Clinical Chemistry

Absolute and Relative Kinetic Changes of High-Sensitivity Cardiac Troponin T in Acute Coronary Syndrome and in Patients with Increased Troponin in the Absence of Acute Coronary Syndrome

Bob Barrett: This is the podcast from *'Clinical Chemistry'.* I am Bob Barrett.

Several major associations including the joint European Society of Cardiology, the American College of Cardiology, the American Heart Association, and the World Heart Federation recommend that a diagnosis of acute myocardial infarction be made utilizing changes in serum concentrations of cardiac troponin in conjunction with other conditions; determining whether these changes reveal a chronic condition or an acute case of myocardial infarction continues to be a challenge for clinicians.

In a paper published in the January 2012 issue of *'Clinical Chemistry'*, Dr. Evangelos Giannitsis, and a team of researchers from the University of Heidelberg evaluated the kinetics of high-sensitivity cardiac troponin T in patients with acute coronary syndrome, and patients with troponin increases not due to acute coronary syndrome to determine if the troponin increases are related to acute myocardial infarction or non-ST elevated myocardial infarction.

Dr. Giannitsis is our guest in this podcast. Doctor, how does the use of more sensitive or highly sensitive cardiac troponin assays influence the interpretation of cardiac troponin results?

Dr. Evangelos Giannitsis: Yes, on the one hand, we will have more patients with two positive troponin elevations, and in the context of an acute coronary syndrome, there will be more diagnosis of the non-ST segment elevation infarctions at the cost of a smaller number of patients with an unstable angina.

On the other hand, we will also detect more patients who do not have an acute coronary syndrome, where the troponin elevation is due to the underlying cardiac pathology, and this might allow also the picture of sub-clinical disease at an earlier stage. This means for example patients with earlier stages of pulmonary artery hypertension or earlier asymptomatic stages of heart failure or earlier stages of heart valve disease, probably also patients with clinical myocarditis and so forth.

Also, it will allow detection of not only acute settings of cardiovascular disease, but also more chronic cardiovascular disease. This is what we have to expect from the use of more sensitive or highly sensitive troponin assays.

© 2012 American Association for Clinical Chemistry

Bob Barrett: Why do we need a rise or fall of cardiac troponin to diagnose acute myocardial infarction?

Dr. Evangelos Giannitsis: Rise and/or fall is a part of the universal infarct definition, in order to indicate the presence of an acute, rather than a chronic troponin elevation. So by this mean, we are able to differentiate between the two main reasons for troponin elevation. But, it's not specific enough to discriminate between let's say an acute infarct or an acute pulmonary embolism.

So we need further information for making a specific diagnosis and let's say we need further information that is done by a rise and/or fall, or by the clinical context to reestablish clinical specificity that we have lost by improving the analytical sensitivity of these high-sensitive troponin assays.

Bob Barrett: How is rise and/or fall of cardiac troponin defined?

Dr. Evangelos Giannitsis: This is really a dilemma currently. So far, the infarct definition proposed a 20% rise and/or fall because this was derived from an earlier recommendation that say this is the three-fold standard deviation of the analytical imprecision of currently sensitive troponin assays. This is a little bit complicated. So this is just a mathematical definition. In clinical settings, other percent changes have been proposed and tested in smaller cohorts, and this percent changes range from 30% to over 250%.

And what is common with all these proposed data changes is the higher the percent change, the higher the clinical specificity for the diagnosis of non-ST segment elevation infarction. But, specificity is increased with loss of sensitivity.

Bob Barrett: Do serial changes allow a better rule-in of acute myocardial infarction?

(00:04:58)

Dr. Evangelos Giannitsis: The serial changes are one of the most important tools we have nowadays to make a diagnosis of an acute infarction as compared to chronic changes, and probably also some important differential diagnosis.

So in the early stage of an infarct, we can anticipate a very rapid increase of the concentrations. So during the first three or six hours or even earlier, you see a substantial rise and/or fall of troponin concentration, and this is able to distinguish an acute

© 2012 American Association for Clinical Chemistry

infarct from another acute setting where this steep rise and/or fall is not seen so commonly.

Bob Barrett: Well, which role does magnitude of baseline high-sensitivity cardiac troponin T level on performance of serial changes play?

Dr. Evangelos Giannitsis: Yeah, this is very important for the performance. At concentrations below the 99th percentile value, this means at very low baseline concentrations, the absolute concentration changes seem to outperform the relative concentration changes.

In the baseline troponin concentration between the 99th percentile and the old WHO definition of infarct for troponin T, this is 100 nanogram per liter, the absolute and relative concentration changes are comparable. There is no statistical difference which serial, which kinetic change criterion you apply. And above 100 nanogram per liter, it means it's the high baseline concentrations. There is again superiority of absolute concentration changes against relative concentration changes.

Bob Barrett: Is there a different timeframe for rule-in or rule-out of myocardial infarction?

Dr. Evangelos Giannitsis: In my opinion, there's clearly a different timeframe. With the use of high-sensitive troponin assays, the current European Society of Cardiology recommendations are to repeat the troponin measurement at three hours for most patients because data have shown that by three hours, 100% of all patients can be ruled out using the 99th percentile value.

However, if a baseline value of troponin is already elevated in presentation, then rule-out is not possible. So our task is now rule-in is diagnosis of myocardial infarction and differentiation of infarction against non-infarct related myocardial damage. So we have the dilemma of rule-in, and rule-in is not possible within three hours.

According to our data, about 25% of all patients with an acute MI that do not fulfill the diagnostic criteria of non-ST segment elevation infarction within the initial six hours. So you need a longer timeframe for rule-in than for rule-out.

Bob Barrett: Doctor, what's your explanation for the superiority of absolute delta changes compared to relative delta changes in the cohort studied?

© 2012 American Association for Clinical Chemistry

Dr. Evangelos Giannitsis: This is a relatively difficult question. To my opinion, the absolute changes give a better estimate of true infarct size, particularly among those patients who present with low baseline troponin concentrations or with very high baseline concentrations. The absolute delta changes are less dependant on time from onset of symptoms to presentation, particularly that's helpful at very low concentrations and very high concentrations.

Bob Barrett: Are there differences regarding performance of serial changes in patients with suspected acute coronary syndrome or unselected patients presenting with equivocal symptoms?

Dr. Evangelos Giannitsis: Yes, based on our data, performance of the delta criteria is by difference, and depends on the target population. So if you have a very selected acute coronary syndrome population, the delta change criteria are different than in mixed cohort that is enriched by patients with acute, or chronic cardiac comorbidities, or high percentage of renal failure, where you can expect troponin elevation in the absence of an acute coronary syndrome.

(00:09:52)

The good news is that the absolute concentration changes are much better, are much useful for the identification of an acute infarction, in such a setting of a mixed population than the relative delta changes.

We have to acknowledge that the different troponin assays that they are commercially available, particularly the troponin I assays, they may have different release kinetics than the troponin T. And the good news again is that our study results and the study results by Reichlin that they are very similar with respect to absolute concentration changes.

But nevertheless, it appears that those new metrics needs to be established for all individual commercially available troponin assays and on all instruments.

Bob Barrett: What are the implications concerning rule-out?

Dr. Evangelos Giannitsis: So rule-out is very straightforward. You can use either the absolute concentration of troponin, that should then be applied repeatedly on presentation, and after three or six hours, so this is very easy; and

© 2012 American Association for Clinical Chemistry

serial changes do not add much diagnostic information for that rule-out, except for the peak troponin concentrations that are measured within the initial six hours. This criterion performs as effectively as absolute concentration changes in that setting.

Bob Barrett: Well, finally doctor, will serial changes, particularly the absolute concentration change criterion enter clinical routine?

Dr. Evangelos Giannitsis: Yeah, this is of course also very difficult, because we don't have too many data. My personal opinion is that I believe they will enter clinical routine, and several studies, new studies now have indicated evidence that these absolute concentration changes might outperform relative changes. However, we need to further validate these very novel study findings.

Bob Barrett: Dr. Evangelos Giannitsis is a professor at the University of Heidelberg in Heidelberg, Germany. He has been our guest in this podcast from '*Clinical Chemistry*'.

I am Bob Barrett. Thanks for listening!

Total Duration: 12 Minutes

© 2012 American Association for Clinical Chemistry