Kidney Disease Progression: How to Calculate & Attenuate Risk

Q When I diagnose patients with minor kidney disease, they often ask if they will require dialysis. I know it is unlikely, but I wish I could give them a better answer. Can you help me?

The diagnosis of chronic kidney disease (CKD) is understandably concerning for many patients. Being able to estimate CKD progression helps patients gain a better understanding of their condition while allowing clinicians to develop more personalized care plans. Tangri and colleagues developed a model that can be used to predict risk for kidney failure requiring dialysis or transplantation in patients with stage III to V CKD. This model has been validated in multiple diverse populations in North America and worldwide.[1]

The Kidney Failure Risk Equation (found at **www.kidneyfailurerisk.com**) uses four variables—age, gender, glomerular filtration rate (GFR), and urine albumin-to-creatinine ratio (ACR)—to assess two- and five-year risk for kidney failure.[1,2] For example

- A 63-year-old woman with a GFR of 45 mL/min and an ACR of 30 mg/g has a 0.4% two-year risk and a 1.3% five-year risk for progression to kidney failure requiring dialysis or transplant.[1]
- Alternatively, a 55-year-old man with a GFR of 38 mL/min and an ACR of 150 mg/g has a 2.9% two-year risk and a 9% five-year risk for progression to end-stage renal disease (ESRD).[1]

Per proposed thresholds, patients with a score < 5% would be deemed "low risk"; with scores of 5% to 15%, "intermediate risk"; and with scores > 15%, "high risk."[1,2]

The Kidney Failure Risk Equation can be incorporated into clinic visits to provide context for lab results. For patients with low risk for progression, optimal care and lifestyle measures can be reinforced. For those with intermediate or high risk, more intensive treatments and appropriate referrals can be initiated. (The National Kidney Foundation advises referral when a patient's estimated GFR is 20 mL/min or the urine ACR is ≥ 300 mg/g.[3]) Providing a numeric risk for progression can help alleviate the patient's uncertainty surrounding the diagnosis of CKD. **—NDM**

1. Tangri N, Grams ME, Levey AS, et al. Multinational assessment of accuracy of equations for predicting risk of kidney failure: a meta-analysis. *JAMA.* 2016;315(2):164-174.
2. Tangri N, Stevens LA, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA.* 2011;305(15):1553-1559.
3. National Kidney Foundation. Renal Replacement Therapy: What the PCP Needs to Know. www.kidney.org/sites/default/files/PCP%20in%20a%20Box%20-%20Module%203.pptx. Accessed December 5, 2016.

Q I overheard a conversation at the hospital in which one of the nephrologists told an internist that allopurinol is better than other medications for treating gout because it slows the progression of chronic kidney disease (CKD). What does the data say?

CKD is a growing problem in America; the number of adults with CKD doubled from 2000 to 2008.[1] Gout is considered an independent risk factor for CKD progression.[2]

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Some randomized controlled trials (RCTs) have shown an association between allopurinol use and decreased proteinuria.[3]

A recent large retrospective review of Medicare charts assessed the correlation between use and dose of allopurinol and incidence of renal failure in patients older than 65.[1] The researchers found that, compared with lower doses, allopurinol doses of 200 to 299 mg/d and > 300 mg/d were associated with a significantly lower hazard ratio for kidney failure, in a multivariate-adjusted model. The findings therefore suggest that doses > 199 mg may slow progression to kidney failure in the elderly.

Despite the strengths of this study, it is worth noting that it did not consider stage of kidney disease, nor did it distinguish comorbidities of the patients. The retrospective chart review format did not allow for identification of concurrent medication use (including OTC and herbal products).

The National Institute of Diabetes and Digestive and Kidney Diseases is currently conducting an RCT to investigate the renoprotective effects of allopurinol versus placebo in diabetic patients. (Clinical Trials.gov identifier: NCT02017171). Enrollment was completed in 2014, and results are expected in June 2019.

One important proviso about allopurinol: While it is inexpensive and generally well tolerated, prescribers should be aware of rare sensitivity reactions, particularly Stevens-Johnson syndrome. **—MRS** **CR**

1. Singh JA, Yu S. Are allopurinol dose and duration of use nephroprotective in the elderly? A Medicare claims study of allopurinol use and incident renal failure. *Ann Rheum Dis.* 2016 Jun 13. [Epub ahead of print]
2. Roughley MJ, Belcher J, Mallen CD, Roddy E. Gout and risk of chronic kidney disease and nephrolithiasis: meta-analysis of observational studies. *Arthritis Res Ther.* 2015;17:90.
3. Kanbay M, Huddam B, Azak A, et al. A randomized study of allopurinol on endothelial function and estimated glomerular filtration rate in asymptomatic hyperuricemic subjects with normal renal function. *Clin J Am Soc Nephrol.* 2011;6(8):1887-1894.