Evaluation of global left ventricular function assessment of non-fluorescent electromechanical endocardial mapping compared with biplane left ventricular contrast angiography

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Background. Little is known about the diagnostic accuracy of global LV function assessment by electromechanical endocardial mapping (EEM). The aim of the present study was to determine the relationship between global left ventricular (LV) function measured by EEM and biplane left ventricular contrast angiography (LVA) after ST-elevation myocardial infarction (STEMI).

Methods. Thirty-seven patients underwent LVA and EEM during routine coronary angiography four months after primary percutaneous intervention for STEMI. Global LV function parameters were available from both techniques in all patients. LVA was regarded as reference standard.

Results. All procedures were carried out without adverse events. Average age was 55 ± 10 years and 84% were male. EEM showed an overestimation of end-diastolic volume (EDV) and end-systolic volume (ESV) of 6.5 ml and 25.5 ml, respectively. Correlation (r) was 0.84 ($p < 0.001$) for

EDV and 0.74 ($p < 0.001$) for ESV. Average left ventricular ejection fraction (LVEF) measured by EEM was 17.2% point ($\pm 11.3\%$ point) lower compared with LVA ($r = 0.69$, $p < 0.001$).

Conclusion. Although global functional parameters by EEM correlated well with LVA, the relatively large differences in terms of absolute values for ventricular volumes and LVEF render the two techniques non-interchangeable for global LV-function-data. (Neth Heart J 2010;18:72-77.)

Keywords: Body Surface Potential Mapping; Ventricular Function, Left; Contrast Media; Coronary Angiography

Prognosis after ST-elevation myocardial infarction (STEMI) is closely related to cardiac volumes, myocardial mass and global left ventricular (LV) function, expressed as left ventricular ejection fraction (LVEF).¹ Accurate assessment of these parameters is required for the prediction of prognosis in individual patients as well as in entire cohorts.²⁻⁴ The introduction of primary percutaneous intervention (PCI) for STEMI has been proven to increase LV rest function in this patient category. However, some patients suffer from symptoms of heart failure as a result of post-infarct deterioration of left ventricular function. One strategy to improve left ventricular function after reperfusion therapy is bone marrow-derived progenitor cell infusion.⁵⁻⁷ The optimal route of delivery is still under debate.^{8,9} Commercially available non-fluoroscopic electromechanical endocardial mapping systems (EEM) that measure both wall motion and electrical activity can aid the interventional cardiologist by providing on-line anatomical and functional information without excessive radiation

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Figure 1. Example of endocardial electromechanical map.

exposure. In addition, these systems can be fitted with dedicated (cell) injection catheters. This technique has proved to be safe and feasible both in the cell- and gene-delivery setting.^{5,10-12} It was hypothesised that besides facilitating cell delivery, the generated maps could provide global LV function assessment, which can be used to measure efficacy of the applied therapy. Since EEM is being used ever more frequently in clinical practice, it is increasingly relevant to assess its diagnostic accuracy for analysis of global LV function parameters. Al-

though there have been many studies focusing on the differentiation between viable and non-viable myocardium, to date only a few studies focusing on the diagnostic accuracy of EEM for assessment of global LV function have been published.^{13,14} Therefore, we sought to investigate the diagnostic accuracy of EEM in a cohort of post-STEMI patients undergoing routine cardiac catheterisation.

Methods

Patients

The present study was conducted at the University Medical Center Groningen. As part of a multicentre randomised controlled trial evaluating the effect of intracoronary infusion of autologous bone marrow derived cells following PCI for STEMI¹⁵ all patients underwent re-catheterisation four months after primary PCI. Due to the specific inclusion and exclusion criteria only patients with a relatively large myocardial infarction were enrolled in the study. All baseline clinical and procedural data were entered in a database. All patients gave written informed consent for participation in the trial.

Electromechanical mapping procedure

EEM maps were obtained four months after primary PCI, as previously described.¹² The mapping NOGA/CARTO system (Biosense Webster, Diamond bar, Ca, USA) comprises a miniature passive magnetic field sensor, an external ultralow magnetic field emitter (location pad), and a processing unit. The catheter tip incorporates standard electrodes that allow recording of unipolar or bipolar signals and the location sensor. The mapping catheter was introduced through an 6F femoral sheath

Figure 2. Example of a biplane left ventricular contrast angiogram with a 30° right anterior oblique (RAO) projection and a 60° left anterior oblique (LAO) projection.

Table 1. Baseline clinical characteristics at primary PCI (n=37.)

Age, years (mean $\pm$ SD)	55.1 $\pm$ 9.6	Stent (n, %)	37 (100)
Male sex (n, %)	31 (84)	Bare metal (n, %)	37 (100)
History of MI (n, %)	0 (0)	Drug eluting (n, %)	0 (0)
History of PCI (n, %)	0 (0)	Stent diameter (mean $\pm$ SD)	3.3 $\pm$ 0.3
History of CABG (n, %)	0 (0)	Length of stented segment (mean $\pm$ SD)	22.8 $\pm$ 9.8
History of stroke (n, %)	2 (5)	Glycoprotein IIb/IIIa receptor blocker (n, %)	36 (97)
Killip class I (n, %)	33 (89)	Intra-aortic balloon pump (n, %)	1 (3)
Killip class II (n, %)	3 (8)	TIMI flow before PPCI	
Killip class III (n, %)	1 (3)	-0 (n, %)	27 (73)
Killip class IV (n, %)	0 (0)	-1 (n, %)	3 (8)
Diabetes mellitus (n, %)	2 (5)	-2 (n, %)	5 (13)
Hypertension (n, %)	11 (28)	-3 (n, %)	2 (5)
Hyperlipidaemia (n, %)	12 (32)	TIMI flow after PPCI	
Current smoker (n, %)	20 (54)	-0 (n, %)	0 (0)
Positive family history (n, %)	17 (46)	-1 (n, %)	2 (5)
Infarct location		-2 (n, %)	5 (14)
- LAD (n, %)	20 (54)	-3 (n, %)	30 (81)
- CX (n, %)	7 (19)	Myocardial blush grade after PPCI	
- RCA (n, %)	10 (27)	0 (n, %)	2 (5)
Number of diseased vessels		1 (n, %)	13 (35)
- 1 (n, %)	31 (84)	2 (n, %)	19 (51)
- 2 (n, %)	4 (11)	3 (n, %)	3 (8)
- 3 (n, %)	2 (5)	Max CK, U/l	3757
Total ischaemic time*	4.1 (2.4-5.4)	(median, interquartile range)	(1739-5649)
(median, interquartile range)		Max CK-MB, U/l	435
Type B2/C lesion (n, %)	36 (97)	(median, interquartile range)	(174-591)

*Total ischaemic time denotes time between onset of symptoms until PPCI; †successful reperfusion denotes TIMI 3 flow and myocardial blush grade 2 or 3. CABG=coronary artery bypass grafting, CX=circumflex coronary artery, CK=creatinine kinase, CK-MB=creatinine kinase myoglobin binding, LAD=left anterior descending coronary artery, MI=myocardial infarction, PCI=percutaneous coronary intervention, PPCI=primary percutaneous coronary intervention, RCA=right coronary artery, SD=standard deviation, TIMI=thrombolysis in myocardial infarction.

and placed in the left ventricle. Another reference catheter, also with a tip sensor, was taped securely to the patient's back. The apex, the inflow and out-flow tract were identified to form the first three dimensional images of the ventricle. After that, the remaining points were measured without fluoroscopy. The stability of the catheter-to-wall contact was evaluated at every site in real time, and points were deleted from the map if one of the following criteria was met: (1) a premature beat or a beat after a premature beat; (2) location stability, defined as a difference of >5 mm in end-diastolic location of the catheter at two sequential heart beats; (3) loop stability, defined as an average distance of >5 mm between the location of the catheter at two consecutive beats at corresponding time intervals in the cardiac cycle; (4) cycle length that deviated >10% from the median cycle length; (5) different morphologies of the local ECG at two consecutive beats; (6) local activation time differences of >5 ms between two consecutive beats; and (7) different QRS morphologies of the body surface ECG. On average around 100 points were measured evenly

distributed throughout the left ventricle in order to complete a representative 3D image. The total time required for the entire procedure varied from 40 to 60 minutes. Fluoroscopy is used for approximately three minutes during the beginning of the procedure. An example of an electro-mechanical cardiac mapping reconstruction is shown in figure 1.

Biplane left ventricular angiography

Biplane cineventriculography was performed using a 30° right anterior oblique projection and a 60° left anterior oblique projection with injection of at least 30 ml of contrast medium at a flow rate of 13 ml/s using a 6 French pigtail catheter. Frame rate was set at 30 Hz. The end-diastolic image was selected manually, as the frame with the largest ventricular silhouette, and the end-systolic image, as the frame with the smallest ventricular silhouette. Analysis of the biplane LV angiograms was performed using a dedicated package for biplane LVA analysis (CAAS, Pie Medical, Maastricht, the Netherlands). End-diastolic volume (EDV) and end-systolic volume (ESV)

Figure 3. Bland-Altman plot comparing end-diastolic volume (EDV) measured by endocardial electromechanical mapping (EEM) with EDV measured by biplane left ventricular contrast angiography (LVA).

Figure 4. Bland-Altman plot comparing end-systolic volume (ESV) measured by endocardial electromechanical mapping (EEM) with ESV measured by biplane left ventricular contrast angiography (LVA).

Figure 5. Bland-Altman plot comparing stroke volume (SV) measured by endocardial electromechanical mapping (EEM) with SV measured by biplane left ventricular contrast angiography (LVA).

Figure 6. Bland-Altman plot comparing left ventricular ejection fraction (LVEF) measured by endocardial electromechanical mapping (EEM) with LVEF measured by biplane left ventricular contrast angiography (LVA).

were determined using biplane Simpson's method. An example of a biplane left ventricular contrast angiogram with a 30° right anterior oblique (RAO) projection and a 60° left anterior oblique (LAO) projection is shown in figure 2.

Data analysis

Bland and Altman's method was used to display the average difference and limits of agreement between EEM and LVA.¹⁶ The results are given in the form of [average - 2x standard deviation (average) average + 2x standard deviation]. A small difference to the reference is associated with high accuracy and small standard deviations are associated with high precision. Pearson's correlation coefficient was cal-

culated to assess the correlation between EEM and LVA. A p value of <0.05 was considered statistically significant

Results

Thirty-seven consecutive patients underwent both EEM and LVA assessment of global left ventricular function parameters during cardiac catheterisation. All procedures were carried out without any revascularisation or adverse events. All baseline patient characteristics are displayed in table 1.

Ventricular volumes

Average EDV measured by EEM was 148.9 ml (± 53.0 ml). Average EDV measured by LVA was

143.0 ml (± 65.5 ml). Average ESV measured by EEM was 97.7 ml. (± 48.7 ml). Average ESV measured by LVA was 72.6 ml (± 61.3 ml). Bland-Altman intervals for EDV and ESV were [-83.0 (6.5) 95.9] and [-40.6 (25.5) 91.6], respectively. Correlation (r) was 0.84 ($p < 0.001$) for EDV and 0.74 ($p < 0.001$) for ESV. The Bland-Altman plots for EDV and ESV are displayed in figures 3 and 4. Average SV measured by EEM was 51.2 ml (± 14.1 ml). Average SV measured by LVA was 70.4 ml (± 24.0 ml) ($r = 0.23$, $p = \text{n.s.}$). The Bland-Altman plot for SV is displayed in figure 5.

Left ventricular ejection fraction

The average LVEF measured by EEM was 36.5% ($\pm 9.1\%$ point). Compared with the average LVEF measurement by LVA of 53.7% ($\pm 15.6\%$ point) there was an average underestimation of -17.3% point ($\pm 11.3\%$ point). The Bland-Altman interval for LVEF was [-39.9 (-17.3) 5.4] (figure 6). The Pearson's correlation coefficient for LVEF was 0.69 ($p < 0.001$).

Discussion

The present study showed that global functional parameters by EEM correlated well with LVA. However, relatively large differences in terms of absolute values for ventricular volumes and LVEF were observed.

The data from the present study confirm the main finding of two earlier studies.^{13,14} In the study by van Langenhove et al. an underestimation of 20% point was observed for LVEF in comparison with LVA. However, in their study this was explained by an underestimation of EDV by EEM (69.1 ml vs. 125.9 ml), while there was far less difference in ESV. In our study the largest differences were seen in ESV, rather than EDV. One possible explanation could be the selected patient population in the present study. Van Langenhove et al. included all comers, where we included only patients after a large STEMI. This difference is illustrated by the larger average EDV in our study. In the study by Grothues et al. the CARTO® system (Biosense-Webster, Diamond Bar, CA, USA) was compared with cardiac magnetic resonance. They observed comparable LV volumes with both modalities. However, RV volumes measured by EEM were larger. Overall, there was a good correlation in both measurements but they concluded that the clinical interchangeability was questionable.

The difference in LVEF between EEM and LVA is considered clinically relevant and they should therefore not be used within the same patient to monitor disease progress. Although most of the difference is probably related to the intrinsic differences between both techniques there are some considerations. First, the fact that both mea-

surements are performed while different catheters are passed through the aortic valve could be responsible for some aortic insufficiency and thereby influence the measurements. Second, EEM provides a 3D image of the left ventricle where biplane LVA only provides two 2D images. Third, the main limitation of EEM is the fact the catheter has to be positioned firmly against the LV wall before a valid EEM point can be recorded. Since the only route into the LV is through the aortic valve, it is conceivable that the entire LV area can not be covered due to natural irregularities such as the chordae tendinae, the papillary muscle and trabecularisation of the LV wall.

Limitations

A limitation of the present study is the fact that LVA is not a tomographic imaging technique. However, it is the only other global LV function assessment which can be performed during a cardiac catheterisation session.

Conclusion

Although global functional parameters by EEM correlated well with LVA, the relatively large differences in terms of absolute values for ventricular volumes and LVEF render the two techniques non-interchangeable for global LV function data. ■

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