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## Stratifying the Risk of Persistent AKI and Clinical Practice

### Announcer:

Welcome to *KDIGO: Conversations in Nephrology*. This episode titled "Stratifying the Risk of Persistent AKI in Clinical Practice" is provided by KDIGO and supported by Baxter Healthcare.

Here's your host, Dr. Kathleen Liu.

### Dr. Liu:

Hello and welcome to KDIGO Conversations in Nephrology. I'm Dr. Kathleen Liu, Professor of Medicine and Anesthesia in the Divisions of Nephrology and Critical Care Medicine at the University of California, San Francisco. And joining me to discuss stratifying the risk of persistent AKI in clinical practice is Dr. Jay Koyner.

Dr. Koyner is Professor of Medicine and the Medical Director of acute dialysis at the University of Chicago. He has a long-standing interest in critical care nephrology having done work around AKI risk assessment and the acute and follow-up care of patients with AKI.

Dr. Koyner, welcome to the program.

### Dr. Koyner:

Thank you. Thanks for having me, Dr. Liu.

### Dr. Liu:

So, to dive right in Dr. Koyner, what is persistent AKI?

### Dr. Koyner:

Right. So, persistent AKI is the idea that AKI that lasts for a while. What that time period is depends on the definition that you use. And there are a couple of different definitions that are out there in the literature. The Acute Disease Quality Initiative, or ADQI group in 2017 proposed that it was KDIGO-based AKI that lasts for at least 48 hours. Other folks including some biomarker studies, have tried to extend that idea to not just 48, but 72 hours. And originally when these time periods for persistent AKI were proposed or suggested, they were based a lot on expert opinion. Since they've hit the literature, multiple different studies have validated the idea that whether it's 48 hours or 72 hours, if you're AKI, regardless of its stage, lasts that long, it's associated with more adverse events for the patient compared to people who have more transient AKI, whether that be less than 48 hours or less than 72 hours.

### Dr. Liu:

Great. Can you tell me, what do you think the difference is between persistent and severe AKI?

### Dr. Koyner:

Yeah. Well, so, I think that persistent and severe AKI are two separate ideas that I'm not sure that everyone thinks about this way, right? Persistence as we just talked about is the idea that it lasts for a longer duration, and severity is the staging system. We have the KDIGO staging system of stage 1, 2, 3 AKI based on changes in serum creatinine or decreases in urine output. And for a long time in the literature, we've had data that the more severe your AKI is the worse the outcomes. Right? Back in 2005 Glenn Chertow and his group in Boston were among the first to demonstrate that if you had a doubling of your creatinine, which wasn't stage 2 AKI then, was just a doubling of creatinine, that you were 6 to 9 times more likely to die in the hospital and that your care was maybe 10 to \$15,000 more. But it didn't necessarily account for how long that AKI lasted. You could have just had AKI that lasted one day versus having it for a week, or for the entire duration of the rest of your life.

Since then, we've learned that if that AKI lasts for longer, it's associated with more costs. So, that pound for pound, if you take someone

who has at least stage 2 AKI, and whether their AKI lasts for 72 hours or less, or 72 hours or more, the folks whose AKI lasts for more or lasts for longer than 72 hours are 3 to 4 times more likely to die in the hospital. Their care costs, again probably in more recent U.S. dollars, somewhere between 15 and \$20,000 more. And the people who have more persistent severe AKI are more likely to be readmitted after their index hospitalization if they survive, and their cost of their readmission is more their cost of their outpatient care is more, and that in general – and I think it makes sense to probably most of the listeners, at every stage along the way, if your AKI lasts for longer, you're more likely to require dialysis, whether that's in the index hospitalization or in a follow-up hospitalization. So that, you know, there are big differences between persistent and severe AKI, and the combination of the two really seem to be the worst.

**Dr. Liu:**

Got it. So, do you use the term severe and persistent AKI in your practice?

**Dr. Koyner:**

So, I do. I mean, I can't ever confess that I write that someone has stage 2 or stage 3 AKI in their note. But where it's probably most useful is my conversations with the people who are consulting me and definitely with the families or the patients themselves. When you have good epidemiologic data, like some of the numbers that I just described to you, it's easy to let someone know, if you're seeing them for the first day and they've got stage 2 AKI, that your goal is to make sure that it's not persistent, or stage 3 AKI for that matter. That your goal is to try to have the ship sort of turn around and have the AKI get better.

And it's easy to use some of that information to put into context for the patients that if things don't get better, your risks of perhaps dying in the hospital, specifically in a place like the ICU, go from maybe 1 in 10 to 1 in 3. And it allows the teams to, sort of, plan appropriately for what sort of care interventions they want to do in terms of trying to take the optimal care of a patient who has AKI, who often times has other problems besides their kidney injury and that their kidney injury is a marker of their shock or some other issue that they're having. I think it's important to be able to use that epidemiologic data to help prognosticate and help inform the teams and the patients because all too often I think for some people, AKI is a little bit of a black box that's either dialysis: yes or no. But there are all these other complications, all these other issues that you want to make sure people are aware of.

**Dr. Liu:**

For those just tuning in, you're listening to the KDIGO podcast on Stratifying the Risk of Persistent AKI in Clinical Practice. I'm doctor Kathleen Liu and I'm speaking with Dr. Jay Koyner. So, you've alluded to this already a little bit, Jay, but what should clinicians pay attention to when they think about persistent AKI?

**Dr. Koyner:**

Yeah. So, I think when people are thinking about persistent AKI I mean it has to be AKI before it becomes persistent AKI. So, folks need to think about why that AKI is happening. On the simplest level, right? You need to continue to check creatinine and monitor patients' urine output, which seem like they're no-brainers, but we've got good data that shows that across multiple settings that sometimes doesn't happen. And then you have to think about why the AKI actually happened and what you can do to make it better or prevent it from getting worse. And that includes things like making sure your drugs are dosed correctly. Kathleen, as you know, many drugs require adjustment in the setting of a changing GFR. You need to make sure that you're perfusing your kidneys, which isn't necessarily the job of the nephrologist but certainly the nephrologists can advocate for the kidneys and say hey we'd like a little bit more blood flow. We think that the issue is that you're still a little bit under-resuscitated.

I think that there's ample data that demonstrates getting nephrology involved early in the setting of AKI, improves patient outcomes. There's some data that shows, yes, you can wind up with less severe AKI, less need for people going on dialysis. But then even for the people who do go on dialysis, who have the time to prepare and implement a treatment program appropriately rather than people crashing into it in the middle of the night.

**Dr. Liu:**

Great. Thanks, Jay. I think you really nicely outlined both what nephrologists can do and how they can advocate for patients in the setting of persistent AKI. So, what new developments do we have to look forward to in the persistent AKI space?

**Dr. Koyner:**

Yeah. So, I think that there are a variety of tools out there that we can use to help prognosticate and help identify these folks. There's a new biomarker, CCL14, that is currently being tested, which has already shown in its original data that it can identify patients who have new stage 2 or stage 3 AKI, and separate out who's going to have persistence to 72 hours, who's going to need dialysis, who's even strong at identifying who's going to die in the hospital compared to those who have a more transient form of AKI. And CCL14 isn't the first one to be able to do that. My group in the past has published around things like the furosemide stress test, which in the setting of people who have established early AKI, can be used to identify who's going to progress. And that, rather than being a biochemical

biomarker, is more functional test where you give the patient either 1 or 1.5 mgs/kg of furosemide and then assess their urine output for the 2 hours after you give them that IV dosing of furosemide.

I think I'm a big believer, personally, that there's not going to be one test that we're ever going to have that's going to replace and tell you everything about every patient, but probably a combination of biomarkers like CCL14, FST, and still keeping an eye on things like urine output and serum creatinine that are going to be able to allow practicing clinicians to take better care of patients with early AKI, and then help triage and risk assess who is at high risk for developing persistent severe AKI.

**Dr. Liu:**

Great. Thanks, Jay. Before we close, are there any final messages you'd like to leave with our listeners?

**Dr. Koyner:**

Yeah, I think that it's important for everyone to sort of always remember that AKI is bad, is associated with all manner of adverse outcomes – longer length of stay, increased morbidity and mortality – but that there are different forms of it, and that the more severe and the more persistent it is the worse that patients do. And so that if you have patients who've got 2-3 days of AKI, you should be prepared for them to acquire other problems outside of their AKI because we know that there's strong epidemiologic data that supports that and that we should do our best to sort of mitigate AKI as quickly as we can, recognizing that I as a nephrologist, certainly know that we don't have the tools to prevent all AKI, or to make all AKI better. But we certainly can take steps to shorten courses. And that the data, as I described, says that if your AKI lasts for three days that's bad. But it's better than if it lasts for 7 days.

**Dr. Liu:**

Great. That's a great way to round out our discussion today. I want to thank my guest Dr. Jay Koyner, for joining me. Dr. Koyner, it was great having you on the program.

**Dr. Koyner:**

Great to be here. Thanks for having me, Doctor Liu.

**Dr. Liu:**

I'm doctor Kathleen Liu. To access this and other episodes in our series, visit [KDIGO.org/podcasts](https://KDIGO.org/podcasts). Thanks for listening.