HEART & LUNG

Effect of coronary revascularization on serum collagen biomarkers and left ventricular remodeling in patients with acute myocardial infarction

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ABSTRACT

Objective: After an acute myocardial infarction (AMI), early coronary revascularization alleviates the synthesis of cardiac collagen and ventricular remodeling. However, the impact of late coronary revascularization on the synthesis of myocardial collagen or on serum collagen biomarkers is unknown. This study aimed to investigate the effects of late coronary revascularization on serum collagen biomarkers after AMI.

Methods: Forty-five patients were divided into early (n = 20) and late (n = 25) coronary revascularization groups. The early coronary revascularization group received either successful percutaneous coronary intervention (PCI) or thrombolytic therapy within 6 hours of their myocardial infarction (MI), whereas the late PCI group received PCI between 12 and 14 days after their MI. Serum type I procollagen (PICP) and type III procollagen (PIIINP) were measured by radioimmunoassay.

Results: In the early coronary revascularization group, the amount of serum PICP on days 60 and 180 was similar to that of week 1 ($P > .05$). The PICP on days 90 and 180 in the late coronary revascularization group was higher than in the early coronary revascularization group at the same time point ($P < .05$). No significant difference was evident in mean serum PIIINP between the two groups on day 60 or 180 after the MI ($P < .05$).

Conclusion: Late coronary revascularization in patients with acute ST-elevation MI was associated with an elevation in serum PICP. Early coronary revascularization should be performed in patients with ST-elevation, to alleviate myocardial remodeling.

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Ventricular remodeling after an acute myocardial infarction (AMI) is one of the major determinants for the long-term prognosis of patients after an AMI.[1] Ventricular remodeling is influenced by several factors, one of which is infarct healing that involves the reformation of extracellular matrix. Type I collagen is one of the most abundant components of the extracellular matrix, and plays a key role in ventricular remodeling during the healing process.[1] The carboxy-terminal peptide of type I procollagen (PICP) appears in the bloodstream during the synthesis of myocardial type I collagen. Serum PICP increases when the synthesis of type I collagen is exaggerated, and the ratio between the number of type I collagen molecules produced and that of PICP released is theoretically 1:1.[2] After an AMI, PICP is significantly correlated with the left ventricular (LV) end systolic and end diastolic volume indices and the LV ejection fraction.[3]

Collagen type III is a major fibrillar constituent of granulation tissues. The amino-terminal propeptide of type III procollagen (PIIINP) is released into serum during conversion from type III procollagen to type III collagen.[4] Elevated serum PIIINP is believed to reflect an enhanced synthesis of collagen III or reduced metabolism.[4,5] Persistent increases of PIIINP after an AMI is associated with poor LV function and high mortality.[6]

Early coronary revascularization through percutaneous coronary intervention (PCI) or thrombolytic therapy leads to myocardial salvage, the preservation of global LV function, and improved patient survival.[7] Late coronary revascularization through PCI 12 hours after a myocardial infarction (MI) diminishes LV dilatation and improves LV function, compared with conservative pharmacotherapy.[8,9] However, a recent study found that late coronary revascularization and conservative drug therapy exerted a similar effect on ventricular volumes or remodeling after MI.[10] In patients successfully treated with coronary revascularization soon after their MI, the levels of serum PICP and PIIINP are lower than in those without successful revascularization, suggesting that early coronary revascularization alleviates the synthesis of cardiac collagen induced by ischemic injury.[11] Little information is available about the impact of late coronary revascularization on the synthesis of myocardial collagen or serum collagen biomarkers. This study sought to investigate the effects of late coronary revascularization on serum collagen biomarkers and LV remodeling after an AMI.

Patients and Methods

Patient Selection

The study was approved by our Institutional Review Board. Written, informed consent was obtained from all participants before the study. Between January 2008 and June 2009, patients with acute ST-elevation MI were selected for this study. Exclusion criteria comprised: (1) age $\geq$80 years; (2) a previous Q-wave MI; (3) a previous diagnosis of congestive heart failure or cardiomyopathy; (4) severe valvular heart disease or severe LV dysfunction (New York Heart Association Function class IV) at admission; (5) noncardiovascular illnesses such as cancer, significant renal or hepatic dysfunction, or respiratory disease; and (6) refusal to give informed consent. The diagnosis of ST-elevation MI was based on typical angina chest pain, ST-elevation according to a body-surface electrocardiogram, and positive results of troponin and creatine kinase-MB (CK-MB) tests. The management of AMI was in accordance with standard protocols in our hospital, including pain relief with morphine, intravenous nitroglycerin, aspirin, heparin, nitrates, β-blockers, statins, and angiotensin-converting enzyme inhibitors. Early or primary PCI is an elective treatment in our department. Its application is determined by the availability of interventional cardiologists and also by the patient's consent. For patients admitted to the hospital within 6 hours after the onset of chest pain, but who did not receive early PCI, thrombolytic therapy was prescribed.

The selected patients were divided into 2 groups. The early coronary revascularization group included patients who had received successful PCI or thrombolytic therapy within 6 hours after their MI. The late coronary revascularization group included patients who did not receive early PCI or who had received unsuccessful thrombolytic therapy within the first 12 hours of MI, or those who presented at the hospital 12 hours or more after their MI. These patients underwent PCI between 10 and 14 days after their MI.

Percutaneous coronary intervention was performed according to standard techniques. The selection of catheters, stents, and adjunctive therapies was left to the discretion of the operators. Successful PCI, which was defined as Thromoblysis In Myocardial Infarction (TIMI) flow grade 2 or 3 and residual stenosis of $\leq$50% at the culprit coronary artery, was achieved in all patients. Successful thrombolytic therapy was defined as the relief of chest pain and a $<$50% reduction of ST-segment elevation 60 minutes after the initiation of thrombolysis therapy.[12]

Echocardiographic Studies

Two-dimensional and Doppler echocardiographic studies were performed within 6 hours after admission, and on days 7, 90, and 180, by a cardiologist using a ViViD7 Cardiac Ultrasound Unit with a 2.5-MHz transducer (General Electric, Erie, PA). The examiner was unaware of each patient's group and clinical data. The LV end-diastolic dimension, LV end-systolic dimension, LV end-diastolic volume, and LV end-systolic volume were measured. The LV ejection fraction was measured from an apical view by Simpson's biplane method. The mean of 3 measurements was used.

Measurement of PICP and PIIINP

Serum samples, which were collected on days 7, 90, and 180 after MI, were stored at -70°C until assay. All