NEW RISK FACTORS FOR HEART DISEASE

By:
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Several less "popular" risk factors have been identified over the past several years, such as CRP, fibrinogen, apolipoproteins, myoglobin, troponins (I & T) & homocysteine.
1. What are CRP?

- **CRP** is a protein released into the bloodstream any time there is active inflammation in the body. (Inflammation occurs in response to infection, injury, or various conditions such as arthritis.) Evidence is accumulating that atherosclerosis is an inflammatory process.
C-Reactive Protein (CRP) has been demonstrated to be a general indicator of major tissue damage. Hence, it can be used to indicate a stroke or heart attack because major blood vessels leading to the heart or brain are damaged and release large quantities of CRP during these disease states.
Some even think that coronary artery disease may be promoted by infection. The fact that elevated CRP levels are associated with an increased risk of heart attack tends to support the proposed relationship between inflammation and atherosclerosis.
hs-CRP
Also known as: High-sensitivity CRP

- People 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 CRP values at the lower end of the normal range.
The CRP molecule itself is **not** a harmful molecule in the body. The higher level of CRP is simply a reflection of higher than normal inflammation. The measurement of CRP does not reflect where the inflammation is. It may come from cells in the fatty deposits in arterial walls that reflect the process of atherosclerosis. It may come from other tissues.
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 CRP, along with the ratio of total cholesterol to HDL cholesterol.
A healthy lifestyle decreases serum CRP levels, while obesity, physical inactivity, and smoking increase them. The CRP level may be influenced more by lifestyle than by genetics. Asians also have lower CRP levels than Westerners. Through improving health and preventing disease, CRP testing may help lower a nation’s health costs.
The AHA/CDC defined risk groups as follows:

- **Low risk:** less than 1.0 mg/L
- **Average risk:** 1.0 to 3.0 mg/L
- **High risk:** above 3.0 mg/L
Taking nonsteroidal anti-inflammatory drugs (like aspirin, Advil, Motrin, and Naproxin) or statins may reduce CRP levels in blood. Both anti-inflammatory drugs and statins may help to reduce the inflammation, thus reducing CRP.
2. Fibrinogen

- *Fibrinogen* is a blood-clotting factor. Most acute myocardial infarctions (heart attacks) are now known to be due to acute thrombosis, or the sudden formation of a blood clot at the site of an atherosclerotic plaque.
Reduced concentrations of fibrinogen may impair the body's ability to form a stable blood clot. Chronically low levels may be related to decreased production due to an inherited condition such as afibrinogenemia or hypofibrinogenemia or to an acquired condition such as end-stage liver disease or severe malnutrition.
Fibrinogen is usually ordered with other blood clotting tests. It helps to evaluate your body's ability to form a blood clot. Fibrinogen may be ordered as a follow-up to an abnormal Prothrombin Time (PT) or Partial Thromboplastin Time (PTT) and/or an episode of prolonged or unexplained bleeding.
What does the test result mean?

- A standard reference range is not available for this test. Because reference values are dependent on many factors, including patient age, gender, sample population, and test method, numeric test results have different meanings in different labs.
Elevated levels may be seen with:
- Acute infections
- Cancer
- Coronary heart disease, Myocardial infarction
- Stroke
- Inflammatory disorders (like rheumatoid arthritis and glomerulonephritis)
- Trauma
3. Apolipoproteins

Why get tested?

- To determine whether or not you have adequate levels of Apo A-I, especially if you have decreased levels of HDL-C, and to help determine your risk of developing coronary artery disease (CAD).
When to get tested?

When you have

- Hyperlipidemia and/or a family history of CAD or peripheral vascular disease.
- When you are trying to assess your risk of developing heart disease;
- When you are monitoring the effectiveness of lipid treatment and/or lifestyle changes.
Deficiencies in Apo A-I appear to correlate well with an increased risk of developing coronary artery disease (CAD) and peripheral vascular disease.
Measurements of apolipoproteins are internationally standardized, automated, cost-effective and more convenient and precise than those for LDL cholesterol. ApoB may also be preferable to the measurement of non-HDL cholesterol.

Measurement of apolipoproteins (apoB and possibly apoA-I) should be routinely added to the routine lipid profile.
Apolipoprotein B is thought to be a better marker of risk of vascular disease and a better guide to the adequacy of statin treatment than any cholesterol index.
4. Myoglobin

- **Why get tested?**

To determine whether muscle, particularly heart muscle, has been injured; to detect high levels in the **urine** that can cause kidney damage after extensive muscle damage.
When to get tested?

- **Every 2-3 hours** for the first several hours after experiencing **chest pain** that is suspected to be due to a heart attack; when there has been severe traumatic injury to skeletal muscle.
Why get tested?
To determine if you have had a heart attack or injury to heart muscle.

When to get tested?
2-3 times during a 12- to 16-hour period if you are having chest pain or other symptoms that may be due to a heart attack.
Early diagnostic efficiency of cardiac troponin I and Troponin T for acute myocardial infarction.

- The cTn-I was significantly more specific for AMI than was the cTn-T, but not significantly better than CK-MB or myoglobin.

- Myoglobin is the biochemical marker having the highest combination of sensitivity, specificity, and negative predictive value for AMI within 2 hours of ED presentation.
When a patient has a heart attack, levels of troponin can become elevated in the blood within 3 or 4 hours after injury and may remain elevated for 10 to 14 days.
How is it used?

- Troponin I and troponin T tests have begun to replace CK and CK-MB tests because they are more specific for heart injury (versus skeletal muscle injury) and are elevated for a longer period of time.
The troponin test will usually be ordered when a patient first comes into the emergency room and then may be ordered again at 6 and 12 hours.

The troponin test is used to help diagnose a heart attack, to detect and evaluate mild to severe heart injury, and to separate it from chest pain that may be due to other causes.
In patients who **have delayed getting treatment** and have been having heart-related chest pain, discomfort, or other symptoms such as sweating, radiating pain in the arms, shoulders, jaw, neck, nausea, and/or lightheadedness for more than a day, the **troponin test** is the test of choice. This is because it will still be elevated in the blood if the symptoms were/are due to heart damage.
6. Homocysteine

What is Homocysteine?

- Homocysteine is an amino acid in the blood. Epidemiological studies have shown that too much homocysteine in the blood is related to a higher risk of coronary heart disease, stroke and peripheral vascular disease.
Other evidence suggests that homocysteine may have an effect on atherosclerosis by damaging the inner lining of arteries and promoting blood clots.
Plasma homocysteine levels are strongly influenced by diet, as well as by genetic factors. The dietary components with the greatest effects are folic acid and vitamins B6 and B12.

Folic acid and other B vitamins help break down homocysteine in the body.
Several studies have found that higher blood levels of B vitamins are related, at least partly, to lower concentrations of homocysteine.

Other recent evidence shows that low blood levels of folic acid are linked with a higher risk of fatal coronary heart disease and stroke.
Why get tested?
To determine if you are at increased risk of a heart attack or stroke;
To determine if you are folate-deficient or B12-deficient;
To help diagnose a rare inherited disorder called homocystinuria.
How is it used?

- Homocysteine is commonly used as a screen for people at high risk for heart attack or stroke. It may be useful in patients who have a family history of coronary artery disease but no other known risk factors.

- Some recommend homocysteine testing in malnourished patients, such as the elderly (who often absorb less vitamin B12 from their diets).
The diagnosis of AMI established by the World Health Organization (WHO) requires at least two of the following criteria:

1. A history of chest pain
2. Evolutionary changes on the ECG
3. Elevation of serial cardiac enzymes and proteins (cardiac markers)
A cardiac marker is a clinical laboratory test useful in the detection of AMI or minor myocardial injury.

Cardiac markers are most useful when individuals have non-diagnostic ECG tracings.

The protein markers of major diagnostic interest include:

- Enzymes such as CK, CK-MB, LDH, AST
- Non-enzyme proteins such as myoglobin and cardiac troponin T & I
## Cardiac markers and time course after onset of AMI

<table>
<thead>
<tr>
<th>Marker</th>
<th>Abnormal activity detectable (hour)</th>
<th>Peak value of abnormality (hour)</th>
<th>Duration of abnormality (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK</td>
<td>3 to 8</td>
<td>10 to 24</td>
<td>3 to 4</td>
</tr>
<tr>
<td>CK-2 (MB)</td>
<td>3 to 8</td>
<td>10 to 24</td>
<td>2 to 3</td>
</tr>
<tr>
<td>LD (Total) &amp; LD1</td>
<td>8 to 12</td>
<td>72 to 144</td>
<td>8 to 14</td>
</tr>
<tr>
<td>AST</td>
<td>6 to 12</td>
<td>24 to 48</td>
<td>4 to 6</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>1 to 3</td>
<td>6 to 9</td>
<td>1</td>
</tr>
<tr>
<td>Troponin I (cTnI)</td>
<td>3 to 8</td>
<td>24 to 48</td>
<td>3 to 5</td>
</tr>
<tr>
<td>Troponin T</td>
<td>3 to 8</td>
<td>72 to 100</td>
<td>5 to 10</td>
</tr>
</tbody>
</table>
Plasma enzyme changes after myocardial infarction

Myoglobin

Multiples of normal levels

Days since onset of chest pain

CK-MB

CK

LDH
- **Ratio of total cholesterol/HDL-cholesterol**: 
  - 3.5 or less is ideal
  - 4.5 average risk
  - 5.1 or higher potentially dangerous
Men with cholesterol levels over 240 mg/dl have a risk that is 2.2-3.6 of those whose cholesterol levels below 200.

Every drop of one point on cholesterol level the risk of ht.dis. Drops by 2 %

For each 4 mg/dl decline in HDL levels there was a 10 % increase in coronary artery disease (CAD)
Role of oxidized lipoproteins in plaque formation in arterial wall

1. In response to endothelial injury caused at least in part by oxidized LDL, monocytes adhere to endothelial cells, move to the subendothelium (intima), and are transformed into macrophages.

2. Macrophages consume excess modified (oxidized) lipoprotein, becoming foam cells.

3. Foam cells accumulate, releasing growth factors and cytokines that stimulate the migration of smooth muscle cells from the media to the intima. There, they proliferate, produce collagen, and take up lipid, potentially becoming foam cells.