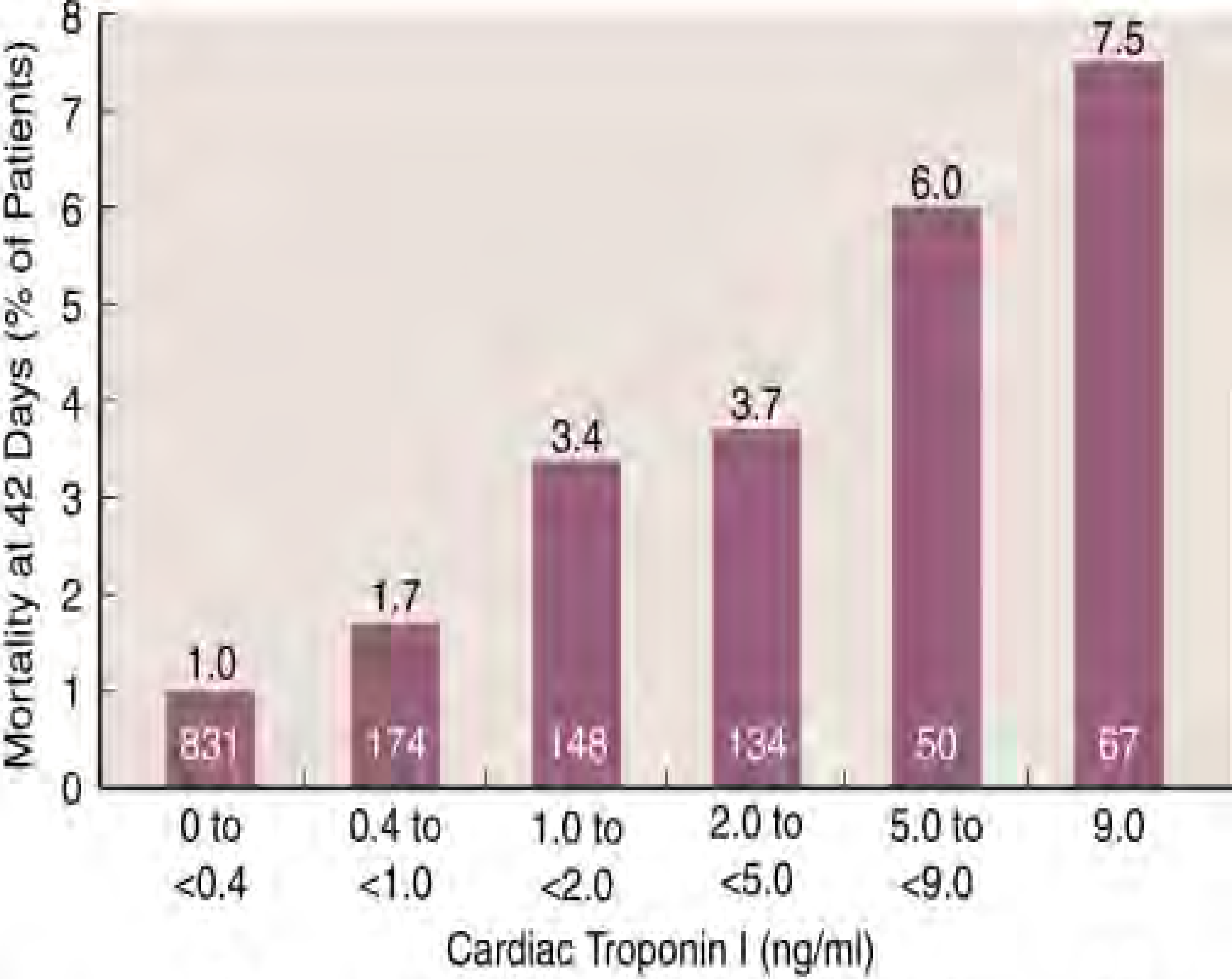
- **What does the test result mean?**

- Normally, cardiac troponin levels are so low that they cannot be measured. Even slight elevations may indicate some degree of damage to the heart. When a patient has significantly elevated troponin concentrations, then it is likely that the patient has had a heart attack or some other form of damage to the heart. When a patient with chest pain and/or known stable angina has normal troponin values, then it is likely that their heart has not been injured.
- Troponin values can remain high for 1–2 weeks after a heart attack.
- **The test is not affected by damage to other muscles, so injections, accidents, and drugs that can damage muscle do not affect troponin levels**.
- **Troponin may rise following strenuous exercise**, although in the absence of signs and symptoms of heart disease, it is usually of no medical significance.

Troponin

- **Is there anything else I should know?**

- Increased troponin concentrations should not be used by themselves to diagnose or rule out a heart attack. **A physical exam, clinical history, and ECG are also important**.
- Some people who have a heart attack will have normal troponin concentrations, and some people with increased troponin concentrations have no apparent heart injury.
- **Troponin levels may also be elevated with acute or chronic conditions such as myocarditis (heart inflammation), congestive heart failure, severe infections, kidney disease, and certain chronic inflammatory conditions of muscles and skin**



Risk Ratio	1.0	1.8	3.5	3.9	6.2	7.8
95% Confidence Interval	–	0.5–6.7	1.2–10.5	1.3–11.7	1.7–22.3	2.6–23.0

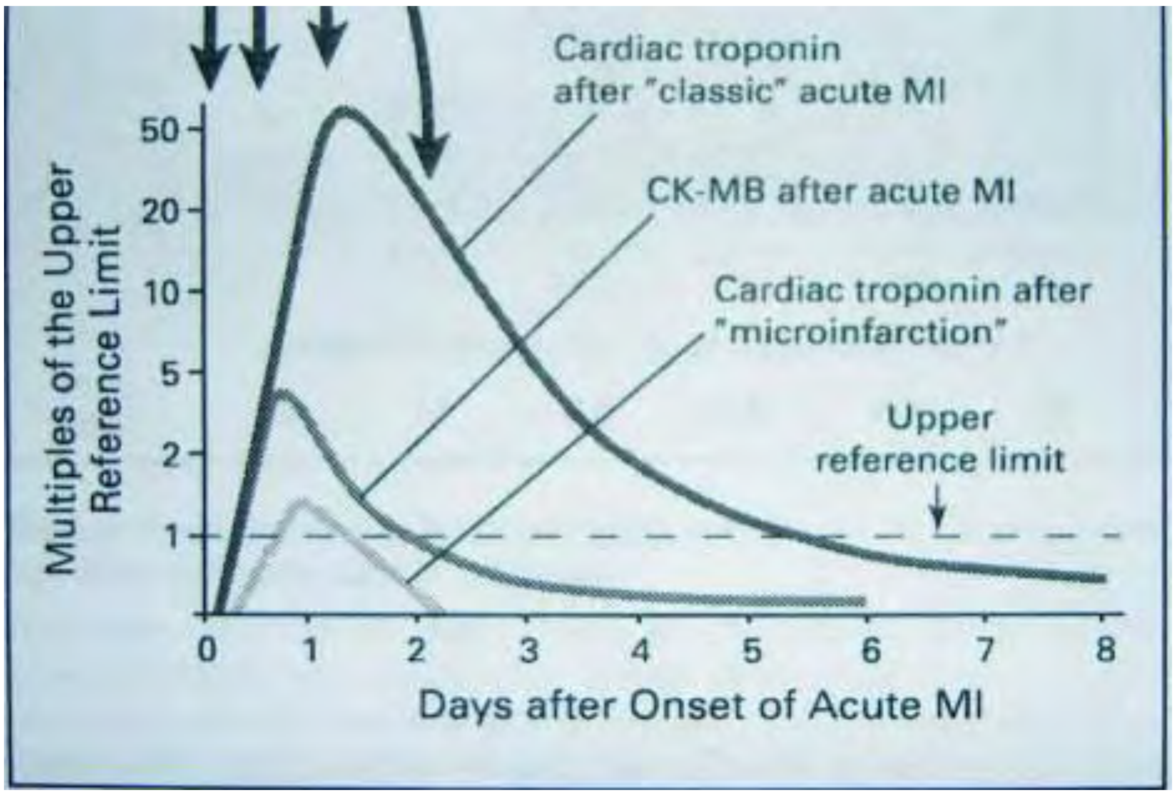
ACC/AHA/ESC 1999

Myocardial infarction: elevation of serum troponin T/I >0.1.

Bedside testing

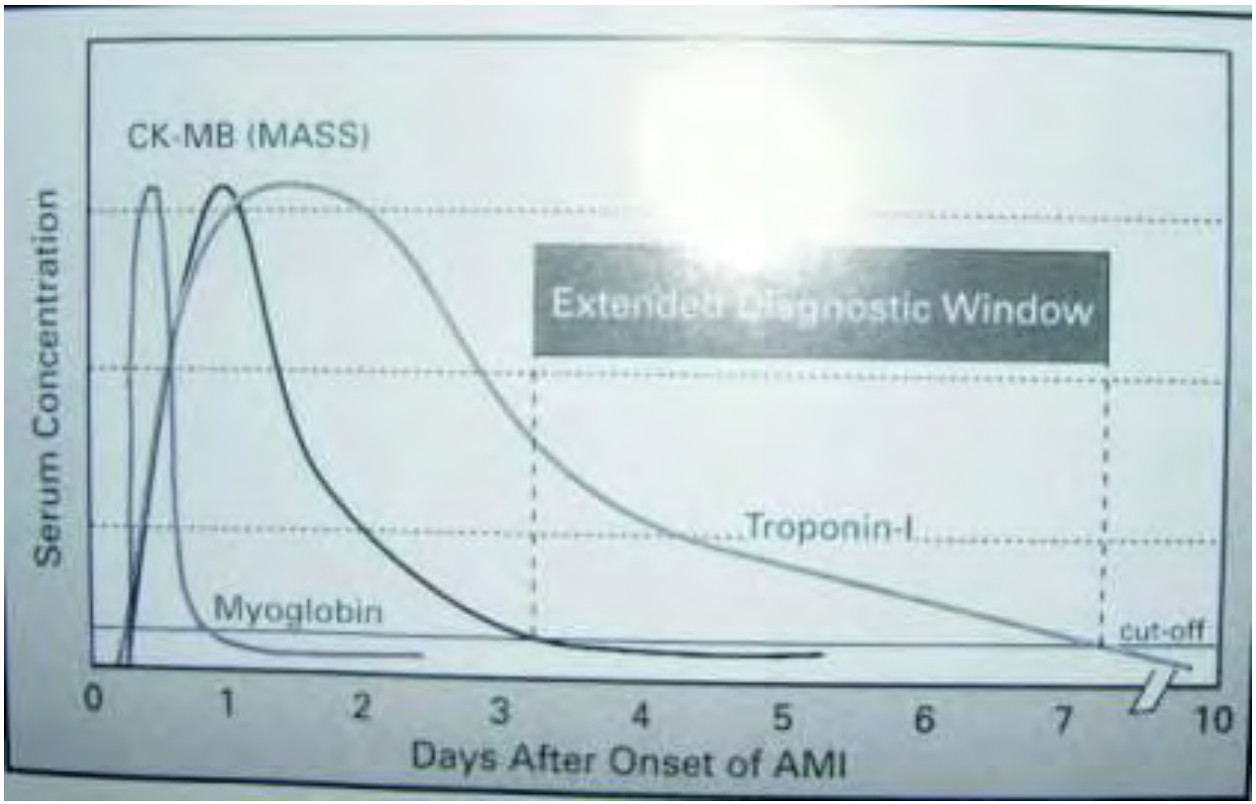
- Trop T and I.
- 96% concordance with quantitative tests.

Comparison



NEJM 2002;Vol.346,No.26:2079-82

Comparison



CK-MB (MASS)
Serum Concentration
Extended Diagnostic Window
Troponin-I
Myoglobin
cut-off
0
1
2
3
4
5
6
7
10
Days After Onset of AMI

مارکر های قلبی

تریاژ کاردیاک مارکر قلبی شامل :

CK-MB / Myoglobin / troponin- I

تفاوت اصلی مارکر های قدیمی و مارکر های جدید قلبی

کراتین کیناز و آسپارتات ترانس آمیناز ولاکتات دهیدروژناز انزیم هائی هستند که با غلظت بالا در عضلات اسکلتی و قلبی تواما یافت می شوند و بدین لحاظ ویژگی این تست ها در تشخیص انفارکتوس قلبی بسیار پایین می باشد در ضمن ظهور این مارکر های قدیمی بسیار با تاخیر رخ می دهد .

نسل جدید مارکرهای قلبی با ویژگی بالاتر و سرعت بالای ظهور مارکرها بر مارکر های قدیمی ارجح می باشند .

Troponin- I مارکر قلبی تروپونین

مارکر طلائی و اختصاصی قلبي تروپونین از جنس میوفیبریل عضلانی قلب می باشد و دارای سه ساب یونیت می باشد

Tn-T ساب یونیت تروپومیوزین تروپونین

Tn- I ساب یونیت مهاری تروپونین

Inhibitory Troponin subunit

Tn-C ساب یونیت کلسیم تروپونین

اختلاف سکانس اسید آمینه بین ایزوفرم عضلانی تروپونین و ایزوفرم قلبی اختصاصیت ویژه ای به مارکر قلبی تروپونین داده است

Troponin- I روش انجام تست مارکر قلبی تروپونین

روش های مختلف کمی و کیفی ایمونو اسی وجود دارد که در این میان بهترین ویژگی و حساسیت را روش کمی انزیم فلوئورو ایمونو اسی(۹۹% ویژگی و ۹۳% حساسیت) دارا می باشد .

بهترین نمونه برای تروپونین سرم یا پلاسما هپارینه است

پلاسما حاوی EDTA منجر به کاهش کاذب تروپونین آی می گردد

همولیز و ایکتریک و لیپمیک بودن سرم در مقادیر بالا تروپونین تداخل جدی حاصل نمی کند ولی در مقادیر مرزی نتایج تاثیر گذار است و بهتر است نمونه مجدد گرفته شود .

تفسیر نتایج تروپونین

در بیمار دارای علامت بالینی مقادیر بالا ۰,۱ در تروپونین نبایست رها گردد و هر ۴ ساعت نمونه مجدد گرفته شود

نتایج بالای ۰,۸ میکرو گرم در لیتر تشخیص انفارکتوس میوکارد حاد را قطعی می نماید خصوصا اگر نتایج در فواصل ۴ ساعت یکبار با افزایش تدریجی رخ داده باشد و از پایین به بالا رسیده باشد .

مقادیر بین ۰,۱ تا ۰,۸ (حد مرزی) می تواند مبین آنژین صدری یا آسیب های نکروتیک مینور قلب باشد و حالت سوم مراحل حدواسط انفارکتوس قلبی حاد است که پس از ۴ ساعت به حد بالای ۰,۸ خواهد رسید .

روماتوئید فاکتور مثبت و آنتي بادی هتروفیل و لخته های فیبرین کوچک نتایج مثبت کاذب حد مرزی (۰,۱ تا ۰,۸) تروپونین را حاصل می نماید .

تفسیر نتایج تروپونین

مطابق پیشنهاد سازمان بهداشت جهانی هرگاه دومعیار از سه معیار زیر مشاهده گردد تشخیص انفارکتوس میوکارد حاد قطعیت می یابد .

۱- درد قلبی مداوم **Prolonged chest pain**

۲- نوار قلبی مثبت **Pos EKG**

۳- افزایش مارکر های تریاژ قلبی

Tn-I / Myoglobin /CK.MB

یا انزیم های قلبی **LDH / CK / AST**

تروپونین نرمال همراه با نوار قلب نرمال اگر با یک درد قلبی مداوم(بیش از ۶ ساعت) همراه باشد بهتر است نمونه دوم و سوم تروپونین با فواصل ۴ ساعت یک بار گرفته شود و بیمار به طور کامل تحت نظر بوده ورهانگردد .

CARDIAC TROPONIN Methodology

Cummins and co-workers were the first to develop a radioimmunoassay to measure cTnI that used polyclonal anti-cTnl antibodies.60 Although the assay showed approximately 2% cross-reactivity with skeletal Tnl, it still had excellent clinical specificity for cardiac muscle injury. The assay was never automated or developed for commercial use.

The first monoclonal ELISA, anti-cTnl antibody-based immunoassay, was described by Bodor et al

CARDIAC TROPONIN Methodology

This assay has less than 0.1% cross-reactivity with skeletal TnI, but it was not suited for clinical use because of the lengthy assay time.

Over the past 15 years, numerous manufacturers have described the development of **monoclonal antibody-based diagnostic immunoassays for the measurement of cTnI in serum**.

Assay times range from 5 to 30 minutes.

over a dozen assays have been approved by the FDA for patient testing within the United States on central laboratory and POCT platforms.

CARDIAC TROPONIN Methodology

- these quantitative assays, several assays have been FDA approved for the qualitative determination of cTnI.
- In practice, two obstacles limit the ease for switching from one cTnI assay to another. First, there is currently no primary reference cTnI material available for manufacturers to use for standardizing their assays. Second, assay concentrations fail to agree because of the different epitopes recognized by the different antibodies used An effort has been underway since 200 I by the AACC Subcommittee on Standardization of cTnI to prepare a primary reference material.50In collaboration with the National Institute for Standards and Technology (NIST),

Quality Specifications-Cardiac Troponin Assays

- **A. Analytical Factors**
- 1. Antibody specificity-recognize epitopes as part of molecule and equimolar for all forms
- 2. Influence of anticoagulants
- 3. Calibrate against natural form of molecule
- 4. Define type of material useful for dilutions
- 5. Demonstrate recovery and linearity of method
- 6. Describe detection limit and imprecision (10% CV)
- 7. Address inferents, i.e., rheumatoid factor, heterophile antibodies
- **B. Preanalytical Factors**
- 1. Storage time and temperature conditions
- 2. Centrifugation effects-gel separators
- 3. Serum-plasma-whole blood correlations

COPeptin
کوپپتین

کوپپتین جدیدترین کاردیاک مارکر شناخته شده و درحال بررسی های تکمیلی است . اندازه گیری همزمان سطح سرمی گلیکو پپتید کوپپتین و تروپونین بلافاصله پس از وقوع انفارکتوس میوکارد و منفی شدن همزمان این دو مارکر تکلیف بیمار مشکوک به حمله قلبی را با ضریب اطمینان ۹۹% قطعی نموده و نیاز به نمونه گیری های مکرر در فواصل ۴ الی ۶ ساعت جهت بررسی افزایش سطح تروپونین را منتفی می سازد.

Copeptin a novel cardiac biomarker

- One of the major challenges in emergency medicine is the early diagnosis of Acute Myocardial Infarction (AMI) in patients presenting with chest pain or other symptoms suggestive of this disease. Until now Troponin is the most effective biomarker. According to study data, **the combination of Troponin and Copeptin, a novel cardiac biomarker from BRAHMS Aktiengesellschaft, allows a rapid and reliable rule out of AMI right at the initial blood draw when the patient presents to the Emergency Department (ED).**

کوپپتین کاردیاک مارکر جدید و نوظهور

یکی از چالش های اصلی طب اورژانس تشخیص زودرس و قطعی انفارکتوس میوکارد حاد در بیماران با درد قفسه صدری و نوار قلبی مبهم می باشد که تاکنون کاردیاک مارکر تروپونین به عنوان کلیدی ترین مارکر تشخیصی انفارکتوس حاد میوکارد شناخته شده است

Copeptin a novel cardiac biomarker

- Approximately 15 million patients present to the Emergency Department (ED) with symptoms suggestive of Acute Myocardial Infarction (AMI) every year.
- The vast majority (70 to 80%) of them finally prove not to have AMI.
- However, **due to a delayed increase of circulating levels of Troponin it takes up to six hours before it can be measured. Therefore serial blood sampling is recommended by the European Guidelines.**
- Study results indicate that **by testing for both markers, along with an Electrocardiogram (ECG) and the clinical findings, approximately two-thirds of the patients would not need to wait those six hours in the ED for the second Troponin test**

Copeptin a novel cardiac biomarker

- **Copeptin levels were significantly higher in AMI patients compared with those in patients having other diagnoses** (median 20,8 pmol/l vs. 6,0 pmol/l, p<0,001).
- **The combination of Troponin and Copeptin at initial presentation resulted in an area under the receiver-operating characteristic curve of 0,97 (95% confidence interval: 0,95 to 0,98), which was significantly higher than the 0,86 (95% confidence interval: 0,80 to 0,92) for Troponin alone (p<0,001)**.
- **A Copeptin level < 14 pmol/l in combination with a Troponin ? 0,01 µg/l correctly ruled out AMI with a sensitivity of 98,8% and a negative predictive value of 99,7%.**

Copeptin

- Copeptin, the C-terminal part of the vasopressin prohormone, is a marker of acute endogenous stress. Arginine vasopressin (AVP) is a key hormone in the human body
- **Copeptin measurement has been shown to be useful in various clinical indications, including the diagnosis of diabetes insipidus and the monitoring of sepsis and cardiovascular diseases**
- Contact:
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Creatine Kinase MB

مارکر قلبی میوگلوبین Myoglobin

۱- میو گلوبین پروتئین حامل اکسیژن می باشد که به طور توام در عضلات قلبی و اسکلتال (ماهیچه ای) موجود است و هرگونه ضایعه نکروتیک یا تخریبی این عضلات منجر به افزایش این مارکر در سطح وسیع می گردد و غلظت ان در جریان خون بالا می رود . مارکر میوگلوبین با اینکه ویژگی پائینی دارد و اختصاصی عضله قلب نمی باشد ولی سریعترین مارکر قلبی می باشد که پس از انفارکتوس حاد قلبی ظهور می نماید

میوگلوبین ۲ دوساعت پس از شروع علائم اولیه انفارکتوس حاد در سطح خون ظاهر می گردد و پس از ۶ الی ۸ ساعت به پیک میرسد و پس از ۱۸ ساعت شروع به کاهش و حذف شدن می نماید بنابراین مارکر میوگلوبین در ۲۴ ساعت دوم پس از علائم انفارکتوس قلبی منفی بوده و غیر قابل پیگیری می باشد .

میوگلوبین علاوه بر انفارکتوس قلبی دربیماری های عضلانی (نظیر دیستروفی عضلانی) و تروما و جراحی و ایسکمی عضلانی بالا رفته لذا ارزش تشخیصی مارکر میوگلوبین در کنار دومارکر دیگر کراتین کیناز قلبی و تروپونین نمود خواهد کرد.

کربنیک CAقبل از شناسائی مارکر اختصاصی تروپونین مارکر غیر اختصاصی عضلانی انهیدراز همراه با میوگلوبین در بیمار مشکوک به انفارکتوس قلبی بررسی می شد اگر کربنیک انهیدراز نرمال موجود بود نشانه بروز انفارکتوس CAمیوگلوبین بالا همراه با قلبی بود اگر هر دو مارکر بالا بود نشانه بیماری غیر قلبی و عضلانی می بود.

Myoglobin

- ✓ Rapid rise
- ✓ Non-specific.
- ✓ Cannot be used alone to confirm MI

CPK-MB

- 15% of cardiac CPK, small amount in skeletal muscle
- Validated as marker for MI.

<u>However:</u>

- Can increase after muscle injury, muscular diseases.
- Can be found in tongue, intestine, diaphragm, uterus, prostate.

Creatine Kinase-MB

- **When to Get Tested?**
- If you have chest pain or other signs and symptoms of a heart attack
- **What is being tested?**
- CK–MB is one of three separate forms (isoenzymes) of the enzyme creatine kinase (CK). CK–MB is found mostly in heart muscle. It rises when there is damage to heart muscle cells.

How is it used?

- CK–MB levels, along **with** total CK, are tested in persons who have chest pain to diagnose whether they have had a heart attack.
- **Since a high total CK could indicate damage to either the heart or other muscles, CK–MB helps to distinguish between these two sources.**
- **If your doctor thinks that you have had a heart attack and gives you a "clot-dissolving" drug, CK–MB can help your doctor tell if the drug worked. When the clot dissolves, CK–MB tends to rise and fall faster. By measuring CK–MB in blood several times, your doctor can usually tell whether the drug has been effective**

When is it ordered?

- CK-MB is usually ordered along with **total CK** in persons with chest pain to determine whether the pain is due to a heart attack. It may also be ordered in a person with a high CK to determine whether damage is to the heart or other muscles.
- **Increased CK-MB can usually be detected in heart attack patients about 3-4 hours after onset of chest pain. The concentration of CK-MB peaks in 18-24 hours and then returns to normal within 72 hours.**
- **Although CK-MB is a very good test, it has been largely replaced by troponin, which is more specific for damage to the heart.**

What does the test result mean?

- If the value of CK-MB is elevated and the **ratio of CK total to CK–MB (relative index) is more than 2.5–3, it is likely that the heart was damaged.**
- A high CK with a relative index below this value suggests that skeletal muscles were damaged

Is there anything else I should know?

- Severe injury to skeletal muscle can be significant enough to raise CK–MB levels above normal, but such injury doesn't usually cause a high relative index. Strenuous exercise may also increase both CK and CK-MB.
- If your doctor suspects injury to both heart muscle and skeletal muscle, troponin is a more accurate test for identifying a heart attack.
- Sometimes persons who are having trouble breathing have to use their chest muscles. Chest muscles have more CK–MB than other muscles, which would raise the amount of CK–MB in the blood.
- Persons whose kidneys have failed can also have high CK–MB levels without having had a heart attack. Rarely, chronic muscle disease, low thyroid hormone (T3, T4, TSH) levels, and alcohol abuse can increase CK–MB, producing changes similar to those seen in a heart attack

Cardiac Biomarkers

- Note: Cardiac biomarkers are not the same tests as those that are used to screen the general healthy population for their risk of developing heart disease. Those can be found under **Cardiac Risk Assessment**

Cardiac Risk Assessment

- Lipid profile;
- hs-CRP;
- Lp(a);
- Lp-PLA2

Routin CHD marker panel

- Biochemical test
- FBS,TG,ch,HDL,LDL,HS CRP
- other
- BMI,BP(Bloodpressure),smoking,exercise, familial background

Specific CHD marker panel

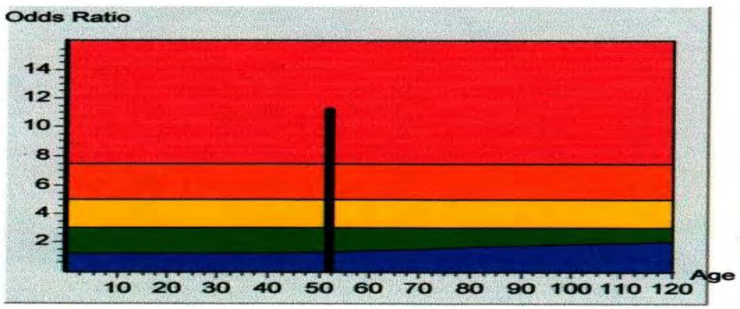
- **Biochemical test**
- Homocystein,fibrinogen,APO A_1(Apo lipoprotein A_1 ,APO E,APO B
- HS CRP(High sensitive CRP), FBS,TG,ch,HDL,LDL ,U.A
- **other**
- BMI,BP(Bloodpressure),smoking,exercise,f amilial background

Farvardin Pathobiology Lab
Tehran, Karoon St, sepah Cr.ss
Tel: 66367914 Tel/Fax: 66837167

CHD Risk Estimation Report
CHD Marker

Name	Ahmadi Ali	Exercise Level	Low	Birthday	1335/06/06
		Weight (Kg)	89	Age	52
Smoking	Yes	Tall (m)	1.6	Date of Sampling	1387/06/05
Familial History of CHD	No	BMI (Kg/m^2)	35	Date of Report:	1390/09/22

Test	Result	Unit	Normal Range	Test	Result	Unit	Normal Range
Bloodp.(S)	12	MM/Hg	≤ 140	Uric Acid	8.9	Mg/dL	3.5 - 6.9
Bloodp.(D)	8	MM/Hg	≤ 90	APO E	Neg.		-----
FBS	162	Mg/dL	75 - 110	APO B	88	Mg/dL	75 - 150
Triglycerid	890	Mg/dL	≤ 180	HS CRP	2.3	Mg/L	1 - 5
Cholesterol	501	Mg/dL	≤ 200	Homocystein	90	µmol/L	≤ 12
HDL	21	Mg/dL	40 - 80	Fibrinogen	302	Mg/dL	200 - 400
LDL	90	Mg/dL	≤ 100	APO A1	151	Mg/dL	110 - 170



CHD risk 11.17 Odds Ratio

Farvardin Pathobiology Lab
Lab Director

Offer

CHD risk score is 11.17 (high risk (danger)) for ten years;
The patient should be advised for more exercise;
The Patient is heavy somker and is high-risk for CHD, and lung disease;
The patient is obese. Diet and exercise should be modified;
The patient is high-risk for diabetes;
Serum liver enzymes should be evaluated for possibility of fatty liver;

Description

The calculated risk by CHD Marker depends on the accuracy of the information provided by the referring physician.

Basic science textbooks

Harrison's Advances In Cardiology
Health An Introduction for Nurses
Methods For The Prediction of Coronary Heart Disease Risk
American Heart Journal January 1990; 293-8

تفسیر این گزارش بر عهدهٔ پزشک می باشد

Age Risk | Low Risk | High Risk (Border line) | High Risk (Alarm) | High Risk (Danger)

low Density Lipoprotein
LDL

کلسترول قسمت عمده کلسترول توتال است که منبع عمده آن از LDL در کبد حاصل می گردد. VLDLکاتابولیسم

مقدار مرجع:

کمتر از ۱۳۰در بالغین و کمتر از ۱۱۰ در کودکان

۱۳۰الی ۱۶۰ گروه مرزی

بالای ۱۶۰ گروه پر خطر

رابطه مستقیم با بیماری های قلبی عروقی و اترواسکلروزیس دارد LDLمیزان .

نحوه محاسبه با فرمول فریدوالد:

$$LDL = Chol\ total - (VLDL + HDL)$$

$$VLDL = TG / 5$$

فرمول فرید والد برای تری گلیسرید های بالا ۴۰۰ فاقد ارزش گزارش و محاسبه می باشد

ApoLipoprotein

apoA / apoBجز پروتئینی لیپو پروتئین ها آپو پروتئین نامیده می شود که اصلی ترین انها شامل:
و مسئولیت اتصال لیپو پروتئین ها به رسپتور سطح سلول را دارند

apoA پلی پپتیداصلی لیپو پروتئین LP(a) /
می باشد که به دوشکل apoA-1(75%) / apoA-2(25%) می باشد :

apoA-1

باشد HDLرابطه مستقیم برای تشخیص ریسک اترواسکلروزیس دارد و حتی تست بهتری نسبت به رابطه مستقیم با افزایشHDLو دارد.

apoB-48 / می باشد که دو نوع شایع ان شامل : LDL پلی پپتید اصلی تشکیل دهنده apoB می باشد .apoB-100

می باشد که این امر را با تمایل به چسبیدن به رسپتور LDL مکانیسم اصلی انتقال apoB100 در سطح سلول های محیطی نشان می دهد . کاهش اپوپروتئین(ب ۱۰۰) رابطه مستقیم با LDL شاخص LDLافزایش رسوب کلسترول در جدار عروق و اترواسکلروزیس دارد و حتی از استانداردتری می باشد .

مسئول انتقال لیپید های داخل روده ای به خون است و در شیلو میکرون ها یافت می شود apoB-48 و منشا روده ای دارد.

می باشد و یک ساختار apoA / apoB-48: لیپو پروتئین کوچک متشکل از از دوجز اپوپروتئینی LP(a) شبه پلاسمینوژن دارد که با رقا بت با پلاسمینوژن لیز لخته ها و میکرو ترومبوز ها را به تاخیر می اندازد و نهایتاً با مهار تخریب فیبرین در میکروترومبوز ها منجر تشدید ضایعه اترواسکلروزیس در دیواره شریان و بروز انوریسم می گردد.

ترکیبات تشکیل دهنده لیپوپروتئین ها

	شیلومیکرون%	VLDL%	LDL%	HDL%
کلسترول	۶	۱۰	۴۵	۲۰
تری گلیسرید	۸۷	۷۲	۱۰	۴
فسفولیپید	۴	۱۰	۲۵	۳۰
کربوهیدرات	<۱	۱	<۲	<۱
پروتئین	۱	۱۰	۲۰	۴۸
آپوپروتئین	A B C E´	A B C D E	B	A C E
نسبت پروتئین -لیپید	۱:۱۰۰	۱:۱۰	۱:۴	۱:۱

Total cholesterol as an indicator of risk of CHD (mg/dl / si units : mmol/L)

High risk	Moderate risk	low risk	Age
>185 [4.8]	171-185	<170 [4.4]	2-19
>220 [5.7]	201-220	<200 [5.5]	20-29
>240 [6.2]	221-240	<220 [5.7]	30-39
>260 [6.8]	241-260	<240 [6.2]	>40

ApoLipoprotein Normal findings

- ApoA-I
- Adult! elderly
- Male: 75-160 mg/dl
- Female: 80-175 mg/ dl
- Child
- Newborn
- Male: 41-93 mg/dl
- Female: 38-106 mg/dl
- 6 months-4 years
- Male: 67-167 mg/dl
- Female: 60-148 mg/dl
- 5-17 years: 83-151mg/dl
- ApoB
- Adult/elderly
- Male: 50-125 mg/dl
- Female: 45-120 mg/dl
- Child
- Newborn: 11-31mg/dl
- 6 months-3 years: 23-75 mg/dl
- 5-17 years:Male: 47-139 mg/dl /Female: 41-132 mg/dl

WHOطبقه بندی فردریکسون
طبقه بندی بر اساس الگوی الکتروفورز

طبقه بندی فردریکسون	شکل الکتروفورز	نوع لیپو پروتئین افزایش یافته
تیپ ۱	افزایش شیلومیکرون	chylomicrons
تیپ ۲	افزایش بتا لیپوپروتئین	LDL
تیپ 2b	افزایش پره بتا لیپوپروتئین	VLDL /LDL
تیپ ۳	باند بتا پهن	IDL
تیپ ۴	افزایش پره بتا لیپوپروتئین	VLDL
تیپ ۵	افزایش شیلومیکرون و پره بتا	VLDL / chylomicrons

homocysteine

- **When to Get Tested?**

- **1- vitamin B12 or folate deficiency**

- **2-**infant or young person **homocystinuria**

- **3- a heart attack or stroke and do not have traditional risk factors**, as part of a **cardiac risk assessment**

چه زمانی تست هموسیستئین درخواست می گردد؟

۱- کمبود شدید ویتامین ب و فولات

۲-ارزیابی هموسیستینوری در نوزادان و کودکان

۳-ارزیابی ریسک بیماری قلبی عروقی

homocysteine

- **What is being tested?**

- This test determines the level of homocysteine in the blood or urine.
- Homocysteine is a product of methionine metabolism. Methionine is one of the eleven "essential" amino acids - amino acids that must be derived from the diet since the body cannot produce them. In healthy cells, homocysteine is quickly converted to other products.
- Vitamins B6, B12, and folate are necessary to metabolize homocysteine. **People who are deficient in these vitamins may have increased levels of homocysteine.**
- **excess homocysteine may promote atherosclerosis by damaging blood vessel walls and supporting the formation of inappropriate blood clots, but there is not a direct link between the two. The benefit of using homocysteine levels for risk assessment of cardiovascular disease (CVD), peripheral vascular disease, and stroke** is uncertain given that several studies indicate no benefit or lowering of CVD risk with folic acid and B vitamin supplementation

homocysteine

- **How is it used?**

- A doctor may order both a urine and blood homocysteine to help **diagnose homocystinuria if she suspects that an infant** may have this inherited disorder. In some states, babies are tested for excess methionine as **part of their newborn screening**.
- If a baby's test is positive, then urine and blood homocysteine tests are often performed to confirm the findings.

homocysteine

- **How is it used?**
- **Homocysteine** may also be ordered as part of **a screen for people at high risk for <u>heart attack</u> or <u>stroke</u>**.
- It may be useful in someone who has a family history of <u>coronary artery disease</u> but no other known risk factors.

hs-CRP

- **Why Get Tested?**
- May be helpful in assessing risk of developing heart disease, cardiovascular disease, or other processes involving inflammation
- **When to Get Tested?**
- No current consensus exists on when to get tested; **hs-CRP is most often done in conjunction with other tests that are ordered to assess risk of heart disease, such as a lipid profile** (cholesterol, triglycerides, HDL-C, LDL-C

hs-CRP

- **What is being tested?**
- C-reactive protein (CRP) is made by the liver and secreted into the bloodstream. It can be measured with two different tests: the CRP test and the high-sensitivity CRP (hs-CRP) test, each measuring different ranges of CRP levels in the blood. **The hs-CRP test can more accurately detect lower concentrations of the protein (it is more sensitive) than the standard CRP test**.
- CRP increases with inflammation and infection as well as following a myocardial infarction (MI, heart attack), surgery, and trauma.
- **As a result, CRP is one of several proteins that are often referred to as acute phase reactants and is used to monitor changes in inflammation associated with many infectious and autoimmune diseases**

hs-CRP

- It is now believed that inflammation plays a major role in atheroslcerosis (the narrowing of blood vessels due to build-up of cholesterol and other lipids), which is often associated with cardiovascular disease (CVD). Studies have shown that measuring CRP with the improved methodology of the highly sensitive assay can identify the risk level for CVD in apparently healthy people. For these high-risk individuals, this more sensitive test allows for measurement of lower concentrations of CRP that may be within the normal range but consistently at the higher end of the range. **These normal but relatively high levels of CRP in otherwise healthy individuals have been found to be predictive of the future risk of a heart attack, stroke, sudden cardiac death, and peripheral arterial disease, even when cholesterol levels are within an acceptable range.**

How is it used?

- There are two different tests for CRP. The standard test measures a much wider range of CRP levels but is less sensitive in the lower ranges.
- **The hs-CRP test can more accurately detect lower concentrations of the protein (it is more sensitive), which makes it more useful than the CRP test in predicting a *healthy* person's risk for cardiovascular disease.**
- hs-CRP is promoted by some as a test for determining the potential risk level for cardiovascular disease, heart attacks, and strokes. The current thinking is that hs-CRP can play a role in the evaluation process before one encounters one of these health problems. More clinical trials that involve measuring hs-CRP levels are currently underway in an effort to better understand its role in cardiovascular events and may eventually lead to guidelines on its use in screening and treatment decisions

Recommendations of a Joint Committee of the American Heart Association and the Centers for Disease Control and Prevention on CRP Testing to Assess CHD Risk

- if inflammatory markers are to be used in assessment of CHD risk, hsCRP is the current analyte of choice •
- Optimally, hsCRP results should be averaged from two specimens drawn about 2 weeks apart. If a level > 10 mg/L is identified, there should be a search for an obvious cause of infection or inflammation; that result should then be discarded, and another test done 2 weeks later
- • **Decision intervals are: < 1 mg/L, low risk; 1–3 mg/L, intermediate risk; > 3–mg/L, high risk (approximately corresponding to tertiles in the adult population)**
- • Patients most likely to benefit from an hsCRP test would be those in whom the risk estimate from established factors is moderate (i.e., approximately 10–20% risk of CHD in the next 10 years), and the physician desires additional information to guide preventive therapy
- • The role of hsCRP in secondary prevention (i.e., prevention of disease progression in patients with established CHD) is limited, because it is not likely to alter management (which needs to be aggressive, regardless of additional information provided by CRP or other markers)
- • Universal hsCRP screening of the adult population is *not* warranted.

hs-CRP

- **When is it ordered?**
- hs-CRP usually is ordered as one of several tests in a cardiovascular risk profile, often along with tests for cholesterol and triglycerides. Some experts say that the best way to predict risk is to combine a good marker for inflammation, like hs-CRP, along with the lipid profile.
- **What does the test result mean?**
- **People with higher hs-CRP values have the highest risk of cardiovascular disease, and those with lower values have less of a risk.**
- Specifically, **individuals who have hs-CRP results in the high end of the normal range have 1.5 to 4 times the risk of having a heart attack as those with hs-CRP values at the low end of the normal range.**

High-sensitivity C-reactive protein (hs-CRP)

- Studies have shown that measuring CRP with a high sensitivity test can help identify risk of cardiovascular disease (CVD).
- **hs-CRP test is different from the regular CRP test**, which detects elevated levels of CRP in people with infections and inflammatory diseases.
- **The hs-CRP test measures CRP that is in the normal range for healthy people. It can be used to distinguish people with low normal levels from people with high normal levels.**
- **High normal levels of hs-CRP in otherwise healthy individuals have been found to be predictive of the future risk of heart attack, stroke, sudden cardiac death, and peripheral arterial disease, even when lipid levels are within acceptable ranges.**

Lipoprotein A (Lp(a)):

- Lp(a) is a lipoprotein consisting of an LDL molecule with another protein (Apolipoprotein (a)) attached to it.
- **Lp(a) is similar to LDL-C but does not respond to typical strategies to lower LDL-C such as diet, exercise, or most lipid-lowering drugs. Since the level of Lp(a) appears to be genetically determined and not easily altered**, the presence of a high level of Lp(a) may be used to identify individuals who might benefit from more aggressive treatment of other risk factors.

BNP

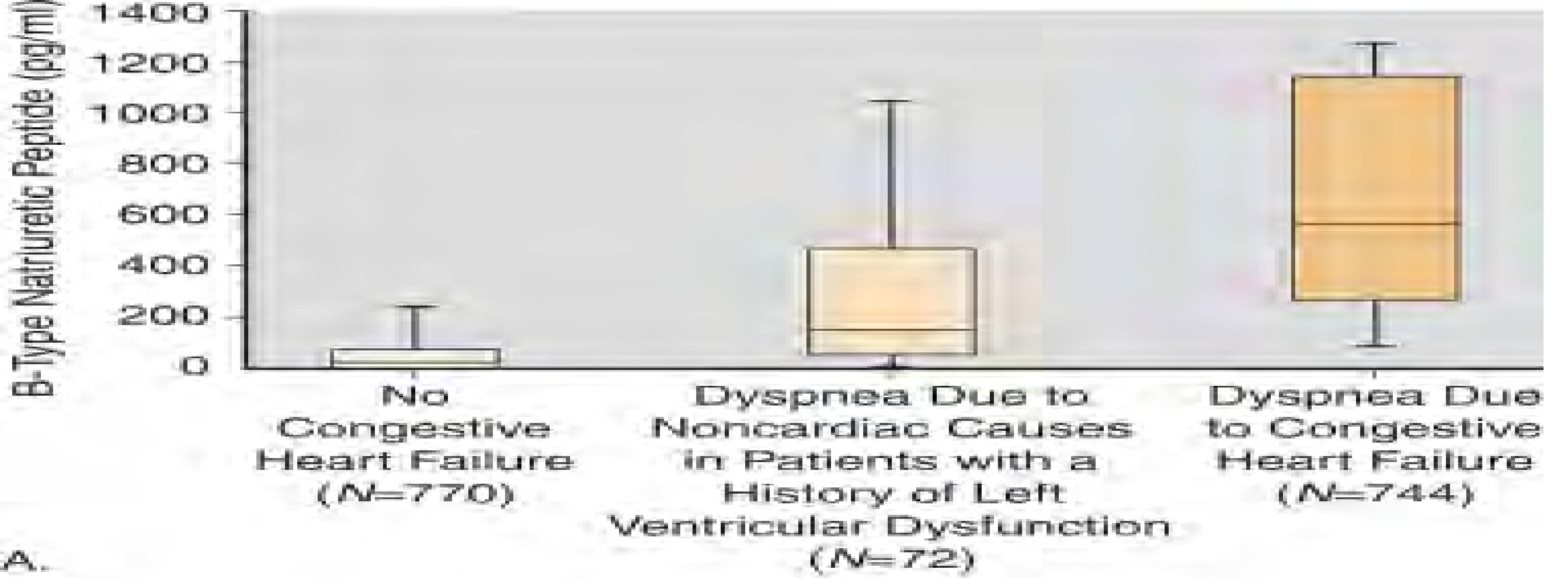
پروتئین دفع کننده سدیم که از بخش ونتریکولار یا بطنی میوکارد ترشح می گردد و با تاثیر بر کلیه ها منجر به افزایش ترشح سدیم و آب می گردد از تست های مناسب و جدید در تشخیص و مانیتورینگ نارسائی مزمن قلبی می باشد

B-type natriuretic peptid (BNP)

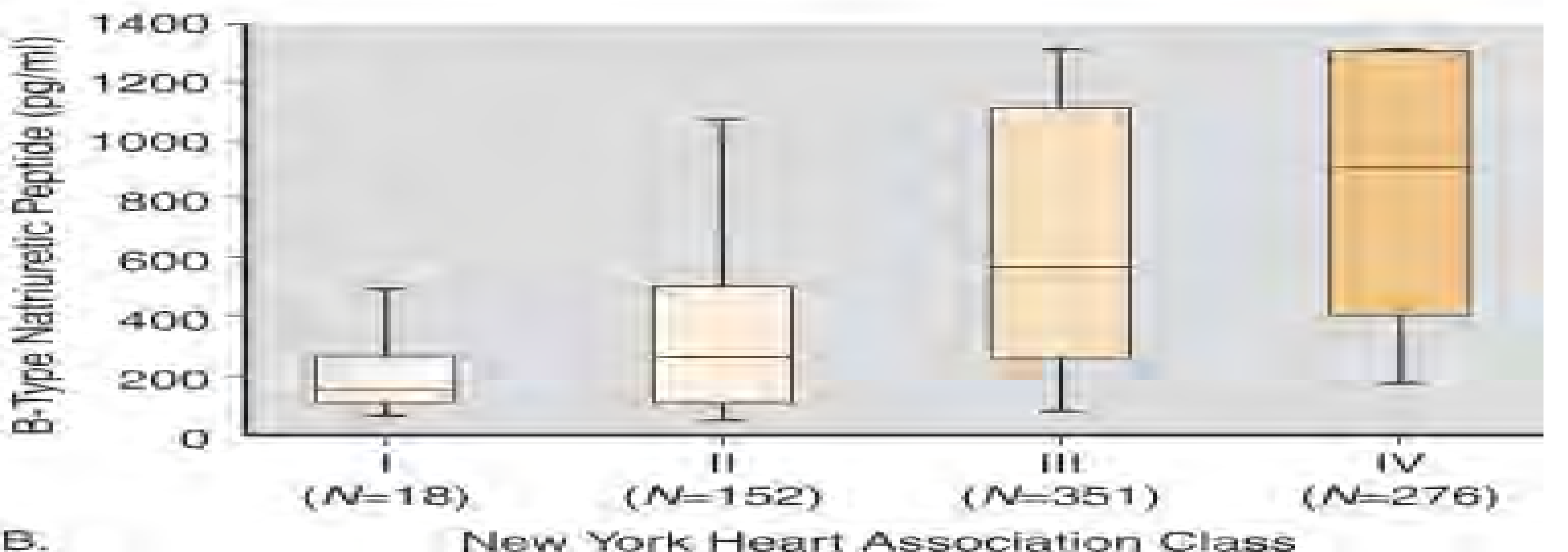
N-terminal pro b-type natriuretic peptide

- **Why Get Tested?**

- To help diagnose the presence and severity of **heart failure**


B-Type Natriuretic Peptide (pg/ml)
1400
1200
1000
800
600
400
200
0
No Congestive Heart Failure (N=770)
Dyspnea Due to Noncardiac Causes in Patients with a History of Left Ventricular Dysfunction (N=72)
Dyspnea Due to Congestive Heart Failure (N=744)

A.


B-Type Natriuretic Peptide (pg/ml)
1400
1200
1000
800
600
400
200
0
I (N=18)
II (N=152)
III (N=351)
IV (N=276)
New York Heart Association Class

B.

What is being tested?

- These tests measure the concentration of BNP or NT-proBNP in the blood. The heart normally produces low levels of a precursor protein, pro-BNP, which is cleaved to release the active hormone BNP and an inactive fragment, NT-proBNP.
- The purpose of BNP is to help regulate blood volume and, therefore, the work that the heart must do in pumping blood throughout the body.
- **Both BNP and NT-proBNP are produced mainly in the heart's left ventricle** (the organ's main pumping chamber). When the left ventricle is stretched from having to work harder, the concentrations of BNP and NT-proBNP in blood can increase markedly. This situation may occur in **heart failure** as well as other diseases that affect the heart and circulatory system.

How is it used?

- Either BNP or NT-proBNP may be used to **help diagnose heart failure and to grade the severity of that heart failure.**
- There are various causes of heart failure. Currently, the condition is diagnosed by the presence of symptoms such as swelling in the legs (edema), difficulty breathing, shortness of breath, and fatigue, in addition to chest X-rays and an ultrasound test called echocardiography. However, heart failure is still often confused with other conditions.
- **BNP and NT-proBNP levels can help doctors differentiate between heart failure and other problems, such as lung disease.**
- An accurate diagnosis is important because heart failure can be successfully managed with various medical treatments.

When is it ordered?

- A BNP or NT-proBNP test may be ordered under these circumstances:
- **In your doctor's office, if you have symptoms that could be due to heart failure.**
- **In the emergency room, if you are in crisis and doctors need to quickly determine whether you are suffering from heart failure or some other medical problem.**
- **To monitor the effects of therapy for heart failure.**

What does the test result mean?

- Higher-than-normal results suggest that a person is in **heart failure**, and the **level of BNP or NT-proBNP in the blood is related to the severity of heart failure.**
- Higher levels of BNP or NT-proBNP also may be associated with a worse outlook (prognosis) for the patient.

Is there anything else I should know?

- BNP and **NT-proBNP levels decrease in most patients who have been taking drug therapies for heart failure, such as ACE inhibitors, beta blockers, and diuretics**.
- Levels of both BNP and NT-proBNP tend to **increase with age**.
- Levels of NT-proBNP and BNP are increased in persons with kidney disease.
- While both BNP and NT-proBNP will rise with left ventricle dysfunction and either can be measured, they are not interchangeable and the results cannot be directly compared.