Left ventricular function, strain, and infarct characteristics in patients with transient ST-segment elevation myocardial infarction compared to ST-segment and non-ST-segment elevation myocardial infarctions

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Aims	This study aims to explore cardiovascular magnetic resonance (CMR)-derived left ventricular (LV) function, strain, and infarct size characteristics in patients with transient ST-segment elevation myocardial infarction (TSTEMI) compared to patients with ST-segment and non-ST-segment elevation myocardial infarctions (STEMI and NSTEMI, respectively).
Methods and results	In total, 407 patients were enrolled in this multicentre observational prospective cohort study. All patients underwent CMR examination 2–8 days after the index event. CMR cine imaging was performed for functional assessment and late gadolinium enhancement to determine infarct size and identify microvascular obstruction (MVO). TSTEMI patients demonstrated the highest LV ejection fraction and the most preserved global LV strain (longitudinal, circumferential, and radial) across the three groups (overall $P \leq 0.001$). The CMR-defined infarction was less frequently observed in TSTEMI than in STEMI patients [77 (65%) vs. 124 (98%), $P < 0.001$] but was comparable with NSTEMI patients [77 (65%) vs. 66 (70%), $P = 0.44$]. A remarkably smaller infarct size was seen in TSTEMI compared to STEMI patients [1.4 g (0.0–3.9) vs. 13.5 g (5.3–26.8), $P < 0.001$], whereas infarct size was not significantly different from that in NSTEMI patients [1.4 g (0.0–3.9) vs. 2.1 g (0.0–8.6), $P = 0.06$]. Whilst the presence of MVO was less frequent in TSTEMI compared to STEMI patients [5 (4%) vs. 53 (31%), $P < 0.001$], no significant difference was seen compared to NSTEMI patients [5 (4%) vs. 5 (5%), $P = 0.72$].

Conclusion   TSTEMI yielded favourable cardiac LV function, strain, and infarct-related scar mass compared to STEMI and NSTEMI. LV function and infarct characteristics of TSTEMI tend to be more similar to NSTEMI than STEMI.

Keywords   myocardial tissue characteristics • infarct size • strain • transient ST-segment elevation myocardial infarction • cardiovascular magnetic resonance imaging

Introduction

Acute myocardial infarction (MI) is generally categorized as ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI).[1] These two MI types encompass different electrocardiogram (ECG) changes, infarct characteristics, and functional outcomes which has led to two-tailored treatment strategies.[2,3] However, approximately one out of four patients with STEMI may express complete normalization of ST-elevation and relief of symptoms before revascularization by the primary percutaneous coronary intervention (PCI).[4,5] This condition is commonly referred to as 'transient ST-segment elevation myocardial infarction' (TSTEMI).[6]

The TSTEMI syndrome possesses a presentation markedly different from the typical STEMI presentation. At first medical contact, patients show signs of ST-segment elevation on the ECG, suggesting transmural ischaemia due to a coronary occlusion similar to STEMI. As time progresses, these patients develop normalization of ST-segment elevations and generally have a significant coronary stenosis with TIMI 2–3 flow at angiography, most likely as a result of early spontaneous reperfusion. Since the initial presentation is accompanied by ST-segment elevations, these patients are mostly treated as STEMI. The most recent guidelines, considering the results of the TRANSIENT trial,[7] do not advocate an immediate (<2 h) invasive strategy for the management of TSTEMI patients,[3] but still identify transient ST-segment elevation as a high-risk criterion within the NSTEMI spectrum for which an invasive procedure is required within 24 h. To date, it has not been fully elucidated is to what extent myocardial injury in TSTEMI patients relates to patients with either STEMI or NSTEMI.

Cardiovascular magnetic resonance imaging (CMR) is considered the reference gold standard to evaluate cardiac volumes and function and it provides the most accurate *in vivo* scar tissue assessment.[8] Recently, CMR-derived scar tissue characteristics have been compared between TSTEMI and STEMI, reporting smaller infarcts in TSTEMI than STEMI,[9] but it remains unknown how these characteristics compare to NSTEMI. Moreover, to our knowledge, no data are available on CMR-derived left ventricular (LV) strain, a superior measure of LV function and performance, in TSTEMI patients.

We hypothesize that TSTEMI is more alike NSTEMI in terms of functional outcome and infarct characteristics, even though it initially typically presents as STEMI. Our objective was to assess CMR-derived myocardial function, strain, and infarct size in TSTEMI patients and to compare these findings to STEMI and NSTEMI populations.

Methods

Study population

For the present study, patients with STEMI were enrolled from two prospective studies, including the multicentre REDUCE-MVI trial (n = 110)[10] and the PREDICT-MVI study (n = 60).[11] Patients with TSTEMI were recruited from the multicentre TRANSIENT trial (n = 141).[7] Detailed inclusion and exclusion criteria for each prospective study are provided in Supplementary data online, File S1. The patients with NSTEMI (n = 108) were prospectively and consecutively enrolled at Amsterdam UMC-location VUmc (n = 57) and Maastricht UMC+ (n = 51). All projects were in accordance with the Declaration of Helsinki and have been approved by their respective local ethics committees, and patients provided written informed consent for participation. Exclusion criteria for all patients were congestive heart failure, creatinine clearance <30 mL/min, haemodynamic instability, and contraindication for CMR examination. Finally, patients were excluded from the study, if the diagnosis of MI was retrospectively rejected for a different diagnosis. The data that support the findings of this study are available at reasonable request to the corresponding author.

Study design

All patients had a routine pre-treatment of acetylsalicylic acid, a P2Y12 inhibitor, and heparin at first medical contact (i.e. at the emergency department or in the ambulance). STEMI patients were eligible for participation when they presented with STEMI <12 h after onset of symptoms. The entire study cohort was treated in accordance with the recent guidelines.[2,3] In this study, we included two trials with randomized arms (REDUCE-MVI and TRANSIENT). We regarded each trial cohort as one cohort, as infarct size and 1-month clinical outcome were found comparable between the randomized arms for both trials. The REDUCE-MVI trial patients were randomized to either ticagrelor or prasugrel treatment arms.[10] Both treatments are recommended with a Class IA indication by the current STEMI guidelines.[2] TRANSIENT trial was designed based on the fact that the optimal timing of revascularization is unclear for TSTEMI patients. TSTEMI patients were randomly assigned to either an immediate or a delayed invasive approach (within 24 or 72 h, depending on the GRACE risk score).[7] Considering the results of the TRANSIENT trial, the most recent guidelines recommend an invasive procedure within 24 h for TSTEMI patients.[3] The median symptom to coronary angiography (CAG) time for TSTEMI patients in this study [10.5 (3.1–25.9) h] closely corresponds with this recommended time-frame. Finally, the REDUCE-MVI patients were initially planned to undergo coronary CAG at 1 month and required to have concomitant intermediate lesion in the non–infarct-related vessel(s) to avoid repeating invasive procedures solely for study purposes.

Coronary angiography analysis

The following data obtained during catheterization are reported: identification of infarct-related artery, extension of vessel disease, TIMI-flow

grades (pre- and post-PCI), treatment choice, and medication. CAG procedures were analysed in an independent core lab (Amsterdam UMC-Location VUmc), blinded to the clinical parameters and outcomes of the patients.

CMR function and strain analysis

All participants underwent CMR imaging 2–8 days after the index event. CMR examination was performed on either 1.5-T scanner (Siemens Healthcare, Erlangen, Germany) or 3-T scanner (Achieva, Philips, Best, The Netherlands), using a phased-array cardiac receiver coil. All images are ECG-gated and acquired during mild end-expiration breath-holding. The scanning protocol included cine and late gadolinium enhancement (LGE) imaging. LV volumes, mass, and ejection fraction were measured on a consecutive stack of short-axis cines, using a balanced steady-state free precession (b-SSFP) pulse sequence using commercially available software (QMASS version 7.6, Medis, Leiden, The Netherlands). Myocardial LV feature tracking analysis was performed on the b-SSFP cine images using dedicated commercial software (Circle Cardiovascular Imaging version 5.13, Inc., Calgary, Canada). All LV contours were traced at the end-diastolic phase. Tracing on the two- and four-chamber views was done to derive global longitudinal strain, and on the short-axis cines for global circumferential and radial strain. Accurate tracking of the LV wall was ensured by visually examining tracking performance and manually adjusting the contours when needed. In case of unsatisfactory detection of tracking even after manual adjustment, the cases were excluded from the strain analysis. Fifteen randomly selected subjects were reanalysed for assessing the intra- and interobserver agreement of global LV strain measurements. A reanalysis was performed by N.v.P., blinded to the previous contouring and the results; and interobserver agreement was assessed between two independent observers (N.v.P. and A.D.), blinded to the other readers contouring and the results. The reliability index was represented by the intra-class correlation coefficient.

CMR infarct characteristics analysis

LGE images were acquired 10–15 min after administration of a gadolinium-based contrast agent (0.15 mmol/kg), using a T1-weighed segmented inversion-recovery gradient-echo pulse sequence, with slice positions identical to the cine images. The presence of infarction was determined based on the LGE images. Infarct size was calculated on the short-axis LGE images using the full-width-at-half-maximum method and expressed in grams, as well as a percentage of entire LV mass.[12] Areas of microvascular obstruction (MVO) were identified on the LGE images as a hypo-intense core within the gadolinium-enhanced myocardium and were included in the calculation of infarct size. LGE images were analysed using commercially available software (QMASS version 7.6, Medis, Leiden, The Netherlands).

All CMR images were analysed in an independent core laboratory (Amsterdam UMC-location VUmc) for quality control and blinded analysis. Typical CMR acquisition parameters are provided in Supplementary data online, *File S1*.

Statistical analysis

Continuous variables were summarized by mean ± standard deviation for normally distributed data and median and interquartile range (IQR) for non-normally distributed data. Categorical variables were summarized by frequency and percentage. Comparison between the groups (TSTEMI, NSTEMI, and STEMI) for continuous variables was performed using one-way ANOVA or Kruskal–Wallis test, depending on the normality of the data. In case the overall ANOVA test was significant, *post hoc* pairwise comparisons were performed using a Bonferroni correction for three pairwise comparisons. Differences between groups on categorical

variables were tested using χ^2 test or the Fisher's exact, where the latter was used if expected cell counts were below 5. *P*-values <0.05 were considered statistically significant. Linear regression analysis was used to assess whether differences in CMR characteristics remained significant after correcting for age, sex, and smoking. Additionally, linear regression was used to identify factors predicting infarct-size. Univariable analyses were first performed, followed by a multivariable regression analysis using backward elimination. Only candidate predictors with $P < 0.2$ were considered in the multivariable analysis. Statistical analysis was performed using SPSS Statistics, version 26 (IBM Corp, Armonk, NY, USA).

Results

Patient population

The final study population consisted of 407 patients with a diagnosis of acute MI following the inclusion criteria (Supplementary data online, *File S2*). Of these patients, 98 (24%) were NSTEMI, 139 (34%) were TSTEMI, and 170 (42%) were STEMI. Baseline characteristics of the three main MI groups are provided in *Table 1*. The mean age was comparable across the three MI groups, although STEMI patients tend to be younger. Patients with TSTEMI and NSTEMI had a similar proportion of male patients, but there were fewer males in the TSTEMI compared to STEMI group. With respect to medical history and smoking, no statistical difference was observed between TSTEMI patients compared to NSTEMI and STEMI patients. Finally, peak troponin T levels were lower in patients with TSTEMI than patients with NSTEMI and STEMI ($P < 0.001$, for both).

A comparison of angiographic and procedural findings is presented in *Table 2*. Patients with TSTEMI and STEMI more frequently had the right coronary artery as culprit compared to NSTEMI ($P < 0.01$, for both). A substantial part of TSTEMI patients ($n = 116$, 83%) and NSTEMI patients ($n = 67$, 69%), and all patients with STEMI were treated with PCI. Prior to PCI, low (0–1) grade TIMI-flow was observed only in 3 (2%) TSTEMI patients, whereas this was observed in 10 (12%) patients with NSTEMI and in 114 (67%) patients with STEMI. After PCI, no patients in TSTEMI and NSTEMI demonstrated low-grade TIMI-flow, whilst 6 STEMI patients had low-grade TIMI-flow.

LV function and strain

CMR analyses of the cine images were performed in 350 patients (86%). The reasons for missing CMR analyses are listed in the Supplementary data online, *File S2*, and no significant difference was observed for baseline and CAG characteristics between the patients with and without CMR analyses (Supplementary data online, *File S3*). All CMR findings for the three groups are summarized in *Table 3*. All groups underwent CMR examination at a similar time point (4.4 ± 2.1 days) after admission to the hospital. Patients with TSTEMI demonstrated the lowest end-systolic and end-diastolic LV volume, and highest LV ejection fraction across the groups ($P < 0.001$, for all) (*Figure 1*). The LV ejection fraction was markedly higher in TSTEMI compared to STEMI patients, whereas no difference was found when comparing TSTEMI to NSTEMI patients.

The global LV strain analysis was performed across all MI types using the CMR-derived feature tracking technique. The excluded case frequencies due to unsatisfactory myocardial tracking from the MI cohorts were 13 (9%) STEMI, 7 (5%) TSTEMI, and 12 (12%)

Table 1 Baseline characteristics

	STEMI (n = 170)	TSTEMI (n = 139)	NSTEMI (n = 98)	Overall P value
Demographics on admission				
Age (years)	60 ± 9	63 ± 12	63 ± 10	0.07
Male (n, %)	141 (83%)	97 (70%)	63 (64%)	0.001[a,b]
BMI (kg/m^2)	27 ± 4	27 ± 4	27 ± 4	0.20
Initial physical examination				
Systolic BP (mmHg)	123 ± 17	133 ± 24	142 ± 23	<0.001[a,b,c]
Diastolic BP (mmHg)	76 ± 13	77 ± 14	81 ± 13	<0.01[b,c]
HR (bpm)	74 ± 14	72 ± 14	71 ± 14	0.12
Medical history (n, %)				
Hypertension	48 (28%)	52 (37%)	38 (39%)	0.12
Diabetes mellitus	18 (11%)	16 (12%)	15 (15%)	0.50
Family history of CAD	72 (42%)	61 (44%)	37 (38%)	0.62
Hypercholesterolaemia	33 (19%)	33 (24%)	24 (25%)	0.53
Smoking	113 (67%)	77 (55%)	40 (41%)	<0.001[b]
Previous MI	1 (1%)	0 (0%)	0 (0%)	0.44
Previous PCI	4 (2%)	8 (6%)	3 (3%)	0.33
Previous CABG	0 (0%)	3 (2%)	0 (0%)	0.14
Cardiac enzymes (peak)				
CK (U/L)	1161.5 (442.8–2244.8)		175.0 (111.0–411.5)	<0.001[b,d]
CK-MB (U/L)	104.0 (34.2–208.8)	18.0 (8.4–38.2)		<0.001[a,d]
Peak troponin-T (µg/L)	1.8 (0.5–4.3)	0.4 (0.1–0.8)	0.2 (0.1–0.4)	<0.001[a,b,c]
Hospitalization duration (days)	3.0 ± 3.1	3.7 ± 4.5	4.6 ± 4.7	0.01[b]

BP, blood pressure; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CK, creatine kinase; CK-MB, creatine kinase-myocardial band; HR, heart rate; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, primary coronary intervention; STEMI, ST-segment elevation myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.
Results of *post hoc* pairwise comparisons: [a]TSTEMI is different from STEMI. [b]NSTEMI is different from STEMI. [c]TSTEMI is different from NSTEMI.
[d]Concerns a comparison of two-groups using Mann–Whitney test

NSTEMI. TSTEMI patients demonstrated the most preserved global LV strain (longitudinal, circumferential, and radial) across the three MI groups (overall $P \leq 0.001$). Patients with TSTEMI had favourable global strain values than STEMI patients in all strain directions (*Figure 2*). In comparison to NSTEMI, TSTEMI patients showed favourable circumferential and radial strain, however, longitudinal strain did not statistically differ. Overall, the inter- and intra-class correlation coefficients demonstrated excellent agreement for the global LV strain analysis. The interobserver intra-class correlation coefficients were 0.99 [95% confidence interval (CI) 0.96–1] for longitudinal, 0.99 (95% CI 0.98–1) for circumferential, and 0.99 (95% CI 0.98–1) for radial strain. The intraobserver intra-class correlation coefficients were 0.99 (95% CI 0.98–1) for longitudinal, 0.99 (95% CI 0.98–1) for circumferential, and 0.99 (95% CI 0.99–1) for radial strain.

Infarct characteristics

CMR analyses of the LGE images were performed in 339 patients (83%). One patient had a previous MI and was therefore not included in CMR infarct analysis. Infarct findings are presented in *Figure 3*. CMR-defined presence of infarction was less frequently observed in TSTEMI than STEMI patients [77 (65%) vs. 124 (98%), $P < 0.001$], but it was comparable to NSTEMI patients [77 (65%) vs. 66 (70%), $P = 0.44$]. A remarkably lower infarct size was seen in TSTEMI compared to STEMI patients [1.4 g (0.0–3.9) vs. 13.5 g (5.3–26.8),

$P < 0.001$], whereas no difference was found when comparing TSTEMI to NSTEMI patients [1.4 g (0.0–3.9) vs. 2.1 g (0.0–8.6), $P = 0.06$]. MVO occurred much less frequently in TSTEMI compared to STEMI patients [5 (4%) vs. 53 (31%), $P < 0.001$], but no significant differences were seen between TSTEMI and NSTEMI patients [5 (4%) vs. 5 (5%), $P = 0.72$]. Furthermore, MVO size was small in TSTEMI and NSTEMI patients and significantly smaller than in STEMI patients ($P < 0.001$, for both). *Figure 4* provides an example of typical ECG, CAG, and CMR findings for all three MI types. The statistical differences regarding LV ejection fraction, strain, and infarct characteristics remained unchanged after correcting for the baseline clinical characteristics.

In univariable linear regression analysis, infarct type, gender, smoking, hypertension, symptom to CAG time, culprit location, pre-PCI TIMI-flow, and PCI were associated with infarct size. Multivariable linear regression analysis identified infarct type ($P = 0.02$), culprit location ($P = 0.001$), and pre-PCI TIMI-flow ($P < 0.001$) as independent markers, related to infarct size (*Table 4*).

Discussion

Further insights into the effects of TSTEMI on LV function, strain, and myocardial injury are of importance to understand the position of

Table 2 Coronary angiography characteristics

	STEMI (n = 170)	TSTEMI (n = 139)	NSTEMI (n = 98)	Overall P value
Symptom to CAG time (h)	2.2 (1.5–3.7)	10.5 (3.1–25.9)	50.3 (23.1–76.9)	<0.001[a,b,c]
Infarct-related artery (n, %)				
Identifiable culprit	170 (100%)	125 (89%)	75 (76%)	<0.001[a,b,c]
Left main	0 (0%)	0 (0%)	1 (1%)	0.15
Left anterior descending	66 (39%)	49 (35%)	37 (44%)	0.42
Left circumflex	33 (19%)	18 (13%)	20 (24%)	0.10
Right coronary artery	71 (42%)	58 (42%)	17 (20%)	0.001[a,c]
Extension of vessel disease (n, %)				
Non-significant CAD	0 (0%)	11 (8%)	7 (8%)	<0.001[b,c]
One-vessel disease	45 (27%)	75 (54%)	40 (46%)	<0.001[b,c]
Two-vessel diseases	98 (57%)	30 (22%)	30 (35%)	<0.001[b,c]
Three-vessel diseases	27 (16%)	23 (16%)	10 (11%)	0.55
TIMI flow pre-PCI (n, %)				
Grade 0–1	114 (66%)	3 (2%)	0 (0%)	<0.01[a,b,c]
Grade 2	28 (17%)	14 (10%)	4 (7%)	0.26
Grade 3	28 (17%)	122 (88%)	58 (93%)	<0.01[a,b,c]
TIMI flow post-PCI (n, %)				
Grade 0–1	6 (4%)	0 (0%)	6 (4%)	0.04[b,c]
Grade 2	18 (10%)	10 (9%)	18 (10%)	0.60
Grade 3	146 (86%)	106 (91%)	146 (86%)	0.15
Treatment choice (n, %)				
PCI	170 (100%)	116 (84%)	67 (69%)	<0.001[a,b,c]
CABG	0 (0%)	8 (6%)	9 (9%)	0.01[b,c]
No intervention	0 (0%)	15 (10%)	22 (22%)	<0.001[a,b,c]
Remaining stenotic segment (n, %)	140 (83%)	47 (34%)	47 (56%)	<0.001[b,c]
Additional PCI of a non-culprit (n, %)	14 (8%)	20 (14%)	19 (27%)	0.001[c]
Medication during PCI				
Heparin	50 (29%)	128 (92%)	80 (82%)	<0.001[b,c]
Bivaluridin	57 (34%)	10 (7%)	0 (0%)	<0.001[a,b,c]
GpIIb/IIIa inhibitor	30 (18%)	9 (7%)	2 (2%)	<0.001[b,c]

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CAG, coronary angiography; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, primary coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.
Results of *post hoc* pairwise comparisons: [a]TSTEMI is different from NSTEMI. [b]TSTEMI is different from STEMI. [c]NSTEMI is different from STEMI.

TSTEMI within the range of MI types and to tailor treatment. This is the first study to evaluate LV function, strain, and infarct size in TSTEMI compared to both STEMI and NSTEMI by means of CMR. We found that patients with TSTEMI have the lowest LV end-systolic volume, the highest LV ejection fraction, and the most favourable global LV strain values including longitudinal, circumferential, and radial directions within the spectrum of MI types. Furthermore, the presence of CMR-defined infarction, infarct size, and frequency of MVO in TSTEMI patients are considerably lower compared to STEMI patients but are comparable with NSTEMI patients. The significance level of the results remained the same even after adjustment of the baseline clinical characteristics for all MI types.

The pathophysiological mechanism of MI consists of a ruptured or eroded plaque with an overlying thrombus or spasm in the epicardial coronary artery.[13] Although there is a lack of solid evidence, specifically TSTEMI may rely on both pathophysiological mechanisms. Thus, spontaneous reperfusion and ST-resolution in TSTEMI may be due

to coronary muscle relaxation, thrombus dissolution, or a combination of both, as these mechanisms may trigger each other.[14,15] Whilst the specific pathophysiological mechanism has not been clearly identified for TSTEMI yet, the unique clinical presentation of TSTEMI warrants further research into the causes and outcome characteristics.

In this study, the comparison of LV volume and ejection fraction results in TSTEMI patients to STEMI and NSTEMI populations is in line with previous echocardiography-based studies assessing LV end-systolic diameter and ejection fraction.[5,16] LV ejection fraction is a clinical cornerstone marker for functional assessment, however, it does not provide a detailed assessment of cardiac mechanics, as it only relies on LV volume changes. Recent studies demonstrated that LV strain analysis soon after acute MI may provide additional prognostic insights.[17,18] In this study, we investigated global LV strain using CMR-derived feature tracking analysis for the first time in TSTEMI patients and assessed these results within the range of MI types. The

Table 3 Cardiovascular magnetic resonance characteristics

	STEMI ($n = 132$)	TSTEMI ($n = 121$)	NSTEMI ($n = 97$)	Overall P value	Adjusted overall P value*
Time from inclusion to CMR (days)	4.4 ± 1.6	4.5 ± 1.6	4.3 ± 3.7	0.88	0.71
LVEDM (g)	124 ± 30	98 ± 23	105 ± 29	<0.001[a,b]	<0.001[a,c]
LVEDMi (g/m^2)	60 ± 13	49 ± 9	41 ± 15	<0.001[a,b,c]	<0.001[a,b,c]
LVEDV (mL)	179 ± 38	153 ± 35	168 ± 40	<0.001[a,c]	<0.001[a]
LVEDVi (mL/m^2)	87 ± 17	78 ± 15	66 ± 26	<0.001[a,b,c]	<0.001[a,b,c]
LVESV (mL)	87 ± 28	65 ± 20	74 ± 28	<0.001[a,b,c]	<0.001[a,b]
LVESVi (mL/m^2)	42 ± 14	33 ± 9	30 ± 16	<0.001[a,b]	<0.001[a,b,c]
LVSV (mL)	92 ± 18	89 ± 20	93 ± 22	0.16	0.049[c]
LVSVi (mL/m^2)	45 ± 7	45 ± 8	37 ± 13	<0.001[b,c]	<0.001[b,c]
LVEF (%)	52 ± 8	58 ± 6	57 ± 8	<0.001[a,b]	<0.001[a,b]
LV longitudinal strain (%)	13.9 ± 0.3	15.3 ± 0.3	14.4 ± 0.3	0.001[a]	0.001[a]
LV circumferential strain (%)	14.4 ± 0.3	16.4 ± 0.2	15.0 ± 0.3	<0.001[a,c]	<0.001[a,c]
LV radial strain (%)	22.6 ± 0.5	26.6 ± 0.6	23.7 ± 0.6	<0.001[a,c]	<0.001[a,c]
CMR-defined infarction (n, %)	124 (98%)	77 (65%)	66 (70%)	<0.001[a,b]	<0.001[a,b]
Infarct size (g)	13.5 (5.3–26.8)	1.4 (0.0–3.9)	2.1 (0.0–8.6)	<0.001[a,b]	<0.001[a,b]
Infarct size (% of LV mass)	11.3 (4.7–20.0)	1.4 (0.0–3.8)	2.4 (0.0–7.3)	<0.001[a,b]	<0.001[a,b]
Presence of MVO (n, %)	53 (31%)	5 (4%)	5 (5%)	<0.001[a,b]	<0.001[a,b]

CMR, cardiovascular magnetic resonance; EDV, end-diastolic volume; ESV, end-systolic volume; g, gram; i, indexed; LVEDM, left ventricular end-diastolic mass; LVEF, left ventricular ejection fraction; MVO, microvascular obstruction; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; SV, stroke volume; TSTEMI, transient ST-segment elevation myocardial infarction.
Results of *post hoc* pairwise comparisons: [a]TSTEMI is different from STEMI; [b]NSTEMI is different from STEMI; [c]TSTEMI is different from NSTEMI.
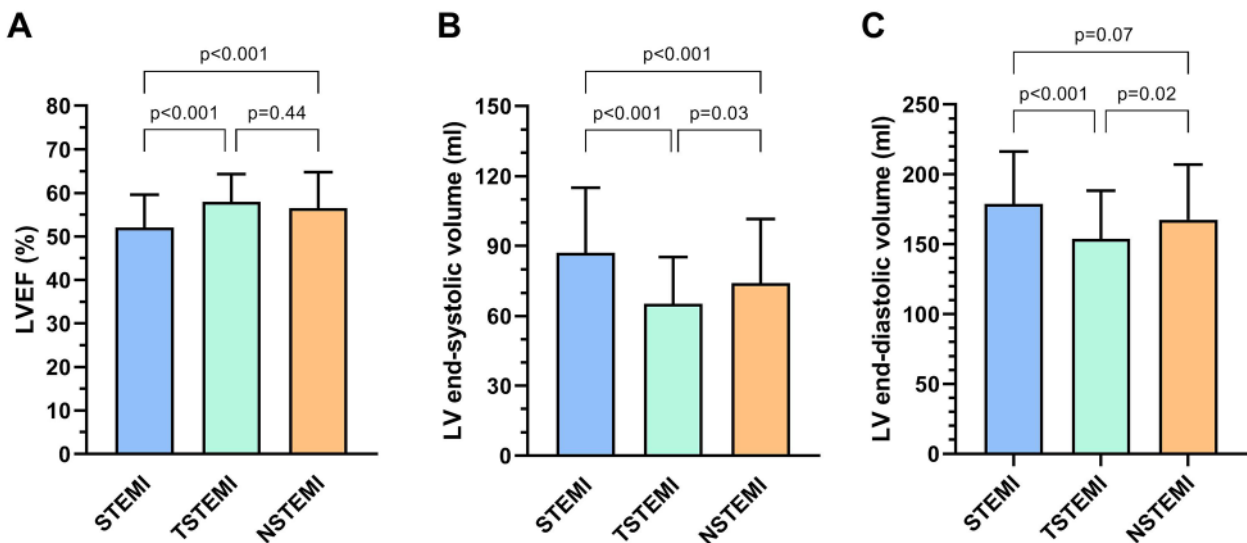*The differences in CMR characteristics were assessed after correcting for age, sex, and smoking.

Figure 1 Comparison of post-infarct cardiovascular magnetic resonance derived function and volume characteristics across three main myocardial infarction types (STEMI, TSTEMI, and NSTEMI). Data are shown as mean ± standard deviation. LVEF, left ventricular ejection fraction; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.

TSTEMI patients presented distinctly more favourable global LV strain values than STEMI patients in all myocardial fibre directions (longitudinal, circumferential, and radial). These results indicate that TSTEMI patients suffer less LV functional damage than STEMI patients also on the myocardium fibre contraction patterns. Moreover, although LV ejection fraction was comparable between TSTEMI and NSTEMI patients, the global LV circumferential, radial, and longitudinal strain values appeared to be less impaired in TSTEMI patients than
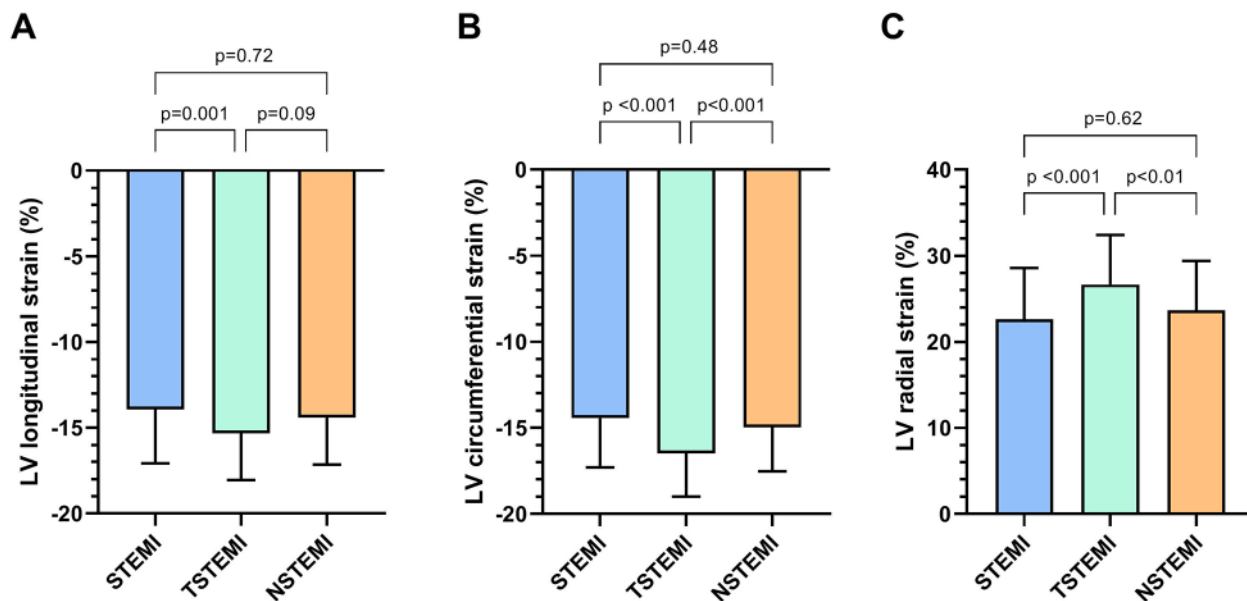
Figure 2 Comparison of post-infarct cardiovascular magnetic resonance derived global LV strain characteristics across three main myocardial infarction types (STEMI, TSTEMI, and NSTEMI). Data are shown as mean ± standard deviation. LV, left ventricle; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.
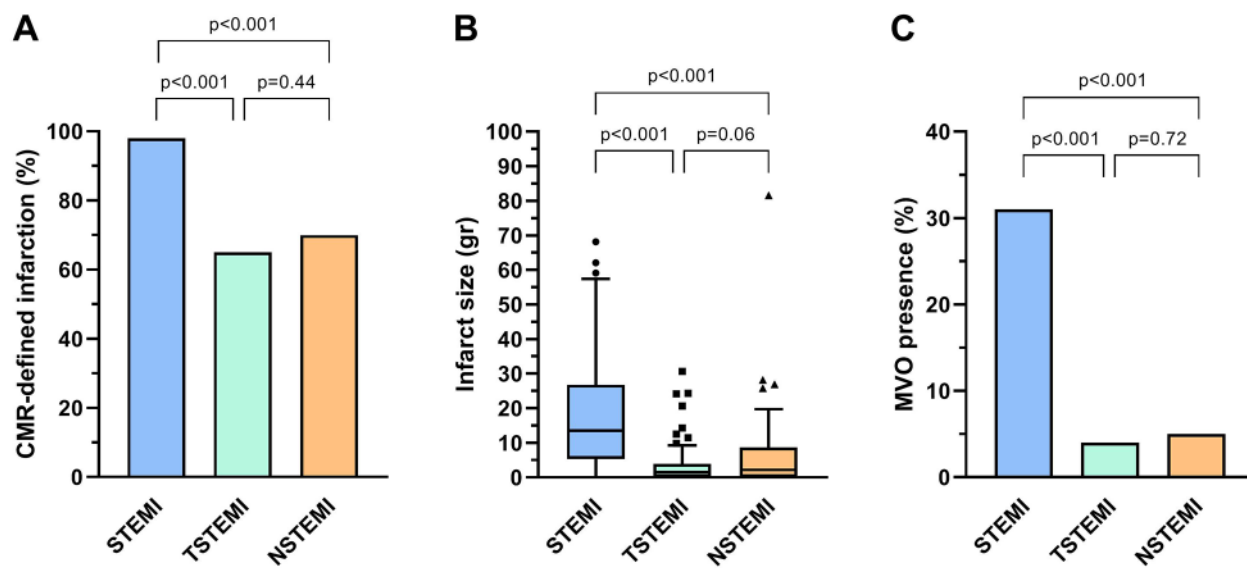

Figure 3 Comparison of cardiovascular magnetic resonance derived infarct characteristics across three main myocardial infarction types (STEMI, TSTEMI, and NSTEMI). Data are shown as percentage or median and interquartile range (Q1–Q3) with Tukey method. CMR, cardiovascular magnetic resonance imaging; LGE, late gadolinium enhancement; LV, left ventricle; MVO, microvascular obstruction; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.

NSTEMI patients. These results may qualify the advanced role of full LV strain analysis to determine the actual extent of functional damage in the setting of an acute myocardial injury, despite preserved LV ejection fraction. Future research is needed to test whether these differences in global LV strain across MI types relate to long-term clinical outcome.
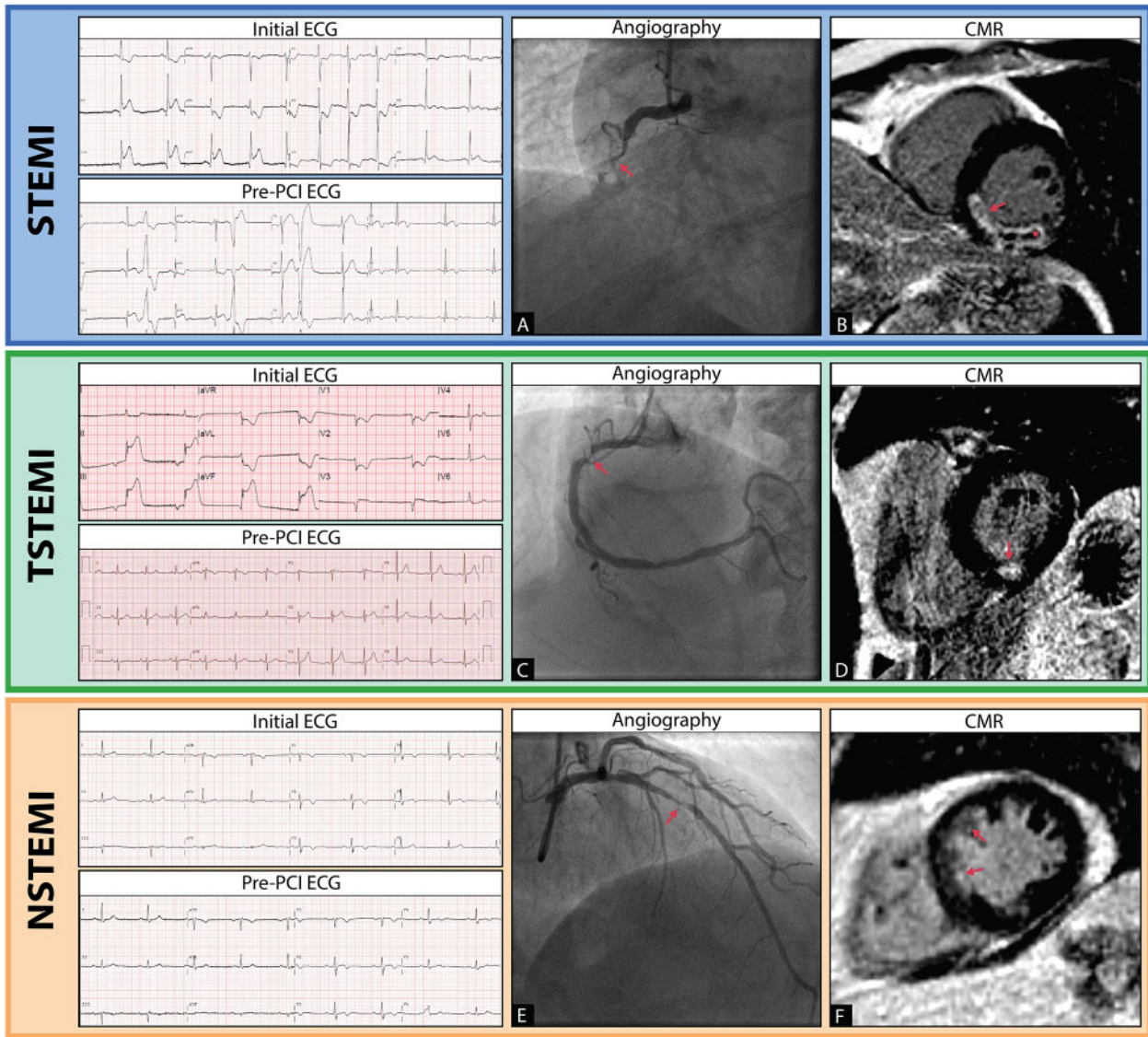
Figure 4 Representation of typical findings of ECG, CAG, and CMR for all myocardial infarction types including STEMI (top), TSTEMI (middle), and NSTEMI (bottom). On the left side, an initial ECG which was taken after the first medical contact and a Pre-PCI ECG which was performed right before the revascularization procedure, were displayed. In the middle, the angiographic appearances of the culprit arteries were shown and on the right side, acquired short-axis LGE images through infarct core during CMR examination days after the index event were demonstrated. In STEMI and NSTEMI, dynamic characteristic ECG changes (e.g. negative T-waves and ST elevations) are seen throughout the MI process. However, in TSTEMI, complete normalization of ST elevations in the Pre-PCI ECG is noted. Concerning CAG, while STEMI exhibits a total occlusion, TSTEMI and NSTEMI are presented with a partly occluded lesion with a residual flow. On the LGE images, in STEMI, a large amount of scar tissue (arrow) and as well as MVO (asterisk) are observed. However, in NSTEMI, a relatively small amount of scar tissue without MVO is noted and in TSTEMI, even a smaller amount of scar mass without MVO is marked. ECG, electrocardiography; CAG, coronary angiography; CMR, cardiovascular magnetic resonance; LGE, late gadolinium enhancement; MVO, microvascular obstruction; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.

In this study, we found that TSTEMI patients have a markedly lower infarct mass and a lower incidence of MVO in comparison to STEMI patients. Our findings are in accordance with previous results.[9] An important cause of these findings can be that nearly all TSTEMI patients demonstrated spontaneous reperfusion (grade 2–3 TIMI flow) before PCI, whereas spontaneous reperfusion was much less common before PCI in the STEMI patients (34% of the patients). This implies that in general, TSTEMI patients experienced shorter periods of transmural myocardial ischaemia compared to STEMI patients. As it is generally believed, early spontaneous reperfusion may have mitigated reperfusion injuries, such as MVO.[19] Moreover, the dynamic nature of TSTEMI may have a role in protecting the myocardium

Table 4: Univariable and multivariable analysis for association with infarct size

	Univariable analysis			Multivariable analysis		
	β	95% CI	P value	β	95% CI	P value
Myocardial infarction type			<0.001			0.025
NSTEMI vs. TSTEMI	2.83	(-0.23, 5.90)	0.07	1.00	(-2.91, 4.91)	0.62
STEMI vs. TSTEMI	14.96	(12.1, 17.8)	<0.001	5.55	(1.40, 9.70)	0.009
Age (per year)	-0.09	(-0.23, 0.04)	0.17	NS		
Gender (male relative to female)	5.40	(2.30, 8.51)	0.001	NS		
Smoking (yes relative to no)	3.31	(0.52, 6.09)	0.02	NS		
Hypertension (yes relative to no)	-3.48	(-6.45, -0.50)	0.02	NS		
Diabetes mellitus (yes relative to no)	-0.51	(-5.00, 3.98)	0.82			
Hypercholesterolaemia (yes relative to no)	-3.10	(-6.52, 0.33)	0.08	NS		
Symptom to CAG time (per hour)	-0.05	(-0.09, -0.02)	0.003	NS		
Culprit location			0.03			0.001
LAD vs. Cx	-2.04	(-6.26, 2.18)	0.34	-2.81	(-6.46, 0.84)	0.13
RCA vs. Cx	2.45	(-1.72, 6.62)	0.25	3.06	(-0.56, 6.68)	0.097
Pre-PCI TIMI-flow			<0.001			<0.001
Grade 2 vs. 0–1	-16.2	(-20.1, -12.2)	<0.001	-14.2	(-18.7, -9.72)	<0.001
Grade 3 vs. 0–1	-16.8	(-19.4, -14.2)	<0.001	-12.8	(-17.0, -8.66)	<0.001
PCI (yes relative to no)	7.9	(4.0, 11.7)	<0.001	NS		

NS included in multivariable analysis, but removed from model in multivariable analysis.
CAG, coronary angiography; Cx, circumflex; LAD, left anterior descending artery; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, primary coronary intervention; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction; TSTEMI, transient ST-segment elevation myocardial infarction.

against ischaemia/reperfusion-related injury. Repetitive cycles of occlusions and reperfusion may result in a further improvement in ventricular remodelling and diminish infarct size through a mechanism similar to ischaemic conditioning, although the net clinical benefit of this mechanism is still under much debate.[20]

Our results do not show any significant differences between TSTEMI and NSTEMI concerning infarct size and the occurrence of MVO. Spontaneous reperfusion may be an important contributor to the lower infarct size in TSTEMI and NSTEMI patients, as we found that most patients in the TSTEMI (98%) and NSTEMI (88%) groups showed high-grade[2,3] TIMI-flow before PCI. Besides, whilst TSTEMI and NSTEMI cohorts demonstrated moderate and similar frequencies of CMR-defined infarction, almost every STEMI patient revealed infarct findings on the LGE images. Taken together, these findings support the notion that TSTEMI is more alike NSTEMI than STEMI with regard to its CMR-derived infarct characteristics. Of course, we cannot exclude the possibility that some NSTEMI patients may have been unrecognized TSTEMI patients, with spontaneous myocardial reperfusion before the first medical contact; however, the majority will be true NSTEMI patients.

The literature findings suggest that the culprit artery remains unidentified in an important proportion of NSTEMI patients during the index catheterization.[21] In this study, the culprit lesion could be determined in 76% of the NSTEMI patients and in 89% of the TSTEMI patients, whereas this was achieved for every STEMI patient. Although the culprit lesion could be identified in 89% of the TSTEMI patients, MI was identified in only 65% of the patients on the LGE images. For these TSTEMI patients, the underlying pathogenesis may

be either atherosclerotic or vasospastic, or both, though with fortunately favourable effects of early restoration of epicardial flow due to antithrombotic therapy or spontaneous reperfusion.

Our results demonstrate that, even after adjustment for possible confounding factors, infarct type is associated with infarct size which is a strong prognostic indicator for clinical outcome. TRANSIENT and REDUCE-MVI trial cohorts demonstrated low mortality rates (<4%) at 1 and 1.5 years, respectively.[22,23] This is most likely due to the efficacy of guideline-recommended medical therapy and the early and widespread use of reperfusion treatments. Studies with a longer period of follow-up are needed to investigate whether long-term differences between the three MI types exist, since up until now, studies have shown inconsistent results.[9,16]

Limitations

This study must be considered as an observational study comparing different infarct types which is subject to limitations related to the patient selection criteria of the randomized studies. Importantly, all patients were recruited consecutively and prospectively and were treated in accordance with the contemporary guidelines. Furthermore, in the REDUCE-MVI cohort, 42 (40%) patients received an additional PCI for concomitant lesion(s) in a non-culprit artery at the 1-month CAG following haemodynamic measurements, as postulated in the study protocol.[10] CMR-derived infarct characteristics were assessed within the first week of the MI and the effect of coronary stenosis in the non-culprit artery can be neglected, as infarct size is principally caused by ischaemia and reperfusion in the culprit artery.

Conclusion

TSTEMI patients have preserved left ventricular function, strain, and smaller infarct-related scar mass compared to NSTEMI and STEMI patients. In addition, LV function and infarct characteristics of TSTEMI patients tend to be more similar to NSTEMI than STEMI patients.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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