AXINON® Clearance Check*

Metabolomics-Based GFR Determination

AXINON® Clearance Check – A Deeper Insight Into Kidney Function

- Simple serum test with the accuracy of tracer-based plasma clearance methods
- Accurate determination of GFR (glomerular filtration rate) based on a metabolite constellation
- Deeper understanding of underlying kidney pathophysiology

The most important parameter in assessing kidney function is the glomerular filtration rate (GFR). Accurate measurement of GFR by determining renal or plasma clearance (mGFR) is a very expensive, time-consuming and impractical process. Thus, clinicians currently rely on estimating GFR by the use of equations based on the concentration of serum creatinine which can be measured by a simple blood test (eGFR) [1]. However, despite being commonly used this approach is associated with an uncertainty in the creatinine blind range between 60-89 ml/min/1.73 m² and below [2].

The new test *AXINON® Clearance Check* provides an advanced determination of GFR which is not based on a single marker, but on multi-parametric metabolomics (GFR_{NMR}) analysis. It is based on a metabolite constellation analyzed by *Magnetic Group Signaling™ (MGS®)* empowered NMR spectroscopy. The test is as simple as eGFR but almost as accurate as tracer-based GFR clearance measurements.

Additionally, *AXINON® Clearance Check* allows a deeper insight into kidney pathophysiology. It provides a metabolite panel with serum concentrations of eight metabolites that are associated with kidney function.

Clinical Utility and Use Cases

AXINON® Clearance Check is a simple and convenient blood test to accurately monitor kidney function.

AXINON® Clearance Check can be used to diagnose and stage chronic kidney disease.

AXINON® Clearance Check provides a more reliable GFR than creatinine-based GFR estimations–especially in the creatinine blind range between 60-89 ml/min/1.73 m² and below.

AXINON® Clearance Check is more suitable in a broader subset of patients than creatinine-based GFR estimations, e.g. patients with reduced muscle mass or patients with chronic liver failure.

AXINON® Clearance Check supports a deeper understanding of underlying pathophysiology by providing serum concentrations of metabolites associated with kidney function.

Performance Data

The performance of GFR_{NMR} delivered by *AXINON® Clearance Check* was evaluated by the P30 value. P30 indicates the amount of the GFR values provided by *AXINON® Clearance Check* differ by no more than 30 percent from the gold standard value (mGFR).

The overall P30 value for *AXINON® Clearance Check* was 81% which is significantly better than eGFR and almost as accurate as plasma clearance (Fig. 1).

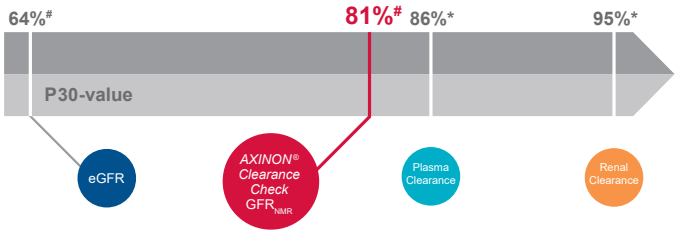

Fig. 1: Overall performance (based on P30 value) of *AXINON® Clearance Check* compared to currently applied methods to estimate and measure GFR (#numares validation study; *Am J Kidney Dis. 2014; 64(3): 411-424).

The performance of *AXINON® Clearance Check* was analyzed in chronic kidney disease (CKD) stages I to IV and compared to the widely accepted CKD-EPI equation which estimates GFR based on serum creatinine (eGFR). *AXINON® Clearance Check* showed a significantly higher clinical performance than creatinine-based GFR estimations–especially in the creatinine blind range between 60-89 ml/min/1.73 m² (CKD stage II) and below (Fig. 2).

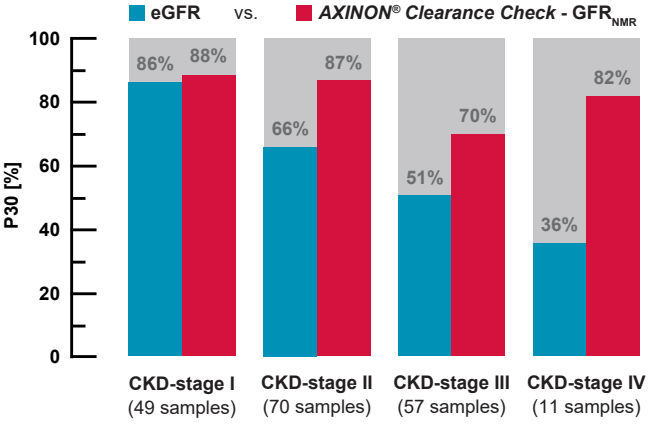

Fig. 2: Performance characteristics of *AXINON® Clearance Check* in comparison to eGFR (based on CKD-EPI equation). Definition of CKD stages was based on mGFR values: CKD stage I: mGFR ≥ 90 ml/min/1.73 m², CKD stage II: mGFR 60 - 89 ml/min/1.73 m², CKD stage III: mGFR 30 - 59 ml/min/1.73 m², CKD stage IV: mGFR 15 - 29 ml/min/1.73 m².

Interpretation

AXINON® Clearance Check offers two perspectives for early detection and management of chronic kidney disease: Firstly, an accurate estimation of glomerular filtration rate and secondly, a deeper insight into pathophysiological processes via the metabolite panel.

** Available as a CE-labeled in vitro diagnostic product in the European Union and as Research-Use-Only product in the United States. numares´ products have not yet been approved or cleared by the U.S. Food and Drug Administration.*

Glomerular Filtration Rate

AXINON® Clearance Check provides an accurate calculation of GFR based on metabolite constellations (GFR_{NMR}). This parameter is used for the assessment of kidney function and allows early detection and reliable classification of CKD.

Metabolite Panel

Beyond GFR calculation, *AXINON® Clearance Check* supports understanding of kidney pathophysiology by providing serum concentrations of distinct metabolites that are known to be associated with kidney function (a list of all provided metabolites is shown in the table below).

Substance	Pathophysiology	References
Creatinine**	Altered filtration, reabsorption, secretion	[3]
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Myo-inositol**	Altered filtration, reabsorption, secretion; oxidative stress; tubular hyperosmolality	[6-8]
Dimethyl-sulfone**	Altered filtration, reabsorption, secretion; changes of microbiome; oxidative stress	[9-13]
Glycerol	Altered filtration, reabsorption, secretion	[14-16]
Dimethyl-amine	Altered filtration, reabsorption, secretion; changes of microbiome	[17-19]
Valine**	Altered filtration, reabsorption, secretion; metabolic acidosis	[20-23]
Isoleucine	Altered filtration, reabsorption, secretion; metabolic acidosis	[20-23]

*Tab.: Substances delivered by AXINON® Clearance Check (**indicates substances used for GFR_{NMR} calculation).*

Case Example

AXINON® Clearance Check was used for the assessment of kidney function in three different patients (A, B and C; Fig. 3). All three showed a moderately decreased GFR of 78 ml/min/1.73 m². A further look at the metabolic panel reveals that the respective GFR values were based on distinct metabolite constellations.

The metabolite constellation of patient A was characterized by high serum levels of creatinine together with highly increased concentrations of valine. In contrast, patient B showed high creatinine levels together with highly elevated myo-inositol. The GFR of patient C was also based on high myo-inositol, however, in this case associated with very low levels of creatinine.

This understanding can help to further stratify patients with equal GFR values.

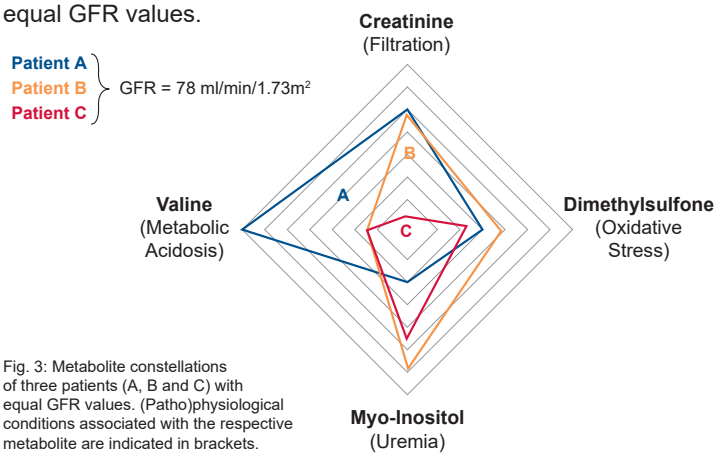

Fig. 3: Metabolite constellations of three patients (A, B and C) with equal GFR values. (Patho)physiological conditions associated with the respective metabolite are indicated in brackets.

How to Use the Test

Specimen Collection, Storage and Transport

The *AXINON® Clearance Check* test is performed on human serum samples collected according to standard techniques for laboratory testing. Appropriate tubes without anti-coagulation additives must be used. If measurement cannot be performed in a timely manner or specimens are to be shipped, specimens should be frozen at -20°C or below.

Test Principle

Samples are prepared with the *AXINON®* serum kit 2.0 and measured using a qualified *AXINON®* 600 MHz NMR system. The NMR measurement is controlled by the *AXINON® Software* and produces standardized NMR spectra which are interpreted by the *AXINON® Clearance Check* test.

The GFR_{NMR} result is determined by a multi-parametric assay of a metabolite constellation of biomarkers associated with kidney function. The concentration of each metabolite delivered by *AXINON® Clearance Check* is calculated by mathematical functions fitted to substance-specific signals in the NMR spectra. The GFR_{NMR} result is determined by mathematically combining the serum concentrations of creatinine, myo-inositol, valine and dimethylsulfone. Utilization of metabolite constellations instead of a single marker allows the calculation of more stable and accurate results.

Literature

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