Quantification of Regional Contractile Function After Infarction: Strain Analysis Superior to Wall Thickening Analysis in Discriminating Infarct From Remote Myocardium

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OBJECTIVES  Using two-dimensional wall thickening (WT) (expressed as percentage) and strain analysis, regional contractile myocardial function was quantified and compared in 13 control subjects and 13 patients with a first myocardial infarction (MI). The findings in the patient group were related to global ventricular function and infarct size.

BACKGROUND  In patients with coronary artery disease, regions with dysfunctional myocardium cannot be differentiated easily from regions with normal function by planar WT analysis. Physiologic factors, in combination with limitations of conventional imaging techniques, affect the calculation of WT. Quantitative assessment of contractile function by magnetic resonance (MR) tissue tagging and strain analysis may be less affected by these factors.

METHODS  Two-dimensional regional WT and strain were calculated in three short-axis MR cine and tagged images, respectively. Left ventricular volumes and ejection fraction (EF) were obtained from a series of contiguous short-axis cine images.

RESULTS  In patients with infarct-related ventricles, WT and strain analysis both revealed reduced myocardial function, as compared with control subjects (p < 0.005 and p < 0.001, respectively). However, WT analysis yielded no significant regional differences in function between infarct-related and remote myocardium (p = 0.064), whereas strain analysis did (p < 0.005). For detecting dysfunctional myocardium of electrocardiographically and angiographically defined infarct areas, WT analysis had a sensitivity of 69% and a specificity of 92%, whereas strain analysis demonstrated a sensitivity of 92% and a specificity of 99%. The EF correlated with WT (r = 0.76, p < 0.005) and strain (r = 0.89, p < 0.001).

CONCLUSIONS  Two-dimensional strain analysis is more accurate than planar WT analysis in discriminating dysfunctional from functional myocardium, and it provides a strong correlation between regional myocardial and global ventricular function. (J Am Coll Cardiol 2001;37: 808–17) © 2001 by the American College of Cardiology

One of the most important hallmarks of ischemic heart disease is regional myocardial dysfunction (1–3). The extent and degree of contractile dysfunction after myocardial infarction (MI) are both important factors in determining the long-term prognosis after MI (4–6). An accurate variable of regional myocardial function is systolic wall thickening (WT) (expressed as a percentage) (7,8). Wall thickening is directly related to myocardial function, and abnormalities in WT are correlated with the extent of infarct size (3,7,9).

Magnetic resonance (MR) imaging has emerged as an important imaging modality for accurate assessment of regional myocardial function by quantitative WT analysis (8–11). Quantification of WT depends on accurate myocardial border delineation, which is facilitated by the high image quality provided by MR imaging. Detection of the excursion of endocardial and epicardial surfaces is affected by through-plane motion and the curvature of the heart wall (12), which can be compensated by three-dimensional WT analysis (13). However, the lack of traceable reference points within the myocardium prevents a quantitative description of intramural function. Zerhouni et al. (14) introduced MR tissue tagging, a method for noninvasive selective labeling of myocardial tissue. This was followed by the introduction of grid-tagging, which provides a large number of traceable tags within the myocardium (15,16). Using this grid-tagging technique in conjunction with two-dimensional strain analysis, quantitative analysis of regional intramural function can be performed independent of accurate border delineation (17–19). In the present study, regional myocardial function was expressed by two different variables: 1) planar WT, and 2) two-dimensional strain. Our aim was to assess the most accurate variable for quantification of regional function after MI. The following comparative investigations were performed, for both WT and strain as the dependent variables. First, regional function in the infarct-related region was tested in patients versus control subjects. Second, within the patient group, regional func-

See page 731
tion was tested in the infarct region versus the remote noninfarct-related region. Third, also within the patient group, regional function was tested against global left ventricular function.

METHODS

Subjects. The Committee on Research Involving Human Subjects of the University Hospital, “Vrije Universiteit,” in Amsterdam, approved the study protocol, and all subjects gave written, informed consent. Thirteen patients (12 men, age 57 ± 11 years) with a first MI were included. Thirteen age-matched male volunteers (age 53 ± 7 years) with no clinical evidence or history of cardiac disease served as control subjects. The diagnosis of MI was based on a typical history of chest pain, electrocardiographic changes compatible with infarction and an increase in plasma creatinine phosphokinase levels of more than twice the upper limit of normal, with an associated increase in the creatinine phosphokinase-MB fraction. Based on angiographic and electrocardiographic findings, it was confirmed that the left anterior descending (LAD) coronary artery was the infarct-related coronary artery in all patients. The patients were studied 103 ± 17 days after MI.

MR imaging. Cardiac-triggered MR imaging was performed at 1.5-tesla (Vision, Siemens Medical Systems, Erlangen, Germany), using a phased-array body coil. Patients were imaged in the supine position.

CINE IMAGES. Localizing scout images were followed by a horizontal long-axis, four-chamber cine series. Using the end-diastolic frame of the horizontal long-axis view for positioning, 7 to 11 single breath-hold, short-axis series were acquired to encompass the whole left ventricle to calculate ventricular volumes, ejection fraction (EF) and mass. A gradient-echo pulse sequence with segmented k-space was applied. Acquiring 7-ky lines per heartbeat, the temporal resolution within the cardiac cycle was 30 ms. The flip angle used was 15°, repetition time was 10 ms and echo time was 3.8 ms. The matrix size was 144 × 256, the field of view was 250 × 250 mm and the corresponding resolution was 1.74 × 0.98 mm. The slice thickness was 6 mm. The entire imaging session, including both cine and tagged gradient-echo images, lasted 35 min.

Image analysis. CINE IMAGES: WT AND GLOBAL FUNCTION. The short-axis cine images were processed using the MASS software package (Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands) loaded on a Sun Sparc station (Sun Microsystems, Mountain View, California). The analysis procedures for calculation of systolic WT, left ventricular volumes, EF and mass have been described previously (23,24). Briefly, the end-diastolic phase was defined as the phase obtained directly after detection of the R-wave. The end-systolic phase was defined as the image frame with the smallest left ventricular cavity. Epicardial and endocardial contours were manually traced. The papillary muscles, trabeculae and epicardial fat were excluded from the analysis.

WALL THICKENING. After tracing, the centerline method was employed at the end-diastolic and end-systolic contours to calculate WT at both time frames (Fig. 1) (8). Only data obtained from cine images corresponding with the level of the three tagged images were used for WT analysis. To ensure proper matching of the cine and tagged short-axis slices, the right ventricle insertion sites, papillary muscle location and base-to-apex location were used as landmarks.

GLOBAL FUNCTION. The end-diastolic and end-systolic volume indexes (EDVI and ESVI, respectively) were calculated by summation of the product (area × slice distance) for all slices and indexed for body surface area. From these volumes, stroke volume index and EF were calculated.

TAGGED IMAGES. STRAIN ANALYSIS. The tagged short-axis images were processed on a Silicon Graphics workstation using a dedicated software package (SPAMMVU, University of Pennsylvania, Philadelphia, Pennsylvania) (17). The tagging grid was automatically marked and followed during contraction (25). The tag intersection points were used to define triangular elements of the myocardium across the heart wall (Fig. 1). Homogeneous strain analysis was used to
compute the deformation of each triangle (16,17). The strain components—radial stretch ($e_r$) and circumferential shortening ($e_c$)—were computed with respect to the radial and circumferential directions, respectively (see Appendix). Positive radial strains ($e_r$) represent the local contribution to WT. Negative values for $e_r$ imply local wall thinning. Negative circumferential strains ($e_c$) quantify local circumferential shortening. Positive circumferential strains represent circumferential lengthening. The reproducibility of results using these strain variables has been reported (26).

**SEGMENTAL ANALYSIS**. For regional analysis of myocardial function, 12 circumferential segments of 30° each were defined at each of the three tagged and corresponding short-axis cine images. Assignment of a centerline or triangular element to a segment was determined by the position of the centerline or triangle's centroid at end-diastole. The values of WT derived from the centerlines and the values of the strain variables derived from the triangular elements were averaged within these segments, yielding 12 regional values of the myocardial function variables per each short-axis level—36 in total. Segments with values for WT, $e_r$ and $e_c$ that exceeded the mean value ± 2 SD of the control group were defined as abnormal, indicating dysfunctional myocardium.

**DEFINITION OF INFARCT-RELATED, ADJACENT AND REMOTE AREAS**. To compare the regional contractile function of patients with that of corresponding healthy volunteers, the anteroseptal and anterior segments at the basal level, the septal and anterior segments at the midventricular level and the septal, anterior and anterolateral segments at the apical level were considered specific for the perfusion territory of the LAD, and thus for the infarct-related area. The two segments adjacent to each side of the defined infarct area were considered the adjacent area. The segments in between the two adjacent areas and opposite of the infarct area were considered to be the remote area (Fig. 2). The distribution
of the perfusion territory of the LAD and the corresponding distribution of the circumferential segments specific for the infarct area were based on previous reports (21,27).

Statistical analysis. Statistical analysis was performed using the SPSS software package, version 7.5. The function in infarct-related, adjacent and remote myocardium in the infarct group was compared with that in comparable regions in the control group by using the nonparametric Mann-Whitney $U$ test. In the infarct group, the differences in function between the infarct and remote areas were analyzed by using the Wilcoxon test for paired samples. Receiver-operating characteristic curves were created to evaluate the sensitivity and specificity of WT and strain analysis, respectively, for the detection of abnormal contractile function in the perfusion territory of the infarct-related coronary artery. Linear regression analysis was performed to correlate regional function quantified by WT and strain analysis (averaged for the 36 segments) to global ventricular function and enzymatic infarct size, respectively. A $p$ value $<0.05$ was considered to be significant. Data are presented as the mean value $\pm$ SD.

RESULTS
All patients received reperfusion therapy: seven patients had thrombolysis and six had primary percutaneous transluminal coronary angioplasty. The averaged peak creatine kinase, MB level was $238 \pm 119$ U/liter. Angiography was per-
formed in all but one patient, confirming that the LAD was the infarct-related vessel. Nine patients received angiotensin-converting enzyme inhibitors and beta-blockers at the time of image acquisition. The clinical characteristics are shown in Table 1.

**Regional function.** WT ANALYSIS. As shown in Table 3, regional WT in the infarct group, as compared with the control group, was reduced in all areas of the left ventricle, including the infarct-related area (p < 0.005), the adjacent area (p < 0.05) and the remote area (p = 0.005). In the infarct group, WT in the infarct area was not significantly different from WT in the remote area (p = 0.064) (Fig. 3). In Figure 4A, WT in 12 circumferential segments at the midventricular level is shown in patients and control subjects. Despite the fact that all patients had sustained an anterior MI, in none of the 12 segments, WT in the infarct group exceeded the mean values ± 2 SD of the control group. Receiver-operating characteristic curve analysis for WT analysis indicates the optimal cutoff value for the detection of dysfunctional myocardium in the perfusion territory of the infarct-related coronary artery—the LAD. A cutoff value of 35% was found to correspond with the highest sensitivity (69%) and specificity (92%).

**WT ANALYSIS IN RELATION TO GLOBAL FUNCTION.** The EF correlated with the mean ventricular contractile function, expressed as WT averaged for all 36 segments (r = 0.76, p = 0.002) (Fig. 5A). No correlation between EF and the number of segments with abnormal WT (r = 0.17, p = NS), indicating the extent of the area with dysfunctional myocardium, was found.

**STRAIN ANALYSIS.** Strain analysis demonstrated significant differences in regional function between the infarct group and the control group in all areas of the left ventricle (infarct-related and adjacent areas: p < 0.001 for $\varepsilon_r$ and $\varepsilon_c$; remote area: p < 0.001 for $\varepsilon_r$ and p < 0.01 for $\varepsilon_c$) (Table 3). The infarct group demonstrated significant differences in regional function between the infarct and remote areas ($\varepsilon_r$: 9 ± 7% vs. 20 ± 7%, p = 0.001; $\varepsilon_c$: −10 ± 7% vs. −16 ± 4%, p < 0.005) (Fig. 3). In Figure 4, B and C, $\varepsilon_r$ and $\varepsilon_c$ at the midventricular level are shown. In the infarct group, four segments were found with values for $\varepsilon_r$ that exceeded the mean values ± 2 SD of the control group. In the same four segments, values for $\varepsilon_c$ also exceeded the mean values ± 2 SD of the control group. These septal and anterior segments were highly concordant with the perfusion territory of the infarct-related LAD (Fig. 2). By using receiver-operating characteristic curves, the optimal cutoff value for the detection of dysfunctional myocardium in the perfusion territory of the LAD by strain analysis was found to be 20% for $\varepsilon_r$, with a corresponding sensitivity of 92% and a specificity of 99%. For $\varepsilon_c$, the best cutoff value was found to be −20%, with a sensitivity of 92% and a specificity of 92%.

**STRAIN ANALYSIS IN RELATION TO GLOBAL FUNCTION.** The correlation between EF and mean contractile function, as quantified by strain analysis, was higher than that found for WT ($r = 0.84$ for $\varepsilon_r$, p < 0.001) and ($r = -0.89$ for $\varepsilon_c$, p < 0.001), as shown in Figure 5, B and C, respectively. In contrast to WT analysis, a close relationship between global ventricular function and the number of segments with abnormal strain values was observed. For $\varepsilon_r$, the correlation coefficient (r) was 0.83 (p < 0.001), and for $\varepsilon_c$, r = 0.91 and p < 0.001.

**DISCUSSION**

Accurate assessment of regional contractile function is important for determining long-term prognosis and patient management after MI. It has been demonstrated that WT is a useful measure of regional function and is more precise than wall motion analysis (3,7). However, the differentiation of regions with abnormal contractile function from regions with normal function by planar WT in patients with coronary artery disease is difficult because of the wide range

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**Table 1. Clinical Characteristics of Patients With Left Anterior Descending Coronary Artery-Related Infarcts (n = 13)**

| Age (years) | 57 ± 11 |
| Peak CK-MB (U/liter) | 238 ± 119 |
| Therapy |  
| Thrombolysis | 7/13 (53.8%) |
| PTCA | 6/13 (46.2%) |
| CAG results |  
| SVD | 6/13 (46.2%) |
| MVD | 6/13 (46.2%) |
| ACE inhibitor | 9/13 (69.2%) |
| Beta-blocker | 9/13 (69.2%) |
| MRI (days after infarction) | 103 ± 17 |

Data are presented as the mean value ± SD or number (%) of patients.  
ACE = angiotensin-converting enzyme; CAG = coronary angiographic findings obtained within one week after infarction; CK-MB = creatine kinase, MB fraction; MRI = magnetic resonance imaging; MVD = multivessel disease; PTCA = percutaneous transluminal coronary angioplasty; SVD = single-vessel disease.

**Table 2. Global Ventricular Function of Patients and Age-Matched Control Subjects**

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 13)</th>
<th>Control Subjects (n = 13)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDVI (ml/m²)</td>
<td>94 ± 30</td>
<td>66 ± 9</td>
<td>0.009</td>
</tr>
<tr>
<td>ESVI (ml/m²)</td>
<td>54 ± 29</td>
<td>21 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SVI (ml/m²)</td>
<td>40 ± 11</td>
<td>46 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>EF (%)</td>
<td>46 ± 16</td>
<td>68 ± 5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are presented as the mean value ± SD.  
EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; SVI = stroke volume index.
of thickening in normal and abnormal regions. In the present study, regional myocardial function was expressed by two different variables—planar WT and two-dimensional strain. Our aim was to assess the most accurate variable for quantification of regional function after MI.

**Observations in the present study.**

**Contractile Function in Normal Volunteers.** In healthy subjects, the mean WT (59%) was comparable with those values from previous reports. Pflugfelder et al. (10) reported an overall mean WT (59%) was comparable with those values from previous reports. Pflugfelder et al. (10) reported an overall mean WT ranging from 18% to 100% in normal subjects. The maximal WT was found to be in the lateral free wall (67%), and the minimal WT was found in the septum (56%). This heterogeneity in function has been recognized previously (10,11,29,30) and can be explained by different physiologic factors, including the myocardial fiber architecture (31), wall stress and heterogeneity of myocardial perfusion (32). For $e_r$, the same distribution was found as for WT, with greater values in the lateral regions (34%) and lower values in the septal regions (28%). The variance in $e_r$ was smaller than that found for $e_c$. This finding has been addressed before by Young et al. (19) and Waldman et al. (33) and can be explained by the fiber architecture of the myocardial wall, which is heterogeneous in the transmural direction and more uniform in the circumferential orientation, and by strain that varies most in the radial direction.

**Regional Contractile Function in Infarct-Related Ventricles.** In infarct-related ventricles, WT and strain analysis both demonstrated reduced myocardial function in all segments, including the noninfarct-related lateral segments. This may be considered an adaptive mechanism. Different loading conditions and the tethering effect of the infarct-related myocardium may reduce function in the remote myocardium. Reduced function in the noninfarct-related myocardium will lead to redistribution of regional wall stress and smaller compliance mismatch between functioning and nonfunctioning myocardium. Reduction of wall stress in the infarct-related ventricle is important, because wall stress determines oxygen consumption and is a stimulus for ventricular remodeling. Our results are in line with the experimental findings in canine hearts of Azhari et al. (37). Using three-dimensional WT and strain analysis, they also found better results for strain analysis for mapping ischemic myocardial regions. However, the difference between these two methods was less, compared with our study, probably because of the higher accuracy of three-dimensional WT analysis. The correlation between global ventricular and regional myocardial function quantified by WT was $r = 0.76$, $p = 0.002$ was higher than that previously reported. Germain et al. (29) found no correlation between EF and the WT score was $r = -0.01$, whereas Sheehan et al. (38) reported a correlation between EF and the hypokinesia score was $r = -0.47$. The correlation between EF and myocardial function was even higher when myocardial function was quantified by two-dimensional strain analysis was $r = 0.84$, $p < 0.001$. The findings in this study suggest that strain analysis may be of greater help than WT analysis to understand the complicated interaction between regional dysfunction and long-term deterioration of global function after MI.

**Study limitations.** Because of the limited number of patients, the results should be interpreted with care. Nevertheless, even with these small numbers, the strain data seem convincingly superior to WT in detecting and discriminating dysfunctional myocardium. The effect of through-plane motion and the curvature of the ventricular wall are important factors influencing planar WT analysis. It has been demonstrated by Beyar et al. (13) that three-dimensional

| Table 3. Regional Myocardial Function in the Perfusion Territory of the Left Anterior Descending Coronary Artery (LAD-Infarct Area) and the Area Adjacent to and Remote From the LAD Perfusion Territory, as Assessed by Wall Thickening and Strain Analysis |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                 | Infarct          | Adjacent        | Remote          | Mean Value      | Infarct          | Adjacent        | Remote          | Mean Value      |
| **WT (%)**                     | 31 ± 20          | 35 ± 25         | 42 ± 23         | 35 ± 20         | 56 ± 16         | 59 ± 19         | 67 ± 15         | 59 ± 15         |
| $e_c$ (%)                      | 9 ± 7            | 15 ± 8          | 20 ± 7          | 14 ± 7          | 28 ± 4          | 29 ± 5          | 34 ± 8          | 30 ± 5          |
| $e_r$ (%)                      | -10 ± 7          | -13 ± 3         | -16 ± 4         | -13 ± 5         | -22 ± 2         | -19 ± 1         | -19 ± 3         | -20 ± 1         |

Patients versus control subjects: †$p < 0.05$; ‡$p < 0.01$; §$p < 0.005$; ¶$p < 0.001$.

$e_c$ = circumferential shortening; $e_r$ = radial stretch; WT = (systolic) wall thickening.

**Figure 3.** Contractile function in patients with MI in the infarct-related and remote myocardium, as quantified by WTh analysis and strain analysis. Strain analysis revealed significant differences in contractile function between infarct-related and remote myocardium, whereas WTh did not. $e_r$ = radial stretch; MI = myocardial infarction; WTh = wall thickening.
Figure 4. (A), The percent WTh in 12 circumferential segments at the midventricular level in patients and control subjects. The strain variables, $\varepsilon_r$ (B) and $\varepsilon_c$ (C). In the control group, the mean value (thick dashed line with diamonds) $\pm$ 2 SD (thin dashed lines) is shown. In the infarct group, the mean value (thick line with triangles) is shown. Despite the fact that all patients had a major MI, in none of the 12 segments, the mean WTh (expressed as a percentage) in the infarct group was below the mean values $\pm$ 2 SD of the control group. For $\varepsilon_r$ and $\varepsilon_c$, the same four segments were found to have reduced function, as compared with that of the control subjects. These segments were highly concordant with the septal and anterior regions of the ventricle (i.e., perfusion territory of the LAD) (see Fig. 2). $\varepsilon_c$ = circumferential shortening; $\varepsilon_r$ = radial stretch; LAD = left anterior descending coronary artery; WTh = wall thickening.
WT analysis is more accurate than planar analysis. The former method reduces artifacts induced by image planes oriented obliquely through the ventricular wall, allowing less variability in normal thickening and thus better discrimination of an ischemic from a nonischemic zone. In this study, WT analysis is based on manual tracing, whereas strain analysis is performed automatically. This may have increased the variability in the thickening measurements as compared with the automatically performed strain measurements. The more detailed visualization of trabeculae provided by the improved image quality of the newer MR systems is another factor contributing to the problem of accurate border delineation. One effect is that the individual trabeculae are often excluded from the wall in diastole; during systole, these trabeculae join and are included within the wall. This confluence of trabeculae mimics WT (24). With tagging, myocardial material points are marked and a mere confluence of trabeculae cannot mimic radial strain. All these factors contribute to the large standard deviation of the measurements and, therefore, reduce the accuracy of planar WT analysis. Radial strain is the local contribution of myocardial deformation to WT. Using strain analysis, a gradual increase in radial stretch from the epicardium to the endocardium can be observed (39). Therefore, the contribution of regional myocardial deformation to WT is dependent on localization. In this study, using a tag-to-tag distance of 7 mm, the number of material points within the heart wall is limited. Therefore, the transmural distribution of myocardial strain cannot be calculated. Consequently, the mid-wall function is more heavily weighted, as compared with the epicardial and endocardial function. Refinement of the tagging grid, with a smaller tag-to-tag distance, may help to address this limitation. In the present study, only two-dimensional homogeneous strains were measured. A more comprehensive measurement method and analysis would account for three-dimensional strains. In addition, by using finite element methods, both two-dimensional and three-dimensional analyses could be generalized to be continuous and nonhomogeneous when using all data simultaneously and interpolating them (33).

CONCLUSIONS

Two-dimensional strain analysis is more accurate than WT analysis in discriminating dysfunctional from functional myocardium and, therefore, it improves the detection of regional differences in function. Two-dimensional strain analysis provides a strong correlation between regional myocardial function and global ventricular function.

APPENDIX

For the two-dimensional strain computation of a triangle, we first transformed the two vectors describing the short sides $X_1$ and $X_2$ of the triangle into the radial-circumferential coordinate system. The deformation gradient tensor $F$ was then computed by solving $[X_1, X_2] = F$.
\[ [X_1, X_2, X_3], \text{ where } X_1', X_2', X_3' \text{ denote the vectors of the triangle in the deformed state. Polar decomposition, } F = R \cdot U, \text{ is a mathematical operation that separates the rigid body rotation, } R, \text{ from stretch, } U; \text{ the radial and circumferential strains were computed from the diagonal elements of the stretch tensor, } U, \text{ by } e_r = U_{rr} - 1 \text{ and } e_c = U_{cc} - 1.\]

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