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EDITORIAL COMMENTARY

Measuring glomerular filtration rate from plasma clearance of ^{51}Cr-EDTA: quality assurance

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The glomerular filtration rate (GFR) is the most important single parameter describing the complex functions of the kidney. GFR estimates are recommended for the definition, classification, screening and monitoring of kidney diseases. For nearly 100 years GFR has been evaluated by endogenous creatinine. In the individual patient the reciprocal concentration of creatinine in the blood is proportional to GFR. However, the correlation between creatinine concentration and GFR differs between patients because the production of creatinine in the muscles is not the same, i.e. the greater the muscle mass the higher is the concentration of creatinine in the blood. Consequently, creatinine concentration offers only a rough estimate of GFR.

The production rate of creatinine can be measured by its excretion in urine, but this is both cumbersome and unreliable. During recent years, it has become more common to estimate creatinine production from empirical equations. Instead of measuring the production rate of creatinine in the individual patient, values from former studies in similar patients are used. The MDRD formula is the most often recommended [1]. The so-called estimated GFR (eGFR) is a more accurate measurement of GFR than the creatinine concentration. However, eGFR is not a superior method for monitoring changes in GFR to creatinine concentration.

Estimating GFR from creatinine is simple and cheap. However, the use of exogenous tracers for the measurement of GFR offers important advantages. After intravenous injection of a tracer, which is excreted from the body by glomerular filtration only, GFR can be measured from its plasma clearance, i.e. excretion rate relative to the plasma concentration or from the ratio between the injected dose and the area under the plasma concentration curve. Collection of urine is not needed, making the technique very reliable. ^{51}Cr-EDTA is the most often used tracer but the x-ray contrast medium iohexol has become popular in recent years. The plasma clearance technique is recommended when a reliable value of GFR is needed, e.g. in patients treated with nephrotoxic drugs for cancer. Treatment dose is adjusted according to GFR (the lower the GFR, the smaller the dose). For this purpose eGFR is unreliable [2].

Plasma clearance of ^{51}Cr-EDTA involves a single intravenous injection followed by blood sampling from 2 or 3 to 4, 5 or 24 h. The lower the GFR, the later is blood sampling needed. The method is associated with several potential errors, including failure in injecting the dose, errors in preparing the standard dilution, in pipetting, in blood sampling and in counting. Therefore, when measuring GFR in clinical routine there is a need for quality control of the result. Unfortunately, international guidelines for measuring renal function do not deal with quality assurance [3]. Plasma clearance is a functional test in the intact organism and not a clinical chemical analysis. This means that quality control cannot be done by sending a "standard" for analysis to the department doing the plasma clearance studies. Furthermore, evaluation of results by comparison with other methods for estimating GFR is of no help because the plasma clearance technique is much more reliable than other methods, e.g. eGFR. Therefore, quality assurance must be done in a different way. Nevertheless, quality assurance is possible, e.g. the distribution volume of ^{51}Cr-EDTA, which equals the extracellular fluid volume (ECV), can be estimated from the plasma curve and the GFR from the slope of the curve and ECV. GFR assessed from plasma clearance and from the slope of the curve should agree [4]. Furthermore,

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GFR varies substantially between patients, but the ECV relative to body weight, or better to body surface area (BSA), is very tightly regulated. Quality assurance can be done on the estimates of ECV/BSA, which should be within "normal values".

In this issue of EJNMMI, Michael Peters and coworkers present a comparative study of the variation in ECV relative to BSA measured from plasma clearance data [5]. Their study included 1,878 renal donors from 15 departments in the United Kingdom. They found significant differences in the coefficient of variation in the ECV/BSA ratio among the 15 centres, indicating differences in quality (the greater the variation in ECV/BSA, the less reliable the GFR). In 2004, the British Nuclear Medicine Society published guidelines for the measurement of GFR using plasma sampling with the purpose of assisting specialists in nuclear medicine in recommending, performing, interpreting and reporting the results of GFR studies [6]. However, the guidelines do not seem to have led to homogeneous quality. Centres undertaking routine GFR measurements in renal donors may use the kidney transplant database of Peters et al. to assess the technical robustness of their GFR values. However, the database may not be valid for patients with lower GFR and probably greater variation in the ECV scaled to BSA. Plasma clearance of ^{51}Cr-EDTA is used in the clinical setting when a reliable value of GFR is needed. To meet this demand it is necessary to have guidelines not only for how to do the study but also for the subsequent quality control of the results.

References

1. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145:247–54.
2. Hartlev LB, Rotbøl CB, Bluhme H, Palshof T, Rehling M. Monitoring renal function in patients treated with cytostatics. Ugeskr Laeger. 2008;170:3664–67. In Danish.
3. Blaufox MD, Aureli M, Bubeck B, Fommei E, Piepsz A, Russell C, et al. Report of the Radionuclides in Nephrourology Committee on Renal Clearance. J Nucl Med. 1996;37:1883–90.
4. Bird NJ, Peters C, Michell AR, Peters AM. Using the slope-only technique and estimated glomerular filtration rate for checking the reliability of slope-intercept measurement of glomerular filtration rate. Nucl Med Commun 2008;29:1086–92.
5. Peters AM, Howard B, Neilly MD, Seshadri N, Sobnack R, Hooker CA, et al. The reliability of glomerular filtration rate measured from plasma clearance: a multi-centre study of 1,878 healthy potential renal transplant donors. Eur J Nucl Med Mol Imaging. 2012. doi: 10.1007/s00259-011-2024-5.
6. Fleming JS, Zivanovic MA, Blake GM, Burniston M, Cosgriff PS. Guidelines for the measurement of glomerular filtration rate using plasma sampling. Nucl Med Commun. 2004;25:759–69.