

# Global and regional myocardial deformation mechanics of microvascular obstruction in acute myocardial infarction: a three dimensional speckle-tracking imaging study

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**Abstract** Microvascular obstruction (MVO) and transmural infarct size are prognostic factors after acute myocardial infarction (AMI). We assessed the value of myocardial deformation patterns using 3D speckle tracking imaging (3DSTI) in detecting myocardial and microvascular damage after AMI. One hundred patients with first ST-segment elevation MI from the REMI Study were prospectively included. Transthoracic echocardiography with 3DSTI and CMR were performed within 72 h after revascularization therapy. Global (3DG) and segmental (3DS) values of LV longitudinal (LS), circumferential and radial area strain were obtained. Late gadolinium enhancement (LGE) and MVO was quantified as transmural (>50 %) or non-transmural (<50 %). Predictive performance was assessed by area under the receiver operating curve characteristic (AUC). Mean LVEF<sub>CMR</sub> was

45.8 ± 9.2 % with 22.2 ± 12.7 % transmural LGE. MVO was present in 55 patients (MVO transmural extent 11.4 ± 11.8 %). In global analysis, all 3DG strain values were correlated with LVEF<sub>CMR</sub> and infarct size, with the best correlation obtained for 3DGAS ( $r = -0.678$ ;  $p < 0.0001$ ). All 3DG strain values, with the exception of LS, were significantly different between patients with and without MVO. In segmental analysis, all 3DS strain values were significantly lower in transmurally infarcted segments than in non-infarcted segments, and all 3DS values except 3DSRS were significantly lower in non-transmural infarcted segments than in non-infarcted segments. The best 3DS strain for detecting non-viable segments with MVO (MVO > 75 %) was 3DSAS [AUC 0.867 (0.849–0.884), 78.0 % sensitivity and 81.1 % specificity for 3DSAS = -16.1 %]. Importantly, 3DSRS and 3DSAS were associated with an increase in diagnostic accuracy of both transmural LGE and MVO over 3DSLS (all increase in AUC > 0.04, all  $p < 0.01$ ). The newly developed 3DSTI, especially 3DSAS, is a sensitive and reproducible tool to predict and quantify the transmural extent of scar. This new early imaging strategy improve the prediction of MVO while enabling to assess the success of reperfusion and the risk of late systolic remodeling in STEMI.

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## Introduction

Left ventricular (LV) ejection fraction (EF) remains the main prognostic indicator for adverse outcomes after an acute myocardial infarction (AMI) [1]. However, with the

enhanced performance of new revascularization therapies, risk stratification has become increasing challenging in patients with smaller infarct sizes.

A significant association between infarct size and major adverse cardiac events has been demonstrated although the correlation between infarct size and LVEF is modest in patients with relatively preserved LVEF and ST-elevation MI (STEMI) undergoing revascularization [2].

Microvascular obstruction (MVO) has been recently extensively studied and found to have additional predictive value for adverse LV remodeling, permanent inability to recover contractility and subsequent cardiovascular events, regardless of infarct size [3]. Additionally, cardiac magnetic resonance imaging (CMR) has gained a pivotal role in assessing myocardial viability and in defining microvascular damage and salvaged myocardium [4]. Unfortunately, CMR is rarely performed in the acute phase of STEMI mainly due to lack of machine time and to hemodynamic and/or respiratory instability [5].

Two-dimensional (2D) deformation parameters derived from speckle tracking imaging (STI) have been introduced as markers of systolic function and display better correlation with infarct size than conventional transthoracic (TTE) LVEF [6]. Previous studies have mainly focused on 2D longitudinal strain (2DLS), probably because of its easier collection from the 3 apical views as compared to radial (RS) and circumferential (CS) components calculated from short axis acquisitions which are more likely to have poorer tracking quality. [7]. But several studies have highlighted the additional value of CS to differentiate transmural from non-transmural lesions as well as in predicting remodeling [8]. These results emphasize the need for a distinct assessment of longitudinal, radial and circumferential functions in order to avoid the loss of useful information. Accordingly, three-dimensional STI (3DSTI) has been validated as a new and reliable quantification tool to assess the 3 components of deformation [9] in addition to providing supplemental deformation information called area strain. Since the latter takes into account both longitudinal and circumferential components of myocardial deformation, it allows a more accurate assessment of regional function, a parameter of growing interest in ischemic myocardial diseases [10, 11].

The aim of the present study was to evaluate the feasibility and accuracy of 3DSTI to detect the presence, extent and degree of scar transmural and microvascular damage (MVO) in the acute phase of STEMI as compared to CMR late gadolinium enhancement (LGE).

## Materials and methods

### Populations

The study population encompassed all patients with successfully reperfused first acute STEMI included in a prospective monocentric cohort study (relation between aldosterone and cardiac remodeling after myocardial infarction—REMI Study) designed to determine whether aldosteronemia is predictive of cardiac remodeling in the 6 months following a STEMI performed in a university hospital between April 2010 and December 2013. Acute STEMI was confirmed by: <12 h of typical chest pain onset and angiographically-confirmed coronary artery acute occlusion or subocclusion (Thrombolysis In Myocardial Infarction flow grade 0–1). The Ethics Committee approved the trial and all patients provided written informed consent.

Cardiac function was assessed by CMR and echocardiography between the second and fifth day (median delay between TTE and CMR 155 min) following percutaneous transluminal coronary angioplasty (PTCA). Exclusion criteria were any counter-indication with CMR examination or inability to participate in a long-term trial.

A total of 111 patients with first STEMI were enrolled in the study of which 11 could not be analyzed due to lack of interpretable 3D echocardiographic images ( $n = 7$ ; poor image quality; low frame rate, stitching artefacts) and/or of CMR study ( $n = 4$ ; poor image quality of LGE sequence). A control group comprised of 100 healthy adults from a monocentric familial longitudinal cohort of STANISLAS COHORT; 88 males, mean age  $54.9 \pm 12.0$  years, NS vs. STEMI group) underwent thorough clinical evaluations to exclude cardiac disease with normal conventional echocardiography.

### Echocardiographic imaging and analysis

Echocardiography was performed with a commercially available standard ultrasound scanner (Vivid 9, General Electric Medical Systems) with a 2.5-MHz transducer and a 3D probe (4 V Volume Phased Array Probe).

### 3D image acquisition

Echocardiographic acquisition was performed according to EAE/ASE guideline recommendations for 3DTTE image acquisition [12]. From this acquisition, an automated software (4D Auto LV Quantification tool; EchoPAC PC, version 110.1.0, GE Healthcare) was used to obtain both standard and 3DSTI derived parameters. The software

provides the following standard 3D echocardiographic parameter values: end-diastolic (3DLVEDV, ml) and end-systolic volumes (3DLVESV, ml) and LV ejection fraction (3DLVEF, %).

In addition, the software provides peak systolic values of longitudinal, radial and circumferential strain (S) of each of the 17 LV segments and of their mean values [3D global longitudinal strain (3D GLS), 3D global circumferential strain (3D GCS) and 3D global radial strain (3D GRS)] and area strain (3D GAS). Feasibility and reproducibility were studied including the tracking rate (Fig. 1).

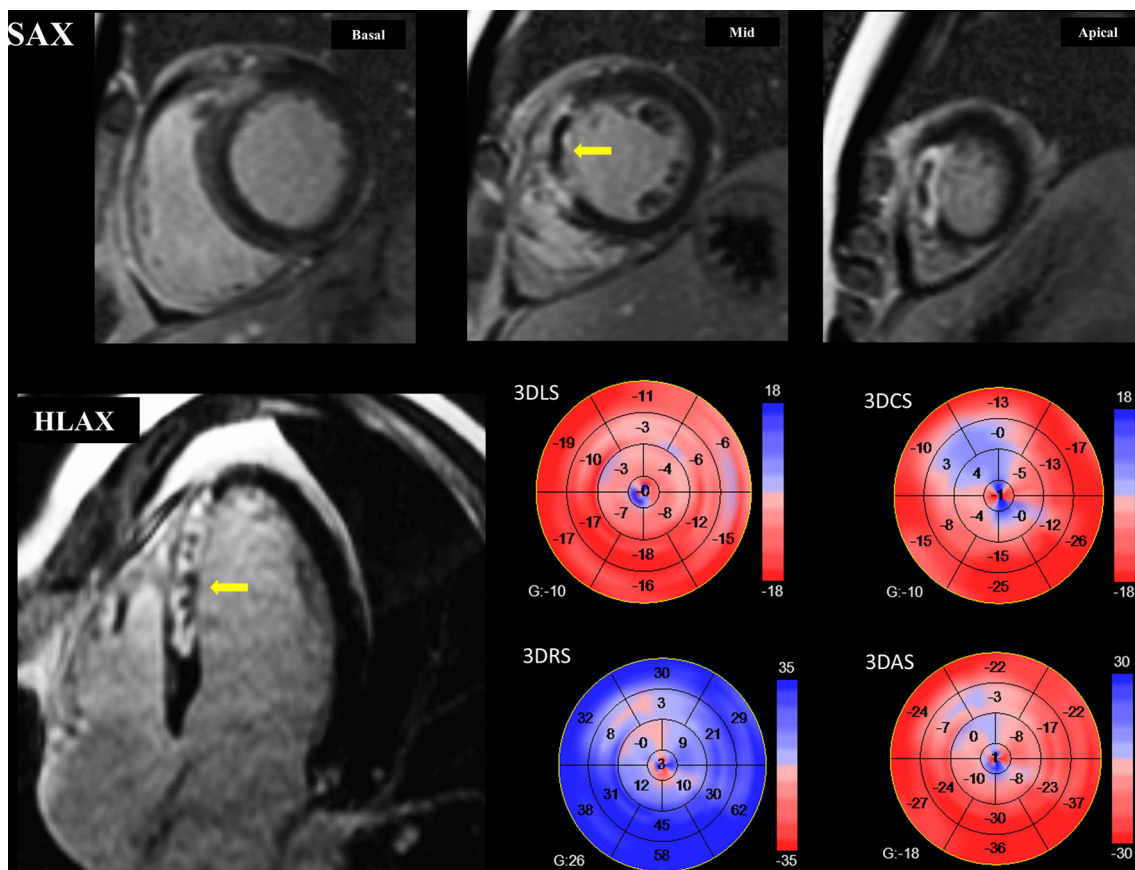
### Cardiac magnetic resonance

CMR was performed between the second and fifth day on a GE 3T system (General Electric 3T signa HDxt) with a phased-array cardiac coil, ECG gating and breath-holding in expiration. Cine imaging for cardiac morphology and function was performed by the steady-state free precession technique. The endocardial contours of the left and right

ventricle were traced manually on all phases and slices using standard software (Mass Analysis +, 4 version, Medis, Netherlands).

Late gadolinium-enhanced (LGE) imaging was acquired 10–15 min after a cumulative total dose of 0.3 mmol/kg Gd contrast in matched short and long-axis planes with a T1-weighted 2D segmented inversion recovery gradient-echo sequence during diastolic standstill. The LGE imaging parameters included a 4.8/1.3 ms repetition time/echo time with a 200–300 ms inversion time adjusted to null normal myocardium.

Transmural LGE extent was assessed visually and scored on a 17-segment model on 3 matched short-axis slices (basal, mid, apical) [13]. The segmental extent of the LGE was considered as non-infarcted if there was no LGE. In case of hyperenhancement, infarcted segments were classified as transmural if LGE > 50 % of mural extent, non-viable if LGE > 75 % and non-transmural if LGE < 50 %. MVO was identified by the presence of a central hypoenhancement within the bright signal within the infarcted segments,



**Fig. 1** 3D transthoracic echocardiography and representative case of anterior infarction related to the occlusion of the proximal left anterior descending coronary artery. CMR late gadolinium enhancement slices of left ventricular short axis (SAX) and horizontal long axis (HLAX) showing transmural extension of myocardial infarct in

anterior and antero-septal zones and central hypoenhancement defining microvascular obstruction (yellow arrow); and Bull eye's view of 3D Segmental longitudinal (3DLS), radial (3DRLS), circumferential (3DCLS) and area strain (3DAS) measured by 3D speckle tracking imaging

usually located in the subendocardium and included as part of the infarct. In presence of MVO, the infarcted segment was defined as transmural (MVO > 50 %) or non-transmural (MVO < 50 %). Analysis of MVO and LGE series was performed independently from, and blinded to, the results of 3D echocardiography.

### Statistical analysis

Statistical analysis was performed using SPSS for Windows (SPSS version 20, Chicago, IL). Quantitative values are expressed as mean values  $\pm$  SD. Intergroup comparisons were performed by the independent samples Student *t* test or Mann–Whitney *U* test when appropriate. For multiple comparisons, analysis of variance along with a post hoc Bonferroni test was performed. Pearson correlation was used to study correlation and concordance between 3DTTE and CMR. As used previously, receiver-operator characteristic (ROC) along with tracing of the area under the curve (AUROC) was performed to identify a 3D segmental strain value to define LGE and MVO transmural (>75 %) [14]. Direct comparisons of AUC were then performed to quantify the increase in diagnostic accuracy between techniques.

3D strain measurements were repeated by two independent observers. Inter- and intra-observer reproducibility of 3D strain measurement was analyzed among 15 patients of the STEMI group. Agreements were assessed using the intraclass correlation coefficient (ICC) for quantitative 3DSTI values and using Kappa analysis for qualitative CMR LGE data.

For all tests, a *p* value < 0.05 was considered to indicate statistical significance.

## Results

### Baseline characteristics

One hundred patients had both CMR and 3DTTE assessments. Mean age was  $55.8 \pm 10.4$  years with most patients being men (87/100, 87 %). The mean delay between CMR and TTE was  $19.2 \pm 23.1$  h.

Fifty-six patients (44 %) had inferior MI, among whom 9 (9 %) had infero-lateral MI, and 44 (56 %) had anterior MI. Reperfusion therapy was achieved in a delay of  $277.7 \pm 199.3$  min after symptoms onset. The culprit vessel was left anterior descending coronary artery (LAD) in 53 patients (53 %), diagonal LAD branch in 6 patients (6 %), circumflex artery (Cx) in 6 patients (6 %), marginal Cx branch in 3 patients (3 %) and right coronary artery in 35 patients (35 %) (Table 1).

### Global left ventricular function assessment

The overall mean LVEF<sub>CMR</sub> was  $45.8 \pm 9.2$  % and 3DLVEF<sub>TTE</sub>  $52.9 \pm 8.1$  % (Table 2). A moderate correlation was observed between LVEF<sub>CMR</sub> and global 3DSTI parameters (3DGLS *r* = 0.595; 3DGCS *r* = 0.608; 3DGRS *r* = 0.632; 3DGAS *r* = 0.678; all correlation *p* values *p* < 0.0001) which were similar or superior to 3DLVEF<sub>TTE</sub> (*r* = 0.569). Weaker correlations between the percentage of transmural infarct size and echocardiographic 3DSTI parameters were observed (*r* = 0.386 for 3DLVEF<sub>TTE</sub>, 0.400 for 3DGLS, 0.397 for 3DGCS, 0.418 for 3DRS and 0.446 for 3DGAS, *p* < 0.0001).

### Infarcted segment analysis

Overall, 1577 of 1700 segments (92.7 %) were analyzable by CMR and 3DSTI. CMR identified 441 infarcted segments (378 with transmural and 63 with non-transmural extent) which accounted for 25.95 % of total myocardium, and 1136 non-infarcted segments (figure supplemental material).

A decrease absolute 3D strain value was noted in all infarcted segments compared to non-infarcted segments. Among myocardial necrotic segments, all absolute 3D strain values were significantly decreased compared to control values and all absolute strain values were also significantly lower in segments with transmural comparatively to segments with non-transmural scar extent (Fig. 2). Furthermore, non-infarcted segments had significantly lower absolute values than control segments for all strains with the exception of radial strain (Table 3).

Among infarcted and non-infarcted segments 3DAS, 3DCS and 3DRS had an AUROC > 0.80 in detecting the transmural non-viable segments (LGE > 75 %) suggesting good predictive values whereas 3SDLS had lower AUROC (0.752) (Fig. 3). Importantly, 3DSRS, 3DSAS and 3DSCS were significantly associated with an increase in diagnostic accuracy of transmural LGE (LGE > 75 %) over 3DSLS (all increase in AUC > 0.05, all *p* < 0.001). 3DSRS was associated with an increase in prediction of transmural LGE of 0.072 (0.054–0.090) over 3DSLS (*p* < 0.001) and of 0.017 (–0.001 to 0.033) over 3DSCS (*p* = 0.06). Likewise, 3DSAS as associated with an increase in prediction of transmural LGE of 0.073 (0.056–0.091) over 3DSLS (*p* < 0.001) and of 0.018 (0.000–0.035) over 3DSCS (*p* = 0.04). 3DSCS was also associated with a significant increase in diagnostic accuracy of transmural LGE over 3DSLS [AUC delta 0.055 (0.023–0.087), *p* < 0.001] but to a lower extent that what was observed with 3DSRS and 3DSAS.

**Table 1** Clinical, biological and hemodynamic characteristics in the entire study population and according to the presence of a microvascular obstruction (MVO+)

	All patients (n = 100)	MVO– (n = 45)	MVO+ (n = 55)	<i>p</i>
Age (years)	55.7 ± 10.4	55.1 ± 9.4	56.2 ± 11	0.18
Gender M/F (%)	88/12	39/6	48/7	0.86
Heart rate (bpm)	75.6 ± 13.9	74.4 ± 14.4	77.5 ± 14.1	0.84
Revascularization delay (min)	277.7 ± 199.3	258.8 ± 181.4	294.2 ± 213.3	0.32
Culprit lesion (n, %)				
LCX–Mg	6–3 (9 %)	2–2 (4 %)	4–1(5 %)	0.83
RCA	35 (35 %)	17(17 %)	18(18 %)	0.76
LAD–Dg	53–6 (56 %)	23–2(25 %)	30–4(34 %)	0.42
Maximum troponin	65.4 + 35.4	46.83 ± 35.2	81.2 ± 27.2	<0.0001
Maximum total creatine kinase (IU/L)	2633 ± 1776	1890 ± 1412	3339 ± 1776	<0.0001
Blood pressure at admission (mmHg)				
SBP	125 ± 20	123 ± 17	126 ± 23	0.03
DBP	74 ± 13	73 ± 9	75 ± 13	0.08
Killip class (n, %)				
1	93 (93)	41	48	0.85
2	7 (7)	2	5	0.63
3/4	0 (0)	0	0	NA

LCX indicates left circumflex; Mg, marginal; RCA, right coronary artery; LAD, left anterior descending artery; Dg, diagonal; SBP, systolic blood pressure; DBP, diastolic blood pressure

**Table 2** Global transthoracic echocardiographic parameters and cardiac magnetic resonance imaging parameters in the entire study population and according to the presence of a microvascular obstruction (MVO+)

Variable	All patients (n = 100)	MVO– (n = 45)	MVO+ (n = 55)	<i>p</i>
<b>3DTTE</b>				
LVEF <sub>TTE</sub> (%)	52.9 ± 8.1	55.5 ± 8.1	51.0 ± 7.6	0.005
LVEDV (mL)	114.1 ± 26.3	110.6 ± 23.8	116.9 ± 28.1	0.782
GLS (%)	–13.3 ± 3.6	–13.9 ± 3.5	–12.9 ± 3.7	0.678
GCS (%)	–14.1 ± 3.7	–15.0 ± 3.9	–13.3 ± 3.3	0.021
GRS (%)	36.7 ± 11.1	39.1 ± 11.8	34.7 ± 10.1	0.046
GAS (%)	–24.6 ± 5.6	–26.0 ± 5.6	–23.5 ± 5.4	0.034
<b>CMR</b>				
LVEF <sub>CMR</sub> (%)	45.8 ± 9.2	49.0 ± 8.4	43.2 ± 9.2	0.002
LVEDV <sub>CMR</sub> (mL/m <sup>2</sup> )	88.3 ± 15.3	85.7 ± 14.6	90.5 ± 15.6	0.706
Transmural LGE infarct % (n)	22.2 ± 12.7 (378)	15.5 ± 11.4 (263)	27.7 ± 11.1 (115)	0.001
Non-transmural LGE % (n)	3.7 ± 12.7 (63)	4.8 ± 5.7 (37)	2.8 ± 4.2 (26)	0.043
Transmural MVO % (n)	6.6 ± 10.4 (107)	0	11.4 ± 11.8 (107)	NA
Non-transmural MVO % (n)	3.8 ± 6.1 (65)	0	6.9 ± 6.8 (65)	NA

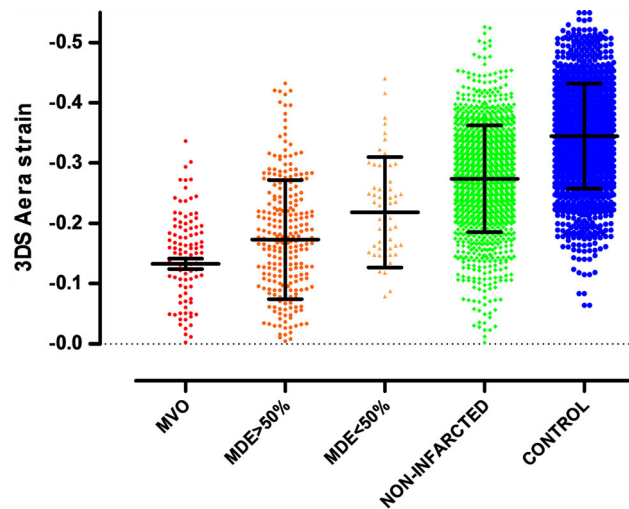
Global GLS, longitudinal strain; GCS, circumferential strain; GRS, radial strain; GAS, area strain; MVO, microvascular obstruction; LGE, late gadolinium enhancement; 3DTTE, 3D transthoracic echocardiography; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; TTE, transthoracic echocardiography; CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement; NA, not available

### Microvascular obstruction segment analysis

MVO was diagnosed in 172 segments (107 with transmural and 65 with non-transmural extent) in 55 patients (55 %) accounting for a mean MVO extent of 10.4 % of total

myocardium. Patients with MVO had significantly larger myocardial infarct size, lower LVEF and higher total creatinine kinase peak (Table 1). Transmural segments with transmural MVO had significant lower segmental strain value than other transmural segments (Table 3).





**Fig. 2** 3D area strain segmental value measured by 3STI in 1577 segments from the STEMI patient group according to the degree of late gadolinium enhancement and the presence of a microvascular obstruction (LGE Myocardial delayed enhancement)

The distinction between transmural segments with and without MVO was also more accurate using area strain as opposed to using the isolated longitudinal component of myocardial deformation (Table 3). When considering non-viable transmural MVO segments (LGE > 75 and MVO > 75 %), 3DAS and 3DRS had an AUROC > 0.85 while 3DLS and 3DCS strains had an AUROC > 0.80 (Fig. 3). Importantly, 3DSRS and 3DSAS were associated with an increase in diagnostic accuracy of transmural MVO (LGE > 75 and MVO > 75 %) over 3DSLS and 3DSCS (all increase in AUC > 0.03, all  $p < 0.05$ ). Specifically, 3DSRS was associated with a significant increase in prediction of MVO of 0.047 (0.018–0.076) over 3DSLS ( $p = 0.001$ ) and of 0.041 (0.009–0.073) over 3DSCS ( $p = 0.01$ ). Likewise, 3DSAS was associated with a significant increase in prediction of MVO of 0.044

(0.015–0.073) over 3DSLS ( $p = 0.003$ ) and of 0.037 (0.005–0.070) over 3DSCS ( $p = 0.03$ ). In contrast, 3DSCS was not associated with an increase in diagnostic accuracy of MVO over 3DSLS (AUC delta 0.007 (–0.052 to 0.065),  $p = 0.82$ ).

### Inter- and intra-observer variability

Inter- and intra-observer variability for 3D segmental strain with tracking quality assessment and CMR segmental qualification (LGE and MVO segments) is described in Table 4.

### Control group

By definition, the 100 patients of the control group had normal systolic function (3DLVEF<sub>TTE</sub>  $62.6 \pm 4.4$  %; 3DLVEDV  $88.0 \pm 26.7$  mL/m<sup>2</sup>) and mean deformation values of  $-34.8 \pm 8.9$  % for 3DGAS,  $-19.9 \pm 5.9$  % for 3DGLS,  $-19.5 \pm 6.2$  % for 3DGCs and  $56.2 \pm 19.1$  % for 3DGRS [15].

### Discussion

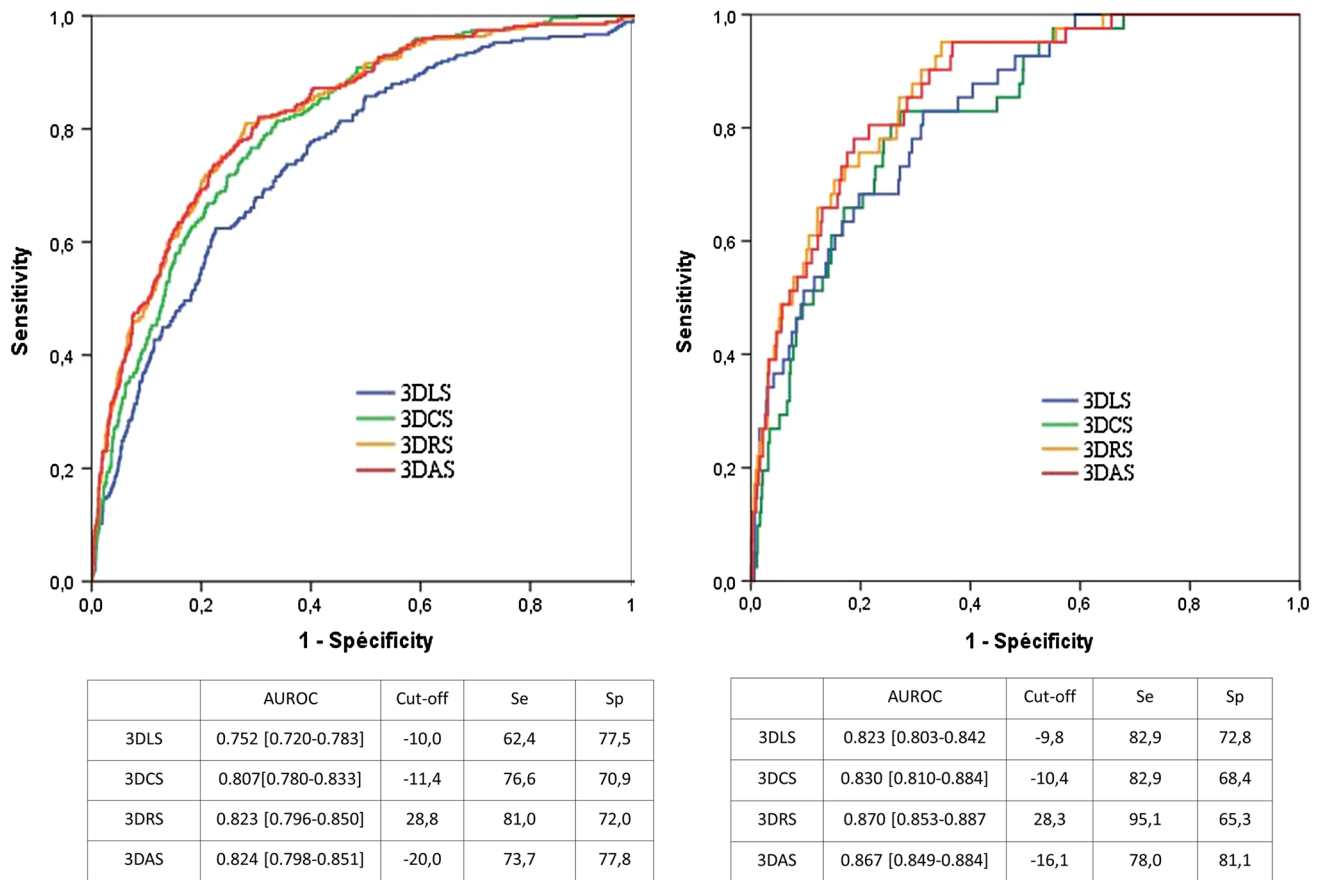
The main findings of this study can be summarized as follows: (1) in patients with STEMI undergoing early PTCA, 3D global strain values were better correlated with LVEF<sub>CMR</sub> than 3DLVEF<sub>TTE</sub> and had a good predictive value of transmural extent; (2) MVO as determined by CMR was a relatively frequent finding being present in 55 % of cases and was well differentiated by all 3D strains except longitudinal strain; (3) with regard to segmental analysis, 3DSAS, which takes into account both longitudinal and circumferential motion, represented the best tool

**Table 3** 3D Segmental deformation value measured by 3STI of 1577 segments from the STEMI patient group according to the degree of late gadolinium enhancement and the presence of a microvascular obstruction

	STEMI group					Control group (n = 1470)
	MVO		LGE			
	Transmural (>50 %) (n = 107)	Non-transmural (<50 %) (n = 65)	Transmural (>50 %) (n = 378)	Non-transmural (<50 %) (n = 63)	Non-infarcted segments (n = 1136)	
3DSLS	$-8.3 \pm 5.8^{*,\dagger}$	$-9.6 \pm 6.8^{*,\dagger}$	$-9.9 \pm 8.3^{*,\dagger}$	$-13.5 \pm 6.1^{*,\dagger,\S}$	$-14.5 \pm 6.0^*$	$-19.9 \pm 5.9$
3DSCS	$-6.4 \pm 5.3^{*,\dagger,\S}$	$8.4 \pm 5.8^{*,\dagger}$	$-9.2 \pm 6.5^{*,\dagger}$	$-10.4 \pm 6.1^{*,\dagger}$	$-16.0 \pm 6.9^*$	$-19.5 \pm 6.2$
3DSRS	$17.8 \pm 12.6^{*,\dagger,\S}$	$22.4 \pm 14.2^{*,\dagger}$	$24.3 \pm 16.2^{*,\dagger}$	$31.3 \pm 15.9^{*,\S}$	$41.3 \pm 17.9^*$	$56.2 \pm 19.1$
3DSAS	$-13.5 \pm 0.09^{*,\dagger,\S}$	$-16.4 \pm 0.9^{*,\dagger}$	$-17.3 \pm 9.9^{*,\dagger}$	$-21.8 \pm 9.2^{*,\dagger,\S}$	$-27.4 \pm 8.9^*$	$-34.8 \pm 8.9$

SLS, segmental longitudinal strain; SCS, circumferential strain; SRS, radial strain; SAS, area strain; MVO, microvascular obstruction, LGE, late gadolinium enhancement

\*  $p < 0.05$  vs. control segments; †  $p < 0.05$  vs. non-infarcted segments; §  $p < 0.05$  vs. transmural infarcted segments



**Fig. 3** ROC curves of 3D segmental longitudinal (3DSLS), radial (3DLS), circumferential (3DCLS) and area strain (3DAS) measured by 3D speckle tracking imaging for distinction of non-viable

segments (Late gadolinium enhancement >75 %) on the left panel and microvascular obstruction >75 % on the right panel

to discriminate LGE with or without MVO in non-viable segments.

As previously reported, we found that 3DLVEF<sub>TTE</sub> overestimated LVEF as measured by CMR along with a modest correlation between infarct size and 3DLVEF<sub>TTE</sub> [16]. Meanwhile, the 3DSTI technique for LV volume measurements has been validated and demonstrated superior accuracy and reproducibility over previously used 2DSTI technique [17]. In our study, all global 3D strains showed good to moderate correlations with the gold standard LVEF<sub>CMR</sub> and infarct size, with 3DGAS having the highest correlation coefficient among all strain parameters.

At the segmental level, our data confirmed a significant difference in longitudinal function between non-transmural and transmural infarcted segments. Longitudinal function is known to be attenuated independently of scar transmurality [18]. Indeed subendocardial fiber layers have the most significant contribution to long-axis function compared to the middle and subepicardial layers which mainly contribute to wall thickening as well as radial and circumferential function. Indeed, Takeuchi et al. [19] showed

that longitudinal function was altered in small subendocardial MI whereas circumferential deformation and short axis function were initially preserved. This longitudinal alteration is usually associated with compensatory circumferential mechanics thus becoming a key determinant of preserved global LV function [20].

Numerous studies have already shown the potential diagnostic value of circumferential strain in discriminating non-transmural and transmural infarction although only using 2DSTI [21]. However, 2D assessment of circumferential strain requires acquisition of 3 short axis views and heart rate; in addition, loading conditions may change between different acquisitions and therefore influence deformation values. Moreover, only one parasternal short axis view at the level of the papillary muscle was performed in most of the above studies. To the best of our knowledge, the present study is the first to assess radial and circumferential deformation over the 17-segments in 3 dimensions. Beyond the analysis of LV volumes, 3DSTI allows the assessment of the different myocardial layer functions by avoiding poor speckle tracking as encountered in monoplane 2D analysis.

**Table 4** Inter- and intra-observer variability for 3D segmental speckle tracking echocardiography (STE) with tracking quality assessment and for CMR segmental qualification

Reproducibility	Intra observer			Inter observer		
Intraclass correlation	ICC			ICC		
3D STE reproducibility and feasibility on 15 patients						
3D SLS	0.852 (0.806–0.888)			0.841(0.790–0.879)		
3D SCS	0.909 (0.881–0.931)			0.844 (0.794–0.882)		
3D SRS	0.911 (0.883–0.932)			0.849(0.801–0.886)		
3D SAS	0.920 (0.896–0.932)			0.870 (0.829–0.902)		
Feasibility	Reader 1			Reader 2		
Percentage of poor tracking	20/255 (7.8)			15/255 (5.8 %)		
Excluded segment n (%)						
Segmental qualitative value CMR LGE	Intra observer			Inter observer		
	R1	R2	κ value	R1	R2	κ value
CMR segmental reproducibility on 20 patients						
Infarcted segments (n = 340)						
Non infarcted	263	263	0.96*	268	263	0.91*
Non transmural	19	18		15	19	
Transmural	58	59		57	58	
MVO segments (n = 340)						
Non MVO	308	309	0.95*	308	308	0.81*
Non transmural	22	19		7	22	
Transmural	10	12		0	10	

Inter- and intra-observer variability for 3D segmental longitudinal and area strain with tracking quality assessment

3D, 3-dimensional; Segmental SLS, Longitudinal strain; SRS, radial strain; SCS, circumferential strain; SAS, area strain, ICC, intraclass correlation coefficient; MVO, micro vascular obstruction; late gadolinium enhancement; R: reading/reader

All \* $P < 0.0001$  with Kappa statistics

Motion assessment of all 17 myocardial segments is performed in a single analysis step, which significantly reduces analysis time. In the present series, we observed a gradual decrease in absolute strain values in the 3 directions of myocardial motion in parallel with the gradual importance of transmural damage. A threshold value of  $-20.0\%$  was defined herein for 3DSAS enabling to discriminate LGE transmural ( $>75\%$ ) with good diagnostic values. Previous studies with smaller patient samples concluded that 3DSTI can determine transmural involvement and therefore the viability of the infarcted segment [22].

There is currently no consensus as to how and when MVO should be assessed after AMI. Accurate detection and quantification of MVO is important since previous studies have shown that MVO is independently associated with adverse ventricular remodeling and patient prognosis [3]. In our study, although 100% of the patients had a TIMI flow grade 3 after PTCA with acceptable revascularization delay, MVO was nonetheless diagnosed by CMR in 55% of cases at day 3. Hence, there is clearly a need for

“in-lab” tools able to assist in the early identification of patients at increased risk of MVO. Rather than ECG or per procedural myocardial blush grade, CMR is currently considered to be the most reliable method for determining MVO in the first days after reperfusion [23]. However, CMR has a number of limitations, including cost and accessibility. Our findings furthermore indicate that  $<10\%$  patients have CMR in the first month following AMI. In the acute phase of MI, segmental and global 2DLS have been shown to be significantly altered by the presence of MVO in addition to MI size [24]. 2DSTI has recently emerged as valuable tool to precociously assess microvascular damage, after a STEMI as well as a marker for persistent akinetic territories [25]. Herein, we confirm a close association between myocardial deformation and the degree of MVO. Our data reveal that both 3DSRS and 3DSCS were further decreased with MVO while displaying a marked decrease in their absolute values in segments with MVO  $>50\%$ . Moreover, the combined analysis of longitudinal and circumferential deformation through 3DSAS was the main indicator in differentiating transmural non-viable segments



with or without MVO. On the other hand, 3DLS was shown to be altered irrespective of the presence or absence of MVO. These results thus support the theory of cross-fiber shortening suggesting that passive radial thickening of segments with non-transmural infarction is generated by the shortening of viable epicardial fibers. In the case of transmural no-reflow segments, the circumferential fibers, which are predominant in the mid layer of myocardium, are severely damaged [26].

Assessment of the presence and extent of MVO is a surrogate endpoint for therapeutic strategies due to adverse LV remodeling in case of MVO. The ACC/AHA guidelines for management of STEMI have stressed the importance of the development of simple, accurate, readily available noninvasive techniques to assess adjunctive reperfusion agents and revascularization therapy strategies and to evaluate the no-reflow phenomenon within the first hours of MI [27]. After a STEMI, CMR is increasingly used for coronary microvascular status assessment and quantification of infarct size [28]. Unfortunately, CMR is rarely performed in acute phase of MI (<10 %) in most countries and hospitals due mainly to a lack of machine time [5]. 3DSTI is an accessible prognostic marker that could identify patients with microvascular dysfunction after reperfusion at the acute phase of MI. Indeed, the assessment of segmental deformation can be used to identify the localization of MI and monitor microvascular damage. As a result, 3DSTI could represent a useful tool to detect those patients with MVO in whom access to MRI is difficult during their initial hospital stay for AMI. Given the high prognostic value of MVO after MI, therapeutic interventions and the intensity of follow-up could hence be adequately adapted in patients likely to have MVO based on 3DSTI evaluation. Further studies assessing the pragmatic clinical usefulness of this 3DSTI-based strategy are warranted.

### Limitations

The main limitation of the present study is the small infarct size with low proportion of transmural segments, which may explain the modest correlations of LVEF<sub>CMR</sub> and infarct size with TTE parameters. However, these limited infarct sized are the reflection of the evolution of modern cardiology, especially in tertiary centers. In addition, it is in these patients with limited infarct size that risk assessment is the most difficult, thus increasing the potential usefulness of new 3DSTI methods in this population.

### Conclusions

The use of 3D deformation in the acute phase of a MI may represent an easy, fast and reliable means to assess myocardial deformation of MVO in the infarcted area.

Global deformation analysis helps in the assessment of MI and, more specifically, the new area strain parameter is best correlated with the reference LVEF<sub>CMR</sub> and differentiates patients with and without MVO. In addition, regional 3D deformation can estimate LV regional mechanics of scarring and yield reliable results in discriminating transmural from non-transmural extent. Indeed, results herein demonstrated a close association between myocardial deformation in patients with a recent AMI and the degree of diminished microcirculation. Circumferential strain value was severely altered in the no-reflow segment and showed notable diagnostic value in the differentiation of infarcted segments with and without no-reflow.

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**Conflicts of interest** None.

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