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### Screening for CKM syndrome

#### Dr. Floege:

It's a great pleasure that you want to listen to a kidney guy. And I think it's really time we talk to each other more. My good friend Niko Marx and I founded one of the first heart and kidney wards in Germany, and I tell you, it's been a blessing realizing that we have huge overlap.

So these are my disclosures, and it's nice to show them, because 5 to 10 years ago, this would have been almost empty. It's another blessing that, finally, pharmaceutical industry discovers kidney. Kidney was considered complex, difficult, multimorbid, let's stay away. It's time we talk to each other.

So I was asked to talk about screening for CKM syndrome. This is screening in people less than 21 years, and we're really talking pediatric screening here, clearly screened for overweight and obesity. I just have to look at my own children. We have 6. Out of these 6, 2 are obese, but they are grown-ups. Mental and behavioral health screening, I don't want to talk about my children. Blood pressure assessment. In children, blood pressure assessment, go to a GP office and see how many 20-year-olds have a blood pressure being taken. Fasting lipid levels, family history, screen for glucose intolerance in teenagers. We are not used to doing that. And then assign the appropriate stage.

If you're older than 21, have a BMI and a waist circumference, a blood pressure, HbA1c, lipid panel, albuminuria – we'll come back to that – and serum creatinine measurements. Screen for fatty liver disease, what we used to call NASH and is now MASLD. And look for coronary artery calcification, as directed for by guidelines. And again, as a kidney guy, I want to come back to coronary artery calcification, because the moment chronic kidney disease comes into play, and in particular advanced stages like GFR below 30, which is not really that uncommon, you have a massive confounder in your screening. This is troponins related to GFR, and we all know that low-molecular-weight proteins such as troponins do accumulate in kidney failure because they are simply not excreted. Everything increases, starting with insulin, ending with BNP and light chains.

This is a guy, and we know this from autopsy, who has massive, massive arterial calcification. And we know from autopsy that this is not atherosclerotic calcification. This is simply aging. This is medial sclerosing. This guy had a GFR of 10.

Advanced kidney disease is a stage of accelerated aging, and clearly, today's imaging methods cannot distinguish between aging, even if it's accelerated by chronic kidney disease and atherosclerosis, and it cannot do so in the coronaries; that is an issue. We don't know the relevance of atherosclerotic versus medial sclerotic vascular calcification. Nevertheless, we are very certain that chronic kidney disease is an amplifier of cardiovascular risk. It's one of the most potent risk factors you can have for cardiovascular disease. We know that low GFR and albuminuria independently increase the risk for MACE and CV death. These are the famous KDIGO heat maps. CKD and diabetes precipitate peripheral artery disease. Vascular calcification is very common in CKD, and as I just showed you, it makes your life a little more difficult to decide what is the culprit. CKD is a proinflammatory stage. Heart failure is extremely common if you have kidney failure. And anemia is common in CKD, but that's probably less of an issue.

This is a famous study by Alan Go. Alan Go looked at people who are all in an integrated health system in the US and then looked at how high is the likelihood of CV events and mortality as you go down with your kidney function. And you can see this dramatic 37-fold

increase in CV events if your kidney function is below a GFR of 15. And it gets even higher if you make it onto dialysis, if you make it onto that, because your likelihood of dying on the way to dialysis is about tenfold higher than reaching dialysis. So ironically, dialysis patients are the survivors, the good ones.

ACI is also an independent predictor of cardiovascular mortality, and it's really nice to see that, at least in my hospital, Niko Marx and his cardiology group have decided that everybody admitted to the hospital, to the cardiology ward, will receive an albuminuria test. And it was very nice to see the many hands that went up earlier. So very clearly, the higher your albuminuria, your albumin creatinine ratio, the higher your risk for cardiovascular mortality. And please lay away terms like microalbuminuria, which suggests it's mild, not relevant. It's relevant. What we used to call microalbuminuria, which would be here in the region between 10 and 30, already has a 50% increase in cardiovascular mortality. eGFR is seemingly a little less potent and seemingly only starts at 75, but that's likely an artifact, because you all know how insensitive eGFR measurements, estimates are in the normal range and how much they fluctuate, how tiny changes in your serum creatinine cause seemingly large swings in GFR.

This is the famous KDIGO heat map I referred to earlier, and in fact, this is for CKD classification, but it's a great table because you can exchange the title and you can have 10 different titles and the heat map looks exactly the same: risk of dialysis, risk of death, risk of cardiovascular event, risk of peripheral artery event. The heat map is identical in all those cases. So it's really nice memorizing the albuminuria categories, which are normal to mildly increased. That replaces the so-called microalbuminuria, moderately increased, severely increased, and then the GFR stages.

And even more importantly, there's good data to show that if your albuminuria decreases, the darker blue box here, then your risk of CKD decreases. If it increases, your risk of CKD increases. So it's a very good surrogate marker for what will happen in the future.

So very clearly, albuminuria screening should be part of our everyday life, but let's have a look at German real life, almost half a million patients. These are data that were published 2 months ago. So it's real, current data. And they looked at offices of 1,244 GPs, out of which 35% were internists working as GPs and 65% were GPs. They looked at a fairly typical German population, 65 years, BMI at 29, blood pressure at 140, etc., etc. And most of these had hypertension; many had CV disease and diabetes; 7.5% had high-risk hypertension, CVD, and diabetes. And then they looked, for an average of 1.7 years, what happened in the GP practice? So just looking at the high-risk cohort, 33,000 patients, out of these, in the next 1.7 years, 53% had a determination of serum creatinine. That's fine, but it could be better. 22% had a dipstick for albuminuria. In this super high-risk population, 1% had an albuminuria measurement. There's room for improvement. And clearly, guideline-recommended CKD screening is inadequate. I know you're not from Germany. I know in your country, it's better, but even if it's 2%, it's not real good.

Thank you.