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Two-dimensional longitudinal strains and torsion analysis to assess the protective effects of ischemic postconditioning on myocardial function: A speckle tracking echocardiography study in rabbits

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ABSTRACT

The reperfusion injury that occurs in the early reperfusion often results in myocardial dysfunction. This study evaluated global and regional left ventricular (LV) function using speckle tracking echocardiography (STE) in a rabbit ischemia–reperfusion (I/R) model with and without ischemic postconditioning (I-PostC). The aim is to investigate the potential benefit of I-PostC for myocardial function and validate whether regional longitudinal strain is an appropriate index to indicate myocardial dysfunction. Forty rabbits were divided into an ischemia–reperfusion group (group I) and an I-PostC group (group II). After the coronary arteries were ligated, LV systolic strain and twist parameters decreased, and absolute value of strain rate of isovolumetric relaxation period (SRivr) and post-systolic strain index (PSI) increased significantly in both groups (all $p < 0.05$). After reperfusion, regional longitudinal systolic strain rate (SRsys), systolic strain (Ssys), LV twist and untwisting rate increased, and SRivr and PSI decreased in group II. These changes were not seen in group I. All STE parameters were correlated with area of necrosis (AN)/area at risk (AR) (all $p < 0.05$). The correlations were more relevant between SRsys and AN/AR ($r = -0.673$) and between Ssys and AN/AR ($r = -0.777$) (both $p < 0.001$). The intra- and inter-observer repeatability of STE parameters were good with correlation coefficients (CCs) >0.8 or 0.6. The sensitivities of GSRsys, GSsys, SRsys, Ssys, and LV twist to detect the myocardial infarction were 81.3%, 62.5%, 87.5%, 93.8% and 81.3%, respectively. And the specificities of those parameters were 75.0%, 81.2%, 75.0%, 87.5% and 68.7%. These results indicate that STE is useful for quantitative detection on myocardial function improvement induced by I-PostC in a rabbit I/R model. The regional index—Ssys is an appropriate parameter to indicate myocardial dysfunction because of its sensitivity, specificity, and repeatability.

1. Introduction

Acute myocardial infarction (MI) is caused by severe reduction or complete blockage of coronary artery flow, resulting in myocardial cell death and reduction of ventricular function. MI is a serious worldwide health issue [1], and the incidence is increasing in many countries, especially in younger populations [2,3]. Early and effective restoration of perfusion to ischemic myocardium is necessary to prevent myocardial cell death. However, some studies found that myocardial injury was more likely to occur during the early period of reperfusion than during the period of ischemia [4]. This is termed reperfusion injury (RI), and may result in arrhythmias, myocardial systolic and diastolic dysfunction, abnormal metabolism, and changes in myocardial ultrastructure including cell apoptosis and necrosis [5,6]. RI is the main reason why it is difficult to improve clinical parameters after restoration of perfusion to ischemic myocardium, or even to aggravate clinical parameters.

It is important to protect the ischemic myocardium from RI as much as possible. Ischemic postconditioning (I-PostC) is a good method of improving tissue tolerance to RI. The main advantage of I-PostC is that cardioprotective therapy can be implemented at the time of reperfusion [7,8]. I-PostC is therefore a more valuable method of cardioprotection in myocardial ischemia–reperfusion (I/R) than ischemic preconditioning.

To date, assessment of the effects of I-PostC has been mainly focused on laboratory and clinical indicators, such as cytokine expression, apoptotic cells, myocardial enzyme levels, and infarct size [9–12]. Few studies have investigated changes in myocardial function in an I-PostC model, even though this is of clinical importance. Accurate evaluation of global and regional myocardial

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function is important for the assessment of reperfusion effects and the selection of therapeutic strategies. Many methods of quantitative evaluation of regional myocardial function have been described in recent years. Doppler tissue imaging has been a standard method, because it has good sensitivity and repeatability. However, the inherent limitations of Doppler imaging make it difficult to evaluate radial and rotational myocardial motions with this method. These motions are often affected by factors such as the position and breathing of the patient, twisting of the heart, and motions of adjacent myocardial segments. Although some previous studies evaluated the cardioprotective effects of I-PostC in patients using magnetic resonance imaging [13,14], they only assessed global function by measurement of left ventricular ejection fraction (LVEF), which often does not change after I-PostC treatment. Methods used to assess myocardial function should ideally be non-invasive and objective, and should not have angular dependence or be influenced by the effects of stretch. Speckle tracking echocardiography (STE) is an appropriate method with above characteristics. It tracks the displacement of segment end points with a high frame rate and calculates strain from the change of length between them. Then the curves of myocardial strain, strain rate, displacement, velocity, and heart rotation can be extracted [15]. As the tracking is based on grayscale B-mode images, it is in principle angle independent. Speckle tracking can track cardiac longitudinal motion, as well as myocardial radial, circumferential, and rotational motion, and can evaluate regional myocardial function and global deformation. It provides a non-invasive and quantitative method for the assessment of LV myocardial deformation and overcomes the shortcomings of Doppler echocardiography [16].

This study evaluated the myocardial function changes after ligation and reperfusion using STE in a rabbit I/R model with and without I-PostC. And it compared the correlations of STE parameters with AN/AR and the repeatabilities and sensitivities of them to detect MI. The aim is to investigate the potential benefit of I-PostC for myocardial function improvement after reperfusion and validate whether regional longitudinal strain is an appropriate index to indicate myocardial dysfunction.

2. Materials and methods

2.1. Animals and experimental protocol

All experimental protocols were approved by the Institutional Animal Care and Use Committee and Animal Ethics Committee of Harbin Medical University. Forty-six healthy adult Japanese white rabbits of either sex weighing between 2.00 and 2.75 kg were initially selected. Six rabbits were excluded from the study because of death. The remaining 40 rabbits were randomized into two groups: (1) I/R (group I, $n = 20$), the LV branch of left anterior descending coronary artery (LAD) was reversibly occluded for 45 min followed by 180 min reperfusion; (2) I-PostC (group II, $n = 20$), the LV branch was reversibly occluded for 45 min followed by three cycles of 30 s reperfusion and 30 s reocclusion, and then reperfusion for a total of 180 min.

2.2. Preparation for surgery

All animals were anesthetized with an intravenous injection of pentobarbital sodium (30 mg/kg) into a marginal ear vein, and the trachea was intubated with a 14-gauge endotracheal tube. Deep anesthesia was maintained with intermittent intravenous injections of pentobarbital sodium (10–15 mg/kg). Animals were ventilated with oxygen using a small animal ventilator at a rate of 20–30 breaths/min with a tidal volume of 30 ml/kg. An external electrocardiogram (ECG) was recorded. The chest was opened via a left thoracotomy through the fourth or fifth intercostal space and expanded using a small chest expander. The pericardium was incised and the heart was exposed. The left atrium was clamped and was retracted upwards to expose the LV branch of LAD. A 1.0 polypropylene suture was placed around the LV branch of LAD at 2.0 mm below the left atrium. The ends of the suture were threaded through a piece of tubing to form a reversible snare. Myocardial infarction was confirmed by observation of changes in color and motion of LV wall, and ST segment elevation on ECG.

2.3. Conventional echocardiography

Echocardiography was performed by an experienced operator using a Vivid 7 Dimension ultrasound scanner (GE Healthcare, Horten, Norway) by timed collection of effluent at baseline, 45 min after ligation, and 180 min after reperfusion in open chest rabbits. M-mode and two-dimensional (2D) echocardiography data were collected using a 10-MHz pediatric sector transducer. The minimal frame rate was 100 frames/s. The echo pattern, shape, and motion of the ventricular walls were observed. The left atrial diameter and LV end-diastolic diameter were measured according to the recent guidelines of the American Society of Echocardiography [17]. The LV ejection fraction (LVEF), LV end-diastolic volume, LV end-systolic volume, and stroke volume were calculated by the biplane Simpson's method. The heart rate was obtained by ECG. 2D movies of three consecutive cardiac cycles in three standard apical views (4-chamber, 2-chamber, and long-axis of LV) and three LV short-axis views (at the levels of the mitral valve annulus, the papillary muscle, and the apex) with clear endocardial and epicardial borders were collected and stored digitally on an EchoPac 7.0 workstation (GE Medical Systems, Horten, Norway) for further analysis.

2.4. STE

Analysis of STE images and acquisition of curves were performed in an off-line EchoPac computer. The speckle tracking analysis was performed by the same trained operator for all images. The images were analyzed in the end-diastolic frame. The endocardial border was traced, and the width of analyzed myocardium was adjusted according to the epicardial border. The software algorithm automatically divided the LV long-axis and short-axis views into six segments each for speckle tracking throughout the cardiac cycle. A total of 18 segments in three long-axis views and 18 segments in three short-axis views were therefore analyzed. The tracking quality was automatically inspected, and the results for every segments were marked as V for successfully tracked segments or X for unsuccessfully tracked segments. If the results were satisfactory for at least five segments in each view, the tracking was accepted. End-systole was defined as the frame showing aortic valve closure. The segmental longitudinal strain and strain rate, circumferential strain and strain rate, radial strain and strain rate, and rotation and rotation rate curves can be constructed and then averaged to obtain global strain and strain rate curves. The longitudinal strain and strain rate curves were obtained from the apical views. The strain value was negative when the local myocardium was shortening, and positive when it was lengthening. The ultrasound system and software calculated the segmental myocardial rotation angle of the region of interest and provided the rotation curves from short-axis views when the LV short-axis center was assumed to be the center of cardiac rotation. From the apical direction, clockwise rotation was recorded as negative and counterclockwise rotation as positive.

Strain rate and strain profiles were averaged over three consecutive cardiac cycles to derive mean strain rate and strain. The mean values of the three cycles were used for statistical analysis. The