Cardiac-Troponin-Guided Heart Failure Management
– Is It Possible in Clinical Practice? –
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Biomarker-based management has been increasing in clinical practice because of its advantages, which include high reproducibility, and simplicity in handling and interpreting results, even by non-specialists. B-type natriuretic peptide (BNP) is established as a representative biomarker in the field of heart failure (HF), indicating the effectiveness of diagnosis and risk stratification together with screening of cardiac dysfunction and guiding optimal treatment. A recent published guideline for HF biomarkers states class I–II indication of BNP measurement for HF management. Although this guideline mostly concentrates on the usefulness of BNP, an exceptional reference was made to the contribution of cardiac troponins (cTn) in prognostic judgment as class IIb, presumably due to low evidence levels.

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cTn, including the 2 subtypes of T and I, have been utilized as a key diagnostic tool for acute coronary syndrome (ACS). International guidelines have only recently recommended the use of cTn in order to make a diagnosis of acute myocardial infarction. Notably, in HF patients the levels of cTn are generally lower than those in patients with ACS. These findings have led to a caution that a low-sensitivity assay of biomarkers may misinterpret or overlook the prognostic risk in cases of HF with relatively low levels of cTn under the detectable level. We must keep in mind that it is artificial to distinguish between normal and elevated biomarker levels especially when using low-sensitivity methodology.

In this issue of the Journal, Kawahara et al demonstrate for the first time the prognostic value of highly sensitive cTnT (hs-cTnT) in HF patients with nonischemic dilated cardiomyopathy using a commercially-available measurement kit. The most important issue was that hs-cTnT, but not conventional cTnT, was an independent predictor for HF prognosis, suggesting that the measurement of hs-cTnT could be used to determine high-risk HF patients from those within the normal range of conventional cTnT. On the other hand, the cutoff value to discriminate cTnT must be used with caution when evaluating for risk stratification of HF. Using the new high-sensitivity assays, measurable levels of circulating cTn can be found in a high proportion of apparently healthy individuals in the general population. The conventional assays for cTn may be inadequate for risk stratification of patients with HF, especially those who are stable. As both the severity and pathogenesis of HF vary widely, the cutoff value of cTn may differ according to the patient population being studied. Apart from the diagnostic value of BNP measurement, cTn plays a limited role in terms of supporting the clinical decision regarding the prognostic risk for HF patients. Hence, these tests seem to be less useful in the clinical setting if an effective intervention cannot be recommended to patients with a cTn level higher than the cutoff value, leading to biomarker-guided strategy. Without a definitive plan of action, serial measurement is wasteful and increases costs. Although a prior study of Latini et al demonstrated a strong association between adverse outcome and detectability of cTnT, especially using the highly sensitive assay in chronic HF, hs-cTnT added only modestly to risk discrimination and did not improve calibration of risk models.

Recently, several clinical studies have demonstrated the clinical utility and limitations of BNP-guided HF management. Although diverse clinical outcomes may be deduced from the variety of study subjects and management protocols, including target BNP values, intensifying medical therapy seems to be the key to a better clinical outcome in almost all BNP-guided trials. HF management tools in recent years can be simply divided into 2 groups: ‘visible’ treatment and ‘invisible’ treatment. The ‘visible’ treatment means prompt relief of visible signs and symptoms. On the other hand, the recommended drugs for ‘invisible’ treatment to improve prognosis are the angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, β-blockers and aldosterone antagonists, based on the evidence from clinical trials using HF cases of systolic dysfunction. In BNP-guided management, ‘invisible’ treatment must be intensified in such cases with BNP higher than target levels toward the drugs and dosages recommended by the guidelines. Although some small studies have suggested that routine measurement of cTn could help to identify HF patients in need of intensive therapy, there have been no clinical trials to demonstrate the clinical efficacy of cTn-guided management based on strict pharmacological intervention. cTn and BNP convey different as well as complementary clinical information: BNP may be viewed as a marker of myocardial load and neurohumoral crosstalk, whereas cTn is a marker of in situ ongoing myocyte damage derived from leakage of the cytosolic pool of Tn through the cell membrane with altered permeability or proteolysis of myocardial contractile proteins. It is unwarranted in cTn-guided management, therefore, to state that intensified ‘invisi-

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ble’ treatment can lead to an improved prognosis, which is different from the BNP-guided strategy.

Now we have received the good news from Kawahara et al of a new effective diagnostic tool, hs-cTnT, but simultaneously we may have the problematic issue of how to deal with the increasing number of HF patients who are ‘positive’ for cTn in clinical practice. Prospective clinical trials to determine definitive cut-off values and a systematic treatment protocol are necessary to establish the clinical utility of this new biomarker.

References


