References

1. Jennette JC, et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; 65:1–11. doi: 10.1002/art.37715
2. Robson JC, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis. *Arthritis Rheumatol* 2022; 74:393–399. doi: 10.1002/art.41986
3. Suppiah R, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for microscopic polyangiitis. *Arthritis Rheumatol* 2022; 74:400–406. doi: 10.1002/art.41983
4. Scott DGI, Watts RA. Epidemiology and clinical features of systemic vasculitis. *Clin Exp Nephrol* 2013; 17:607–610. doi: 10.1007/s10157-013-0830-8
5. Merkel PA, et al. Identification of functional and expression polymorphisms associated with risk for antineutrophil cytoplasmic autoantibody-associated vasculitis. *Arthritis Rheumatol* 2017; 69:1054–1066. doi: 10.1002/art.40034
6. Lyons PA, et al. Genetically distinct subsets within ANCA-associated vasculitis. *N Engl J Med* 2012; 367:214–223. doi: 10.1056/NEJMoa1108735
7. Unizony S, et al. Clinical outcomes of treatment of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis based on ANCA type. *Ann Rheum Dis* 2016; 75:1166–1169. doi: 10.1136/annrheumdis-2015-208073
8. Lionaki S, et al. Classification of antineutrophil cytoplasmic autoantibody vasculitides: The role of antineutrophil cytoplasmic autoantibody specificity for myeloperoxidase or proteinase 3 in disease recognition and prognosis. *Arthritis Rheum* 2012; 64:3452–3462. doi: 10.1002/art.34562
9. Gisslander K, et al; FAIRVASC consortium. Data-driven subclassification of ANCA-associated vasculitis: Model-based clustering of a federated international cohort. *Lancet Rheumatol* 2024; 6:e762–e770. doi: 10.1016/S2665-9913(24)00187-5

Calculators Help Estimate GFR for Adolescents Transitioning to Adult Nephrology Care

By Karen Blum

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The transition from adolescence to adulthood is a critical time in development, and estimating the glomerular filtration rate (GFR) at this juncture can help nephrologists best determine care for their patients. Fortunately, there are several calculators available to help.

Historically, physicians have used separate formulas to estimate GFR, developed in two different populations: those younger than 18 years and those aged 18 or older. These measures included the Chronic Kidney Disease in Children (CKiD) formula and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, said Susan Furth, MD, PhD, chief scientific officer, executive vice president, and an attending physician at the Children's Hospital of Philadelphia, PA, in a presentation at Kidney Week 2024.

Of the two formulas, Furth offered, "But it's important in our work to look at longitudinal changes in GFR, to look at effects on GFR decline." She explained, "For clinical decision-making, the period around late teens to early adulthood is a really vulnerable period for individuals with CKD. Being able to accurately assess GFR for finding when one should accelerate treatments to try to slow progression, or make plans for transplantation, is a really important criteria."

The CKiD study, authored by Furth and colleagues, has evaluated over 1100 participants with mild to moderate CKD, assessing risk for kidney function progression—as well as cardiovascular disease risk factors—and CKD effects on growth and neurocognitive development. They are now recruiting for the fourth cohort, targeting adolescents ages 14–17 years to follow them through transitions to adult care.

Through the study, investigators have conducted direct measurement of GFR annually for the first 2 years and every-other year after, using plasma clearance of iohexol. To date, they have calculated nearly 2700 GFR measurements.

Furth said that nephrologists who care for patients in this age group have recognized for a long time that there were "big gaps" when going from a pediatric to an adult equation. Her team previously used the revised Bedside Schwartz formula from 2009 and then compared results with the CKD-EPI equation, including age, sex, and race, and the CKiD serum creatinine and cystatin C equation in 2012. However, she said, using those measures when a child turned 18 years old could return big variances in estimated GFR (eGFR).

In a 2018 study (1), Furth's team reviewed all visits (N = 548) from 219 CKiD study participants with a median age of 19 years, of which 279 person-visits had measured iohexol GFR from 187 individuals. The CKiD serum creatinine and cystatin C equation demonstrated agreement with iohexol GFR, but both the serum creatinine CKiD equation and the CKD-EPI equation showed substantial biases in opposite directions, she said. "A simple fix was to take an average of the CKD-EPI and CKiD serum creatinine equations. This resulted in an overall valid estimate of GFR," Furth said.

As she and her colleagues continued to collect data from CKiD formulas, and some of this population moved into young adulthood, Furth and her team wanted to revisit the equations. "We knew that we needed valid, accurate estimates of GFR," she said, noting that although GFR direct measurement is more exact, it is not generally available in clinical care. "We wanted to have the best estimates possible, particularly during this transition to adult care…. We knew there were challenges in the 18-to-25-year age group, with pediatric equations underestimating GFR and adult equations overestimating GFR. We were hoping to develop equations that would be applicable across the life course for pediatric to young adult [populations with CKD]."

The team developed the CKiD U25 equation (U25) (2), which can be used to monitor kidney function and disease progression over time, for patients ages 1 to 25 years with mild to moderate kidney diseases. The equation estimates GFR using either serum creatinine or cystatin C alone or the average of both factors. U25 eGFR with sex- and age-dependent κ values can be used without bias across the pediatric age spectrum into adulthood, Furth said.

The equation can be accessed online through QxMD (qxmd.com or via the free mobile application). It factors in patient age, sex, serum creatinine, height, and cystatin C to provide serum creatinine eGFR, cystatin eGFR, and the average of both. Although it is just an estimate, it is a useful tool to have at the bedside, Furth said.

The code and software are available online for download at the CKiD study site (ckidstudy.org), under the Investigator Resources tab. Several children's hospitals have incorporated this into their electronic health records, Furth noted.

A recent study (3) compared U25 with CKD-EPI among 1491 participants from 21 studies. The mean age was 31.7 years and mean measured GFR was 92.7 mL/min/1.73 m^2. At higher GFR levels, U25 did not perform as well as CKD-EPI, she said, indicating that when working with young adults in their 20s and 30s, there is a substantial underestimation of GFR using U25.

Another available marker is the European Kidney Function Consortium (EKFC) eGFR calculator, designed to overcome the limitations of equations like U25 and CKD-EPI regarding age and race modeling. Its key element is the Q-value, the median normal value of serum creatinine in a given population. The calculator is available online through EKFC (ekfccalculator.pages.dev/) and MDApp (mdapp.co).

A recent study published in *The New England Journal of Medicine* (4) showed the performance of different equations to estimate GFR with respect to bias and P30 (the conventional measure of precision) according to age. For children known to have had CKD in childhood, who are now in their later teenage years with only mild or modest decreases in GFR, the EKFC equation or the CKD-EPI equation may perform better than U25, Furth said.

References

1. Ng DK, et al. Combination of pediatric and adult formulas yield valid glomerular filtration rate estimates in young adults with a history of pediatric chronic kidney disease. *Kidney Int* 2018; 94:170–177. doi: 10.1016/j.kint.2018.01.034
2. Pierce CB, et al. Age- and sex-dependent clinical equations to estimate glomerular filtration rates in children and young adults with chronic kidney disease. *Kidney Int* 2021; 99:948–956. doi: 10.1016/j.kint.2020.10.047
3. Inker LA, et al. Performance of GFR estimating equations in young adults. *Am J Kidney Dis* 2024; 83:272–276. doi: 10.1053/j.ajkd.2023.06.008
4. Pottel H, et al. Cystatin C-based equation to estimate GFR without the inclusion of race and sex. *N Engl J Med* 2023; 388:333–343. doi: 10.1056/NEJMoa2203769