**EDITORIAL COMMENT**

**Left Ventricular Electromechanical Mapping for Determination of Myocardial Function and Viability**

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Left ventricular electromechanical mapping (LVEMM, also termed NOGA or Biosense procedure) is derived from a diagnostic and navigational guidance tool that utilizes ultralow magnetic-field sources and location sensor-tipped catheter electrodes that trace the catheter-tip position in three-dimensional (3D) space (1–3). The system reconstructs electromechanical maps of the left ventricle with minimal utilization of X-ray fluoroscopy. Primarily, LVEMM was designed for electrophysiology application for electrical activation and voltage mapping (CARTO system, Cordis-Webster, Diamond Bar, California) and ablation of arrhythmogenic foci (4–6). More recently, this system was investigated for catheter-based diagnosis of myocardial function, viability, and ischemia in the cardiac catheterization setting (7). It has been theorized that maps generated by the LVEMM system could be utilized for localization and identification of viable myocardial regions based on integration of endocardial electrical potentials and mechanical signals (8). Also, this platform technology has been used to investigate the safety, feasibility, and efficacy of strategies designed for intramyocardial therapeutics using either integrated laser energy or intramyocardial injection catheters for angiogenic gene and cell transplantation investigational strategies for alternative myocardial revascularization (9–11).

Because the system collects endocardial electrical signals (unipolar and bipolar voltages), those signals may reflect the status of myocardial viability (presence of normal or reduced voltage), and mechanical maps (end-systolic and end-diastolic volumes, ejection fraction, and local endocardial shortening) can provide global and regional contractility data for the left ventricle, compared simultaneously with those derived from electrical signals (12–14). Analysis of mapping details is based on color-coded unipolar and bipolar endocardial potentials recorded from sensor-tipped electrodes, and mechanical function represented as local endocardial shortening maps. Using the LVEMM system in various in vivo models, the average maximal and mean errors for repeated same location measurements was found to be as accurate as 1.26 ± 0.08 mm and 0.54 ± 0.05 mm, and the overall mean error for location distances measured was 0.73 ± 0.03 mm (2). Location accuracy assessment in patients was found to be 0.95 ± 0.80 (median 0.86) mm (3).

The LVEMM system was used in several animal models to identify electrical and mechanical changes during acute and chronic myocardial ischemia and myocardial infarction (12–17). Significant reduction (by ~50 to 70% from baseline values) was found in measured peak-to-peak unipolar and bipolar voltage amplitudes and local endocardial shortening signals in infarcted regions after coronary occlusion compared with baseline or noninfarcted areas (8,13–15). Using models that simulated chronic myocardial ischemia (rather than infarction), electrical signals were found to be mildly attenuated (by ~10% to 25%) in ischemic regions, while mechanical signals were significantly impaired compared with nonischemic regions (16). It was, thus, presumed that the mapping technique can provide a unique insight into myocardial ischemia from “dissociated” electromechanical measurements (mechanical impairment in stunned or hibernating myocardium and relative preservation of electrical activity vs. a decline in both parameters in infarcted segments). Moreover, in a canine model of myocardial infarction, it has been suggested that the catheter-based LVEMM technique could delineate between infarcts varying in transmurality by using electrical information derived from endocardial voltage potentials (17).

In a pilot clinical study, unipolar voltage and local endocardial shortening were measured in 18 patients with symptomatic chronic angina and preserved left ventricular function, who had reversible or fixed myocardial perfusion defects using single-photon emission computed tomography (SPECT) dual isotope imaging study (18). The results showed significant differences in voltage potentials and local shortening values between the examined myocardial segments. The average voltage potentials (14.0 ± 2.0 mV) and endocardial shortening values (12.5 ± 2.8%) were highest when measured in myocardial segments with normal perfusion and the lowest (7.5 ± 3.4 mV and 3.4 ± 3.4%) when measured in myocardial segments with fixed perfusion defects. Myocardial segments with reversible perfusion defects had intermediate voltage amplitudes and shortening values (8). Those findings were recently confirmed by another group of investigators (19), suggestive that, in patients with myocardial ischemia, electromechanical mapping enables a catheter-based assessment of myocardial viability in the cardiac catheterization laboratory.

In this issue of the Journal, Keck et al. (20) report a series of 51 patients undergoing LVEMM and correlates the maps to results of SPECT and positron emission tomography (PET) nuclear imaging and transthoracic echocardiography. The correlations found in this study between

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See page 1067

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LVEMM parameters, echocardiography, nuclear perfusion, and metabolic imaging were reasonably good. The strongest correlation that had sufficient sensitivity and specificity to have potential clinical implications was found between 99mTc tetrofosmin uptake and unipolar voltage, both obtained at rest and, in particular, when excluding the basal myocardial segments from analysis. Both electrical and mechanical parameters were highest in normally perfused segments (11.2 ± 5.0 mV and 8.2 ± 5%) and in segments with reversible ischemia (11.7 ± 4.7 mV and 7.6 ± 7.3%), as compared with segments with fixed perfusion defects (6.3 ± 3.0 mV and 3.5 ± 4.0%, p = 0.001 vs. normal and ischemic segments). Similar observations were made when calculating the QRS "fragmentation index." However, even for this correlation, it should be acknowledged that, to have a sensitivity of 90% to detect scar tissue, one must find unipolar voltage as low as 6 mV, and, to have 90% specificity to exclude the presence of scar tissue, unipolar voltage as high as 10 mV should be found. As the authors correctly pointed out in their paper, it means that a relatively large intermediate zone exists of ill-defined values and myocardial viability status. In this "gray zone," the mapping system may not be able to distinguish accurately between ischemic, scar, and normal tissue. This conclusion is also valid for the fragmentation index and, even more so, for the local endocardial-shortening algorithm, which also shows the greatest degree of scattered values.

Perhaps the most interesting finding of this study is derived from the comparison between LVEMM and PET fluorine-18 fluorodeoxyglucose (FDG) metabolic imaging in myocardial segments identified as "scar" using SPECT imaging. "Fixed" segments with preserved FDG uptake that identified preserved glucose metabolism had a significantly higher unipolar voltage and lower fragmentation index than scar tissue that had no FDG uptake using PET metabolic imaging (7.2 ± 2.7 mV vs. 6.5 ± 2.6 mV vs. 5.0 ± 3.1 mV for normal vs. limited vs. no FDG uptake, respectively, p = 0.029). The latter finding implies that in some cases LVEMM may define areas with preserved myocardial functionality in regions wherein SPECT nuclear perfusion shows no signs of myocardial viability. However, even for those signals, a wide variability of measured electrical and mechanical values exists that makes individual interpretation somewhat difficult for purposes of individual working algorithms.

Interestingly, in the current study the authors could not demonstrate changes in average unipolar voltage amplitudes within regions defined as ischemic per SPECT compared with normal perfusion areas. Whether ischemic changes can be detected by peak-to-peak unipolar voltage potential measurements is still a matter of controversy. However, based on our recent clinical report (21), it is probable that only regions with the most severe degree of myocardial ischemia (i.e., lowest perfusion grades), that extends throughout the resting phase, may cause electrical abnormalities that can be depicted by reduced voltage amplitudes recording at rest. In a recent study from our laboratory (21), we demonstrated a gradual and proportional reduction in voltage and shortening values in relation to 201Tl uptake score at rest and redistribution studies in 61 ischemic patients with relatively preserved left ventricular function. According to those findings, unipolar voltage >7.4 mV and local shortening >5.0% had a sensitivity of 78% and 65%, respectively, with a specificity of 68% and 67% to detect viable myocardial segments. Also, unipolar voltage values of 12.3 mV and 5.4 mV had 90% specificity and sensitivity, respectively, to predict viable tissue, data similar, although not identical, to those of Keck et al. (20).

In another study (22) the use of LVEMM was evaluated to distinguish between nonviable and viable myocardium in 31 patients with ischemic cardiomyopathy having a mean ejection fraction of 30%. Unipolar voltage amplitudes and local shortening was compared with dysfunctional regions, identified by 3D echocardiography and characterized as nonviable using PET imaging. The optimum nominal discriminatory unipolar voltage amplitude between nonviable and viable dysfunctional myocardium was 6.5 mV in that study. As in other works, a great overlap was observed between groups of viable and nonviable myocardial segments. Between-patient variability was the main component responsible for the large variability of measured data. However, when normalized amplitudes were used in this particular study (e.g., highest amplitude expressed as 100%), an improved discriminatory value was found, with a 78% sensitivity and specificity for the normalized value compared with 68% of the nominal value in distinguishing between a viable and nonviable myocardium. It was, thus, appropriately concluded that, although endocardial electrical amplitude mapping allows distinction between viable and nonviable areas in ischemic cardiomyopathy patients, this technique displays a wide scatter and that a better distinction could be obtained using individual normalization of voltage amplitude values.

A major question that arises from the above cited works is: "What is the potential merit of LVEMM as an invasive diagnostic method designed for assessing myocardial viability or ischemia in the cardiac catheterization laboratory?" It has been proposed by the authors (20) as well as others (7), that, in patients without recent assessment of myocardial viability who undergo coronary revascularization, information concerning regional viability might be useful for clinical decision-making before revascularization procedures. Also, this mapping technique may assist efficient delivery of catheter-based therapy in patients with left ventricular dysfunction who undergoing catheterization by providing online assessment of viability. However, the study by Keck et al. (20) also highlights that more data is still needed for enabling improved differentiation between viable and nonviable regions and between ischemic and normally perfused myocardium. As observed in most previous studies that involved validation of LVEMM, this study found considerable overlap in the electromechanical mapping values
between groups. The overlap is probably caused by differences in methods of LV segmentation used for the 3D LVEMM compared with the nuclear, metabolic, and echocardiographic imaging techniques where regions of normal, ischemic, viable, and scarred myocardium do not fall exactly within segmental borders. As a result, each segment may traverse the boundaries between regions of differing viability and contractility. Scattering may also result from a true variability between individual patients in endocardial voltage amplitudes "output" and the impact of left ventricular thickness and dimension upon measured values and algorithms used to assessing global and regional mechanical activity. A greater overlap between scattered nominal data is still a limitation of the mapping technique that could be improved by normalizing measured electrical and mechanical values by using improved electromechanical algorithms. It should be notable that the threshold values to define myocardial viability are not uniform among the studies. Voltage amplitudes within a range of 7 mV to 9 mV might represent viable tissue in one patient as in another case this may represent a nonviable tissue, especially when high (e.g., >15 mV) normal "reference" electrical values coexist. Another limitation of using the LVEMM technique is the lack of viability assessment in relation to changes in regional mechanical or electrical functions after coronary revascularization procedures. A recent study showed that voltage mapping enabled the prediction of functional recovery in regional and global left ventricular function among 46 patients with prior myocardial infarction who underwent coronary revascularization and compared with FDG PET and Tc-99m sestamibi SPECT (23). Regional unipolar electrogram amplitude was 11.0 ± 3.6 mV in regions with normal perfusion, 9.0 ± 2.8 mV in regions with reduced perfusion and preserved FDG-uptake, and 6.5 ± 2.6 mV in scar regions (p < 0.001). At a threshold amplitude of 7.5 mV, the sensitivity and specificity for detecting viable (by PET/SPECT) myocardium were 77% and 75%, respectively. Functional recovery was further assessed in 25 patients with a follow-up angiography using the centerline method. In infarct areas with electrogram amplitudes >7.5 mV, improvement of regional wall motion from −2.4 ± 1.0 per chord to −1.5 ± 1.1 per chord (p < 0.01) was observed, whereas, in infarct areas with amplitudes <7.5 mV, wall motion remained unchanged at follow-up. More data are needed, however, to validate those promising findings. In addition, the appropriate thresholds for defining myocardial viability and ischemia should be determined more definitively before a widespread use of this technique could be recommended for routine diagnostic purposes. Finally, mapping techniques should become: 1) faster; 2) simplified; and 3) uniformly taught and practiced to enable more generalized use of the technique and adequate comparison between operators and centers.

Before such data from endocrical mapping will be useful in decision-making about whether to perform revascularization procedures, considerably more work is required and especially in patients with impaired myocardial function who are candidates for conventional (e.g., angioplasty or bypass surgery) or "alternative" (e.g., direct myocardial revascularization or angiogenesis-promoting interventions) myocardial revascularization procedures. It remains to be established whether such precise localized diagnosis directed towards viable myocardial zones and coupled with myocardial revascularization would enhance the therapeutic benefit obtained by myocardial revascularization procedures whether or not preceded by noninvasive studies. The answer to these questions will dictate whether left ventricular mapping is, indeed, ready for "prime time" as a diagnostic cardiac procedure.

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