Int J Clin Exp Med 2016;9(2):3334-3343
www.ijcem.com /ISSN:1940-5901/IJCEM0018473

Original Article

Protective effect of edaravone post-conditioning on myocardial ischemia-reperfusion injury in rabbits: a speckle tracking imaging study

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Received October 25, 2015; Accepted January 21, 2016; Epub February 15, 2016; Published February 29, 2016

Abstract: Edaravone, an effective free radical scavenger, can alleviate myocardial ischemia-reperfusion injury (IRI) by decreasing reactive oxygen species (ROS) accumulation. The speckle tracking imaging (STI) could precisely and objectively evaluate the global and regional myocardial deformation. The aim of our study was to assess the protective effect of edaravone postconditioning on IRI in rabbits by quantitatively detecting the global and regional deformation characteristics of left ventricle using STI. In the present study, Japanese big ear rabbits were randomly divided into IRI group, ischemia postconditioning group, edaravone postconditioning (intravenous group), and edaravone postconditioning (intra-arterial group). The absolute value of global and regional longitudinal, circumferential and radial strain and strain rate of left ventricle was decreased after coronary artery obstruction. Ischemia-reperfusion could not restrain the changes of myocardial deformation parameters. Edaravone postconditioning, performed the same functions as ischemia postconditioning, effectively promoted myocardial function by enhancing the myocardial strain and strain rate. Moreover, edaravone postconditioning and ischemia postconditioning could improve twist function by increasing the absolute value of peak twist (Ptw), untwisting rate (Untw R), peak twisting velocity (PTV) and peak untwisting velocity (PUV). In conclusion, edaravone postconditioning plays important protective roles in the global and regional deformation characteristics. Meanwhile, our study showed that there was no obvious difference between the two different drug-delivery systems in the recovery of myocardial deformation except in circumferential strain, which further demonstrated the wide application prospect of edaravone.

Keywords: Ischemia-reperfusion injury, ischemia postconditioning, edaravone postconditioning, speckle-tracking imaging

Introduction

Cardiovascular disease is one of the most common fatal diseases in the world. In recent years, with the rapid development of modern social-economic, the life style and living standard of people have shifted dramatically. Increasing prevalence of cardiovascular risk factors such as smoking, obesity, hypertension and hyperglycaemia has pushed cardiovascular disease as the leading killer of people. Coronary atherosclerotic heart disease (CAD) is the leading cause of cardiovascular disease death. About 50% patients with cardiovascular disease were died of CAD throughout the world [1]. CAD with high morbidity and bad prognosis is seriously harmful to human health. Therefore, the search for effective prevention and treatment for CAD has great social and economic value.

A large number of studies have demonstrated that the clear of coronary blockages, which recover the blood perfusion of ischemic myocardium, is the key of cardiac function recovery. So coronary artery angioplasty and stenting is frequently adopted to revascularization in clinic. However, further impairments are usually caused during operation, which aggravate cardiac muscle tissue necrosis, myocardial apoptosis and no-reflow: this is called IRI [2]. It proves that the excessive production of ROS in ischemic area is the key trigger factor of IRI [3]. At present, there are mainly three therapies for IRI including ischemia preconditioning (I-PreC),

ischemia postconditioning (I-PostC), and pharmacologic postconditioning (P-PostC). Edaravone (3-Methyl-1-phenyl-2-pyrazolin-5-one) is a new-style free radical scavenger, which could alleviate IRI by eliminating the ROS in the ischemia area. The intensive exploration of the protective effect of edaravone postconditioning on IRI has important clinical value and extensive application prospect.

STI, also known as two dimensional strain (2DS), is a new technology which could qualitatively and quantitatively evaluate the global and regional myocardial deformation based on high frame two dimensional gray scale ultrasonic images. Studies show that the parameter values of myocardial infarction detected by STI are closely related to the ventricular wall motion scoring evaluated by tissue Doppler imaging (TDI) which is widely used in the clinic [4, 5]. Compared with other means, STI is a repeatable, accurate and economical method for evaluation of cardiac function in clinic. In addition, the global longitudinal strain detected by STI can serve as a prognostic indicator of IRI and the accuracy of it is as much as 20 percent greater than left ventricular ejection fraction (LVEF) in identification of a large infarct area [6]. Thus it can be seen that STI has remarkable advantage in diagnosis of coronary heart disease and IRI.

In our study, rabbits were injected with edaravone via aortic root or ear vein after artery ligation. STI was applied to evaluate the variations of global and regional myocardial deformation parameters in left ventricle. The improvement effect of edaravone on IRI was compared among different experiment groups.

Materials and methods

Animals

Big-eared Japanese rabbits (2.00-2.75 kg) were provided by the Animal Experiment Center of Harbin Medical University. The rabbits without coronary artery malformation were feed separately with free access to water at room temperature. One week before experiment, the eating, activities and faeces of rabbits were observed every morning and night. Only healthy rabbits were chosen for the following experiments. All animal experiments were performed strictly in accordance with the National Institutes of Health Guide concerning the Care and Use of Laboratory Animals. The experiments were approved by the Institutional Animal Care and Use Committee of Harbin Medical University.

Animal experimental groups

36 rabbits were randomly divided into four groups: IRI group (The left ventricle branch was completely blocked for 45 min followed by 2 h reperfusion.); I-PostC group (The left ventricle branch was completely blocked for 45 min followed by serial blocking and reperfusion for 30 s for four times.); edaravone (intra-arterial group) (The left ventricle branch was completely blocked for 45 min, then edravone was injected via aortic root within 5 minutes at the top of the reperfusion for 2 h.) and edaravone (intravenous group) (The left ventricle branch was completely blocked for 45 min, then edaravone was injected via ear vein within 5 minutes at the top of the reperfusion for 2 h).

Animal procedures

Six hours before experiment, there was no food and water for the rabbits. After anesthetizing animals by injection of 2.5% pentobarbital sodium via ear vein, the heart was exposed by thoracic surgery. The IRI model was produced according to previous method with some adjustments [7]. Through superficial layer of myocardium 2 mm below left auricle, ligature was knotted loosely. Then a water-filled latex balloon was inserted between blood vessel and ligature and tied up. The myocardial ischemia was caused by increasing balloon pressure via a force pump. After reducing the balloon pressure, reactive hyperaemia of regional myocardial indicated successful reperfusion. STI was used to detect myocardial function for each group at the following three time points: before blocking, after blocking for 45 min and reperfusion for 2 h.

Echocardiography examination

All rabbits underwent a standardized two dimensional echocardiography using a GE Vivid 7 system (GE Healthcare, Germany) with a 10 s 4.4-11.4 MHz probe especially for small animal. The morphology and movement of segmental wall in left ventricular was observed. The heart chamber sizes were calculated. Left

Table 1. Comparisons of conventional echocardiographic index among each group

	Before blocking	After blocking for 45 min	Reperfusion for 2 h			
			IRI group	I-PostC group	Edaravone (intravenous group)	Edaravone (intra-arterial group)
LAD (cm)	0.76±0.06	0.73±0.07	0.74±0.05	0.81±0.12	0.79±0.10	0.83±0.11
LVEDD (cm)	1.53±0.38	1.48±0.21	1.58±0.35	1.49±0.51	1.57±0.42	1.55±0.27
LVEF (%)	73.00±4.47	67.57±3.60*	70.20±5.07	66.20±3.27	70.20±5.07	69.75±3.30
SV (ml)	3.00±0.58	2.57±0.79	2.75±0.50	2.60±0.55	3.50±0.58	3.25±0.50
HR (beats/min)	250.00±8.54	222.29±17.42*	209.00±11.91#	238.00±13.91	235.00±12.91	241.00±15.91

LAD, left atrial diameter; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; SV, stroke volume; HR, heart rate. *$P<0.05$, compared with index before blocking; #$P<0.05$, compared with index after blocking for 45 min.

ventricular ejection fraction (LVEF), end-diastolic volume (EDV), end-systolic volume (ESV) and stroke volume (SV) were measured by Simpson's method. The long axis three sections and short axis three horizontal sections of the left ventricle were used. 2D gray scale dynamic images were captured in three stable consecutive cardiac cycles at a frame rate >90 frames/s. STI quantitative offline analysis was performed on the EchoPAC 7.0 workstation (GE Healthcare). At the end systolic phase manually outlined the endocardial region from mitral annulus to the border region of basal segment of ventricular septum and aortic valve. The region of interest (ROI) was automatically generated and the width of ROI could be adjusted to cover the whole left ventricle wall thickness. Timing of aortic valve closure (AVC) was selected accurately and then the program was run using the 18-segments-model. The global and regional deformation parameters were generated by software including longitudinal/circumferential/radial strain, peak strain and strain rate. Twist functional parameters such as peak twist, untwisting rate, peak twisting velocity, and peak untwisting velocity were also analyzed.

Statistical analysis

All data were presented as mean ± SD. The comparison among multiple groups was analyzed by one-way analysis of variance followed by Bonferroni post hoc test using Gaphpad Prism 5.0 software. A *P* value less than 0.05 indicates a statistical significant.

Results

Comparing the conventional echocardiographic index

The conventional echocardiographic indexes were shown in **Table 1**. The LVEF and HR were decreased obviously after blocking for 45 min. There was no difference in other indexes before and after blocking. The HR in IRI group was significantly decreased compared with that after blocking.

Comparing the strain parameters of 2D STI

To explore the effect of edaravone postconditioning on left ventricle function, we detected the global and regional longitudinal/circumferential/radial strain and strain rate of left ventricle respectively by STI. The longitudinal/circumferential/radial strain curves of normal and myocardial infarction model were shown in **Figure 1**.

The global and regional longitudinal strain and strain rate of left ventricle in each group were described in **Table 2**. According to the results, GLSsys, GLSp, GLSRsys, LSsys, LSp, LSRsys and LSRd were obviously decreased after blocking for 45 min compared to those before blocking. The value of these parameters was not enhanced in IRI group. In I-PostC group and edaravone-PostC groups there were statistical differences in most of these parameters except GCSsys compared with IRI group. However, there was no difference in the improvement of myocardial function among I-PostC group, Edaravone (intravenous group) and Edaravone (intra-arterial group). The circumferential strain and strain rate were also determined and shown in **Table 3**. GCSsys, GCSp, GCSRsys, CSsys, CSp, CSRsys and CSRd were decreased between the two groups before and after blocking. The I-PostC and edaravone-PostC could improve myocardial function via increasing the value of these parameters. The effect of intra-arterial administration of edaravone on GCSp, CSsys and CSp is better than that of intravenous administration. There was no difference between I-PostC group and edaravone-PostC

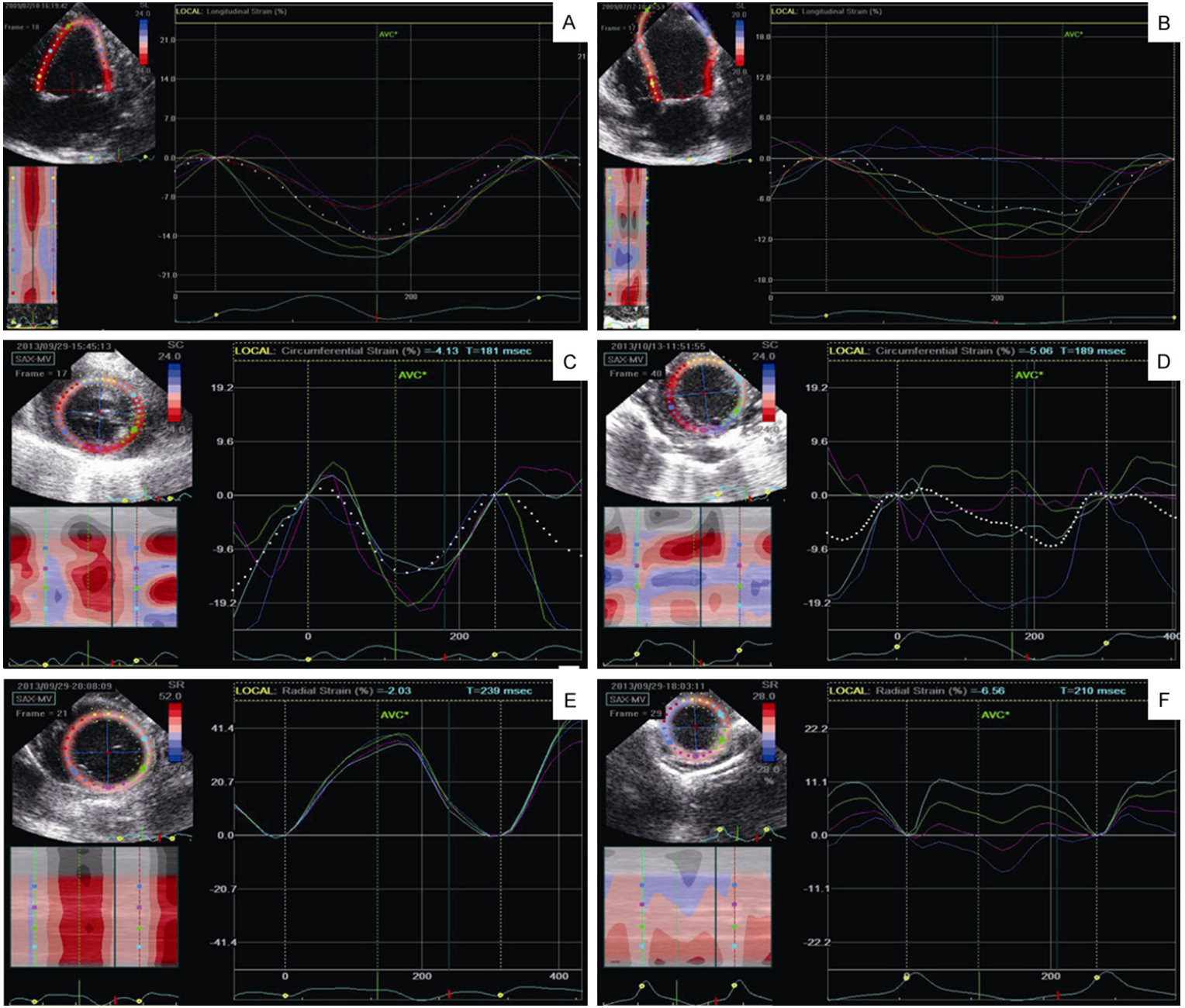
A
LOCAL: Longitudinal Strain (%)
AVC*
B
LOCAL: Longitudinal Strain (%)
AVC*
C
LOCAL: Circumferential Strain (%) =-4.13 T=181 msec
AVC*
D
LOCAL: Circumferential Strain (%) =-5.06 T=189 msec
AVC*
E
LOCAL: Radial Strain (%) =-2.03 T=239 msec
AVC*
F
LOCAL: Radial Strain (%) =-6.56 T=210 msec
AVC*

Figure 1. Speckle tracking images from the rabbits before and after blocking for 45 min. A. Curve image of the longitudinal strain before blocking. B. Curve image of the longitudinal strain after blocking for 45 min. C. Curve image of the circumferential strain before blocking. D. Curve image of the circumferential strain after blocking for 45 min. E. Curve image of the radial strain before blocking. F. Curve image of the radial strain after blocking for 45 min.

Table 2. Comparisons of left ventricular global and regional longitudinal strain and strain rate among groups

	Before blocking	After blocking for 45 min	Reperfusion for 2 h			
			IRI group	I-PostC group	Edaravone (intravenous group)	Edaravone (intra-arterial group)
GLSsys (%)	-16.47±2.80	-7.80±1.36**	-8.61±1.29	-13.61±2.59$^{▲,\#}$	-11.80±1.77$^{▲,\#}$	-11.95±2.03$^{▲,\#}$
GLSp (%)	-17.72±3.01	-8.50±1.70**	-8.58±1.29	-15.75±2.99$^{▲,\#}$	-13.19±2.05$^{▲,\#}$	-13.05±2.22$^{▲,\#}$
GLSRsys (s^{-1})	-2.47±0.49	-0.76±0.15*	-1.06±0.26	-1.15±0.39	-1.26±0.46	-1.21±0.38
GLSRd (s^{-1})	2.49±0.52	1.03±0.18	1.32±0.22	1.44±0.49	1.41±0.32	1.50±0.38
LSsys (%)	-15.89±1.19	-7.28±0.90**	-9.16±1.83	-13.43±1.88$^{▲▲,\#}$	-13.96±1.28$^{▲▲,\#}$	-15.08±1.48$^{▲▲,\#\#}$
LSp (%)	-17.19±0.86	-7.24±0.48**	-9.28±1.73	-14.26±1.37$^{▲,\#}$	-15.82±0.31$^{▲▲,\#\#}$	-16.60±0.45$^{▲▲,\#\#}$
LSRsys (s^{-1})	-3.03±0.16	-0.82±0.09*	-0.97±0.19	-2.59±0.07$^{▲,\#}$	-2.17±0.04$^{▲,\#}$	-2.51±0.08$^{▲,\#}$
LSRd (s^{-1})	2.64±0.04	0.94±0.17*	1.62±0.05	2.58±0.05$^{▲,\#}$	2.36±0.05$^{▲,\#}$	2.37±0.03$^{▲,\#}$

GLSsys, global longitudinal systolic strain; GLSp, global longitudinal peak systolic strain; GLSRsys, global longitudinal systolic strain rate; GLSRd, global longitudinal diastolic strain rate; LSsys, regional longitudinal systolic strain; LSp, regional longitudinal peak strain; LSRsys: regional longitudinal systolic strain rate; LSRd, regional longitudinal diastolic strain rate. $^{*}P<0.05$, $^{**}P<0.01$, compared with index before blocking; $^{▲}P<0.05$, $^{▲▲}P<0.01$ compared with index after blocking for 45 min; $^{\#}P<0.05$, $^{\#\#}P<0.01$ compared with IRI group.

Table 3. Comparisons of left ventricular global and regional circumferential strain and strain rate among groups

	Before blocking	After blocking for 45 min	Reperfusion for 2 h			
			IRI group	I-PostC group	Edaravone (intravenous group)	Edaravone (intra-arterial group)
GCSsys (%)	-17.96±3.19	-7.63±1.14**	-8.06±2.42	-9.25±1.13	-10.36±2.68	-10.09±2.62
GCSp (%)	-20.39±4.27	-8.34±1.67**	-9.58±-2.01	-19.03±4.76$^{▲▲,\#\#}$	-18.06±2.71$^{▲▲,\#\#}$	-18.97±2.66$^{▲▲,\#\#,\&}$
GCSRsys (s^{-1})	-2.88±0.59	-1.62±0.12**	-1.80±0.36	-2.09±0.42$^{▲,\#}$	-1.96±0.43$^{▲,\#}$	-2.05±0.48$^{▲,\#}$
GCSRd (s^{-1})	2.54±0.73	1.45±0.20	1.56±0.29	1.63±0.52	1.75±0.43	1.83±0.35
CSsys (%)	-15.44±2.32	-8.99±1.71**	-10.14±1.93	-13.99±2.94$^{▲▲,\#}$	-12.45±2.37$^{▲,\#}$	-13.87±2.91$^{▲▲,\#,\&}$
CSp (%)	-16.93±3.39	-8.37±1.67**	-10.88±2.18$^{▲}$	-14.92±3.28$^{▲▲,\#\#}$	-13.51±2.84$^{▲▲,\#\#}$	-15.49±3.41$^{▲▲,\#\#,\&}$
CSRsys (s^{-1})	-3.44±0.65	-1.31±0.25*	-1.92±0.37	-2.91±0.52$^{▲▲,\#\#}$	-2.88±0.63$^{▲▲,\#\#}$	-2.85±0.43$^{▲▲,\#\#}$
CSRd (s^{-1})	3.29±0.66	0.95±0.19*	1.83±0.33	2.48±0.45$^{▲,\#}$	2.41±0.36$^{▲,\#}$	2.53±0.48$^{▲,\#}$

GCSRsys, global circumferential systolic strain rate; GCSp, global circumferential peak strain; GCSsys, global circumferential systolic strain; GCSRd, global circumferential diastolic strain rate; CSsys, regional circumferential systolic strain; CSp, regional circumferential peak strain; CSRsys, regional circumferential systolic strain rate; CSRd, regional circumferential diastolic strain rate. $^{*}P<0.05$, $^{**}P<0.01$ compared with index before blocking; $^{▲}P<0.05$, $^{▲▲}P<0.01$ compared with index after blocking for 45 min; $^{\#}P<0.05$, $^{\#\#}P<0.01$ compared with IRI group; $^{\&}P<0.05$ compared with Edaravone (intravenous group).

group. As shown in **Table 4**, after blocking the coronary artery for 45 min, RSsys, RSp, RSRsys and RSRd were significantly decreased. Compared with myocardial infarction group, the value of these indicators in IRI group demonstrated trend of increase but had no statistical difference. However, in I-PostC group and edaravone-PostC group these parameters were all enhanced remarkably as compared with IRI group. There was no statistical difference between intravenous administration and intra-arterial administration of edaravone.

Comparing the twist function parameters of 2D STI

To further confirm the beneficial effect of edaravone-PostC, we also investigated the twist function of cardiac muscle. As shown in **Table 5**, the absolute value of Ptw, Untw R, PTV and PUV were significantly reduced in myocardial infarction group. Compared with IRI group, the absolute value of Ptw, Untw R, PTV and PUV were significantly increased in I-PostC and edaravone-PostC groups. There was no difference

Table 4. Comparisons of left ventricular radial strain and strain rate among groups

	Before blocking	After blocking for 45 min	Reperfusion for 2 h			
			IRI group	I-PostC group	Edaravone (intravenous group)	Edaravone (intra-arterial group)
RSsys (%)	28.07±5.61	19.41±2.62**	21.12±4.65	25.24±4.90▲▲,#	27.48±4.67▲▲,##	27.21±5.51▲▲,##
RSp (%)	30.71±5.84	15.52±3.41**	19.60±3.72	29.87±5.97▲▲,##	29.41±5.59▲,#	29.99±4.80▲▲,##
RSRsys (s^{-1})	5.12±0.97	1.96±0.25**	2.21±0.46	3.47±0.66▲,#	3.71±0.59▲,#	3.45±0.55▲,#
RSRd (s^{-1})	-5.30±1.01	-1.98±0.25*	-2.26±0.43	-4.36±0.87▲,#	-4.21±0.80▲,#	-3.84±0.61▲,#

RSsys, radial systolic strain; RSp, radial peak strain; RSRsys, radial systolic strain rate; RSRd, radial diastolic strain rate; *P<0.05, **P<0.01 compared with index before blocking; ▲P<0.05, ▲▲P<0.01 compared with index after blocking for 45 min; #P<0.05, ##P<0.01 compared with IRI group.

Table 5. Comparisons of left ventricular twist function parameters among groups

	Before blocking	After blocking for 45 min	Reperfusion for 2 h			
			IRI group	I-PostC group	Edaravone (intravenous group)	Edaravone (intra-arterial group)
Ptw (°)	11.75±2.35	7.01±1.12**	8.34±1.42	10.94±2.30▲,#	10.59±1.80▲,#	11.28±1.92▲,#
UntwR (%/ms)	2.57±0.44	1.16±0.24*	1.55±0.33	2.26±0.38▲▲,#	2.19±0.46▲,#	2.36±0.49▲▲,#
PTV (°/s)	191.20±40.15	116.72±18.68**	127.51±21.68	176.14±36.99▲,#	169.46±28.81▲,#	170.45±28.98▲,#
PUV (°/s)	-184.61±31.38	-115.82±23.16**	-116.05±24.37	-150.59±24.09▲,#	-130.18±22.13▲,#	-144.18±23.07▲,#

Ptw, peak twist; Untw R, untwisting rate; PTV, peak twisting velocity; PUV, peak untwisting velocity. *P<0.05, **P<0.01 compared with index before blocking; ▲P<0.05, ▲▲P<0.01 compared with index after blocking for 45 min; #P<0.05, ##P<0.01 compared with IRI group.

Table 6. Results of ROC curves comparing different 2D-STI parameters for their accuracy to assess myocardial function

Parameter	AUC	Standard error	*P* value	95% CI	Cut off	Sensitivity (%)	Specificity (%)
GCSRsys	0.812	0.046	0.000	0.722 to 0.902	-2.12	85.9	79.2
GCSp	0.848	0.057	0.000	0.736 to 0.959	-2.52	86.1	75
GLSp	0.815	0.049	0.000	0.719 to 0.910	-13.12	79.2	72.5
GLSRsys	0.769	0.05	0.000	0.671 to 0.868	-13.14	77.8	70.8
Ptw	0.81	0.047	0.000	0.719 to 0.902	9.41	79.2	75
PTV	0.703	0.059	0.003	0.587 to 0.819	151.02	66.7	70.8

in these parameters between intravenous and intra-arterial administration.

ROC curves drew by SPSS software were performed to detect the sensitivity and specificity of GCSp, GCSRsys, GLSp, GLSRsys, Ptw, and PTV in assessing myocardial function. The results were shown in **Table 6** and the ROC curves were presented in **Figure 2**. According to the results, GCSp (0.848) had the highest AUC, followed by GLSp (0.815), GCSRsys (0.812), Ptw (0.81), GLSRsys (0.769) and PTV (0.703).

Discussion

Edaravone is an important free-radical scavenger. Research showed that edaravone could significantly alleviate IRI and improve myocardial function by eliminating free radical, inhibiting intracellular calcium overload and myocardial cell apoptosis [8]. STI could quantitatively evaluate the global and regional deformation characteristics of myocardium without angle dependence, which has advantage in myocardial motion analysis [9]. Studies show that the myocardial strain parameters detected by STI have good correlation with the assessment results by other mature medical inspection technologies [5, 10]. Up to now, there have been no reports on the effect of edaravone postconditioning on myocardial ischemia-reperfusion injury by STI.

Our previous study found that I-PostC effectively relieved IRI with 2D-STI. However, I-PostC is an invasive procedure and has potential risk.

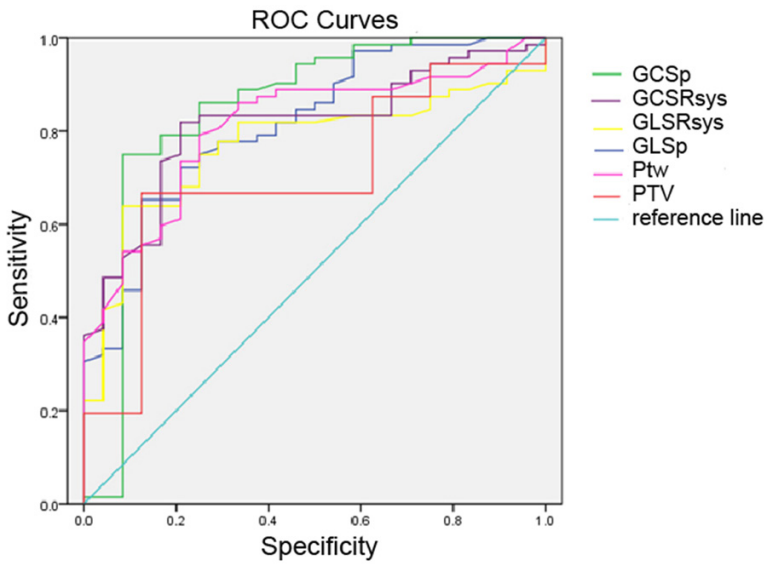

Figure 2. ROC curves for different echocardiographic parameters for the prediction of myocardial function.

The repeated balloon dilatation may obviously promote plaque rupture and acute thrombosis, which increases the risk of plaque or thrombus detachment. So at present, the research hotspots focus on the P-PostC, which is a drug treatment within minutes at the top of the reperfusion and could alleviate IRI [10]. Based on the above situation, our present study aimed at evaluation the effect of edaravone postconditioning on myocardial deformation characteristics compared with I-PostC using 2D-STI and the protective effect of edaravone based on different administration methods was also observed.

The left ventricular longitudinal diastolic and systolic function plays a pivotal role in the maintenance of heart function [11]. The study of longitudinal myocardial function in patients with coronary heart disease has important actual implication. The longitudinal strain and strain rate have a higher sensitivity than circumferential/radial strain and strain rate during acute myocardial ischemia. This is mainly because longitudinal myocardial function is determined by endocardium, which is the only part involved in early myocardial ischemia [12]. So left ventricle dysfunctions could be diagnosed early and exactly by detection of long-axis longitudinal myocardial strain and strain rate. A previous study proved that the global longitudinal strain and strain rate in patients with coronary heart disease were obviously decreased compared with those in healthy people [13]. Liang et al. found that the longitudinal diastolic and systolic strain in ischemic myocardium was significantly lower than that in normal myocardium [14]. Study by Zuo et al. showed that the regional longitudinal strain was lower than global longitudinal strain in 143 patients with coronary heart disease [15]. In our study, the GLSsys, GLSp were obviously decreased and regional strain and strain rate were all reduced after blocking of left coronary arterial for 45 min. There was no obvious improvement in myocardial function after reperfusion for 2 h because of IRI. Arterial and intravenous administration of evarovone could effectively increase global and regional longitudinal strain and strain rate and the results had no significant difference compared with I-PostC group. This is the evidence that evarovone postconditioning has the same protective effect as I-PostC on IRI. Consistent with previous studies, the improvement in regional function was more obvious than that in global function.

Not only the longitudinal strain/strain rate from the long axis view, but also the circumferential and radial strain/strain rate from short axis view can be determined by STI. Circumferential motion is telescopic and rotational motion of midmyocardium along short axis and radial motion reflects the thickening of heart muscle fibers from epicardium to endocardium [16]. STI is an ideal means of evaluating the left ventricle short axis motor functions. Study by Popovic et al. found that left ventricle circumferential and radial regional strain changes were more sensitive than LVEF in patients with coronary heart disease assessed by STI [17]. In the present study, edaravone effectively alleviated IRI by inhibiting global and regional circumferential strain parameters changes. CSsys and CSp in artery group were higher than that in vein group, which indicated that edaravone given through artery was better than vein. Our findings were consistent with those of previous

studies [18, 19]. Similar changes of radial strain parameters have been also observed. The RSsys, RSp, RSRsys and RSRd in edaravone postconditioning group were obviously higher than ischemia-reperfusion group, which was more proof of the protective effect of edaravone on IRI.

Our results also showed that the longitudinal strain parameters were not more sensitive than circumferential and radial parameters from short axis view. There were differences only in circumferential strain parameters of different edaravone delivery system. A possible explanation is that transmural myocardial infarction model in rabbits was used in our study. Study by Treguer found that when transmural extension of myocardial infarction is over 0.75, the circumferential and radial strain parameters were to be more sensitive and accurate in a rat model of ischemia-reperfusion [20]. Moreover, our results showed that the tracking success rate of short axis was 92.52%, which was about 2% higher than long axis. The results also demonstrated that the AUC of GCSp was 0.848 and the sensitivity and specificity were 86.1% and 75%, which were higher than others. Considering the above the circumferential strain parameters showed advantages for evaluation myocardial motor function in our study.

Previous study shows that myocardial motion not only depends on myocardial contraction but also on cardiac twist [21]. The twist motion binds the ventricular systole and diastole tightly together. The elastic energy stored by twist motion is quickly released during isovolumic relaxation, which promotes the ventricular filling by the production of intraventricular pressure gradients. Untwisting, unaffected by heart load, mainly happens during the isovolumic relaxation period and may accurately reflect cardiac diastolic function [22, 23]. The untwisting rate correlates strongly with intraventricular pressure gradients [24]. The left ventricle twist motion could be evaluated by STI through measuring twist and untwisting parameters. Park et al. found that the left ventricle twist and untwisting rate were significantly decreased in patients with coronary heart disease and negatively correlated with disease severity [25]. A study by Takeuchi et al. demonstrated that left ventricle twisting angle was decreased in patients with anterior myocardial infarction and positively correlated with LVEF [26]. In our present study, we also evaluated the systolic and diastolic function by detection the left ventricle twist motion. The results showed that the twisting angle, twisting velocity, untwisting rate and velocity were significantly decreased in IRI group, which could be elevated by edaravone postconditioning. This is the evidence that edaravone has a protective effect on ventricular twist function after IRI.

In conclusion, our results demonstrated that edaravone postconditioning could improve left ventricle long-axis and short-axis function and twist function in rabbit model of myocardial ischemia-reperfusion injury. STI could objectively and quantitatively evaluate the protective effect of edaravone on IRI, which makes the results much more scientific and accurate. However, there are still some insufficiencies that need further improvements in our study. The study of the protective effect of edaravone on IRI is still in the preliminary stage. The clinical appropriate administration method of edaravone needs to be investigated and verified in future.

Acknowledgements

This study was supported by a grant from the National Nature Science Foundation of China (No. 81201093).

Disclosure of conflict of interest

None.

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