

THE EFFECT OF HIGH-DOSE VALSARTAN ON LEFT VENTRICULAR FUNCTION FOLLOWING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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The study by Kim et al.¹⁾ revealed that while improvement of regional function by valsartan was more effective in the high-dose (160 or 320 mg) valsartan group, compared with the low-dose group, high-dose valsartan did not have effects on left ventricular ejection fraction (LVEF) and left ventricular (LV) size.

Angiotensin-receptor blockers (ARBs) should be used in post-ST-segment elevation myocardial infarction (STEMI) patients with evidence of LV dysfunction who are intolerant to angiotensin-converting enzyme (ACE) inhibitors.²⁾ ARBs reduce mortality and morbidity rates in patients with heart failure (HF) and reduced LVEF. Investigators of the Val-HeFT³⁾ and CHARM⁴⁾ trials reported that high doses of ARBs improved clinical outcomes. Recently, the HEAAL study⁵⁾ demonstrated that high-dose (losartan 150 mg) is superior to low-dose ARB (losartan 50 mg) in patients with HF and reduced LVEF. In contrast to the latter ARB trials, the VALIANT study⁶⁾ focused on patients with HF after acute myocardial infarction (MI) and demonstrated that a high-dose ARB (valsartan 320 mg) was not inferior to an ACE inhibitor (captopril 150 mg). However, the VALIANT study did not evaluate dose-dependent clinical outcomes.

The study by Kim et al.¹⁾ is helpful to understand changes in dose-dependent LV remodeling. However, this study has several limitations in terms of dose-dependent echocardiographic changes. First, the study population size was too small to compare LVEF and LV size between two groups. In the VALIANT Echo study, the small improvement in LVEF was observed in 610 patients. Second, baseline LVEF was too high (mean EF $52.7 \pm 8.1\%$) to evaluate LV remodeling, compared to other remodeling studies such as the VALIANT

(EF $\leq 35\%$) and HEAAL (EF $\leq 40\%$) studies. Third, the results do not definitively answer the question of why improvement of segmental wall motion was better in the high-dose than in the low-dose group. If additional information, such as myocardial microcirculation by myocardial contrast echocardiography and drugs affecting LV function were provided, the results would be more convincing.

Valsartan (Diovan) is an oral angiotensin II-receptor antagonist with specificity for the angiotensin II type 1 receptor subtype. It has been shown to attenuate the progression of chronic HF and to reduce mortality in patients with myocardial infarction. Although based on clinical trials high-dose ARB (Valsartan 160 mg BID) is recommended for the improvement of LV function in heart failure, low-dose ARB is preferred in clinical practice in patients with HF. The ARB dose may vary according to race and personal preferences. In the VALIANT study, discontinuation of valsartan (160 mg BID) was observed in 1,675 (34%) patients. However, in the study by Kim et al.¹⁾, discontinuation of high-dose valsartan was seen in 43 (68%) patients.

By comparing two groups prospectively after randomization, the present study concludes that high-dose valsartan is more effective than low-dose valsartan in improving segmental wall motion. Even though this is a small study to compare dose-dependent echocardiographic LV remodeling, it reveals the benefit of high-dose treatment, which may allow recommendation of high-dose valsartan even in post-STEMI cases.

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