

Claims

1. Use of a marker set comprising at least creatinine, dimethyl sulfone, and valine in an in vitro method for calculating a glomerular filtration rate of an individual and/or in an in vitro method for providing an indicator of a pathophysiologic factor of an impaired glomerular filtration rate.
2. Use according to claim 1, **characterized** in that the marker set comprises creatinine, dimethyl sulfone, myo-inositol, and valine.
3. Use according to claim 1, **characterized** in that the marker set comprises creatine, creatinine, dimethyl sulfone, glycerol, and valine.
4. Use according to any of the preceding claims, **characterized** in that the pathophysiologic factor is at least one of the group consisting of renal failure, renal co-morbidity, extra-renal co-morbidity, altered renal filtration, reabsorption and/or secretion capability, uremia, renal metabolic acidosis, renal oxidative stress, altered renal gluconeogenesis, amyotrophy, creatinine to muscle mass ratio, changes of gut microbiome and/or tubular hyperosmolality.
5. Marker set comprising at least creatinine, dimethyl sulfone, and valine for use in diagnostics of renal function.
6. In vitro method for calculating a glomerular filtration rate of an individual, comprising the following steps:
 - a) providing a blood sample from an individual,
 - b) determining the concentration of at least three substances, namely, of at least creatinine, dimethyl sulfone, and valine in the blood sample by analyzing the blood sample with a suited measuring technique, and
 - c) calculating a predicted glomerular filtration rate from the determined concentrations of the substances.

7. Method according to claim 6, **characterized** in that the predicted glomerular filtration rate is calculated by applying at least one of the following equations:

a)
$$GFR = a - b \log(\text{substance 1}) - c \log(\text{substance 2}) \\ * d \log(\text{substance 3})$$
 Equation 3

wherein

- a is a number in the range of 100 to 260;
 b is a number in the range of 10 to 100;
 c is a number in the range of 1 to 10;
 d is a number in the range of 10 to 100; and
 (substance n) denotes the concentration of the respective substance n;

b)
$$GFR = \exp(f) * (\text{substance 4})^{-g} * (\text{substance 5})^{-h} \\ * (\text{substance 6})^i$$
 Equation 4

wherein

- f is a number in the range of 1 to 20;
 g is a number in the range of 0.1 to 2.0;
 h is a number in the range of 0.1 to 2.0;
 i is a number in the range of 0.1 to 2.0; and
 (substance n) denotes the concentration of the respective substance n;

c)
$$GFR_A = \exp(-j) * (\text{substance 7})^{-k} * (\text{substance 8})^l \\ * (\text{substance 9})^m * (\text{substance 7})^{o \log(\text{substance 8})},$$
 Equation 5

$$GFR_B = p - q \log(\text{substance 7}) - r \log(\text{substance 10})$$
 Equation 6

wherein

- j is a number in the range of 0.1 to 10;
 k is a number in the range of 0.1 to 2.0;
 l is a number in the range of 0.1 to 10;
 m is a number in the range of 0.1 to 2.0;

o is a number in the range of 0.1 to 2.0;

p is a number in the range of 100 to 360;

q is a number in the range of 10 to 100;

r is a number in the range of 1 to 40;

(substance n) denotes the concentration of the respective substance n;

GFR_A denotes the predicted GFR for a first GFR range and

GFR_B denotes the predicted GFR for a second GFR range;

$$\begin{aligned} \text{d)} \quad GFR_A &= \exp(s) * (\text{substance } 11)^t * (\text{substance } 12)^u \\ &\quad * (\text{substance } 11)^{-v \log(\text{substance } 13)}, \end{aligned} \quad \text{Equation 7}$$

$$\begin{aligned} GFR_B &= w - x \log(\text{substance } 14) - y \log(\text{substance } 15) \\ &\quad - z \log(\text{substance } 14) * \log(\text{substance } 13) \end{aligned} \quad \text{Equation 8}$$

wherein

s is a number in the range of 0.1 to 10;

t is a number in the range of 0.1 to 10;

u is a number in the range of 0.1 to 2.0;

v is a number in the range of 0.1 to 2.0;

w is a number in the range of 50 to 220;

x is a number in the range of 10 to 100;

y is a number in the range of 1 to 40;

z is a number in the range of 1 to 40;

(substance n) denotes the concentration of the respective substance n;

GFR_A denotes the predicted GFR for a first GFR range and

GFR_B denotes the predicted GFR for a second GFR range.

8. Method according to claim 6 or 7, **characterized** in that at least a first equation and a second equation are combined for calculating the predicted glomerular filtration rate, wherein the first equation is optimized for a first glomerular filtration rate range and the second equation is optimized for a second glomerular filtration rate range, wherein the first glomerular filtration rate range and the second glomerular filtration rate range are spaced apart from each other, adjoin or partially overlap.
9. Method according to claim 8, **characterized** in that the first glomerular filtration rate range comprises glomerular filtration rates indicative for hypofiltration and in that the second

glomerular filtration rate range comprises glomerular filtration rates indicative for hyperfiltration or normal glomerular filtration.

10. Method according to claim 8 or 9, **characterized** in that the first equation is weighted by a first weighing factor and the second equation is weighted by a second weighing factor, wherein a) the first weighing factor is bigger than the second weighing factor if the predicted glomerular filtration rate, when calculated using the non-weighted first equation and/or the non-weighted second equation, falls within the first glomerular filtration rate range but not within the second glomerular filtration rate range, or b) the first weighing factor is smaller than the second weighing factor if the predicted glomerular filtration rate, when calculated using the non-weighted first equation and/or the non-weighted second equation, falls within the second glomerular filtration rate range but not within the first glomerular filtration rate range.
11. Method according to any of claims 8 to 10, **characterized** in that a third equation is combined with the first equation and the second equation, wherein the third equation is optimized for a third glomerular filtration rate range, wherein the first glomerular filtration rate range, the second glomerular filtration rate range, and the third glomerular filtration rate range are spaced apart from each other, adjoin or partially overlap with at least one of the respective other glomerular filtration rate ranges.
12. Method according to any of claims 6 to 11, **characterized** in that a classification of the individual, the blood sample of whom is analyzed, into a predefined class is performed based on a pattern of the determined concentrations of the substances.
13. Method according to claim 12, **characterized** in that the classification is supplemented by an indication of a likelihood that the individual is in transition to another predefined class.
14. Method according to any of claims 6 to 13, **characterized** in that in case that the calculated glomerular filtration rate is indicative of hypofiltration or hyperfiltration, the determined concentrations of the substances are additionally used to provide an indicator of a pathophysiologic factor of an impaired glomerular filtration rate, wherein the determined concentration of at least one substance is compared with the concentration of the same substance in the blood of another individual having a similar glomerular filtration rate.

15. Method according to claim 14, **characterized** in that the indicator of a pathophysiologic factor of an impaired glomerular filtration rate and optionally the predicted glomerular filtration rate are used for at least one of assisting in assessing the eligibility of diabetic patients for metformin therapy; assisting in evaluating a contribution of kidney dysfunction to edema formation for congestive heart failure patients; supporting a diagnosis of kidney disease in children; assisting in identifying suitable candidates for live kidney donation; assisting in evaluating kidney function after renal allograft transplantation; supporting an evaluation of the eligibility of chronic kidney disease stage IV patients to enter kidney transplant waiting list; assisting in evaluating the risk for acute kidney injury peri liver transplantation and/or post liver transplantation; assisting GFR estimation in patients having a body constitution significantly differing from the body constitution of a healthy standard population; assisting in evaluating the necessity of liver and kidney co-transplantation; and assisting in adapting a drug dose administered to a patient.