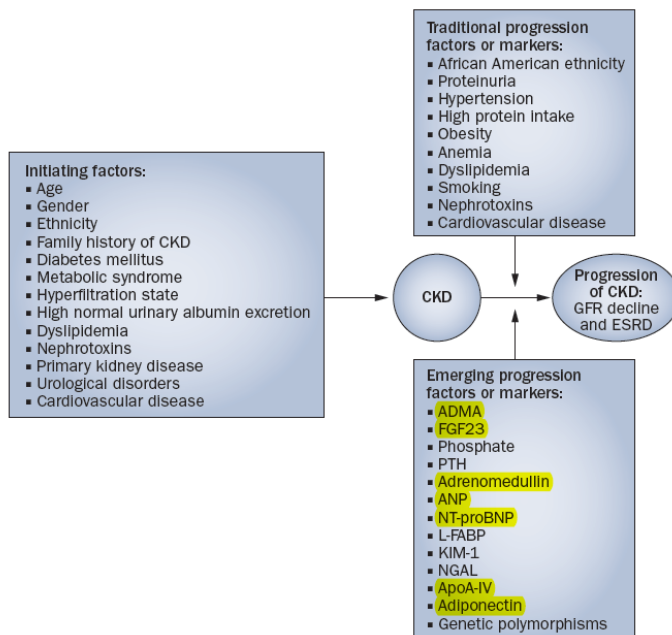


Mild to Moderate Kidney Disease Study (MMKD)

Principal Investigators: [Florian Kronenberg](#)

Background and rationale for the MMKD Study: Chronic kidney disease (CKD) is a common condition and its prevalence is increasing. CKD has a number of related comorbidities and the prognosis is poor: many patients experience disease progression. Recognizing the factors associated with CKD progression allows high-risk patients to be identified and given more intensive treatment if necessary (Figure 1). The identification of new predictive markers might also improve our understanding of the pathogenesis and progression of CKD.



The "Mild to Moderate Kidney Disease" (MMKD) Study was established in the mid nineties and aims to investigate possible risk factors or risk markers for the progression of CKD. More than half of the recently identified risk markers for the progression of CKD were the first time described in the MMKD Study (for review, see reference [1]).

Figure 1: Risk factors and markers for the initiation and progression of chronic kidney disease. Markers for the first time described in the MMKD Study are highlighted in yellow. Figure adapted from reference [1].

Baseline investigation: We recruited at baseline 227 Caucasian patients between the ages of 18 and 65 years with non-diabetic CKD and various degrees of renal impairment (see detailed description in references [2,3,4]). These individuals were recruited from eight nephrology departments in Germany, Austria, and South Tyrol (Italy). The patients had stable renal function for at least three months before entry into the study. The primary cause of CKD was glomerulonephritis in 97 patients (biopsy-confirmed in 90), adult polycystic kidney disease in 37 patients, interstitial nephritis in 24 patients, other types of kidney disease in 43 patients, and unknown in 26 patients. Main exclusion criteria were serum creatinine >6 mg/dL, diabetes mellitus and nephrotic syndrome. GFR at baseline was measured using the iohexol clearance technique. All parameters studied in the context of progression of chronic kidney disease (see below) were measured in the baseline samples.

Prospective follow-up: After the baseline investigation patients were followed prospectively until the primary study endpoint or the end of the observation period (year 2002/03) was reached. The primary endpoint was defined as doubling of baseline serum creatinine and/or terminal renal failure necessitating renal replacement therapy. A total of 177 patients (78%) from the baseline cohort could be assessed during the follow-up, 65 of them experienced a progression of chronic kidney disease.

Emerging risk markers associated with progression of CKD (Figure 2): Besides parameters of calcium-phosphate metabolism [5], we found the following parameters to be associated with progression of CKD: fibroblast growth factor 23 (FGF23) [5], asymmetric dimethylarginine (ADMA) [6], the natriuretic peptides A-type natriuretic peptide (ANP), adrenomedullin (ADM) [7], NT-pro brain natriuretic peptide (NT-proBNP) [8], apolipoprotein A-IV (apoA-IV) [9], adiponectin (only in men) [10], cystatin C and beta-trace protein [11]. **It has to be pointed out that these parameters predicted progression of CKD independently of GFR and proteinuria which are well-known progression factors.**

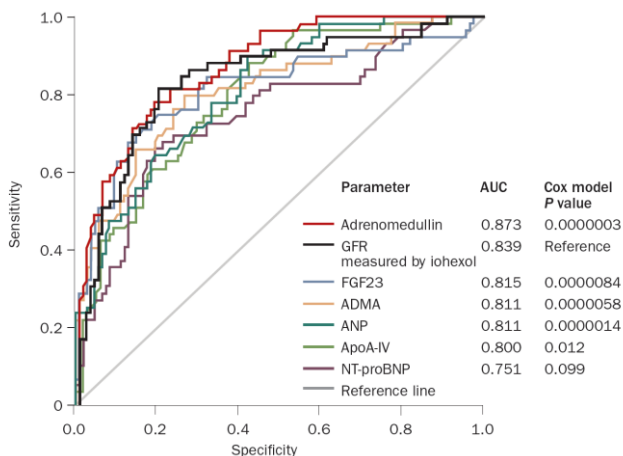


Figure 2: Receiver operating curves from the MMKD Study for GFR measured by iohexol, asymmetric dimethylarginine (ADMA), fibroblast growth factor 23 (FGF23), apolipoprotein A-IV (apoA-IV) and the natriuretic peptides atrial natriuretic peptide (ANP), NT-pro brain natriuretic peptide (NT-proBNP) and adrenomedullin (ADM) to predict progression of CKD. Area under the curve (AUC) values for each of these parameters are shown and P values for the addition of each of the particular variables to a Cox reference model adjusted for age, sex, proteinuria and GFR. ADM showed the greatest AUC reflecting discriminative capability between patients who will and those who will not experience a progression of CKD. This was even better than that of GFR measured by iohexol. Figure is from reference [1].

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Selected Publications:

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11. Spanaus K-S*, Kollerits B*, Ritz E, Hersberger M, Kronenberg F*, von Eckardstein A*: Serum creatinine, cystatin C, and β -trace protein in diagnostic staging and predicting progression of primary nondiabetic chronic kidney disease. ***Clinical Chemistry*** 56:740-749, 2010. [\[Pub-Med\]](#)

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