What diagnostic tools are reliable for assessing renal function:
Options: creatinine, cystatin C, 99Tc-DPTA GFR and other clearance studies

IT IS CLEAR FROM KDIGO GUIDELINES THAT RENAL FUNCTION MUST BE ASSESSED

Creatinine as a poor marker of GFR in patients with SB initially suggested in paper in 1997 by Quan et al comparing relationship with serum cr and iothalamate clearance study. Many studies suggest cr is a poor marker for renal function in patients with SB and suggest other markers to utilize. GFR using Schwarz formula significantly overestimates DPTA GFR in nonambulatory patients and there is poor correlation between DPTA GFR and Schwartz formula. No large studies exist. I believe there is a consensus that if patient is non-ambulatory, that creatinine is not good marker for renal function and that IN ADDITION to creatinine another measure should be obtained. Creatinine Schwartz based GFR formulas require height, which MUST be measured accurately. Adult creatinine based formulas may or may not require an anthropometric measure (MDRD--no, Crockoft-Gault—weight.)

Cystatin C: there are GFR formulas based on cystatin C that have been assessed in small studies of patients with SB. Studies have suggested that these equations do not require anthropometric data and might be better in patients with SB. Some studies reported good correlation between cystatin based GFR studies and DPTA GFR studies. Studies are small and single center. In addition, cystatin C is not a routine lab test, is not available in many centers labs and thus is a send out. Many physicians are not accustomed ordering cystatin C or interpreting results or using these formulas outside of studies.

Clearance studies GFR: (inulin, iohexol, 51-cr-EDTA, recent radioisotope: 99Tc-DPTA)—have been considered the gold standard in the past. Likely readily available and easily performed (requires injection, and multiple timed blood draws) and should be correlated with serum creatinine at the same time to determine difference in particular patient between creatinine as marker and DPTA GFR. There are criticisms in the literature on DPTA GFR calculations because body surface area must be calculated (anthropometric measure) and given the difficulties in assessing inht/wt in patients with SB, this may also result in some inaccuracies.

GUIDELINES: KDIGO 2012 CKD GUIDELINES
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IMPORTANCE OF ASSESSING FOR GFR!!!!!!

1.4.3: Evaluation of GFR
We recommend using serum creatinine and a GFR estimating equation for initial assessment. (1A)

We suggest using additional tests (clearance measurement) for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate. (2B)

We recommend that clinicians (1B):

- Use a GFR estimating equation to derive GFR from serum creatinine (eGFR_{creat}) rather than relying on the serum creatinine concentration alone. Understand clinical settings in which eGFR_{creat} is less accurate.

We recommend that clinical laboratories should (1B):

- Measure serum creatinine using a specific assay with calibration traceable to the international standard reference materials and minimal bias compared to isotope-dilution mass spectrometry (IDMS) reference methodology.
- Report eGFR_{creat} in addition to the serum creatinine concentration in adults and specify the equation used whenever reporting eGFR_{creat}.
- Report eGFR_{creat} in adults using the 2009 CKD-EPI creatinine equation. An alternative creatinine-based GFR estimating equation is acceptable if it has been shown to improve accuracy of GFR estimates compared to the 2009 CKD-EPI creatinine equation.

When reporting serum creatinine:

- Concentration be reported and rounded to the nearest whole number when expressed as standard international units (\(\text{lmol/l}\)) and rounded to the nearest 100\(^{\text{th}}\) of a whole number when expressed as conventional units (\(\text{mg/dl}\)).

When reporting eGFR_{creat}:

- We recommend that eGFR_{creat} should be reported and rounded to the nearest whole number and relative to a body surface area of 1.73 m\(^2\) in adults using the units ml/min/1.73 m\(^2\).
- eGFR_{creat} levels less than 60 ml/min/1.73 m\(^2\) should be reported as “decreased.”

1.4.3.5: We suggest measuring cystatin C in adults with eGFR_{creat} 45–59 ml/min/1.73 m\(^2\) who do not have markers of kidney damage if confirmation of CKD is required. (2C)

- If eGFR_{cys}/eGFR_{creat-cys} is also <60 ml/min/1.73 m\(^2\), the diagnosis of CKD is confirmed.
- If eGFR_{cys}/eGFR_{creat-cys} is >60 ml/min/1.73 m\(^2\),
the diagnosis of CKD is not confirmed.

1.4.3.6: If cystatin C is measured, we suggest that health professionals (2C): use a GFR estimating equation to derive GFR form serum cystatin C rather than relying on the serum cystatin C concentration alone. Understand clinical settings in which eGFRcystatin and eGFRcreat-cys are less accurate.

1.4.3.7: We recommend that clinical laboratories that measure cystatin C should (1B):

measure serum cystatin C using an assay with calibration traceable to the international standard reference material.

report eGFR from serum cystatin C in addition to the serum cystatin C concentration in adults and specify the equation used whenever reporting eGFRcys and eGFRcreat-cys.

report eGFRcys and eGFRcreat-cys in adults using the 2012 CKD-EPI cystatin C and 2012 CKD-EPI creatinine-cystatin C equations, respectively, or alternative cystatin C-based GFR estimating equations if they have been shown to improve accuracy of GFR estimates compared to the 2012 CKD-EPI cystatin C and 2012 CKD-EPI creatinine-cystatin C equations.

When reporting serum cystatin C:

We recommend reporting concentration rounded to the nearest 100th of a whole number when expressed as conventional units (mg/l).

When reporting eGFRcys and eGFRcreat-cys:

We recommend that eGFRcys and eGFRcreat-cys be reported and rounded to the nearest whole number and relative to a body surface area of 1.73 m² in adults using the units ml/min/1.73 m².

We recommend eGFRcys and eGFRcreat-cys levels less than 60 ml/min/1.73 m² should be reported as decreased

1.4.3.8: We suggest measuring GFR using an exogenous filtration marker under circumstances where more accurate assessment of GFR will impact on treatment decisions (2B)

Studies that suggest other measures of renal function to utilize:
1. Quan, Albert et al; Serum Creatinine is a poor marker of glomerular filtration rate in patients with spina bifida. Developmental Medicine and Child Neurology, 39:808-810, 1997  
   a. This study compared Cr and 125I-iothalamate GFR studies and suggested that obtaining a GFR from a clearance study and not serum creatinine was only reliable measure to assess renal function.  
      i. 19 patients, age 3-18

   a. Best review of all the options for measurement of GFR.

   a. Specific analysis in spina bifida cohort with comparison to other groups.  
      i. Filleq and Schwartz formulas strikingly overestimated IoGFR (iothalamate) compared with other formulas, whereas the cysCrEq GFR estimate WHICH CONTAINS A TERM FOR PRESENCE OF SPINA BIFIDA was extremely similar to IoGFR.  
      ii. CysCrEq table 3, has a special formula for spina bifida.

   a. Although comparing multiple studies and GFR studies, does have section on Zapitellicyscreq and sensitivity and specificity and diagnostic accuracy and comparison to DPTA GFR

   a. compares cystatin C Filler and Lepage equation, Schwartz formula and DOTA GFR in 28 children with SB  
      i. suggests correlation between DPTA GFR and Filler cystatin C equation, not Schwartz formula. Also suggests using cystatin based formula due to lack of need for anthropometric data. Majority had normal GFR

   a. 65 patients with spinal dysraphism in Sweden  
   b. Compared chromium 51 EDTA clearance and cystatin C.  
      i. Agreed with prior studies that showed that at mild impaired GFR, a full clearance study can not be replaced by measurement of cystatin c. 10 patients with slight to moderate reduced GFR by clearance study had cystatin C in normal range. Using Filler cystatin C formula, 4/10 with low clearance GFR were identified.

   a. 69 patients. Suggests use of Cystatin C, but not compared to clearance study. But has good review of pros and cons of use of cysatin c, and
limitations of use-. Also suggests use as a screen to determine need for other testing to save money (use this prior to clearance GFR or DMSA renal scan).

Once upper tract changes occur are they reversible?

Will be important in this discussion to discuss difference between findings on imaging of upper tract which might be reversible, such as NEW HYDRONEPHROSIS, as a marker of change in bladder dynamics and something that with intervention will change and prevent upper tract scarring versus renal scarring, which is not reversible.

There is plenty of old data on renal scarring in obstructive uropathy and reflux nephropathy and resultant renal scarring and CKD. More important to this discussion would be ongoing surveillance for NEW FINDINGS that suggest change, and use of urodynamics and other evaluation (?tethered cord?) to assess reasons for change, implement treatment, to PREVENT RENAL SCARRING.

The effects of delayed diagnosis and treatment in patients with an occult spinal dysraphism.
Satar N1, Bauer SB, Shefner J, Kelly MD, Darbey MM.

These observations confirm that older children and adults with occult spinal dysraphism are more likely to present with irreversible urological and neurological findings than younger children, and so it is imperative that a diagnosis be made and treatment be instituted as early as possible.

Renal cortical deterioration in children with spinal dysraphism: analysis of risk factors.
DeLair SM1, Eandi J, White MJ, Nguyen T, Stone AR, Kurzrock EA.

By limiting the definition of renal deterioration to cortical loss, we identified relevant risk factors: reflux, female sex, and delayed initiation of clean intermittent catheterization.
Prevention of chronic kidney disease in spina bifida.
Filler G1, Gharib M, Casier S, Lödige P, Ehrich JH, Dave S.

Discussion on implementation of treatment for prevention of renal scarring.
Development of secondary VUR as marker of renal risk
Urodynamic studies can predict risk of hydronephrosis and reflux and prognosticate renal damage.
Highlights tools for surveillance and proactive approach for early intervention.

Renal preservation in children with neurogenic bladder-sphincter dysfunction followed in a national program.
Wide P1, Glad Mattsson G, Mattsson S.

\Single center review on bladder findings and renal scarring and emphasizes importance of follow-up (many patients with scarring were not compliant with treatment and follow-up)

Diagnostic accuracy of Tc-99m DMSA scintigraphy and renal ultrasonography for detecting renal scarring and relative function in patients with spinal dysraphism.
Veenboer PW1, Hobbelink MG2, Ruud Bosch JL1, Dik P3, van Asbeck FW4, Beek FJ5, de Kort LM1.

USE OF DMSA TO ASSESS FOR RENAL SCARRING, MISSED BY US