Clinical Chemistry

Imputation of Baseline LDL Cholesterol Concentration in Patients with Familial Hypercholesterolemia on Statins or Ezetimibe

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Guest: Dr. Isabelle Ruel is Clinical Biochemist at the Research Institute of the McGill University Health Center, Royal Victoria Hospital in Montreal Quebec and is the National Coordinator of the Canadian Registry on Familial Hypercholesterolemia.

Bob Barrett: This is a podcast from *Clinical Chemistry,* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

Familial hypercholesterolemia is a frequent genetic disorder encountered in clinical practice and is associated with high levels of serum LDL cholesterol known as the "bad cholesterol." A diagnosis of familial hypercholesterolemia has important clinical implications with respect to risk of cardiovascular disease and a requirement for intensive pharmacological therapy. Often, the baseline LDL cholesterol before treatment is not available because the patient has initiated and continues on lipid lowering therapy, especially statins. Furthermore, the original baseline LDL cholesterol may predate the current status by many years and cannot be easily retrieved.

The February 2018 issue of *Clinical Chemistry* published a paper describing a method to obtain an imputed, or estimated, baseline LDL cholesterol concentration in these patients who are already taking cholesterol lowering drugs. Both a computer program and a smartphone app are available from links in the paper. We are pleased to have the lead author of that paper as a guest on this podcast. Isabelle Ruel is a Clinical Biochemist at the Research Institute of the McGill University Health Center Royal Victoria Hospital in Montreal, Quebec, and is currently the national coordinator of the Canadian Registry on Familial Hypercholesterolemia.

Doctor, how is the diagnosis of familial hypercholesterolemia usually made?

Dr. Isabelle Ruel: A patient with familial hypercholesterolemia will be diagnosed first through clinical criteria and DNA testing can be done after to confirm the presence of a mutation known to cause FH. The concentration of baseline LDL cholesterol or untreated cholesterol is essential for a clinical diagnosis of FH, but it is often not available because the patient will be screened while already on a lipid-lowering medication. So

this is why the study was done. When we realized that many patients who have high cholesterol were already on treatment with a statin or Ezetimibe, we wanted to know what was their baseline LDL cholesterol before the treatment according to the medication and the dose or the intensity of the of the treatment.

Bob Barrett: Okay, so what did you do to go back to the baseline cholesterol concentrations of these patients, and well, what did you find out?

Dr. Isabelle Ruel: We based ourselves on published literature to find the effect of every statin and the drug Ezetimibe in various doses with respect to the lowering of LDL cholesterol. We examined more than a thousand patients with the FH from whom we had a known baseline LDL cholesterol as well as a value while on the lipid lowering therapy and we found that our estimated baseline LDL cholesterol, what we call the imputed LDL cholesterol, was not different from the patient's true baseline.

Bob Barrett: Could you please tell our listeners how this will be useful to physicians?

Dr. Isabelle Ruel: This should enable physicians who have a patient on statin therapy with or without Ezetimibe to determine what was the baseline, so in other words, what was the LDL cholesterol before the treatment? And this will be useful to determine whether the patient has a high likelihood of having the genetic lipoprotein disorder of familial hypercholesterolemia. Once a patient is diagnosed with FH, CAT scan screening which is the screening of all first degree relatives of the patient is usually done to efficiently identify additional affected individuals and make sure they receive proper healthcare.

Bob Barrett: How can physicians have a quick access to your method of estimating the baseline LDL cholesterol?

Dr. Isabelle Ruel: We have already included the numbers from the imputed LDL cholesterol algorithm in an app called the CardioRisk Calculator where physicians using a drop-down menu can use the patient's information such as the on-treatment LDL cholesterol and the medication used to determine the probability of the patients who have familial hypercholesterolemia. This app is available at circl.ubc.ca.

Bob Barrett: Well, thanks so much doctor. Finally, is there anything else in the field that our listeners should know about?

Dr. Isabelle Ruel: We are trying to raise awareness both in healthcare providers and in the general public on the high prevalence of familial hypercholesterolemia and the fact that once

identified early in childhood or in early adulthood, life expectancy will be a completely normalized with appropriate treatment.

Bob Barrett: Dr. Isabelle Ruel is Clinical Biochemist at the Research Institute of the McGill University Health Center, Royal Victoria Hospital in Montreal Quebec and is the National Coordinator of the Canadian Registry on Familial Hypercholesterolemia. She has been our guest in this podcast looking at calculation of baseline LDL cholesterol concentrations. I'm Bob Barrett. Thanks for listening.