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Biomarkers for Acute Kidney Injury: Where Are We Today? Where Should We Go?

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Guest:
Dr. John Lieske is a Professor of Medicine and Director of the Renal Function Laboratory in the Department of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota.

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

Acute kidney injury is an important health problem. Patients who develop acute kidney injury have increased in-hospital mortality, and if they do survive, they still suffer long-term increased morbidity and mortality. For that reason there has been great interest in the development of biomarkers that could identify kidney injury in its earliest stages, at a time when interventions might be more successful.

The February 2014 issue of Clinical Chemistry featured a question and answer article on biomarkers for acute kidney injury. The moderator of that expert panel was Dr. John Lieske, a Professor of Medicine and Director of the Renal Function Laboratory in the Department of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota. Dr. Lieske is our guest in this podcast.

Doctor, what exactly is acute kidney injury and how does it differ from chronic kidney disease that we have read so much about lately?

Dr. John Lieske: Acute kidney injury is sort of a consensus term and it really describes abrupt loss of kidney function and this results in retention of things like urea and creatinine and other waste products and also the acute ability not to regulate your blood volume and electrolyte composition.

Typically, acute kidney injury is something that happens in hospitalized patients that's often associated with other illnesses. Chronic kidney disease is by definition something that lasts longer, and I think it has to be more than three months in duration. Oftentimes it's much longer in onset. So it's something that develops over many years in a given person and sort of slowly gets worse over time.

Bob Barrett: Well, who is at risk of acute kidney injury and how important a health problem is it?

Dr. John Lieske: Typically, it's something that occurs amongst hospitalized patients, so often causes include things like acute tubular necrosis. This is something where the tubular cells in the kidney actually die. So oftentimes this can be due to decreased blood flow to the kidney, so there is ischemic damage.

There can be specific toxins that damage the kidneys, some antibiotics can cause this. And it's often something that occurs with severe infection, so sepsis. So that's often a part of the picture and often an important cause of decreased renal blood flow.

Less common things might be urinary obstruction. So people that have say, prostate problems or other issues with bladder drainage, might get acute kidney injury, or there can be specific kidney diseases; glomerulonephritis, some drug reactions like allergic reactions, like interstitial nephritis; but all of these kind of fall under the general term of acute kidney injury.

And quite often people will have more than one of these going on. So when we see somebody in the hospital with this they will have, for example, exposure to a drug, which we know can cause some damage and then they will also have a bad infection at the same time.

People that are older, as well as people that have other preexisting co-morbidities are more susceptible. A younger healthy person might get the same kind of exposures, but not develop acute kidney injury as someone who is older or someone that has already has some chronic kidney disease. Diabetes is often an important preexisting risk factor as well.

Bob Barrett: Well, currently how are cases of acute kidney injury diagnosed?

Dr. John Lieske: The traditional way to diagnose it is really -- there's two things that go into it. One is a drop in your urine output, and then the second is a rise in something that's a marker of filtration. The thing that we have used traditionally has been serum creatinine.

In the last couple of years this has been more formalized. There is actually a Acute Kidney Injury Network and they have developed a staging system for this called the AKIN Staging System, and you can have a stage one or two or three acute kidney injury, and it's defined by how much your creatinine goes up, and then how much your urine flow has decreased from baseline, and then also how long both of those things have been going on.

So obviously stage one, it tends to be more mild and more potentially reversible, and stage three would be a more severe and longer lasting form.

Previously there was another similar scoring system called the RIFLE criterion, which was conceptually the same two parameters and stages. Between both of these, this is really -- I think it has been a big step forward, so that now there are these actual formalized definitions on what is acute kidney injury, what stage you are, and then this has allowed for more standardized studies, both for describing acute kidney injury and then also for identifying patients for studies so that they can be standardized between different centers.

Bob Barrett: What role do biomarkers play in the diagnosis of acute kidney injury?

Dr. John Lieske: I think that the areas where people are looking for biomarkers to make a difference are three different things: one would be for early diagnosis, one would be for identifying prognosis once it is diagnosed, how likely is it to get worse or get better quickly, and then for predicting recovery from acute kidney injury.

Of these I would say there has been great interest in developing one that could identify acute kidney injury at its earliest stage.

One of the issues with creatinine, it does go up when you develop acute kidney injury, but there can be a lag phase of as much as one or two days between the injury before your blood creatinine levels will start to go up. And this has really been thought to be a reason why a lot of interventions have not really worked very well. That in animal models there are certain growth factors and other interventions that have worked pretty well in experimental models, but when used in clinical trials really haven't, and the thought is that if you had a biomarker that went up quicker than creatinine, so you knew very quickly when an injury occurred and we did these sort of interventions, that would be a big breakthrough.

Even the things that we have today, there is standardized supportive measures to volume resuscitate people with intravenous fluids and other things we do that we know can make a difference and identifying by these biomarkers that they do work, the people where we really need to use these things aggressively, could probably change the outcome.

Then I think that the other area where it becomes helpful is that once you do have a patient in the hospital that has

acute kidney injury and is on dialysis, oftentimes the question is, will they get better and recover their own kidney function, and this can be somewhat frustrating for everyone in that just basically at the present time we have to wait until they do show signs of recovery versus if we had some kind of a biomarker that could predict that, that would be very helpful.

Bob Barrett: Well, finally then, what do you think are the most promising biomarkers for acute kidney injury?

Dr. John Lieske: I think right now we are sort of maybe at the beginning of the very early development stage. I think there have been several biomarkers that have been identified that seem to have some correlation with the sort of parameters we have been talking about.

And just to sort of list them off, I think the six that people are looking at most at this point in time are something called NGAL or neutrophil gelatinase-associated lipocalin, interleukin-18, Kidney Injury Molecule-1 (KIM1), Liver Associates Fatty Acid Binding Protein (L-FABP), Tissue Inhibitor of Matrix Metalloproteinase-2 or TIMP-2, and then IGF Binding Protein-7.

So those are six that have been shown in various trials, some more than others, recently, that have some utility for acute kidney injury, diagnosis, and monitoring. These are all still kind of in the research phase, so none are FDA approved test yet for acute kidney injury, but there's a lot of interest I would say in all of these at the present time, and it may turn out that some of these are better for others.

So some may go up in situations where you have ischemic injury very early after something like cardiac surgery; whereas others may detect it better in a more complicated setting, such as sepsis in the ICU, where others of these may be better in predicting when you know someone has acute kidney injury whether they will progress to go on to develop a more severe injury, others of these may be helpful there.

So I think all these sort of questions are being worked out in a lot of trials now, but I think that eventually we will have some tools to do that.

Bob Barrett: Dr. John Lieske is a Professor of Medicine and Director of the Renal Function Laboratory in the Department of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota. He has been our guest in this podcast from Clinical Chemistry.

I am Bob Barrett. Thanks for listening!