Octogenarian Patients With Heart Failure
Commonly Encountered in Clinical Practice but Only a Minority in Clinical Trials

Kazuhiro Yamamoto, MD

Heart failure is a global burden in industrialized countries, and the number of heart failure patients will continue to increase. One of the reasons for the increase is that the incidence of heart failure increases with aging, particularly after 80 years of age. The increase in octogenarian patients leads to elevation of the rehospitalization rate as well as mortality in heart failure patients. Octogenarian patients are also characterized by worse renal function, which is one of the risks of diuretic resistance. The ATTEND registry has revealed that the prevalence of octogenarian patients is already more than one third of patients hospitalized for acute decompensated heart failure (ADHF) in Japan, and how to treat them in the current era has become a critical issue.

It is well known that β-blockers improve the prognosis of patients with heart failure and reduced ejection fraction, and guidelines recommend the administration of β-blockers in patients without contraindication. However, their use is avoided in elderly patients in Japan. Why is adherence to guidelines low in the treatment of elderly patients? This may be partly explained by the fact that elderly, particularly octogenarian, patients were excluded from the subjects or only a small number were included in previous clinical trials that investigated the effects of β-blockers in heart failure patients. One may argue that the past evidence is not generalizable and cannot necessarily be extrapolated to the treatment of octogenarian heart failure patients. To overcome such discrepancy between guidelines and clinical practice, additional data on the effects in elderly populations that had sufficient percentages of octogenarian patients is needed. Although both were observational, not randomized studies, the findings suggest the risk of underutilization of β-blockers in octogenarian heart failure patients and raise the importance of clinical data in “real world” patients.

Diuretic therapy is frequently required in patients hospitalized for ADHF because most of the symptoms and signs of heart failure are attributed to congestion. The Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST) showed that the vasopressin V2 receptor antagonist tolvaptan provided additive diuretic effects to standard therapy including diuretics and improved heart failure signs and symptoms in patients hospitalized for ADHF; although there was no long-term benefit in its use during the hospitalization. It is very useful in clinical practice to relieve the symptoms due to congestion in patients with resistance to loop diuretics; however, tolvaptan acutely increased the urine volume by more than 50%, raising concerns about acute hypovolemia. To avoid hypovolemia, recognition of thirst is very helpful in clinical practice, and the administration of tolvaptan to patients who cannot feel thirst is prohibited in Japan. It is reasonable and justified to be worried about administration of tolvaptan to elderly patients. In addition, Inamura, et al reported that elderly patients were significantly resistant to tolvaptan treatment compared with younger patients, although the number of study subjects was too small. Therefore, the safety and efficiency of tolvaptan in elderly patients remain controversial.

In a study published in this issue of International Heart Journal, Kinugawa, et al revealed that tolvaptan is well-tolerated and effective in heart failure patients ≥ 80 years old as well as in those < 80 years old. This observational study was conducted in Japan, included more than 900 octogenarian patients hospitalized for ADHF, and showed that the administration of tolvaptan reduced body weight and improved symptoms to a similar degree in both groups of patients. In addition, although the incidence of thirst was significantly lower in patients ≥ 80 years old than in those < 80 years old, the frequency of adverse events including hypernatremia and hypovolemia was not different between the 2 groups. These results strongly suggest that the administration of tolvaptan should be considered in patients hospitalized for ADHF even if they are octogenarian. In addition, this study has provided other important information. The incidence of hypernatremia in octogenarian patients decreased after May 2013 in association with the decrease in the initial dose of tolvaptan. Analysis showed a close relation...
between the initial dose of tolvaptan and the incidence of hypernatremia in patients ≥ 80 years old. In particular, the treatment with a high initial dose of tolvaptan in octogenarian patients with serum Na ≥ 135 mEq/L at baseline was associated with a high incidence of hypernatremia. There was no significant correlation between the incidence of hypernatremia and the initial dose or serum Na level at baseline in patients < 80 years old. Therefore, to obtain the same efficiency and safety in the treatment with tolvaptan in octogenarian patients with ADHF as in patients < 80 years old, special attention should be paid to the initial dose of tolvaptan and serum Na level at baseline. Data collection in this study was started in 2011, and the mean value of the initial dose of tolvaptan was about 9–10 mg/day. The Japanese Circulation Society and The Japanese Heart Failure Society released a joint statement in October 2013 that stated the initial dose of tolvaptan should be 7.5 mg/day (http://www.asas.or.jp/jhfs/topics/20131107.html, in Japanese), and the current data support the statement, in particular for octogenarian patients.

Hypernatremia is another risk of diuretic resistance and is a risk for poor prognosis in elderly patients hospitalized for ADHF. Tolvaptan is likely to provide long-term benefits in patients with extremely low serum Na (< 130 mEq/L) at baseline. Kinugawa, et al described the safety of tolvaptan in octogenarian patients, and thus, administration of tolvaptan may be the treatment of choice for ADHF patients with pronounced hypernatremia, regardless of their age. β-Blockers are most likely effective even in elderly patients with heart failure, however, β-blocker tolerance is slightly attenuated with aging. The relationship between tolerability and age does not mean β-blockers are ineffective in elderly patients, but only cautions us against careless increases in the dose of a β-blocker. Such cautions may well improve the utilization of β-blocker therapy for heart failure patients in clinical practice. For example, the prescription rate of β-blockers in elderly patients has increased in our institute, and this may be at least partly explained by the accumulation of evidence concerning points to consider as well as the beneficial effects of β-blocker therapy in elderly patients. The subjects of clinical trials are not necessarily representative of heart failure patients that are usually encountered in clinical practice. Observational studies with “real world” patients may help to resolve issues left unanswered by clinical trials.

References