Lipoprotein Biomarkers and Risk of Cardiovascular Disease: A Laboratory Medicine Best Practices (LMBP) Systematic Review

Article:
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Guest:
Dr. Paramjit Sandhu of the Laboratory Research and Evaluation Branch, Division of Laboratory Systems of the Centers for Disease Control and Prevention in Atlanta, Georgia.

Randye Kaye: Hello and welcome to this edition of "JALM Talk" from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

It is well-known that cardiovascular disease, or CVD, is the leading cause of death in the United States, and that 50% of the risk of developing CVD is associated with abnormalities in lipid levels, such as total cholesterol, low density lipoprotein cholesterol, and triglycerides, as well as other non-lipid risk factors such as high blood pressure, smoking, diabetes, age, gender, diet, and obesity.

Recently, there has been a growing interest in the investigation of other lipid-related biomarkers including apolipoprotein B, apolipoprotein A1, the apoB-apoA1 ratio, and non-high density lipoprotein cholesterol and how they pertain to CVD risk. A review article entitled "Lipoprotein Biomarkers and Risk of Cardiovascular Disease: A Laboratory Medicine Best Practices (LMBP) Systematic Review" published in the September 2016 issue of JALM is based upon a literature review that set out to determine the effectiveness of these other lipid-related biomarkers in improving a CVD risk prediction model.

This model already includes traditional lipid levels and the other risk factors mentioned above. The first author of this article is Dr. Paramjit Sandhu from the Laboratory Research and Evaluation Branch, Division of Laboratory Systems of the Centers for Disease Control and Prevention in Atlanta, Georgia. Dr. Sandhu is our guest for today's podcast. Dr. Sandhu, this study was done with the Laboratory Medicine Best Practices (LMBP) methodology. Can you briefly describe what this is?

Dr. Sandhu: Sure. Thank you very much, Randye. Laboratory Medicine Best Practices, or LMBP, is a CDC program that evaluates the effectiveness of laboratory practices to improve the health and safety of the patients, based on an evidence-

based methodology called LMBP A6 Strategy. So as the name states, the LMBP A6 method includes six A's representing six steps to conduct systematic review. So I will describe each step very briefly starting with step A1 which is Ask. This involves the conceptualization and development of potential research questions that need to be addressed in a systematic review.

Step two is Acquire, which means search for the evidence in existing literature; recommendations for best laboratory practice are based on the findings from the total evidence. The next step is A3 which is Appraise. That includes the screening and selection of qualifying studies from the total retrieved evidence. Each study is graded according to the standardized quality scoring criteria. Only the studies that fit the inclusion criteria are included in the total evidence.

And here I would also like to clarify that we include both published and unpublished evidence to base best laboratory practice recommendations. Step four stands for Analyze, where the information is abstracted from each qualifying study and other qualifying sources. It's summarized to make final conclusions and to develop recommendations for the best laboratory practices.

As far as the steps A5 and A6, although these steps do not contribute to the development of recommendations, but as they stand for Apply and Assess, step five, which is Apply, involves the dissemination and implementation of the recommendations. And finally, step A6, which is Assess, involves the assessment of the recommendations in the field.

So in addition generally, for conducting systematic reviews, the topics are vetted to the oversight by an independent LMBP work group committee and also, an expert panel is formed to help guide the reviews. The foundation of LMBP reviews is a formulation of questions and for this study, the research question was "What laboratory practices are effective to improve the cardiovascular disease risk prediction among the population at risk for developing cardiovascular events?"

Randye Kaye: All right. Thank you. That makes a lot of sense. The six "A questions," kind of lines it up. Second question here, why was the decision made to investigate the utility of non-traditional lipid biomarkers in identification and prevention of CVD risk factors?

Dr. Sandhu: Cardiovascular disease, or the CVD, remains the leading cause for morbidity and mortality in the United States. For the early identification and the timely treatment of the risk factors that can lead to CVD events are much needed, in

order to accelerate disease prevention and also the related morbidity improvement. Although conventional risk prediction algorithms and guidelines are made available on presence of major CVD risk factors identified in disease population, still, there is a growing interest to investigate whether non-tradition lipid biomarkers such as apoB, apoA1, apoB and apoA1 ratio, non-HDL cholesterol, could add incremental values to the existing conventional algorithms in order to improve CVD risk prediction.

This can be best examined by combining them to a model with traditional risk factors to predict the chances of developing long-term CVD-related events among the populations at risk.

Randye Kaye: So, what was the objective of your study?

Dr. Sandhu: Well the main objective of our study was to investigate the incremental utility of non-traditional lipid biomarkers in improving the CVD risk prediction among the populations at risk when they're added to the conventional model of traditional risk factors. So in this study, we evaluated the effectiveness of three non-traditional lipid biomarkers which include apolipoprotein B, apoA1, and non-HDL cholesterol for improved long-term risk prediction of CVD events such as ischemic heart disease, congestive heart failure, angina, myocardial infarction and associated mortality.

Randye Kaye: So based on the findings of this study, what conclusions were made?

Dr. Sandhu: The findings of the study showed that the non-traditional biomarkers apoB and the ratio of apoB and apoA1, when they were added to the traditional diagnostic markers, they resulted in significant improvement in long-term CVD assessment among the populations at risk.

Randye Kaye: It sounds very important. What would you say is the bottom line here? Should physicians be using these non-traditional biomarkers as diagnostic markers along with those traditional lipid profiles for everyone for CVD risk prediction?

Dr. Sandhu: As I mentioned earlier, our study was focused on the incremental utility or added value of these non-traditional markers only among the populations at risk. These are populations with high blood pressure, diabetes, family history of premature heart disease, and also individuals who smoke cigarettes, and the individuals who are obese or physically inactive, and among the male populations of 35 and females over 45 years of age. To answer your question, no, the findings of this review on incremental utility of non-traditional biomarkers as diagnostic

biomarkers for CVD risk prediction are not applicable for everyone.

Randye Kaye: Just mostly for those at risk, is that correct?

Dr. Sandhu: Yes, absolutely.

Randye Kaye: Okay. Thank you. Now, if anybody is interested to find out more details about these methods, where can they go?

Dr. Sandhu: If anybody is interested to find more details about the LMBP A6 methods that were used to develop this recommendations, please visit the CDC website, https://wwwn.cdc.gov/futurelabmedicine.

Randye Kaye: All right. Thank you so much for being our guest today.

Dr. Sandhu: Thank you so much for having me.

Randye Kaye: That was Dr. Paramjit Sandhu from the Centers for Disease Control and Prevention in Atlanta talking about the JALM article "Lipoprotein Biomarkers and Risk of Cardiovascular Disease: A Laboratory Medicine Best Practices Systematic Review" for this podcast. Thanks for tuning in for "JALM Talk." See you next time and don't forget to submit something for us to talk about.