

Impact of septal myectomy on diastolic function in patients with obstructive hypertrophic cardiomyopathy

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Background: The impact of septal myectomy on diastolic function in patients with obstructive hypertrophic cardiomyopathy is not well studied.

Methods: A transcatheter hemodynamic study was performed before and 3 to 6 months after septal myectomy in 12 patients with obstructive hypertrophic cardiomyopathy (HCM).

Results: Postoperative hemodynamic studies were done 4.4 ± 1.2 months after myectomy. The left ventricular outflow tract peak-to-peak gradient decreased from 83.2 ± 43.3 mmHg preoperatively to 11.6 ± 4.3 mmHg after myectomy (P<0.00). The left ventricular diastolic time constant (Tau) was 64.2 ± 26.1 ms before surgery and 42.2 ± 15.7 ms postoperatively (P=0.029). The average left atrial pressure (LAP) decreased from 20.2 ± 7.0 to 12.1 ± 4.5 mmHg after myectomy (P=0.008). Pulmonary artery hypertension was present in 6 patients preoperatively and remained in 2 patients after myectomy. Mean pulmonary artery pressure decreased from 29.3 ± 16.2 to 20 ± 6.7 mmHg after surgery (P=0.05), and the systolic pulmonary artery pressure decreased from 46 ± 26.9 to 30.5 ± 8.3 mmHg (P=0.048). Pulmonary vascular resistance decreased from 5.7 ± 4.1 to 3.6 ± 1.6 wood after surgery (P=0.032).

Conclusions: Septal myectomy improved left ventricular diastolic function and subsequently relieved the right ventricular congestion in patients with obstructive HCM.

Keywords: Obstructive hypertrophic cardiomyopathy; myectomy surgery; diastolic function; cardiac catheterization; pulmonary hypertension

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Introduction

Obstructive hypertrophic cardiomyopathy (HCM) is characterized by left ventricular outflow tract (LVOT) obstruction and diastolic dysfunction, which are the main causes of symptoms in many patients. In most symptomatic patients with obstructive HCM, appropriate management of the LVOT obstruction leads to a dramatic improvement of the symptoms. Septal myectomy is one of the most favorable options for the management of LVOT obstruction (1-3). The abnormal ejection hemodynamics are corrected immediately after myectomy. Septal myectomy showed excellent long-term outcomes in patients with obstructive

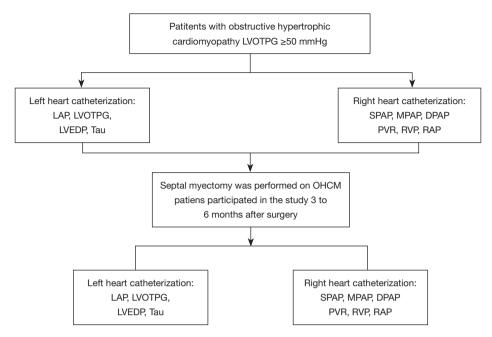


Figure 1 The flowchart of the study. LVOTPG, left ventricular outflow tract pressure gradient; LAP, left atrial pressure; LVEDP, left ventricular end diastolic pressure; SPAP, pulmonary artery systolic pressure; MPAP, mean pulmonary artery pressure; DPAP, pulmonary artery diastolic pressure; PVR, pulmonary vascular resistance; RVP, right ventricular pressure; RAP, right atrial pressure; OHCM, obstructive hypertrophic cardiomyopathy.

HCM whose symptoms were refractory to maximal medical treatment (4,5).

The improvement of symptoms following septal myectomy may also be due to improvements of diastolic functions. Indirect data derived from imaging studies suggested decreased left atrial pressure (LAP) and pulmonary pressure after myectomy (6-12). However, the intrinsic relaxation of the left ventricle (LV) was not studied. Due to the complex diastolic hemodynamics in the presence of LVOT obstruction, estimates of the myocardial relaxation of the LV using a noninvasive approach were less reliable (13-15).

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi. org/10.21037/jtd-21-902).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Fuwai Hospital approved this study (NO. 2019-1206). All patients signed informed consents for the use of their data for research. Catheter examinations were performed approximately one week

before the extended septal myectomy. Patients who voluntarily participated in a postoperative study came back to our institute for 3 to 6 months after surgery. Twelve patients completed preoperative and postoperative cardiac catheterization. *Figure 1* shows the flowchart of this study.

Study population

Inclusion criteria: (I) age: 16–60 years old; (II) Class II– III cardiac function [New York Heart Association (NYHA) classification]; and (III) left ventricular outflow tract pressure gradient (LVOTPG) \geq 50 mmHg at rest or on provocation.

Exclusion criteria: (I) the patient had a catheter examination within 1 month; (II) Contraindications for catheterization, such as stenosis or occlusion of peripheral arteries; (III) patients needed concomitant cardiovascular surgery at the time of septal myectomy or had prior cardiovascular surgeries; (IV) prior alcohol septal ablation; and (V) patients with coronary heart disease.

Cardiac catheterization

A standard procedure was used following guidelines,

including right heart catheterization (16) and left heart catheterization. A designated senior interventional physician performed cardiac catheterization in a catheterization room within 1 week before surgery and 3-6 months after surgery. The enrolled patients were examined in the supine position at rest. At the end of expiration, 3-5 cardiac beat pressure curves were obtained at each site. When obtaining the pressure curves, interferences, such as premature ventricular contraction and baseline instability, were excluded. The frequency of data collection was 240 times per second. All patients in this study underwent echocardiography before cardiac catheterization, and right cardiac catheterization followed by left cardiac catheterization during cardiac catheterization. The detailed catheterization method is described in the supplementary information. After obtaining a continuous pressure curve, 3-5 cardiac beats with stable left ventricular pressure curves were selected, we used monoexponential model to calculate the Tau value as previously reported by Weiss and associates (17,18).

Statistical analyses

Continuous variables are presented as the means \pm standard deviation or the median (interquartile range). The normality of data was tested with the Kolmogorov-Smirnov test. Oneway analysis of variance was used to compare continuous variables between groups. The Kruskal-Wallis test was used for nonnormally distributed variables. Categorical data are expressed as the percentage frequency and were compared using the χ^2 test or Fisher's exact test. Statistical analyses were performed using SPSS software (IBM SPSS Statistics for Macintosh, version 22.0; IBM Corp, Armonk, NY, USA). A P value <0.05 was considered statistically significant.

Results

Clinical characteristics

A total of 32 patients had preop study over the 8 months following the first enrollment. However, only 12 patients came back for postoperative test. Twelve patients met the inclusion criteria and agreed to be included in the study. Preoperatively, all patients exhibited medically refractory symptoms. Symptoms and NYHA class significantly improved after septal myectomy surgery. There was no significant difference in pre-myectomy and post-myectomy heart rate or hemoglobin level. No medication changes was made between the two cardiac catheterizations.

As previously described (9), a modified Morrow procedure was applied in this study. The weight of the myocardium removed was 12 ± 6.7 g. None of the study patient died during hospitalization or follow-up, and none required MV replacement. Non had postoperative constrictive pericarditis or other complication. The average time from surgery to postoperative echocardiography was 4.7 ± 1.4 months. Septum thickness decreased from 21.4 ± 4.5 mm before surgery to 11.8 ± 4.7 mm after surgery (P=0.03). The resting pressure gradient decreased from 69.5 ± 23.7 mmHg before surgery to 8.3 ± 1.6 mmHg after surgery (P<0.001). The baseline clinical characteristics and the clinical outcomes in the 12 study patients are summarized in *Table 1*.

Preoperative and postoperative cardiac catheterization outcomes

Postoperative cardiac catheterization was done 4.5 ± 1.2 months after myectomy. The left heart catheterization showed that the peak pressure gradient decreased from 83.2 ± 43.3 mmHg before surgery to 11.6 ± 4.3 mmHg after surgery (P<0.001). The right heart catheterization showed that mean pulmonary artery pressure (MPAP) decreased from 29.3 ± 16.2 mmHg preoperatively to 20 ± 6.7 mmHg (P=0.05) postoperatively, and the systolic pulmonary artery pressure decreased from 46 ± 26.9 to 30.5 ± 8.3 mmHg (P=0.048). Pulmonary vascular resistance (PVR) decreased from 5.7 ± 4.1 wood before surgery to 3.6 ± 1.6 wood after surgery (P=0.032). *Tables 2* and 3 show the comparisons of heart catheterization.

The outcomes of cardiac catheterization on ventricular diastolic function

Common indicators of left ventricular diastolic function, such as left ventricular end diastolic pressure (LVEDP) measured in various parts of the LV did not change significantly after surgery. Tau is defined as the time constant of isovolumic pressure decay in the early period of left ventricular relaxation, and it is calculated using the natural logarithm-time linear regression equation of left ventricular pressure (17,18). This study also compared the pre- and postoperative changes in Tau of the right and LVs. The results showed that the preoperative Tau of the right ventricle was 62.4 ± 75.6 ms, and the postoperative Tau was 71.0 ± 47.5 ms. There was no significant difference (P=0.766).

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 Table 1 Clinical characteristics before and 3–6 months after surgery

Parameters	Preoperative	Postoperative	P value
Age (years)	38.7±11.7		
Female gender	4 (33.3)		
Shortness of breath	12 (100.0)	1 (8.3)	
Palpitation	3 (25.0)	1 (8.3)	
Chest pain	3 (25.0)	0	
Syncope	2 (16.7)	0	
NYHA functional class			<0.001
NYHA I	0	7 (58.3)	
NYHA II	8 (66.7)	5 (41.7)	
NYHA III	4 (33.3)	0	
NYHA IV	0	0	
HR	73.8±7.6	70.7±11.7	0.363
AF	1 (8.3)	1 (8.3)	-
RBBB	2 (16.7)	2 (16.7)	_
LBBB	1 (8.3)	1 (8.3)	_
Pacemaker implantation	1 (8.3)	1 (8.3)	_
Medications			
Diuretic	2 (16.7)	1 (8.3)	_
Beta-blocker	12 (100.0)	12 (100.0)	_
Calcium channel blocker	0	0	_
Pulmonary inodilators	0	0	
Hb (g/L)	140.5±25.2	141.4±21.9	0.619
Echocardiography parameters			
LAD (mm)	44.5±10.8	38.9±6.3	0.049
LVEDD (mm)	41.7±5.4	45.6±5.7	0.038
LVEF (%)	70.2±4.3	63.7±4.3	0.019
Interventricular septum thickness (mm)	21.4±4.5	11.8±4.7	0.03
Maximal resting LVOT gradients (mmHg)	69.5±23.7	8.3±1.6	<0.001
Resting MR	1.5±0.8	0.7±0.3	<0.001
1	5	12	
2	4	0	
3	2	0	
4	1	0	
PH	1 (8.3)	0	

Values are presented as the means ± SD, medians (IQR) or n (%). The degree of MV regurgitation was a graded on a scale from 0 to 4 (0= none, 1= mild; 2= moderate; 3= moderate to severe; and 4= severe). PH, pulmonary hypertension; IQR, interquartile range; NYHA, New York Heart Association; HR, heart rate; AF, atrial fibrillation; RBBB, complete right bundle branch block; LBBB, complete left bundle branch block; Hb, hemoglobin; LAD, left atrium diameter; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; MR, mitral valve regurgitation.

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Table 2 Comparison of right heart catheterization

Parameters	Preoperative	Postoperative	P value
RAP-A peak (mmHg)	10.5±4.3	11.4±6.3	0.667
RAP-V peak (mmHg)	8.1±3.7	11.0±7.3	0.239
MRAP (mmHg)	6.7±3.4	8.3±5.3	0.384
MRVP (mmHg)	19.7±12.4	13.1±3.8	0.139
SRVP (mmHg)	46.3±25.7	31.0±8.3	0.058
DRVP (mmHg)	6.9.0±5.5	5.1±3.3	0.0335
MPAP (mmHg)	29.3±16.2	20.0±6.7	0.05
SPAP (mmHg)	46.0±26.9	30.5±8.3	0.048
DPAP (mmHg)	19.7±10.2	13.7±5.9	0.062
Pulmonary circulatory blood volume (L/min)	5.9±1.9	6.3±1.6	0.613
PVR, wood	5.7±4.1	3.6±1.6	0.032
MPAP ≥25 mmHg	6 (50%)	2 (16.7%)	-
MPAP 25–34 mmHg	4 (33.3%)	2 (16.7%)	-
MPAP 35–44 mmHg	0	0	-
MPAP ≥45 mmHg	2 (16.7%)	0	-

Values are presented as the means ± SD or n (%). IQR, interquartile range; RAP, right atrial pressure; MRAP, mean right atrial pressure; MRVP, mean right ventricular pressure; SRVP, right ventricular systolic pressure; DRVP, right ventricular diastolic pressure; MPAP, mean pulmonary artery pressure; SPAP, pulmonary artery systolic pressure; DPAP, pulmonary artery diastolic pressure; PVR, pulmonary vascular resistance.

The preoperative Tau of the LV Tau was 64.2 ± 26.1 ms, and the postoperative Tau was 42.2 ± 15.7 ms, which was significantly different (P=0.029). *Figure 2* shows a typical change of LV change of pressure at follow-up. *Figure 3* shows a change of time of left ventricular relaxation at follow-up. *Table 3* presents the outcomes of cardiac catheterization on ventricular diastolic function.

Tau went down in 7 of the 12 patients and remained the same in the other 5 patients. The preop Tau was XX in the 7 decreased patients and YY in the 5 non-decreased patients. The 7 patients with higher preop Tau had their Tau reduced significantly postoperatively. The 7 patients with higher preoperative Tau have higher LOPTPG before surgery. *Table 4* compares clinical parameters between Tau decreased patients and non-decreased patients.

Discussion

The present study investigated diastolic function using catheterization in patients with obstructive HCM before and after septal myectomy. The pressures of the left and right hearts were thoroughly investigated via direct measurement. The filling pressure and myocardial relaxation were significantly improved following myectomy, which are consistent with prior studies that showed a decrease in left atrial (LA) size (7-9), improvement of pulmonary artery hypertension (10-12), and reverse remodeling of the LV (9,19). The results from the present study suggested that improvement of the diastolic function may be an important reason for the increased functional capacity following myectomy in patients with obstructive HCM, by improving cardiopulmonary function and NYHA.

LVOT obstruction is the main cause of symptoms in patients with HCM. For patients who are refractory to medical treatment, septal myectomy produces an excellent effect on the improvement of functional capacity and survival (1-5). An intraoperative hemodynamic study showed that the improvement of functional capacity may be due to the relief of obstruction and the increase in stroke volume (20). Many studies also showed that septal myectomy was associated with the improvement of diastolic function using an imaging approach (6-9). The method of evaluating

 Table 3 Outcomes of left heart catheterization and ventricular diastolic function

Parameters	Preoperative	Postoperative	P value
LAP-A peak (mmHg)	28.3±5.9	19.8±6.0	0.002
LAP-V peak (mmHg)	27.1±12.3	16.1±6.0	0.013
MLAP (mmHg)	20.2±7.0	12.1±4.5	0.008
SAO (mmHg)	101.1±11.4	114±13.9	0.027
DAO (mmHg)	67.3±6.7	72.4±8.3	0.213
MAO (mmHg)	81.3±16.3	86.1±7.5	0.359
SLVP-apex (mmHg)	187.7±51.1	129.6±17.5	0.005
MLVP-apex (mmHg)	76.1±21.5	42.7±13.5	0.001
SLVP-middle (mmHg)	164.4±44.0	127.6±18.6	0.008
MLVP-middle (mmHg)	68.5±14.9	41.5±15.6	0.001
SLVP-outflow tract (mmHg)	111.0±14.0	120.9±17.8	0.229
MLVP-outflow tract (mmHg)	54.4±14.5	40.0±17.1	0.056
DLVP-apex (mmHg)	15.9±5.2	17.6±8.8	0.626
DLVP-middle (mmHg)	15.2±6.0	15.1±11.5	0.982
DLVP-outflow tract (mmHg)	13.2±5.9	14.1±8.7	0.812
LVOT gradients (mmHg)	83.2±43.3	11.6±4.3	<0.001
LV-Tau (ms)	64.2±26.1	42.2±15.7	0.029
RV-Tau (ms)	62.4±75.6	71.0±47.5	0.766

Values are presented as the means ± SD. IQR, interquartile range; LAP, left atrial pressure; MLAP, mean left atrial pressure; SAO, aortic systolic pressure; DAO, aortic diastolic pressure; MAO, mean aortic pressure; SLVP-apex, left ventricular apex systolic pressure; MLVP-apex, mean left ventricular apex pressure; SLVP-middle, left ventricular middle segment systolic pressure; MLVP-middle, mean left ventricular middle segment pressure; SLVP-outflow tract, left ventricular outflow tract systolic pressure; MLVP-outflow tract, mean left ventricular outflow tract pressure; DLVP-apex, left ventricular apex diastolic pressure; DLVP-middle, left ventricular outflow tract, left ventricular outflow tract, left ventricular outflow tract; LV, left ventricle; RV, right ventricle; Tau, time constant of isovolumic pressure decay in early period of left ventricular relaxation.

diastolic function using imaging was derived from simpler hemodynamic circumstances and may not apply to the complex hemodynamics in patients with obstructive HCM (13-15). For example, Doppler echocardiographic estimates of left ventricular filling pressure using transmitral flows and mitral annular velocities modestly correlate with direct measurements of LAP (13).

Notably, the LA pressure and LV filling pressure decreased following septal myectomy, which were reported in many studies using different methods. Improvement of mitral valve regurgitation and increase in forwarding stroke volume significantly decrease the LA congestion. However, the improvement of myocardial relaxation was not well determined due to methodological limitations. Sorajja *et al.* found a variable effect of septal ablation on myocardial relaxation in patients with HCM (21). However, the postoperative measurements were performed during the ablation procedure and may have been affected by the acute myocardial necrosis. Postoperative measurements in the present study were performed three to six months after myectomy, when the hemodynamics and myocardium had recovered from the acute surgical phase. The data showed a decrease in the Tau value after myectomy, which indicates an improvement in LV relaxation. Several changes after myectomy may induce the improvement. Myocardial ischemia has a vital impact on the Tau value, and it is present in many patients with HCM (22). The relief of LVOT obstruction considerably decreases the oxygen consumption of the myocardium. These factors together contribute to the improvement of myocardial ischemia and stiffness.

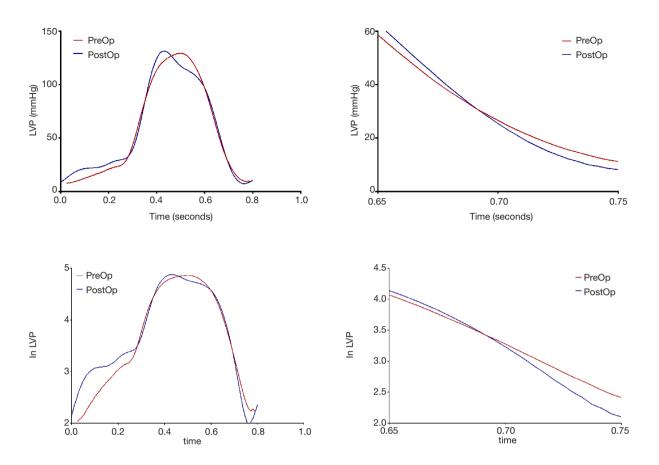


Figure 2 LV pressure tracings before and after septal myectomy. The height of the pressure curve has been adjusted. The upper left panel shows the LV pressure in a heartbeat before septal myectomy and a heartbeat at a 3-month follow up, and the upper right panel shows the part of the pressure tracings in LV relaxation. The pressure tracings show the LV pressure decreases faster at follow-up. The lower left panel shows the converted LV pressure by natural logarithm, and the lower right panel shows the LV relaxation part of ln (LV pressure). The steeper slope of follow-up ln (LV pressure) in LV relaxation demonstrates the decrease of tau value. LV, left ventricle.

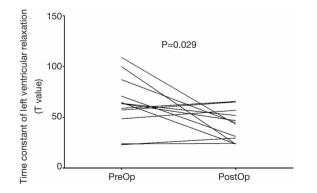


Figure 3 Change of tau value at a 3-month follow-up. The tau value decreased overall at follow-up and the decrease is especially significant in those who have a large tau value before myectomy.

Thinning of the ventricular septum may be another reason for the improvement of myocardial relaxation. The LV in patients with obstructive HCM is generally characterized by asymmetric hypertrophy, which predominantly presents as septal hypertrophy, especially basal septal hypertrophy. This hypertrophy is an important cause of the LV systolic and diastolic dysfunction. Septal myectomy may improve global LV compliance by thinning the thickest part of the LV, which was demonstrated by the echocardiographic data in the present study and prior studies (9,19,23). There was a regression in the left ventricular hypertrophy following myectomy. A prior study also showed a continuous decrease of N-terminal pro-brain natriuretic peptide months after myectomy (24). Therefore, the reverse remodeling of the

Table 4 Com	parisons of clin	cal parameters	between Ta	u decreased	patients and	non-decreased	patients
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Parameters	Tau decreased group (N=7)	Tau non-decreased group (N=5)	P value	
Age (years)	38.9.3±11.8	38.4±12.9	0.950	
Female gender (mmHg)	3 (42.9%)	1 (20%)	0.408	
NYHA functional class			0.735	
NYHA I	0	0		
NYHA II	5 (71.4%)	4 (80%)		
NYHA III	2 (28.6%)	1 (20%)		
NYHA IV	0	0		
NT-proBNP (pg/mL)	846.1 (106.1, 3,116.0)	956.5±623.8	1.000	
Echocardiography parameters				
LAD (mm)	47.6±12.6	41.2±0.8	0.291	
LVEDD (mm)	43.1±5.5	39.4±4.3	0.235	
LVEF (%)	72.0±4.4	68.0±2.5	0.102	
Interventricular septum thickness (mm)	20.3±3.0	23.2±5.6	0.263	
LVOT gradients (mmHg)	82.3±25.0	56.0±5.4	0.045	
LV-Tau (ms)	79.8±18.9	42.3±17.7	0.006	

Values are presented as the means ± SD, medians (IQR) or n (%). IQR, interquartile range; NYHA, New York Heart Association; LAD, left atrium diameter; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; LV, left ventricle.

LV may also contribute to the improvement of diastolic function.

Our results showed that the 7 patients with higher preoperative Tau had their Tau reduced significantly postop. And the 7 patients with decreased Tau seems to have higher LOPTPG before surgery. In 5 patients, Tau did not change significantly due to a relatively lower baseline value. We speculate patients with worse diastolic function and higher LOPTPG may benefit more from myectomy surgery, and the Tau decreased more significantly postoperatively. We conclude that septal myectomy decreased the Tau, especially in those who had an increased baseline Tau. Though we need to prove our speculation by increasing the sample volume.

There was also a significant improvement in pulmonary artery hypertension. Pulmonary circular volume increased, and pulmonary artery pressure decreased. Notably, pulmonary vascular resistance also decreased. This result is consistent with prior studies on post-myectomy changes of pulmonary artery pressure using imaging methods (10-12,25). The mechanism may be improvement of the vascular congestion. However, the right ventricular and right atrial pressure were not apparently affected.

Limitations

There were several limitations in the present study. The study size was relatively small, which limited the power of the conclusions. Patients voluntarily decided whether to undergo the postoperative study, so the comparison was done in only 12 patients. There may be a selection bias in sampling.

Conclusions

Patients with obstructive HCM have improved diastolic function following septal myectomy, especially in those who had an increased baseline Tau. The improvement was indicated by decreased LA and LV filling pressures and improved LV relaxation. Cardiac output and pulmonary vascular congestion were also improved.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by The Institutional Review Board of Fuwai Hospital (NO.2019-1206) and informed consent was taken from all the patients.

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