Short Editorial

Cardiac Myosin Inhibitors in Patients with Hypertrophic Cardiomyopathy

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Short Editorial referring to the article: Efficacy of Cardiac Myosin Inhibitors in Symptomatic Hypertrophic Cardiomyopathy: An Updated Meta-Analysis and Systematic Review

In recent years, we have witnessed a significant shift in the management of symptomatic Hypertrophic Cardiomyopathy (HCM). For decades, treatment relied on medications that provided hemodynamic support without directly addressing sarcomeric hypercontractility, the primary pathophysiological driver of the disease. The emergence of Cardiac Myosin Inhibitors (CMIs), particularly mavacamten and aficamten, has transformed this landscape.[1,2] In an article published in this issue of the International Journal of Cardiovascular Sciences, Fogaça PHT *et al*.[3] present an updated systematic review and meta-analysis that reinforces the efficacy of this class of medications while providing important insights into their effects in both obstructive and non-obstructive HCM.

The study pooled data from six randomized controlled trials. Five included patients with obstructive HCM, whereas one – the MAVERICK-HCM trial – included patients with non-obstructive HCM.[1,2,4-7] The inclusion of non-obstructive patients represents a distinctive aspect of this analysis, as the benefits of CMIs in the absence of left ventricular outflow tract (LVOT) obstruction remain less well established.

The efficacy results were robust. The proportion of patients who improved by at least one New York Heart Association (NYHA) functional class was significantly higher in the CMI group (59.1%) than in the placebo group (26.4%). Likewise, the mean change from baseline in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) favored treatment with CMIs. LVOT gradients, both at rest and following the Valsalva maneuver, were significantly reduced in patients receiving CMIs compared with those receiving placebo. Among the secondary outcomes, peak oxygen consumption (pVO_2) improved in the CMI group, further supporting the functional benefits of these agents beyond symptomatic improvement. A reduction in left ventricular ejection fraction (LVEF) was also observed, an effect consistent with the mechanism of action. Although this finding warrants monitoring, it rarely results in clinically significant heart failure. Importantly, no significant heterogeneity was observed among the included studies after exclusion of the MAVERICK-HCM trial because of concerns regarding the randomization process. This finding strengthens the consistency and reliability of the pooled estimates.

These results are largely consistent with those of a recently published meta-analysis by Yassen *et al*.[8] Both studies demonstrated the superiority of CMIs over placebo in improving NYHA functional class, LVOT gradients, KCCQ-CSS, and pVO_2 in patients with obstructive HCM. However, the review by Fogaça et al.[3] incorporates more recent clinical trials, includes data from patients with non-obstructive HCM through the MAVERICK-HCM trial, and provides a more detailed assessment of heterogeneity across studies.

In doing so, the authors address an important question: whether CMIs may have a therapeutic role in patients with non-obstructive HCM. Current evidence remains inconclusive in this population, and studies such as MAVERICK-HCM and ODYSSEY-HCM have demonstrated only modest effects.[5,8]

At present, mavacamten and aficamten represent major therapeutic advances for patients with symptomatic obstructive HCM, offering a truly disease-targeted treatment strategy. However, one of the greatest barriers to their widespread adoption remains limited access due to their high cost. Until issues related to cost-effectiveness and equitable access are not adequately addressed, these therapies may remain unavailable to many patients who could potentially benefit from them.

Keywords

Hypertrophic Cardiomyopathy; Cardiac Myosins; Therapeutics

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