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Prediction for the Progression of Chronic Kidney Disease (CKD) in Various Situation

Hiroshi BANDO[1,2*]
[1]Tokushima University / Medical Research, Tokushima, Japan
[2]Japan Low Carbohydrate Diet Promotion Association (JLCDPA), Kyoto, Japan

Corresponding Author: **Hiroshi BANDO, MD, PhD, FACP** ORCID iD
Address: Tokushima University /Medical Research, Nakashowa 1-61, Tokushima 770-0943, Japan. Tel: +81-90-3187-2485; Email: pianomed@bronze.ocn.ne.jp
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Abstract
The discussion of chronic kidney disease (CKD), kidney replacement therapy (KRT), and end-stage kidney disease (ESKD) has been important. Recently, a useful predictive model of CKD progression to renal failure was reported by the German CKD study group. They include a novel 6-variable risk score (Z6), composed of creatinine, albumin, cystatin C, urea, hemoglobin, and urinary alb/cre ratio (UACR). CKD patients were studied in 3 groups based on educational attainment. Hazard ratios compared to low vs high groups showed mortality of 1.48, MACE 1.37, and renal failure 1.54, respectively. For the prediction of CKD progression, UACR and estimated glomerular filtration rate (eGFR) are useful.

Keywords
Chronic Kidney Disease, Kidney Replacement Therapy, End-Stage Kidney Disease, Urinary Alb/Cre Ratio, Estimated Glomerular Filtration Rate

Abbreviations
CKD: Chronic Kidney Disease; KRT: Kidney Replacement Therapy; ESKD: End-Stage Kidney Disease; UACR: Urinary Alb/Cre Ratio; EGFR: Estimated Glomerular Filtration Rate

Renal diseases have been still large challenges for health and medicine, which lead to pathophysiological research and optimal care. Among them, metabolomics has been a quantitative investigation of small organic compounds that has become more important in nephrology development [1]. They include analytical, statistical and bioinformatics data with metabolomics cohort investigation. For clinical treatment and decision-making, stratification of patients with chronic kidney disease (CKD) has been important. They are at risk for exacerbation to kidney failure requiring kidney replacement therapy (KRT) [2]. Several studies have been found for prospective cohort trials. Recently, meaningful independent observational cohort studies have been reported [3].

Among the latest topics for renal diseases and CKD, a useful predictive model leading to the progression of CKD to renal failure was reported from a German CKD study group. They proposed novel 6 variable risk

scores (Z6), which are composed of creatinine, albumin, cystatin C, urea, hemoglobin, and urinary alb/cre ratio (UACR). Concerning the re-sampling method approach, Z6 showed a median C statistic (0.909) after 2 years of baseline visit. Consequently, the newly proposed risk equation using 6 routine variables can facilitate the judgement for the identification of CKD cases who will be at higher risk of progressing to KRT [3]. CKD has been a globally important medical issue that is characterized by a high burden of mortality and comorbidities [4]. The usual CKD prevalence seems to be 13.4% worldwide, and it is about 15% higher in lower-income countries. People of lower educational attainment tend to have more risk factors of CKD compared with higher groups. They usually include diabetes, obesity, and hypertension [5]. These tendencies suggest elevated incidence ratios of CKD and renal failure [6].

The latest significant report is found from the German CKD (GCKD) Cohort, Kidney International Reports [7]. Several relationships were investigated among educational attainment, mortality, CKD etiology, major adverse cardiovascular events (MACEs), and renal failure requiring hemodialysis. Participants included 5095 cases with 30-60 ml/min of eGFR divided into three groups from the educational attainment, which were followed for 6.5 years. The protocol calculated the hazard ratio (HR) in comparison with low vs high educational attainment. The results were HR 1.48 for mortality, 1.37 for MACE, and renal failure for 1.54. Related mediators for low educational attainment and mortality included higher BMI, smoking, history of CV disease, lower income, higher CRP, and others. Furthermore, positive relationships were found for diabetic nephropathy (odds ratio, OR 1.65) and CKD after acute renal failure (OR 1.56) [7].

The progression rate of CKD, end-stage kidney disease (ESKD), all-cause mortality, and CVD events vary in each country [8]. Generally, CKD progression ratio is 40 events/1000 person-year, 28 for ESKD, 29 for CVD events, and 41 for death [9]. The adjusted hazard ratio (aHR) for ESKD per baseline eGFR showed 2.02 in the Chronic Renal Insufficiency Cohort (CRIC) Study in the United States and 3.01 in the Canadian study of prediction of death, dialysis, and interim cardiovascular events (CanPREDDICT) [10]. Consequently, several risks may be observed differently in countries. For identifying CKD cases who will progress to ESKD, plasma biomarkers were studied for predicting high-risk patients [11]. The patients included 894 diabetic cases with chronic renal failure (CRF) and <60 ml/min per 1.73 m^2 of eGFR. The protocol showed the measurement of several biomarkers related to fibrosis and tubular injury and inflammation. They include 6 markers of TNFR-1, TNFR-2, KIM-1, MCP-1, YKL-40, and suPAR. As a result, higher values of 6 markers were observed for elevated risk of DKD progression. Among them, TNFR-2 showed the highest risk level of aHR 1.61.

Regarding long-term risk of renal failure, some biomarkers were investigated in hospitalized patients with CKD and acute kidney injury [12]. Applying 1538 cases in admission for multicenter studies, uromodulin (UMOD), monocyte chemoattractant protein 1 (MCDP-1/DDL2) and YKL-40 (CHI3L1) were measured in the urine specimen. As a result, higher UMOD was observed for smaller eGFR decrease and lower ratio of composite renal outcome, and higher MCP-1 and YKL-40 were found for larger eGFR decrease and larger ratio of composite renal outcome.

Concerning the prediction of advanced CKD, an observational cohort study was conducted for changes in two biomarkers [13]. They are eGFR and UACR. The cases were 91 thousand primary care patients; which data were from clinical practice research datalink in England for 16 years. The primary outcome for changes in eGFR and UACR was categorized as increased >30%, stable, or decreased >30%, for alone or combined changes, over a 3 years period. The results showed that i) 77.7% was diabetic, ii) 2541 cases were progressed to advanced CKD. In comparison with stable levels, hazard ratios (HRs) for decreased eGFR and increased UACR were 7.53 and 1.78, respectively. When compared with both stable cases, combined changes of eGFR and UACR showed HRs 15.15. Prediction using both biomarkers showed better than either alone, and this method would be an alternative outcome for progression of CKD [13].

Related to the progression of CKD to ESRD, proton nuclear magnetic resonance (NMR) spectroscopy was investigated [14]. This method could improve the performance of the equation for renal failure risk. It has been called the Tangri score, in which Fundamental clinical variables included age, gender, eGFR and UACR. For 4640 CKD cases from the GCKD study, 185 cases (3.99%) developed to ESRD for 3.70 years on average who required hemodialysis or kidney transplantation. The original Tangri risk equation showed 0.863 of C statistics. When putting higher weights to the model, some factors were beneficial such as HDL, creatinine, glycoproteins and valine. As these factors are accompanied with NMR features, C statistic increased to 0.875, where predominance was found in 94 out of 100 samples [14].

In order to evaluate the nephrology referral situation in the light of current guideline referral, observational cohort study was conducted [15]. The subjects were 399,644 veterans with CKD and investigated for 1 year. From a referral point of view, 66,276 cases met laboratory indications for referral. Among them, 11,752 (17.7%) cases were referred to the nephrology department. Among all cases meeting the referral criteria, two-year predicted renal failure risk in median would be 1.5%.

In summary, recent topics concerning CKD, KRT and ESKD were introduced. This article would be hopefully useful for future practice and research in nephrology development.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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