Cardiac amyloidosis and aortic stenosis: Great masquerader back again!

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Central Message

Degenerative aortic stenosis shares a common demographic and clinical profile with amyloidosis. Cardiac amyloidosis appears to be a vastly underrecognized entity in patients undergoing AVR.

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Cardiac involvement is a common finding in patients with all types of systemic amyloidosis, including hereditary and age-related (senile) forms, and it often goes unrecognized.^{1,2} The presence of cardiac amyloidosis carries a poor prognosis; patients with the hereditary type have been reported to have a median survival of 24 to 66 months, and patients with age-related amyloidosis (wild-type transthyretin) have been reported to have a median survival of 75 months.³

Degenerative aortic stenosis and age-related amyloidosis share common demographic and clinical characteristics. Cardiac amyloidosis could cause excessive cardiac remodeling or a restrictive physiology that might mimic paradoxical low-flow, low-gradient aortic stenosis (AS), which may easily be missed, making the clinical management challenging. Both surgical aortic valve replacement and transcatheter aortic valve replacement (TAVR) provide excellent outcomes in elderly patients with isolated AS. It is well known, however, that some patients benefit less than others from any heart valve replacement procedure, whether transcatheter or surgical. Previous reports have suggested the potential negative impact of transthyretin amyloidosis in patients with severe AS. At 2-year follow-up among 146 patients who underwent surgical aortic valve replacement, the presence of amyloidosis was associated with death, with a hazard ratio of 9.5.⁴ In a retrospective study of 171 patients with transthyretin amyloidosis and without AS, mortality was the same irrespective of aortic valve replacement, suggesting that transthyretin amyloidosis may have a deleterious contribution to outcomes.⁵ Whether amyloidosis affects mortality synergistically with severe AS or whether it is the primary driver of poor outcomes in patients needs further exploration in large cohorts. Nietlispach and associates⁶ reported that myocardial amyloidosis was present in nearly one-third of all autopsy cases after TAVR and might have contributed to death from progressive heart failure.⁶

In this issue of the *Journal*, Java and colleagues⁷ present the results of a series of 16 patients with confirmed

amyloidosis, undergoing surgical AVR (n = 11) or transfemoral TAVR (n = 5) to treat AS. Their results show excellent perioperative outcomes. Although follow-up was rather heterogeneous, 4 patients died later than 1 year after surgery. Java and colleagues⁷ suggest that aortic valve replacement, either surgical or TAVR, in patients with cardiac amyloidosis is a safe procedure and should be considered for all patients who are deemed good candidates. They provide little detail about the degree of cardiac infiltration and measures of cardiac involvement, whether measured by echocardiography, magnetic resonance imaging, or positron emission tomography. It is well known that these patients can present with different degrees of involvement with amyloid infiltration, which might significantly alter the prognosis.

As mentioned by Java and colleagues⁷ in their discussion of limitations, there is an inherent selection and referral bias in zooming in on the 16 patients who were referred from among more than 2600 patients in their amyloidosis clinic. The effect of aortic valve replacement on outcomes in patients with amyloidosis and AS would be better delineated by also looking at the natural history of patients who did not undergo aortic valve replacement. The similar mortality observed by Sperry and colleagues⁵ in patients with amyloidosis with or without AS justifies the search for less invasive treatment options, of which TAVR is one.

The presence of concomitant cardiac amyloidosis is an important and probably vastly underrecognized entity in elderly patients undergoing aortic valve replacement. Most recently, Scully and colleagues⁸ reported that 13.9% recipients of TAVR have occult cardiac amyloidosis. The question of recognizing it and determining the early and midterm outcomes of patients after surgery is therefore of extreme importance for appropriate risk stratification and to choose the appropriate therapy. It is clear that operative decision making is complex, and the decision to operate should depend on the type of amyloidosis, the severity of the cardiac involvement, and the overall prognosis. Current data support the contention that aortic valve replacement can be performed with low operative risk and provides excellent symptom relief, but the data are insufficient to inform us regarding whether aortic valve replacement will improve long-term survival.

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