# Improving risk stratification after acute myocardial infarction : focus on emerging applications of echocardiography

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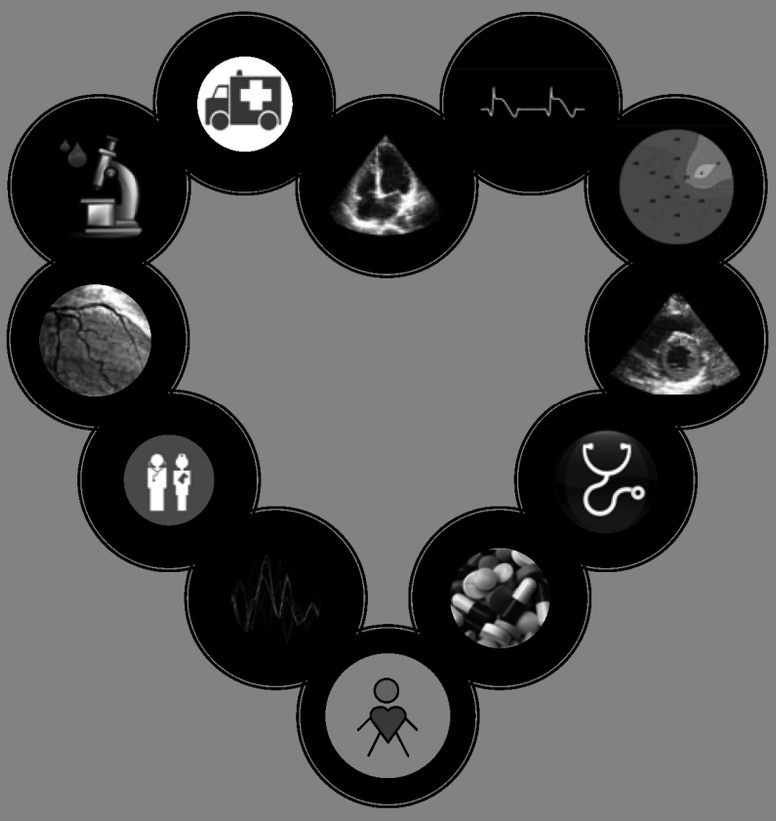
# *Part II*

## *Systolic Function after Acute Myocardial Infarction*



*Chapter 7*

# *Prognostic Importance of Strain and Strain Rate after Acute Myocardial Infarction*

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## Abstract

### Objectives

Recently, strain and strain rate have been introduced as novel parameters reflecting left ventricular (LV) function. The purpose of the current study was to assess the prognostic importance of strain and strain rate after acute myocardial infarction (AMI).

### Methods and results

A total of 659 patients after AMI were evaluated. Baseline echocardiography was performed to assess LV function with traditional parameters and strain and strain rate. During follow-up, 51 patients (8%) reached the primary endpoint (all-cause mortality) and 142 patients (22%) the secondary endpoint (a composite of revascularization, reinfarction and hospitalization for heart failure). Strain and strain rate were both significantly related with all endpoints. After adjusting for clinical and echocardiographic parameters, strain was independent related to all endpoints and was found to be superior to LV ejection fraction (LVEF) and wall motion score index (WMSI). Patients with global strain and strain rate higher than -15.1% and -1.06$s^{-1}$, demonstrated HRs of 4.5 (95%CI 2.1 – 9.7) and 4.4 (95%CI 2.0 – 9.5) for all-cause mortality, respectively.

### Conclusions

Strain and strain rate provide strong prognostic information in patients after AMI. These novel parameters were superior to LVEF and WMSI in the risk stratification for long-term outcome.

## Introduction

It has been well recognized that left ventricular (LV) systolic function is a major predictor of outcome after acute myocardial infarction (AMI).[1-4] The most commonly used and recommended measurements for echocardiographic quantification of global and regional LV systolic function are LV ejection fraction (LVEF) and wall motion score index (WMSI).[5] However, these measurements have limitations. Biplane assessment of LVEF can be difficult because of poor endocardial border definition and is often time-consuming and poorly reproducible.[6] Thereby, LVEF may appear normal in patients with remote, compensatory hyperkinesis, despite myocardial damage at the infarct zone. WMSI is an alternative to LVEF, which also reflects regional systolic function. However, the assessment of WMSI is semi-quantitative and experience-dependent.[5]

Over the past years, echocardiographic techniques have been developed that can assess more subtle changes in LV function. Strain and strain rate have been introduced as novel quantitative measurements reflecting LV function.[7] These novel parameters use two-dimensional (2D) speckle-tracking imaging and enable angle-independent quantification of myocardial deformation.

Whether strain and strain rate provide prognostic information after AMI has not been evaluated. Accordingly, the objective of the current study was to evaluate the individual prognostic importance of strain and strain rate, together with other established clinical and echocardiographic predictors of adverse (cardiac) events after AMI.

## Methods

### Patient selection and study protocol

Since February 2004 consecutive patients admitted with an AMI treated with primary percutaneous coronary intervention (PCI) were included in an ongoing registry. All patients were treated according to the institutional AMI protocol, which includes a prehospital, inhospital, and outpatient clinical framework for decision making and treatment. This protocol, designed to improve care around AMI, includes structurized medical therapy, 2D echocardiography performed within 48 hours of admission and standardized outpatient follow-up, as described previously.[8] Echocardiography was used to assess LV function by traditional and novel parameters. During follow-up the occurrence of adverse events was

scored. The final study population comprised patients included in the registry who underwent echocardiography <48 hours of admission and completed at least 1-year follow-up.

## Echocardiography

Patients were imaged in the left lateral decubitus position using a commercially available system (Vivid 7, General Electric-Vingmed, Horton, Norway). Data acquisition was performed using a 3.5-MHz transducer, at a depth of 16 cm in the parasternal and apical views. Standard M-mode and 2D images were obtained during breath hold and saved in cine-loop format from 3 consecutive beats. Analysis was performed offline by 2 experienced observers (EchoPac version 7.0.0, General Electric-Vingmed). The LV end-systolic volume, end-diastolic volume were traced and LVEF was calculated using the biplane Simpson's technique.[5] The LV was divided into 16 segments and each segment was analyzed individually and scored based on its motion and systolic thickening (1 = normokinesis, 2 = hypokinesis, 3 = akinesis, 4 = dyskinesis). The WMSI was calculated as the sum of the segment scores divided by the number of segments scored.[5] Left atrial (LA) size was quantified by calculating the volume according to the ellipsoid model.[5] Severity of mitral regurgitation (MR) was graded semiquantitatively from the jet area of color-flow Doppler data and by measuring the width of the vena contracta. MR was characterized as: mild = jet area/LA area <20% and vena contracta width <0.3 cm, moderate = jet area/LA area 20% to 40% and vena contracta width 0.3 – 0.69 cm, and severe = jet area/LA area >40% and vena contracta width ≥0.7 cm.[9] Pulsed-wave Doppler of the mitral valve inflow was obtained by placing the Doppler sample volume between the tips of the mitral leaflets. Peak early (E) and late (A) diastolic velocities and deceleration time (DT) were measured. E/E'-ratio was obtained by dividing E by E' measured by color-coded tissue Doppler imaging at the basal septal segment.[10]

## Strain and strain rate analysis

Peak systolic longitudinal strain and strain rate were assessed on apical 2-chamber, 4-chamber and long-axis views using speckle tracking analysis.[15] This novel software analyzes motion by tracking frame-to-frame movement of natural acoustic markers on

standard ultrasonic images in 2 dimensions. All images were recorded with a frame rate of ≥40 fps for reliable analysis. The LV endocardial border was manually traced at end-systole and the automatically created region of interest was adjusted to the thickness of the myocardium. Peak systolic strain and strain rate were determined in all 18 segments from the 3 apical views (Figure 1). Segments were discarded if tracking was of poor quality. Strain analysis was feasible in 98% of segments and strain rate analysis in 89% of segments.

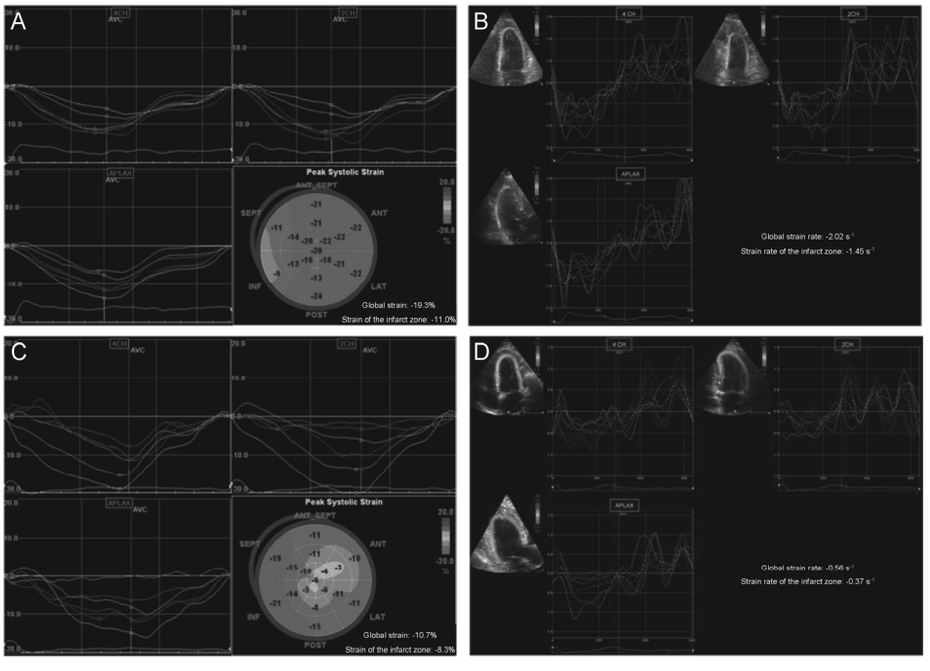


**Figure 1.**

Examples of longitudinal strain (A,C) and strain rate (B,D) curves from the three apical views of the left ventricle. Baseline strain (A) and strain rate (B) were preserved in patients without events, whereas baseline strain (C) and strain rate (D) were diminished in patients with events during follow-up.

Global strain for the LV was provided by the software as the average value of the peak systolic longitudinal strain of the three apical views. Global strain rate is not provided by the software and was calculated as the mean value of all segments. Strain and strain rate of

the infarct zone were calculated as the mean values of the segments supplied by the culprit vessel. The left anterior descending artery was considered to supply the anterior, anteroseptal, apical and mid septal segments, the right coronary artery to supply the inferior and basal septal segments, and the circumflex to supply the posterior and lateral segments.[12]

### Follow-up and endpoint definitions

Standardized follow-up was performed according to the institutional AMI protocol.[8] Data about the occurrence of adverse events was obtained from the patient's hospital or general practitioner. The primary endpoint was all-cause mortality. The secondary endpoint was a composite of nonfatal reinfarction, coronary revascularization and hospitalization for heart failure. Nonfatal reinfarction was defined based on criteria of typical chest pain, elevated cardiac enzyme levels, and typical changes on the electrocardiogram[13] All coronary revascularizations after discharge of the index infarction were included for the secondary endpoint.

### Statistical analysis

Continuous data are presented as mean ± standard deviation and categorical data are presented as frequencies and percentages. Differences in baseline characteristics between patients who died versus survivors were evaluated using the unpaired Student's *t*-test and chi-square test. Continuous variables which were not normally distributed (as evaluated by Kolmogorov-Smirnov tests), were presented as medians and corresponding $25^{th}$ and $75^{th}$ percentiles and were compared using Wilcoxon Rank-Sum test. In addition, Kaplan-Meier analysis was performed for the analysis of survival and cumulative event rates. Therefore, global strain and strain rate were subdivided according to the median. Differences in the occurrence of primary and secondary endpoints were evaluated by log-rank tests. Univariable and multivariable Cox proportional hazards regression analyses were performed to relate clinical parameters (age, current smoking, diabetes, hyperlipidemia, hypertension, prior myocardial infarction, multivessel disease, peak cardiac enzymes and QRS duration) and echocardiographic parameters (LVEF, WMSI, LA volume, E/A-ratio, DT, E/E'-ratio and moderate or severe MR) to the primary and secondary endpoints. All continuous variables were assessed per 1 unit change in each variable. The number of

covariables had to be limited because of the relatively small number of endpoint events. Therefore, separate clinical and echocardiographic multivariate models were constructed. Variables with a p value ≤0.25 in univariable analysis were considered as potential predictors of endpoint events. The clinical and echocardiographic multivariate models were based on this selection, and were constructed by backward deletion of the least significant variable, until all variables had a p value ≤0.15. When both peak cardiac enzymes were significant in univariate analysis, peak cardiac troponin T level was selected for the multivariate model to avoid co-linearity. The novel parameters global strain and strain rate, and strain and strain rate of the infarct zone were added individually to a final multivariate model, which combined the above mentioned clinical and echocardiographic multivariate models, to evaluate their independent prognostic importance. In addition, univariate analysis was performed for global strain and strain rate divided according to the median and all endpoints. To check the proportional hazard assumption (ie, that the HR for 2 subjects with fixed predictors is constant over time), log (–log[survival probability]) for different categories was plotted against time to ensure that the curves were reasonably parallel. In general, all proportionality assumptions were appropriate. Finally, 20 patients were randomly selected to test the intra-and interobserver variability for strain and strain rate measurements by Bland-Altman analysis. All statistical tests were two-sided, and a p value <0.05 was considered to be statistically significant. All statistical analyses were performed with SPSS software (version 16.0, SPSS Inc., Chicago, Illinois).

## Results

### Baseline characteristics

A total of 726 patients were included. Nine (1.2%) patients died during hospitalization before echocardiographic assessment could be performed, and in 22 (3.0%) patients echocardiographic assessment was not available <48 hours of admission due to logistic reasons. An additional 36 (4.9%) patients were lost to 1-year follow-up. The final study population therefore comprised 659 patients. Table 1 summarizes the baseline characteristics of the study population. Mean age was 60 ± 12 years and most patients were men (517 patients, 78%). Mean LVEF was 46 ± 8.0% and median E/E'-ratio was 12 (9, 15). Moderate or severe MR was observed in 46 patients (7.0%). Global strain and strain

rate were significantly higher than strain and strain rate of the infarct zone (-15.3 ± 4.5% vs. -10.6 ± 5.3%, p <0.001 and -1.1 ± 0.31 $s^{-1}$ vs. -0.81 ± 0.33 $s^{-1}$, p <0.001). Bland-Altman analysis demonstrated a good intra-observer and inter-observer agreement with a small non-significant bias for strain and strain rate. Mean differences ± 2SDs for global strain and global strain rate were -0.090 ± 2.2% and -0.019 ± 0.12 $s^{-1}$ for intra-observer agreement and -0.20 ± 1.1% and -0.020 ± 0.12 $s^{-1}$ for inter-observer agreement.

**Table 1a.Baseline clinical characteristics**

| | ***All Patients (N = 659)*** | ***All-cause mortality (N = 51)*** | ***Survivors (N = 608)*** | ***P**** |
|---|---|---|---|---|
| Age (years) | 60 ± 12 | 70 ± 12 | 60 ± 11 | <0.001 |
| Male gender | 517 (79%) | 39 (77%) | 478 (79%) | 0.72 |
| Current smoking | 331 (50%) | 22 (44%) | 309 (51%) | 0.35 |
| Diabetes | 64 (10%) | 8 (16%) | 56 (9%) | 0.13 |
| Family history of CAD | 269 (41%) | 14 (29%) | 255 (42%) | 0.07 |
| Hyperlipidemia | 131 (20%) | 11 (22%) | 120 (20%) | 0.76 |
| Hypertension | 203 (31%) | 25 (49%) | 178 (29%) | <0.05 |
| Prior myocardial infarction | 49 (7.4%) | 7 (14%) | 42 (6.9%) | 0.08 |
| LAD culprit vessel | 311(48%) | 27 (53%) | 288 (47%) | 0.44 |
| Multivessel disease | 315 (48%) | 39 (78%) | 276 (46%) | <0.001 |
| TIMI 2 – 3 flow | 651 (99%) | 50 (98%) | 601 (99%) | 0.52 |
| Peak CPK level (U/l) | 1925 (925, 3448) | 3693 (1757, 5985) | 1820 (902, 3266) | <0.001 |
| Peak cTn T level (µg/l) | 5 (2, 9) | 13 (6, 25) | 5 (2, 9) | <0.001 |
| QRS duration (ms) | 90 (86, 100) | 100 (90, 121) | 90 (84, 100) | <0.001 |
| Medication at 6 months follow-up | | | | |
| ACE inhibitor / ARB | 612 (98%) | 21 (100%) | 591 (98%) | 0.47 |
| Anticoagulants | 627 (100%) | 21 (100%) | 606 (100%) | 1.00 |
| Beta-blocker | 575 (92%) | 18 (86%) | 557 (92%) | 0.31 |
| Statin | 657 (98%) | 20 (95%) | 597 (99%) | 0.24 |

**Table 1b. Baseline echocardiographic characteristics**

| | ***All Patients (N = 659)*** | ***All-cause mortality (N = 51)*** | ***Survivors (N = 608)*** | ***P**** |
|---|---|---|---|---|
| LVESV (ml) | 57 ± 22 | 62 ± 29 | 56 ± 21 | 0.20 |
| LVEDV (ml) | 101 ± 38 | 104 ± 34 | 104 ± 34 | 0.56 |
| LVEF (%) | 46 ± 8.0 | 40 ± 8.9 | 46 ± 8.3 | <0.001 |
| WMSI | 1.5 (1.3, 1.7) | 1.6 (1.3, 1.9) | 1.5 (1.3, 1.6) | <0.001 |
| LA volume (ml) | 31 (24, 38) | 32 (23, 41) | 31 (24, 38) | 0.53 |
| E/A-ratio | 0.9 (0.7, 1.1) | 0.9 (0.7, 1.3) | 0.9 (0.7, 1.1) | 0.57 |
| DT (ms) | 205 (157, 253) | 190 (152, 250) | 206 (159, 254) | 0.29 |
| E/E'-ratio | 12 (9, 15) | 14 (11, 18) | 12 (9, 15) | <0.05 |
| Moderate or severe MR | 46 (7.0%) | 12 (25%) | 34 (6%) | <0.001 |
| Global strain (%) | -15.3 ± 4.5 | -10.8 ± 4.5 | -15.6 ± 4.4 | <0.001 |
| Global strain rate ($s^{-1}$) | -1.1 ± 0.31 | -0.83 ± 0.26 | -1.1 ± 0.30 | <0.001 |
| Strain of the infarct zone (%) | -10.6 ± 5.3 | -6.4 ± 3.6 | -10.9 ± 5.2 | <0.001 |
| Strain rate of the infarct zone ($s^{-1}$) | -0.81 ± 0.33 | -0.54 ± 0.16 | -0.83 ± 0.33 | <0.001 |

*P values are given for the comparison of patients who died of all-cause mortality versus patients who survived.

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CAD: coronary artery disease; CPK: creatine phosphokinase; cTnT: cardiac troponin T; DT: deceleration time; E/A: mitral inflow peak early velocity (E) / mitral inflow peak late velocity (A); E/E': mitral inflow peak early velocity (E) / mitral annular peak early velocity (E'); LA: left atrium; LAD: left anterior descending coronary artery; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; MR: mitral regurgitation; TIMI: thrombolysis in myocardial infarction; WMSI: wall motion score index.

## Follow-up

Mean follow-up duration was 21 ± 13 months. During follow-up, 179 patients (27%) reached one or more endpoints: 51 patients died (8%), 16 patients (2%) had a nonfatal reinfarction, 123 patients (19%) underwent revascularization and 29 patients (4%) were hospitalized for heart failure. Among the 123 patients who underwent revascularization after discharge, PCI was performed in 90 patients, 29 patients underwent coronary artery bypass grafting (CABG) and 4 patients underwent CABG and PCI.

Survival analysis showed a survival of 95% (95%CI 93% – 97%) at 1 year, 93% (95%CI 90% – 95%) at 2 years and 89% (95%CI 85% – 92%) at 3 years. Event-free survival for the combined primary and secondary endpoints was 80% (95%CI 77% – 83%) at 1 year, 71% (95%CI 67% – 75%) at 2 years and 68% (95%CI 64% – 73%) at 3 years.

## Primary endpoint

Baseline characteristics for the 51 patients (8%) who reached the primary endpoint (all-cause mortality) are shown in Table 1. Parameters which were significant associated with all-cause mortality at univariate analysis are shown in Table 2. The final multivariate model comprised age, hypertension, multivessel disease, peak cardiac troponin T level, QRS duration, LVEF and moderate or severe MR. In this model global strain (HR 1.2, 95%CI 1.1 – 1.3, p = 0.002), strain of the infarct zone (HR 1.2, 95%CI 1.0 – 1.3, p = 0.004), and strain rate of the infarct zone (HR 14, 95%CI 2.4 – 84, p = 0.003) demonstrated to be independently associated with all-cause mortality (Table 2).

Kaplan-Meier analysis for global strain and strain rate are shown in Figure 2. For patients with a global strain <-15.1% a mortality rate at 3 years of 6% (95%CI 1% – 10%) was observed and 15% (95%CI 10% – 20%) for patients with a global strain ≥-15.1%. Analysis for global strain rate showed a mortality rate at 3 years of 4% (95%CI 0% – 7%) for patients with global strain rate <-1.06$s^{-1}$ and 17% (95%CI 11% – 24%) for patients with global strain rate ≥-1.06$s^{-1}$.

Univariate analysis demonstrated an increased risk for patients with global strain of ≥-15.1% and global strain rate of ≥-1.06$s^{-1}$ for all-cause mortality of 4.5 (95%CI 2.1 – 9.7, p <0.001) and 4.4 (95%CI 2.0 – 9.5, p <0.001) times, respectively.

**Table 2.Correlations with the primary endpoint***

| | *Univariate analysis* | | | *Multivariate analysis* | | |
|---|---|---|---|---|---|---|
| | ***HR*** | ***95%CI*** | ***P*** | ***HR*** | ***95%CI*** | ***P*** |
| Age (years) | 1.1 | 1.1 – 1.1 | <0.001 | 1.0 | 1.0 – 1.1 | 0.03 |
| Hypertension | 2.2 | 1.3 – 3.8 | 0.005 | | | |
| Multivessel disease | 4.0 | 2.0 – 7.7 | <0.001 | 2.5 | 1.2 – 5.3 | 0.01 |
| Peak CPK level (U/l) | 1.0 | 1.0 – 1.0 | <0.001 | | | |
| Peak cTnT level (µg/l) | 1.1 | 1.1 – 1.1 | <0.001 | 1.1 | 1.0 – 1.1 | <0.001 |
| QRS duration (ms) | 1.0 | 1.0 – 1.1 | <0.001 | 1.0 | 1.0 – 1.0 | 0.02 |
| LVEF (%) | 0.92 | 0.89 – 0.95 | <0.001 | | | |
| WMSI | 13 | 4.7 – 35 | <0.001 | | | |
| E/E'-ratio | 1.1 | 1.0 – 1.1 | 0.001 | | | |
| Moderate or severe MR | 5.0 | 2.6 – 9.6 | <0.001 | 3.9 | 1.9 – 8.1 | <0.001 |
| Global strain (%) | 1.3 | 1.2 – 1.4 | <0.001 | 1.2 | 1.1 – 1.3 | 0.002 |
| Global strain rate ($s^{-1}$) | 29 | 8.1 – 103 | <0.001 | | | |
| Strain of the infarct zone (%) | 1.3 | 1.2 – 1.4 | <0.001 | 1.2 | 1.0 – 1.3 | 0.004 |
| Strain rate of the infarct zone ($s^{-1}$) | 67 | 16 – 291 | <0.001 | 14 | 2.4 – 84 | 0.003 |

*Final multivariate model with global strain is shown. CPK: creatine phosphokinase; cTnT: cardiac troponin T; E/E': mitral inflow peak early velocity (E) / mitral annular peak early velocity (E'); LVEF: left ventricular ejection fraction; MR: mitral regurgitation; WMSI: wall motion score index.

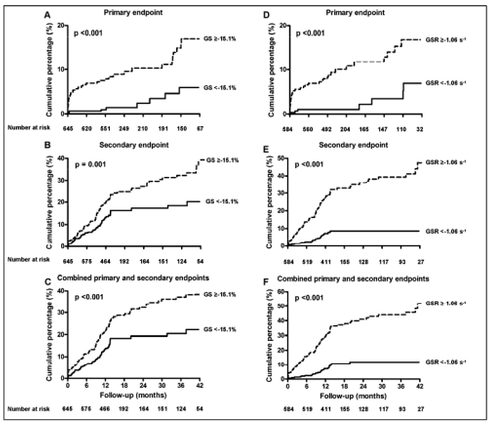


**Figure 2.**

Kaplan-Meier curves for global strain (A – C) and global strain rate (D – F) divided according to the median and the primary (all-cause mortality), secondary (reinfarction, revascularization and hospitalization for heart failure) and combined endpoints.

## Secondary endpoint

The secondary endpoint (a composite of reinfarction, revascularization and hospitalization for heart failure) was reached by 142 patients (22%). Parameters which were significant associated with the secondary endpoint at univariate analysis are shown in Table 3. The final multivariate model comprised current smoking, diabetes, multivessel disease, QRS duration and LVEF. In this model, global strain (HR 1.0, 95%CI 1.0 – 1.1, p = 0.04), global strain rate (HR 22, 95%CI 11 – 48, p <0.001) and strain rate of the infarct zone (HR 15, 95%CI 7 – 34, p <0.001) appeared to be independent associated with the secondary endpoint (Table 3).

**Table 3.Correlations with the secondary endpoint**

| | *Univariate analysis* | | | *Multivariate analysis* | | |
|---|---|---|---|---|---|---|
| | ***HR*** | ***95%CI*** | ***P*** | ***HR*** | ***95%CI*** | ***P*** |
| Current smoking | 1.3 | 0.95 – 1.8 | 0.10 | 1.5 | 1.1 – 2.2 | 0.02 |
| Diabetes | 1.7 | 1.1 – 2.8 | 0.02 | | | |
| Multivessel disease | 2.4 | 1.7 – 3.8 | <0.001 | 2.2 | 1.5 – 3.2 | <0.001 |
| QRS duration (ms) | 1.0 | 1.0 – 1.0 | 0.01 | 1.0 | 1.0 – 1.0 | 0.02 |
| LVEF (%) | 0.97 | 0.95 – 0.99 | 0.001 | | | |
| Global strain (%) | 1.1 | 1.0 – 1.1 | 0.002 | 1.0 | 1.0 – 1.1 | 0.04 |
| Global strain rate ($s^{-1}$) | 29 | 14 – 61 | <0.001 | 22 | 11 – 48 | <0.001 |
| Strain rate of the infarct zone ($s^{-1}$) | 20 | 8.7 – 44 | <0.001 | 15 | 7 – 34 | <0.001 |

Event rates at 3 years ranged from 18% (95%CI 13% – 24%) for patients with global strain <-15.1%, to 32% (95%CI 26% – 39%) for patients with a global strain ≥-15.1% and from 8% (95%CI 5% – 12%) for patients with global strain rate <-1.06$s^{-1}$, to 39% (95%CI 32% – 47%) for patients with global strain rate ≥-1.06$s^{-1}$.

Univariate analysis demonstrated an increased risk for patients with global strain of ≥-15.1% and global strain rate of ≥-1.06$s^{-1}$ for the secondary endpoint of 1.8 (95%CI 1.2 – 2.5, p = 0.002) and 4.9 (95%CI 3.1 – 7.7, p <0.001) times, respectively.

### Combined primary and secondary endpoints

During follow-up, 179 patients (27%) reached one or more endpoints. Parameters which were significant associated with the combined endpoints at univariate analysis are shown in Table 4. The final multivariate model comprised diabetes, multivessel disease, peak cardiac troponin T level, QRS duration and LVEF. In this model, global strain (HR 1.1, 95%CI 1.0 – 1.1, p = 0.006), global strain rate (HR 18, 95%CI 10 – 35, p <0.001) and strain rate of the infarct zone (HR 12, 95%CI 6 – 25, p <0.001) appeared to be independent associated with the combined endpoints (Table 4). Representative examples of patients with and without events during follow-up are shown in Figure 1.

The event rates at 3 years ranged from 21% (95%CI 16% – 26%) for patients with global strain <-15.1%, to 40% (95%CI 33% – 46%) for patients with a global strain ≥-15.1% and from 13% (95%CI 8% – 17%) for patients with global strain rate <-1.06$s^{-1}$, to 46% (95%CI 39% – 54%) for patients with global strain rate ≥-1.06$s^{-1}$.

Univariate analysis demonstrated an increased risk for patients with global strain of ≥-15.1% and global strain rate of ≥-1.06$s^{-1}$ for the combined endpoints of 2.0 (95%CI 1.5 – 2.8, p <0.001) and 4.8 (95%CI 3.2 – 7.2, p <0.001) times, respectively.

**Table 4.Correlations with the combined endpoints**

| | *Univariate analysis* | | | *Multivariate analysis* | | |
|---|---|---|---|---|---|---|
| | ***HR*** | ***95%CI*** | ***P*** | ***HR*** | ***95%CI*** | ***P*** |
| Age (years) | 1.0 | 1.0 – 1.0 | <0.001 | | | |
| Diabetes | 1.7 | 1.1 – 2.5 | 0.01 | | | |
| Hypertension | 1.4 | 1.0 – 1.9 | 0.03 | | | |
| Prior myocardial infarction | 1.7 | 1.1 – 2.7 | 0.02 | | | |
| Multivessel disease | 2.4 | 1.8 – 3.3 | <0.001 | 2.1 | 1.5 – 2.9 | <0.001 |
| CPK-level (U/l) | 1.0 | 1.0 – 1.0 | 0.03 | | | |
| cTnT-level (µg/l) | 1.0 | 1.0 – 1.1 | <0.001 | | | |
| QRS duration (ms) | 1.0 | 1.0 – 1.0 | <0.001 | 1.0 | 1.0 – 1.0 | <0.001 |
| LVEF (%) | 0.96 | 0.94 – 0.97 | <0.001 | | | |
| WMSI | 2.1 | 1.2 – 3.6 | 0.007 | | | |
| E/E'-ratio | 1.0 | 1.0 – 1.1 | 0.04 | | | |
| Moderate or severe MR | 1.9 | 1.2 – 3.1 | 0.007 | | | |
| Global strain (%) | 1.1 | 1.1 – 1.1 | <0.001 | 1.1 | 1.0 – 1.1 | 0.006 |
| Global strain rate ($s^{-1}$) | 26 | 13 – 50 | <0.001 | 18 | 10 – 35 | <0.001 |
| Strain of the infarct zone (%) | 1.1 | 1.0 – 1.1 | 0.001 | | | |
| Strain rate of the infarct zone ($s^{-1}$) | 22 | 11 – 46 | <0.001 | 12 | 6 – 25 | <0.001 |

*Final multivariate model with global strain is shown.

CPK:creatine phosphokinase; cTnT:cardiac troponin T; E/E':mitral inflow peak early velocity (E) /mitral annular peak early velocity (E'); LVEF:left ventricular ejection fraction; MR:mitral regurgitation; WMSI:wall motion score index.

## Discussion

The major findings of this study can be summarized as follows. (1) After adjusting for the strongest clinical and traditional echocardiographic predictors, strain and strain rate, measured early after AMI, were found to be independent associated with all-cause mortality, reinfarction, revascularization and hospitalization for heart failure. (2) Patients with global strain ≥-15.1% demonstrated a 5 times increased risk for all-cause mortality and 2 times higher risk for reinfarction, revascularization and hospitalization for heart failure. (3) Patients with global strain rate ≥-1.06$s^{-1}$ demonstrated a 4 times increased risk for all-

cause mortality and 5 times increased risk for reinfarction, revascularization and hospitalization for heart failure was observed. (4) Strain and strain rate appeared to be superior to LVEF and WMSI in the risk stratification after AMI.

## Risk stratification after AMI

The prognosis of patients after AMI is determined by the interaction of a large number of factors. Lee et al. [14] showed in a large population of the GUSTO-I trial that clinical determinants of 30-days mortality after AMI are multifactorial and complex. In that study, several clinical characteristics including age, medical history and medical treatment were identified as important factors determining the prognosis of an individual patient. Besides the importance of clinical parameters, several studies have described the use of 2D echocardiography for risk stratification after AMI.[15] 2D echocardiography permits noninvasive assessment of LV function, which has been defined as one of the most important prognostic parameters. According to the current guidelines LV systolic function can be assessed by LVEF and WMSI.[5] Although these factors have important prognostic value, both LVEF and WMSI have limitations for risk stratification after AMI.[1-3,4] To overcome these limitations, novel parameters have been developed to assess LV systolic function. Strain and strain rate have been introduced as quantitative measurements reflecting global and regional LV systolic function.[7] These parameters have been validated as accurate measurements of LV systolic function in patients after AMI.[11] However, whether strain and strain rate provide prognostic value after AMI has, thus far, not been evaluated.

## Strain and strain rate analysis

Strain and strain rate are measurements of the magnitude of active deformation of the regional myocardium and the time course of this deformation. The feasibility to differentiate between myocardial segments with active deformation and passive motion due to tethering may overcome the major limitation of LVEF.[14] In addition, speckle-tracking imaging is angle-independent and semi-automated, which may overcome the potential misinterpretations of WMSI analysis and increase the reproducibility of quantification of LV systolic function.

Data on the prognostic value of strain and strain rate are scarce. In patients undergoing dobutamine stress echocardiography, strain rate was superior over WMSI for the prediction of outcome. In 646 patients with suspected or known coronary artery disease, studied by Bjork et al., strain rate was the only independent predictor of all-cause mortality.[17] In patients with AMI, utilization of strain and strain rate was found to be able to differentiate between transmural and non-transmural infarctions and to predict infarct size.[18, 19] Thus far, the only study about the prognostic importance of strain and strain rate in patients with AMI was performed by Park et al., who demonstrated an association between strain and LV remodeling and adverse cardiovascular events in 50 patients with an anterior AMI.[20] Twenty-two patients showed significant LV remodeling and 11 patients developed symptomatic congestive heart failure. The authors demonstrated that patients who showed significant LV remodeling or developed symptomatic heart failure during follow-up had significantly lower baseline strain. In addition, strain was a strong independent predictor of LV remodeling (OR 1.31, 95%CI 1.08 – 1.58) and adverse cardiovascular events (OR 1.46, 95%CI 1.14 – 1.85).

In the current study, strain and strain rate measured early after AMI were of significant prognostic value. After adjusting for clinical and echocardiographic parameters, traditionally used in risk stratification after AMI, strain was found to be independent associated with all endpoints. Thereby, strain appeared to be superior to LVEF and WMSI. These results suggest that strain may provide additional information concerning LV systolic function and may be superior to LVEF and WMSI for the prediction of outcome after AMI. Strain analysis was feasible in 98% of segments and strain rate analysis in 89% of segments. The observation that strain and strain rate are of substantial prognostic importance with a high feasibility and reproducibility may further increase the potential value of these parameters.

### Clinical implications

Quantification of LV systolic function is an important component of the follow-up of patients after AMI. In the present study, the novel parameters strain and strain rate were both significantly related with outcome after AMI. Moreover, the present findings suggest that strain and strain rate provide stronger prognostic information for risk stratification after AMI than the currently recommended measurements of LV systolic function. The semi-automated assessment increases the ease of clinical application of strain and strain rate in daily practice. Although these results are promising, more studies are needed to confirm these findings before strain and strain rate can be applied in the clinical setting as routine analysis after AMI. In addition, the measurements of strain and strain rate are time consuming, but novel automated techniques have been developed which may overcome this limitation.[21]

## Conclusions

Strain and strain rate provide strong prognostic information in patients early after AMI. These novel parameters were superior to LVEF and WMSI in the risk stratification after AMI.

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