COLLEGE of AMERICAN PATHOLOGISTS

Educational Discussion: 2020-A Chemistry Survey (C)

Kidney Biomarkers: the Kidney Profile Order, Urine Albumin-Creatinine Ratio (uACR), and Estimated Glomerular Filtration Rate (eGFR)

The C-C 2019 General Chemistry Survey included questions regarding laboratory practices for ordering the newly introduced Kidney Profile; for ordering and reporting urine albumin, and the urine albumin-creatinine ratio (uACR); and for reporting eGFR from serum creatinine results for adult and pediatric patients. The findings from this Survey are described here.

Kidney Profile

The kidney profile order was introduced in 2018 to encourage and make it easy for physicians to order the correct tests, eGFR from serum creatinine and uACR, for testing and managing patients at risk of or being followed for chronic kidney disease[1,] Among USA participants, 15% of respondents (904 of 5953) offered the Kidney Profile. Among international participants, 26% of respondents (303 of 1152) offered the Kidney Profile. Laboratories are encouraged to work with their clinical colleagues to introduce the Kidney Profile as an orderable test panel.

Urine albumin, and the urine albumin-creatinine ratio

The table below shows which names are used most frequently to order a urine albumin test.

Test order name	USA labs	International labs
Albumin, urine	333	168
Albumin-Creatinine Ratio (uACR)	911	379
Microalbumin	3537	466
Other	681	91
Total responding	5462	1104

The “other” responses for test order names included a large number that do not offer the test and similar responses, and a smaller number of terms with variations of the microalbumin/creatinine ratio. A few laboratories used “Diabetic Nephropathy Screen” as a test order name for uACR. The National Kidney Disease Education Program (NKDEP) recommends using the test order term “Albumin, urine” to be clear what is being measured[2]. The term “Microalbumin” should not be used because there is no such molecule in the urine, and practitioners can be confused by the misunderstanding that a smaller molecular form of albumin is found in the urine or that the term implies a reference interval for the test result from 30-300 mg albumin per g creatinine.

Result reporting practices for urine albumin and the uACR are shown in the following tables.

Test reporting	USA labs	International labs
Urine albumin, urine creatinine and uACR separately	3457	642
Urine albumin by itself	563	81
Urine albumin and creatinine separately without uACR	227	35
Only uACR	216	102
Total responding	4463	860

Test reporting units for uACR	USA labs	International labs
mg/g	2367	327
µg/mg	759	30
mg/mmol	245	348
g/mol	26	23

Other	651	130

The “other” responses for reporting units included a mix of “do not perform the test” and various units that are inconsistent with the type of result suggesting an incorrect response. The NKDEP recommends to always report the uACR because the ratio of albumin to creatinine adjusts for hydration status and has been shown to correlate highly with the 24-hour albumin excretion rate using, preferably, a first morning void or a random, or spot, urine collection. The urine albumin concentration should never be reported alone. The uACR should always be reported for detecting kidney disease as well as stratification of risk. Because different countries and regions use conventional or SI units for creatinine, the NKDEP recommends reporting uACR as mg/g or mg/µmol consistently in a region.

Estimated Glomerular Filtration Rate (eGFR)

eGFR for ADULTS (≥18 years old)

The NKDEP recommends reporting eGFR along with serum (or plasma or whole blood) creatinine for adults because an eGFR value is more easily related to a patient’s kidney function than is the creatinine concentration by itself and eGFR assists practitioners to more easily identify patients with CKD[3].

The eGFR observations are not categorized by US and international laboratories to be consistent with data from prior years’ Surveys. Of the 6217 laboratories that responded, 92% were reporting eGFR for adults as recommended by the NKDEP (Figure 1) that is a consistent reporting practice since 2013. Figure 2 shows that, of those reporting eGFR for adults, 85% reported eGFR with all creatinine results as recommended by NKDEP because most computer systems are not able to discriminate clinical conditions when eGFR is less reliable. Selective reporting of eGFR was practiced by 15% of respondents with 8% only reporting eGFR when requested and 3% only for outpatients. The NKDEP web site cautions that there are clinical conditions when creatinine is less reliable as an indicator of kidney function including: very large or very small body size or muscle mass, clinical conditions which decrease muscle mass (eg, cancer, paraplegia, amputation), nutritional status (eg, meat increases and a vegan diet decreases blood creatinine concentration), pregnancy which increases GFR and decreases creatinine concentration, and patients with serious comorbid conditions or with metabolically unstable kidney function such as for some inpatients and those with acute kidney injury. However, reporting eGFR with all adult creatinine results is still recommended because the clinician is able to determine the suitability of an eGFR result for a patient's condition.

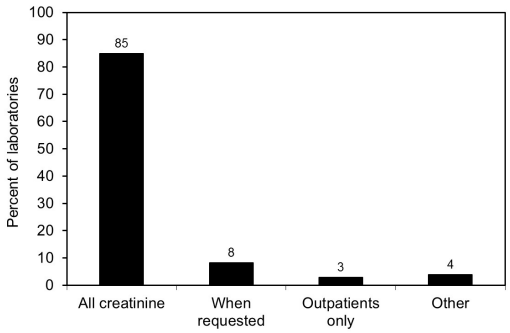

Figure 1. Situations when eGFR is reported

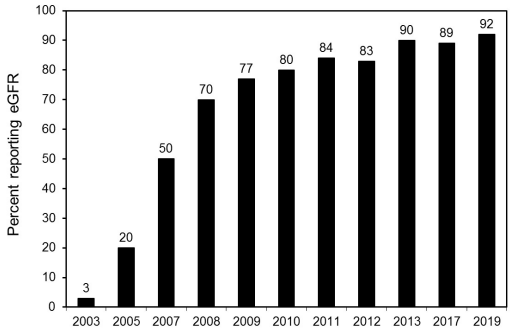

Figure 2. Percent of laboratories reporting eGFR

Figure 3 shows that 76% of laboratories were using an isotope dilution mass spectrometry (IDMS) traceable version of the MDRD 4-variable equation (45%)[4] or the CKD-EPI equation (31%)[5]. This usage represents an increase from 65% of laboratories using an IDMS traceable equation two years ago and a greater proportion using the CKD-EPI equation. All major global manufacturers have now standardized creatinine calibration to be traceable to an IDMS reference measurement procedure. Consequently, all laboratories should be reporting standardized creatinine results and using an eGFR equation that is suitable for standardized creatinine values. The CKD-EPI equation is recommended by the most recent

2012 Kidney Disease Improving Global Outcomes[6] clinical practice guidelines to standardize the equation used, and endorsed in the USA by the Kidney Disease Outcomes Quality Initiative[7].
Of concern in Figure 3 are the 23% of laboratories that are still using the original MDRD 4-parameter, MDRD 6-parameter, Cockcroft-Gault (C-G) or other older equation. IDMS traceable calibration caused a method dependent 5-30% reduction in creatinine results compared to older calibration schemes[8]. Thus, when an IDMS traceable creatinine result is used with an older estimating equation, the eGFR will be erroneously high which may lead to erroneous decisions regarding patient treatment. Laboratories using an older equation should change to the IDMS traceable version of the CKD-EPI equation, preferably, or the IDMS traceable version of the MDRD equation.

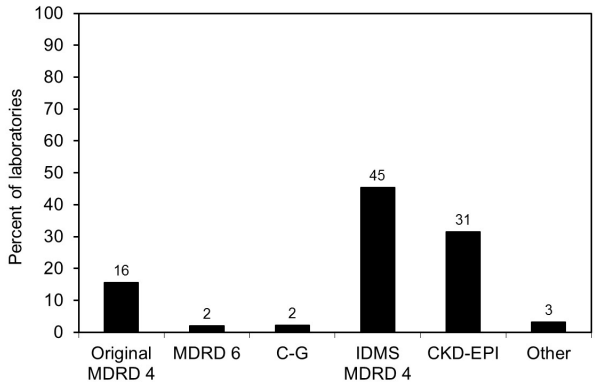

Figure 3. eGFR equation used by laboratories

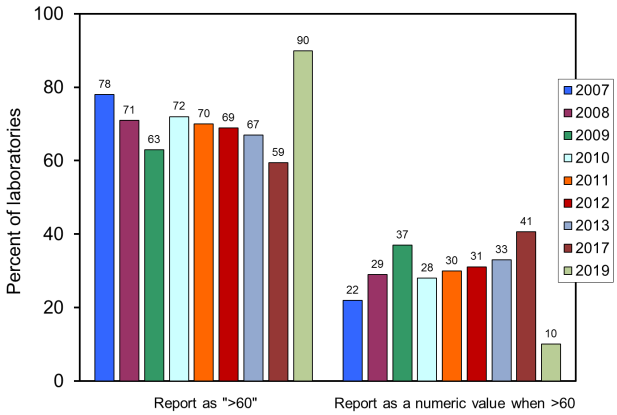

Figure 4. Reporting eGFR values >60 mL/min/1.73m^2

Figure 4 shows that 10% of laboratories are reporting numeric values for eGFR >60 mL/min/1.73 m^2. Since Figure 3 indicates that 31% of laboratories are using the CKD-EPI equation, presumably these laboratories represent those reporting higher eGFR values. The 10% reporting numeric values >60 mL/min/1.73 m^2 is a substantial reduction from preceding years that raises the possibility of misunderstanding the question in the current or earlier years' Surveys. The MDRD equation should not be used to report numeric values >60 mL/min/1.73m^2 because the values are biased lower than true measured GFR values. Laboratories reporting numeric values for eGFR >60 mL/min/1.73 m^2 should be using the CKD-EPI equation. The CKD-EPI equation uses the same variables as the MDRD equation, is more accurate than the MDRD equation at values >60 mL/min/1.73m^2 (2), and may improve classification of patients into risk categories at eGFR values near the 60 mL/min/1.73m^2 decision area[9].

eGFR for CHILDREN (<18 years old)

Among the respondents to the Survey questions, 10% indicated they report eGFR values for pediatric patients calculated from a creatinine result. It is more difficult to automatically report values for pediatric patients because information on the height of the patient is needed which is typically not available in a laboratory information system or instrument middleware computer. Consequently, most laboratories do not report an eGFR for pediatric patients. Estimating equations appropriate for use in children with IDMS standardized creatinine results are not as well developed as for adults. The only equation suitable for use with IDMS standardized creatinine results is referred to as the "bedside" Schwartz equation[10]. The term "bedside" was suggested by Dr. Schwartz to indicate that the value is an estimate suitable for general clinical purposes but may not be suitable for critical decisions such as some drug dose decisions.

In this Survey, only 27% of respondents, no change from this question 2 years ago, are using the correct IDMS "bedside" version of the Schwartz equation, with 39% using the incorrect original Schwartz equation that gives erroneously high estimates of GFR when used with IDMS traceable creatinine results. Of particular concern is the observation that 20% of laboratories are using an adult eGFR equation for pediatric patients. None of the adult equations have been validated for use in children. Laboratories

should use the newer IDMS traceable “bedside” Schwartz equation to estimate eGFR from a creatinine result for children.
Importantly, the “bedside” Schwartz equation requires the height in cm for calculation that may pose availability and laboratory information system challenges for implementation. If the height data cannot be captured, the laboratory should not report an estimate, but instead refer the physician to the “bedside” Schwartz equation [eGFR (mL/min/1.73 m²) = (0.41 × Height in cm) / Creatinine in mg/dL] available at the NKDEP web site[11].

Of all respondents, 7% offer cystatin C in their laboratories with 93% sending the test to a referral laboratory. Cystatin C is not affected by muscle mass after age 1 so eGFR calculated from cystatin C is particularly useful for pediatric patients, those with muscle wasting conditions, amputees, body builders and to supplement eGFR calculated from creatinine in conditions when creatinine is less reliable as mentioned earlier.

Additional information on reporting urine albumin and eGFR is available at the NKDEP web site[12].

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