（博士課程医学領域）　　（別記様式第５号）
（課程・論文博士共通）

論　文　内　容　要　旨

※ 整理番号		（ふりがな） 氏名（自署）	印
論文題目	Persistent Dysfunction of Coronary Endothelial Vasomotor Responses is Related to Atheroma Plaque Progression in the Infarct-Related Coronary Artery of AMI Survivors （急性心筋梗塞患者における梗塞関連動脈の遷延する血管内皮機能障害は動脈硬化進行と関連する）		

論文内容要旨

Aim: Although coronary endothelial vasomotor dysfunction predicts future coronary events, there are few human studies showing the relationship between endothelial vasomotor dysfunction and atheroma plaque progression in the same coronary artery. This study examined whether endothelial vasomotor dysfunction is related to atheroma plaque progression in the infarct-related coronary artery of ST-segment elevation myocardial infarction (STEMI) survivors using serial assessment of coronary plaque size with intravascular ultrasound (IVUS) and coronary vasomotor responses to acetylcholine (ACh).

Methods: This prospective study initially enrolled 210 consecutive patients with a first STEMI due to occlusion of a proximal segment of the left anterior descending coronary artery (LAD), who were admitted to Yamanashi University Hospital between January 2008 and December 2017. Finally, this study included 50 patients with successful reperfusion therapy with percutaneous coronary intervention (PCI). The study also included 20 age- and sex-matched control patients, who were selected from 25 consecutive patients with atypical chest pain and normal coronary angiograms. The control patients served as a reference group for determination of cut-off values of coronary vasomotor dysfunction. IVUS and vasomotor response to ACh in the LAD were measured within two weeks of acute myocardial infarction (AMI) (1st test) and repeated six months (2nd test) after AMI under optimal anti-atherosclerotic therapies. Also, measuring the coronary vasomotor response was performed only once in all of the control subjects. In this study, the greatest dilator response from baseline among the responses to 3 ACh doses (5, 10 and 50 μg/min) was selected as the epicardial coronary vasomotor response to ACh for each patient and control subject. The epicardial coronary response with the least constriction from baseline among the 3 ACh doses was selected for each patient who did not have a dilator response to any ACh dose. Similarly, the greatest increase in coronary flow response from baseline among the 3 ACh doses was selected as the coronary flow response to ACh for each patient and control subject. The coronary vasomotor dysfunction cut-off values in response to ACh were arbitrarily defined as the lower 10% of the distribution of coronary vasomotor responses to ACh in control subjects.

Results: As a whole, patients' Percent atheroma volume (PAV) and total atheroma volume (TAV) at the target lesion decreased over six months. PAV and TAV in the LAD progressed over six months of follow-up in 18 and 14 patients, respectively. The epicardial coronary diameter and coronary flow responses to ACh at the 1st test were similar between patients with and without progression of PAV or TAV. PAV and TAV progression was significantly associated with persistent impairment of epicardial coronary artery dilation and coronary blood flow increase in response to ACh at both the 1st and 2nd tests.

備　考

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PAV and TAV progression had no significant association with traditional risk factors, PCI-related variables, medications, and the coronary vasomotor responses to sodium nitroprusside, an endothelium-independent vasodilator. The change in PAV or TAV over six months had a significant inverse correlation with the difference in epicardial coronary diameter and coronary flow response to ACh from the 1st to 2nd test

Discussion: The present study showed that the percent changes in PAV or TAV over six months of follow-up were inversely correlated with the changes in epicardial coronary diameter and coronary flow responses to ACh. In addition, the progression of PAV and TAV was associated with persistently impaired coronary vasomotor responses to ACh. This is the first study to show that persistently impaired endothelial vasomotor function was related to atheroma plaque progression in the entire infarct-related coronary artery tree of STEMI survivors. Endothelial vasomotor function at baseline (1st test) did not predict plaque progression in the infarct-related coronary artery in the present study. A single assessment of endothelial vasomotor function may not necessarily reflect later atherosclerotic risk burden in the coronary artery because anti-atherosclerotic treatments were initiated after MI onset. Changeable endothelial function after the baseline measurement may explain the association of coronary plaque progression with the change in the endothelial vasomotor function over time, but not with the baseline endothelial function in the infarct-related coronary artery in the present study. The longer endothelial dysfunction persisted, the greater the progression of atherosclerotic plaque in the infarct-related coronary artery of STEMI survivors.

Conclusions: Persistent impairment of endothelial vasomotor function in the conduit arterial segment and the resistance arteriole was related to atheromatous plaque progression in the infarct-related coronary arteries of STEMI survivors.

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