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# Associations between ECG changes and echocardiographic findings in patients with acute non-ST elevation myocardial infarction☆

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ABSTRACT

*Background:* ST segment depression (STD) and T wave inversion (TWI) are typical electrocardiographic (ECG) findings in non-ST elevation myocardial infarction (NSTEMI). In ST elevation myocardial infarction, ST changes represent transmural ischemia. The pathophysiological mechanisms of the ECG changes in NSTEMI are unclear.
*Purpose:* We studied the associations between ECG and the echocardiographic findings in NSTEMI patients.
*Methods:* Twenty patients with acute NSTEMI were recruited during their hospital stay. A comprehensive echocardiography study was performed. The findings were compared with blinded ECG analyses.
*Results:* Nine (45%) patients had STD, and 16 (85%) patients had TWI. In multivariable analysis, STD was independently associated with a lower global early diastolic strain rate ($\beta$=-5.061, p=0.033). TWI was independently associated with lower circumferential strain ($\beta$=0.132, p=0.032).
*Conclusions:* The typical ECG changes in NSTEMI patients were associated with subtle echocardiographic changes. STD was related to changes in diastolic function, and TWI was associated with systolic deterioration.


## Introduction

In ST elevation myocardial infarction (STEMI), acute coronary occlusion causes transmural myocardial ischemia, which is expressed as ST elevations and prominent positive T waves on the electrocardiogram (ECG). The location of the ST elevations on the ECG depends on the ischemic myocardial region [1]. On the other hand, non-ST elevation myocardial infarction (NSTEMI) is a heterogeneous clinical condition with a variable pathophysiological background. ST depression (STD) and T wave inversion (TWI) are the typical ECG changes in NSTEMI patients. STD is most often located in the lateral precordial leads, V4-V6, independent of the coronary anatomy [2–4]. "Wellens' syndrome" - TWI in precordial leads V1–V3/V4 caused by a lesion in the left anterior descending coronary artery (LAD) – is an example of the association between the location of TWI on the ECG and the culprit artery in acute coronary syndrome [4].

Echocardiography has a central role in the diagnosis and risk stratification of acute myocardial infarction (MI) patients [5]. Newer techniques, such as tissue Doppler imaging and speckle tracking echocardiography, have emerged as valuable diagnostic and prognostic tools in patients with acute coronary syndrome [6]. Their roles in the clinical evaluation of NSTEMI patients are being explored.

The goal of our study was to evaluate the relationships between ECG changes and concurrent echocardiographic findings in patients with acute NSTEMI. This comparison may shed some light on the mechanisms behind these ECG changes, which in turn potentially could improve risk stratification in acute coronary syndrome patients. We hypothesize that STD and TWI may differ with respect to their association with echocardiographic systolic and diastolic functional parameters.

## Materials and methods

### *Patient selection*

Patients were recruited at the Heart Center Tampere University Hospital from April 2012 to June 2015. Twenty NSTEMI patients without

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a history of cardiac disease were recruited after coronary angiography. The exclusion criteria were significant valvular stenosis or regurgitation (grade 2 or higher), prior MI, non-sinus rhythm, the presence of a pacemaker, wide QRS complex (>120 ms), and severe lung disease or other significant pathology, such as severe infection or pericardial effusion. The study protocol was approved by the local ethical committee (R11149) and each patient signed an informed consent form before enrollment in the study.

*Cardiac examinations*

All patients underwent coronary angiography during their hospital stay and repeated analyses of biomarkers and 12-lead ECG recordings were conducted according to the normal hospital protocol.

A 12-lead ECG was routinely recorded upon arrival to the hospital and repeated at least once during the hospital stay. The ECG closest to the time of the echocardiographic study was used in the analysis. A manual analysis of the ECG was performed with a magnifying lens by two authors (JR and KN) blinded to the clinical and echocardiographic data. The data were analyzed separately for three anatomic territories corresponding to the coronary artery distribution: anterior territory leads V1-V4 (LAD territory), inferior territory leads II, III and aVF (right coronary artery territory, RCA), and lateral territory leads I, aVL and V5-V6 (left circumflex artery territory, LCX), please see Fig. 1. The cut-off value for STD was ≥0.05 mV at the J point. The corresponding value for TWI was ≥0.1 mV. Both STD and TWI had to be present in at least two contiguous leads (Fig. 2). Pathological Q waves were defined according to current guidelines [7].

Thorough echocardiography was performed within one (0 to 2) day after coronary angiography. Invasive procedures were performed according to the current national and international guidelines and this was also the case for anti-thrombotic and anti-ischemia medical therapy [8]. All echocardiographic examinations were performed with a commercially available cardiac ultrasound machine (Philips iE33 ultrasound system, Bothell, Washington, USA) and a 1-5 MHz matrix-array X5-1 transducer by the same cardiologist (SST). All imaging was acquired at rest with the patients in the left lateral decubitus position. Doppler recordings were acquired at end-expiration. A simultaneous superimposed ECG was used throughout the studies. The images were stored in an external hard drive for off-line analysis (Philips Qlab, Bothell, Washington, USA). For the wall motion score analysis, the left ventricle was divided into 17 segments [9]. Each segment received a grade as follows: 1 - normal, 2 - hypokinesia, 3 - akinesia and 4 - dyskinesia. The total wall motion score was calculated by adding the score of each segment and the wall motion score index was obtained by dividing the total wall motion score by the number of left ventricular segments.

The analysis to compare the ECG and echocardiographic results was conducted in two ways. First, echocardiographic parameters reflecting global changes were compared with the presence of STD or TWI. Second, the left ventricle was divided into the three segments corresponding to the regions perfused by the LAD, RCA and LCX. The regional results reflecting these segments were compared with corresponding changes in the ECG (Fig. 1).

*Statistical analysis*

Data are reported as means and standard deviations for normally distributed variables and as medians with ranges for other continuous variables. Differences in baseline characteristics between the groups were tested with the independent samples Student's t-test for continuous variables and with Fisher's exact test for categorical variables. Differences between the groups were analyzed with independent

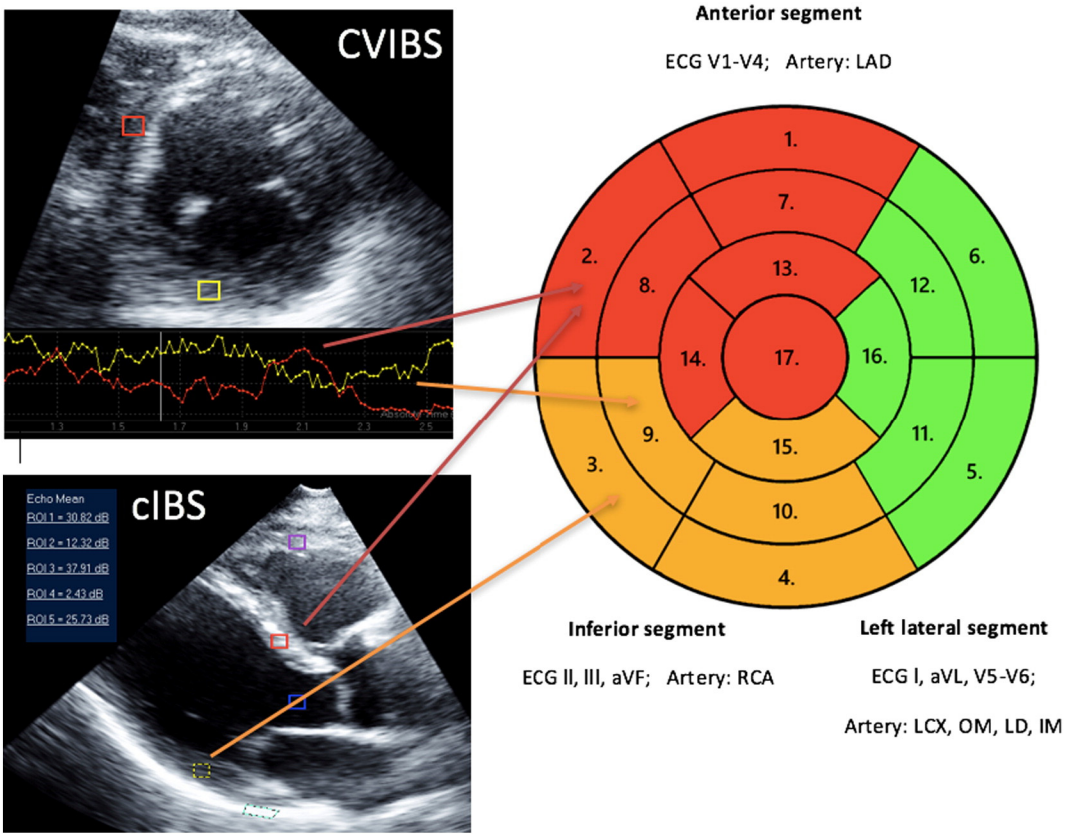


**Fig. 1.** Regional analysis. A 17-segment model of the left ventricle is presented on the right. The colors represent the segment distribution for the speckle tracking analysis. The integrated backscatter analysis is represented on the left with anteroseptal (red) values reflecting the LAD artery distribution area and posterior (yellow) values reflecting the inferior territory (the RCA distribution area). LAD = left anterior descending; RCA = right coronary artery; LCX = left circumflex; OM = obtuse marginal; LD = left diagonal; IM = intermediate branch.

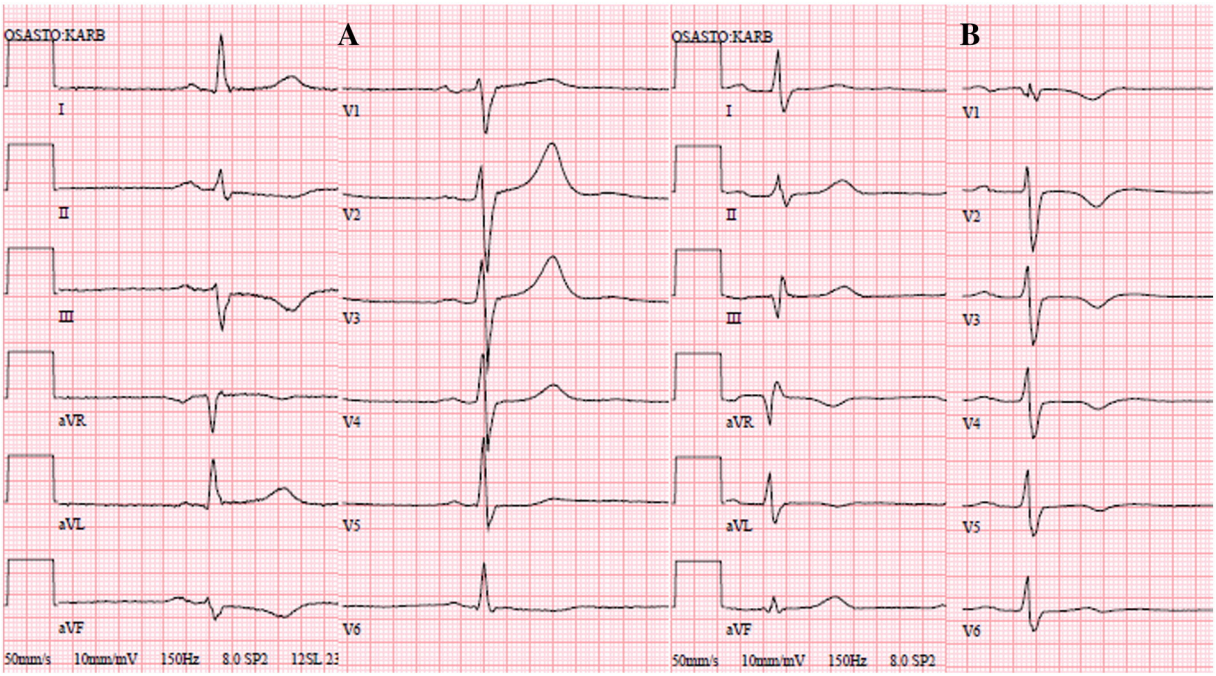


**Fig. 2.** ECG changes in two NSTEMI patients. Patient A (left side) had a 95% stenosis in the right coronary artery without other concomitant lesions. A percutaneous intervention for the stenosed vessel was performed prior this ECG recording and echocardiography. ST depressions and T-wave inversions are present in leads II, III, aVF and 6. In patient B, there are T-wave inversions in leads aVL and V1–V5 and angiography showed 90% stenosis in the left anterior descending coronary artery with less severe lesions in the right posterior descending and left obtuse marginal branches. He had coronary artery by-pass grafting within a week after this recording. The speed of the ECG recordings is 50 mm/s according to national standard.

samples t-tests for normally distributed variables or with the independent samples Mann Whitney U test for variables with skewed distribution and categorical variables were analyzed with the $X^2$/Fishers exact test. Associations between variables were calculated with Spearman correlations. A regression analysis was used to test univariate associations and a linear forward regression analysis was used to test multivariable associations. The tested variables are shown in Tables 3 and 4. Statistical analyses were carried out with IBM SPSS Statistics for Windows, Version 23.

## Results

### *General characteristics*

The patient population had a male predominance (80%) with a mean age of 63 ± 9 years. For other baseline characteristics, please see Table 1. The patient characteristics showed no significant differences across different ECG findings.

The median duration of angina pectoris prior to hospitalization was 2.5 days (0 to 21 days) and coronary angiography was performed within 1 day (0 to 2 days) of hospital admission. The echocardiographic examination was performed 1 day (0 to 6 days) after angiography. Coronary angiography revealed one-vessel disease in eight (40%) patients, two-vessel disease in seven (35%) patients and three-vessel disease in five (25%) patients. None of the patients had left main coronary artery involvement. Three patients had a total occlusion (one proximal LCX, one mid-RCA and one distal RCA); none of these patients were considered "STEMI equivalent" based on the ECG findings. At the time of echocardiography, 14 (70%) patients were treated with percutaneous coronary artery intervention (PCI) with stenting for their culprit lesion. The remaining patients had received medical treatment and four (20%) patients were scheduled to undergo coronary artery by-pass surgery later on.

Regarding myocardial ischemia after invasive evaluations and therapy, 16 (27%) of 60 segments had been treated successfully with PCI, 21 (35%) segments had normal coronary flow, and 23 (38%) segments were still supplied by coronary arteries with significant stenosis (diameter of stenosis ≥ 50%). All patients were stable at the time of echocardiography and were either transferred to a local hospital or discharged from our hospital within 4 (1 to 20) days after hospital admission.

**Table 1**
Characteristics of the study population.

| | The entire group | |
|---|---|---|
| | n = 20 | |
| | Mean/median | SD/($Q_1$, $Q_3$) |
| Age (years) | 63.0 | 9.3 |
| Systolic blood pressure (mm Hg) | 131 | (124, 142) |
| Diastolic blood pressure (mm Hg) | 81 | (68, 89) |
| BMI (kg/m$^2$) | 27.6 | (24.5, 30.0) |
| max hsTnt (ng/l) | 189 | (74, 727) |
| | n | % |
| Sex (male) | 16 | 80 |
| Hypertension | 9 | 45 |
| Diabetes | 4 | 20 |
| High cholesterol | 13 | 65 |
| Familial predisposition for coronary artery disease | 12 | 60 |
| Smoking | | |
| Current | 6 | 30 |
| Previous | 3 | 15 |
| Medical treatment at the time of echocardiography | | |
| Beta blockers | 14 | 70 |
| Calcium channel blockers | 3 | 15 |
| ACE inhibitors/ARB | 13 | 65 |
| Diuretics | 1 | 5 |
| Acetylsalisylic acid | 18 | 90 |
| Clopidrogrel | 11 | 55 |
| Statins | 13 | 65 |
| Diabetes medications | 1 | 5 |

BMI, body mass index; hsTnt, high-sensitivity troponin T; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

*ECG findings*

All patients had sinus rhythm with an average heart rate of 69 ± 16 bpm. No conduction defects were observed. The median QRS-complex width was 93 [83, 104] ms. One patient had a pathological Q wave in the LAD territory without concurrent STD or TWI. Nine (45%) patients had STD and TWI was present in 16 (80%) patients. Three (15%) patients had neither STD nor TWI in their ECGs at the time of echocardiography. At the regional level, STD was observed in 17/60 (28%) of the segments and TWI was observed in 28/60 (47%) of the segments. In 12/60 (12%) segments, both STD and TWI were present and in 27/60 (45%) segments, no abnormal findings were observed in the ST segments or the T waves.

Time delays from hospital arrival or the time from symptom onset to treatment were not different according to the presence or absence of STD or TWI. TWI was more prevalent in segments with ischemia (coronary stenosis) according to coronary angiography ($p = 0.058$). The positive predictive values (PPV) of TWI and STD for segments with ischemia were 79% and 82%, the negative predictive values (NPV) were 47% and 42%, the sensitivity scores were 56% and 36% and the specificity scores were 71% and 86%, respectively. In the absence of both STD and TWI, the existence of significantly stenosed coronary arteries was significantly less prevalent ($p = 0.017$). The PPV to predict a non-ischemic segment was 52%, the NPV was 79%, the sensitivity was 41% and the specificity was 67%.

*Echocardiographic findings*

The echocardiography findings are presented in Table 2. In general, the left ventricle exhibited normal size without overt systolic or diastolic dysfunction. Half of the patients showed no regional changes in contractility and the rest showed hypokinesia in 1.6 ± 1.3 segments.

*Findings in echocardiography in patients with STD*

Compared to patients without STD, patients with STD had longer isovolumetric relaxation time (IVRT) (142 ± 19 ms vs 114 ± 25 ms, $p = 0.007$), lower global early diastolic velocity (e′) in the speckle tracking echocardiography analysis (0.83/s [0.77, 1.02] vs 1.08/s [0.99, 1.21], $p = 0.006$) and lower values of posterior cyclic variation in the integrated backscatter (pCVIBS) analysis (8.9 ± 1.9 dB vs 12.3 ± 2.9 dB, $p = 0.043$). STD showed correlations with diabetes ($r = -0.452$, $p = 0.045$), smoking ($r = 0.596$, $p = 0.006$), pCVIBS ($r = -0.462$, $p = 0.040$), e′ ($-0.619$, $p = 0.004$), and global circumferential strain (GCS) in the speckle tracking echocardiography analysis ($r = -0.457$, $p = 0.049$) and with IVRT ($r = 0.629$, $p = 0.003$). The univariate and multivariable analyses of the factors associated with STD are presented in Table 3. Globally, IVRT and e′ were independently associated with the presence of STD. Regional changes showed independent associations with e′ and STD.

*Findings in echocardiography in patients with TWI*

Compared to patients without TWI, patients with TWI had lower left ventricular ejection fraction (LVEF), (57 ± 6% vs 71 ± 4%, $p = 0.008$) and lower global systolic strain rate (s′) in the speckle tracking echocardiography analysis ($-1.09$/s [$-1.22$, $-0.98$] vs $-1.31$/s [$-1.67$, $-1.15$], $p = 0.050$). TWI showed correlations with smoking ($r = 0.452$, $p = 0.045$), s′ ($r = -0.455$, $p = 00.044$) and LVEF ($r = -0.586$, $p = 0.007$). The results of the univariate and multivariable analyses of TWI are presented in Table 4. Globally, TWI was independently associated with s′ and hypertension. The regional changes were independently associated with circumferential strain. Patients with TWI had lower circumferential strain ($-26.8 \pm 4.4\%$ vs $-29.7 \pm 4.1\%$, $p = 0.013$).

*Cardiac biomarkers*

Cardiac biomarkers were elevated. Upon hospital arrival, the median ($Q_1$, $Q_3$) of the high-sensitivity troponin T (hsTnt) was 117 ng/l (43, 196) (normal <15 ng/l) with a maximum value of 189 ng/l (74, 727) during the hospital stay. Pro-B-type natriuretic peptide (ProBNP) was 1003 ng/l (567, 1464), hemoglobin was 140 ng/l (136, 151), total cholesterol was 4.7 mmol/l (4.1, 5.7), LDL was 3.2 mmol/l (2.5, 4.0) and

**Table 2**
Echocardiographic results of the study population.

| | All patients | | Patients with STD | | | Patients with TWI | | |
|---|---|---|---|---|---|---|---|---|
| | n = 20 | | n = 9 | | | n = 16 | | |
| | Mean/median | SD/($Q_1$, $Q_3$) | Mean/median | SD/($Q_1$, $Q_3$) | p | Mean/median | SD/($Q_1$, $Q_3$) | p |
| Structures | | | | | | | | |
| LVEDD | 49.6 | 4.0 | 50.3 | 3.8 | 0.528 | 50.2 | 3.2 | 0.329 |
| LVEDS | 33.6 | 4.3 | 34.2 | 3.6 | 0.628 | 34.5 | 3.2 | ***0.051*** |
| IVS | 11.3 | (10.8, 11.8) | 11.5 | (10.9, 12.0) | 0.295 | 11.1 | (10.8, 11.8) | 0.682 |
| PW | 11.4 | (10.7, 12.4) | 11.4 | (10.0, 12.2) | 0.710 | 11.6 | (10.5, 12.4) | 0.617 |
| cIBS | −16.5 | 4.1 | −15.4 | 4.8 | 0.884 | −16.1 | 4.0 | 0.871 |
| Diastolic function | | | | | | | | |
| Mitral E-wave | 72 | 21 | 67 | 21 | 0.180 | 70 | 20 | ***0.098*** |
| Mitral ea-ratio | 0.93 | (0.85, 1.39) | 0.90 | (0.81, 0.96) | 0.238 | 0.93 | (0.86, 1.43) | 0.655 |
| IVRT | 127 | 26 | 142 | 19 | **0.007** | 129 | 28 | 0.277 |
| STE global e′ | 1.01 | (0.86, 1.13) | 0.83 | (0.77, 1.02) | **0.006** | 1.00 | (0.79, 1.14) | 0.617 |
| STE global a′ | 1.15 | (0.89, 1.33) | 1.27 | (1.09, 1.48) | 0.331 | 1.10 | (0.94, 1.30) | 0.211 |
| Systolic function | | | | | | | | |
| LVEF | 59 | 8 | 58 | 10 | 0.328 | 57 | 6 | ***0.008*** |
| GLS | −15.4 | 2.4 | −14.8 | 2.6 | 0.136 | −15.2 | 2.2 | 0.524 |
| GCS | −28.4 | 4.3 | −27.3 | 3.6 | 0.123 | −27.9 | 4.6 | 0.322 |
| STE global s′ | −1.10 | (−1.21, −1.00) | −1.12 | (−1.18, −0.99) | 0.824 | −1.09 | (−1.22, −0.98) | ***0.050*** |
| sCVIBS | 8.5 | 2.7 | 7.9 | 1.7 | 0.308 | 8.6 | 2.9 | 0.899 |
| pCVIBS | 10.7 | 3.0 | 8.9 | 1.9 | **0.043** | 10.8 | 3.0 | 0.835 |
| WMSI | 1.00 | (1.00, 1.03) | 1.00 | (1.00, 1.06) | 0.882 | 1.01 | (1.00, 1.03) | 0.750 |

LVEDD and LVEDS, left ventricular end-diastolic and end-systolic diameters; IVS and PW, interventricular and posterior wall thickness; cIBS, calibrated integrated backscatter derived from the parasternal long axis view from the interventricular septum; Mitral E-wave, mitral inflow E-wave velocity; Mitral ea-ratio, ratio between mitral inflow E and a waves; IVRT, isovolumetric relaxation time; STE, speckle tracking echocardiography; LVEF, left ventricular ejection fraction; GLS and GCS, global longitudinal and circumferential strain in STE; sCVIBS and pCVIBS, cyclic variation of the integrated backscatter derived from the septum and posterior wall; WMSI, wall motion score index. The p-value represents the difference between patients with and without changes in STD and TWI.
Bold text indicates statistically significant changes with p<0.05 and text with italics indicates p-value between 0.05–0.10.

**Table 3**
Factors associated with STD

| | Univariate analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | β | SE(β) | p | β | SE(β) | p |
| Global ST depression | | | | | | |
| WMSI | 15.044 | 15.763 | 0.340 | | | 0.845 |
| GLS (%) | 0.325 | 0.219 | 0.138 | | | 0.753 |
| STE systolic strain rate (1/s) | −1.436 | 2.341 | 0.540 | | | 0.985 |
| STE early diastolic strain rate (1/s) | −9.642 | 4.316 | **0.025** | −1.276 | 0.435 | **0.010** |
| GSC (%) | 0.188 | 0.125 | 0.133 | | | 0.826 |
| Mitral inflow E-wave (cm/s) | −0.036 | 0.027 | 0.189 | | | 0.561 |
| IVRT (ms) | 0.061 | 0.029 | **0.032** | 0.007 | 0.003 | **0.029** |
| LVEF (%) | −0.071 | 0.065 | 0.275 | | | 0.888 |
| CVIBS (dB) | −0.254 | 0.258 | 0.324 | | | 0.958 |
| Sex | 0.251 | 1.120 | 0.822 | | | 0.961 |
| Hypertension | 0.875 | 0.931 | 0.347 | | | 0.959 |
| Diabetes | 21.454 | 20096.487 | 0.999 | | | 0.746 |
| High cholesterol | −0.134 | 0.945 | 0.888 | | | 0.987 |
| Age | 0.012 | 0.050 | 0.805 | | | 0.968 |
| Smoking | −1.281 | 1.030 | 0.214 | | | 0.869 |
| Regional ST depression | | | | | | |
| WMSI | 3.296 | 6.059 | 0.586 | | | 0.584 |
| STE longitudinal strain (%) | 0.057 | 0.04 | 0.158 | | | 0.771 |
| STE systolic strain rate (1/s) | −0.355 | 0.960 | 0.727 | | | 0.894 |
| STE early diastolic strain rate (1/s) | −5.498 | 1.791 | **0.002** | −5.061 | 2.376 | **0.033** |
| STE late diastolic strain rate (1/s) | 0.864 | 0.792 | 0.275 | | | 0.274 |
| STE circumferential strain (%) | 0.130 | 0.056 | **0.020** | | | 0.729 |
| CVIBS (dB) | −0.267 | 0.182 | 0.142 | | | 0.103 |
| cIBS (dB) | −0.056 | 0.041 | 0.177 | | | 0.394 |
| Sex | 0.762 | 0.674 | 0.258 | 2.964 | 1.756 | ***0.091*** |
| Hypertension | 1.318 | 0.648 | **0.042** | 2.992 | 1.554 | ***0.054*** |
| Diabetes | 20.602 | 11602.713 | 0.999 | | | 0.239 |
| High cholesterol | 0.018 | 0.600 | 0.976 | | | 0.597 |
| Age | 0.017 | 0.032 | 0.593 | | | 0.504 |
| Smoking | −0.711 | 0.604 | 0.239 | | | 0.290 |

STD, ST-level depression on ECG; WMSI, wall motion score index; GLS and GCS, global longitudinal and circumferential strain; STE, speckle tracking echocardiography; IVRT, isovolumetric relaxation time; LVEF, left ventricular ejection fraction; CVIBS, cyclic variation of the integrated backscatter; cIBS, calibrated integrated backscatter.
Bold text indicates statistically significant changes with p<0.05 and text with italics indicates p-value between 0.05–0.10.

**Table 4**
Factors associated with TWI.

| | Univariate analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | β | SE(β) | p | β | SE(β) | p |
| Global T-wave inversion | | | | | | |
| WMSI | | | | | | 0.391 |
| GLS (%) | 0.168 | 0.252 | 0.504 | | | 0.918 |
| STE systolic strain rate (1/s) | 7.517 | 4.215 | 0.075 | 1.002 | 0.314 | **0.006** |
| STE early diastolic strain rate (1/s) | −1.928 | 2.865 | 0.501 | | | 0.595 |
| GSC (%) | 0.159 | 0.161 | 0.324 | | | 0.422 |
| Mitral inflow E-wave (cm/s) | −0.044 | 0.028 | 0.116 | | | 0.880 |
| IVRT (ms) | 0.028 | 0.025 | 0.273 | | | 0.486 |
| LVEF (%) | −0.449 | 0.240 | 0.062 | | | 0.314 |
| CVIBS (dB) | 9.050 | 21.053 | 0.667 | | | 0.498 |
| Sex | −0.368 | 1.320 | 0.781 | | | 0.167 |
| Hypertension | 1.609 | 1.265 | 0.203 | −0.311 | 0.127 | **0.026** |
| Diabetes | 0.368 | 1.320 | 0.781 | | | 0.851 |
| High cholesterol | −0.788 | 1.136 | 0.488 | | | 0.429 |
| Age | −0.094 | 0.075 | 0.211 | | | 0.958 |
| Smoking | −20.287 | 16408.713 | 0.999 | | | 0.648 |
| Regional T-wave inversion | | | | | | |
| WMSI | 11.236 | 6.981 | 0.108 | | | 0.207 |
| STE longitudinal strain (%) | 0.060 | 0.037 | 0.103 | | | 0.160 |
| STE systolic strain rate (1/s) | 1.928 | 1.085 | ***0.076*** | | | 0.136 |
| STE early diastolic strain rate (1/s) | −1.651 | 1.142 | 0.148 | | | 0.344 |
| STE late diastolic strain rate (1/s) | −0.977 | 0.748 | 0.191 | | | 0.444 |
| STE circumferential strain (%) | 0.1340 | 0.051 | **0.007** | 0.132 | 0.061 | **0.032** |
| CVIBS (dB) | −0.090 | 0.116 | 0.440 | | | 0.261 |
| cIBS (dB) | −0.032 | 0.036 | 0.380 | | | 0.394 |
| Sex | −0.253 | 0.635 | 0.698 | | | 0.988 |
| Hypertension | 0.713 | 0.530 | 0.179 | | | 0.273 |
| Diabetes | −0.167 | 0.646 | 0.796 | | | 0.262 |
| High cholesterol | 0.059 | 0.542 | 0.914 | | | 0.989 |
| Age | −0.041 | 0.030 | 0.171 | | | 0.239 |
| Smoking | −0.838 | 0.577 | 0.146 | | | 0.313 |

TWI, T-wave inversion on ECG; WMSI, wall motion score index; GLS and GCS, global longitudinal and circumferential strain; STE, speckle tracking echocardiography; IVRT, isovolumetric relaxation time; LVEF, left ventricular ejection fraction; CVIBS, cyclic variation of the integrated backscatter; cIBS, calibrated integrated backscatter.
Bold text indicates statistically significant changes with p<0.05 and text with italics indicates p-value between 0.05–0.10.

creatinine was 72 μmol/l (62, 83). We found no associations between biomarker values and ECG changes.

## Discussion

In NSTEMI patients, TWIs were associated with changes in systolic function and their locations corresponded with the anatomic distribution of myocardial ischemia. On the other hand, the distribution of STD in the 12 ECG leads did not correlate with the locations of wall motion abnormalities in echocardiography. STD was associated with global and regional changes in diastolic function.

### *Clinical implications of our findings*

Tissue Doppler imaging and speckle tracking echocardiography have revolutionized the quantitative evaluation of myocardial function. Our study, which utilized these new echocardiographic techniques, provides some new insight into the possible mechanisms behind STD and TWI on the ECG. It is intriguing that STD was associated with diastolic parameter changes and TWI with systolic parameter changes. In NSTEMI, it is evident that these ECG changes are caused by different mechanisms, at least to some extent. First, STD is a robust prognostic factor in non-ST elevation acute coronary syndrome (NSTEMI and unstable angina combined), but the prognostic significance of TWI is controversial [2,10]. Both the presence and the magnitude of STD and the number of leads with these changes have prognostic impact [2,11]. Second, STD is a typical ECG finding during angina pectoris symptoms, while isolated TWI almost never appears during angina pectoris symptoms. Instead, recurrent ischemic symptoms cause "pseudo-normalization" or ST elevations in patients with TWI [12]. Third, TWI, but not STD, tends to be located in the leads that correspond to an ischemic/infarcted region [2,13].

There is clearly a large knowledge gap regarding the possible pathophysiologic mechanisms of STD and TWI in patients with NSTEMI. STD is the hallmark of subendocardial ischemia in patients with stable angina pectoris [4]. Subendocardial MI is a known condition in cardiac imaging, but its association with ECG changes in this context has not been studied in detail [4]. The exploration of the pathophysiological mechanisms behind STD is challenging. In animal experiments, the induction of subendocardial ischemia resulted in a significant increase in the end-diastolic pressure of the left ventricle and loss of left ventricular chamber compliance, indicating diastolic dysfunction [14,15]. The fact that STD in our patients was associated with changes in diastolic function parameters is consistent with the experimental hemodynamic data.

The etiology of TWI in NSTEMI is probably multifactorial. TWI in STEMI patients has been associated with improved outcome related to an open infarct-related artery and restored blood flow [16]. However, TWI has also been associated with non-patency of the culprit artery and worse short-term outcome in late-presenting patients [17]. Interestingly, the results of a recent study with a large number of patients showed that 20% of the patients presenting with NSTEMI and single-vessel disease had a totally occluded culprit artery [18]. Additionally, cardiac magnetic resonance imaging (CMR) data have shown that approximately 25% of NSTEMI patient had transmural infarction [19]. Therefore, it can be speculated that MI patients presenting late may have passed the initial stage showing ST elevation and show only "post-ischemic" TWI on the ECG [12]. It is possible that the rapid restoration of normal myocardial function is not achieved in these patients with therapeutic interventions and they may instead develop varying degrees of myocardial edema and stunning [20]. Indeed, in a small study on a sub-type of NSTEMI with TWI – "Wellens' syndrome" – the patients had myocardial edema on cardiac CMR [21]. In addition, repolarization abnormalities on the ECG and myocardial edema had similar time courses. Our study showed an association between TWI and echocardiographic markers of systolic dysfunction on speckle tracking echocardiography analysis. Interestingly, regional echocardiographic changes correlated with the ischemic regions on the ECG.

*Tissue Doppler and speckle tracking echocardiography - comparison with previous studies*

Data on the clinical roles of the new echocardiographic modalities in coronary artery disease are emerging. Several studies and a recent meta-analysis indicate that speckle tracking echocardiography derived strain is associated with global left ventricular function and has prognostic value in patients with acute STEMI [22,23]. However, data on NSTEMI patients are limited. We are not aware of any previous study that has investigated ECG and echocardiography parameters utilizing newer imaging methods. Considering the high rate of NSTEMI patients with a totally occluded culprit artery and the limitations of the ECG to identify this subgroup, it is important to identify these individuals with other diagnostic modalities such as echocardiography [18]. Study results in 40 NSTEMI patients with preserved left ventricular function indicated that speckle tracking echocardiography may be a more sensitive discriminator of left ventricular dyssynchrony than tissue Doppler imaging [24]. In another study including 111 patients with suspected NSTEMI who received echocardiography within 1 h (median value; interquartile range 0.5–4 h) of admittance, 61% had a clinical diagnosis of NSTEMI, 16% had a diagnosis of unstable angina, and 23% had non-coronary chest pain [25]. Territorial systolic strain, measured by averaging all segmental peak systolic strain values in each territory in the 16-segment left ventricular model, proved to be the most reliable method to identify acute total occlusion. A territorial circumferential strain value >− 10% had 90% sensitivity and 88% specificity for the identification of a totally occluded culprit artery. Symmetrical TWI was present in 33% and 31% of the patients with an occluded and a non-occluded culprit artery, respectively. Our patients had a higher frequency of TWI, but we did not restrict the definition of TWI to symmetrical T waves and in our study, all patients had NSTEMI. In our study, patients with TWI had lower circumferential strain.

## Limitations of our study

Our study has clear limitations. The patient population was small. Therefore, all speculations regarding pathophysiological mechanisms should be considered hypothetical, especially since CMR was not part of the protocol. Additionally, the limited number of patients made it impractical to introduce patients with both STD and TWI as a third group in the statistical analyses.

## Conclusion

In NSTEMI patients with well-preserved global left ventricular systolic function, subtle changes in myocardial imaging were found. STD was associated with changes in diastolic function, and TWI was associated with systolic deterioration. The findings are consistent with the proposed pathophysiologic mechanisms behind these ECG changes.

## Disclosure of interest

The authors state no conflict of interest related to the study.

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