CLINICAL VIGNETTE

Stable, Elevated Serum Creatinine for 10 Years: Problems in Estimation of Chronic Kidney Disease

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Introduction

Estimated glomerular filtration rate (eGFR) is based on a few assumptions. The ideal molecule to estimate GFR would be freely filtered, neither secreted nor absorbed.[1] Creatinine, however, is actively secreted in the proximal convoluted tubule, and does not meet strict criteria for a freely filtered solute.[2] Creatinine is also assumed to be produced at a rate of 1 gram/day, when production varies depending on age, gender, muscle mass, ethnicity, diet, medications and organ system function.[3]

Other equations have been developed to overcome limitations of creatinine-based estimates of renal function. Three equations use multiple factors to estimate eGFR.[4] The Cockcroft Gault equation, the MDRD (Modification of diet in renal disease) equation, and the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) still have limitations in estimating eGFR in healthy individuals, but the MDRD and the CKD epi equations include more variables to adjust for patients of different genders and ethnic groups resulting in more accurate predictions.[5]

Case

A 57-year-old male with hypertension and chronic kidney disease presented for to primary care for a nephrology referral and second opinion about chronic kidney disease. His serum creatinine had been elevated for ten years, ranging between 3.5-4.5 mg/dL with urea nitrogen of 70-90 mg/dL. He reported limited prior evaluations, but had been taking non-steroidal anti-inflammatory drugs for many years, but had stopped prior to his initial visit. He has no family history of renal disease, nor personal nor family history of treated hypertension or diabetes.

He recalls a previous nephrologist informing him that although his creatinine was high, between 3-4 mg/dL, but this was "normal" for him. Another nephrologist noted increasing BUN and recommended initiation of dialysis. The patient reported no uremic symptoms, specifically denying confusion, bleeding or adverse events despite documented high urea nitrogen and creatinine for nearly 10 years. He reported high urine output, estimated at around 3-4 liters per day.

His exam was remarkable for blood pressure 159/81, Pulse 98 and weight of 297 lbs. Labs included urea nitrogen of 71 mg/dL, creatinine 4.12 mg/dL, eGFR 15, sodium 141 mmol/L, potassium 4.1 mmol/L, chloride 103 mmol/L, calcium 10.0 mg/dL, carbon dioxide 28 mmol/L, cystatin C 3.40 mg/L, phosphorus 5.5 mg/dL, hemoglobin 10.1 g/dL, total protein/creatinine ratio 1446 mg/g creatinine. 24-hour urine collection showed total volume of 4609 mL, total protein of 8158 mg, creatinine of 2.67 grams.

He was referred to nephrology. Renal biopsy was not recommended due to the documented chronicity of his chronic kidney disease and he was eventually started on hemodialysis

Discussion

This case highlights the limitations in methods of estimating GFR using creatinine and reviews other methods for estimating GFR. Although the eGFR was only about 15 based on his initial serum lab results, the 24 hr urine collection estimated creatinine clearance of about 45 ml/min versus the eGFR of 15. The 24-hour urinary creatinine does over estimate renal function (due to secretion of creatinine), but is more accurate than serum creatinine-based estimates given the copious urine production of patient (3-4L at times). It also is revealing that the patient's creatinine excretion was so high despite his CKD likely suggesting a very high muscle mass and a high protein intake. The cystatin C measurement of 3-3.4 is significantly lower than the creatinine estimate and this demonstrates the utility of using cystatin C in estimating renal function with a marker less affected by body mass, dietary intake, as well as gender differences.

The "take home" message is the difficulty in estimating eGFR by creatinine alone, the importance of 24-hour urine collections of creatinine and urea clearance (with the caveat that creatinine clearance over estimates eGFR due to secretion in the proximal convoluted tubule while urea clearance under estimates eGFR due to reabsorption in the cortical collecting duct). Finally, it is important to recognize the utility of new surrogates for renal filtration. The most prominent of these is cystatin C, which can be measured in serum and estimate eGFR via equations or to utilize a 24-hour cystatin C clearance measurement.[6,7]

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