Evaluation of inotropic changes in ventricular function by NOGA mapping: comparison with echocardiography

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The assessment of ventricular function is a cornerstone in the field of cardiovascular pathophysiology. The dynamic contraction of the left ventricle (LV) can be assessed by several methods, including echocardiography, magnetic resonance imaging (MRI), electron-beam computed tomography (CT), radioisotope scanning, and contrast ventriculography. Of these, only the last is regularly used in the catheterization laboratory; however, it requires the administration of large amounts of iodine-based contrast medium and relatively high doses of X-ray exposure. Recently, NOGA electromechanical mapping was developed as a means of assessing regional and global ventricular contraction in the catheterization laboratory (1, 7, 11). It has the advantage of providing color-coded quantitative maps of regional LV mechanical and electrical function, superimposed on contracting three-dimensional (3D) reconstructions of the LV endocardial surface. The technique is unique physiologically, as it is the only method in clinical use that uses actual endocardial tissue tracking to measure true endocardial shortening. Our group and others have demonstrated that NOGA can accurately measure ventricular volume (9) and that, on a regional level, it can distinguish between grossly normal and abnormal myocardium (5, 6, 11, 13, 18). However, a thorough quantitative evaluation of the algorithms involved in determining regional and global function is lacking. Also, a search of the literature shows only one direct quantitative evaluation of regional function assessment by NOGA with standard imaging techniques (25), in this case ventriculography.

NOGA has also been developed as a treatment strategy for providing percutaneous myocardial delivery of local therapies via its catheter (10, 12, 14, 15, 21, 22, 24). This requires prior identification of regions of ischemic or malfunctioning myocardium, based on assessment of regional function. The degree of malfunction may vary from mild to severe and may only be elucidated by forms of pharmacological stress. This underscores the importance of assessing the accuracy and sensitivity of the algorithms used to assess regional and global function by NOGA. Clearly, a...
direct numerical comparison between conventional standards and NOGA-derived parameters of LV function and their sensitivity to pharmacological stress is necessary. Because echocardiography is the most widely used method to evaluate LV function in clinical practice, it was chosen as the gold standard.

We, therefore, performed a study in the pig model with the following objectives: 1) to determine the accuracy of NOGA-derived regional function, defined as local shortening (LS), compared with circumferential shortening (CS), as derived by both NOGA (CS\textsubscript{NOGA}) and echocardiography (CS\textsubscript{ECHO}); 2) to compare NOGA-derived global ejection fraction (EF) (EF\textsubscript{NOGA}) with echocardiography-derived EF (EF\textsubscript{ECHO}); 3) to determine the sensitivity of the NOGA system to positive and negative inotropic stimuli (dobutamine and propranolol); and 4) because regional function of the LV is known to be inhomogeneous, we also aimed to evaluate regional differences in LS for the different conditions studied and to compare our results with those from the literature.

**Methods**

**NOGA procedure.** This nonfluoroscopic electromechanical mapping system has been described elsewhere (1, 7–9). Briefly, the system uses ultralow electromagnetic fields, generated by an external triangular magnetic field emitter located at the catheterization table, to accurately determine the localization and orientation of a miniature location sensor situated close to the tip of a 7-F deflectable-tip-tip electrophysiology catheter (NAVISTAR, Biosense Webster), henceforth referred to as “the catheter.” This allows continuous tracking of the exact position of the tip of the catheter over time and thus the location of the endocardial site with which the catheter tip is in contact. The procedure involves sequential mapping of endocardial points until the whole endocardial surface is adequately reconstructed. For each endocardial point, local unipolar and bipolar electrocardiographic signals are obtained, as well as the exact position and motion of the endocardial site in contact with the catheter. Knowledge of the position of the endocardium over time allows one to calculate indexes of regional and global myocardial function, such as EF and regional shortening (6, 9, 17).

**Experimental protocol.** Studies were performed on 10 young pigs, weighing from 30 to 45 kg. The experimental protocol was approved by the Animal Use and Care Committee of the Technion Faculty of Medicine and conforms with the “Guide for the Care and Use of Laboratory Animals” published by the US National Institutes of Health (NIH publication No. 85-23, revised 1996).

The animals were premedicated with 20 mg/kg intramuscular ketamine and 0.5 mg/kg intramuscular diazepam. After establishing intravenous (IV) access, 30 mg/kg IV pentobarbital were administered, and tracheal intubation was performed. Ventilation was maintained with a Harvard mechanical respirator. Anesthesia was maintained with 1.5% isoflurane. IV heparin 5000 U was given to prevent thrombus formation on the catheter. A reference mapping catheter was sutured securely onto the skin on the pig’s back to account for possible movement during the procedure. Cannulation of a carotid artery and jugular vein was performed, and a pacing electrode was placed in the right atrial appendage. Because dobutamine and propranolol are associated with significant changes in heart rate, which may affect myocardial function and make evaluation difficult, each study was performed at a constant heart rate throughout. Pacing was established at a cycle length of 420–440 ms, depending on resting heart rate. Pigs were then placed in the supine position, the catheter was introduced via the carotid artery to the aortic root by using fluoroscopy, and the valve was crossed with the catheter tip in full flexion.

Baseline maps of the entire LV were then acquired, as described previously (1, 7, 9). The first three points were acquired with the aid of fluoroscopy and, thereafter, with only the Silicon Graphics workstation, which depicts, in real time, the catheter tip’s position and direction in relation to the reconstructed LV surface. After the catheter was removed from the LV, each pig was placed in the left decubitus position, and baseline short-axis echocardiographic images of the LV at the papillary muscle level were obtained by using a Vingmed 725CMF machine with a 3.25-MHz mechanical transducer and were recorded on videotape for later off-line analysis.

An infusion of IV 5 μg·kg\(^{-1}\)·min\(^{-1}\) dobutamine was begun, and, after waiting for ~10 min for a steady state to be reached, short-axis echocardiographic images were obtained as described. Thereafter, the pig was remapped with NOGA as before. The original protocol included studying a second dose of dobutamine (10 μg·kg\(^{-1}\)·min\(^{-1}\)); however, it was seen to introduce various problems, including severe irritability of the LV causing arrhythmias and an increase in the heart rate to a rate above the pacing rate. This protocol was thus abandoned after the first four animals. After completion of the NOGA map, dobutamine infusion was stopped. Pacing was also temporarily stopped to monitor the heart rate in normal sinus rhythm. The pig was allowed ~20 min for the effect of dobutamine to wear off, and the heart rate was noted.

Boluses of IV propranolol were then given until the heart rate reached a plateau of ~60–70 beats/min. Pacing at the same cycle length was then restarted, and, after waiting a few minutes for steady state to be reached, echocardiograms and NOGA maps were once again performed. Every 15 min during mapping, a small, additional dose of propranolol (~1 mg) was given. In some experiments, IV lidocaine was given in 40-mg doses as needed to reduce excessive ventricular ectopy. At the end of the experiment, pigs were killed with an overdose of pentobarbital.

**Analysis of NOGA maps.** After mapping the LV, manual editing was performed to remove unsatisfactory points, according to the following criteria: points with signs of poor stability, as described in previous studies (6, 9); internal points; premature beats; points with excessive catheter pressure, as evidenced by ST elevation on the local electrogram; and points on the mitral valve, left atrium, or aorta, identified according to their position and the presence of P waves on the bipolar electrogram. Because mechanical alternans was noted in all pigs during the propranolol stage, all point trajectories underwent a temporal smoothing algorithm, based on the fast-Fourier transform over the 3 s of recorded data (~7 cycles), to produce a representative trajectory at each point. The phenomenon of mechanical alternans has been described previously during rapid pacing (2) and appears to be related to delayed intracellular calcium cycling. Another smoothing algorithm was applied to the trajectories on a spatial level, based on the assumption that nearby trajectories behave similarly. This smoothed cases in which individual points moved differently from their neighbors.

Each reconstructed LV was then divided along its long axis into three equal zones, apex, midzone, and base, and each of
these zones was divided circumferentially into four sectors, septum (30°–150°), posterior wall (150°–230°), lateral wall (230°–310°), and anterior wall (310° through 0°–30°, with 0° being anterior chest wall and anticlockwise direction). To correspond with the parasternal short-axis echocardiographic slice in terms of anatomy, only the midzone sectors were used for regional analysis. Regional midventricular shortening was defined as local endocardial shortening, averaged for the four sectors in the mid-LV (posterior, lateral, and anterior walls, and septum).

**LS.** The fact that any two points on the healthy endocardial surface move closer to each other during contraction is used as the basis of the algorithm, which has been described previously (6, 11) and is briefly summarized. For any point \( p \), it is based on the following equation

\[
LS_p = \sum_{i=1}^{n} \frac{L_{ED}^{p_i} - L_{ES}^{p_i}}{L_{ED}^{p_i}} \cdot \frac{1}{n}
\]

where \( i = 1 \ldots n \) are the sampled points on the map surrounding point \( p \), and \( L_{ED}^{p_i} \) and \( L_{ES}^{p_i} \) are the lengths of the line segments joining \( p \) and \( p_i \) at end-diastole (ED) and end-systole (ES), defined as the time of maximum and minimum ventricular volumes, respectively. A weighting algorithm takes into account the density of the points surrounding \( p \), the volume of the ventricle, and the distance of each point from \( p \), with the aim of giving negligible weight to points that are distant (>15 mm) or too close (<5 mm = noise range).

**CSNOGA and area shortening by NOGA.** Because LS is the only parameter returned by the NOGA system for evaluating regional function, we derived two other functions off-line, to mimic the two echocardiography parameters of the same name, i.e., CS and area shortening (AS). We evaluated a 5-mm-thick short-axis slice of the reconstructed LV, perpendicular to its long axis at the center of mass at ED. Points on the surface of the reconstructed LV were assumed to lie on a single plane at the center of the slice to construct a short-axis two-dimensional (2D) image of the endocardial contour in this plane, resembling the short-axis 2D echocardiogram. At ES, we analyzed the slice of LV that had moved into the exact same zone during contraction, i.e., to mimic the echocardiogram, we did not follow the same endocardial locations from diastole to systole, but chose the previously out-of-plane locations, which had since moved into the plane as defined at ED. From these reconstructed images, AS and CS were calculated.

**Global EFNOGA.** This was calculated from the internal volumes as derived from ED and ES 3D reconstructions (see Fig. 1). Because the endocardial surface can be divided into a series of adjacent triangles, internal volumes could be calculated as the sum of volume tetrahedrons, where each tetrahedron is made up of a triangle of points on the endocardial surface and the center of mass of the ventricle (9).

**Analysis of echocardiographic images.** As described, good-quality parasternal short-axis images at the midpapillary muscle level were recorded on videotape. Two short-axis 2D loops were digitized from the videotape on an Acuson Sequoia ultrasound machine. From each of the two loops, two consecutive cycles were chosen for analysis to control for the effect of the mechanical alternans during the propranolol stage. To overcome the problems presented by the presence of papillary muscles and of the poorer lateral resolution of the images inherent in short-axis images, the endocardial border was visually approximated by the closest fitting ellipse at ED and at ES, defined as the largest and smallest cavities, respectively, during the cycle being analyzed. All analyses were performed by a senior cardiologist with extensive experience in echocardiography. The circumference and areas of the ellipse were calculated and used to calculate CS (CS\(_{\text{Echo}}\)), AS by echocardiography, and global EF (EF\(_{\text{Echo}}\)) by using a modification of the Teichholz et al. formula (23).

**Variability of echocardiographic analysis.** Fourteen sets of short-axis echocardiograms were traced a second time by the same person (J. Lessick) at least 1 mo after the first analysis, and 10 sets were traced independently by a second cardiologist (S. A. Reisner) to enable calculation of intrauser and interuser variability. Intrauser variability was calculated as the absolute percent difference compared with the initial value, and interuser variability was calculated as the absolute percent difference compared with the mean value of the first user.

**Variability of LS.** All maps underwent totally automatic editing to assess the possible bias of manual editing. Automatic editing consisted of removing internal points and unstable points (ED distance between 2 consecutive loops >4 mm, loop stability >4 mm, or cycle length stability >12%) by automatic computer algorithms. Maps of five animals (14 cases) were also edited independently by a second user (G. Hayam) using the criteria described above. The ventricles were then redivided into 12 zones as described, and LS was recalculated for each zone to assess interuser variability for editing.

**Statistical analysis.** Global EF and regional shortening as calculated by the two methods were compared by means of the Pearson linear correlation coefficient and by linear regression analysis. The treatment effect of dobutamine compared with baseline (in 9 pigs) and propranolol compared with baseline (in 6 pigs) in the 12 zones of the LV was examined separately by multivariate ANOVA, with treatment, pig, and LV zone as the independent variables.

Regional variability of LS for each of the three conditions studied was examined by multivariate ANOVA with pig, circumferential zone, and longitudinal zone as the three variables. Individual zones were compared by using Bonferroni \( t \)-tests, when indicated.

**RESULTS**

All 10 pigs completed at least two stages of the protocol (baseline plus either dobutamine or propranolol). Of these, nine completed the dobutamine stage successfully, and six completed the propranolol stage (mean dose 14 mg). Four pigs demised shortly after receiving propranolol, and one pig did not complete the 5 \( \mu \)g·kg\(^{-1}\)·min\(^{-1}\) dobutamine stage because of severe arrhythmias, which disappeared after stopping dobutamine. The 10 \( \mu \)g·kg\(^{-1}\)·min\(^{-1}\) stage of dobutamine was attempted in the first four pigs and was completed successfully in two of them. These two maps were used in analysis, despite this part of the protocol being discontinued thereafter. An additional 11th pig (pig 10) was also studied, but, due to evidence of a large zone of apical akinesis on echocardiography, which appeared during the study, this case was not included in the analysis. An average of 114 ± 32 points/map were sampled, taking 64 ± 20 min/map, with a point density of 1.3 ± 0.4 points/cm\(^2\) endocardial surface area at ED. After automatic editing, 99 ± 26 points/map remained, with a point density of 1.2 ± 0.4 points/cm\(^2\), and, after manual editing, 85 ± 20 points remained, with a point density of 1.0 ± 0.3 points/cm\(^2\).
Regional function. CS by the two techniques showed a correlation of \( r = 0.80 \), with a regression equation \( CS_{\text{NOGA}} = 0.52 \times CS_{\text{Echo}} + 6.9 \) (Fig. 2A) and SE of estimate (SEE) = 4.4%. Actual circumferences (Fig. 3A) showed a correlation of \( r = 0.76 \). ED circumferences averaged 14.1 ± 1.6 cm for NOGA vs. 10.3 ± 1.1 cm for echocardiography, and, at ES, circumferences averaged 11.5 ± 1.9 cm (NOGA) vs. 7.9 ± 1.6 cm (echocardiography). NOGA overestimated the midwall circumference by an average of 29 ± 10%. The percent
overestimation was similar in diastole and systole for low-to-normal CS values; however, at CS >22%, the circumference was overestimated to a greater extent at ES compared with ED (Fig. 3B), resulting in a relative underestimation of CS_{NOGA}. Similarly, AS by NOGA vs. echocardiography showed a correlation of \( r = 0.80 \) and \( r = 0.86 \), respectively.

LS by NOGA correlated even better with \( CS_{	ext{Echo}} \) (\( r = 0.86 \) for manual editing and \( r = 0.88 \) for automatic editing), with a regression equation \( \text{LS}_{	ext{NOGA}} = 0.4 \times \text{CS}_{	ext{Echo}} + 5.4 \) (Fig. 2B) and SEE = 2.5%. LS was also found to correlate highly with \( CS_{	ext{NOGA}} \) (\( r = 0.85 \)), with AS by echocardiography (\( r = 0.87 \)) and with AS by NOGA (\( r = 0.86 \)), and with \( \text{EF}_{	ext{Echo}} \) (\( r = 0.87 \)) and \( \text{EF}_{	ext{NOGA}} \) (\( r = 0.96 \)).

Correlating the change in \( CS_{	ext{Echo}} \) vs. the change in LS by NOGA and \( CS_{	ext{NOGA}} \) yields \( r \) values of 0.84 and 0.79, respectively. In all cases, both LS by echocardiography and \( CS_{	ext{Echo}} \) increased during the dobutamine stage and decreased during the propranolol stage (Fig. 4); however, in two cases, \( CS_{	ext{NOGA}} \) failed to increase in the dobutamine stage. It is notable that 9 of the 10 pigs behave in a similar fashion and appear in Fig. 4 to practically fit onto a straight line, whereas one pig (pig 2) behaves differently, both by echocardiographic and NOGA shortening, appearing to have an inherently worse contractile state in all three stages of the experiment.

During the propranolol stage, in all pigs studied, mechanical alternans was noted by echocardiography after pacing was introduced. To overcome this, mean values of two sets of two consecutive beats are used in calculations.

Mean values and SD for each of the three stages are shown in Table 1. By ANOVA, both LS and CS differ significantly between baseline and dobutamine and between baseline and propranolol (\( P = 0.0001 \)). Values are similar for all of the four mid-LV zones (septum, anterior, lateral, and posterior walls), with similar increases in all zones (Table 2). On a zonal basis, in the mid-LV, 90% of the 67 changes in function after treatment were in the expected direction (improvement of at least 1% LS after dobutamine and reduction of at least 1% LS after propranolol), 6% showed no change, and 4% went opposite to expectation. In the apical and basal segments, expected changes were predicted in 71 and 79%, respectively.

Global function. EF as measured by the two techniques correlated highly (\( r = 0.92 \) for both manual and automatic editing) with a regression equation \( \text{EF}_{	ext{NOGA}} = 0.6 \times \text{EF}_{	ext{Echo}} + 13.7 \) (Fig. 5) and SEE = 4.8%. Correlating the change in \( \text{EF}_{	ext{NOGA}} \) vs. the change
in EF\textsubscript{Echo} yields an $r$ value of 0.93. In all cases, by both echocardiography and NOGA, EF increased during dobutamine administration and decreased after propranolol. Mean values and standard deviation for each of the three stages are shown in Table 1. By ANOVA, EF by both methods differs significantly between baseline and dobutamine and between baseline and propranolol ($P = 0.0001$).

**Regional heterogeneity.** A consistent pattern of regional ventricular heterogeneity of LS was found in all three stages. Basal zones, especially the septal basal zone, corresponding anatomically to the LV outflow tract, tended to have slightly lower LS values during all stages compared with the midzone and apex ($P < 0.05$). Similarly, in the circumferential direction, the interventricular septum had consistently slightly lower LS than the three zones making up the free wall of the ventricle ($P < 0.05$).

The mean percent increases in LS from baseline after dobutamine administration were 32, 41, and 42% for the apex, midzone, and base, respectively, and 42, 47, 38, and 26% for the septum, anterior, lateral, and posterior walls, respectively. Similarly, mean percent decreases in LS after propranolol were 25, 30, and 22% from apex to base and 28, 30, 16, and 29% for the septum, anterior, lateral, and posterior walls, respectively. No difference was found in treatment effect between zones by ANOVA.

**Reproducibility in analysis of echocardiograms.** Intrauser variability was 12.3, 9.4, and 10.4%, respectively. No difference was found in treatment effect between the two sets of measurements. Interuser variability, demonstrated good correlation ($r = 0.92$).

**Table 2. Mean local shortening in each of the 12 zones of the LV through the 3 treatment stages**

<table>
<thead>
<tr>
<th>Zone</th>
<th>Propranolol</th>
<th>Baseline</th>
<th>Dobutamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-LV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septum</td>
<td>7.2 $\pm$ 2.6</td>
<td>12.4 $\pm$ 3.1</td>
<td>17.1 $\pm$ 4.0</td>
</tr>
<tr>
<td>Anterior</td>
<td>9.2 $\pm$ 3.1</td>
<td>12.7 $\pm$ 3.5</td>
<td>20.0 $\pm$ 5.7</td>
</tr>
<tr>
<td>Lateral</td>
<td>9.0 $\pm$ 1.9</td>
<td>12.2 $\pm$ 3.1</td>
<td>16.7 $\pm$ 5.1</td>
</tr>
<tr>
<td>Posterior</td>
<td>9.3 $\pm$ 2.3</td>
<td>12.3 $\pm$ 3.3</td>
<td>16.0 $\pm$ 3.3</td>
</tr>
<tr>
<td>All midzones</td>
<td>8.7 $\pm$ 2.5</td>
<td>12.4 $\pm$ 3.1</td>
<td>17.5 $\pm$ 4.7$^*$</td>
</tr>
<tr>
<td>Apex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septum</td>
<td>9.0 $\pm$ 6.9</td>
<td>11.0 $\pm$ 4.5</td>
<td>15.4 $\pm$ 4.5</td>
</tr>
<tr>
<td>Anterior</td>
<td>8.7 $\pm$ 5.5</td>
<td>13.6 $\pm$ 5.4</td>
<td>18.2 $\pm$ 5.8</td>
</tr>
<tr>
<td>Lateral</td>
<td>10.5 $\pm$ 5.1</td>
<td>12.1 $\pm$ 3.2</td>
<td>14.8 $\pm$ 5.8</td>
</tr>
<tr>
<td>Posterior</td>
<td>8.4 $\pm$ 5.6</td>
<td>12.5 $\pm$ 6.3</td>
<td>16.0 $\pm$ 4.0</td>
</tr>
<tr>
<td>All apical zones</td>
<td>9.2 $\pm$ 5.5</td>
<td>12.2 $\pm$ 4.8</td>
<td>16.1 $\pm$ 5.2$^*$</td>
</tr>
<tr>
<td>Base</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septum</td>
<td>6.0 $\pm$ 3.0</td>
<td>7.9 $\pm$ 1.7</td>
<td>11.8 $\pm$ 3.6</td>
</tr>
<tr>
<td>Anterior</td>
<td>6.5 $\pm$ 2.3</td>
<td>8.8 $\pm$ 5.6</td>
<td>13.2 $\pm$ 6.5</td>
</tr>
<tr>
<td>Lateral</td>
<td>9.5 $\pm$ 1.8</td>
<td>10.3 $\pm$ 3.0</td>
<td>15.9 $\pm$ 3.0</td>
</tr>
<tr>
<td>Posterior</td>
<td>8.8 $\pm$ 1.9</td>
<td>12.8 $\pm$ 3.4</td>
<td>15.3 $\pm$ 3.3</td>
</tr>
<tr>
<td>All basal zones</td>
<td>7.7 $\pm$ 2.6</td>
<td>9.9 $\pm$ 4.0</td>
<td>14.1 $\pm$ 4.5$^*$</td>
</tr>
</tbody>
</table>

Values are means $\pm$ SD (in %). $^*$Significant differences between treatments by ANOVA (propranolol, baseline, and dobutamine), $P < 0.01$. 

**Table 1. Summary of pharmacologically induced changes in LV function as assessed by NOGA and echocardiography**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Dobutamine (5 $\mu$g/kg)</th>
<th>Propranolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>10</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>EF (NOGA), %</td>
<td>37.2 $\pm$ 6.7</td>
<td>51.6 $\pm$ 8.1</td>
<td>27.2 $\pm$ 5.9</td>
</tr>
<tr>
<td>EF (Echo), %</td>
<td>39.4 $\pm$ 5.4</td>
<td>62.6 $\pm$ 11.9</td>
<td>21.9 $\pm$ 2.0</td>
</tr>
<tr>
<td>LS (NOGA), %</td>
<td>12.4 $\pm$ 2.6</td>
<td>17.2 $\pm$ 4.3</td>
<td>8.7 $\pm$ 2.2</td>
</tr>
<tr>
<td>CS (NOGA), %</td>
<td>17.2 $\pm$ 4.4</td>
<td>24.1 $\pm$ 5.2</td>
<td>10.6 $\pm$ 4.0</td>
</tr>
<tr>
<td>CS (Echo), %</td>
<td>18.4 $\pm$ 3.1</td>
<td>33.2 $\pm$ 7.9</td>
<td>9.7 $\pm$ 0.8</td>
</tr>
</tbody>
</table>

Values are means $\pm$ SD; $n$, no. of animals. LV, left ventricle; EF, ejection fraction; LS, local shortening; CS, circumferential shortening; Echo, echocardiography.
was 11.0, 9.4, and 10.0%, and correlation coefficients were 0.98, 0.98, and 0.98, respectively.

**Reproducibility in calculation of LS.** From an initial 119 ± 40 points, the first user remained with 84 ± 25 points and the second with 92 ± 27 points after the original maps were editing. Automatically edited maps retained 99 ± 26 points. Interuser variability was 6.0% for LS (mean midzone value) and 3.7% for EF, and correlation coefficients were 0.994 and 0.996, respectively. When manually edited and automatically edited maps were compared, variability was 7.2% for LS and 4.8% for EF, and correlation coefficients were 0.98 and 0.99, respectively.

To examine reproducibility per zone (12 zones/case), 168 zones (14 cases × 12 zones in 5 animals) were analyzed, and interuser variability was calculated to be 1.4 percentage points absolutely, relative to a mean LS of 11.2 ± 5.5% for all zones in these 5 pigs and 9.8 ± 3.8% for baseline maps only. Variability could not be calculated as percent change in LS in this case, because some values of LS are close to zero. The correlation coefficient between the sets of LS values for the two users was 0.93. Comparing manual to automatic editing, the mean difference in LS per zone was 1.8 percentage points absolutely for all zones. Overall correlation in LS for all zones between manual and automatic editing was 0.88. There was a tendency for variability to be greater near the apex.

**DISCUSSION**

The NOGA system with its LS algorithm is a relatively new, not fully validated catheter-based method for evaluating regional LV function as well as global function. This study was designed to compare NOGA-derived regional midwall LS and EF with echocardiography, which is, in clinical practice, the most common noninvasive technique for assessing LV function. To enable a more direct comparison to be made between the techniques, NOGA-derived CS, which is not incorporated in the usual output of the system, was calculated.

This study has succeeded in showing a close correlation between echocardiographic- and NOGA-derived regional midwall shortening (both LS and CS). However, CS is characterized by a consistent underestimation by NOGA compared with echocardiography at higher values of CS. This results from a greater overestimation of NOGA circumference in systole compared with diastole (Fig. 3B). The reason for this is not obvious; however, a possible mechanism is the pressure applied by the operator on the catheter, causing an increased local afterload, which would tend to decrease regional shortening. This effect could be expected to be greater when shortening is highest, because a larger amount of pressure would be required to achieve catheter stability at any endocardial location. This hypothesis is supported by two pieces of evidence. First, the maps taken during dobutamine infusion tend to show more points with ST segment elevation, which is a definite sign of increased catheter pressure on the endocardium. Second, comparison of absolute circumferences of the short axis slices shows that there is a consistent 29% overestimation of circumference by NOGA compared with echocardiography, suggesting that the endocardial cavity might be artificially expanded by catheter pressure. A previous study, however, suggests that at least part of this overestimation by NOGA is actually an underestimation of volumes by echocardiography (3).

LS by NOGA differs from CS in that it is based on mean endocardial shortening between actual endocardial sites, not limited by a particular plane or direction. Differences in absolute values between LS and CS are predominantly a result of torsion, which has been shown to account for differences in magnitude between fiber shortening and the resultant wall thickening and CS (20, 27). It is notable that LS correlates better and behaves in a more consistent manner than calculated CS, as a result of it being a more robust parameter, less affected by sporadic noise. LS values are of a similar magnitude to those reported for endocardial strains with the use of tagged MRI in the range of −0.1 to −0.2 (20). It is interesting to note that NOGA shortening has values similar to those of sarcomere shortening (up to 15%). The only previous study that performed a quantitative comparison of NOGA LS found a reasonable but less favorable correlation ($r = 0.67$) with ventriculography (25); however, this study looked at angiographic relative wall motion and not shortening.

With respect to global function, one previous study has compared EF$_{NOGA}$ vs. ventriculography in humans (26), demonstrating also a good correlation. However, this study showed consistently lower values of EF$_{NOGA}$, compared with our study, which showed lower values only at higher EF. This paper seems to have overestimated their EF as measured from the ventriculogram, because one-third of patients had an EF >80%! The relation between EF$_{Echo}$ and EF$_{NOGA}$ in our study is almost identical to that seen in the analysis of CS, suggesting a similar mechanism. Another possible mechanism is the greater difficulty in obtaining catheter stability near the papillary muscles and in hypercontractile regions, causing a bias toward measuring the more easily mapped hypococontractile regions.

It is important to note that the changes in LS occur fairly evenly throughout the LV, over all 12 zones (Table 2), with little variability from apex to base and for the four circumferential divisions, with improvements of ~38% after dobutamine and reductions of ~26% after propranolol. This contrasts with the regional heterogeneity found in LS itself, with the basal regions and the septum showing consistently smaller LS under all conditions. Knowledge of these differences in the normal heart is required when interpreting NOGA maps. Several studies have shown a similar apex-base gradient in ventricular function, as assessed by thickening with the use of ultrafast CT (16), by midwall shortening with the use of ultrasonic crystals (19), and by strain analysis with the use of tagged MRI (20). There is less consistency in the literature concerning circumferential heterogeneity; however, Fisher et
al. (4) using MRI and Lessick et al. (16) using ultrafast CT have shown reduced thickening in the septum.

limitations of the study. The LV is mapped in a sequential manner over a period varying from 15 min to 1 h, depending on the amount of detail required in the map, the number of points taken, operator experience, myocardial stability, and the size of the LV. This introduces the possibility of variability in LV function during the time of mapping and, therefore, variability between points mapped at different times. This was partially overcome by pacing the animal, which ensures identical cycle lengths for all points.

Regional function was examined only in the mid-LV region. Because only normal hearts with homogeneous contraction were dealt with, it was not possible (or intended) to analyze the ability to differentiate between different regions with different functions in the same LV, rather only to look at differences between ventricles before or after treatments.

Comparison of EF by the two techniques is limited by significant differences in the methods used: a 3D approach for NOGA vs. a simplified 2D-based geometric model for echocardiography.

Conclusions. This study has demonstrated that the NOGA system is capable of quantitating regional and global myocardial function with reasonable accuracy, compared with echocardiography, although there is a tendency to overestimate the midwall circumference and to underestimate both regional and global function at higher values. It is also able to consistently quantify both improvement and deterioration in myocardial function, both on a global and on a regional basis. Values of parameters in each of the three states (baseline, dobutamine, and propranolol) can be used as reference values for defining normal, hyperkinetic, and hypokinetic myocardium, even though an overlap exists.

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REFERENCES


