Estimation of GFR using the CKD-EPI formula based on SCr has gained increasing acceptance, although it has not been validated specifically in those patients with GN. It may be more accurate than earlier equations, especially at values >60 ml/min per 1.73 m^2. Ethnicity, muscle bulk, sarcopenia, and the method used for creatinine measurement may influence the accuracy of estimated glomerular filtration rate (eGFR) based on SCr. This is less true when one uses a serum cystatin C biomarker to estimate GFR. In NS and hypoalbuminemia, tubular creatinine handling is altered, and CrCl- and eGFR-creatinine-based equations may overestimate true GFR by 50% or more.[16,19] GFR estimations are also unreliable during episodes of acute kidney injury (AKI) and possibly are influenced by altered creatinine generation in patients with chronic glucocorticoid-related myopathy.

In children, there are alternative validated formulas for eGFR, notably the Schwartz or Full Age Spectrum (FAS) formulas.

Practice Point 1.2.8: In children, quantify proteinuria, but goals of treatment should not be different between disease etiologies. A PCR of <200 mg/g (<20 mg/mmol) or <8 mg/m^2/hour in a 24-hour urine should be the goal for any child with glomerular disease. Acceptance of a baseline higher than this should come only with kidney biopsy evidence of kidney scarring.

Practice Point 1.2.9: The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) estimated glomerular filtration rate (eGFR) creatinine equation is preferred in adult patients with glomerular disease, and the modified Schwartz equation is preferred in children. The Full Age Spectrum (FAS) equation may be used in both adults and children (Figure 5).

All creatinine-based eGFR equations tend to overestimate true GFR in patients with NS and hypoalbuminemia. eGFR, cystatin C, or combinations of eGFR, cystatin C, and creatinine may be used in special circumstances when disturbances in creatinine generation are suspected.

Research recommendations

- Evaluation of "spot" versus "timed" urine collections in evaluation of proteinuria in specific kidney diseases
- Evaluation of urine proteomics for diagnosis and prognosis of specific forms of GN
- Evaluation of urinary biomarkers for detection and quantification of kidney fibrosis in GN
- Evaluation of whether validated GFR-estimating equations in patients with marked proteinuria can improve clinical trial outcomes and patient management

1.3 Evaluation of hematuria

Hematuria is one of the cardinal manifestations of glomerular disease. The initial detection of hematuria is often by "dipstick" analysis of a random urine specimen. Dipstick tests are very sensitive for detection of hemoglobin in urine (free or erythrocyte-related) with very few false negatives (except in patients taking large amounts of vitamin C), but with false positives in myoglobinuria or hemoglobinuria. Macroscopic or gross hematuria usually imparts a reddish or brownish "smoky" appearance to voided urine, depending on urine pH. In visible hematuria due to GN, clots do not occur. Typically, hematuria in GN is not accompanied by urinary tract symptoms.

An abnormal dipstick test for blood should be confirmed by a microscopical examination of fresh, centrifuged urine sediment by phase-contrast microscopy or brightfield optics under low- and high-power magnification. Staining of the urine sediment (Sternheimer-Malbin) can aid in the recognition of cells and formed elements. Flow-assisted cell-sorting techniques can greatly aid automated analysis of hematuria.

In patients with GN, the erythrocytes are commonly (50%–80%) misshapen (dysmorphic) and small (microcytic). The presence of casts containing red blood cells or the presence of acanthocytes (>5% of all red blood cells) usually indicates an inflammatory glomerular disease. It should be noted that among the few erythrocytes seen in a normal, properly collected urine, all are of a glomerular (dysmorphic) type.

The prognostic implications of the persistence and magnitude of hematuria can have a very significant impact on long-term outcomes of glomerular disease. Given this, findings often represent continued "low-grade" activity of the underlying glomerular inflammatory process. This aspect of hematuria as a "biomarker" of progression, for example, in IgAN,[23] is now receiving long-overdue attention. Periodic monitoring of the presence and magnitude of hematuria should be a part of the care process for all forms of glomerular disease, in our opinion.

Practice Point 1.3.1: Routine evaluation of urine sediment for erythrocyte morphology and the presence of red cell casts and/or acanthocytes is indicated in all forms of glomerular disease.

Practice Point 1.3.2: Monitoring of hematuria (magnitude and persistence) may have prognostic value in many forms of glomerular disease. This is particularly applicable to immunoglobulin A nephropathy (IgAN) and vasculitis (IgAV; Chapter 2).

Research recommendation

- Further prospective studies of the impact of persistent hematuria on prognosis for specific forms of glomerular disease and its therapeutic implications

1.4 Management of complications of glomerular disease

A number of complications of glomerular disease are a consequence of the clinical presentation rather than the specific histopathologic pattern. Active management of such complications should always be considered to have a positive impact on the natural history of the disease and to significantly improve morbidity and even mortality. These include measures to control edema, reduce proteinuria, treat elevated systemic arterial blood pressure (BP), slow disease progression, and