A growing recognition of chronic kidney disease 

Nagai: At present, an aging society, arteriosclerosis, and other cardiovascular system diseases are on the rise, indeed. For diabetes patients, for dialysis patients, additional afflictions such as arteriosclerosis or heart conditions can have an impact on prognosis. People with bad kidneys face a worsening of heart conditions, and the same holds true vice versa. These bad kidneys have worse kidney problems. To treat kidney and heart diseases have become reciprocal risk factors for complications in each other.

Kimura: That’s right. We have known about the heart-kidney relationship for quite some time now. We are now trying to advance this concept by thinking in terms of “CKD”—chronic kidney disease. CKD is diagnosed when any of the following occur independently, or when both have continued for three months or longer: the first is when laboratory findings indicate a kidney disorder—such findings include albuminuria in blood, urine, etc., blood, palpitation, and so on. The second is when the glomerular filtration rate, or GFR, has been less than 60 mL/minute/1.73 m² for three months or longer. With this definition of CKD in hand, we are trying to view kidney problems and coronary heart disease, stroke, peripheral arterial disease (PAD), kidney failure, etc. in a new way.

In addition, while heart failure and kidney disease are reciprocal risk factors for complications in each other, it is also possible, and it is, that for coronary heart disease, stroke, peripheral arterial disease, kidney disease, diabetes, and hypertension from facing more severe diseases, and the key is to prevent heart and kidney diseases. What do you think?

KIMURA: CKD is indeed a notion that enables us to discover to people in need of expert medical information by asking doctors like leukemia, grades, diabetes, and hypertension patients. In GFR, in addition, as a concept it is easy to understand and illustrates that controlling urinary protein excretion and GFR decline can address the risk of heart and kidney-related diseases, and that those things are measurable.

NAGAI: One fundamental idea in diagnosis is that a doctor in kidney function indicates a problem with the heart, but, with the addition of the CKD concept, there is now also an awareness that guidance must be provided to patients at an earlier stage, when their CKG is beginning to decline.

KIMURA: That’s right. The feeling before now had been that serum creatinine at 1.4 or so meant a light kidney disorder, which was not taken very seriously. Now we know that when calculations are made that take into consideration of multiple indicators in combination.

Further clarification of the relationship between free fatty acids and kidney disease progression.

NAGAI: The kidneys are organs that separate the external environment and the internal environment—thus the body doesn’t need any extra nourishment. Also, they collectively serve as a “sanitary trench” to maintain homeostasis, identifying various substances and giving instructions to other bodily organs. We can learn from our research that the kidneys detect heart stress, and that the kidneys issue commands to inhibit that stress. It appears that the kidney control chronic inflammation in other organs.

KIMURA: That’s certainly very interesting. The kidneys’ epithelial cells work as stress sensors, and that Kruppel-like factor 5 (KLF5) and downstream physiological substances protect the heart. When kidney function is suppressed, the kidneys can no longer protect the heart, and inflammation intensifies, increasing the likelihood of heart failure. Organs in the body are interconnected in this way.

NAGAI: And by the same token, that heart failure is more likely to occur when the renal function of a diabetes patient declines.

NAGAI: We think that arteriosclerosis proceeds more readily when the anti-inflammatory functions of the kidneys decline, which makes it difficult to suppress inflammation. However, inflammation does not always lead to a functional disorder. In fact, in some kind of light inflammation does not occur when an organ is under stress, the biological system can sometimes break down. In other words, organs can experience inflammation as a protective measure in response to stress. Yet when that happens repeatedly, structural changes begin to happen, and finally, gradient and sudden declines, which itself can also be a cause of stress.

KIMURA: And so aged and obese patients are likely to have an increased likelihood of kidney disease progression.

NAGAI: Right. As people age, their stress response changes. The stress response is an organ’s function, serum creatinine levels gradually rise. More research is needed to establish the stress response, and environmental factors are involved in these changes. As the analysis of the human genome moves forward, rare but important genetic factors may also come to light.

It then may be possible to identify subgroups using CKG and GFR. I think it is essential that physicians take into consideration the significance of such parameters, however, we must lean on our long-term perspective.

Fig. 1 FABP urinary excretion within proximal tubule cytoplasm

KIMURA: In the future, there is a tendency for soft markers that are more acute than the serum creatinine to be used as an indicator, individual treatment requires consideration of multiple indicators in combination.

Fig. 2 Evaluation of urinary L-FABP within kidney injury (AKI)