Developing Improved Clinical Markers to Detect Heart Failure and Chronic Kidney Disease
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There are many useful markers/biomarkers for heart failure (HF) and chronic kidney disease (CKD); however, care must be taken to choose markers according to their specific purpose. Some markers may indicate the degree of HF or the exacerbation of CKD, whereas others may indicate the prognosis of patients with HF or with CKD. Some other markers may indicate both the degree of HF and exacerbation of CKD, as well as the prognosis of patients with these conditions. However, although many studies of clinical markers have been conducted, continued research into markers with increased specificity is necessary.

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On the other hand, although many studies have been performed on the evaluation of CKD prognosis, prognostic markers for chronic hemodialysis (HD) have rarely been investigated. The number of patients who require chronic HD remains high in Japan, and advances in management modalities are required for improving the prognosis and quality of life of these patients. The major cause of death in patients undergoing chronic HD is cardiovascular disease, with HF and arrhythmia being the most common conditions. Therefore, factors related to heart disease are important in the search for reliable prognostic markers for patients undergoing chronic HD.

One possible marker is the plasma B-type natriuretic peptide (BNP) level, because it indicates the degree of ventricular dysfunction. The increase in plasma BNP level is likely related to both the severity of HF and exacerbation of CKD. Furthermore, plasma BNP levels are likely to be increased in patients here are many useful markers/biomarkers for heart failure (HF) and chronic kidney disease (CKD); however, care must be taken to choose markers according to their specific purpose. Some markers may indicate the degree of HF or the exacerbation of CKD, whereas others may indicate the prognosis of patients with HF or with CKD. Some other markers may indicate both the degree of HF and exacerbation of CKD, as well as the prognosis of patients with these conditions. However, although many studies of clinical markers have been conducted, continued research into markers with increased specificity is necessary.

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with poorly controlled HD. Thus, the plasma BNP level is a potentially reliable prognostic marker of chronic HD. In addition, it is accepted that HF is a state of increased oxidative stress or low-grade inflammation. Interestingly, plasma BNP levels are probably increased in patients with higher C-reactive protein (CRP) levels. BNP levels would thus be similarly increased to counteract the level of inflammation. The anti-inflammatory effect of natriuretic peptides was confirmed by a study demonstrating that the infusion of human atrial natriuretic peptide (ANP) decreased oxidative stress in patients with HF. Therefore, the plasma BNP level could be a good prognostic marker of hemodynamic deterioration and inflammation related to chronic HD.

As mentioned before, inflammation is a key feature in both HF and CKD. Thus, the CRP level itself may be a prognostic marker in chronic HD patients. Recently, the measurement sensitivity of CRP has improved; CRP levels can now be used to detect low-grade inflammatory status, such as atherosclerosis.

The troponin T (TnT) level is a reliable marker of myocardial injury and can be useful for the detection of acute myocardial infarction. It has recently been established that the TnT level is slightly increased in a variety of cardiovascular diseases, including nonischemic HF. Very low levels of TnT were undetectable previously; however, the sensitivity of TnT assays have recently been improved and even a small degree of myocardial injury can be detected now. Therefore, the TnT level could also be a potential prognostic marker in chronic HD.

Based on these findings, Ishii et al. report in this issue of the Journal on their multimarker approach to risk stratification for long-term mortality in patients with chronic HD. They clearly show that the multimarker approach, consisting of simultaneous assessment of the levels of BNP, CRP, and TnT, each of which independently predicts prognosis, may improve the prediction of long-term mortality in HD patients. Although their prospective study is valuable, several questions remain about the use of this multimarker approach. The authors measured the biomarkers only once at the time of study enrollment. They did not show whether these biomarkers can act as monitoring markers, or whether improvement in the markers affects the clinical outcome of the patients. In addition, they did not evaluate therapies used for each patient; therefore, they did not provide data regarding the effectiveness of treatments for decreasing biomarker levels and improving prognosis. Further studies are necessary to determine whether a treatment policy based on these marker levels decreases the risk of mortality in HD patients. In particular, it should be examined whether guided therapy with these markers is appropriate.

New markers that are easily evaluated, rapidly assessed, and affordable are necessary. Such candidate markers could include the cardiothoracic ratio (CTR) on chest X-ray, serum albumin levels, and hemoglobin levels.

CTR is a simple marker indicating the severity of HF; the marker also reflects the volume status in chronic HD. CTR remains large in patients with poorly controlled HD, thus making this marker a simple, beneficial indicator of prognosis in patients with chronic HD. In this regard, the plasma ANP level, which indicates volume status, may also be effective.

Low hemoglobin and low albumin levels could be important prognostic markers of HF and chronic HD from the nutritional perspective. Anemia has recently been reported as a significant marker linking the heart and kidney, and is predictive of the cardiorenal anemia syndrome. Although a minimum level of hemoglobin has not been identified yet, it is established that anemia can be easily reversed by therapies such as blood infusion and erythropoietin supplementation. On the other hand, hypoalbuminemia is thought to result mainly from malnutrition, inflammation, and cachexia. Hypoalbuminemia facilitates the onset of body edema, which is likely seen in HF. Low plasma oncotic pressure related to hypoalbuminemia induces a fluid shift from the intravascular space to the interstitial space. A dietary survey should be performed and refeeding may be indicated. It is unknown whether targeted nutritional intervention and albumin administration confer benefits to hypoalbuminemic patients; however, hypoalbuminemia could be a potential useful prognostic marker in patients undergoing chronic HD.

It has been established that obesity is a risk factor for atherosclerosis and ischemic heart disease; however, it has been reported that a relatively high body mass index is a prognostic indicator for patients with HF, which has been recognized as an obesity paradox. The obesity paradox should also be examined in Japanese patients with chronic HD, as it has previously been examined in other races. In addition, nutritional conditions such as diabetes and insulin resistance should also be examined.

In conclusion, the study by Ishii and colleagues is valuable in clarifying the clinically available prognostic markers for chronic HD in Japanese patients. Their study demonstrated the importance of searching for other simple and useful markers and the value of combining markers in multimarker approaches (Figure). Hopefully, new markers can be used to guide therapies for improving prognosis.

References