The Efficacy of Cardiac Myosin Inhibitors Versus Placebo in Patients with Symptomatic Hypertrophic Cardiomyopathy

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Introduction: Given the interplay between hypertrophic cardiomyopathy, elevated resting LVOT gradients (≥ 50 mm Hg) and heart failure and cardiovascular death, cardiac myosin inhibitors have recently emerged as a promising novel therapy to improve HCM-related outcomes by regulating myocardial relaxation and contractility, and thereby reducing intracavitary gradients.

Methods: We performed a literature search using PubMed, Embase, and Cochrane Library from inception through May 2022 to assess the impact of novel cardiac myosin inhibitors (Mavacamten and Aficamten) on LVOT gradient and functional capacity in patients with symptomatic hypertrophic cardiomyopathy. The co-primary outcomes were mean percent change from baseline in resting LVOT gradient, Valsalva LVOT gradient, and NYHA Class Improvement ≥ 1. Secondary outcomes included mean percent change from baseline NT ProBNP, Troponin I, and LVEF.

Results: 4 studies (all randomized-control trials, including 3 Mavacamten-focused and 1 Aficamten-focused trials) involving 463 patients were included in the meta-analysis. Compared to patients receiving placebo, the cardiac myosin inhibitor group demonstrated statistically significant differences in percent change in mean resting LVOT gradient (MD -62.48, CI -65.44, -59.51, p <0.00001), Valsalva LVOT gradient (MD -54.21, CI -66.05, -42.36, p <0.00001), and mean percentage in NYHA Class Improvement ≥ 1 (OR 3.43, CI 1.90, 6.20, p <0.0001). Regarding secondary outcomes, the intervention group demonstrated statistically significant reductions in meant percent change from baseline in NT-proBNP (MD -69.41, CI-87.06, -51.75, p < 0.00001), Troponin I (MD, -44.19, CI -50.59, -37.78, p < 0.00001), and LVEF (MD -6.31, CI -10.35, -2.27, p = 0.002).

Conclusion: The use of cardiac myosin inhibitors in patients with symptomatic hypertrophic cardiomyopathy may confer both clinical and symptomatic benefits, at the possible expense of LV ejection fraction. Further trials with large sample sizes are needed to confirm our findings.

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