Online Myocardial Viability Assessment in the Catheterization Laboratory via NOGA Electroanatomic Mapping
Quantitative Comparison With Thallium-201 Uptake

Mariann Gyöngyösi, MD, PhD; Heinz Sochor, MD, FESC; Aliashgar Khorsand, MS; Lior Gepstein, MD, PhD; Dietmar Glogar, MD, FESC

Background—The aim of this prospective study was to investigate the concordance between quantitative resting $^{201}$Tl uptake as an established myocardial viability index and the electrical activity of the heart, determined by NOGA nonfluoroscopic electroanatomic mapping.

Methods and Results—The myocardial resting and late resting thallium uptakes of 384 myocardial segments from 32 patients (27 males aged 65 ± 8 years) with previous myocardial infarction and chronic stable angina were compared with unipolar voltage potentials and local shortening of the left ventricle as assessed by electroanatomic mapping. The quantitative thallium uptake data were analyzed by polar map analysis by division into 12 comparable myocardial segments, as represented in electroanatomic mapping images. Unipolar voltage potentials exhibited a significant logarithmic correlation with both resting and late resting thallium uptake (attenuation corrected: $r=0.660$ and $r=0.744$; non-attenuation corrected: $r=0.623$ and $r=0.721$). Receiver operator characteristic analyses revealed unipolar voltage cutoff points of 12.0 mV (predictive accuracy 0.853, $P<0.001$; sensitivity/specificity 81%) for normal myocardium and 6.4 mV (predictive accuracy 0.901, $P<0.001$; sensitivity/specificity 82%) for nonviable myocardium assessed by attenuation-corrected $^{201}$Tl late resting images and of 12.7 mV (predictive accuracy 0.822, $P<0.001$; sensitivity/specificity 75%) and 6.5 mV (predictive accuracy 0.808, $P<0.001$; sensitivity/specificity 73%) for non-attenuation-corrected late resting $^{201}$Tl images.

Conclusions—These results indicate that the unipolar voltage potentials obtained by electroanatomic mapping correlate well with standard quantitative late resting $^{201}$Tl imaging for the evaluation of myocardial viability; thus, NOGA endocardial mapping provides useful “online” data at the time of catheterization, especially when information from other methods for viability assessment is unavailable. (Circulation. 2001;104:1005-1011.)

Key Words: mapping ■ radioisotopes ■ scintigraphy ■ catheterization ■ coronary disease

In the diagnosis of viable myocardium, $^{201}$Tl resting and late resting myocardial perfusion imaging is an acceptable and frequently applied method that offers the attractiveness of its noninvasive nature paired with its ability to provide regional information. One disadvantage of this viability assessment, shared by other noninvasive imaging techniques, is the time and spatial separation from cardiac catheterization. With the increasing number of percutaneous coronary interventional procedures, online information concerning the presence and extent of viable myocardial territories in the catheterization laboratory would be desirable.

Nonfluoroscopic catheter-based electroanatomic mapping offers the possibility of simultaneous assessment of electrical activation and local mechanical response of the heart. The first preliminary data of Ben-Haim et al4 and Gepstein et al5,6 suggested that an infarcted myocardium could be accurately diagnosed and distinguished from a healthy myocardium by virtue of the reductions in both electrical voltage and mechanical activity assessed by the NOGA (Biosense Webster, Inc) system.4–9 Additionally, the serial recording of left ventricular endocardial ECGs allows the characterization of the 3D architecture of myocardial infarction and the detection of still-viable myocardial zones.4,7,10 Endocardial mapping findings from animal experiments and phantoms, which revealed the possibility of online myocardial viability assessment in the catheterization laboratory, were subsequently quickly used in humans, first by Kornowski et al in 1998.7 Kornowski et al11 also compared the viability assessment of
were performed according to institutional guidelines. Informed consent was obtained from all patients, and all procedures were performed under fluoroscopic control.

The aims of the present prospective clinical study were to evaluate the diagnostic value of endocardial electroanatomic mapping in myocardial viability assessment and to compare the results of this invasive method with those of noninvasive 201 Tl resting and late resting perfusion imaging, applying a comparable quantitative polar map reference system for both techniques.

Methods

Patients

Thirty-two patients (27 males aged 65±8 years) with at least 1 significant coronary artery stenosis, previous myocardial infarction, stable angina pectoris, and left ventricular ejection fraction >30% were enrolled in the study. Patients with valve disease, peripheral vascular disease, left ventricular thrombus, left ventricular ejection fraction ≤30%, unstable angina pectoris, and recent (within 3 weeks before the mapping procedure) myocardial infarction were excluded. All patients underwent 201 Tl resting/late resting myocardial imaging 2±2 days before coronary catheterization and the electroanatomic mapping procedure. Informed consent was obtained from all patients, and all procedures were performed according to institutional guidelines.

NOGA Electroanatomic Mapping

As described previously,4–6 the mapping procedure utilizes the following components: a triangulation location pad with 3 coils that generate an ultralow magnetic field energy, a stationary reference field sensor, and the NOGA silicon graphic monitor. By steering the deflectable mapping catheter tip randomly to multiple left ventricular endocardial sites, the NOGA processing system reconstructs the left ventricular anatomy in 3 dimensions, presented in real time. Normal myocardial cells furnish a resting unipolar potential of ≥15 mV, whereas voltage values <5 mV reflect scar tissue; potentials between 5 and 15 mV suggest still-viable myocardium.3–9 Local linear shortening of the left ventricular wall denotes regional contractility and is calculated on the basis of a formula.5,6 Normal, hypokinetic, akinetic, and dyskinetic myocardium corresponds to regional linear shortening values of ≥12%, 2% to 12%, <2%, and negative values, respectively. After data processing, both electrical and mechanical maps are also displayed as quantitative polar maps.

Electroanatomic Mapping Procedure

After diagnostic coronary angiography and contrast ventriculography were performed, a 7F mapping catheter was introduced into the left ventricular cavity under fluoroscopic control, and electroanatomic mapping was performed. After completion of the map, the mapping points of the internal sites of the left ventricle were deleted. The polar map analysis involved 12 myocardial segments (septal, anterior, lateral, and inferior/posterior, all regions being further divided into apical, mid, and basal segments), and the mean values of the points of each segment were calculated.

Resting and Late Resting Myocardial Perfusion Scintigraphy With 201 Tl

Myocardial single photon emission computer tomography (SPECT) was performed at rest and late rest, immediately and 4 hours after intravenous injection of 3 mCi of 201 Tl. SPECT images were acquired with the use of a noncircular clockwise orbit with a dual detector camera (VertexMCD, ADAC Laboratories). A total of 32 projections (16 per head) were obtained as a 64×64 matrix, with a step-and-shoot acquisition over a 180° arc extending from the 45° right anterior oblique to the 45° left posterior oblique position. The acquisition zoom was 1.46, which gave a pixel size of 6.46×6.46 mm. The energy windows were 70±14 keV and 167±33.4 keV. Images were acquired for 50 seconds per projection for a total imaging time of 13.5 minutes. A transmission scan was made simultaneously with gadolinium, which required 30 seconds per projection. The uncorrected emission data were reconstructed by a filtered back-projection with Butterworth filter (cutoff 0.5 analytic, tenth order). The attenuation-corrected acquisition data were normalized to the reference scan and logarithmic inversion, followed by reconstruction by filtered back-projection with Butterworth filter and a maximum likelihood expectation maximization algorithm with 12 iterations. The software for attenuation and the scatter correction algorithm is fully automated (Vantage, ADAC Laboratories; ExSPECT, Emory University, Atlanta, Ga). SPECT images were transferred to an image-analysis workstation (Onyx, SGI) for image reorientation and polar map analysis with Munich Heart software. Polar map images were subdivided into 12 segments as for electroanatomic mapping, and segmental average values of tracer uptake were derived. Because we reconstructed the polar map of the 201 Tl uptake in a similar mode as in endocardial mapping, a direct comparison of the endocardial voltage/local shortening and 201 Tl tracer uptake was possible (Figure 1).

Statistical Analysis

Data are expressed as mean±SD for continuous variables and as percentages for categorical variables. The unpaired Student t test was used for data comparison between groups. For testing of the correlation between 2 images, regression analysis was used. The cutoff points of unipolar voltage values determining the nonviable,
viable, and normal myocardial areas were established with receiver operating characteristic (ROC) curves, which presented the best cutoff points, the predictive accuracy, and the sensitivity and specificity. Statistical significance was considered present if $P<0.05$. The statistical analyses were performed with the standard SAS package and the CLABROC and LABROC computer software designed by Metz et al.12

Results

Clinical Data
Fifteen patients had had previous anterior, 9 patients infero-posterior, and 8 patients lateral-posterolateral myocardial infarction 4.2±4.1 years before the endocardial mapping procedures. Coronary angiography revealed single-vessel disease in 7 patients, 2-vessel disease in 8 patients, and 3-vessel disease in 17 patients; 11 patients had undergone a previous aortocoronary bypass operation. Contrast ventriculography indicated a mean ejection fraction of 40±8%. Mean endocardial mapping time was 37±13 minutes. The total radiation dose due to fluoroscopy orientation during mapping was 5014±2524 cGy/cm². After careful filtering of the internal points of the left ventricle, the mean number of points drawing the left ventricular silhouette was 81±14. No left ventricular perforation was detected immediately after endocardial mapping assessed by transthoracic echocardiography.

Correlation Between Myocardial Perfusion Scintigraphic Data and Endocardial Unipolar Voltage Values

With the 12-segment analysis of both perfusion scintigraphy and endocardial mapping, 384 segments of the 32 patients were analyzed. Because the septal and posterolateral basal segments in the polar map analysis of the endocardial mapping contain the low-voltage values of the mitral valve apparatus and heart base,7 these basal segments were excluded from additional analyses. Additionally, 19 segments containing fewer than 3 points were also excluded to minimize sampling errors. Thus, the average voltage and local linear shortening values of 269 segments were compared and correlated with the resting and late resting $^{201}$TI tracer uptakes demonstrated by the corresponding polar map analysis.

Frequency distribution analysis revealed normal (gaussian) distribution for linear shortening values and nonnormal distribution of unipolar voltage values, with a peak frequency of 20.3% for values between 10.0 and 12.5 mV. In contrast, all $^{201}$TI uptake images exhibited skewed distributions, with a peak frequency of 22.3% for non–attenuation-corrected late resting images, 26.9% for attenuation-corrected late resting images, 26.8% for non–attenuation-corrected resting images, and 32.4% for attenuation-corrected resting images for uptake values between 70% and 80%. After logarithmic transformation of the unipolar voltage values, the frequency distribution curve of the unipolar voltage values displayed a similarly skewed distribution pattern as for the $^{201}$TI images (Figure 2).

Endocardial voltage values exhibited good logarithmic correlation with attenuation-corrected late resting $^{201}$TI values ($r=0.744, P<0.001$), whereas the correlation between resting $^{201}$TI images and endocardial voltage values was weaker ($r=0.660, P<0.001$; Figure 3). The non–attenuation-corrected $^{201}$TI images showed a somewhat worse correlation with endocardial voltage values (late resting $r=0.721$, $P<0.001$; resting: $r=0.623, P<0.001$). According to the nongaussian distribution of the endocardial voltage values, the logarithmic correlation proved to furnish a better fit than the linear correlation between the voltage values and resting $^{201}$TI uptakes (linear correlation by late resting/resting attenuation-corrected images: $r=0.697$ and $r=0.554$; non–attenuation-corrected late resting/resting images: $r=0.606$ and $r=0.507$). The endocardial voltage values of the anterior (648 total mapping points), septal (679 mapping points), posterior (638 mapping points), and lateral (640 mapping points) myocardial segments furnished similarly good correlations with $^{201}$TI imaging (Table 1).

Because resting $^{201}$TI uptake reflects myocardial perfusion and late resting $^{201}$TI uptake is more closely related to myocardial viability,13 which also indicates the integrity of the myocardial membrane and potassium pool, the results of
late resting $^{201}$TI images were compared with endocardial mapping results in the further viability assessment (Figure 4). Forty-seven segments that exhibited late resting $^{201}$TI uptake between 40% and 60% (most questionable viable areas) displayed a wide scattering of voltage values (range 3 to 10 mV, mean 6.5±2.8 mV) without any significant correlation between the 2 images; however, 62% of the obtained endocardial points of this area exhibited voltage values ≥5 mV, which indicated a still-viable myocardium.

**Endocardial Voltage and Local Linear Shortening Values in Moderate and Severe Perfusion Defects**

In all patients, severe perfusion defects on late resting $^{201}$TI imaging were present in 66 segments ($^{201}$TI uptake ≥50%), whereas 112 segments exhibited moderate defects ($^{201}$TI uptake 51% to 75%) and 91 segments were normal ($^{201}$TI uptake 51% to 75%) and 91 segments were normal ($^{201}$TI uptake <50%). Accordingly, significantly decreased unipolar voltage potential and local linear shortening values were measured in moderate and severe perfusion defects (Table 2).

ROC analyses revealed unipolar voltage cutoff points of 12.0 mV (predictive accuracy 0.853, P<0.001; sensitivity/specificity 81%) and 6.4 mV (predictive accuracy 0.901, P<0.001; sensitivity/specificity 82%) for normal and nonviable myocardium assessed by attenuation-corrected $^{201}$TI late resting images and 12.7 mV (predictive accuracy 0.822, P<0.001; sensitivity/specificity 75%) and 6.5 mV (predictive accuracy 0.808, P<0.001; sensitivity/specificity 73%) for non–attenuation-corrected late resting thallium images, respectively. The relatively low predictive accuracy (<0.6) and low common sensitivity and specificity (<60%) values did not allow calculation of significant cutoff values for linear shortening.

When the myocardium was divided into infarcted and noninfarcted areas on the basis of the clinical and echocardiographic data, the infarcted myocardial zones presented significantly lower $^{201}$TI late resting uptake, endocardial voltage, and linear shortening values than those for noninfarcted myocardium (attenuation-corrected $^{201}$TI late resting uptake 52±18% versus 72±14%, P<0.05; non–attenuation-corrected $^{201}$TI late resting uptake 49±17% versus 69±16%, P<0.05; endocardial unipolar voltage 7.1±2.4 versus 13.3±3.0 mV, P<0.05; local linear shortening 6.1±5.6% versus 10.5±5.2%, P<0.05, respectively).

**Evaluation of Local Linear Shortening Values**

Local linear shortening values correlated only weakly with endocardial voltage values (best correlation with linear regression analyses was $r=0.489$, $P<0.001$). Neither late resting nor resting $^{201}$TI uptake exhibited a significant correlation with local linear shortening values ($r=0.342$ and $r=0.310$ for attenuation-corrected and $r=0.297$ and $r=0.151$ for non–attenuation-corrected $^{201}$TI images, respectively).

Moderately decreased endocardial voltage values with moderately to severely depressed local linear shortening values were observed in 21 (66%) of the 32 patients (Figure 5). Interestingly, the endocardial map showed completely preserved electrical activity with preserved tracer uptake, but severely decreased local wall motion was assessed by NOGA mapping in 3 patients (electromechanical dissociation; Figure 6). In contrast, despite the decreased unipolar voltage, normal linear shortening values were seen in 8 patients with paradoxical wall motion due to an apical aneurysm in 4 patients, complete left bundle-branch block in 1 patient, and a ventricular pacemaker in 3 patients.

**Discussion**

The present study demonstrates that the left ventricular endocardial voltage map parallels viable myocardial tissue...
with sufficient accuracy, displaying a good concordance with late resting 201Tl myocardial uptake, as a classic reference approach for myocardial viability assessment. ROC analyses revealed unipolar voltage cutoff points of 12.0 mV for normal myocardium and 6.4 mV for nonviable myocardium assessed by attenuation-corrected 201Tl late resting images and 12.7 and 6.5 mV, respectively, for non–attenuation-corrected 201Tl late resting images. Twenty-one (66%) of the 32 patients showed concordant moderate decreases in endocardial voltage, local shortening, and 201Tl uptake, whereas contradictory voltage and linear shortening values were present in 11 patients. Good logarithmic correlation between overall endocardial voltage values and late resting 201Tl data were found; the voltage values of the different left ventricular areas displayed a similarly good concordance with attenuation-corrected 201Tl late resting uptake, with a correlation coefficient range between 0.825 (septal) and 0.709 (lateral).

The relationships between 201Tl images and endocardial voltage signals and local shortening values were determined by use of both attenuation-corrected and non–attenuation-corrected 201Tl images because there are questions concerning the commercially available attenuation techniques. For the attenuation correction, we used the package of ADAC Laboratories, which has been proven to provide significant improvements in the normalcy rate without a decline in overall sensitivity. In the present study, the attenuation-corrected 201Tl images showed a better overall correlation with endocardial voltage values and a higher predictive accuracy for the cutoff points that determined viable and nonviable myocardium than the non–attenuation-corrected images.

ROC analyses revealed lower cutoff values for normal myocardium and higher cutoff values for still-viable myocardium than the recommendations of the NOGA guidelines. Further noninvasive viability studies that include other methods are needed to confirm these new cutoff values for endocardial mapping.

Similarly to the semiquantitative analysis of Kornowski et al,11 we found severely depressed endocardial voltage and local shortening values in the myocardial segments that exhibited severe perfusion defects and moderately decreased voltage and local shortening values in segments that dis-
played $^{201}$Tl late resting uptake in the interval of 51% to 75%. The use of 50% peak activity as a threshold for viability determination was based on the value derived for $^{201}$Tl from a variety of studies in which an independent assessment of viability (positron emission tomography and serial scintigraphy) was made.15–17

Theoretically, more precise separation of viable from nonviable myocardium would be desirable at the invasive evaluation in myocardial tissues that exhibit late resting $^{201}$Tl uptake, especially between 40% and 60%. However, these areas contain variable amounts of viable and nonviable cells and are thus characterized by a wide range of voltage values in endocardial mapping; this scatter is undesirable but reflects an almost unavoidable limitation of mapping due to a coexistence of differently viable cells. Nevertheless, 62% of segments in this “intermediate injury” zone did exhibit voltage values suggestive of residual viability (>5 mV).

Infarcted myocardium exhibited significantly lower endocardial voltage and linear shortening values, paralleling the significantly decreased $^{201}$Tl uptake. Interestingly, noninfarcted myocardium in the present series also exhibited slightly decreased voltage and linear shortening values compared with normal values in the published NOGA guidelines, even if the unipolar voltage values of noninfarcted myocardium were just higher than the cutoff values for normal myocardium derived in our patients. Nevertheless, our findings are in accordance with those of Kornowski et al.,11 who found that 3 weeks after left anterior descending coronary artery occlusion in pigs, the remote healthy zone exhibited slightly decreased voltage and linear shortening values. The reason for this can only be speculative: an early or late incipient ventricular remodeling, together with myocardial cell damage, is probably responsible for the phenomenon. An alternative explanation might be remote ventricular strain or presence of multivessel disease.

The parallel myocardial scintigraphy and electroanatomic mapping studies differentiated 2 distinct but partially similar patterns that suggested residual viability. One involved concordant moderate decreases in myocardial perfusion, electrical voltage, and linear shortening, which may result from a reduced voltage in ischemia (slow conduction and reduced amplitude of the action potential in ischemic cells) and/or fibrosis in the mixed area of infarcted and viable tissues. The second was completely preserved electrical activity with normal myocardial perfusion but severely reduced segmental myocardial wall motion. Similar to the latter pattern, Fuchs et al.18 concluded that the electromechanical mapping procedure may be of diagnostic value for identifying zones of hibernat-
ing myocardium. However, myocardial hibernation is much more complex: it is considered a state of persistent left ventricular dysfunction that results from chronically reduced blood flow, which is improved or reversed after successful myocardial revascularization.\textsuperscript{19,20} Although preserved electrical activity with decreased local shortening suggests the presence of hibernating myocardium, it is highly questionable whether endocardial voltage values really represent the electrical status of the transmural myocardium (an extensive subendocardial scar might still have transmural viability) and whether endocardial voltage and linear shortening values improve after coronary revascularization. Because the present study did not furnish follow-up data, we cannot address these questions. There have been no published studies in which baseline and follow-up endocardial mapping have been applied after coronary interventions, and thus the suggestion of hibernating myocardium presented by endocardial mapping remains elusive.

The endocardial mapping procedure exhibited discordant results in 8 patients with normal segmental linear shortening values despite decreased myocardial perfusion and voltage. This is probably related to incomplete determination of local linear shortening values, because the present software calculates local shortening on the basis of the maximum and minimum volumes instead of the ECG-triggered end diastole and end systole. Consequently, paradoxical wall motion that results in increased volume at end systole may lead to paradoxical electromechanical dissociation.

In conclusion, we found a highly significant correlation between endocardial voltage potentials and \textsuperscript{201}Tl late resting uptake, which confirms our hypothesis that endocardial mapping can aid in the diagnosis and distinction of viable and nonviable myocardium online in the catheterization laboratory.

**Study Limitations**

It was necessary to exclude basal septal and posterolateral segments from the analysis, because polar map analysis contains low-voltage values of basal myocardial segments adjacent to mitral valve apparatus. To avoid the misinterpretation of these low-voltage basal areas, 2 steps may be taken: (1) delete basal segmental points before the polar map analysis or (2) modify present software according to this direction, while exclusion of basal segments from the statistical analysis does not resolve the problem of misalignment between NOGA-based and tracer-related maps. However, we tried to minimize this problem by use of a comparable polar map system, further using a segment-averaging approach for actual segmental values. Additionally, there is a fundamental difference in the mode of “sampling” itself; mapping represents a discrete collection of points, whereas tracer uptake is the result of a tomographic imaging technique. Nevertheless, especially for the clinically relevant distinction of normal, moderately reduced, severely reduced, or absent viability, a good concordance was observed.

**References**

Online Myocardial Viability Assessment in the Catheterization Laboratory via NOGA Electroanatomic Mapping: Quantitative Comparison With Thallium-201 Uptake
Mariann Gyöngyösi, Heinz Sochor, Aliashgar Khorsand, Lior Gepstein and Dietmar Glogar

Circulation. 2001;104:1005-1011
doi: 10.1161/hc3401.095099

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/104/9/1005

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/