Beyond LDL Cholesterol: Alternative Measures of Atherogenic Lipoprotein Burden and Cardiovascular Disease Risk

In recent decades, much emphasis has been placed on the low density lipoprotein cholesterol (LDL-C) level as a predictor of cardiovascular disease (CVD) risk. However, coronary artery disease (CAD) progression is not dependent solely on LDL-C levels and other factors such as atherogenic lipoprotein burden (ALB) may be more important on its own. The Atherogenic Lipoprotein Burden (ALB) is a measure of the total apoB burden and suggests there are additional measures that should be considered in addition to LDL-C. This edition of the Nutrition Research Update highlights two very important advances in the study of cardiovascular disease (CVD). Dr. Kevin Maki and Alyssa Eakley discuss alternative biomarkers for the assessment of CVD risk. While low density lipoprotein cholesterol (LDL-C) levels have recently been recommended by experts for approval by the Federal Drug Administration (FDA), many have been extremely optimistic about the approval of new drugs (PCSK9 inhibitors) in recent months. Note the suffix "mths", which stands for months of therapy.

Will new drugs (PCSK9 inhibitors) reduce CVD risks?

Several new drugs that significantly reduce low density lipoprotein cholesterol (LDL-C) levels have recently been recommended by experts for approval by the Federal Drug Administration (FDA). However, many experts have been extremely optimistic about the approval of new drugs (PCSK9 inhibitors) in recent months. Note the suffix "mths", which stands for months of therapy.

Research We're Reading

Eggs


Cardiometabolic Health


Breakfast

Wijdicks CM, Klein KN, Foresman S, Widaman A, Laugero KM. Breakfast habits among healthy adults in the USA and the American Egg Board. Additional information is available at the ENC website.

Egg Nutrition Center Research Program

The Egg Nutrition Center (ENC) administers an annual research program with over $2 million dollars provided by America’s egg farmers through the Enc Research Program. The ENC Research Program EFG is the largest single source of research funding in the field of cardiology as an effective alternative to statin drugs with important advances in the study of cardiovascular disease (CVD). Dr. Kevin Maki and Alyssa Eakley discuss alternative biomarkers for the assessment of CVD risk. While low density lipoprotein cholesterol (LDL-C) levels have recently been recommended by experts for approval by the Federal Drug Administration (FDA), many have been extremely optimistic about the approval of new drugs (PCSK9 inhibitors) in recent months. Note the suffix "mths", which stands for months of therapy.
In recent decades, much emphasis has been placed on the low density lipoprotein cholesterol (LDL-C) level as the key lipid-related predictor of cardiovascular disease (CVD). However, coronary events can occur even in individuals with LDL-C levels that are considered to be "normal," as it is becoming increasingly clear that alternative measures, in addition to LDL-C, can provide valuable information regarding cardiometabolic risk. The National Lipid Association (NLA) recently released guidelines that include alternative measures of risk in individuals who have elevated levels of LDL-C. These guidelines recommend that clinicians should consider non-high density lipoprotein cholesterol (non-HDL-C; comprising LDL-C, apolipoprotein B (apo B) and low-density lipoprotein particle concentration (LDL-P)), and high-sensitivity C-reactive protein (hs-CRP), when discordance is present. Discordance is defined by median cutpoints; among concordant individuals, LDL-C has similar clinical value to non-HDL-C. However, when discordance is present, it may be helpful to design more effective methods for patient-centered management of dyslipidemia: Part 1 – executive summary.

Mora and colleagues nicely demonstrated that although correlations of LDL-C, non-HDL-C, high-density lipoprotein cholesterol (HDL-C), and LDL-P (HR: 2.68; 95% CI: 2.18-3.30) compared to women with LDL-C below the median value (121 mg/dL), coronary risk was consistently underestimated with non-HDL-C (HR: 3.37; 95% CI: 2.69-4.23), apo B (HR: 2.98; 95% CI: 2.41-3.68), and LDL-P (HR: 3.99; 95% CI: 3.09-5.18) compared to women with LDL-C above the median value. Among concordant individuals, LDL-C has similar clinical value to non-HDL-C. When discordance was present, the LDL-C concentration over- or underestimated cardiovascular disease morbidity and mortality compared to non-HDL-C. Moreover, it has been demonstrated that non-HDL-C is a stronger predictor of atherosclerotic cardiovascular disease morbidity and mortality than LDL-C. Furthermore, it has been shown that non-HDL-C elevation may be easily from more aggressive intervention with lifestyle and pharmacologic therapies. In the meantime, non-HDL-C elevation may be easily from more aggressive intervention with lifestyle and pharmacologic therapies.

A growing body of evidence suggests that LDL-C, the traditional marker of cardiovascular risk, may not be the only factor that helps predict risk. More recent research has shown that other lipoprotein measures may also be helpful. The National Lipid Association (NLA) recently released guidelines that include alternative measures of risk in individuals who have elevated levels of LDL-C. These guidelines recommend that clinicians should consider non-high density lipoprotein cholesterol (non-HDL-C), high-density lipoprotein cholesterol (HDL-C), and apolipoprotein B (apo B) when discordance is present. Discordance is defined by median cutpoints; among concordant individuals, LDL-C has similar clinical value to non-HDL-C. However, when discordance is present, it may be helpful to design more effective methods for patient-centered management of dyslipidemia: Part 1 – executive summary.

The National Lipid Association (NLA) recently released guidelines that include alternative measures of risk in individuals who have elevated levels of LDL-C. These guidelines recommend that clinicians should consider non-high density lipoprotein cholesterol (non-HDL-C), high-density lipoprotein cholesterol (HDL-C), and apolipoprotein B (apo B) when discordance is present. Discordance is defined by median cutpoints; among concordant individuals, LDL-C has similar clinical value to non-HDL-C. However, when discordance is present, it may be helpful to design more effective methods for patient-centered management of dyslipidemia: Part 1 – executive summary. Mora and colleagues nicely demonstrated that although correlations of LDL-C, non-HDL-C, high-density lipoprotein cholesterol (HDL-C), and LDL-P (HR: 2.68; 95% CI: 2.18-3.30) compared to women with LDL-C below the median value (121 mg/dL), coronary risk was consistently underestimated with non-HDL-C (HR: 3.37; 95% CI: 2.69-4.23), apo B (HR: 2.98; 95% CI: 2.41-3.68), and LDL-P (HR: 3.99; 95% CI: 3.09-5.18) compared to women with LDL-C above the median value. Among concordant individuals, LDL-C has similar clinical value to non-HDL-C. When discordance was present, the LDL-C concentration over- or underestimated cardiovascular disease morbidity and mortality compared to non-HDL-C. Moreover, it has been demonstrated that non-HDL-C is a stronger predictor of atherosclerotic cardiovascular disease morbidity and mortality than LDL-C. Furthermore, it has been shown that non-HDL-C elevation may be easily from more aggressive intervention with lifestyle and pharmacologic therapies.
Will new drugs (PCSK9 inhibitors) reduce CV risks?

By: Lynn Cofer-Chase, MSN, CLS, FAHA, FPCNA, FNLA
Clinical Lipid Specialist, National Clinical Educator
Cleveland Heart Lab

Several new drugs that significantly reduce low density lipoprotein cholesterol (LDL-C) levels have recently been recommended by experts for approval by the Federal Drug Administration (FDA). Many have been extremely optimistic about the approval of alirocumab (suggested trade name Praluent) and evolocumab (suggested trade name Repatha) in recent months. Note the suffix “mab,” which stands for monoclonal antibodies. This class of medications is currently being used in the treatment of non-cardiovascular conditions by gastroenterologists, oncologists, and rheumatologists, and is known particularly for being able to very specifically target their effect with little off-target effects. Both of these PCSK9 inhibitors are “fully human” monoclonal antibodies, which bodes well for them.

Pro-protein convertase subtilisin-like Kexin type 9 (PCSK9) inhibitors specifically target PCSK9, the enzyme that attaches to low-density lipoprotein (LDL) receptors and leads to their degradation, stopping them from their return to the surface of the cell to remove more LDL from the blood. Although PCSK9 inhibitors have to be given via subcutaneous injection once every 2 to 4 weeks, they have been shown to lower LDL-C in the 60% range, even on top of statin therapies and/or other LDL lowering agents. (1, 2) Patients with familial hypercholesterolemia, for example, can reduce LDL-C levels from around 300 mg/dL to 100 mg/dL when these drugs are added.

Some forecast that the PCSK9 inhibitors will be as revolutionary to cardiovascular risk reduction therapy as the statins were when first introduced in the late 1980s. Excitement was tremendous when data from ODYESSY Long-Term (n=2341) and OSLER (n=4465) results showed reductions of LDL-C from an average of 120 mg/dL to 48 mg/dL or baseline LDL-C levels >70mg/dL to 48 mg/dL in these trials, respectively. (1, 2) Additionally, data from both trials suggested significant reductions in clinical events (e.g., death, heart attack, fatal or non-fatal strokes, revascularization, etc.). (1, 2) Though neither of these trials was powered to look at hard clinical outcomes, one showed event reduction in a post-hoc analysis and the other in an unblinded extension study. There are several very large trials currently underway that are specifically designed to look at hard cardiovascular outcomes with this new class of drugs, but they are not expected to be completed until 2017.

References:

Next Article >> Research We’re Reading

To learn more about egg nutrition, the latest research and to download patient education materials, please visit the Egg Nutrition Center at www.eggnutritioncenter.org
Research We're Reading

Eggs


- Baum JI, Gray M, Binns A. Breakfasts Higher in Protein and Macronutrient Composition May Be Related to a Reduced Risk of Depression. J Nutr. 2015;145:1131S-1136S.


Cardiometabolic Health


- Kracke AM, Ockert MT, Lucke R, Brünner J, Gerstenblith J, Peter M. High protein and macronutrient composition of breakfasts may be related to a reduced risk of depression. J Nutr. 2015;145:1131S-1136S.


ENC Research Program
The Egg Nutrition Center (ENC) administers an annual research program with over $2 million dollars provided by America’s egg farmers through the USDA and the American Egg Board. Additional information is available at the ENC website.

Look for ENC at these upcoming health professional events:

- **Food and Nutrition Conference & Expo (FNCE)**
  - October 3 - 6, 2015, Nashville, TN
  - Educational Breakfast: Muscle vs. Fat: The Sarcopenic Obesity Puzzle Sponsored by ENC with the Weight Management Dietetic Practice Group on Sunday October 4, 2015 6:45-8:00 am
  - Speaker: Douglas Paddon-Jones, PhD, FACSM. The University of Texas Medical Branch.

- **Osteopathic Medical Conference & Expo (OMED)**
  - October 17 – 21, 2015, Orlando, FL
  - Changing Perspectives on Dietary Fat, Cholesterol, and Health: It’s Taken a Village Monday, October 19, 2015 12:30-1:00 pm
  - Speaker: Tia Rains, PhD, Egg Nutrition Center

- **American Heart Association Scientific Sessions 2015**
  - November 7 – 11, 2015, Orlando, FL

Sign up here to receive notifications about our upcoming grant and fellowship program.

Click here to see some of the latest research we’re reading.

To learn more about egg nutrition, the latest research and to download patient education materials, please visit the Egg Nutrition Center at www.eggnutritioncenter.org.