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【 EDITORIAL 】

Pharmacological Strategies for Midventricular Obstruction in Patients with Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a markedly heterogeneous cardiac disorder with a variable clinical presentation (1, 2). Left ventricular intracavitary obstruction is an important pathophysiological feature of patients with HCM, and classically occurs at the outflow-tract level, mainly due to the systolic anterior motion of the mitral valve (1, 2). In a minority of patients, however, the obstruction occurs at the midventricular level, termed midventricular obstruction (MVO), which is reported to be independently associated with poor outcomes (3, 4). However, as this condition is relatively rare, treatment strategies for HCM patients with MVO are poorly described. Although there are several reports on the effects of class I antiarrhythmic drugs, myectomy, and implantable cardioverter-defibrillators, there are few reports on the effects of beta-blockers on pressure gradient reduction in HCM patients with MVO (5-7).

In this issue of Internal Medicine, Tezuka et al. report the case of an HCM patient who received bisoprolol and warfarin as a treatment for MVO with apical aneurysm and intra-aneurysmal thrombus without atrial fibrillation (8). As a result, the pressure gradient in the midventricle successfully improved from 53.9 to 21.8 mm Hg, and the intra-aneurysmal thrombus disappeared. Several case reports on HCM patients with MVO have been published, and more recently, several cohort studies have also been reported (3, 4). These studies provided an overview of the medical treatments and the prognosis of HCM patients with MVO, approximately three quarters of whom received beta-blocker therapy (3, 4). However, the effectiveness of beta-blockers for improving the pressure gradient in the midventricle was still unclear. A previous study reported that the pressure gradient of the midventricle in an HCM patient with MVO who exhibited both mid-cavitary obliteration and segmental wall motion abnormalities of the apex was reduced by propranolol during both diastole and systole (9). Similarly in this case reported by Tezuka et al., the pressure gradient in the midventricle was reduced by bisoprolol during both diastole and systole, and diastolic dysfunction was also improved. These results suggest that beta-blocker therapy might be able to improve the pressure gradient of the midventricle, leading to the improvement of the diastolic function in HCM patients with MVO. In addition, Tezuka et al. started bisoprolol treatment at a low dose (0.625 mg/day) with the dosage being gradually increased, taking the fact that the patient was elderly into consideration. Since there are few reports on the starting dose and bisoprolol dosing method in elderly HCM patients with MVO, this report will be a reference for future bisoprolol therapy for improving the pressure gradient in the midventricle.

Another problem in this reported case by Tezuka et al. was the presence of apical aneurysm formation and intra-aneurysmal thrombus. Previous studies have indicated that MVO is likely to complicate apical aneurysm in patients with HCM (3, 10-12). Maron et al. hypothesized that the apical aneurysm and the associated regional myocardial scarring occur secondary to an increase in left ventricular wall stress, which occurs due to MVO and the elevation of the intracavitary pressure (10). Increased wall stress imposes a greater pressure load on the apical myocardium and increases its oxygen demand, while simultaneously reducing coronary flow through extravascular compression, leading to chronic myocardial ischemia, scarring, and aneurysm formation (10). HCM patients with apical aneurysms therefore represent a high-risk subgroup at risk of a number of adverse HCM-related consequences, including sudden death, thrombus formation, and end-stage heart failure (11). In addition, a substantial proportion of HCM patients with apical aneurysm were identified with thrombus formation within the aneurysm or who had experienced a thromboembolic event, even in sinus rhythm (11). These observations suggest

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that the dyskinetic or akinetic apical chamber can provide a structural basis for intracavitary thrombus formation, which strongly suggests that anticoagulation should be considered for all patients with apical aneurysm (11).

As Tezuka et al. reported, beta-blocker therapy and anticoagulation may be the first choice for the initial treatment of MVO-HCM patients with apical aneurysm formation. However, it is not entirely clear whether beta-blockers are effective for mid-cavitary obstruction as well as outflow-tract obstruction. In order to establish beta-blocker therapy for HCM patients with MVO, further clinical research rather than case reports will be necessary. In addition, symptom reduction is also an important goal of medical therapies for HCM (1, 2). Although our previous study demonstrated that the New York Heart Association (NYHA) functional class in patients with MVO was higher than that in those without MVO (NYHA class ≥II 71.7% vs. 44.4%) (3), it is still unclear whether beta-blockers are effective for symptom reduction in HCM patients with MVO. However, gradient reduction with negative inotropic agents (i.e., beta-blockers) might be expected to provide relief from dyspnea, wall stress, myocardial scarring, and apical aneurysm formation in patients with MVO. Furthermore, although HCM patients with apical aneurysm are considered to have a higher risk of thromboembolic events than those without aneurysm, it is not entirely clear whether anticoagulation is effective for primary stroke prevention in HCM patients with apical aneurysm and sinus rhythm. In this respect, further studies are required to determine the most appropriate treatment strategies for gradient and symptom reduction, stroke prevention, and achieving better outcomes in MVO-HCM patients with apical aneurysm formation.

The authors state that they have no Conflict of Interest (COI).

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