CLINICAL RESEARCH

Automated function imaging:
a new operator-independent strain method
for assessing left ventricular function

Imagerie paramétrique fonctionnelle automatique :
une nouvelle méthode d’étude de la fonction ventriculaire gauche
de la déformation, indépendante de l’expérience de l’opérateur

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Summary

Background. — Speckle tracking is a new technique based on pure 2D grayscale ultrasound
acquisition allowing calculation of segmental strains. To facilitate clinical application, speckle
tracking has been integrated into the most recent echocardiographic systems for quick,
automated evaluation of left ventricular function (Automated Function Imaging, AFI).
Objective. — To evaluate the feasibility, calculation time, accuracy and reproducibility of
global longitudinal strain (GLS) from AFI in determining LV function in comparison to reference
echocardiographic and angiographic methods—whatever the operator’s experience.
Methods. — Echocardiography was performed in 65 patients scheduled for cardiac catheterization
using a Vivid 7 system. They were divided into 3 groups according to EF (>55%, 35\leq EF\leq55%, <35%).
Image quality, global LV function parameters (ejection fraction, aortic flow, dp/dt) and
segmental contraction were analyzed by one experienced operator and one beginner. GLS was
obtained from apical 2, 3 and 4 chamber views. GLS was compared to both echocardiographic
and angiographic EF, as well as to other echocardiographic parameters.
Results. — GLS was obtained successfully in 97% of patients. Mean calculation time including
correction of endocardial detection was less than 60 seconds. GLS was significantly different
between the 3 groups, respectively -18.1\pm2.5 \%, -11.5\pm2.1\% and -6.0\pm1.2\% (p<0.01). Strong
correlations were observed between GLS and LV function (r from 0.68 to 0.87) with a high level
of reproducibility. No difference was observed between experienced and inexperienced
operators.
Conclusion. — AFI is clinically applicable and an effective means of assessing LV function due
to its short acquisition time, feasibility and accuracy, whatever the experience of the operator.

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KEYWORDS
Speckle tracking; Regional left
ventricular function; Strain;
AFI.
Introduction

There are still limitations to the quantification of myocardial contraction by echocardiography. First, it relies on measurements such as wall motion that are susceptible to overall cardiac movement and the tethering of normally and abnormally contracting myocardial segments. In addition, measurement techniques are imperfect, often subjective, and time-consuming. Importantly, today’s echographic measurements are far from perfectly reproducible [1] and are strongly dependent on the operator’s experience.

Measurements of myocardial deformation, such as strain and strain rate, have provided alternatives which overcome the influence of overall cardiac movement and tethering. Contractile performance is compared for two myocardial points against each other rather than against a fixed reference such as the transducer. The initial method to calculate strain from ultrasound recordings used an algorithm applied to a Doppler dataset [2]. However, such strain measurements derived from Doppler are angle-dependent and lack both reproducibility and robustness when it comes to identifying abnormalities in the clinical setting [3]. Speckle tracking, an innovative technique based on pure, two dimensional greyscale ultrasound acquisition, has recently been implemented to calculate global and regional strains [3]. Compared to other tools, such as tissue Doppler velocity recordings, regional strain has the advantages of independence from translation and tethering. To facilitate clinical application, this strain technique called Automated Function Imaging (AFI) has been simplified and has been integrated into echocardiographic instruments to generate a parametric image of myocardial strain throughout the left ventricle (LV).

The assessment of LV function by this new comprehensive strain approach has never been rigorously compared with current techniques and the purpose of this study was to establish the relationship between the new strain-based quantitative assessment of LV function and standard LV volume and ejection fraction (EF) readings. Feasibility, calculation time, accuracy and reproducibility of the technique in determining LV function were evaluated in comparison to standard echocardiographic and angiographic methods by two operators: one experienced and one beginner.

Methods

Successive patients with sinus rhythm who had been referred for cardiac catheterization for standard clinical indications (coronary artery disease 48%, dilated cardiomyopathy 24%, ischemic cardiomyopathy 28%) were enrolled. Patients with atrial fibrillation and severe valve disease were excluded. For each patient, transthoracic echocardiography and cine-angiography were performed within 3±1 days. None of the patients manifested any change in clinical status during this interval. All patients provided written informed consent for the study, which was approved by the Institutional Clinical Research and Ethics Committee.
Echocardiography

Echocardiography was performed with standard views and the patient in the left lateral decubitus position using a commercially available machine (GE Vivid 7, General Electric Ultrasound) equipped with a 2.5 MHz probe functioning in the tissue harmonic imaging mode. Digital loops were stored on the hard disk of the echocardiography machine for on-line and off-line analysis, and they were also transferred to a workstation (EchoPac, Vingmed, General Electric) for off-line analysis.

Selection of region of interest and strain measurement

Strain measurement was performed as follows by two operators, one with experience with the software (>200 analyses) (EXP) and one beginner (<10 analyses) (BEG). Digital loops with three successive cardiac cycles were acquired from apical 2, 3, and 4-chamber views. The frame rate for these recordings was set at 40 to 60 frames/s. Analysis was performed directly on the echocardiography system for each of the three apical views with the operator manually identifying 3 points: two on each side of the mitral valve and a third at the apex of the left ventricle. The software automatically detected the endocardium at end-systole, tracked myocardial motion during the entire cardiac cycle, and created U-shaped regions of interest (ROI) that encompassed basal, mid, and apical segments of 2 opposite LV walls (figure 1). Tracking quality was assessed by the operator and scored by the software. If the tracking was poor, the operator could repeat the imaging, readjust the endocardial tracing or change software parameters such as ROI width and smoothing until a better tracking score was achieved. Inadequately tracked segments were automatically excluded from analysis.

Longitudinal strains for each individual segment were measured and the software calculated global longitudinal strain (GLS) by averaging local strains along the entire LV.

Conventional echocardiographic measurements

Analysis was performed off-line by a second blinded operator. Using Simpson’s biplanar method, end-diastolic and end-systolic LV volumes and EF were determined by manual tracing of end-diastolic and end-systolic endocardial borders using standard apical four-chamber and two-chamber views. According to the recommendations of the American Society of Echocardiography, tracings were performed with the papillary muscles and trabeculations allocated to the LV cavity. Aortic VTI (cm) was measured conventionally using pulsed-wave Doppler in the apical 5-chamber view. Continuous-wave Doppler spectra of mitral regurgitation (MR) jets were analyzed in 31 patients with mild to moderate MR. Doppler-derived dp/dt was determined as follows: the two points on the MR spectrum corresponding to 1 m/s and 3 m/s were identified. These points correspond to LV-left atrial pressure gradients of 4 mmHg and 36 mmHg using the modified Bernoulli equation ($P = 4v^2$). Doppler-derived dp/dt was defined as $dp/dt = 36-4/dt$ mmHg/s. Three dp/dt measurements were determined for each patient and the average dp/dt was calculated.

Cineventriculography

Standard cineventriculography was performed using a biplanar projection (RAO/LAO) with injection of at least 30 mL of contrast using 4F-6F pigtail catheters. The frame rate was set at 25 Hz. Semi-automatic border tracking was used to define the end-diastolic image, based on the frame with the largest ventricular contour, and the end-systolic image was the frame with the smallest ventricular silhouette. LV end-diastolic and end-systolic volumes were determined using Simpson’s method with biplanar cineventriculography in all patients. Angiographic examinations with at least two successive cardiac cycles without extrasystolic beats were considered interpretable and a prerequisite for inclusion in the study.

Figure 1. Global longitudinal strain measurement from one apical view (A) and “Bull’s-eye” representation of regional strain (B).
Reproducibility

Interobserver variability in the measurement of echocardiographic strain was evaluated in 18 randomly selected patients by 2 independent observers blinded to the echocardiographic and cineangiographic LVEF results. These investigators had 2 months of experience with speckle tracking echocardiography. We also evaluated interobserver variability between an experienced investigator and a third observer with little experience with speckle strain in 44 randomly selected patients.

To assess intraobserver variability, the same experienced observer blinded to clinical information re-evaluated echocardiographic strain in 10 randomly selected patients.

Intra and inter-observer variability in the assessment of global strain was determined by percentage of measurement error.

Statistical analysis

Data were analysed using standard statistical software (StataCorp LP, College Station, Texas). Results are expressed as mean values ± SD. Quantitative data were analyzed using Student’s t test and linear regression with correlation coefficients (r). A p value less than 0.05 was considered statistically significant. Reproducibility was assessed by calculating inter-observer and intra-observer variations in 20 successive subjects.

Results

Baseline characteristics

The study included 65 patients (50 men and 15 women: average age 60.2±11.1 years) who had been referred for cardiac catheterization. The baseline clinical, echocardiographic and angiographic characteristics of the patients included in the study are summarized in Table 1. LV function was normal in 32 patients (49%), moderately impaired in 20 (31%) and substantially impaired in 13 (20%).

Feasibility and calculation time of global longitudinal strain

A valid global longitudinal strain (GLS) measurement was obtained in 63 of the 65 patients included in the study (97%). In one patient, the measurement was not possible in all views because of poor echogenicity and in another, the anterior wall could not be visualized in the apical 2 chamber view. Mean calculation time including correction of endocardial detection was less than 60 seconds. Fully automatic, validated tracing by the software was obtained in 44 patients whereas a short operator correction (<30 sec) was necessary in 19.

Comparison between 2D strain and LVEF, aortic VTI and Doppler-derived dp/dt

Mean strain was calculated for patients with preserved LV systolic function by angiography (group 1: LVEF >55%), those with moderately altered LV systolic function (group 2: LVEF between 35% and 55%), and patients with severely altered LV systolic function (group 3: LVEF <35%): the results were respectively -18.1±2.5%, -11.5±2.1% and -6.0±1.2%. Mean strain was significantly different between these 3 groups (p<0.01). No difference was observed between EXP and BEG measurements (p ns). A high level of correlation was observed between GLS and echocardiographic LVEF (r=0.87) and between GLS and angiographic LVEF (r=0.82, p<0.01). The correlation of GLS with angiographic LVEF was similar to the correlation of echo and angio LVEF. The correlations between GLS and aortic VTI and between GLS and dp/dt were also good: 0.69 and 0.68 respectively (p<0.05) (figure 2). For patients with ischemic heart disease, we found similarly strong correlations between GLS and echocardiographic LVEF (r=0.83) and angiographic LVEF (r=0.81) (p<0.01). Identical level of correlation was observed between EXP and BEG (figure 3).

Reproducibility

Inter-observer variability between two experienced observers and between an experienced and an inexperienced operator were respectively 7.1 and 8.7% (table 2). The intra-observer average percentage error was lower than 4%. Inter and intra observer variability for the same observers for echocardiographic LVEF was 14.5% and 12.9% respectively.

Table 1 Baseline clinical, echocardiographic, and angiographic characteristics of the study population.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>60,2±11,1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>male (n, %)</td>
<td>50 (76%)</td>
</tr>
<tr>
<td>female (n, %)</td>
<td>15 (24%)</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
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<tr>
<td>Ischemic (n, %)</td>
<td>35 (54%)</td>
</tr>
<tr>
<td>Valvular (n, %)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Dilated (n, %)</td>
<td>14 (21%)</td>
</tr>
<tr>
<td>Normal (n, %)</td>
<td>13 (20%)</td>
</tr>
</tbody>
</table>

LVEF

>55% (n, %) | 32 (49%) |
35-55 % (n, %) | 20 (31%) |
<35% (n, %) | 13 (20%) |

LVIdd (mm) | 52±10 |
LVIDs (mm) | 38±11 |
Strain global (%) | -14.2±4.9 |
Echocardiographic LVEF (%) | 50,1±15,1 |
Angiographic LVEF (%) | 54,6±19 |
Doppler-derived dp/dt (mmHg/s) | 1025±377 |
Aortic VTI (cm) (mean ± SD) | 17,8±4,1 |

Data presented are mean ± SD or number of patients.
LVIdd: left ventricular internal diameter at end-diastole.
LVIDs: left ventricular internal diameter at end-systole.
Discussion

An assessment of LV function is essential for the evaluation and management of patients with heart disease but the evaluation of this parameter suffers from problems of subjectivity, reproducibility and accuracy as well as being dependent on the experience of the operator. Our study is the first to compare a global measurement of longitudinal strain to conventional parameters of LV function (e.g. angiography) whatever the operator’s experience. The 2D strain approach was easy to implement and reproducible regardless of operator experience, and the results correlated well with conventional parameters of LV function.

LV function assessment

The conventional indices of global LV function, such as ejection fraction and volumes, are load-dependent, and standard echocardiographic approaches to their measurement may be influenced by image quality. Furthermore, technical considerations such as off-axis imaging and measurement error may compromise the accuracy of ultrasound quantification. Assessment of regional function remains highly subjective and requires rigorous training. The introduction of a new generation of ultrasound technology, enabling high frame rate second harmonic imaging, has helped to compensate for the above limitations.

Alternative methods such as tagged magnetic resonance imaging (MRI) have been shown to be more accurate [4-7]
but are very complex and expensive for the routine evaluation of LV function.

Myocardial strain is a dimensionless index of change in myocardial length in response to an applied force and is expressed as fractional or percentage change [8]. The strain rate is the time derivative of strain expressed per second (s⁻¹) representing the differential velocity of 2 points normalized for the distance separating them. Initial measurements of strain required invasive techniques and involved tracking the movement of implanted radio-opaque markers by biplanar cineangiography [9, 10], or using sonomicrometric crystals embedded in the myocardium [11]. More recently, strain parameters have been measured noninvasively by echocardiography using M-mode, Doppler tissue velocity data, or two-dimensional imaging [12].

Doppler-derived tissue velocity imaging is the most commonly used method for the assessment of myocardial strain. Several clinical studies have shown good correlation between tissue velocity-based strain and traditional echocardiographic parameters of global LV systolic function (Simpson’s biplanar method, wall motion score index (WMSI), Doppler-derived dp/dt) [13], as well as between tissue velocity-based strain and MRI-derived strain [14, 15]. However, Doppler-derived strain measurements have a number of potential pitfalls [12]: firstly, the quality of tracings is exquisitely sensitive to signal noise and reverberation artifacts; secondly, spatial resolution is dependent on temporal resolution [16]; and finally, like all Doppler techniques, tissue velocity-based strain is sensitive to alignment, with errors related to suboptimal interrogation angling possible [17, 18].

**Speckle tracking echocardiography**

Recently, 2-dimensional strain echocardiography (2DSE) has been introduced as a new non-Doppler based method. It calculates myocardial deformation from frame-by-frame tracking of a small image block of myocardial backscatterers (“natural acoustic markers”). The appearance of these acoustic markers is considered to be relatively stable between subsequent image frames, so that a change in their position is assumed to follow tissue motion. Tracking is based on searching for the new location of the marker in the subsequent frame. Two-dimensional strain and strain rate are then calculated from the displacement and rate of displacement of each marker [19, 20]. Since tracking is based on gray-scale B-mode images, it is in principle angle-independent and affords good temporal and spatial resolution.

Different speckle tracking methods have been applied in *vitro* and *in vivo*, and several experimental studies have validated speckle tracking echocardiography against reference techniques such as sonomicrometry and MRI tagging [21, 22], but there have been few clinical studies [3, 21-23] and the results are inconsistent. Reisner et al. [23] compared 2D strain and wall motion score index (WMSI) in 27 patients after myocardial infarction and found a general correlation between WMSI and strain and strain rate (r=0.68 and 0.67 respectively). However, this retrospective study evaluated only a small group of patients with myocardial infarction; furthermore, reproducibility was not tested. A recent study [22] found only moderate correlations between 2D strain, tissue velocity-based strain and tagged harmonic-phase MRI, making it difficult to reach definitive conclusions about the accuracy of echocardiographic strain in evaluation of LV systolic function.

In the present study, we compared 2D strain with angiographic and echocardiographic measurement of LVEF and other conventional echocardiographic parameters of LV systolic function. Our study population included patients with ischemic, dilated and valve-based cardiomyopathies as well as healthy subjects. Patients had variable degrees of impairment of LV systolic function with EFs ranging from 15% to 85%. Thus, the accuracy and reliability of 2D longitudinal strain as an index of global systolic LV function was tested in a variety of different clinical situations.

**Feasibility and calculation time of GLS**

Measurement of global longitudinal strain was feasible in most patients with good temporal and spatial resolution. The measurement could be performed in 63 out of 65 patients (97%). Global strain could not be measured using this technique in patients with poor echogenicity and those in whom the anterior or the anteroseptal walls were difficult to image but this only represents a small proportion (approximately 1/30).

Mean strain calculation time using GLS was less than 60 seconds, allowing a rapid and real-time analysis of global systolic LV function. Furthermore, the use of 3 references planes is a significant advantage compared to usual echocardiographic methods of evaluation of LVEF, and to other available techniques of strain measurement as tissue velocity based strain and MRI.

We found good correlation between GLS and both echocardiographic and angiographic EF. GLS also correlated with Doppler-derived dp/dt and aortic VTI (r=0.69, and r=0.70); strong correlations were observed in patients with ischemic heart disease as well as in patients without coronary artery disease. The correlation between GLS and angiography was the same as that between echocardiography and angiography. These results support the use of 2D longitudinal strain as a

**Table 2 Inter and intra-observer variabilities of strain measurements.**

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Mean difference ± SD</th>
<th>Percentage of error</th>
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</thead>
<tbody>
<tr>
<td>Inter-observer variability *</td>
<td>18</td>
<td>-0.45±1.1%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Inter-observer variability †</td>
<td>44</td>
<td>-0.25±1.6%</td>
<td>8.7%</td>
</tr>
<tr>
<td>Intra-observer variability (EXP)</td>
<td>10</td>
<td>0.30±0.7%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Intra-observer variability (BEG)</td>
<td>10</td>
<td>0.33±0.8%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>

* inter-observer variability between 2 experienced operators. † inter-observer variability between an experienced and an inexperieneced operator.
reliable parameter in the evaluation of LV systolic function. However, radial strain may give better correlation since EF is mainly related to the radial component independently of heart disease. Unfortunately, the current radial strain technique lacks robustness and reproducibility.

Reproducibility

Reproducibility of GS measurement was also very satisfactory. The intra-observer percentage error was only 3.1%. Inter-observer variability ranged between 7.1 and 8.7% compared to the results of echo LVEF of 14.5 and 12.9% respectively. This represents a remarkable improvement in intra- and inter-observer variability compared to echocardiographic and angiographic measurements of LVEF for which the percentages of error are generally reported to be between 10 and 15% [24]. This low inter-observer variability is better than that for MRI [24] supporting the idea that 2D strain could be a useful way of measuring systolic LV function on a regular basis.

Limitations

In this study, the software evaluated global longitudinal strain from apical views. Radial and circumferential strains are not taken into consideration for the estimation of global strain, largely because longitudinal strain is more reproducible and more accurate for immediate clinical application. In the near future, 3D strain could allow the accurate assessment of all components. Although we tried to include patients with a variety of heart diseases, the population studied was limited to patients who had a clinical indication for coronary angiography. These results should be extended to other patient populations to compare two-dimensional strain with reference techniques such as MRI or radionuclide ventriculography.

Conclusion

The application of echocardiography has often resembled “ultrasonic fluoroscopy” with qualitative but without true quantitative assessment. Two-dimensional global longitudinal strain obtained from AFI technology provides objective and quantitative assessments of LV function. It should prove to be superior to conventional measurements due to its independence of cardiac motion and tethering. It is a simple, accurate, reproducible, and rapidly obtained parameter which has the potential to become a standard for real-time automatic echocardiographic assessment of cardiac function and patient follow-up.

References