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www.reachmd.com
info@reachmd.com
(866) 423-7849

AHA Identifies CKM Syndrome: A First Step in Managing Patients with CVD

Dr. Butler:

For the first time, the American Heart Association has identified a new condition that reflects a strong overlap between heart disease, kidney disease, and obesity. Recognizing cardiovascular-kidney-metabolic, or CKM, syndrome is the first step in earlier diagnosis and treatment of individuals who are at risk of dying from cardiovascular disease.

You're listening to *Heart Matters* on ReachMD. I am Dr. Javed Butler, and joining me today is Dr. Chiadi Ndumele, who is an Associate Professor of Medicine and the Director of Obesity and Cardiometabolic Research at the Johns Hopkins University and is the lead author of the American Heart Association Presidential Advisory, which was published in the journal *Circulation* in 2023. Today, he'll dive into this, along with the treatment and management of CKM syndrome.

Dr. Ndumele, welcome to the program.

Dr. Ndumele:

Thank you so much for having me, Javed. It's a pleasure to be here.

Dr. Butler:

So let's jump right into it. Can you just give us a little bit of a background as to why this presidential advisory was commissioned in the first place? What are the overlapping issues with these disease states, and what was the background that led to you explaining to us about CKM syndrome?

Dr. Ndumele:

Of course. So cardiovascular-kidney-metabolic, or CKM, syndrome, is really most easily defined as a health disorder that's resulting from the close interplay and connections among risk factors, such as obesity and diabetes, chronic kidney disease, and the cardiovascular system. The major clinical consequence of CKM syndrome is multi-organ dysfunction with a particularly high incidence and burden of cardiovascular disease, and the result of this is premature morbidity and mortality that's mostly due to cardiovascular mortality. So as a result, it's really important for us to focus on defining this and identifying individuals with CKM syndrome.

It's worth noting that CKM syndrome is really disproportionately present in those individuals with adverse social determinants of health, and as a consequence of that, it's really a major contributor to cardiovascular disease disparities in the population. And from a definition standpoint, it's worth emphasizing that the CKM syndrome definition includes those individuals who are at risk for CVD as a consequence of metabolic risk factors, chronic kidney disease or both, as well as those with existing CVD where the presence of metabolic risk factors or chronic kidney disease can lead to really important unique considerations for care.

The urgency behind this from a public health standpoint and clinical standpoint is clear because of the bad outcomes associated with CKM syndrome, but there's also a tremendous opportunity for improving CKM health in the population both now because there's a growing recognition of the importance of obesity in this syndrome, therapeutic options to address not only obesity but other metabolic risk factors in kidney disease, and all of these having a beneficial impact on cardiovascular outcomes. So our goal is to provide a framework to help healthcare professionals identify these individuals and to provide more timely and appropriate care.

Dr. Butler:

Well, certainly very important but also very innovative way of thinking about these multiple risk factors. Can you highlight some of the guidelines included in this advisory?

Dr. Ndumele:

That's a very good question. So it's important to emphasize that this was a multidisciplinary effort that was spearheaded by the American Heart Association. So this brought together not only both preventive cardiologists and cardiologists who have specific focus on chronic coronary disease or heart failure or stroke, but then also it brought together nephrologists, endocrinologists, primary care physicians, pediatric and adult physicians, and also nurses and pharmacists, which really reflects the interdisciplinary nature and the multisystem consequences of CKM syndrome. So we included several different guidelines, both American and European, that focused on prevention, metabolic risk factors, such as obesity and diabetes, where there was statements on those by the American Heart Association and by the American Diabetes Association, chronic kidney disease, as spearheaded by KDIGO, and really bringing in the AHA, ACC, and ESC guidelines on heart failure, atrial fibrillation, PAD, as well as general prevention, hypertension, cholesterol, because really this touches on a lot of these different conditions. And what we're doing is we're bringing all these together in one place to emphasize holistic approaches to maximizing and optimizing CKM health for our patients.

Dr. Butler:

For those just joining us, you're listening to *Heart Matters* on ReachMD. I'm Dr. Javed Butler, and I'm speaking with Dr. Chiadi Ndumele about cardiovascular-kidney-metabolic syndrome. So can you talk a little bit about the diagnosis now that we understand some of the background? How do we identify these patients with CKM? How do we categorize them? Do you propose a scoring system?

Dr. Ndumele:

Yes, that's a very important point. And I think one of the key take-homes from this work was a focus on early identification of individuals who are in the early spectrum of CKM syndrome, as well as a life course approach to prevention, and the key aspect of that is this CKM staging system. So it starts with CKM stage 0, which is individuals who really don't have any of these significant CKM risk factors, who are fairly healthy, and we're focusing really on primordial prevention, preventing the development of risk factors. And we know that we see this most often in young adults and in youth, but this is something we want to preserve as much as possible in the population.

CKM stage 1 is a focus on excess, and/or dysfunctional adiposities. Those are individuals with overweight or obesity, so measures like waist circumference could help us start to understand who has that central adiposity that contributes to metabolic risk. And then we also bring in this concept of dysfunctional adiposity, which has several different processes pathophysiologically associated with that, but at the end of the day, the consequence of that is impaired glucose tolerance. So we focus on impaired glucose tolerance, which can occur even in individuals who don't have excess adiposity using traditional anthropometric measures.

Stage 2 is really individuals who have metabolic risk factors, like diabetes, hypertension, dyslipidemia, particularly hypertriglyceridemia, metabolic syndrome, or moderate-to-high risk chronic kidney disease, most of which is downstream from this excess and dysfunctional adiposity.

And then stage 3 in those individuals who have subclinical cardiovascular disease or risk equivalents, which are high predicted risk using our risk calculator, or individuals who have very high risk of chronic kidney disease.

And then stage 4 are individuals with overt clinical cardiovascular disease that's overlapping with metabolic risk factors and/or chronic kidney disease.

And the reason for that staging system is because it really reflects the pathophysiologic progression of CKM syndrome. It gives us windows for prevention, and the stages also promote the concept of CKM stage regression as we know that with substantial lifestyle change and with weight loss that's substantial, we can actually see people go backwards in terms of their CKM stage as well.

Dr. Butler:

So very logical, makes total sense, but I have a conceptual question for you. Is this primarily for risk prediction and prevention, or are there treatment implications as well?

Dr. Ndumele:

Yeah, so that's a great question, and it's for both. We know that the outcomes are best when we identify these risk factors early, and we know that a lot of these risk factors are underrecognized in the population as they are, so the staging construct and the associated screening can help for better identification. We also have developed a new risk prediction tool that was also aligned with this effort that better reflects the CKM risk factors in the population and focuses on both short- and long-term risk among individuals now ages 30 through 79 for total CVD, as well as ASCVD and heart failure. But there are very clear treatment implications for individuals who are in these various stages. We know that we have these cardioprotective anti-hypoglycemics, the SGLT2 inhibitors, GLP-1 receptor agonists. We know we have agents to help with kidney disease, including the SGLT2s, ACE inhibitors, and ARBs, as well as finerenone. And really what we try to do is provide a framework for how and when we consider these therapies, where we'll think about combination therapies, which is those individuals with higher CKM risk, particularly in the setting of CVD. So each stage in this construct is tied to specific therapeutic recommendations, but the larger point is that the intensity of the therapies should increase as the stage is higher and as the absolute CVD risk is higher.

Dr. Butler:

Is there a role of a multidisciplinary team also for prevention and treatment as well?

Dr. Ndumele:

Yeah, so that's a very good point. So there's two overarching themes that we have, and one is multidisciplinary care. And there's two aspects that we think of. One is that we see that individuals in the real-world settings don't just have diabetes or chronic kidney disease or cardiovascular disease. Usually, we see a confluence of multiple conditions because these are so interrelated, and that really necessitates having involvement from multiple specialties, and also having us all be on the same page. So we really describe a couple of approaches, and one is an approach where individuals have somewhat lower-risk disease where there's more remote interdisciplinary support using a CKM coordinator that brings together interdisciplinary support to help individuals make sure that we're following the appropriate guidance for care, and especially for those individuals who we want to prevent from developing kidney failure, prevent from developing cardiovascular disease, and we know we can get these protective agents on sooner makes an impact.

We also then want to think about coordinating care for those individuals who have multiple severe conditions that are seeing multiple providers, so we give a framework for referrals for those individuals, but then also want to support cohesive care and support navigation for patients across those multiple providers, so the CKM coordinators playing a role there as well in terms of bringing individuals in that journey across providers and making sure we help them in their journey to optimal CKM care.

I also want to emphasize social determinants of health, which are really key to the development of so much of CKM syndrome. So we emphasize screening for social determinants of health, and then having individuals on the care team who can actually help with addressing those when they're present, adverse social determinants of health.

Dr. Butler:

I hope I'm not exaggerating in saying that the CKM syndrome is probably one of the most important medical needs of our time from a population perspective, so really, thank you very much for taking on this effort. Before we close, I will give you the podium if you want to share any final thoughts about what the current or the future research is for this condition.

Dr. Ndumele:

First of all, thank you so much for having me. And I think this is a really exciting and important area from a public health standpoint. We do need to know a few more things in terms of the science moving forward, how we better understand some of the mechanisms of cardiovascular disease development, these kidney-heart interactions that occur and are more common when metabolic risk factors are present, and why that is occurring and how we can mitigate that, the science of CKM progression along that staging spectrum, why some people progress more frequently, more rapidly than others, and differences across demographic groups. And then, we definitely need more robust research on interdisciplinary care approaches, and also the impact of systematically addressing social determinants of health. But I agree with you that this is really a fundamentally important area for our public health future and our clinical future, so I'm

happy to have played a role.

Dr. Butler:

This has been an important update on the treatment and management of CKM syndrome, and I'd like to thank my guest, Dr. Chiadi Ndumele, for sharing his insights with me today. Dr. Ndumele, thanks so much for joining me.

Dr. Ndumele:

Thank you so much for having me. I really appreciate the opportunity.

Dr. Butler:

For ReachMD, I'm Dr. Javed Butler. To access this and other episodes in our series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.