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Early Kidney Stress Signals: Risk Assessment Imperatives

ReachMD Announcer:
You're listening to ReachMD. This medical industry feature, titled "Early Kidney Stress Signals: Risk Assessment Imperatives," is sponsored by bioMérieux. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to ReachMD. I'm Dr. Charles Turck, and joining me to discuss the importance of early risk assessment of acute kidney injury, or AKI for short, is Dr. Anthony Dempsey, who's the Chief of Surgical Services and Perioperative Medicine at Marshall Health Network. He's also the Medical Director of Cardiovascular and Thoracic Critical Care at St. Mary's Medical Center, and an Assistant Professor of Anesthesiology at the Joan C. Edwards Marshall University School of Medicine in Huntington, West Virginia.

Dr. Dempsey, it's great to have you with us today.

Dr. Dempsey:
Well thank you for having me!

Dr. Turck:
So why don't we begin with some background information on AKI. Dr. Dempsey, can you tell us what the burden of AKI currently looks like in the United States?

Dr. Dempsey:
Of course. But first, let's define what AKI is. AKI is a rapid loss of kidney function within about 48 hours, according to the global nonprofit organization KDIGO, which stands for Kidney Disease: Improving Global Outcomes. And AKI includes, but isn't limited to, acute renal failure.[1]

Now AKI is a very common, costly, and deadly burden. It occurs in 57.3 percent of patients in the U.S. on day *one* of their ICU stay,[2] and another 42 percent of critically ill patients with sepsis will develop AKI.[3] In addition, AKI treatment, especially when renal replacement therapy is required, contributes significantly to healthcare expenditures. For patients undergoing surgery, the risk-adjusted average cost of care was $26,700 for patients with no AKI versus $42,600 for patients with any AKI.[4]

To complicate things even further, AKI is difficult to identify and assess the risk of, and it's been described as a "silent killer." Because unlike myocardial infarction and stroke, AKI presents with minimal symptoms.[5] But any delays in recognizing AKI can potentially lead to irreversible injury.[6]

And unfortunately, current diagnostic tools are inadequate for assessing the risk of AKI,[7,8] and there is a 25 percent overall mortality rate for AKI in critically ill patients.[2]

Dr. Turck:
So why are current diagnostics inadequate for determining AKI risk?

Dr. Dempsey:
Well, there are a couple of different reasons in my opinion. First, when you look across a spectrum of patients you may see some clues as to which patients are more likely to develop AKI, perhaps those with cardiovascular or respiratory compromise. But in the end, it's really difficult to tell who's going to end up with the AKI, which is why it's often misdiagnosed or under-recognized, and also why early

risk assessment is so important.[9]

And second, we know that there are AKI risk factors related to disease states, like if a patient has sepsis or needs major surgery, and then there are patient risk factors like advanced age, poorly controlled diabetes, or dehydration.[1]

Now KDIGO *does* have staging criteria based on increases in serum creatinine and decreases in urine output that assess and stratify AKI into mild, moderate, or severe levels, but these lagging indicators are present when the patient *already has* an injured kidney. And in a kidney that isn't actually injured yet, but has a high risk for AKI, we may not see low urine output or increases serum creatinine.[1]

So instead, my goal is to try and assess signs of kidney stress *before* it advances to kidney injury, dysfunction, or failure.

Dr. Turck:
Now with that being said, Dr. Dempsey, what can clinicians do to assess kidney stress before it's too late?

Dr. Dempsey:
Well, the good news is…is that we can look for renal biomarkers that indicate signs of stress in the kidneys.

Biomarkers known as urinary tissue inhibitor of metalloproteinases-2 and insulin-like growth factor-binding protein-7, also known as TIMP-2 and IGFBP-7 respectively, are actually produced during episodes of stress before significant and widespread damage to the kidney occurs.[10,11]

The biomarkers are expressed in renal tubular cells in response to stress, resulting in G1 cell cycle arrest. We think this process prevents *potentially damaged* cells from dividing.[10,11]

Now this is important to note because these particular biomarkers represent a significant improvement in renal testing over the past 60-plus years. In fact, a prospective examination of a variety of AKI biomarkers identified TIMP-2 and IGFBP-7 as relevant for early kidney stress.

In this exam, more than 300 candidate AKI biomarkers, including NGAL, Cystatin C, and KIM-1, were studied and analyzed from two observational clinical trials across 37 sites. And of the candidates, TIMP-2 and IGFBP-7 were validated to be significantly superior to all other markers of AKI in more than 1,200 critically-ill or ICU patients with diverse illnesses, such as sepsis, major surgery, trauma, all types of shock, and more.[11]

So as we can see, urinary TIMP-2 and IGFBP-7 are valid indicators of kidney stress in response to a wide variety of tissue insults.[10]

And the combination of urinary TIMP-2 and IGFBP-7 has been studied as a predictive biomarker that can help to identify patients at risk for imminent AKI.[12]

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Anthony Dempsey about early assessment of acute kidney injury.

So, Dr. Dempsey, now that we've discussed AKI detection with urinary biomarkers, what tools are available to help clinicians assess a patient's risk of AKI?

Dr. Dempsey:
So we have an FDA-cleared test for the risk assessment of AKI using TIMP-2 and IGFBP-7 called the VIDAS® NEPHROCHECK® assay. [10]

It's intended to be used in conjunction with clinical evaluation in ICU patients who currently have or have had acute cardiovascular and/or respiratory compromise within the past 24 hours. This tool aids in identifying patients at risk of moderate or severe AKI within 12 hours of clinical assessment. But it's only intended to be used in patients 21 years of age or older.[10]

Now in terms of how it works, the VIDAS® NEPHROCHECK® is an automated test that's used on the VIDAS® 3 instrument.[10]

Using the VIDAS® 3 instrument, the VIDAS® NEPHROCHECK® assay produces an AKIRISK™ score by calculating the product of the measured concentration of TIMP-2 and IGFBP-7. A negative AKIRISK ™ score is less than or equal to the cutoff of 0.30, meaning the patient is at a lower risk of developing moderate to severe AKI within 12 hours of assessment.[10]

But a positive score greater than 0.30 means the patient is at risk for moderate to severe AKI within 12 hours.[10]

The threshold is set at 0.30 to cast a wide net to identify a large number of patients at risk for moderate to severe AKI.[10]

Or in other words, a positive score is designed for high sensitivity while also preserving an acceptable specificity in identifying a majority of at-risk patients.[10]

And an assay cutoff of greater than 0.30 has been established based on the results of clinical studies to achieve this high sensitivity. In one study of 399 patients, a cutoff of 0.30 had a sensitivity of about 90 percent and a negative predictive value of 95.5 percent in predicting moderate to severe AKI. And in another study of 126 patients, there was about an 83 percent sensitivity with an 89 percent negative predictive value.[10]

So high sensitivity and negative predictive value are important in risk assessment to ensure that the majority of patients who will develop AKI actually test positive and there are few patients with a negative test result who are at risk of developing AKI.[10]

It's also important to note that AKIRISK Scores aren't elevated in acute non-AKI conditions or for patients with stable chronic comorbidities, like chronic kidney disease, diabetes, or heart disease—unless there's an acute-on-chronic injury.[10]

Dr. Turck:
So what does all this mean for our patients who are at risk of AKI?

Dr. Dempsey:
Well, I think the biggest way the VIDAS® NEPHROCHECK® assay can impact patients is by providing an early AKI risk assessment *before* significant damage occurs.[6,10,11]

As we know, serum creatinine is elevated after 50 percent of kidney function loss has already occurred, putting our patients at risk for kidney failure and even death by the time we've assessed the risk of AKI.[8]

But with the ability to assess a risk patient factor for AKI when they're asymptomatic and *before* injury occurs, we have the opportunity to implement earlier intervention, such as the KDIGO bundle, to potentially prevent AKI and improve patient outcomes.[9,13]

Dr. Turck:
Now we're almost out of time, so before we close, Dr. Dempsey, would you mind summarizing the key highlights from our discussion today?

Dr. Dempsey:
Absolutely. So AKI comes with a heavy burden for our patients because it's very common and costly—not only in terms of financial expenditures, but also in lives lost as it has a 25 percent overall mortality rate in critically ill patients.[2] And because AKI often presents without signs or symptoms, it can be very difficult to identify and assess the risk of.[5]

But VIDAS® NEPHROCHECK® gives us the opportunity to assess a patient's risk for AKI *before* significant damage occurs.[6,10,11] And with its high sensitivity and negative predictive value capabilities I've found that this assay helps me to be more proactive in the ICU.

For example, in cardiac surgery patients, Meersch et al showed that using the AKIRISK score and implementing the KDIGO bundle reduced moderate and severe AKI.[14]

And so for me, this evidence of a bedside test that can help me improve patient outcomes with early intervention of the KDIGO bundle changed the way I practice in the ICU. [9,14]

Dr. Turck:
That's a great way to summarize our discussion, and as that brings us to the end of today's program, I want to thank my guest, Dr. Anthony Dempsey, for joining me to talk about how we can assess our patients' risk of acute kidney injury.

Dr. Dempsey, it was great speaking with you today.

Dr. Dempsey:
Well Dr. Turck, thank you so much for having me. I really appreciate the chance to talk.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. Please stay tuned to hear some Important Safety Information.

ReachMD Announcer:
IMPORTANT INFORMATION

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This medical industry feature was sponsored by bioMérieux. If you missed any part of this discussion visit ReachMD.com, where you can Be Part of the Knowledge.

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