Can global longitudinal strain predict reduced left ventricular ejection fraction in daily echocardiographic practice?

Le strain longitudinal global peut-il prédir la dysfonction systolique du ventricule gauche en pratique échocardiographique de routine?

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Summary
Background. — Transthoracic echocardiography (TTE) is the most commonly used method for measuring left ventricular ejection fraction (LVEF), but its reproducibility remains a matter of controversy. Speckle tracking echocardiography assesses myocardial deformation and left ventricular systolic function by measuring global longitudinal strain (GLS), which is more reproducible, but is not used routinely in hospital practice.
Aim. — To investigate the feasibility of on-line two-dimensional GLS in predicting LVEF during routine echocardiographic practice.
Methods. — The analysis involved 507 unselected consecutive patients undergoing TTE between August 2012 and November 2013. Echocardiograms were performed by a single sonographer. Echogenicity was noted as good, moderate or poor. Simple linear regression was used to assess the relationship between LVEF and GLS, overall and according to quality of echogenicity. Receiver operating curve (ROC) analysis was used to identify the threshold GLS that predicts LVEF ≤ 40%.

Abbreviations: ESC, European Society of Cardiology; GLS, Global longitudinal strain; HCM, Hypertrophic cardiomyopathy; LV, Left ventricular; LVEF, Left ventricular ejection fraction; TTE, Transthoracic echocardiography.

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GLS for predicting reduced LVEF

Results. — Mean LVEF was 64 ± 11% and GLS was –18.0 ± 4.0%. A reasonable correlation was found between LVEF and GLS ($r = –0.53; P < 0.001$), which was improved when echogenicity was good ($r = –0.60; P < 0.001$). GLS explained 28.1% of the variation in LVEF, and for one unit decrease in GLS, a 1.45 unit increase in LVEF was expected. Correlations between LVEF and GLS were –0.51 for patients in sinus rhythm ($n = 490$) and –0.86 in atrial fibrillation ($n = 17$). Based on ROC analysis, the area under the curve was 0.97 for GLS $\geq –14$, allowing detection of LVEF $\leq 40$% with a sensitivity of 95% and specificity of 86%.

Conclusion. — Two-dimensional GLS is easy to obtain and accurately detects LVEF $\leq 40$% in unselected patients. GLS may be especially helpful when a suboptimal acoustic window makes LVEF measurement by Simpson’s biplane method difficult and in atrial fibrillation patients with low heart rate variability.

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Introduction

Echocardiography is the most commonly used diagnostic tool for left ventricular (LV) systolic dysfunction. Given the poor prognosis associated with this condition, early detection is warranted [1]. Simpson’s biplane method is the reference approach for calculating LV ejection fraction (LVEF), but it is time consuming to perform and is prone to intra- and interobserver variability.

New echocardiographic techniques are now available for assessing LV systolic function, one of which is speckle tracking. This technique can be used to study global myocardial deformation using global longitudinal strain (GLS) [2]. Measurement of this index is now possible on-line during the ultrasound examination, with no requirement for post-processing. The aim of this study was to determine the value of GLS in measuring LVEF and identifying LV systolic dysfunction during routine in-hospital echocardiographic practice in consecutive patients, regardless of the indication for transthoracic echocardiography (TTE).

Methods

The study population comprised consecutive patients undergoing TTE at Fondation Rothschild Hospital, Paris, France, between August 2012 and November 2013.

Echocardiographic analysis

TTEs were performed using a commercial ultrasound system (Vivid 7; GE Health Medical, Horten, Norway) with a 4 MHz transducer. All echocardiograms were performed by one experienced cardiologist (NB).

Standard TTE included LV analysis, LVEF calculation (using Simpson’s biplane method in patients in sinus rhythm and by visual evaluation in patients in atrial fibrillation), Doppler tissue imaging and calculation of LV GLS. First, a comprehensive analysis of the cardiac anatomy was performed. Importantly, the patient’s echogenicity was noted as good, moderate or poor, to allow further analysis by ‘acoustic window’ subgroups. The quality of the acoustic window had to be sufficient to allow the calculation of LVEF and GLS, otherwise the TTE was excluded.

As the aim was to evaluate GLS in detecting LV systolic dysfunction in everyday clinical practice, no rereading by a second observer was done. All measurements were performed on-line, without post-processing. Final results of LVEF were obtained by averaging two to three measures. Simpson’s biplane LVEF was calculated using the manual tracing. All of the images were stored digitally on EchoPAC imaging analysis software (EchoPAC; GE Health Medical).

Speckle tracking global longitudinal strain analysis

The three apical views (four-, two- and three-chamber) were recorded, with a frame rate of between 70 Hz and 80 Hz. Careful manual tracing of the endocardial contour was performed on-line and the entire thickness of the myocardium had to be covered correctly to ensure good tracking. GLS values were calculated during the standard TTE as the mean of the global longitudinal strains of each apical view. Using this method, myocardial deformation was assessed in a semi-automatic manner, based on grey-scale images. Segmental strain values were also recorded, according to a 19-segment model.

Statistical analysis

Values are presented as means ± standard deviations, medians (interquartile ranges) or absolute counts and frequencies. Pearson’s test was used to seek correlations, and simple linear regression was used to assess the relationship between LVEF and GLS. The tests were repeated for each class of echogenicity and according to cardiac rhythm (sine or atrial fibrillation). Logistic regression was used to determine the threshold of GLS that predicts abnormal LVEF in this population. Thus, receiver operating characteristic curve analysis was used to identify the optimal cut-off value and the sensitivity and specificity of GLS in detecting an LVEF ≤ 40%. A P value of < 0.05 was considered to be statistically significant. Statistical analyses were performed using STATA® software, version 13 (StataCorp LP, College Station, TX, USA).

Results

A total of 558 TTEs were performed, 51 (9.1%) of which were excluded from the analysis for the following reasons: 19 patients were in atrial fibrillation and had important variability in heart rhythm; and in 32 patients the image quality was insufficient to use the speckle tracking technique and/or to assess LVEF by Simpson’s biplane method. The study population therefore comprised 507 consecutive TTEs.

The indications for TTE were as follows: ischaemic stroke or transient ischaemic attack and haemorrhagic stroke (n = 235), multiple sclerosis (n = 44), dyspnoea (n = 24), evaluation of various treatments (n = 19), heart murmur exploration and control of valvular disease, endocarditis and suspicion of endocarditis (n = 17), LVEF evaluation and/or heart failure (n = 17), preoperative assessment (n = 15), hypertension (n = 12), diabetes mellitus (n = 11), assessment of the pericardium (n = 5), occlusion of the central retinal artery (n = 4), ischaemic heart disease (n = 4), dissection of supra-aortic vessels (n = 4), subarachnoid haemorrhage (n = 3), assessment of pulmonary pressures (n = 3) and other indications (n = 90).

Table 1 displays the main clinical and echocardiographic characteristics of the population. Of note, the study population was relatively young, with a mean age of 59 ± 18 years; the median age was 60 years. The two youngest patients were aged 8 years and 14 years, and the oldest patient was aged 95 years.

Echogenicity was considered good in 48.1% of cases, moderate in 36.9% and poor in 15.0%. Mean LVEF was 64 ± 11% (median 65% [59%–70%]) and mean GLS was −18.0 ± 4.0% (median −19% [−21%–16%]). LV wall-motion abnormalities (LVWMAs) were present in 20.3% of TTEs. Lower values were recorded for both LVEF and GLS in the presence of LVWMAs (Table 2).

In the entire series, the correlation between GLS and LVEF was reasonable (r = −0.53, P < 0.001), and was improved
Table 1 Main clinical and echocardiographic characteristics (n = 507).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59 ± 18</td>
</tr>
<tr>
<td>Men</td>
<td>272 (53.7)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>17 (3.4)</td>
</tr>
<tr>
<td>LVM indexed to body surface (g)</td>
<td>96.7 ± 33.3</td>
</tr>
<tr>
<td>Wall-motion abnormality</td>
<td>103 (20.3)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td></td>
</tr>
<tr>
<td>Overall, mean</td>
<td>64 ± 11</td>
</tr>
<tr>
<td>Overall, median</td>
<td>65 (59, 70)</td>
</tr>
<tr>
<td>According to Teichholz</td>
<td>68 ± 10</td>
</tr>
<tr>
<td>Without LVWMA</td>
<td>67 ± 8</td>
</tr>
<tr>
<td>With LVWMA</td>
<td>54 ± 15</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>18.0 ± 4.0</td>
</tr>
<tr>
<td>Overall, median</td>
<td>19 (21, 16)</td>
</tr>
<tr>
<td>A3C</td>
<td>17.9 ± 4.8</td>
</tr>
<tr>
<td>A4C</td>
<td>17.6 ± 4.1</td>
</tr>
<tr>
<td>A2C</td>
<td>18.4 ± 4.5</td>
</tr>
<tr>
<td>Without LVWMA</td>
<td>19.1 ± 3.0</td>
</tr>
<tr>
<td>With LVWMA</td>
<td>13.6 ± 4.7</td>
</tr>
<tr>
<td>Echogenicity</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>244 (48.1)</td>
</tr>
<tr>
<td>Moderate</td>
<td>187 (36.9)</td>
</tr>
<tr>
<td>Poor</td>
<td>76 (15.0)</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation, number (%) or median (interquartile range). GLS: global longitudinal strain; LVM: left ventricular mass; LVWMA: left ventricular wall-motion abnormality.

Table 3 Pearson’s correlation coefficients between global longitudinal strain and left ventricular ejection fraction, overall and according to acoustic window quality and cardiac rhythm.

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>−0.53</td>
<td>−0.59, −0.46</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Echogenicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>−0.60</td>
<td>−0.67, −0.51</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Moderate</td>
<td>−0.54</td>
<td>−0.63, −0.43</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Poor</td>
<td>−0.53</td>
<td>−0.67, −0.35</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cardiac rhythm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>−0.51</td>
<td>−0.57, −0.45</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>−0.86</td>
<td>−0.95, −0.65</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

a Using Fisher’s z transformation.

when the echogenicity was good ($r = −0.60$, $P < 0.001$) (Table 3). When investigating the relationship between GLS and LVEF according to cardiac rhythm, the correlation coefficients were reasonable for patients in sinus rhythm ($r = −0.51; n = 490$) and high for those with atrial fibrillation ($r = −0.86; n = 17$) (Table 3).

Fig. 1 depicts the simple linear regression analysis between GLS and LVEF, in the entire series (Fig. 1A) and according to level of echogenicity (Fig. 1B). GLS explained 28.1% of the variation in LVEF and for one unit decrease in GLS, a 1.45 unit increase in LVEF was expected (Fig. 1A). For good echogenicity, GLS explained 36.3% of the variation in LVEF, and for one unit decrease in GLS, a 1.71 unit increase in LVEF was expected. Corresponding data were 28.3% and

Table 2 Left ventricular ejection fraction and global longitudinal strain according to the presence or absence of left ventricular wall-motion abnormality.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>GLS (%)</th>
<th>95% CI</th>
<th>P</th>
<th>LVEF (%)</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>404</td>
<td>−19.1 ± 3.0</td>
<td>−19.4, −18.8</td>
<td>&lt; 0.001</td>
<td>67 ± 8</td>
<td>66–68</td>
<td>0.001</td>
</tr>
<tr>
<td>Present</td>
<td>103</td>
<td>−13.6 ± 4.7</td>
<td>−14.5, −12.7</td>
<td></td>
<td>54 ± 15</td>
<td>51–56</td>
<td></td>
</tr>
</tbody>
</table>

CI: confidence interval; GLS: global longitudinal strain; LVEF: left ventricular ejection fraction.
a Data are mean ± standard deviation.

1.70 for moderate echogenicity, and 26.6% and 1.48 for poor echogenicity. Hence, the obtained regression equation for LVEF by GLS was, in the whole series: $LVEF = −1.45 \times GLS + 38.04$ (Fig. 1A). Such a relationship has already been reported in the literature [3]; however, the one we cite was based on the assessment of only 22 patients.

The results of the linear regression analysis according to cardiac rhythm are shown in Fig. 2. GLS explained 25.8% of the variation in LVEF in sinus rhythm and 73.8% in atrial fibrillation. On logistic regression, the AUC was 0.97 (95% CI 0.95–0.99) for $GLS \geq −14%$, with a sensitivity in detecting $LVEF \leq 40%$ of 95% and a specificity of 86% (Fig. 3).

Discussion

This is, to the best of our knowledge, the first prospective study to evaluate myocardial deformation using speckle tracking imaging in a large cohort of consecutive patients, with GLS calculation on-line and taking into account the quality of the acoustic window. Our results indicate the feasibility of this approach in predicting LVEF during routine echocardiographic practice.

To carry out speckle tracking successfully, all three apical views have to be of sufficient quality to enable correct definition of the endocardium, and the entire thickness of the myocardium has to be covered correctly to ensure good tracking. In our study, which involved the spectrum of patients treated in everyday echocardiographic practice in our echolab, less than one-tenth of TTEs were excluded...
because they failed to meet these two criteria, and GLS calculation was therefore possible in 90% of cases.

Heart failure due to systolic LV dysfunction is associated with a poor prognosis [1] and early detection is important to ensure that patients benefit from recommended therapies as soon as possible, even when asymptomatic (angiotensin-converting enzyme inhibitors). LVEF has an important prognostic value—the lower the LVEF the poorer the survival—yet LVEF values and normal ranges are dependent on the imaging technique employed, the method of analysis and the individual operator [4]. European Society of Cardiology (ESC) guidelines recommend performing TTE in all patients with suspected heart failure. The apical biplane method of discs (the modified Simpson’s rule) is used to measure LVEF [4,5], which relies on accurate tracing of the endocardial border, and an insufficient acoustic window (or poor echogenicity) may preclude its measurement [4].

Speckle tracking imaging is a relatively new, angle-independent technique that allows the study of myocardial

**Figure 1.** Simple linear regression analysis between global longitudinal strain (GLS) and left ventricular ejection fraction (LVEF) in (A) the whole series and (B) according to echogenicity.
deformation. While speckle tracking imaging previously required post-treatment processing, on-line evaluation of myocardial deformation is now possible. The feasibility of two-dimensional strain for calculating strain and strain rate on real-time myocardial function was investigated in a small study, which reported that the technique can achieve real-time wall-motion analysis, and could become a standard for real-time automatic echocardiographic assessment of cardiac function [6]. Furthermore, a high level of agreement and reproducibility has been found with two vendor-dependent software products, using off-line post-processing for speckle tracking GLS [7]. In view of the limited data available, deformation imaging has not yet been included in the ESC guidelines, which state: “deformation imaging is more sensitive than ejection fraction in detecting minor changes in LV systolic function. However, issues of reproducibility and standardization currently limit the routine clinical use of deformation imaging” [4].

GLS has been studied in the general population [8] as well as in various clinical settings [9–11], but we are not aware of any large-scale studies that have evaluated the contribution of GLS for the detection of LV dysfunction in “real-life” echocardiographic practice, particularly in routine in-hospital practice, which often involves suboptimal acoustic windows and/or imaging. Our findings were obtained despite the fact that echogenicity is often worse in hospitalized patients than outpatients, with hospitalized patients comprising approximately 90% of our population. Indeed, fewer than half of the scans had good echogenicity, with the quality of the other scans affected by, for example, disease severity, presence of lung disease or scars and inadequate positioning. While prediction of LVEF by GLS was best with good echogenicity, the results were still reasonable with moderate or poor echogenicity.

Our results also give a threshold of GLS—-independent of clinical setting—that detects LV systolic dysfunction (GLS ≤ −14%), with a sensitivity of 95% and a specificity of 86%. Of interest, the correlation between GLS and LVEF was excellent in patients in atrial fibrillation (r = −0.86). However, LVEF was assessed visually in this group of patients, and only 17 TTEs were involved, so these results require confirmation in a larger study.

We have to take into consideration that our series included very few cardiac conditions, such as hypertrophic cardiomyopathy (HCM) and cardiac amyloidosis. Indeed, despite apparently normal LV systolic function, all components of strain have been reported to be significantly reduced in HCM, probably reflecting a subtle LV systolic dysfunction while LVEF is preserved [12]. Myocardial deformation was also reported to be significantly decreased in patients with confirmed cardiac amyloidosis [13]. However, our objective was the “screening” of LV systolic dysfunction in the setting of an echocardiographic activity, hence favoring sensitivity, not specificity.

It may be important to notice here that GLS and LVEF represent two different aspects of LV function and are not exchangeable. To date, they are complementary and each could predict the other in most cases, in the absence of structural cardiac diseases. Whenever possible, we believe that both should be done. In case of impossibility (when the technique is not available on the ultrasound system or if the calculation is impossible for some reason), each will be useful separately.

There are other interesting applications for GLS, such as detecting subclinical global systolic dysfunction in patients with preserved LVEF [12], differentiating athlete’s heart from HCM [14] and predicting clinical events in heart failure as a prognosticator [15]. However, these were not the subject of our study.

Potential clinical applications

While speckle tracking imaging has been standardized and evaluated in different cardiac conditions, the role of this technique has yet to be clearly defined in the European guidelines [4]. GLS may be useful for detecting an LVEF ≤ 40% when TTE is performed by novice echographers, or in emergency departments and intensive care units. TTE, due to its portability, is now widely used by intensivists [5], who do not perform comprehensive assessments, but look for serious anomalies, such as pericardial effusion, pulmonary hypertension and, of course, LV systolic dysfunction. In our study, the evaluation of GLS was feasible in about 90% of cases and was quick and easy to perform, and therefore deserves consideration in this setting. GLS may also be helpful when a suboptimal echocardiographic window precludes LVEF measurement by Simpson’s biplane method, as GLS is less dependent on the endocardial definition and is more dependent on the whole thickness tracking. Finally, GLS of the LV seems to be accessible and to accurately predict LVEF in atrial fibrillation, provided that heart rate variability is low.

Study limitations

All the measurements were performed on-line, without off-line processing, and there was no rereading by a second observer. However, this was part of the underlying philosophy of this study, which aimed to assess, in consecutive unselected patients in real-life practice, the feasibility of speckle tracking and its contribution to interpretation of TTE results and the detection of LV dysfunction.
Our study population was relatively young, with a rather preserved ejection fraction. Mean LVEF was 64 ± 11%, median LVEF was 65%, the smallest value was 13% and the highest value was 94%. Only 21 patients had an LVEF ≤ 40%.

Furthermore, few cases of HCM were included and LVEF was assessed visually in patients with atrial fibrillation. Indeed, averaging would have had little meaning, would require too many cycles and thus would be time consuming, which was not the aim of our study. Hence, these results should be interpreted with caution and tested on larger-scale atrial fibrillation populations.

Conclusions

This study was exclusively driven by a practical goal of improving the assessment of systolic function in echocardiographic routine daily practice.

Two-dimensional GLS, assessed in a semiautomatic manner, is easy to perform and sufficiently quick to obtain on-line, and accurately detects LVEF ≤ 40% in patients representative of routine in-hospital echocardiographic practice. A GLS of ≥ −14% predicted an LVEF ≤ 40% with a sensitivity of 95% and a specificity of 86%. This technique may be especially helpful when echogenicity is poor and/or when TTE is performed by novice echographers or non-cardiologists, and may be of value in atrial fibrillation, provided heart rate variability is low.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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