Effects of Valsartan, an Angiotensin II Receptor Blocker, on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction Who Receive an Angiotensin-Converting Enzyme Inhibitor

(ACE 阻害薬内服中の急性心筋梗塞患者における冠動脈硬化進行に アンギオテンシン II 受容体拮抗薬追加投与が与える影響)

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Introduction: Patients with acute myocardial infarction (AMI) have a greatly increased risk of subsequent cardiovascular event even if after successful revascularization therapy was performed. Pharmacotherapy for secondary prevention is mandatory in this clinical setting. The Survival and Ventricular Enlargement (SAVE) trial was large randomized, double-blind, placebo-controlled trial in 2231 patients within 3 to 16 days after AMI and left ventricular ejection fraction of 40 percent or less but without overt heart failure or symptoms of myocardial ischemia. In this trial, mortality from all causes was significantly reduced in an angiotensin-converting enzyme inhibitor (ACE-I) group as compared with the placebo group (Pfeffer et al, 1992). Japanese Circulation Society guidelines for secondary prevention for myocardial infarction also recommend Angiotensin II receptor blocker (ARB) is an alternative approach to renin-angiotensin-aldosterone system inhibition. Recent trials have demonstrated that ARBs are as effective as ACE-I in improving survival and reducing cardiovascular morbidity in patients with congestive heart failure. Preclinical data demonstrate that RAS activation plays an important role in atherosclerosis and that renin-angiotensin-aldosterone system (RAS) inhibition may have a direct beneficial effect on the arterial wall (Ferrario and Strawn, 2006; Yusuf et al, 2000). Our hypothesis is that the combined effects of these drugs might have higher anti-atherosclerotic efficacy. We assessed the effects of the ARB on coronary plaque progression in patients of AMI after successful coronary revascularization who received an ACE-I.

Methods: After local ethics committee approval and obtaining informed consent, 116 patients with AMI were randomly assigned to receive a combination of valsartan and captopril or captopril alone. Non-culprit intermediate coronary atherosclerosis was assessed by intravascular ultrasound. The primary and secondary end points were the nominal change in percent atheroma volume (PAV) and the percent changes in lumen volume (%ΔLV), respectively. The target lesion was measured at 1-mm intervals. The luminal/intimal borders were traced manually to determine the lumen cross-sectional area (CSA). The external elastic membrane (EEM) CSA, which represents the area
encompassed by the medial/adventitial border, was measured by tracing the leading edge of the adventitia. Atheroma volume (AV) was calculated as the sum of the differences between the EEM and lumen CSAs across all evaluable slices: atheroma volume = Σ (EEM CSA – lumen CSA). Percent atheroma volume (PAV) was calculated as AV/Σ EEM CSA × 100. The primary end point, the nominal change in PAV, was calculated with the following formula: PAV (follow-up) – PAV (baseline). The secondary endpoint, the percent change in lumen volume (%ΔLV), was calculated with the following formula: (follow-up lumen volume – baseline lumen volume)/baseline lumen volume × 100.

**Results:** The combination group showed a significant lower systolic blood pressure (117 vs. 125 mm Hg; p = 0.02) and a lower plasma aldosterone level (56 vs. 75 pg/ml; p = 0.02) at follow-up. The nominal change in PAV was slightly lower in the combination group than in the ACE-I group (-1.9 vs. -0.68%, p = 0.06). %ΔLV was -0.3% in the ACE-I group and was 4.3% in the combination group (p = 0.03). Logistic regression analysis showed that additional ARB therapy was independently associated with lumen volume enlargement (odds ratio 2.144; 95% confidence interval, 1.818 to 5.618; p = 0.03).
Discussion: In this study of patients with AMI, additional ARB therapy had minimal impact on the progression of coronary atherosclerosis as compared with an ACE-I alone. The absence of a decrease in plaque in the combination group as compared with the ACE-I group in our study is in accordance with the results of these pivotal clinical trials, although whether coronary plaque progression is
directly related to outcomes remains to be determined. RAS inhibition with an ACE-I alone may be sufficient and dual blockade might not confer any additional benefits in terms of reducing the progression of coronary atherosclerosis in patients with AMI. However, we cannot exclude the possibility that ARB induced a change in the histologic composition of plaque, which was not assessed in this study. Further study must be required to evaluate the impact of RAS inhibition in human coronary atherosclerosis.


Publication list

I 主論文
Effects of valsartan, an angiotensin II receptor blocker, on coronary atherosclerosis in patients with acute myocardial infarction who receive an angiotensin-converting enzyme inhibitor


III 参考論文
1. Influence of omeprazole and famotidine on the antiplatelet effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes: a prospective, randomized, multicenter study

2. B-type natriuretic peptide as a predictor of ischemia/reperfusion injury immediately after myocardial reperfusion in patients with ST-segment elevation acute myocardial infarction

3. Impact of plaque rupture on infarct size in ST-segment elevation anterior acute myocardial infarction

4. Long-term survivor with pulmonary veno-occlusive disease