Chronic Kidney Disease
Creatinine Determination Most Effective Test

Widespread diseases such as high blood pressure and diabetes may ultimately have a severe effect on the kidneys. The functional impairment of the kidney is surprisingly common worldwide, and its incidence is increasing. In order to avoid costly and cumbersome therapies culminating in kidney replacement, it is essential to diagnose impaired kidney function early.

The best marker for kidney function is the glomerular filtration rate (GFR). It is also the earliest indicator for clinically silent cases of impaired kidney function. A list of gender and age-specific reference values is given in table 1. Nowadays, a cost-effective way to assess GFR is through estimation of creatinine clearance using endogenous markers, while the calculation using specified exogenous markers is considered the gold standard. The calculation of a creatinine-based estimated GFR (eGFR) according to defined formulae takes parameters such as age, weight, gender, ethnic background and the serum creatinine result into account. The following formulae are widely used:

1. Cockroft-Gault formula

CCr* (ml/min) = (140-age in years) x Serum creatinine (mg/dl)$^{-1}$ x (body weight (kg)/72)
(Correction factor for women: 0.85) *=Creatinine Clearance
This formula estimates a creatinine clearance without considering tubular creatinine clearance. This results in a systematic overestimation of the GFR. Since this formula includes a weight factor, it is considered suitable for the monitoring of renal function under medications affecting kidney performance.

2. MDRD forumla

eGFR ((ml/min x (1.73 m^2)$^{-1}$) = 175 x (Serum creatinine in mg/dl)$^{-1.154}$ x (age in years) $^{-0.203}$
(Correction factor for women: 0.742)
(Correction factor for Africans: 1.18)
This formula includes age, gender and ethnic background and is therefore capable of detecting GFR impairment earlier than serum creatinine alone. However, in early and middle stages of renal impairment, the GFR estimate is too high, which makes the formula less suitable for the monitoring of chronic kidney disease progress and for children.

3. Counahan-Barratt formula

eGFR (ml/min) = 0.43 x height in cm x (Serum creatinine in mg/dl)$^{-1}$
This formula significantly overestimates GFR by 20-30% and is mainly used for children.

Another internal marker for renal function is cystatin C. Reliable tests to quantify this parameter have been on the market for some time. Its great advantage is the fact that it is not dependent on muscle mass, age and gender up to 50 years of age. However, this parameter is affected by nicotine abuse, hyperthyroid disease and glucocorticoid therapy. Another advantage of cystatin C is that only the serum value is needed for the GFR estimation formula:

1. Hoek et al. formula
eGFR ((ml/min x (1.73 m^2)$^{-1}$) = 80.35 x (serum cystatin C in mg/l – 4)$^{-1.68}$
This formula is often used for adult patients, as it is more sensitive than the MDRD formula.

2. Grubb et al. formula
eGFR ((ml/min x (1.73 m^2)$^{-1}$) = 84.69 x (serum cystatin C in mg/l)$^{-1.68}$ x 1.384
This cystatin C based formula is mainly used for children < 14 years due to its improved reliability over the Counahan-Barratt formula.

Summary:
A number of suitable test parameters exist to determine impaired renal function. Apart from issues of sensitivity and reliability, the laboratory will also take economical aspects into account. The most cost-effective test is a creatinine determination using the Jaffe method. More precise, but also more expensive, is a creatinine determination using an enzymatic test. A cystatin C test is approximately 20-30 times more expensive than a creatinine test and may therefore be restricted to selected patient groups.

(Source: Dtsch Arztebl Int 2009; 106 (51-52): 849-54)

Table 1: Reference Ranges of GFR

Age	Men	Women	Units
Prematurely born	> 0.5		ml x min^{-1} x kg^{-1}
Newborn	> 10		ml x min^{-1} x kg^{-1}
2 - 8 weeks	16.3 - 44.6		ml x min^{-1} x $(1.73m^2)^{-1}$
3 - 12 months	> 70		ml x min^{-1} x $(1.73m^2)^{-1}$
1 - 20 years	> 80		ml x min^{-1} x $(1.73m^2)^{-1}$
20 - 29 years	77 - 179	71 - 165	ml x min^{-1} x $(1.73m^2)^{-1}$
30 - 39 years	70 - 162	64 - 149	ml x min^{-1} x $(1.73m^2)^{-1}$
40 - 49 years	63 - 147	58 - 135	ml x min^{-1} x $(1.73m^2)^{-1}$
50 - 59 years	56 - 130	51 - 120	ml x min^{-1} x $(1.73m^2)^{-1}$
60 - 69 years	49 - 113	45 - 104	ml x min^{-1} x $(1.73m^2)^{-1}$
70 - 79 years	42 - 98	39 - 90	ml x min^{-1} x $(1.73m^2)^{-1}$
80 - 89 years	35 - 81	32 - 75	ml x min^{-1} x $(1.73m^2)^{-1}$