New Cardiac Biomarkers

Dr. mehrdad vanaki
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
- STEMI
  Immediate reperfusion therapy and admission

Normal or nonspecific ECG
- POSSIBLE UA / NSTEMI
  Serial ECGs and cardiac markers over up to 24 hours

Positive findings
- UA / NSTEMI
  Admit for appropriate treatment

All tests negative
- ACS EFFECTIVELY RULED OUT
  Patient may still have had an episode of cardiac ischemia. Exercise stress test.

Positive
- TREAT APPROPRIATELY

Negative
- 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) – 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

<table>
<thead>
<tr>
<th>TEST</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK/CK-MB</td>
<td>3-12 hours</td>
<td>18-24 hours</td>
<td>36-48 hours</td>
</tr>
<tr>
<td>Troponins</td>
<td>3-12 hours</td>
<td>18-24 hours</td>
<td>Up to 10 days</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>1-4 hours</td>
<td>6-7 hours</td>
<td>24 hours</td>
</tr>
<tr>
<td>LDH</td>
<td>6-12 hours</td>
<td>24-48 hours</td>
<td>6-8 days</td>
</tr>
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</table>
Myoglobin, or CK-MB isoform ratio

Transaminase, total CK, or CK-MB

LD-1

cTnl or cTnT

Marker Concentration (% of Maximum)

Hours After Onset of Chest Pain
<table>
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<tr>
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<th>WHAT IT IS</th>
<th>TISSUE SOURCE</th>
<th>REASON FOR INCREASE</th>
<th>TIME TO INCREASE</th>
<th>TIME BACK TO NORMAL</th>
<th>WHEN/HOW USED</th>
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<tr>
<td>CK</td>
<td>Enzyme - three different isoenzymes of CK also in skeletal muscle</td>
<td>Heart, brain, and skeletal muscle</td>
<td>Heart-related isoenzymes of CK</td>
<td>4 to 6 hours after heart attack, peaks in 12 to 20 hours</td>
<td>48 to 72 hours, unless due to continuing injury</td>
<td>Performed in combination with CK-MB</td>
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<td>CK-MB</td>
<td>Heart and other muscle cells</td>
<td>Heart primarily, but also in skeletal muscle</td>
<td>Injury to heart and/or muscle cells</td>
<td>4 to 6 hours after injury, peaks in 8 to 10 hours</td>
<td>24 hours</td>
<td>Less specific than troponin, may be ordered when troponin is not available</td>
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<tr>
<td>Myoglobin</td>
<td>Oxygen-storing protein</td>
<td>Heart and other muscle cells</td>
<td>Injury to muscle and/or heart cells</td>
<td>Within one day after injury, peaks in 8 to 12 hours</td>
<td>24 to 48 hours, unless new or continuing damage</td>
<td>Performed in combination with troponin to provide early diagnosis</td>
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<td>Troponin</td>
<td>Cardiac regulatory protein complex. Two cardiac-specific isoforms: T and I</td>
<td>Heart</td>
<td>Injury to heart</td>
<td>4 to 8 hours</td>
<td>Remains elevated for 7 to 14 days; degree of damage assessed</td>
<td>Diagnose heart attack, assess degree of damage</td>
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**Cardiac Biomarker Tests**

**Commonly Used Cardiac Biomarker Tests**

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<td>hs-CRP</td>
<td>Protein</td>
<td>Inflammation</td>
<td>May help determine risk of future cardiac events in patients who have had a heart attack</td>
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<td>BNP and NT-proBNP</td>
<td>Hormone</td>
<td>Heart failure</td>
<td>Help diagnose and evaluate heart failure, prognosis and to monitor therapy</td>
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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.
**Tropomyosin:**

**Troponin T,**
**Troponin I,**
**Troponin C.**

**Actin** and **tropomyosin**

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**C. THIN FILAMENT**

**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.
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.
Mortality at 42 Days (% of Patients)

Cardiac Troponin I (ng/ml)

- 0 to <0.4: 1.0 (831)
- 0.4 to <1.0: 1.7 (174)
- 1.0 to <2.0: 3.4 (148)
- 2.0 to <5.0: 3.7 (134)
- 5.0 to <9.0: 6.0 (50)
- 9.0: 7.5 (67)

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
مکارکر های قلبی

تربیت کاردیاک مکارکر قلبی شامل:

CK-MB / Myoglobin / troponin-I

تفاوت اصلی مکارکر های قدمی و مکارکر های جدید قلبی

کراتین کیناز و آسپارتاک اتیراس آمیناز و لاکتات

دهیدروژنژن انزیم هایی هستند که با غلتی بالا در

عضلات اسکلتوی و قلبی تواما یافته می شوند و بدين

لذا لواز و پوزگی این تست است در تشخیص انفارکتوس قلبی

پسیار پایین می باشد در ضمن ظهور این مکارکر های

قدمی بسیار با تأخیر خمی دهد.

نسل جدید مکارکر های قلبی با ویژگی بالاتر و سرعت

پلاعی ظهور مکارکر ها بر مکارکر های قدمی ارجح می

پاشند.
مارکر قلبی تروپونین

مارکر طلایی و اختصاصی قلبی تروپونین از جنس میوپیریل عضلانی قلب می باشد و دارای سه ساب یونیت می باشد.

ساب یونیت تروپومیوزین تروپونین

ساب یونیت مهاری تروپونین

Inhibitory Troponin subunit

 ساب یونیت کلسیم تروپونین

اختلاف سکانس اسید آمینه بین ایزومیر عضلانی تروپونین و ایزومیر قلبی اختصاصیت ویژه ای به مارکر قلبی تروپونین داده است.
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 (99% ویژگی و 93% حساسیت) دارا می‌باشد.

بهترین نمونه برای تروپونین سرم یا پلاسما هپارینه است پلاسما حاوی EDTA می‌گردد همچنین و ایکتریک و لیپمیک بودن سرم در مقادیر بالا تروپونین تداخل جدی حاصل نمی‌کند ولی در مقادیر مرزی نتایج تأثیر گذار است و بهتر است نمونه مجدد گرفته شود.
تفسیر نتایج تروپونین

در بیمار دارای علامت بالینی مقادیر بالا ۱۰۰ در تروپونین نبایست رها گردد و هر ۲ ساعت نمونه مجدد گرفته شود.

نتایج بالای ۰.۸ میکرو گرم در لیتر تشخیص انفارکتوس می‌کند. هاد را قطعی می‌نماید خصوصاً اگر نتایج در فواصل ۴ ساعت یک‌بار با افزایش تدريجی رخ داده باشد و از پایین به بالا رسیده باشد.

مقادیر بین ۱۰ تا ۸۰۰ (حد مرزی) می‌تواند میان آن‌های صدری یا آسیب‌های نکروتیک مینور قلب باشد و حالت سوم مراحل حدواست انفارکتوس قلبی حاد است که چه پس از ۳ ساعت به حد بالای ۰.۸ خواهد رسید.

روماتوئید فاکتور مثبت و آنتی باده هتروفیل و لخته های فیبرین کوچک نتایج مثبت کاذب حد مرزی (۰.۱، تا ۰.۸) تروپونین را حاصل می‌نماید.
مطالعه بهداشت جهانی هرگاه دومیار از معیار زیر مشاهده گردد تشخیص ایفاکتوس میوکارد حاد قطعیت می‌یابد.

1. درد قلبی مداوم
2. نوار قلبی مثبت
3. افزایش مارکر های تریگر قلبی

Tn-I / Myoglobin / CK.MB
LDH / CK / AST

یا انزیم های قلبی

تروپونین نرمال همراه با نوار قلب نرمال اوگر با یک درد قلبی مداوم (بیش از ۶ ساعت) همراه باشد بهتر است نمونه دوم و سوم تروپونین با فواصل ۶ ساعت یکبار گرفته شود و بیمار به طور کامل تحت نظر بوده وراهانگردید.
Cummins and co-workers were the first to develop a radioimmunoassay to measure cTnl that used polyclonal anti-cTnl antibodies. 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 Tnl, 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 cTnl 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 cTnl.
- In practice, two obstacles limit the ease for switching from one cTnl assay to another. First, there is currently no primary reference cTnl 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 2001 by the AACC Subcommittee on Standardization of cTnl to prepare a primary reference material. In 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

کوپپتين جديدترین كاردياک ماركر شناخته شده و در حال بررسی هاي تكميلي است. اندازه گيري همزمان سطح سرمي گليكپپتین پپتيد کوپپتين و تروپيونين بلافاصله پس از وقوع انفارکتوس ميوکارد و منفقي شدن هموزمان اين دو ماركر تكليف بيمار مشكوك به حمله قلبی را با ضريب اطمینان 99% قطعی نموده و نياز به نمونه گيري هاي مكرر در فواصل 6 اى 6 ساعت جهت بررسيا افزايش سطح تروپيونين را منتفي مي سازد.
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).
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:
BRAHMS Aktiengesellschaft
Ingo Buchholzer
Public Relations Manager
Phone: +49 3302 883-637
Fax: +49 3302 883-635
Mobile: +49 172 323 4087
E-mail: i.buchholzer@brahms.de
1- ميوغلوبين بروتينين حامل اكسيشن مي باشد كه به طور توانام در عضلات قلبى و اسكلتال (ماهيچه ای) موجود است و هرگونه ضایعه نکروتیک يا تخريبي اين عضلات منجر به آفزايش اين ماركر در سطح وسبع مي گردد و غلظت ان در جريان خون بالا مي رود. ماركر ميوغلوبين با اينكه ويژگي پانيني دارد و اختصاصي عضله قلب نمي باشد ولی سريعترین ماركر قلبی مي باشد كه پس از انفارکتوس حاد قلبی ظهور مي نماید.

ميوغلوبين 2 دوساعت پس از شروع علائم اوليه انفارکتوس حاد در سطح خون ظاهر مي گردد و پس از 6 تا 8 ساعت به پيك ميرسد و پس از 18 ساعت در ميان ماركر ميوغلوبين سبب شروع به كاهش و حذف شدن مي نماید.

در 24 ساعت دوم پس از علائم انفارکتوس قلبی منفي بوده و غير قابل پيگيري مي باشد.

ميوغلوبين علاوه بر انفارکتوس قلبی دربيمارى های عضلانى (نظرى ديستروفى عضلانى) و تروما و جراحى و ايسکمي عضلانى بالا رفته لذا ارزش تشخيصى ماركر ميوغلوبين در كنار دوماركر دىگر كراتين كيناز قلبى و تروپونين نمود خواهد كرد.

کربنیک CA انهيدراز همراه با ميوغلوبين در بيمار مشکوك به انفارکتوس قلبی بررسي مي شد اگر کربنیک انهيدراز ترمال موجود بود نشانه بروز انفارکتوس ميگيب مييوغلوبين بالا همراه با قلبى بود اگه هر دو ماركر بالا بود نشانه بيمارى غير قلبی و عضلانى مي 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.

**However:**

- 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.
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 (Blood pressure), smoking, exercise, familial background
Specific CHD marker panel

- **Biochemical test**
  - Homocysteine, fibrinogen, APO A₁ (Apolipoprotein A₁), APO E, APO B
  - HS CRP (High sensitive CRP), FBS, TG, ch, HDL, LDL, U.A
- **other**
  - BMI, BP (Blood pressure), smoking, exercise, familial background
# CHD Risk Estimation Report

**CHD Marker**

<table>
<thead>
<tr>
<th>Name</th>
<th>Exercise Level</th>
<th>Weight (Kg)</th>
<th>Age</th>
<th>Birthday</th>
<th>Date of Sampling</th>
<th>Date of Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ali Ahmadi</td>
<td>Low</td>
<td>89</td>
<td>52</td>
<td>1335/06/06</td>
<td>138/06/05</td>
<td>1390/09/22</td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes</td>
<td>Tall (m)</td>
<td>1.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Familial History of CHD</td>
<td>No</td>
<td>BMI (Kg/㎡)</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

**Odds Ratio**

![Odds Ratio Chart]

**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 smoker 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
LDL کلسترول قسمت عمده کلسترول توتال است که منبع عمده آن از VLDL در کبد حاصل می‌گردد.

مقدار مرجع:
کمتر از ۱۳۰ در بالغین و کمتر از ۱۱۰ در کودکان
۱۳۰ تا ۱۶۰ گروه مرزی
۱۶۰ تا ۲۰۰ گروه پر خطر

رابطه مستقیم با بیماری‌های قلبی عروقی و اترواسکلروزیس دارد.

نحوه محاسبه با فرمول فریدوالد:

\[ \text{LDL} = \text{Chol total} - (\text{VLDL} + \text{HDL}) \]

\[ \text{VLDL} = \frac{\text{TG}}{5} \]

فرمول فرید والد برای تری‌گلیسرید های بالا ۴۰۰ فاقد ارزش گزارش و محاسبه می‌باشد.
ApoLipoprotein

ژر پروتئین لیپید پروتئین ها اپو پروتئین نامیده می شود که اصلی ترین انها شامل:
apoA / apoB
و مسئولیت اتصال لیپید پروتئین ها به رستور سطح سلول را دارند
/ LP(a) پلی پپتید اصلی لیپید پروتئین apoA

می باشد که به دو نماد (75%) / apoA-1 (75%) می باشد:
apoA-1

رابطه مستقیم برای تشخیص ریسک اتروواسکلروزیس دارد و حتی تست بهتری نسبت به
HDL باشد
رابطه مستقیم با افزایش
HDL و دارد.
apoB

می باشد که این امر را با تماشای به چسبیدن به رستور
apoB-48 / apoB-100 (75)

می باشد که این امر را با تماشای به چسبیدن به رستور
apoB

Mکانیسم اصلی انتقال LDL مکانیسم اصلی انتقال LDL
در سطح سلول های محيطی تنشان می دهد. کاهش اپوپروتئین( ب 100 ) رابطه مستقیم با
apoB-48

شاخص افزایش رسوب کلسترول در جدار عروق و اتروواسکلروزیس دارد و حتی از
LDL

استانداردتری می باشد.

مسنول انتقال لیپید های داخل روده ای به خون است و در شیلی میکرونها یافته می شود و
apoB-48

و منشا روده ای دارد.

LP(a) لیپید پروتئین کوچک متشکل از از دوزج اپوپروتئینی

شبه پلاسمینز دارد که با رقابت با پلاسمینز لیز لخته ها و میکرو ترومبوز ها را به تأخیر می اندازد و

نهاپتا با مهار تخریب فیبرین در میکروترومبوز ها منجر تشکیل ضایعه اتروواسکلروزیس در دیواره شریان و

پروژ اتئوریسم می گردد.
## Lipoprotein Fractions Composition

<table>
<thead>
<tr>
<th>HDL%</th>
<th>LDL%</th>
<th>VLDL%</th>
<th>Shilomikron%</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>65</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>30</td>
<td>25</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>40</td>
<td>82</td>
<td>81</td>
<td>1</td>
</tr>
<tr>
<td>88</td>
<td>20</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>B</td>
<td>A</td>
<td>A B C D E E</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1:1 A B C E</td>
</tr>
</tbody>
</table>

**Control**

**Triglycerides**

**Phospholipids**

**Triglycerides**

**Proteins**

**Lipoproteins**

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

<table>
<thead>
<tr>
<th>High risk</th>
<th>Moderate risk</th>
<th>low risk</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;220 [5.7]</td>
<td>201-220</td>
<td>&lt;200 [5.5]</td>
<td>20-29</td>
</tr>
</tbody>
</table>
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: 83-151 mg/dl
- **ApoB**
  - Adult/elderly
    - **Male:** 50-125 mg/dl
    - **Female:** 45-120 mg/dl
  - **Child**
    - **Newborn:** 11-31 mg/dl
  - 6 months-3 years: 23-75 mg/dl
  - 5-17 years: **Male:** 47-139 mg/dl / **Female:** 41-132 mg/dl
<table>
<thead>
<tr>
<th>نوع لیپو پروتئین</th>
<th>شکل الکتروفورز</th>
<th>طبقه بندی فردیکسون</th>
</tr>
</thead>
<tbody>
<tr>
<td>chylomicrons</td>
<td>افزایش شیلومیکرون</td>
<td>تیپ 1</td>
</tr>
<tr>
<td>LDL</td>
<td>افزایش بتا لیپوپروتئین</td>
<td>تیپ 2</td>
</tr>
<tr>
<td>VLDL / LDL</td>
<td>افزایش پره بتا لیپوپروتئین</td>
<td>تیپ 2b</td>
</tr>
<tr>
<td>IDL</td>
<td>باند بتا پهن</td>
<td>تیپ 3</td>
</tr>
<tr>
<td>VLDL</td>
<td>افزایش پره بتا لیپوپروتئین</td>
<td>تیپ 4</td>
</tr>
<tr>
<td>VLDL / chylomicrons</td>
<td>افزایش شیلومیکرون و پره بتا</td>
<td>تیپ 5</td>
</tr>
</tbody>
</table>
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
**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.
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 heart attack or stroke.

It may be useful in someone who has a family history of coronary artery disease 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 atherosclerosis (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.
پروتئین دفع کننده سدیم که از پخش ونتریکولار یا بطنی میوکارد ترشح می‌گردد و با تأثیر بر کلیه‌ها منجر به افزایش ترشح سدیم و آب می‌گردد از تست‌های مناسب و جدید در تشخیص و مانیتورینگ نارسائی مزمن قلبی می‌باشد.
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
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.