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Released: 04/06/2023
Valid until: 04/06/2025
Time needed to complete: 53m

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

Primary care role in CKD

Hello, I'm Richard Hobbs, Head of Academic Primary Care at the University of Oxford. I'm pleased to be talking about the primary care role in chronic kidney disease in this session. Those are my competing interests.

Let's look at what I'm going to talk about in this brief presentation. I'm going to cover the definition and how we diagnose CKD. I'm going to talk about why it's an important topic, increasingly important topic actually, for doctors to focus on, and discuss the evidence base around management.

First, around CKD definition. It's basically a condition of decline in renal function. That's determined by both markers of renal impairment, which we use the measure of estimated glomerular filtration rate, plus evidence of renal damage. There are a number of ways that we can assess that, and they're listed on the slide. Most commonly the evidence of proteinuria. There may be imaging evidence of cardiac damage or history. The other important consideration in diagnosing chronic kidney disease though, is that there needs to have some duration associated with these biomarkers. Single measures aren't sufficient and you need to have repeat measures of both impairment and damage over a three-month period to reach a classification of chronic kidney disease. If you looked at the impairment classifications, those are the classic stages, 1 to 5, determined by eGFR, with most of the action once patients have got an eGFR below 45. If we look at the renal damage biomarker, which is a measurement of protein excretion from the kidney, and in most health systems, it's probably albumin-creatinine ratio that you'll be most used to. There are the cutoffs that define either mild, moderate, or severe proteinuria based on milligrams per millimole or milligrams per gram.

What about the burden of CKD? It's basically, as with many diseases, predominantly in the elderly. Once you get to 75 plus, around 50% of patients are going to have, effectively, CKD. It is common in middle ages onwards. The risk factors are classic risk factors for vascular disease in terms of smoking, obesity, diabetes, hypertension, and indeed any evidence of existing vascular factors such as events like MI or stroke. Why is it such an important topic? Indeed, that's partially because it's become a more important driver of death. If you look at this global burden of disease data, you can see that CKD is now within the top 20 causes of death on the planet, that impact on mortality is increasing. It also actually has big burden for health systems because it doesn't just increase death.

You can see on the left there in green, those are the data on death, and they're graded by stage of CKD. As you can see, from stage 3 onwards; stage 3, 4 and 5, significantly increased rates of death. In yellow there, in the middle, you can see increased rates of hospitalization. On the right in red, vascular events such as MI or stroke. Importantly, if you have CKD, if you have an event such as MI on the left there or stroke on the right, then you are going to have a worse prognosis. You'll have a poorer recovery, and you're more likely to suffer recurrent events. Threefold increased rate of repeat cardiac events if you have pre-existing CKD, and doubling of stroke risk.

What about its diagnosis? Basically, it requires the measurement of these biomarkers. What should happen in clinical practice, particularly in the community in general practice, is that all patients who've got hypertension, diabetes, existing CVD, family history of CKD, or other multisystem diseases should basically have their eGFR measured. If that shows levels of impairment, then it should be accompanied by measurement of protein excretion, ACR, which then will stage the patient. As I've said, you will need to repeat that when you first detect any impairment. If somebody has mild impairment, eGFR greater than 60, then it needs to be something you repeat on at least an annual basis. Based on these two biomarkers, you're going to get an interaction between the impairment and

damage. Basically, that's going to put your patient into either a high risk, which is red there. That's the very high risk. High risk in orange, so any level of protein denotes some high level of risk. Moderate risk in yellow, or green monitoring the patient. It's only if patients have got mild renal impairment with eGFRs above 60 where treatment is basically monitoring and assessing future decline.

When to refer from primary care. Having made an assessment, what the primary care physician needs to do is consider whether there's already evidence to refer the patient in. That would be if a patient meets stage 4 or 5 CKD already, or if there are high levels of protein or even moderate levels of protein excretion associated with hematuria, or somebody's rapidly declining in their renal function, those patients should be referred straight away in for specialist follow-up. For most patients, you basically are going to be considering therapeutic management.

Here are the main aims of treatment. It's basically renoprotection, delaying the progression of CKD. That's to both avoid end-stage renal failure, but it's also to reduce proteinuria, which is, as I said, the measure of renal damage, or slow down eGFR decline. It's going to decline with age, but what you want to do is slow down the rate of decline. In addition to that, there are cardioprotective reasons for therapy. In the bottom of the slide, you can see that the evidence-based treatments are basically lipids, blood pressure treatment and RAS blockade, and now, SGLT2is.

Just a brief word about statins. Basically, you get a similar protective effect in terms of cardioprotection if you have CKD than if you don't have CKD. Because vascular outcomes are an important risk factor of CKD, you should initiate cardioprotection with statins. Indeed, that's true in primary prevention as well. JUPITER trial showing that basically, patients with CKD who go on to a statin treatment have similar outcomes to patients who have no CKD and are on placebo.

Then in terms of blood pressure treatment, that's important because patients with CKD are more likely to have uncontrolled hypertension. You can see on this data in red there that the average patient, unfortunately, is going to shift and be more likely to have uncontrolled blood pressure. All the blood pressure treatments are effective. If you treat blood pressure effectively, then you are going to reduce the burden of vascular disease consistently to the way you actually reduce risk in patients without CKD. The biggest improvement up till recently in CKD renoprotection was through RAS blockade. We know that ARBs, for example from IDNT and renal trials are effective at slowing progression of diabetic nephropathy. They also, compared to other classes of drugs, will reduce protein excretion as well.

The big improvement we have relates to SGLT2 inhibition. This meta-analysis basically shows as the SGLT2is have a big effect on cardioprotection against all the vascular outcomes in patients who have got established disease. You can see on the bottom of that odds plot that, in fact, in patients for primary prevention, they appear to have lower benefits. However, for two outcomes, which is heart failure and cardiovascular death, you actually do see benefits, even in patients in primary prevention. That's particularly true in heart failure, where SGLT2is have now got primary indications for preventing hospitalization associated with heart failure in both secondary and primary prevention. Their biggest therapeutic benefit is seen in renoprotection in the effects on reducing renal worsening, progression to end-stage renal disease, or renal death, where they collectively have about a 50% risk reduction in this important outcome. Indeed, importantly, what we now have data from the DAPA-CKD trial is that renoprotection is maintained. Even in patients who don't have diabetes, most of the data in the previous meta-analysis was based on patients who have diabetes and CKD, and in the DAPA-CKD trial, about a third of patients didn't have diabetes, and yet, as you can see from this slide, they had a very similar treatment benefit in terms of renoprotection. Also, consistently in the subgroups, patients who have more severe renal disease, patients who had renal impairment or greater levels of proteinuria, similar benefits in terms of the dapagliflozin, in terms of its treatment effect. Importantly, very safe, no episodes of hypoglycemia in this population. In fact, there's less glycemic effect once eGFR gets below 60, so borne out in a trial, really no signals to worry about. The only side effect that is reasonably common in treatment is genital infections, which obviously, if you're excreting a lot of glucose in the urine, that's more likely, and that just requires sensible conversations with patients about hygiene in the perineum and treatment with simply anti-fungal creams, if they develop infection.

In conclusion, I've demonstrated the importance of CKD, the fact that it's actually becoming a more important condition to manage in primary care. Therefore, it’s very important conditions for us to diagnose both earlier, but then, initiate evidence-based treatments with our patients. The evidence base for treatments is basically statins and treating hypertension for cardioprotection, plus the renoprotective effects of RAS blockade, and now the additional renoprotective and cardioprotective effects in addition to all those other agents from SGLT2is and the recent data from dapagliflozin that actually that is effective in patients with and without diabetes.

Thank you.