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Diagnostic and Therapeutic Strategy for Female Patients With Cardiac Amyloidosis
— Reply —

We are grateful to Drs. Imamura and Nakamura for their interest in and comments on our study,[1] and for highlighting some issues regarding the diagnostic and therapeutic strategies for female patients with wild-type transthyretin amyloidosis (ATTRwt) in an aged Japanese community.

First, Imamura and Nakamura focused on differences in clinical symptoms between female and male patients with ATTRwt. In our experience, the most frequent profile leading to diagnosis was heart failure, and the second most frequent was arrhythmia, in both female and male patients. However, female ATTRwt patients had heart failure symptoms even at the stage of mild left ventricular hypertrophy and preserved ejection fraction. Regarding extracardiac symptoms, there was no significant difference between female and male patients in the prevalence of carpal tunnel syndrome or lumbar spinal canal stenosis. A more detailed investigation of the differences in clinical manifestation by gender in ATTRwt is needed.

Next, Imamura and Nakamura asked whether it was necessary to aggressively pursue a diagnosis of ATTRwt in elderly patients. As points of concern, they raised the lack of a definitive therapeutic strategy for elderly patients with ATTRwt and the cost-effectiveness of tafamidis therapy. We partially agree with their comments, particularly the remarkably high cost of tafamidis. With regard to tafamidis therapy, for all patients with newly diagnosed ATTRwt, we confirm the patient requirements for administration of tafamidis by the Japanese Circulation Society (JCS).[2,3] Furthermore, there is discussion among several physicians about whether to start tafamidis therapy with consideration of various factors including the patient's age, disease severity or progression, patient's will, patient's frailty or activity, and comorbidities. In our initial experiences of tafamidis therapy for ATTRwt over the past 2 years, we administered tafamidis to 46% of patients diagnosed with ATTRwt. In a total of 11 female patients with ATTRwt (mean age of 82.8±5.6 years), 5 patients (mean age of 80.1±5.2 years) were administered tafamidis and the remaining 6 patients (mean age of 84.4±5.8 years) were not administered tafamidis.

However, even for patients without a suitable indication for tafamidis therapy, we think that appropriate diagnosis remains meaningful. For those patients, an understanding of the progressive and life-threatening disease may be important in their future lives and also for their families and clinicians in order to make plans for the rest of their life and to manage optimal care as a viewpoint of an advanced care planning approach. Furthermore, a correct diagnosis of cardiac amyloidosis is important to avoid potentially harmful therapies that may otherwise be standard heart failure treatments. For patients with cardiac amyloidosis, data are scarce supporting the prognostic benefit of standard heart failure treatments. Calcium channel blockers and digoxin are potentially toxic, and β-blockers are regarded as a relative contraindication. Therefore, we strive to make an accurate diagnosis of ATTRwt, even in elderly patients, except in patients who do not want to undergo a detailed examination.

Imamura and Nakamura also raised the use of neurohormonal blockers for patients with mid-range or reduced ejection fraction as a concern in the therapeutic strategy for patients with ATTRwt. We have not proactively used neurohormonal blockers for patients with ATTRwt. In the 27 patients with an ejection fraction <50% in our study,[1] the mean systolic blood pressure measured at the time of right heart catheterization was 118±19 mmHg, the stroke volume index was 28.9±7.9 mL/m^2, and the estimated glomerular filtration rate was 47±18 mL/min/1.73 m^2. As described in the JCS guidelines,[2] in such patients neurohormonal blockers may be poorly tolerated and induce adverse effects such as hypotension, low cardiac output, concomitant autonomic dysfunction, and worsening renal function. However, few studies have shown the safety and tolerability of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients with cardiac amyloidosis.[4] Further investigations of the implications of the use of neurohormonal blockers for patients with ATTRwt are warranted in the future.

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Disclosures

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IRB Information

This study was approved by the Ethics Committee on Medical Research of Kochi Medical School (Reference no. ERB-002080) and was performed in accordance with the Declaration of Helsinki.

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