Deterioration of longitudinal, circumferential, and radial myocardial strains during acute coronary flow reduction: which direction of strain should be analyzed for early detection?

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Abstract

Purpose: Longitudinal myocardial strain is considered to deteriorate in the early ischemic stage compared to circumferential and radial strains because the subendocardial inner oblique fibers are generally directed along the longitudinal axis. However, it is unclear whether the decrease in longitudinal strain precedes a decrease in circumferential and radial strains during acute coronary flow reduction.

Methods: The left anterior descending artery was gradually narrowed in 13 open-chest dogs. Whole-wall and subendocardial longitudinal, circumferential, and radial strains were analyzed at baseline and during flow reduction. Peak systolic and end-systolic strains, the postsystolic strain index (PSI), and the early systolic strain index (ESI) were measured in the risk area; the decreasing rate in each parameter and the diagnostic accuracy to detect flow reduction were evaluated.

Results: Absolute values of peak systolic and end-systolic strains gradually decreased with flow reduction. The decreasing rate and diagnostic accuracy of longitudinal systolic strain were not significantly different from those in other strains, although the diagnostic accuracy of radial systolic strain tended to be lower. PSI and ESI gradually increased with flow reduction. In these parameters, a lower diagnostic accuracy with respect to radial strain was not demonstrated.

Conclusion: During acute coronary flow reduction, the decrease in longitudinal systolic strain did not precede that in circumferential systolic strain; however, the decrease in radial systolic strain may be smaller than that of other systolic strains. In contrast, there appeared to be no differences in the PSI and ESI values among the three strains.

Keywords: Early systolic lengthening, Ischemia, Myocardial strain, Postsystolic shortening, Speckle-tracking echocardiography

Introduction

Speckle-tracking echocardiography was developed to noninvasively quantify global and regional myocardial deformation and allows the evaluation of longitudinal, circumferential, and radial functions of the left ventricle (LV). Many studies have demonstrated that longitudinal function deteriorates in the early stage of various cardiac diseases and that global longitudinal strain is especially useful for predicting a prognosis [1-3]. Impairment of the subendocardial inner oblique fibers, which are generally directed along the longitudinal axis, is considered a reason for early longitudinal dysfunction [1-3].

With respect to the diagnosis of acute myocardial ischemia, it has also been suggested that longitudinal strain is impaired earlier than circumferential and radial strains because the subendocardium is vulnerable to ischemia [4-8]. However, several studies have reported that longitudinal strain is not the most sensitive response to acute ischemia [9, 10]. Thus, the vulnerability of longitudinal, circumferential, and radial strains during acute ischemia has been controversial. We therefore investigated whether the decrease in longitudinal strain precedes that in circumferential and radial strains in a dog model with acute coronary flow reduction.

Material and Methods

Animal preparation

All animal studies were performed in accordance with the institutional guidelines for the care and use of laboratory animals. A total of 13 open-chest dogs (9.9 ± 1.0 kg) were used in this study. Dogs were anesthetized with intramuscular xylazine (0.5 mg/kg), followed by intravenous pentobarbital (25.9 mg/kg) injection, and then were intubated and ventilated using a respirator pump. Oxygen saturation was monitored by a pulse oximeter and maintained within the normal range, and continuous electrocardiographic monitoring was performed. Buprenorphine (4 μg/kg) was administered intramuscularly as an analgesic. Pentobarbital (6 mg/kg/h) and midazolam (0.18 mg/kg/h) were continuously injected to maintain a sufficient depth of anesthesia. LV pressure was measured by a 5-F micromanometer (Millar, Houston, Texas, USA), which was placed in the LV through the right carotid artery. The heart was suspended in a pericardial cradle through a left parasternal thoracotomy in the longitudinal direction. The proximal portion of the left anterior descending coronary artery (LAD) was carefully dissected from the surrounding tissues, and a hydraulic occluder was placed around the artery. An ultrasonic perivascular flow probe was placed on the artery immediately distal to the hydraulic occluder and was connected to a digital flowmeter (Transonic Systems, Ithaca, New York, USA) for the continuous measurement of the mean LAD flow.

Echocardiography

Two-dimensional echocardiography for speckle-tracking analysis was performed using Vivid E9 with a 6S transducer (GE Healthcare, Horten, Norway). The transmission frequency was 2.7 MHz, whereas the receiving frequency was 5.4 MHz, and the frame rate was 109.3 frames/s. The apical 4-chamber and apical short-axis views were acquired with a water bath as a standoff. Since the risk area in this model has been confirmed to be located in the apical anterior and apical septal segments in our previous study [11], the apical 4-chamber view was slightly modified in advance to visualize the apical anteroseptal segment. The timing of aortic valve closure (AVC) was determined by the aortic component of the second heart sound derived from phonocardiography.

Experimental protocol

After the simultaneous acquisition of hemodynamic and echocardiographic data at baseline, the LAD was narrowed up to three times to create various degrees of flow-limiting stenosis. Before coronary flow reduction, heparin (100 U/kg) was intravenously administered to prevent coronary thromboembolism. Hemodynamic and echocardiographic data were acquired 2 min after the steady state in hemodynamics was achieved during coronary flow reduction. After relieving stenosis, a sufficient return of hemodynamics and myocardial wall motion to the baseline level was allowed, and then the hydraulic occluder was further inflated to achieve more than a 5% coronary flow reduction from the previous stage. Echocardiographic views during coronary flow reduction were carefully aligned in comparison with the views stored at baseline. Finally, the risk area was visually determined as the area with wall motion abnormalities observed during graded flow reduction.

Data analysis

Hemodynamic parameters, namely, the heart rate, LV systolic pressure, LV end-diastolic pressure, maximum and minimum time derivatives of LV pressure (dP/dt_{max} and dP/dt_{min}, respectively), and time constant of LV pressure decay during the isovolumetric relaxation period (tau), were averaged across five consecutive cardiac cycles. Data obtained during coronary flow reduction were categorized into three groups according to the level of coronary flow reduction normalized by the baseline value: <30% flow reduction (mild), ≥30% and <60% flow reduction (moderate), and ≥60% flow reduction (severe).

The speckle-tracking analysis was performed offline on the clip containing the captured images using EchoPAC BT13 software (GE Healthcare, Horten, Norway). The endocardial border in the end-systolic frame was manually traced, then the wall thickness was adjusted to a width even with that of the myocardium. The longitudinal strain was analyzed in the apical anteroseptal segment of the modified apical 4-chamber view. The circumferential and radial strains were analyzed in the anteroseptal segment (60°) of the apical short-axis view, which was manually adjusted carefully to correspond with the same segment obtained from the modified apical 4-chamber view. The longitudinal and circumferential strains were calculated using whole-wall and subendocardial analyses, whereas the radial strain was calculated using whole-wall analysis only. End-diastole was defined at the onset of the QRS complex on the electrocardiogram, and end-systole was defined at the timing of AVC.

Peak systolic and end-systolic strains were measured from the strain-time curve. When postsystolic shortening (PSS) was observed, the postsystolic strain index (PSI) as a parameter of PSS was calculated using the following formula: ([peak strain after end-systole] − [end-systolic strain])/(maximum amplitude) [12]. When early systolic lengthening (ESL) was observed, the early systolic strain index (ESI) as a parameter of ESL was calculated using the following formula: (peak lengthening during systole)/(maximum amplitude during systole) [12]. When these motions were not observed, these parameters were assigned a value of zero. Myocardial strain parameters were averaged across three consecutive cardiac cycles.

As described later, the numbers of datasets were smaller in mild and severe flow reduction than in moderate flow reduction, resulting in the mean strain values at baseline corresponding to each flow reduction group being different. Since this difference complicated the comparison between the groups, the decreasing rate from the baseline value was calculated for peak systolic and end-systolic strains. The decreasing rate was not calculated for the PSI and ESI because both parameters included baseline values of zero.

Interobserver and intraobserver variabilities

Ten image datasets, which consisted of the modified apical 4-chamber and apical short-axis views, were randomly selected from the total data to assess interobserver and intraobserver variabilities in each strain parameter. To determine the interobserver variability, the analysis was repeated by a second observer who was blinded to the values obtained by the first observer. To determine the intraobserver variability, the analysis was repeated more than 2 weeks later by the same observer.

Statistical analysis

Data are expressed as the mean ± standard deviation. The comparison between baseline and coronary flow reduction datasets for each hemodynamic parameter was performed by one-way analysis of variance, followed by the Dunnett test. The relationship between coronary flow reduction and myocardial strain parameters (the decreasing rate in peak systolic and end-systolic strains, PSI, and ESI) was fitted by an exponential expression, which was used in a previous study [13]. The comparison between whole-wall longitudinal, circumferential, and radial strain parameters was performed by one-way analysis of variance, followed by the Tukey-Kramer test or the Games-Howell test. The comparison between subendocardial longitudinal and circumferential strain parameters was performed by an unpaired t-test. The diagnostic accuracy of each myocardial strain parameter to detect moderate or severe flow reduction is shown as the area under the curve (AUC) derived from the receiver operating characteristic (ROC) curve analysis. The comparison between AUCs was conducted using the method of Delong. Interobserver and intraobserver variabilities were determined using the intraclass correlation coefficient. Statistical analyses were performed using SPSS Statistics version 20.0 (IBM, Armonk, New York), Origin 2017 (OriginLab, Northampton, Massachusetts), and MedCalc version 15.2.2 (MedCalc Software, Ostend, Belgium). A value of $p < 0.05$ was considered to be statistically significant.

Results

Thirty-three datasets of coronary flow reduction were acquired from 13 dogs, but three datasets were excluded due to unstable strain-time curves. Therefore, a total of 13 baseline datasets and 30 coronary flow reduction datasets (9, mild flow reduction; 13, moderate flow reduction; and 8, severe flow reduction) were included in the final analysis. In all dogs, the apical anteroseptal segments that we used in the speckle-tracking analysis were included in the risk areas.

Coronary flow and hemodynamics

The LAD flow tended to be reduced with increasing coronary flow reduction severity. Hemodynamic changes were small; LV end-diastolic pressure tended to increase, dP/dt_{max} and the absolute value of dP/dt_{min} tended to decrease, and tau tended to be prolonged during severe flow reduction (Table 1).

Peak systolic and end-systolic strains

At baseline, standard deviations of peak systolic and end-systolic strain values were larger in the radial strain compared to the longitudinal and circumferential strains (peak systolic strain values in the whole-wall analysis: longitudinal, −15.8 ± 4.7%; circumferential, −17.0 ± 3.4%; radial, 32.2 ± 11.8%; end-systolic strain values in the whole-wall analysis: longitudinal, −15.7 ± 4.7%; circumferential, −17.0 ± 3.4%; radial, 32.1 ±11.7%).

Absolute values of peak systolic and end-systolic strains began to decrease during moderate flow reduction and markedly decreased during severe flow reduction. Representative strain-time curves in the risk area are shown in Figure 1. The relationships between coronary flow reduction and the decreasing rate of systolic strains could be fitted by exponential expressions (Figure 2). Because the majority of radial strains during mild and moderate flow reduction tended to be higher than baseline values, the decreasing rate of radial strain was smaller than those of longitudinal and circumferential strains during less than moderate flow reduction.

In the whole-wall analysis, the decreasing rates of peak and end-systolic strains tended to be smaller in radial strain than other strains, although there were no significant differences among all strains (Figure 3). Similarly, in the subendocardial analysis, there were no significant differences between longitudinal and circumferential strains.

PSS and ESL

At baseline, the standard deviations of the PSI and ESI values were almost the same among all directions (PSI values in the whole-wall analysis: longitudinal, 0.03 ± 0.03; circumferential, 0.02 ± 0.03; radial, 0.02 ± 0.03; ESI values in the whole-wall analysis: longitudinal, 0.18 ± 0.13; circumferential, 0.14 ± 0.08; radial, 0.14 ±0.07).

PSS and ESL tended to appear during moderate flow reduction and were markedly augmented during severe flow reduction (Figure 1). The relationships between coronary flow reduction and the PSI and ESI could also be fitted by exponential expressions (Figure 4). There were no significant differences among all directions at baseline or during coronary flow reduction (Figure 5).

Diagnostic accuracy of coronary flow reduction

With respect to the diagnostic accuracy of peak systolic and end-systolic strains to detect moderate flow reduction, the AUCs for all strains were not significantly larger than the line of no information (AUC = 0.5) (Figure 6). The AUC for longitudinal strain was not significantly larger than that for other strains in the whole-wall and subendocardial analyses. During severe flow reduction, the AUCs for longitudinal and circumferential strains were significantly larger than the line of no information, but that for radial strain was not. There were no significant differences between the AUCs for longitudinal and circumferential strains; however, the AUC for radial strain tended to be smaller than those for other strains.

With respect to the diagnostic accuracy of the PSI and ESI to detect moderate and severe flow reduction, the AUC for longitudinal strain was not significantly larger than that for other strains. A tendency of lower diagnostic accuracy with respect to radial strain was not demonstrated (Figure 6).

Interobserver and intraobserver variabilities

Interobserver and intraobserver variabilities in the randomly selected image datasets were excellent in all myocardial strain parameters (Table 2).

Discussion

The main findings of this study were as follows: the decrease in longitudinal systolic strain did not precede that in circumferential systolic strain, although the decrease in radial systolic strain tended to occur later than that in other strains. With respect to the diagnostic accuracy to detect coronary flow reduction, significant differences were not shown between longitudinal and circumferential systolic strains, whereas that for radial systolic strain tended to be relatively lower. In contrast, there were no differences in the PSI and ESI values among the three strains.

Deterioration of longitudinal function during acute ischemia

Myocardial damage during ischemia expands from the subendocardium to the subepicardium. The subendocardial myocardial fibers show an oblique clockwise orientation mainly in the longitudinal direction and most significantly contribute to longitudinal function. The midmyocardial fibers run circumferentially and contribute to circumferential function. The subepicardial fibers are longitudinally oriented in an oblique counterclockwise direction [14]. Radial function is determined by the sum of the complicated dynamics of the myocardial fibers and sheets [15].

Previous studies have reported that global and regional longitudinal strains are significantly decreased in patients with coronary artery disease, and it has been speculated that longitudinal strain may decrease more sensitively during ischemia than circumferential and radial strains due to subendocardial fiber orientation [5, 7, 8]. However, comparisons between longitudinal strain and the circumferential or radial strain were not shown in these studies.

In studies that compared global strains, global longitudinal strain allowed better detection of significant coronary stenosis than other strains [4, 6]. However, these studies have a limitation because the global longitudinal strain was analyzed from two or three apical views, whereas the global circumferential and radial strains were analyzed from the midpapillary short-axis view only.

Although a few studies have compared the three strains in the same ischemic region, the results are inconsistent. Tanaka et al. assessed three directions using color tissue Doppler echocardiography and demonstrated greater deterioration in circumferential strain than in other strains during dobutamine stress in patients with coronary artery stenosis [9]. Reant et al. simultaneously measured and compared the three directions of myocardial strain in two different pig ischemia experiments; one experiment demonstrated that the decrease in longitudinal strain significantly preceded that in circumferential and radial strains [16], whereas another experiment showed that longitudinal and circumferential strains decreased in the same manner, although radial strain deteriorated later [10].

Comparison of peak systolic and end-systolic strains in three directions

In the present study, the decreasing rates of longitudinal peak systolic and end-systolic strains were not significantly larger than those of circumferential strain. Although subendocardial shortening has been suggested to be more susceptible to ischemia than subepicardial shortening [17], the subendocardial analysis in our experiment demonstrated the same results as the whole-wall analysis. In a previous study using sonomicrometry crystals placed in the subendocardium, the decreasing rate of longitudinal function was almost the same as that of circumferential function during acute ischemia, as was the case in the present study [18]. This finding indicates that the deterioration in longitudinal strain does not occur earlier than that in circumferential strain in the acute ischemic myocardium. Simultaneous impairment in both directions appears to be reasonable because shortening of the inner oblique fibers in the subendocardium involves not only longitudinal but also circumferential components.

The decreases in radial peak systolic and end-systolic strains tended to be inferior to those in longitudinal and circumferential strains in our results. Previous studies have reported the same result [11, 19]. Although the possibility of a preserved radial strain at an early stage during ischemia cannot be denied, larger standard deviations in radial strain appear to be a main reason that the radial strain is less sensitive. This variation may have caused some positive changes in the decreasing rate of radial strain, resulting in the lower diagnostic accuracy of radial strain.

Comparison of PSS and ESL in three directions

PSS and ESL are known as subtle motions that appear in the ischemic myocardium, and their amplitudes increase concomitantly with the decrease in systolic shortening. These motions occur as the result of segmental interactions between ischemic and nonischemic regions [20]. In the present study, the PSI and ESI exponentially increased with the severity of coronary flow reduction. The diagnostic accuracies of the PSI and ESI in the radial direction were not lower than those in other directions. The reason appears to be that the PSI and ESI were almost zero at baseline, resulting in smaller standard deviations even in the radial direction.

Both PSS and ESL are considered more sensitive than systolic strains to detect ischemia in previous studies [21, 22]. Nevertheless, the AUCs for PSI and ESI were not superior to those for systolic strains in this study. The area perfused by the LAD is small in dogs. Thus, subtle PSS or ESL might not have been detected because the diagnostic accuracy of speckle-tracking echocardiography is affected by the spatial extent of abnormal motion [23].

Study limitations

First, since the total number of datasets was relatively small, the results may be potentially subject to type II errors. In the decreasing rate, there seemed to be small (but not significant) differences between the longitudinal and circumferential systolic strains during mild flow reduction in the subendocardial analysis. However, the decreasing rate in longitudinal strain was approximately 8% on average, which indicates a decrease of less than 2% in the absolute strain value. Therefore, even if this difference is significant, it would be difficult to detect the decrease in regional strains because there is nonnegligible test-retest variability (approximately 3-5% in the average difference) in current speckle-tracking echocardiography techniques [24].

Second, only the flow-limiting stenosis model was assessed in this study because we focused on investigating the relationship between strain parameters and the severity of coronary flow reduction. A model of demand ischemia induced by dobutamine stress should be tested in further studies.

Third, in repetitive ischemia, we secured time for a sufficient return of hemodynamics and myocardial wall motion to the baseline level; however, preconditioning of the myocardium may have affected the change in the decreasing rate.

Finally, since we used 2-dimensional speckle-tracking echocardiography, modified apical 4-chamber and short-axis views were not acquired simultaneously. In contrast, 3-dimensional speckle-tracking echocardiography can analyze strain components in all three directions from one image acquisition. However, we did not use the 3-dimensional method due to its low temporal and spatial resolution.

Clinical implications

Echocardiographic assessments of regional wall motion are valuable for identifying myocardial ischemia because wall motion abnormalities occur relatively upstream in the ischemic cascade. Three apical views are frequently used for this purpose, but clear apical images may not always be acquired. Our results indicate that circumferential analysis provides the same diagnostic accuracy as longitudinal analysis if clear short-axis views are obtained. Moreover, in the PSS or ESL analysis, it has been historically unclear from which direction these motions should be analyzed. Our results suggest that there are no significant differences among the three directions in the PSS and ESL analyses.

Conclusions

In a dog model with acute coronary flow reduction, the decrease in longitudinal systolic strain did not precede that in circumferential systolic strain, although the decrease in radial systolic strain may be smaller than that in other systolic strains. This result suggests that circumferential systolic strain allows early detection of the impaired myocardium during acute ischemia as well as longitudinal strain. In contrast, there appeared to be no difference in the PSI and ESI among the three strains.

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Figure legends

Figure 1 Longitudinal (upper), circumferential (middle), and radial (lower) strain-time curves derived from the apical anteroseptal segment (white arrows) in the whole-wall analysis. Peak systolic strain (red circles) and end-systolic strain (blue circles) gradually decreased during moderate to severe flow reduction. Conversely, postsystolic shortening and early systolic lengthening gradually increased. AVC = aortic valve closure.

Figure 2 Relationships between coronary flow reduction and the decreasing rate of peak systolic and end-systolic strains from the baseline value. The relationships could be fitted by exponential expressions. The decreasing rate of radial strain tended to be lower during mild and moderate flow reduction than those of other strains due to the presence of positive values.

Figure 3 Comparisons of the decreasing rates of longitudinal, circumferential, and radial systolic strains. Numerical values show p-values. In the whole-wall analysis, the decreasing rates of peak and end-systolic strains tended to be smaller in radial strain than in other strains, although there were no significant differences among all strains. Similarly, in the subendocardial analysis, there were no significant differences between longitudinal and circumferential strains.

Figure 4 Relationships between coronary flow reduction and the postsystolic strain index (PSI) and early systolic strain index (ESI). Exponential increases in PSI and ESI with severity of coronary flow reduction were observed in all directions. The increase in radial strain appeared to be similar to that in other strains.

Figure 5 Comparison between longitudinal, circumferential, and radial directions with respect to the postsystolic strain index (PSI) and the early systolic strain index (ESI). Numerical values show p-values. There were no significant differences among all directions at baseline and during coronary flow reduction.

Figure 6 Receiver operating characteristic curves for the detection of moderate or severe flow reduction. With respect to peak systolic and end-systolic strains, there were no significant differences between the areas under the curve (AUCs) for longitudinal and circumferential strains; however, the AUC for radial strain tended to be smaller than those for other strains. With respect to the postsystolic strain index (PSI) and the early systolic strain index (ESI), there appeared to be no significant differences among all strains. CI = confidence interval.