Heart failure is the common feature of the endstage for any type of cardiovascular disease (CVD) and is one of the most important causes of high morbidity and mortality in developed countries. This is also the situation in Japan, mainly because of rapid aging of the population, and increased survivors of serious CVD because of the recent advances in therapeutic strategies. Although it has been thought that both the prevalence and mortality of chronic heart failure (CHF) are relatively low in Japan, an early multicenter prospective cohort study (The Chronic Heart Failure Analysis and Registry in the Tohoku District 1 Study: CHART-1) clarified that the number of patients with HF in Japan was more than we thought, and that prognosis was as poor as that in Western countries. The most prevalent etiology of HF in the CHART-1 Study was nonischemic cardiomyopathy (28.6%), and coronary artery disease (CAD) accounted for only 25.4% of the total HF patients, which was considerably low compared with Western HF studies. On the other hand, Gheorghiade et al reported that admission for acute heart failure syndrome (AHFS) is a key event in the progression of CHF, which suggests that the process of CHF is largely modulated by the severity and frequency of AHFS, thus making the pathophysiology and prognosis of CHF varied. In fact, it is reported that hospitalized HF patients are a heterogeneous group with a wide range of 30-day mortality (1.7–7.2%) and a high post-discharge event rate, approaching 40% at 90 days. Since both the characteristics of such patients at high risk and the pathophysiology of the transition to decompensated HF from stable HF status remain uncertain, Shiba et al started a large-scale multicenter prospective cohort study, named the Chronic Heart Failure Analysis and Registry in the Tohoku District 2 (CHART-2) Study, in which consecutive patients at high risk for progression of CVD or HF because of the development of AHFS were investigated.

In their report of the CHART-2 Study in this issue of the Journal, Shiba et al examined the trend in the etiology of HF patients and their characteristics as compared with the CHART-1 Study. A total of 10,219 patients from 24 hospitals located in the Tohoku district with overt HF, structural cardiac disorders but without HF, or CAD were enrolled, making this study the largest multicenter prospective cohort of HF performed in Japan. The work of their head office, including 8 clinical research coordinators, and the newly developed web-based entry system would be a good model for future clinical study in Japan. They divided the study patients into 3 groups: (1) patients with CAD but without HF, (2) patients in Stage-B or Stage-C, and (3) those in Stage-D. In the present study, 5,484 (53.7%) patients did not have HF but had either CAD or cardiac structural disorders. The Stage-C group included 4,640 patients and accounted for 45.4% of the entire cohort, while 95 patients (0.9%) were classified as Stage-D. Initial data from CHART-2 Study provide important insights into the clinical characteristics of patients with HF and those at risk of disease progression because of developing AHFS, and the patterns of treatment of HF. First, when comparing the CHART-2 and CHART-1 patients, increasing trends of ischemic etiology (26.4–47.1%) and comorbidity with diabetes (19.5–23.3%) and hypertension (47.4–74.3%) in Japanese HF patients are evident, whereas those risks have been more prominent in patients with HF in Western countries. Consistent with this study, the MIYAGI-AMI Registry Study demonstrated a steady trend of an increasing incidence of acute myocardial infarction over the past 30 years in Japan, and JCARE-CARD demonstrated that the comorbidities of diabetes and hypertension was evident in Japan. Second, the findings from the CHART-2 Study indicate that ~54% of patients are classified as either Stage-B or CAD without overt HF in the real-world clinical setting. In those patients, the plasma concentration of B-type natriuretic peptide (BNP) was mildly elevated and their cardiovascular risk profile was also similar compared with patients in either Stage-C or D. Consistent with this study, it is reported that Stage-A/B patients with high plasma BNP levels have a similar or even worse prognosis than Stage-C/D patients with low plasma BNP levels. Thus, the plasma BNP levels may contribute to confirmation of the diagnosis in such patients. Third, the severity of prognostic risks, including reduced ejection fraction (EF), elevated plasma BNP levels, comorbidity of chronic kidney disease, and low hemoglobin level, were progressively exacerbated as HF stage progressed in the CHART-2 patients. Fourth, the prevalence of HF with preserved EF (HFeEF) was higher among the CHART-2 patients compared with the patients in the CHART-1 Study (44.6–68.7%) or other studies of HF, including JCARE-CARD. Because patients with HFeEF have similar mortality risks and readmission rates,
changes in the prevalence of HFpEF may contribute to changes in the natural history of patients at high risk for progression of CVD. Because no proven therapy for HFpEF currently exists, there is a need for coordinated efforts to address this growing problem. Fifth, both body mass index and the prevalence of metabolic syndrome (MetS) were significantly decreased in the CHART-2 patients as HF stage increased. A recent meta-analysis reported that MetS is associated with a 2-fold increase in cardiovascular outcomes and 1.5-fold increase in all-cause mortality. Furthermore, it is reported that the prevalence of MetS in CHF patients is 45% in males and 19% in females, which is more than double compared with the general population in Japan. Although the prognostic influence of MetS in HF patients remains uncertain, the results will become clearer by the time of completion of the follow-up period. Finally, the use of standard medications, such as renin-angiotensin-system inhibitors and β-blockers, in the CHART-2 patients was increased compared with the CHART-1 patients, but was still insufficient, especially in the Stage-B patients. Because prevention is always better than treatment, it is important to develop strategies to prevent the onset of HF. CHART-2 will provide the framework for improved management strategies for patients with HF. It is also of interest that CHART-2 was performed in the Tohoku area, a district of Japan that can be compared with the rest of Japan, Asia and the world, because lifestyle and genetic background may vary, even in Japan, and we are interested to discover whether the observations in the present study are also the case in Japan generally. Such a nationwide cohort study of HF should be seriously considered by the Japanese Circulation Society.

References