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THE AUTHORS REPLY:

The data presented by Dr. Sperry and colleagues are complementary to our recent report (1). Together, the 2 papers show an ample epidemiological overlap between wild-type transthyretin (TTR)-related amyloidosis (wt-ATTR) and degenerative aortic stenosis (AS). In our series, ~13% of patients with AS (and low flow-low gradient, or other echocardiographic red flags) also had wt-ATTR, and in the series reported by the Cleveland group, ~10% of patients with wt-ATTR had associated severe AS. The coexistence of these 2 conditions in the same patient has important clinical, pathophysiological, and prognostic implications.

In both series, the low flow-low gradient hemodynamic profile is particularly frequent and is probably the result of a reduction of myocardial systolic function (not necessarily associated with a reduced left ventricular ejection fraction). The observation of this hemodynamic finding can serve as a red flag for cardiac amyloidosis and prompt a search for other echocardiographic markers such as pericardial effusion and increased thickness of atrioventricular valves, interatrial septum, and right ventricular free wall or a mismatch between left ventricular wall thickness and QRS voltages. The diagnosis can then easily and noninvasively be confirmed by bone-tracer scintigraphy (^{99m}Tc-3,3-diphosphono-1,2 propanodicarboxylic acid in Europe and technetium-99 m pyrophosphate scintigraphy in the United States), which is becoming the gold standard for the diagnosis of TTR-related cardiac amyloidosis.

Despite the fact that the clinician has the possibility of diagnosing coexisting AS and wt-ATTR, this does not yet translate into specific established changes in current decision making. The similar mortality observed by Dr. Sperry and colleagues in wt-ATTR patients with and without AS is thought provoking, and we share their concern regarding the benefit-risk ratio of a surgical strategy. However, transcatheter aortic valve replacement (TAVR) also appears to have incremental risks in this population, including atrioventricular block requiring permanent pacemaker implantation (2) and fatal heart failure (3). At our center, patients with coexistent wt-ATTR and severe AS are currently cautiously managed with repeated balloon valvuloplasties (4) or TAVR. Nonetheless, it must be emphasized that the concomitant presence of wt-ATTR cannot at present be considered an absolute contraindication to aortic valve replacement and that larger prospective studies are urgently required to clarify this issue.

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http://dx.doi.org/10.1016/j.jcmg.2015.11.019

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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