

First pass contrast enhanced MRI shows disparate manifestations in exercise-induced perfusion improvement in non-transmural infarcted and remote myocardium

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Introduction

Exercise-based rehabilitation has been well documented to increase exercise capacity and reduce recurrent cardiovascular events. Several studies also demonstrated that exercise training can improve myocardial perfusion for patients with myocardial infarction (MI). Currently, the improvement of myocardial perfusion after exercise training has been proved by reduced coronary vascular resistances and increased capillary density in post infarcted rat model (1). Although, the effect of exercise training influences myocardial perfusion in the infarcted and non-infarcted remote zone has been studied in vivo (2,3), but the effect of exercise training on the non-transmural infarcted myocardium and residual viable myocardium still remains unclear. Therefore, our aims of the present study were: first, to investigate the effects of exercise training on myocardial perfusion in the infarcted and non-infarcted remote zone; second, to assess the perfusion change of the residual viable myocardium in the non-transmural infarcted zone after exercise training.

Materials and Methods

Study protocol A total of 39 patients presenting with a first acute MI at least 6 months ago were recruited and randomized into two groups, a training group (N=20, age: 52±8 yrs) who attended a 3-month exercise program and a control group (N=19, age: 52±9 yrs; p=NS) who did not join the exercise program. The training group received two MR studies, one before and one after the 3-month exercise program. The control group also received two MR studies which were three months apart. The first MR studies served as a baseline for comparing with the second MR studies.

Cardiac rehabilitation protocol Exercise sessions were performed three times a week for 3 months. The exercise included a 5-min warm up, a 20-min bicycle exercise combined with treadmill walking, and a 5-min cool down. The exercise intensity was prescribed according to the ventilatory threshold (51–59% of maximal heart rate reserve) and the Borg's scale 12 rating of perceived exertion of 12 to 13 (fairly light to somewhat hard).

MR acquisition All subjects underwent both rest and stress first-pass contrast-enhanced MR studies on a 3T MR scanner (Trio, Siemens, Germany). Three short-axis slices at basal, mid left ventricle (LV) and apical levels were acquired using an SR-prepped Turbo FLASH pulse sequence. Right after the scanning started, gadolinium-DTPA (0.025mmole/kg) was bolus injected via left antecubital vein at a rate of 4–6ml/sec. The stress study was performed approximately 10 min after the rest study. Vasodilator (dipyridamole, 140µg/kg/min) was infused intravenously for 4 min and the image acquisition began at the 7th min when the maximal vasodilatation was achieved. Gadolinium-DTPA (0.2 mmole/kg) was administered after the perfusion study, and delay-enhancement (DE) MR imaging was performed 10 min after to assess the myocardial scarring.

Image analysis

1. **Residual viable myocardium quantification:** From DE MRI, the non-transmural infarcted zone was defined by a sector bounded by two ends of hyperenhanced region and the rest of the myocardium was defined as the remote zone. In the non-transmural infarcted zone, a pixel was counted as scar if its signal-intensity (SI) was higher than two standard deviations (SD) above the mean SI of the remote zone. The residual viable-myocardial ratio, VMR, of the non-transmural infarcted zone was quantified by the percentage of the total pixels of non-scar pixels relative to the total pixels in the non-transmural infarcted zone:

$$VMR = \frac{\text{total pixels of infarct zone} - \text{scar pixels}}{\text{total pixels of infarct zone}} \times 100\%$$

2. **Regional perfusion quantification:** Myocardial perfusion (MP) was measured in the same zones as those determined on DE MRI (Fig 1). The MP at rest and hyperemic status, in the unit of ml/min/g, was quantified by model-independent deconvolution method (4). (MPR = hyperemic MP/rest MP)
3. **Estimation of perfusion in residual viable myocardium:** The MP in the residual viable myocardium was evaluated by estimating the MP augmentation during maximal vasodilatation. Regional MP in the non-transmural infarcted zone (Pregion) can be considered as a result of linear combination of the perfusion in the scar tissue (Pscar) and the perfusion in the viable myocardium (Pviable). Pviable can be estimated as follows:
$$P_{\text{viable}} = (P_{\text{region}} - (1 - VMR) P_{\text{scar}}) / VMR$$
 Assuming that the scar tissue failed to augment during the hyperemic challenge and that MP measured during resting is similar for both residual viable myocardium and scar tissue, Pscar can be replaced by the rest MP in the non-transmural infarcted zone. In this way, Pviable can be estimated based on the measured regional MBFs at rest and stress as well as VMR.

Statistical Analysis

Data were presented as mean±SD. Paired differences in rest, stress MP and MPR between two MR studies were tested using a paired Kolmogorov-Smirnov test. The differences in rest, stress MP and MPR between non-transmural infarcted and remote myocardium were also analyzed using a 2-sample Kolmogorov-Smirnov test. Statistical significance was considered if p<0.05.

Results

In the control group, there was no significant change in MP and MPR between two MRI studies in both non-transmural infarcted and remote zones. After 3 months training, the remote zone showed no significant change in stress perfusion (3.57±1.34, 3.83±1.21; p=NS), but significant decreased in rest perfusion (1.50±0.70, 1.10±0.22; p=0.016). This resulted in significant improvement in MPR (2.60±1.26, 3.59±1.43; p=0.035). For the non-transmural infarcted zone, exercise training did not significantly change the perfusion at both rest and hyperemia states. However, the estimated stress perfusion of the residual viable myocardium in the non-transmural infarcted zone showed significant improvement after 3 months of exercise training (2.88±1.31, 4.13±1.92; p=0.041)(Figure 2).

Conclusion

In infarcted animal model, exercise training has been proved to reduce coronary vascular resistance and increase capillary density after myocardial injury (1). Our results suggest that the effects of exercise training on the non-transmural infarcted and non-infarcted remote zone might be different. In the remote zone, improvement of MPR after exercise training is mainly due to reduced rest myocardial oxygen demand. For the residual viable myocardium in the non-transmural infarcted zone, the observed increased stress perfusion might be attributed to exercise-induced angiogenesis.

References

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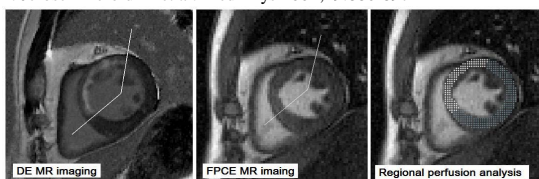


Fig. 1. Regional myocardial perfusion was measured from the infarct and remote zone which were determined from DE MRI.

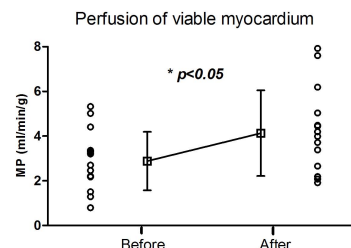


Fig 2. Perfusion of residual viable myocardium showed significant increased after exercise training.