Cardiovascular Health Markers For All Ages

CRP, Lp-PLA2, LDL-P, Apo B, Lp(a)

TheFatNurse R.N.
Before reading please understand that I am not an expert in this field. This comic is to simply pique the interest of cardiovascular markers and heart disease that you may not have heard about before. Therefore, much of the information presented here is super simplified and I recommend additional research for anything that interests you.

The cardiovascular markers selected in this comic were based on their mention in the 2011 National Lipid Association expert panel review, "Clinical Utility of inflammatory markers and advanced lipoprotein testing: Advice from an expert panel of lipid specialists" in the Journal of Clinical Lipidology. Therefore, cardiovascular markers should not be limited to what is in this comic.

If anything in here is of interest, you may find the original journal at www.lipid.org/cg. Additionally, I highly recommend looking up the works of Peter Attia M.D., Thomas Dayspring M.D., Tara Dall M.D., and Ronald Krauss M.D. These individuals have more or less commented or done original research on the biomarkers presented here.

- TheFatNurse R.N.
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***This comic is meant for educational and entertainment purposes only and not clinical advice. Consult with your primary care provider if you have any medical questions***
TheFatNurse (TFN), I've got a question, you mentioned earlier that measuring cholesterol levels might not be accurate for some people...who?

TFN: That's right! the traditional LDL-C is discordant for some people

Eh...Discordant?

TFN: Yeap! For many people having normal LDL-C also means having normal LDL-P. But not always. For certain people, they may have a normal LDL-C while having a high LDL-P. This is discordant

Certain people?

TFN: Yes, there are many reasons of discordance but one factor is insulin resistance and diabetes. LDL-C levels may not reflect LDL-P that accurately for these ppl.

With the rise in diabetes, it is important to understand these concepts.

New Cases of Diagnosed Diabetes Among U.S. Adults Aged 18–79 Years, 1980–2009

Number (in Thousands)


O H MY GAWDZ Look at those rates! We're doomed!

TFN: Whoa uhhh hey...it's okay man! Hug it out, there's hope!

Many healthcare providers are becoming interested in using other biomarkers to predict Cardiovascular (CV) risk, some of which include looking at:

CRP, Lp-PLA2, LDL-P, Apo B, Lp (a)
Eh...some of these things look familiar, but how are they related to CV risk?

TFN: Glad you asked! We'll go over this in the following pages!

Therefore CRP is great for knowing when cellular injury is occurring

CRP: OMG there is inflammation everywherez!!
Okay but from where?

However, CRP by itself is general and may be hard to pinpoint where the inflammation is occurring

CRP: Oh uhh maybe heart? Lungs? Bowels? Dunno!

However, clinicians can use a high-sensitivity CRP test to try an estimate heart disease risk.

Regardless, when CRP sees inflammation it tries to help by complementing our immune system. However, some believe this may inadvertently promote atherogenesis!

TFN: Relax! It is just a theory so far and targeting CRP is not considered a treatment goal!

Now to our next guest: Lp-PLA2 otherwise known as Lipoprotein-associated phospholipase A2

LP-PLA2 is mainly tied with LDL-P but can be found in HDL-P, LP(a) and other lipoproteins as well.

It's produced by cells of the immune system as well as the liver.

Up first is CRP which stands for C-reactive protein. CRP is made in the liver when there is inflammation in the body and detects phosphocoline from injured cells, pathogens and oxidized LDL

Dying Cell: Uh...if I was ok you wouldn't have been made dummy
That's all fine and dandy but how does this relate to heart disease?

TFN: To the right is a picture of an artery with atherosclerotic legions off the heezy. Some studies show an increase activity in LP-PLA2 upregulation when this occurs.

One theory is the highly inflammatory byproducts of LP-PLA2 (lysophosphatidylcholine and oxidized fatty acids) trigger a series of reactions involving cells of the immune system that eventually lead to plaque formation & rupture.

LP-PLA2: Oops my bad

OMG! Inflammation!

Therefore LP-PLA2 is associated with early atherosclerosis!

**OH GOD**

**WHY**

TFN: No worries! There is currently research going on to see if selective inhibition of LP-PLA2 is beneficial.

My GAWD....WE'RE DOOMED

Now our next guest is Apo B. He's very special because of his association with LDL-P. About 90% of Apo B is associated with LDL-P.

In our previous comic we went over what lipoproteins and LDL particles were including a car analogy.
We had mentioned in that comic that there is one Apo-B per LDL-P. Therefore we can indirectly measure LDL-P by looking at the Apo-B! Remember, it's about the cars (LDL-P) not the passengers (LDL-C)!

No matter how big or small the car (LDL-P) it will only have one steering wheel (Apo-B)! Remember, we want less LDL-P!

Remember how we talked about discordance earlier? When we get a normal LDL-C reading we are hoping that it shows risk of heart disease due to concordance with LDL-P. However, for some individuals there is discordance and they have normal LDL-C while having high LDL-P! Which means we may not accurately know their risk!

**Concordance**

LDL-C LDL-P

**Discordance (uh oh)**

LDL-C LDL-P

**Wow, so if we get 10 Apo Bs does that mean we have 10 LDL- Ps?**

TFN: Close but remember those other lipoproteins from the previous comic? VLDL and IDL? They have Apo B in them as well! However, Apo B is more associated with LDL-P since LDL-P is around 9 times more than VLDL-P!

**Oh good! This sounds like excellent news!**

TFN: Well, you might not like our next guest as much...Lp(a) he's quite the troll

Lp(a) is where an Apo A hitchs a ride with Apo B which, as we just covered, is also attached to an LDL-P. Remember our previous comic and the "crashing" analogy of LDL-P into artery walls to trigger heart disease? This is how Lp(a) collects in the artery walls.

Apo B: get off me!

For simplicity, we will refer to Apo A and Lp(a) as the same for rest of comic

Apo B: LDL-P

Lp(a)

Up next: special guest Sir plasminogen!
Before continuing on with Lp(a) we need to know about Sir Plasminogen. This Sir is a connoisseur of fibrin and loves to degrade fibrin whenever he can.

Wait but what does Fibrin do?
TFN: Fibrin has many functions but for our related purposes it is essential for clot formation. However, too much fibrin can lead to thrombogenesis and thus cardiovascular complications!

That sounds scary! So how does Lp(a) come into this?
TFN: Just watch!

Plasminogen: mmm...yes quite a day of fibrin drinking today...so sleepy now. I'll just leave my top hat and specs on the bedz

Lp(A): <yoink!>

Plasminogen: zzz...

Fibrin Winery

Halt! Who goes there?
Lp(a): why it's me, Sir Plasminogen!

My mistake Sir Plasminogen! You just look a little bit different is all! Enter!

Sir Plasminogen: Converts to Plasmin to breakdown fibrin

Lp(a): Resembles Sir plasminogen and thus takes his spot at the fibrin dinner table!

Fibrin Winery

Sorry Sir Plasminogen, I already let one of you in! It's full!

TFN: So you see, Lp(a) competitively inhibits Sir plasminogen from breaking down fibrin by taking his dinner spot! This increases the risk of thrombogenesis and cardiovascular events!

What a douchebag!

TFN: There is more tho!
TFN: What I just told you is only 1 of several theories on how Lp(a) is related to heart disease!

TFN: No need to rage out! Lots of future research questions are being proposed to help understand Lp(a) better! It's okay!

***ACTUALLY...***

TFN: Wow uhh...you do know that rage is a risk factor for heart disease right? Okay I'm gonna move onto our last guy LDL-P...

Why is LDL-P laughing out loud?
TFN: I think he's just happy to know that people are starting to realize how important he is in risk prediction.

TFN: Measuring the LDL-Ps is exactly like what it sounds - we are getting the number of LDL particles which, like using Apo B, may be discordant in certain people compared to LDL-C

Right, because using the LDL-C is old school! Get outta here gramps!
TFN: -Wait now hold on a minute!

Again, it's all about concordance and discordance! As we mentioned before, it's only for certain conditions like when triglycerides are excessively high, or if there is insulin resistance when LDL-C may be discordant with LDL-P!
For most people who don't meet the criteria, LDL-C is concordant with LDP-P! Which means LDL-C still has a role. Now go kiss and makeup with granny!

Wait... I got a question. If measuring LDL-P predicts risk and and Apo-B indirectly measures LDL-P...which test is better?

Apo B vs LDL-P...which is better?

That is primarily determined by clinician preference, cost and access if your clinician decides its necessary

In fact many of the markers discussed today are only necessary depending on how high your clinician feels the risk of heart disease is. Not everyone needs to get the markers discussed today measured! **CHALLENGE CONSIDERED**

Hmm... do I need more than a standard lipid profile for my patient?

Change is coming and more people in healthcare are starting to realize how important other markers are for heart disease outside the standard lipid profile. The five markers in this comic are becoming more known and driving the thirst for more research into heart disease and lipids. Much of the research is breaking down old medical dogmas that people never bothered questioning like "LDL bad HDL good."

As such, if may also be possible that future research will make everything covered in this comic obsolete as well. However, TheFatNurse looks forward to being wrong as much as being right since both options mean taking a step closer to the truth.

-TheFatNurse R.N.
**Glossary**

**Apolipoprotein B** (APOB or ApoB) are the primary apolipoproteins of chylomicrons and low-density lipoproteins (LDL - known commonly by the misnomer "bad cholesterol" when in reference to heart disease), which is responsible for carrying cholesterol to tissues. While it is unclear exactly what functional role APOB plays in LDL, it is the primary apolipoprotein component and is absolutely required for its formation.

**Atherosclerosis** (also known as arteriosclerotic vascular disease or ASVD) is a condition in which an artery wall thickens as a result of the accumulation of fatty materials such as cholesterol. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, caused largely by the accumulation of macrophage white blood cells and promoted by low-density lipoproteins.

**Concordance:** similar with respect to one or more particular characters.

**C-reactive protein** (CRP) is a protein found in the blood, the levels of which rise in response to inflammation (i.e. C-reactive protein is an acute-phase protein). Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex.

**Cytokines** (Greek cyto-, cell; and -kinos, movement) are small cell-signaling protein molecules that are secreted by numerous cells and are a category of signaling molecules used extensively in intercellular communication.

**Discordance:** dissimilar with respect to one or more particular characters—compare concordant.

**Insulin resistance** (IR) is a physiological condition where the natural hormone insulin becomes less effective at lowering blood sugars. The resulting increase in blood glucose may raise levels outside the normal range and cause adverse health effects.

**LDL-C:** low-density-lipoprotein cholesterol (passenger).

**LDL-P:** Low-density lipoprotein particle (Car).

**Lp-PLA_2** is involved in the development of atherosclerosis. In human atherosclerotic lesions, 2 main sources of Lp-PLA_2 can be identified, including that which is brought into the intima bound to LDL (from the circulation), and that which is synthesized de novo by plaque inflammatory cells (macrophages, T cells, mast cells).

It is used as a marker for cardiac disease.
A meta-analysis involving a total of 79,036 participants in 32 prospective studies found that Lp-PLA₂ levels are positively correlated with increased risk of developing coronary heart disease and stroke.

**Lipoprotein(a)** (also called Lp(a)) is a lipoprotein subclass. Genetic studies and numerous epidemiologic studies have identified Lp(a) as a risk factor for atherosclerotic diseases such as coronary heart disease and stroke.

**Macrophages** function in both non-specific defense (innate immunity) as well as help initiate specific defense mechanisms (adaptive immunity) of vertebrate animals. Their role is to phagocytose (engulf and then digest) cellular debris and pathogens, either as stationary or as mobile cells.

**Monocytes** are a type of white blood cell and are part of the innate immune system of vertebrates including all mammals (including humans), birds, reptiles, and fish. Monocytes play multiple roles in immune function.

**Phosphocholine:** one of the binding targets of C-reactive protein (CRP).[3] Thus when a cell is damaged, CRP binds to phosphocholine beginning the recognition and phagocytic immunologic response.

**Plasminogen:** Precursor to Plasmin.

**Plasmin** is an important enzyme (EC 3.4.21.7) present in blood that degrades many blood plasma proteins, most notably, fibrin clots. The degradation of fibrin is termed fibrinolysis.

***Definitions taken from Wikipedia***