Interpreting Cardiac Troponin Results from High-Sensitivity Assays in Chronic Kidney Disease without Acute Coronary Syndrome

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett. Chronic kidney disease has recently come to the forefront of public health concerns. Although chronic kidney disease is associated with an increased risk of cardiovascular disease, interpretation of cardiac biomarkers, particularly cardiac troponin in the setting of kidney disease, has been controversial.

In the September 2012 issue of *Clinical Chemistry*, Dr. Christopher deFilippi, Associate Professor of Medicine with the Division of Cardiology, University of Maryland School of Medicine, and his colleagues in Baltimore and Boston evaluated new cardiac troponin assays in patients with renal disease in an ethnically and medically diverse population. Dr. deFilippi is our guest in this podcast.

Dr., there have been a lot of prior investigations into interactions between kidney disease and cardiac troponin tests, so what's new here?

Dr. Christopher deFilippi: Well, this study that's being published in *Clinical Chemistry* that myself and my colleagues performed evaluates two new highly sensitive cardiac troponin T and I assays. So these assays, particularly in the United States, are now becoming the de facto standard. And what's important about them compared to the conventional assays that we still use here in the United States is they have a low-end sensitivity that is often about ten to sometimes a hundredfold higher than the assays currently in clinical use.

So this recent possibility of more and earlier detection of patients with myocardial infarction, which is the reason that they were designed, and however, it's more critical to understand the influences of other non-acute coronary syndrome or myocardial infarction conditions that could result in elevated levels.

Bob Barrett: Okay. Well, let's talk about your article. What exactly did you study in this presentation?

Dr. Christopher deFilippi: Well, we did a cross-sectional analysis of 140 patients who had chronic kidney disease, who are not on dialysis, who are essentially asymptomatic from a cardiovascular standpoint, who presented to outpatient clinics at the Mass General Hospital or the University of Maryland Medical Center or the Baltimore VA Medical Center, for routine follow up of their kidney disease. And what we did is we did

several measures of cardiovascular disease, and this included CT scans for coronary calcium and it included echocardiography for evaluation of left ventricular function and left ventricular mass and hypertrophy.

We also made several different measures of renal function by using the marker cystatin C to calculate the estimated glomerular filtration rate, as well as calculating the estimated glomerular filtration rate using a creatinine based formula and we measured urine albumin and creatinine to get the urine albumin/creatinine ratio. We then correlated these findings with the presence and severity with cardiac and renal abnormalities, with the levels of the highly sensitive troponin I and T, and we also correlated these cardiac and renal findings with cardiac troponin I and T as measured by conventional assays.

Lastly, we did an exploratory analysis where we followed these patients for all-cause mortality over a period of two to three years to determine whether elevated levels is determined by the highly sensitive I and T assays correlated with a higher risk of cardiovascular death.

Bob Barrett: Okay. Well, let's get to some results. What were your main findings?

Dr. Christopher deFilippi: Well, here I am going to outline four main findings. We found importantly that concentration of both cardiac troponin I and T as measured with these highly sensitive assays were above the 99th percentile, which is a typical cutoff as determined in a normal young healthier population in the majority of patients when using the highly sensitive troponin T assay and a large minority of patients when using the highly sensitive troponin I assay. So, importantly, one can anticipate when using a highly sensitive troponin assay of either T or I that there will frequently be elevated values in these asymptomatic patients with chronic kidney disease. To put this in context, a much smaller proportion, to the tune of about 12% or 13% using the conventional troponin T assay and on the order of several percent using the conventional troponin I assay, had elevated values as above the 99th percentile. Again, that’s using the conventional assay.

Now, number two, both highly sensitive troponin assays were significantly associated with multiple cardiac and renal abnormalities. This was less so once you adjusted for typical clinical confounders.

Once you factored in a patient's age, troponin concentrations were no longer independently associated with the extent of coronary calcium, but they did remain highly associated with the extent of left ventricular hypertrophy.

And thirdly, interesting, even though there was a discordance between the tests, for example, you could have an elevation as measured by the highly sensitive troponin T above the 99th percentile, but the highly sensitive troponin I was below its 99th percentile value, these patients with discordance values frequently had evidence of cardiac pathology and much more so than individuals who had low values by both tests.

And lastly, when values of either troponin test were measured as high by the highly sensitive assay, this identified individuals at increased risk of death over the next several years.

Bob Barrett: So Dr., based on your findings can you say that the cardiac troponin are influenced by cardiac disease, renal disease, or both?

Dr. Christopher deFilippi: Well, this is difficult to determine on the basis of this study alone. So this is in large part a cross-sectional analysis, so we can only look for associations between the concentrations of the cardiac troponins and findings of cardiac pathology, whether it's coronary calcium, or increases in left ventricular mass, or evidence of renal dysfunction, whether it's measured by estimated glomerular filtration rate or albumin/creatinine ratio.

We found that both tests were in fact associated with left ventricular mass and renal function even after adjusting for clinical risk factors. These would include the general demographic risk factors, such as age and gender and race, and then measures of cardiovascular risk factors, such as the presence of diabetes, the presence of hypertension, or known coronary disease.

But since we believed that the troponin proteins that are measured by these assays are released only from the heart, even in patients with renal disease, the influence of renal disease is present for both troponin T and I, though it appears that T may be somewhat more influenced by the presence of renal disease than troponin I when utilizing these highly sensitive assays.

We can't determine from this study if the influence of renal disease on the concentrations is the result of a decrease in clearance of the troponin proteins or an increased production by mechanisms of cardiac injury, that can't be detected by the cardiac imaging we use.

Bob Barrett: Well, Dr., finally, what's the take home message for clinical chemists who get calls from clinicians about how to interpret these tests in their patients who have renal disease, but are not on dialysis?

Dr. Christopher deFilippi: So to us the reason to do this study, and my authors and I are a combination of clinical cardiologists, clinical nephrologists, and clinical chemists, we think there are several take home messages.

When using these highly sensitive assays, irrespective of whether you are going to measure cardiac troponin I or T, elevated concentrations are going to be common in patients with chronic kidney disease, not on dialysis, in the absence of any acute coronary syndrome. This is in contrast to the contemporary assays that are now used for both I and T in the United States.

Second, concentrations of both assays are associated with cardiac pathology, but in this chronic setting this appears to be more of a myocardial pathology, i.e., left ventricular hypertrophy and not so much coronary disease, at least as measured by coronary calcium.

And lastly, of course acute coronary syndromes are common in patients with chronic kidney disease, and one should refer to or refer clinicians to the recently revised definition, now the third definition of myocardial infarction, to confirm the presence or absence of other objective findings consistent with the myocardial infarction, such as symptoms or electrocardiographic changes, along with an elevated troponin value. And of course one should, as one is already doing, be careful in the interpretation of the troponin values and look for rise and fall of these values over a period of at least several hours.

Bob Barrett: Dr. Christopher deFilippi is from the Division of Cardiology, University of Maryland School of Medicine in Baltimore. He has been our guest in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening!