Use of cystatin C for precise assessment of kidney function and cardiovascular risk

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ABSTRACT: In many situations, it is essential that the physician knows a patient’s kidney function as precisely as possible. The glomerular filtration rate (GFR) is calculated in order to assess kidney function. Various equations and methods exist in that regard, each of which has its advantages and disadvantages. As a paper published today in NDT [1] has now shown, there are clear scientific findings on how to calculate GFR optimally for best possible precision.

The glomerular filtration rate (GFR) is normally specified as a measure of kidney function. The GFR is the volume of blood that the kidneys filter per minute (the unit of measurement, in relation to a standardized body surface area, is therefore ml/min/1.73 m²). To calculate or estimate GFR (eGFR= estimated GFR), an equation based, inter alia, on the laboratory parameter serum creatinine is mostly applied. Creatinine, a non-protein nitrogenous substance, is a breakdown product of muscle metabolism that is released continuously and excreted in urine (making it a urinary substance). If kidney function is impaired, eGFR decreases and serum creatinine increases. However, because the body’s own creatinine production depends on various factors (e.g. age, gender and muscle mass), the significance of creatinine-based eGFR (eGFRcr) is a recurrent topic of discussion among specialists. For example, the kidney function of a delicate elderly lady (with low muscle mass and correspondingly lower serum creatinine) may be wrongly assessed as normal, based on her creatinine level,
even though her kidney function may be significantly reduced. Conversely, the muscular creatinine production in a bodybuilder may cause elevated serum creatinine values and thus lead arithmetically to a low eGFR (despite normal kidney function). The endogenous protein Cystatin C (Cys-C), which is permanently released in the metabolism of almost all body cells, therefore appears to be more suitable as a marker than serum creatinine. The volume of Cys-C amount is independent of age, gender and muscle mass – potential confounding factors in cystatin-based eGFR estimation (eGFR$_{cys}$) are inflammation, cancer, thyroid dysfunction or steroid therapy. Cys-C measurement is also more expensive than creatinine, and the test is not available in every laboratory.

An equation for estimating eGFR that includes both parameters (eGFR$_{cr-cys}$) has been shown to provide the most accurate approximation of true GFR, not only in early stages, but also in late stages of kidney disease. This may be due to the fact that the confounding factors of the two parameters are independent of each other and play a less significant role in the combined equation eGFR$_{cr-cys}$, according to the authors. eGFR$_{cr-cys}$ is particularly suitable, therefore, when it is important to know how well kidneys function as precisely as possible and at an early stage (e.g. to calculate the dosage of certain drugs, for enrolment in studies, or in the case of potential kidney donors).

“Accurate measurement is needed for the early detection of CKD. The ERA-EDTA recommends that eGFR$_{cys}$ and eGFR$_{cr-cys}$ be implemented as the new standard”, emphasizes Professor Denis Fouque, Lyon/France, NDT’s Editor-in-chief.

Restriction of kidney function is known to worsen the prognosis of patients with cardiovascular disease. “eGFR$_{cys}$ and eGFR$_{cr-cys}$ could be used in anybody with an eGFR$_{cr}$ of 45-60 or 60-90 ml/min/1.73 m$^2$ plus another cardiovascular risk factor to confirm diagnosis/staging of CKD. The lowest identified eGFR should be used for forward planning”, explains corresponding author, Dr. Jennifer Lees, Glasgow. “EGFR$_{cys}$ should be used in parallel with traditional cardiovascular risk factors in order to produce a more exact prediction of individual risk and to optimize the primary prevention cardiovascular disease.”


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