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Impact of significant functional mitral regurgitation and aortic stenosis on outcome of HFrEF patients

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Background: Concomitant aortic stenosis (AS) and functional mitral regurgitation (FMR) are common in patients with left ventricular dysfunction. We evaluated the impact of significant valve diseases on outcome of patients with reduced left ventricular ejection fraction (HFrEF, LVEF < 40%).

Methods: A total of 1264 consecutive HFrEF patients referred to our department between 2009 and 2017 were screened. Transthoracic echocardiography was performed at baseline visit in all patients. Patients with primary MR or received mitral valve operation before or after baseline visit (n = 64) as well as patients underwent aortic valve replacement (AVR) before baseline visit (n = 66) were excluded. Finally, 1134 HFrEF patients were included for final analysis, and all completed a median clinical follow-up of 26 (12-40) months by medical record review or telephone interview. The primary endpoint was all-cause mortality or heart transplantation (HTx).

Results: Moderate or severe FMR or AS was detected in 902 (79.5%) and in 119 (10.5%) patients by echocardiography, respectively. Of patients with significant AS, 47 patients underwent AVR shortly after baseline visit. In total, 353 (31.2%, including HTx n = 11) HFrEF patients died or underwent HTx during follow-up.

Age, body mass index, diabetes, atrial fibrillation, coronary artery disease, chronic respiratory diseases, and renal dysfunction (all P < 0.05) were defined as clinical covariates associated with all-cause mortality/HTx and served as potential confounders in the multivariable Cox regression models. All-cause mortality/HTx was significantly higher in HFrEF patients with significant FMR than patients without significant FMR (33.8% vs. 20.7%, P < 0.001).

Multivariable Cox regression analysis showed significant FMR remained as an independent determinant of all-cause mortality/HTx in patients with HFrEF after adjusted for above mentioned confounders (HR 1.39, 95% CI 1.02-1.90, P = 0.035).

Patients with significant AS without AVR faced increased risk of all-cause mortality/HTx as compared to patients without significant AS (HR 2.34, P < 0.001), while risk of all-cause mortality/HTx was significantly lower in patients with significant AS and underwent AVR as compared to patients without significant AS after adjustment for confounders (HR 0.36, P = 0.008).

In the subgroup of HFrEF patients with significant FMR, significant AS without AVR was independently associated with increased all-cause mortality/HTx as compared to patients without significant AS (HR 2.30, P < 0.001), while outcome is better in AS and FMR patients underwent AVR as compared to patients with significant FMR and without significant AS (survival: 85.4% vs. 67.5%, P < 0.001; HR 0.34, P = 0.010) after adjustment for potential confounding factors.

Conclusion: Moderate to severe FMR and/or AS is incrementally related to higher all-cause mortality/HTx in HFrEF patients. AVR could significantly improve the survival of HFrEF patients with concomitant significant AS and FMR.