////Title: Artificial Intelligence Predicts the Worsening of Chronic Kidney Disease.

////Standfirst: Our kidneys are primarily responsible for filtering waste out of the body and into urine. However, with aging, kidney dysfunction begins to develop. Although no symptoms appear for years, this dysfunction can eventually progress to severe kidney failure. If caught early, the adverse outcomes of kidney dysfunction can be prevented. But unfortunately, the detection and management of kidney disease remain far from optimal. Professor Eiichiro Kanda (Eye-CHI-ro KAN-da) of the Kawasaki (Ka-wa-SA-ki) Medical School has established a new model based on statistics and artificial intelligence to predict the risk factors and likelihood of kidney disease progression.

////Body text:

The kidneys act as molecular sieves in our bodies. These fist-sized organs, one on each side of our lower back, filter blood to eliminate waste substances, regulate fluids, and maintain an electrolyte balance. Blood filtered through the kidneys has adjusted salt, sugar, mineral, and water levels, and can safely return to the rest of the body. Waste substances, such as ammonia and bile by-products, are converted to urine and travel from the kidneys to the bladder for elimination.

With age, the kidneys' ability to carry out their normal function declines. By the age of 65, it is believed that 1-in-5 males and 1-in-4 females have some degree of kidney dysfunction. This common condition is referred to as chronic kidney disease (CKD). In some cases, no symptoms appear at all, while in other cases, CKD can lead to tiredness, breathlessness, nausea, swelling of limbs, and the appearance of blood in the urine. Even though symptoms can be mild, CKD is a serious condition because it can lead to kidney failure, heart disease, and even death.

CKD can be diagnosed in its early stages. It is most commonly diagnosed by measuring creatinine levels in blood, and the presence of excess protein, such as albumin, in the urine. Creatinine is a natural waste product during muscle breakdown. Increased levels of creatinine in the blood indicate a reduced ability of the kidneys to filter waste. The glomerular filtration rate, or eGFR (EE-gee-ef-arr), is thus said to decrease. A decrease in eGFR from 90 to 60 millilitres/minute/1.73m2 indicates CKD. Other conditions, such as the presence of blood in urine and the appearance of cysts in the kidneys, are also useful in the diagnosis of CKD.

The severity of kidney disease is classified using eGFR on a scale of G1 to G5, ranging from mild kidney dysfunction to kidney failure. It is also classified from A1 to A3 on the basis of the albumin-to-creatine ratio in the urine.

The progression of CKD can be prevented if it is diagnosed early, that is, at the G1 or G2 stages. However, because most patients have very mild or no symptoms, most cases remain undiagnosed until it is too late. In addition, confounding diseases such as high blood pressure, diabetes, and abnormal levels of lipids, such as cholesterol, in the blood make it difficult to predict how CKD will progress. For these reasons, a clear clinical protocol for the management of early kidney disease is required.

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Professor Eiichiro Kanda of Kawasaki Medical School in Japan has proposed that predicting the future progression of CKD can be best achieved using artificial intelligence (AI). Prompted by the high incidence of CKD in Japan, Professor Kanda and his colleagues wanted to develop an efficient way of predicting disease progression. They followed a group of 7,465 workers in Yamagata Prefecture over 7 years, from 2009 to 2016. The workers were apparently healthy, i.e., not previously diagnosed as having CKD. Results of medical examinations of the individuals in 2009 were compared to those in subsequent years of the study.

Professor Kanda and his team used Bayesian (BAy-zian) networks to establish the risk factors associated with disease progression. These networks enable the calculation of the probability that two events are related or dependent on each other. They also used AI models to identify patients at risk of developing severe kidney disease. These AI models can be trained using a set of clear examples to classify any patient into a disease severity group.

Results showed that the CKD stage was stable for 7-in-10 participants, but other data such as eGFR and proteinuria changed every year. The study of the long-term trends showed that the G1 stage progressed more rapidly than the G2 stage. These results showed that periods of 1 or 2 years were not long enough to evaluate kidney function, and a period of at least 3 years was required to monitor progression in a healthy population.

To identify the factors associated with CKD progression, the Bayesian network was used to evaluate the complicated relationships among eGFR, proteinuria, and other factors. The Bayesian network indicated that workers showing yearly progression of CKD and high blood pressure were at higher risk of worsening CKD. These results suggest the importance of a yearly follow-up assessing kidney function. Moreover, although other studies of kidney disease confirm this finding and suggest that high-level cholesterol can harden or block blood vessels in the kidneys and cause severe kidney failure, interestingly, diabetes, age, weight, and gender were not identified as strong risk factors for kidney disease in this study.

Professor Kanda and co-workers took a step further and developed AI models to predict the progression of CKD. The AI models show the high probabilities of CKD progression as heat maps. When patients were shown to be at very high risk, this risk remained very high seven years later. However, the AI models also detected the patients who showed high possibilities of CKD progression seven years later among the patients at low risk at the start of the study. It was also shown that at least a three-year observation period is required to identify such patients.

Finally, Professor Kanda and his team recommend a minimum monitoring period of three years for people regardless of the risk of developing kidney failure. This study is very important for preventive medicine, informing health check-ups to assess the progression of early CKD, and improving the lifestyle guidance provided to patients.

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