**Table S1.** Correlation amongst baseline urinary biomarker excretions (n=302)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Albumin | |  | IgG | |  | β2MG | |  | KIM-1 | |  | HFABP | |  | NGAL | | |  | MCP-1 | |
|  | **St. β** | **p.val** |  | **St. β** | **p.val** |  | **St. β** | **p.val** |  | **St. β** | **p.val** |  | **St. β** | **p.val** |  | **St. β** | | **p.val** |  | **St. β** | **p.val** |
| Albumin | *NA* | |  | 0.551 | <0.001 |  | 0.339 | <0.001 |  | 0.415 | <0.001 |  | 0.481 | <0.001 |  | 0.443 | | <0.001 |  | 0.332 | <0.001 |
| IgG | - | **-** |  | *NA* | |  | 0.295 | <0.001 |  | 0.311 | <0.001 |  | 0.220 | <0.001 |  | 0.316 | | <0.001 |  | 0.444 | <0.001 |
| β2MG | - | **-** |  | - | - |  | *NA* | |  | 0.209 | <0.001 |  | 0.347 | <0.001 |  | 0.139 | | 0.02 |  | 0.287 | <0.001 |
| KIM-1 | - | **-** |  | - | - |  | - | - |  | *NA* | |  | 0.195 | 0.001 |  | 0.326 | | <0.001 |  | 0.511 | <0.001 |
| HFABP | - | **-** |  | - | - |  | - | - |  | - | - |  | *NA* | |  | 0.278 | | <0.001 |  | 0.162 | 0.005 |
| NGAL | - | **-** |  | - | - |  | - | - |  | - | - |  | - | - |  | *NA* | | |  | 0.304 | <0.001 |
| MCP-1 | - | **-** |  | - | **-** |  | - | **-** |  | - | **-** |  | - | **-** |  | - | **-** | |  | *NA* | |
| Correlations among the biomarkers are calculated using Pearson Correlation. The biomarkers were log transformed to fulfill the criteria of linear regression.  *Abbreviations are:* IgG, immunoglobulin G; KIM-1, Kidney Injury Molecule 1; β2MG, β2 microglobulin; HFABP, Heart-type Fatty Acid Binding Protein; MCP-1, monocyte chemotactic protein 1; NGAL, Neutrophil Gelatinase-Associated Lipocalin. | | | | | | | | | | | | | | | | | | | | | |

**Table S2.** Cross-sectional association baseline urinary biomarker excretion with baseline eGFR (n=302)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Crude** | |  | **Model 1** | |  | **Model 2** | |
|  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |
| **General** |  |  |  |  |  |  |  |  |
| - Albumin | -0.20 | 0.001 |  | -0.22 | <0.001 |  | -0.20 | <0.001 |
| **Glomerular** |  |  |  |  |  |  |  |  |
| - IgG | -0.16 | 0.005 |  | -0.19 | 0.001 |  | -0.16 | 0.006 |
| **Proximal tubular** |  |  |  |  |  |  |  |  |
| - β2MG | -0.24 | <0.001 |  | -0.26 | <0.001 |  | -0.25 | <0.001 |
| - KIM-1 | -0.17 | 0.004 |  | -0.18 | 0.002 |  | -0.14 | 0.01 |
| **Distal tubular** |  |  |  |  |  |  |  |  |
| - HFABP | -0.36 | <0.001 |  | -0.35 | <0.001 |  | -0.34 | <0.001 |
| **Inflammatory** |  |  |  |  |  |  |  |  |
| - NGAL | -0.23 | <0.001 |  | -0.34 | <0.001 |  | -0.31 | <0.001 |
| - MCP-1 | -0.11 | 0.06 |  | -0.22 | <0.001 |  | -0.16 | 0.02 |
| Standardized beta’s and p-values were calculated using multivariate linear regression. Dependent variable is eGFR. Biomarkers were log-transformed to fulfill the criteria of the linear regression analyses.  *Abbreviations are:* IgG, immunoglobulin G; β2MG, β2 microglobulin; KIM-1, Kidney Injury Molecule 1; HFABP, Heart-type Fatty Acid Binding Protein; NGAL, Neutrophil Gelatinase-Associated Lipocalin; MCP-1, monocyte chemotactic protein 1  Model 1: Adjusted for age and sex  Model 2: as model 1 plus additional adjustment for baseline htTKV | | | | | | | | |

**Table S3.** Cross-sectional association baseline urinary biomarker excretion   
with baseline htTKV (n=302)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Crude** | |  | **Model 1** | |  | **Model 2** | |
|  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |
| **General** |  |  |  |  |  |  |  |  |
| - Albumin | 0.21 | <0.001 |  | 0.17 | 0.002 |  | 0.14 | 0.02 |
| **Glomerular** |  |  |  |  |  |  |  |  |
| - IgG | 0.26 | <0.001 |  | 0.22 | <0.001 |  | 0.19 | 0.001 |
| **Proximal tubular** |  |  |  |  |  |  |  |  |
| - β2MG | 0.09 | 0.13 |  | 0.05 | 0.91 |  | 0.00 | 0.98 |
| - KIM-1 | 0.25 | <0.001 |  | 0.21 | <0.001 |  | 0.18 | 0.001 |
| **Distal tubular** |  |  |  |  |  |  |  |  |
| - HFABP | 0.12 | 0.04 |  | 0.12 | 0.04 |  | 0.00 | 0.95 |
| **Inflammatory** |  |  |  |  |  |  |  |  |
| - NGAL | 0.09 | 0.11 |  | 0.20 | 0.001 |  | 0.15 | 0.02 |
| - MCP-1 | 0.45 | <0.001 |  | 0.41 | <0.001 |  | 0.38 | <0.001 |
| Standardized beta’s and p-values were calculated using multivariate linear regression. Dependent variable is log transformed baseline htTKV. Biomarkers were log-transformed to fulfill the criteria of the linear regression analyses.  *Abbreviations are:* IgG, immunoglobulin G; β2MG, β2 microglobulin; KIM-1, Kidney Injury Molecule 1; HFABP, Heart-type Fatty Acid Binding Protein; NGAL, Neutrophil Gelatinase-Associated Lipocalin; MCP-1, monocyte chemotactic protein 1  Model 1: Adjusted for age and sex  Model 2: as model 1 plus additional adjustment baseline eGFR | | | | | | | | | |

**Table S4.** Longitudinal association of baseline urinary biomarkers excretion with annual change in eGFR (n=152)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Crude** | |  | **Model 1** | |  | **Model 2** | |  | **Model 3** | |
|  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |
| **General** |  |  |  |  |  |  |  |  |  |  |  |
| - Albumin | -0.27 | 0.002 |  | -0.24 | 0.005 |  | -0.15 | 0.08 |  | -0.16 | 0.07 |
| **Glomerular** |  |  |  |  |  |  |  |  |  |  |  |
| - IgG | -0.20 | 0.02 |  | -0.18 | 0.04 |  | -0.13 | 0.14 |  | -0.15 | 0.09 |
| **Proximal tubular** |  |  |  |  |  |  |  |  |  |  |  |
| - β2MG | -0.29 | 0.001 |  | -0.27 | 0.002 |  | -0.21 | 0.01 |  | -0.20 | 0.02 |
| - KIM-1 | -0.29 | 0.001 |  | -0.27 | 0.002 |  | -0.21 | 0.02 |  | -0.24 | 0.006 |
| **Distal tubular** |  |  |  |  |  |  |  |  |  |  |  |
| - HFABP | -0.31 | <0.001 |  | -0.33 | <0.001 |  | -0.25 | 0.006 |  | -0.26 | 0.004 |
| **Inflammatory** |  |  |  |  |  |  |  |  |  |  |  |
| - NGAL | -0.23 | 0.007 |  | -0.26 | 0.003 |  | -0.16 | 0.08 |  | -0.17 | 0.07 |
| - MCP-1 | -0.29 | 0.001 |  | -0.24 | 0.01 |  | -0.17 | 0.09 |  | -0.19 | 0.04 |
| Standardized beta’s and p-values were calculated using multivariate linear regression. Dependent variable is annual change in eGFR.  *Abbreviations are*: IgG, immunoglobulin G; β2MG, β2 microglobulin; KIM-1, Kidney Injury Molecule 1; HFABP, Heart-type Fatty Acid Binding Protein; NGAL, Neutrophil Gelatinase-Associated Lipocalin; MCP-1, monocyte chemotactic protein 1.  Model 1: Adjusted for age and sex  Model 2: As model 1 plus additional adjustment for baseline eGFR and htTKV  Model 3: As model 2 plus additional adjustment for *PKD* mutation analysis | | | | | | | | | | | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Crude** | |  | **Model 1** | |  | **Model 2** | |  | **Model 3** | |
|  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |  | **St. β** | **p-val.** |
| **General** |  |  |  |  |  |  |  |  |  |  |  |
| - Albumin | 0.05 | 0.62 |  | -0.02 | 0.83 |  | -0.07 | 0.46 |  | -0.09 | 0.38 |
| **Glomerular** |  |  |  |  |  |  |  |  |  |  |  |
| - IgG | 0.09 | 0.32 |  | 0.04 | 0.65 |  | 0.02 | 0.80 |  | 0.01 | 0.89 |
| **Proximal tubular** |  |  |  |  |  |  |  |  |  |  |  |
| - β2MG | 0.14 | 0.14 |  | 0.07 | 0.43 |  | 0.04 | 0.64 |  | 0.05 | 0.56 |
| - KIM-1 | 0.11 | 0.27 |  | 0.05 | 0.58 |  | 0.02 | 0.80 |  | -0.00 | 0.99 |
| **Distal tubular** |  |  |  |  |  |  |  |  |  |  |  |
| - HFABP | 0.13 | 0.17 |  | 0.05 | 0.61 |  | -0.01 | 0.89 |  | -0.02 | 0.84 |
| **Inflammatory** |  |  |  |  |  |  |  |  |  |  |  |
| - NGAL | -0.12 | 0.22 |  | -0.04 | 0.69 |  | -0.11 | 0.29 |  | -0.11 | 0.29 |
| - MCP-1 | 0.16 | 0.09 |  | 0.09 | 0.36 |  | 0.08 | 0.45 |  | 0.07 | 0.51 |
| Standardized beta’s and p-values were calculated using multivariate linear regression. Dependent variable is annual change in htTKV.  *Abbreviations are*: IgG, immunoglobulin G; β2MG, β2 microglobulin; KIM-1, Kidney Injury Molecule 1; HFABP, Heart-type Fatty Acid Binding Protein; NGAL, Neutrophil Gelatinase-Associated Lipocalin; MCP-1, monocyte chemotactic protein 1.  Model 1: Adjusted for age and sex  Model 2: As model 1 plus additional adjustment for baseline eGFR and htTKV  Model 3: As model 2 plus additional adjustment for *PKD* mutation analysis | | | | | | | | | | | | | |

**Table S5.** Longitudinal association of baseline urinary biomarkers excretion with annual change in htTKV (n=132)

**Table S6.** Baseline characteristics independent cohort (n=95)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **All patients**  (n=95) | **Rapid progressors**  (n=38) | **Slow progressors** (n=57) | **p-value** |
| Female, n (%) | 39 (41.1) | 11 (28.9) | 28 (49.1) | 0.05 |
| Age (years) | 39.6 ± 11.1 | 38.1 ± 10.0 | 40.5 ± 11.7 | 0.31 |
| Weight (kg) | 84.3 ± 16.7 | 86.8 ± 16.5 | 82.7 ± 16.7 | 0.24 |
| Height (cm) | 180 ± 10.4 | 183 ± 9.93 | 179 ± 10.4 | 0.08 |
| BSA (m2) | 2.03 ± 0.23 | 2.07 ± 0.22 | 2.00 ± 0.23 | 0.13 |
| SBP (mmHg) | 128 ± 12 | 128 ± 10 | 129 ± 13 | 0.62 |
| DBP (mmHg) | 80 ± 9 | 79 ± 9 | 80 ± 9 | 0.87 |
| AHT, n (%) | 71 (74.7) | 29 (76.3) | 42 (73.7) | 0.77 |
| RAASi, n (%) | 64 (67.4) | 24 (63.2) | 50 (70.2) | 0.48 |
| eGFR (ml/min/1.73m2) | 78.6 ± 29.6 | 75.7 ± 30.8 | 80.6 ± 28.9 | 0.44 |
| htTKV (ml/m) | 852 (510-1212) | 1152 (790-1516) | 669 (423-932) | <0.001 |
| *PKD* mutation, n (%) |  |  |  | 0.25 |
| * *PKD1* truncating | 44 (46.3) | 18 (47.4) | 26 (45.6) |  |
| * *PKD1* non-truncating | 27 (28.4) | 13 (34.2) | 14 (24.6) |  |
| * *PKD2* | 12 (12.6) | 2 (5.3) | 10 (17.5) |  |
| * No mutation detected | 1 (1.1) | 0 (0.0) | 1 (1.8) |  |
| * Missing | 11 (11.6) | 5 (13.2) | 6 (10.5) |  |
| Variables are presented as mean ± SD, or as median (IQR) in case of non-normal distribution. P-values for vast versus slow progressors are calculated using independent sample *t* test in case of normal distribution, Mann Whitney U in case of non-normal distribution and Chi-Square in case of categorical data*.* Rapid and slow progressors were defined as patients with an annual change in eGFR ≤ -3.5 or > -3.5 ml/min/1.73m2, respectively.  *Abbreviations are*: BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure; AHT, anti-hypertensive therapy; RAASi, RAAS inhibitors; eGFR, estimated glomerular filtration rate; htTKV, height adjusted total kidney volume; *PKD*, polycystic kidney disease. | | | | |

**Figure S1.** Intra-individual variation in urinary biomarker excretion. The line was calculated with orthogonal regression analysis and the st. β and p-values with Pearson Correlation.



**Figure S2.** Proportion of patients with rapidly progressive disease (upper panel) and annual change in eGFR (lower panel) according to Mayo htTKV class in case of typical ADPKD. Rapid and slow progressors were defined as patients with an annual change in eGFR ≤ -3.5 or > -3.5 ml/min/1.73m2, respectively. Differences in proportion p=0.26 across the different classes.



**Figure S3.** Proportion of patients with rapidly progressive disease (upper panel) and annual change in eGFR (lower panel) according to PROPKD score. Rapid and slow progressors were defined as patients with an annual change in eGFR ≤ -3.5 or > -3.5 ml/min/1.73m2, respectively. Differences in proportion p=0.54 across the PROPKD score (left panel) and p=0.04 across risk categories based on the PROPKD score (right panel).



**Figure S4.** Proportion of patients with rapidly progressive disease (upper panel) and annual change in eGFR (lower panel) according to urinary biomarker score, calculated by combining tertiles of β2MG excretion and MCP-1 excretion in an external validation cohort. Rapid and slow progressors were defined as patients with an annual change in eGFR ≤ -3.5 or > -3.5 ml/min/1.73m2, respectively. Differences in proportion p=0.002 across urinary biomarker score.

