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EDITORIAL COMMENT

Echocardiography in Cardiac Amyloidosis

From Identification to Classification

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Cardiac amyloidosis (CA) is an infiltrative cardiomyopathy characterized by the accumulation of insoluble amyloid fibrils derived from misfolded soluble precursor proteins. CA is classified based on the type of amyloidogenic protein, with immunoglobulin light chain cardiac amyloidosis (AL-CA) and transthyretin-related cardiac amyloidosis (ATTR-CA) being the primary subtypes. ATTR-CA can be further divided into hereditary transthyretin-related cardiac amyloidosis (ATTRv-CA) and wild-type transthyretin-related cardiac amyloidosis (ATTRwt-CA), based on the presence or absence of TTR gene alteration.[1] The prognosis varies significantly among different subtypes of CA, highlighting the importance of precise etiological diagnosis for appropriate management and prognostic stratification.[2]

Endomyocardial biopsy remains the gold standard for diagnosing CA. However, multimodality imaging techniques, including echocardiography and cardiac magnetic resonance imaging, are increasingly recognized and utilized in the diagnostic evaluation of CA.[3] Echocardiography, with its simplicity, safety, lack of radiation, and bedside availability, often provides the first clue for diagnosing CA,[4] and is recommended as a Class Ib diagnostic tool in the 2022 ESC Cardio-Oncology Guidelines.[5]

Identification of CA by echocardiography can effectively guide subsequent diagnostic work-up and optimize the diagnostic pathway.[6] These readily available echocardiographic red flags, when combined together, demonstrate good diagnostic accuracy.[7,8] Prior researches have mainly concentrated on characterizing the echocardiographic features of CA to differentiate it from other causes of left ventricular hypertrophy.[9-12] In this issue of *JACC: Asia*, Kitada et al[13] advanced this understanding from identification of CA to classification of CA types. The authors conducted a multicenter, retrospective study analyzing echocardiographic data from 172 patients with ATTRwt-CA, 98 with AL-CA, and 41 with ATTRv-CA, to identify key clinical and echocardiographic findings that differentiate ATTRwt-CA from other subtypes of CA. The study observed that higher age, male sex, diabetes mellitus, hyperlipidemia, carpal tunnel syndrome, and paroxysmal atrial fibrillation, along with echocardiographic parameters such as increased left ventricular mass index (LVMI) with relatively modest interventricular septum thickening and papillary muscle (PM) hypertrophy, can enhance the accuracy of screening echocardiography for ATTRwt-CA.[13] The discriminant model achieved an accuracy of 83.8%, with a positive predictive value of 86.0% and a negative predictive value of 81.4%.[13]

Clinically, AL-CA and ATTR-CA exhibit distinct features. Researches indicated that advanced age, male sex, and carpal tunnel syndrome can hint at the likelihood of ATTR-CA.[14-16] Additionally, ATTR-CA patients exhibit higher rates of diabetes mellitus, coronary artery disease, and atrial fibrillation compared with AL-CA patients,[17,18] aligning with the findings of Kitada et al.[13] Despite similarities in echocardiographic findings between AL-CA and ATTR-CA,[7] subtle differences do exist, which may aid in their differentiation.[19] In this study, patients with ATTR-CA were found to have a higher LVMI.[13] However, significant overlap in LVMI between the 2 subtypes has been noted, making accurate differentiation challenging

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based solely on LVMI.[20] Notably, this study also identified that patients with ATTRwt-CA have a larger PM diameter,[13] which may serve as a red-flag sign for ATTRwt-CA and guide further investigation. PM hypertrophy has traditionally been regarded as a unique sign of Fabry disease on both echocardiography and cardiac magnetic resonance imaging.[21,22] However, recent study has shown that PM hypertrophy appears to be more pronounced in patients with CA.[23] PM hypertrophy may serve as a feature of infiltrative cardiomyopathies and storage disorders, often becoming more pronounced in advanced stages of disease.[23] Given that ATTRwt-CA is often considered a disease of the elderly, it is plausible that patients with ATTRwt-CA are more prone to developing PM hypertrophy.

In summary, Kitada et al[13] constructed a discriminant model that holds significant value for improving the accuracy of screening echocardiography in the diagnosis of ATTRwt-CA. These findings could further refine our understanding of the echocardiographic features of different amyloidosis subtypes. Nevertheless, it should be noted that while echocardiography is a valuable tool for identifying CA, it cannot confirm the diagnosis directly.[4,7] Despite the continuous emergence of new echocardiographic techniques to aid in differentiating amyloidosis,[24,25] other noninvasive imaging modalities and biopsy remain essential for definitive diagnosis.

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