

Assessment of myocardial segmental function with coronary artery stenosis in multi-vessel coronary disease patients with normal wall motion

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Abstract. – **OBJECTIVE:** To discover the impact of the various degrees of coronary artery stenosis (CAD) on the left ventricular systolic dysfunction in steady state with quantitative analysis of the regional systolic myocardium in longitudinal, radial and circumferential direction in patients with coronary artery disease by two-dimensional speckle tracking imaging (STI).

PATIENTS AND METHODS: Forty-three normal wall motion-multi vessel coronary artery disease (NWM-MVD) patients labeled as the experimental groups and forty-two subjects with little risk of CAD marked as the control group were enrolled in this study. The two-dimensional STI was obtained in the apical long axis and three levels of the short axis of the left ventricle. The left ventricular wall was divided into 18 segments. The affected myocardia were divided into three groups: group B (coronary stenosis degree $\leq 50\%$), group C (coronary stenosis degree 50%-99%) and group D (coronary stenosis degree $\geq 99\%$). Using the Q-analysis software, the longitudinal, radial and circumferential systolic strain (SL, SR, SC) and strain ratio (SrL, SrR, SrC) of the myocardium were analyzed.

RESULTS: The bradycardia in the NWM-MVD group is greater than that in the control group (16/43 vs. 7/42, $p < 0.05$). Compared with the control group, the SL and SR of group B, group C and group D decreased significantly ($p < 0.05$). Compared with group C, the SL of group D also decreased significantly ($p < 0.05$). However, there was no SC difference among the four groups. Meanwhile, compared with group A, the SrL, SrR and SrC of group B, group C and group D decreased significantly ($p < 0.05$). Compared with group A, group B and group C, the SrL and SrC of group D also decreased ($p < 0.05$). Compared with group A and group C, the SrR of group D decreased. The SrL was equal to 1.085 for the cut-off value, and the sum (1.348) of sensitivity

(0.673) and specificity (0.675) were the greatest. Bland-Altman analysis showed that there was myocardium conformity of in both the multi-vessel CAD patients and the control subjects.

CONCLUSIONS: Myocardial systolic function was impaired in the MVD patients of group B (coronary stenosis degree $\leq 50\%$), group C (coronary stenosis degree 50%-99%) and group D (coronary stenosis degree $\geq 99\%$), especially the longitudinal and radial systolic function, even though they had normal wall motion. The SrL equaled 1.085 for the cut-off value, and the sums (1.348) of sensitivity (0.673) and specificity (0.675) were the greatest. Bradycardia might be a compensatory mechanism in NWM-MVD patients.

Key Words:

STI (Speckle tracking imaging), Myocardium function, Left ventricle, Multi vessel coronary artery disease.

Introduction

Many studies demonstrate that it is not unusual for multi-vessel coronary artery disease (CAD) patients to have a normal wall motion in steady state¹⁻³. Multi-vessel CAD is defined as having, at least, luminal stenosis (degree $\geq 50\%$) of the two main coronary arteries. Multi-vessel CAD patients may account for 50% of the coronary heart disease patients⁴⁻⁶. Worse, the mortality ratio of the multi-vessel CAD patients is very high because of the dangerous hardening of the multi-vessel coronary artery⁷⁻⁹. Therefore, early diagnosis for multi-vessel disease patients, especially those with normal wall motion, is important for the as-

assessment of the patient's condition, treatment and long-term prognosis.

Two-dimensional speckle tracking imaging (STI) is a new method for evaluating myocardial systolic function by measuring the local myocardial deformation¹⁰⁻¹¹. This study assesses the segmental myocardial systolic function with various degrees of coronary artery stenosis in multi-vessel CAD patients with normal wall motion.

Patients and Methods

Patients

The experimental group consisted of 43 normal walls motion-multi vessel coronary artery disease (NWM-MVD) patients (34 male, 9 female, aged from 44 to 74) who were randomly selected from our hospital and had coronary stenosis (degree $\geq 50\%$). There were, at least, two experienced echocardiogramphists doctors who confirmed that all multi-vessel CAD patients had normal wall motion. Moreover, all subjects had no myocardial infarction according to their clinical history and data. The control group consisted of 42 patients (26 male, 16 female, aged from 45-81) with suspected coronary heart disease and confirmed coronary stenosis (degree $< 50\%$). All subjects had no diseases that could have affected cardiac function.

Apparatus and Methods

The M3S probe (1.5 to 4.0 MHz) of GE Vivid 7 Dimension was used. First, the clients were hooked up to the electrocardiogram (ECG) monitors while lying on the left side to record their heart rate. With the parasternal left ventricular long axis view, the left ventricular end-diastolic diameter (LVEDD) and the left ventricular anteroposterior diameter (LAD) were measured. With the M3S probe, the left ventricular ejection fraction (LVEF) was measured. With an apical four-chamber view, the mitral diastolic velocity peak (E and A values) were measured, and E/A was calculated. Using the Tissue Doppler echocardiography (TDE), diastolic peak velocity e' and a' of the ventricular septal basal was measured and e'/a' was calculated. Using Simpson's biplane method, the LVEF was measured.

The stable two-dimensional images of the left ventricular short axis, apical four-chambers and two-chambers based on the 3-5 cardiac cycle of the mitral valve, papillary and apical apex were measured. After importing the image to the EchoPAC workstation, the Q-analysis software automatically divi-

ded the left ventricular wall into 18 segments after importing the images to the EchoPAC workstation, then adjusted the frame within the systolic end and sketched out the endocardial boundary. Finally, the two-dimensional STI software will display the sarcomere strain and strain ratio curve. Then, the longitudinal, radial and tangential strain and strain ratio of each segmental systolic peak would be recorded. After the analysis of the 18 segments ventricular wall motion. The records were divided into four groups: Group A – myocardial segments records of control group patients; Group B – coronary stenosis (degree $\leq 50\%$) records of multi-vessel CAD patients; Group C – coronary stenosis ($50\% \leq \text{degree} \leq 99\%$) records of multi-vessel CAD patients; Group D – coronary stenosis (degree $\geq 99\%$) records of multi-vessel CAD patients. Then, a random sample (30 myocardial segments records) was analyzed by two observers. Meanwhile, one observer needed to analyze the sample again a week later to evaluate for inter-observer variation. Then, the intra-observer and inter-observer variation would be calculated by percentage difference (deviation between two times value/mean of two times value) $\times 100\%$. Finally, we tried to find out the conformity between the experimental group and control group using the Bland-Altman analysis method.

Statistical Analysis

Using the SPSS 13.0 statistical software to perform the analysis, the mean $\pm$ standard deviation ($\bar{x} \pm s$) represented the continuous numerical variables. With a single factor variance analysis, the comparisons between the multiple groups were performed. Using the Dunnett t -test, each myocardial segment between the experimental and the control group was compared. The Chi-square test was used to compare the ratios of the enumeration data. The ROC curve analyzed the accuracy of the multi-vessel CAD patients with coronary stenosis (degree $\geq 99\%$) according to left ventricular systolic peak strain parameter. Then, the conformity in the experimental and control groups was analyzed using the Bland-Altman. A $p < 0.05$ was considered statistically significant.

Results

Comparison of the Clinical Data

Since there was no significant age and sexual difference between the two groups, the patients' heart rate in the experimental group was slower than that of the control group and the patients si-

Table I. Comparison of general clinical data between multi-vessel CAD group and control group.

	Age	Male ratio	BMI $\geq$ 24	HR	Cardiac Arrhythmia
Multi-vessel CAD group	61.08 $\pm$ 7.26	33/43 (76.7%)	19 (44.2%)*	61.78 $\pm$ 6.76*	16/43 (37.2%)*
Control group	60.13 $\pm$ 9.62	26/42 (61.9%)	9 (21.4%)	66.13 $\pm$ 6.24	7/42 (16.7%)
p-value	0.653	0.138	0.026	0.008	0.033

Note: *Comparative differences between Multi-vessel CAD group and Control group are statistically significant.

nus bradycardia was greater, and the patients with BMI $\geq$ 24 was higher as well (Table I).

Comparison of the Conventional Ultrasonic Measurements

The LAD of the multi-vessel CAD group was obviously higher than that of the control group, but the LVEDD had no difference between the two groups. The LVEF was normal (EF $>$ 50%) and showed no difference between the two groups. Moreover, there was no significant difference between the two groups in the E/A, e', e'/a', E/e' and IVRT (Table II).

Comparison of strain and strain ratio of each segment systolic peak of the left ventricular wall

The 43 multi-vessel CAD patients with normal ventricular wall motion were enrolled (Figure 1). Among them, 27 patients had triple vessel disease and 16 patients had double vessel disease. Among the 28 total coronary occlusion or subtotal coronary occlusion patients, 19 patients had triple vessel disease, 9 patients had double vessel disease, and 16 patients had right coronary artery occlusion, 8 patients had anterior descending branch

occlusion, and 4 patients had cyclotron branch occlusion. Coronary angiography showed that there were 18 patients with collateral, and they all had total coronary occlusion or subtotal coronary occlusion. Meanwhile, 16 patients had right coronary artery occlusion, 5 patients had anterior descending branch occlusion and 1 patient had cyclotron branch occlusion.

After analyzing the 18 segments ventricular wall motion, the multi-vessel patients with normal ventricular wall motion were divided into three groups based on coronary stenosis levels.

1) After analyzing the various levels of coronary artery stenosis, the result (Table III-1) of the left ventricular systolic strain peak comparison showed that the SL and SR of group B, C and D was significantly lower than group A ($p < 0.05$) which had statistical differences. The SL and SR of group D was significantly lower than group C which had statistical differences too. However, there was no significant difference among the four groups in SL ($p > 0.05$). Meanwhile, the results (see Table III-2) of the left ventricular systolic strain ratio peak comparison showed that the SrL, SrC and SrR of group B, C and

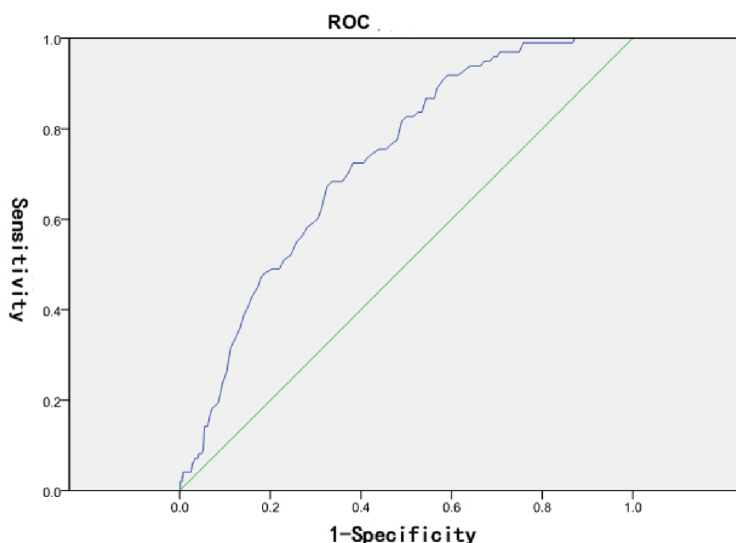


Figure 1. ROC curves of myocardial segments with $\geq$ 99% supplying coronary artery stenosis in multi-vessel CAD patients with normal wall motion diagnosed by SrL.

Table II. Comparison of conventional ultrasonic measurement between Multi-vessel CAD group and Control group

	LA (mm)	LV (mm)	LVEF (%)	Simpson's LVEF (%)	E (m/s)	e' (m/s)	E/A<1	e'/a<1	E/e'	IVRT (ms)
Control group	33.58±2.93	46.29±2.25	65.35±4.64	65.10±3.82	0.75±0.20	0.07±0.02	23/42 (54.8%)	30/42 (71.4%)	10.26±2.26	67.11±34.80
Multi-vessel CAD group	35.31±3.62*	46.92±2.64	65.11±4.15	66.00±4.10	0.70±0.14	0.07±0.02	31/43 (72.1%)	37/43 (86.0%)	11.03±2.40	80.00±17.12
p-value	0.038	0.305	0.821	0.357	0.239	0.113	0.097	0.099	0.211	0.084
p-value	0.653	0.138	0.026	0.008	0.033					

Note: *Comparative differences between Multi-vessel CAD group and Control group are statistically significant

Table III-1. Comparison of peak strain of left ventricular systolic strain between group A, B, C, D (±s).

Group	SL	SC	SR
A group	-21.7326±4.0969 (717)	-23.8832±7.1125 (621)	51.6888±19.5440 (556)
B group	-20.4257±4.3104▲ (58)	-22.8827±10.3117 (74)	39.2073±16.6155 (70)▲
C group	-20.9821±5.1226▲ (607)	-22.6497±8.8622 (458)	43.7605±21.5386 (530)▲
D group	-19.0659±4.5364▲● (104)	-22.1492±6.5538 (79)	44.6357±18.5062 (96)▲

Note: ▲The difference was statistically significant compared with that of group A; *The difference was statistically significant compared with that of group B; ●The difference was statistically significant compared with that of group C.

Table III-2. Comparison of peak strain rate in left ventricular systolic strain rate between group A, B, C, D (±s).

Group	SrL	SrC	SrR
A group	-1.3227±0.3135 (659)	-1.7244±0.4642 (615)	2.0020±0.6168 (624)
B group	-1.2152±0.2921 (60)▲	-1.6289±0.4172 (74)▲	1.7843±0.6353 (72)▲
C group	-1.2256±0.3634 (599)▲	-1.6312±0.4747 (460)▲	1.8569±0.5449 (546)▲
D group	-1.0228±0.2236 (95)▲●	-1.4684±0.3109 (82)▲●	1.6687±0.4861 (91)▲●

Note: ▲ The difference was statistically significant compared with that of group A; * The difference was statistically significant compared with that of group B; ● The difference was statistically significant compared with that of group C.

D was significantly lower than group A. The SrL and SrC of group D were significantly lower than group A, B and C, and the SrR of group D was lower than group A and C, which had statistical differences too.

Diagnosis Accuracy of the Total Coronary Occlusion or subtotal Coronary Occlusion by Parameters of the Left Ventricular Systolic Strain Peak

The area under the SrL ROC curve was $0.727 > 0.700$ (Figure 2) and if $SrL = -1.085$ was regarded as the cut-off value, the sum (1.348) of sensitivity (0.673) and specificity (0.675) would be the most.

Conformity of the Strain Measurements in Both Groups Analyzed by Bland-Altman Method

The Bland-Altman figure showed that there was good conformity in the strain value in both groups (Figure 3). Ninety percent of the measurements were within the 95% confidence interval.

Discussion

The study evaluates the indicators of the ventricular wall motion such as quantitative measurement of ejection fraction through conventional echocardiography, systolic endocardial motion range through observation, and the analysis of the abnormal segmental ventricular wall motion, obtained by traditional ultrasonic cardiogram method¹²⁻¹⁴. Because of this, the thickening ratio of the ventricular wall could only report the radial motion of the ventricular wall motion. What's more, the experience and skill of observers would directly influence the final measurements¹⁵. Thus, there were no differences in both the left ventricular end diastolic diameter and the ejection fraction through conventional echocardiography. There was no abnormal segmental ventricular wall motion too, though part of patients were diagnosed with total or subtotal occlusion of the right coronary artery¹⁶.

However, longitudinal, circumferential and radial myocardial motion strain ratio could be measured comprehensively and accurately by STI⁷⁻⁹. The subjective factors could also be avoided by STI too. Moreover, the strain measurements result showed a good conformity between both groups by Bland-Altman analysis^{17,18}.

The results of this study show that the longitudinal, circumferential and radial systolic function of each segment were impaired. Perhaps the reason behind this was that the left ventricu-

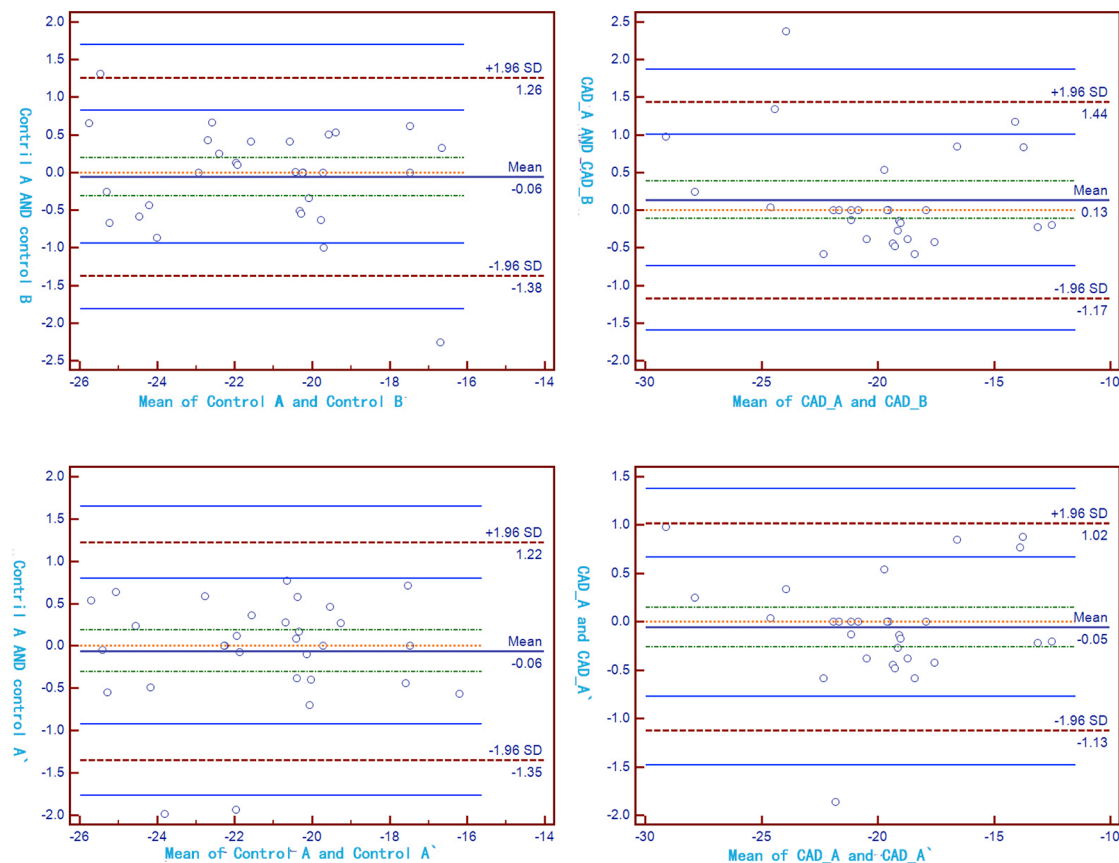


Figure 2. The Consistency of Bland-Altman analysis of strain measurement in the CAD Multi-vessel group and the control group.

lar endocardial myocardial artery was issued at the right angle while 2/3 of the right myocardial arteries had many dendritic branches¹⁹. The impact produced from deeply oppressed and buried coronary branches in the myocardium during cardiac contraction on coronary blood flow was more obvious too²⁰. Thus, the endocardial myocardial fibers were more sensitive to ischemia, and the left ventricular longitudinal motion was produced by contracting longitudinal myocardial fibers²¹. Subendocardial myocardial, mid myocardium and subepicardial myocardium of radial movement endocardium accounted for 58%, 25% and 17% of the radial motion. Meanwhile, the circumferential motion was produced by mid circular fiber. Thus, longitudinal and radial systolic function changed earlier than the circumferential systolic function.

The results showed that the circumferential strain ratio of each segment in the multi-vessel CAD groups was slower than that in the control group. The circumferential strain had no diffe-

rence among all groups that related to strain and strain ratio²². Therefore, the strain ratio change was more sensitive than the strain change.

The comparison results of the left ventricular systolic strain peak showed that the absolute value of SL SrL, SrC and SrR was demonstrated as group A > group C > group B > group D. This may relate to the establishment of coronary collateral circulation and blood flow redistribution. There was numerous anastomosis veins²³ with diameters ranging from 20 to 350 μm in the hearts of normal people and those with coronary disease. Under severe coronary stenosis, the myocardium would render blood flow from “non-ischemic” to “ischemic” by its metabolites-adenosine, to present myocardial blood flow redistribution, which would protect the myocardium well.

Research showed that radial strain would significantly reduce only over 75% of the transmural myocardial infarction²⁴. However, this research showed that the SrR of group B, group C and group D were markedly reduced, and it reported that

although the conventional ultrasound inspection showed that NWM-MVD patients had normal ventricular wall motion in steady-state, long-term low perfusion led to serious myocardial ischemia of the regional myocardial. Although collateral circulation can improve clinical symptoms, the net effect is not enough to compensate for blood flow reduction caused by severe coronary stenosis or simultaneous occlusion.

Bradycardia lengthened the diastole and increased artery shear stress to induce neovascularization, which increased coronary blood flow. Besides, bradycardia could reduce oxygen consumption of the myocardium to improve the myocardial tolerance to hypoxia. Hence, bradycardia and sinus bradycardia might be a compensatory mechanism in NWM-MVD patients.

Conclusions

The myocardial systolic function was impaired in MVD patients of group B (coronary stenosis degree $\leq 50\%$), group C (coronary stenosis degree $50\%-99\%$) and group D (coronary stenosis degree $\geq 99\%$), especially the longitudinal and radial systolic function. Moreover, there was myocardium conformity of in both the multi-vessel CAD patients and the control subjects.

Limitations of this Research

The sample of this research was limited; this study did not classify as multi vessel disease and the impacts from different lesions on the final result could not be excluded.

There was no load test which could increase oxygen consumption of the myocardium and detected ischemia more easily for this research.

Conflicts of interest

The authors declare no conflicts of interest.

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