Help with the Headlines

HEALTH NEWS IN PERSPECTIVE

Topic: "Good" Cholesterol & Heart Health

A study published online Oct. 31, 2016 in the Journal of the American College of Cardiology found that low levels of HDL cholesterol were unlikely to represent a specific risk factor for cardiovascular disease.

It was reported Oct. 31, 2016 by United Press International.

What's the most important thing I should know about this study related to my health?

People and health care professionals should continue to assess "good" HDL-C cholesterol levels and be aware of the association of low HDL-C and cardiovascular disease and cancer risk and of high HDL-C and non-cardiac, non-cancer risk. However, we should be more aware that there may well be other factors that directly cause the increase in death rates and that low/high HDL-C is simply a marker rather than a cause.

A RECENT STUDY FOUND THAT LOW LEVELS OF "GOOD" CHOLESTEROL WERE UNLIKELY TO INCREASE RISK OF HEART DISEASE.

What are "Bad" and "Good" Cholesterol?

Bad cholesterol has traditionally been identified as LDL-C, (low-density lipoprotein cholesterol). Think "L for Lousy." Elevated LDL-C has been shown to have a causal relationship in the development of heart attack and stroke (atherosclerotic cardiovascular disease).

Good cholesterol has traditionally been identified as HDL-C, (high density lipoprotein cholesterol). Think "H for Happy." Low HDL-C levels have been correlated with increased risk for heart attack.

What was this study seeking to determine? Has this been done before?

This study was seeking to reappraise the association of HDL-C with cardiovascular and non-cardiovascular causes of death, using data from a large dataset: the CANHEART (Cardiovascular Health in Ambulatory Care Research Team) dataset, in an observational study.

Although studies observing the association of HDL-C with causes of mortality (both cardiovascular and cancer-related) have been performed before, this study design had some unique aspects. First, the approach of using what researchers call big data is a relatively new concept. In big data studies, data from different health sources are combined to generate a very large population which may be examined observationally. Examination of big data is a new capability given the advent of electronic medical records and data-keeping across wide health systems. Traditionally, observational data analyses have occurred in one confined population, as opposed to a large population such as the one CANHEART created from multiple sources. Secondly, given the large population, for the first time researchers were able to investigate associations of HDL-C across the entire spectrum of HDL-C, both low and high.

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March 2017

How were the data obtained for this study?

The study was performed on the CANHEART (Cardiovascular Health in Ambulatory Care Research Team) dataset, which was created by linking together 17 different individual-level data sources in Canada. The average length of time from an initial data collection and follow up was about five years.

People were included if they were between 40 and 105 years old, living in Ontario, Canada, without previous cardiovascular conditions (no prior heart attack, heart failure, stroke, or coronary revascularization) or severe existing chronic conditions (no prior cancer; dementia; blood vessel disease outside the brain and heart; enlargement of the main blood vessel that supplies the abdomen, pelvis, and legs; or blood clot in the vein), and had an outpatient fasting cholesterol measurement in the prior year.

The average age of the 631,762 participants was 57 years, and 55% were women.

What did the researchers measure? What was the primary outcome they looked for?

The primary outcome was cause-specific mortality (death). Information on cause of death was obtained from the Ontario Vital Statistics Database, which categorizes cause of death using special codes.

What were the results?

The participants were split into groups based on HDL-C levels in milligrams per deciliter (mg/dL <30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90 and >90) to allow for examination of the relationship between HDL-C levels and mortality. Based on previous studies, the HDL-C ranges of 41-50 mg/dL in men and 51-60 mg/dL in women were selected as the references for comparison.

Individuals with lower HDL-C levels were more likely to have low incomes, unhealthy lifestyles, higher triglyceride levels, other cardiac risk factors, and other existing chronic medical conditions. Individuals with lower HDL-C levels were independently associated with higher risk of cardiovascular disease, cancer, and other causes of death compared with individuals in the reference ranges of HDL-C levels. In addition, individuals with higher HDL-C levels (>70 mg/dL in men and >90 mg/dL in women) had increased risk of non-cardiovascular death. The authors concluded that HDL-C is unlikely to represent a cardiovascular-specific risk factor given similarities in its associations with non-cardiovascular outcomes.

Did the study reveal any differences concerning women or other subgroups?

The results were similar to the overall findings. In women, a pattern was observed where individuals with lower HDL-C levels had significantly higher age-standardized risk for all-cause mortality and cause-specific mortality compared with the overall rate. Also similar to the overall findings, women with a very high HDL-C level (>90 mg/dL), had a higher risk of age-adjusted mortality for noncardiac/noncancer mortality.

Does this research fall in line with previous studies? Was anything surprising?

For the past several decades, it has been widely accepted that HDL-C plays an important role in the development of cardiovascular death and disease. Early studies consistently demonstrated an inverse relationship between HDL-C levels and cardiovascular events. However, recent studies have cast doubts about the predictive value of HDL-C level as a modifiable risk factor. Trials of niacin and cholesterol ester transfer protein inhibitors have clearly demonstrated their ability to increase HDL-C substantially. However, none of these trials exhibited improved clinical outcomes compared with a placebo, an inactive substance used to test the effectiveness of a treatment by comparison. Genetic studies using a statistical method to examine the effect of very low HDL-C levels
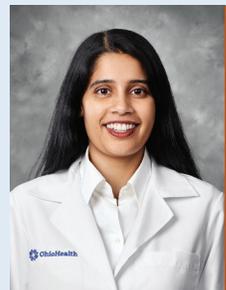
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found no association with premature coronary heart disease. Therefore, the causal role for low HDL-C in the development of cardiovascular disease has been called into question recently, doubts advanced in this new study.

In addition, this study was among the first to describe a relationship between low HDL-C and cancer and among the first to demonstrate a higher occurrence of noncardiac/noncancer mortality among individuals with very high HDL-C levels.

Did the researchers offer an explanation for the results?

The researchers explained their findings by noting low HDL-C is associated with low incomes, unhealthy lifestyle, higher triglyceride levels, other cardiac risk factors, and existing chronic medical conditions. They noted that these other factors may contribute more to outcomes than HDL-C, rendering HDL-C a variable with highly uncertain causal impact.

What were the strengths of this study's design and execution?

A strength of this study was its big data approach, examining the relationship of HDL-C levels and cause-specific mortality in more than 630,000 individuals without previous cardiovascular conditions. Given sheer size, HDL-C levels across their entire spectrum were evaluated.

Were there any shortcomings in the study design and execution?

The study's strength was also its weakness. The big data approach utilized by the researchers is observational only and not a randomized clinical trial. It is difficult to make any conclusions regarding the biological development of disease in this study design. The researchers' conclusions are observations only, not proven facts tested by isolating variables using a control group and randomly assigning subjects to experimental groups manipulating their HDL-C levels.

Unfortunately, it remains very difficult to isolate the effects of HDL-C on cardiovascular risk alone, given its association with complicating factors. This has rendered study of its specific role in cardiovascular disease risk difficult for many years. Randomized control trials specifically addressing HDL-C levels remain the gold standard for evaluation. Statistical genetic studies provide additional strong evidence as well.

Further assessment of HDL-C's effect on cardiovascular disease risk utilizing novel methods of assessment will be necessary to clarify HDL-C's role in cardiovascular disease risk.

What should people and health care professionals do differently in the face of these findings? What are the challenges to addressing this issue?

People and health care professionals should continue to assess HDL-C and be aware of the association of low HDL-C and cardiovascular disease and cancer risk and of high HDL-C and non-cardiac, non-cancer risk. However, we should be more aware that there may well be other factors that directly cause the increase in mortality and that low/high HDL-C is simply a marker rather than a cause.

Given the association with unhealthy lifestyles, high triglycerides, and other existing chronic medical conditions with low HDL-C, it becomes imperative that we as a society focus on adequate diet and exercise habits to prevent the development of chronic disease. If low HDL-C is a marker for a pre-disease state, and if low HDL-C is present in a certain stereotypical pattern of individuals (i.e., with less heart-healthy lifestyles), then we should be striving to prevent those behaviors and promote healthy patterns in all.

The challenges to the promotion of healthy behavior are staggering, related to our society's current habits of physical inactivity and poor intake of fruits and vegetables. The association of low income and low HDL-C also implies that individuals of low socioeconomic status face unique barriers to developing good habits for preventing heart disease.

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