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Left ventricular global longitudinal strain in the evaluation of left ventricular heart failure and ischaemic heart disease in modern echocardiography

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Abstract. Since its introduction into echocardiology around 20 years ago, speckle tracking (ST) has developed significantly, finding its place in daily clinical practice. Many applications have been tested and proposed for different modalities of ST. Longitudinal strain (LS) and, specifically, global longitudinal strain (GLS) have become the most utilised and studied modalities of ST. Due to their diagnostic/treatment complexities, heart failure (HF) and ischaemic heart disease (IHD) have become an important domain for the development of GLS. In recent years, many clinical studies, meta-analyses, and systematic reviews have tried to define the clinical applications of GLS in these pathologies and estimate its reliability and predictive value for diagnostic/prognostic purposes. The results from these studies have prompted international institutes such as the European Society of Cardiology (ESC) and the American Society of Echocardiography (ASE) to add GLS to the diagnostic protocols in their recent guidelines. In this review we examine this novel, advanced, echocardiographic method and discuss its most relevant clinical applications in HF and IHD. Fig. 4, Tab. 1, Ref. 45, on-line full text (Free, PDF) www.cardiologyletters.sk

Key words: speckle tracking – global longitudinal strain – echocardiography – heart failure – ischaemic heart disease – left ventricular systolic function

The human heart is composed of a complex three-dimensional structure of varying-orientation folds of myocardial bands creating three muscular layers: the transversely oriented circular layer, the inner oblique layer, and the outer oblique layer (1). These muscular layers, during their contraction, create a sophisticated myocardial deformation, which is needed for the optimal pumping activity of the heart in each cardiac cycle. In echocardiography (ECHO), this compound process of deformation is described in the form of three principle (radial, circumferential, and longitudinal) changes, called strains (1). Radial strain represents myocardial thickening along its radius, longitudinal strain represents shortening of the cardiac cavity along its long axis, and circumferential strain represents a reduction in the circumference of the ventricle during contraction (1). Moreover, during

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systole, the left ventricle (LV) undergoes rotation around its long axis. The base (clockwise) and apex (counter-clockwise) of the LV rotate in opposite directions to each other to create a twisting "torsion" movement (2). In reality, cardiac systolic–diastolic functions are dependent on and influenced by all of the described myocardial deformations.

Although the complex structure of the myocardium has been known for some time, until recently, a method for the comprehensive quantification of myocardial strain during cardiac cycles was not available (2). The first non--invasive measurement of myocardial strain was obtained via cardiac magnetic resonance (CMR) tracing in the late 1980s (1). Despite the proposal to apply echocardiography to estimate myocardial strain in the early 1980s, it was not achieved clinically until the 1990s. In the 1990s, one-dimensional myocardial strain assessment through the post-processing of tissue Doppler imaging (TDI) was performed (3). The main disadvantage of this method was the angle dependency of TDI. During the early 2000s, through the further development of computing abilities and advances in technology, two-dimensional speckle tracking echocardiography (2D-STE) was introduced into clinical practice (3).

In STE, the echo machine produces particular acoustic markers, called speckles, through the interaction of the ultrasound beam and the myocardial tissue. Speckles can be tracked in their displacement during the whole cardiac cycle, hence providing information about myocardial deformation (3). Since its introduction in 2004 by Reisner et al. using GLS, STE has become increasingly useful in the evaluation of myocardial function (1). STE is now used not only to estimate the function of the left ventricle, but also in the evaluation of the function of the right ventricle and atria (4). Its use has been expanded to assess a multitude of diseases, with or without the involvement of the myocardium (such as amyloidosis, rheumatoid arthritis, inflammatory disease, and neoplasia), and in the evaluation of cardiac structures for pre-operational decision-making and/or post-operational follow-up (5). The independence of STE from the angle of insonation, the automated or semi-automated evaluation of the obtained echo, the reproducibility of the results, and the greater availability in comparison to CMR support the utility of this method in daily clinical practice. Advances in echocardiography and the emergence of three-dimensional STE (3D-STE) in recent years, achieved by tracking myocardial motion in 3D space and overcoming the inherent limitations of 2D-STE, provide opportunities for the powerful quantification of subclinical myocardial dysfunctions. Today, the European Association of Cardiovascular Imaging (EACVI) and ASE consider STE a "state-of-the-art" approach for patient management and an "invaluable tool" in the detection of "subclinical" LV systolic dysfunction and "specific cardiac conditions" that are not possible to assess otherwise by any "currently used echocardiographic parameters" (3).

However, it is important to highlight that, as an advanced diagnostic modality, despite the automatisation of the process analysis and online–offline evaluation of the obtained images using sophisticated software, STE is still reserved for more experienced echocardiographers. The person performing this examination should be very familiar with cardiac imaging, quality 2D-3D echocardiographic visualisation, and important technical optimisations such as the omittance of ventricular foreshortening, noise minimisation, gain correction, frame rate, and depth and focus variations. Such a person is then able to refine the images obtained and is accustomed to the standard of image quality required to obtain translatable clinical results. Only under these conditions are the examinations reproducible, reliable, and able to provide accurate clinical information. This should not demotivate inexperienced echocardiographers from pursuing STE training. Studies have demonstrated that the measurement of some well-known conventional values, such as the LV ejection fraction (EF), can be far more variable than STE. For example, in a study published by Nagishi et al., the authors evaluated the effect of experience and training on the precision of strain measurement (6). Interestingly, inter-observer variation was greater in the measurement of EF than in LV-GLS (6). They remarked that although experience is important, the inter-observer precision in the measurement of LV-GLS is high (6).

Inter-vendor variation bias, caused by different algorithms in the analysis and software used by manufacturers, is another important consideration. Several studies have tried to address this, although concerns still remain. For example, in a study published by Farsalinos et al., nine different ultrasound machines and software packages were tested to determine the variability of LV-GLS and to compare this method with EF. They found that STE LV-GLS was more reproducible than EF measurement, and the differences in the results between different vendors were statistically significant (2).

Among the different modalities of STE, LV-GLS is the most widely studied and used application in practice today. Global circumferential strain (GCS), LV radial strain (LV-RS), and torsion of the left ventricle (LV twist) each have proposed clinical applications for the evaluation of left ventricular function, and, in some instances, their indexed values have been shown to be superior to GLS. For example, studies have shown that in the evaluation of hemodynamic deterioration during the acute phase of STEMI, the diagnostic value of LV-GCS is superior to LV-GLS in discriminating transmural from subendocardial necrosis (7, 8). Generally, however, it is accepted that among the different indices of STE, GLS is the most robust myocardial deformation marker available today (9-11). The superiority of GLS over other indices is due to the inherently higher resolution of images obtained from the axial plane, hence its ability to incorporate a larger region of interest (ROI) (more myocardia can be tracked through the longitudinal axis than in the short-axis view) (9-11).

As addressing all of the proposed applications of STE was not possible in this short review, we focused on the implications of LV-GLS examination in the detection and/or prognostic evaluation of HF and IHD. We discussed the EACVI/ASE standardised methodology in order to obtain a technically acceptable GLS acquisition and to present the most important optimisations of the 2D and 3D modalities.

Two-dimensional longitudinal strain of the left ventricle

LS represents the shortening of the myocardium along its long axis (12). Strain (derived from the Lagrangian strain equation) is an index that is able to estimate the deformation of an analysed segment of myocardium (by tracking the movement of speckles), expressed as a percentage (12). Negative values of strain indicate shortening or compression of the segment under deformation (meaning two tracked speckles are moving closer to each other), while positive values define myocardial stretching or expansion (12).

Hence, LS is described by negative values (curves) during systole and positive values (curves) during diastole (12). Left ventricular LS is evaluated in apical two-, three-, and four-chamber views separately. Then, we obtain a mean value from all three regional deformations, captured as a so-called "global" LS, which represents an important index of LV function/deformation (12). The LV-GLS is always a negative value (12). Since this negative nature of GLS can cause confusion when expressing an increase or decrease in strain, the ESC and ASE recommend referring to global strain changes using only "increased or decreased" terminology (12).

To perform the measurement of LV-GLS (based on EACVI and ASE guidelines for cardiac chamber quantification (12)), we need to proceed as follows:

1. Optimise the image quality with good endocardial definition and minimise the foreshortening.
2. Maximise the frame rate. The high frame rate is due the nature of STE as an examination method. In STE, the pattern of the ultrasound signal is tracked frame-by-frame to assess the myocardial deformation. As the accuracy of STE is highly dependent on the temporal resolution, a higher frame rate is required in order to obtain reliable strain values.
3. Capture images with approximately similar pulse rates in different views (12). The R-R interval defines the cardiac cycle for the system in 3D acquisitions. Higher pulse rates decrease the R-R interval and cause variation in the cardiac cycle time frame acquired.
4. Image depth should be adjusted so that it includes the mitral annulus (to obtain all needed ROIs) and the whole apex during diastole (12). Decreasing depth (and sector width) will help to increase the frame rate, and thereby increase the quality of tracking (12).

Following these adjustments, GLS measurements should be performed in three standard apical views and then averaged (12).

To obtain the LV-LS, the echocardiographer should begin the measurement from the three-chamber apical view (apical long-axis view), visualising the aortic valve (**Figure 1B**) (12). This is due to recognition of end-systole (aortic valve closure) as the defining point in the cardiac cycle used by the software to represent the time of peak

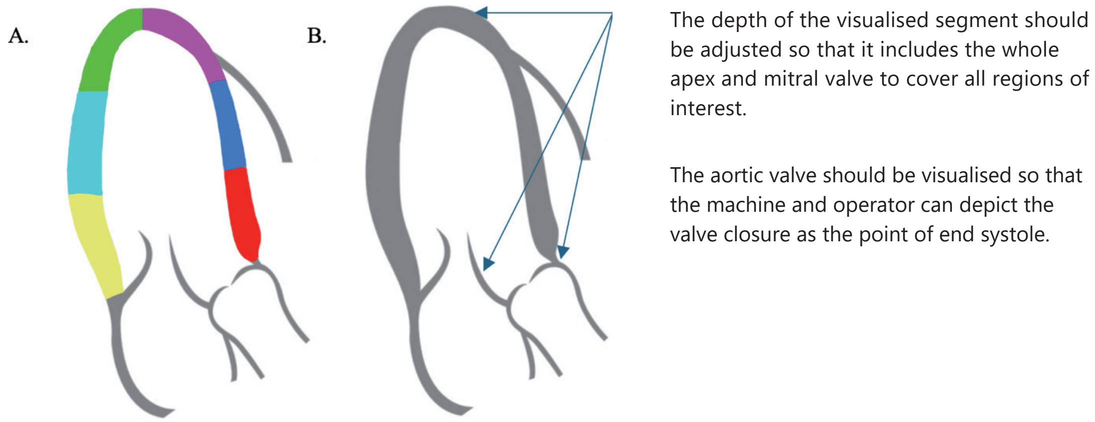

Figure 1 Three-chamber (long axis) apical view with visualisation of the aortic valve
A: Graphical depiction of the six segmented (colour-coded) regions of interest used in the measurement of the longitudinal strain of left ventricle in the long-axis apical view. The machine calculates the deformation changes of each coloured section during the cardiac cycle and presents the results in the form of six (negative) values (curves, Figure 2), one for each segment. B: Long-axis apical view.

systolic strain (12). This is when we expect to observe the peak systolic shortening of the myocardium in all segments (**Figure 2**).

Then, the operator should start from an accurate point and click the delineation of the endocardial border (12). The software then converts the traced area into six segments or ROIs (three for the anteroseptal, basal, medial, and apical segments, and three for the inferolateral wall). In newer automated software, after capturing a proper apical three-chamber view, the machine recognises the six segments and automatically shows them in different colours (**Figure 1A**). The operator can, at any time, correct any designated area if needed. Importantly, the ROI should not include the hyperechogenic pericardium (12). Then, the software determines whether the tracking phase was correct (indicated by a green tick) or not (red cross) for each segment. This indicates correct or incorrect endocardial delineation, which can be manually corrected/modified by the operator for every segment. Once six green ticks have

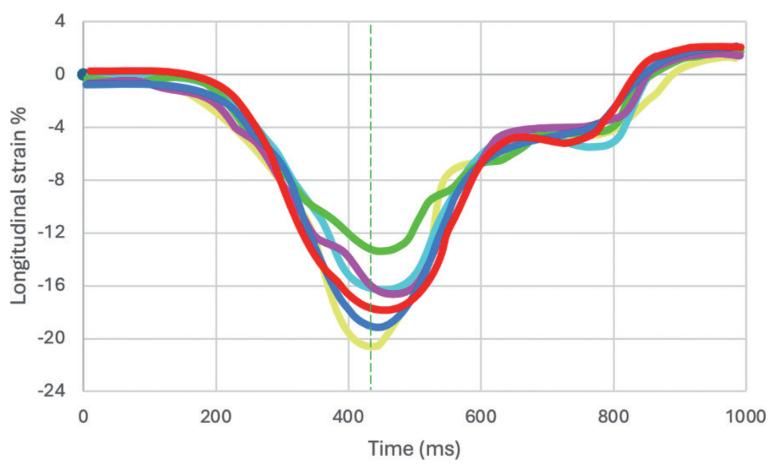

Figure 2 Longitudinal strain curves measured by the machine during the cardiac cycle
Each curve represents the deformation (contraction percentage) of a delineated segment of myocardium (the same segments are shown in the same colours) during the cardiac cycle. The green dotted line in the middle represents the time of aortic valve closure, defining end systole, where the peak systolic strain is expected. Post-systolic shortening is seen when the negative peak of a given segment's curve is located after the green dotted line.

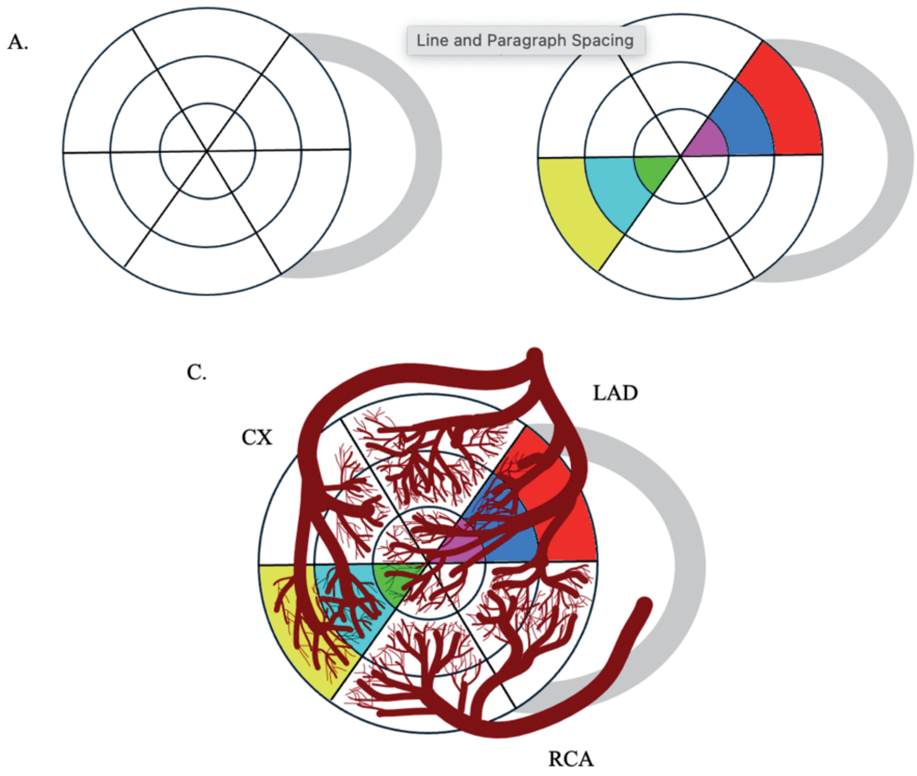

Figure 3 Eighteen segmented bullseye plots of the left ventricle
A: Eighteen segmented bullseye plots of the left ventricle, B: Bullseye plot depicting the six colour-coded segments (base to apex) of regions of interest evaluated through the long-axis apical view based on longitudinal strain, C: Demonstration of the (approximate) coronary artery tree blood supply, based on the segmented plot of LV. This orientational tree is used to appreciate the extension/place of coronary artery pathology once wall motion abnormalities (through strain results) of a given segment are recorded. CX: circumflex artery, LAD: left anterior descending artery, RCA: right coronary artery.

been achieved (meaning optimal tracking), the software processes the image and provides LV curves and peak systolic strain values (**Figure 2**). When regional tracking is suboptimal in one or two segments in a single view, the measurement of GLS should be avoided (12).

This process then has to be repeated in the two- and four-chamber views in the same manner, with the same frame and pulse rates. Every obtained view gives six regional peak systolic strain values (shown in numbers and curves), from which a mean LS value for the given view can be calculated by the software. After obtaining all three mean regional LS values, the software automatically provides an average value of GLS. Six regional strain values captured from three different views are normally presented in the form of 18 segmented bullseye maps/polar maps by the software (**Figure 3**).

Due to age and load dependency, serial assessment of GLS in individual patients using the same vendor and same software (to omit inter-vendor bias) is recommended (12).

The absolute cut-off or normal value of GLS has still not been defined. The American College of Cardiology's last publication on STE indicated that as the GLS normal value varies with "age, sex, and LV loading conditions, defining a norm is not straightforward" (10). They concluded that, in adults, GLS values of more than -18% can be considered normal, GLS values of less of -16% can be considered abnormal, and GLS values of -16% to -18% can be considered borderline (10).

Three-dimensional speckle tracking of the left ventricle

3D-STE tracks the three-dimensional motion trajectory of myocardial speckles between successive volume frames within the ROI, frame by frame, and so provides various deformation parameters of the myocardium throughout the cardiac cycle (13). The movement tracking ability of this modality in three dimensions overcomes the limitations of 2D-STE (13). Importantly, it can be achieved as long as the speckles remain in the sample volume (13). Since the whole process is automatic, the 3D-STE is more reproducible (13). To acquire the 3D full volume, the probe is placed at the apical position of the four-chamber view, including all LV myocardium in the pyramidal volume data (3, 13, 14). Then, the acquired image is divided by the software into 2D apical and transverse sections, and both the endocardial and epicardial borders are identified (14). The operator can correct or modify the delineation of the acquired images manually during the process if needed. Then, the borders are tracked during the whole cardiac cycle (14). For correct template matching, electrocardiogram (ECG) recording is essential. This is because the acquisition of the volumetric frame is based on the R-R interval on the ECG (11). Hence, the repetition of the acquisition and the comparison examination have to be undertaken at the same pulse rate (11). After processing the image, the software analyses the entire cardiac cycle and obtains information such as the global and segmental 3D strain.

The major flaws of 3D-STE are the low temporal and spatial resolution (11). If the thickness of the ROI is too wide, the tracking may be impaired, and the strain variability may increase if the thickness of the ROI is over-focused (11, 13). The modality is highly dependent on the frame rate and image quality (13). Low-quality acquisitions will make endocardial and epicardial border tracking very complicated. Moreover, as in 2D-STE, the results are vendor-dependent, and inconsistency can occur in the results across different vendors (13).

Clinical applications

The implementation of GLS in diagnostic/prognostic modalities and follow-up has been extensively studied in recent years (8, 15, 16). Many clinical applications have been proposed and validated for GLS (17). The use of LV-GLS in the evaluation of HF, IHD, cardiomyopathies, valvular heart disease (VHD)/post operative follow-up, or systematic diseases such as arterial hypertension (AH) and diabetes mellitus (DM), is becoming increasingly common in daily practice (3). This is due to the ability of this method to detect early, subclinical, and sub-endocardial changes in the primary stages of diseases or during mild chronic progression of diseases, where other conventional echocardiographic examinations are unable to detect (3). Many studies have demonstrated that in the early stages of the aforementioned pathologies, despite normal standard echocardiographic parameters, GLS results are abnormal, and through the course of disease/treatment, GLS changes can provide valuable prognostic information (3, 15, 18, 19). The results derived from metanalyses, and systematic reviews agree that, in general, a decrease in GLS is associated with adverse outcomes; hence, it is commonly accepted that this method can be used for the risk stratification of underlying pathologies (3).

Heart failure

Due to the inherent limitations of EF in the evaluation of the state of disease or estimation of prognosis in patients with HF for whom the EF value is normal, the implementation of LV-GLS as a new index to evaluate the function of LV in a novel way has been proposed (4, 15, 18). The initial efforts towards the evaluation of the clinical value of GLS were focused on cohorts of HFpEF patients. The results showed that GLS can identify abnormalities in these patients that other conventional indices fail to. The accumulated data demonstrated that nearly half of patients (52%) with a diagnosis of HFpEF had abnormal GLS values but a normal EF (20). The follow-up of these patients with abnormal GLS and normal EF showed that they are significantly more prone to systolic deterioration and HF-related hospitalisation than patients with a normal GLS at baseline (20). These findings showed that conventional indices of heart systolic function, such as EF, are insufficient. The left ventricular EF defines the function of LV based on relative volume changes, relying on geometrical assumptions of the chamber, which are strongly influenced by its shape (20). It does not provide a measure of the contractility of LV and can overestimate the systolic function in patients with mitral or aortic abnormalities (4, 13, 18, 19). Ejection fraction is historically interwoven to HF, it is still the best defining tool of stages of the disease with clear cut-offs, and is the only internationally accepted and understood determinant of the function of LV. However, based on new findings, GLS is increasingly being incorporated into definitions of systolic function and ventricular contractility (20). Newer studies have demonstrated that the predictive value of GLS is not limited only to HFpEF patients. Chimed et al. in their article on the prognostic relevance of LV-GLS in patients with HF with reduced EF (HFrEF), reported that LV-GLS is "independently associated with HF hospitalisation and all-cause mortality", and provided incremental prognostic value despite the traditional risk factors (**Table 1**) (21). The European Journal of Heart Failure, in a manuscript published in 2023, claimed that abnormal LV-GLS is a strong predictor of adverse clinical events and future systolic deteriorations within a median of three years in patients with HF (**Table 1**) (20). As mentioned earlier, despite unclear cut-off for an abnormal GLS, the value of < -16% was consistently used in different publications for such assessments (20).

Additional to its prognostic qualities in HF patients, GLS has been shown to have predictive value for the clinical outcomes and treatment prognosis of patients with moderate to severe VHD concomitant to HF and regardless of EF. For example, in a study published by Kaperidis et al., patients with dilated cardiomyopathy (HFrEF) and similar EFs at baseline were divided into a group with severe MR and a group without severe MR. They demonstrated that despite similar EFs in all patients, the baseline GLS was significantly lower in patients with severe MR (22). This correlation was believed to be due to the better ability of GLS to quantify myocardial deformation and structural changes, such as fibrosis. Based on these findings, studies have been designed to evaluate the prognostic value of GLS in HFrEF improvement after valvular therapy or medical optimisation. The results from these studies showed that LV-GLS improvement at 6-months follow-up was

Table 1 The main clinical applications of left ventricular global longitudinal strain

Clinical pathology	Diagnostic application	Prognostic application
Heart failure	An accurate LV functional index correlates with the extent of myocardial fibrosis in advanced HF (44). Stratification of asymptomatic patients with moderate to severe VHD for consideration of valvular repair in HFpEF patients (14).	Predictor of worsening of HF (HR: 0.94; 95% CI, 0.90 to 0.99, p = 0.032) or all-cause mortality (HR: 0.94; 95% CI, 0.90 to 0.97, p = 0.001) in HFrEF patients, GLS of ≤10%, (median follow-up of 60 months) (21). Predictor of systolic deterioration and HF-related hospitalisation (HR: 2.23; 95% CI, 1.16 to 4.28, p = 0.016) and cardiovascular death (HR: 3.20; 95% CI, 1.44 to 7.12, p = 0.004) in a median of 3 years in HFpEF patients (cut-off of <-15.8%) (15). Prognostic value for the estimation of post-operational systolic function improvement with a median of 6 months after valvular repair in HFrEF patients (22).
Coronary artery disease	Diagnostic support in inconclusive IHD patients where conventional tests cannot identify the diagnosis (5, 35). Diagnosis of ACS in patients with chest pain and inconclusive ECHO or lab results (5, 35). Diagnosis of chronic IHD/stable angina following an inconclusive conventional stress test (34).	Lack of improvement of GLS soon after PCI is an independent predictor of long-term negative LV remodelling (37). LV-GLS is a predictor of event-free survival after AMI (NSTEMI and STEMI, HR = 3.27; 95% CI = 1.691–6.157, p < 0.001, cut-off -13%) (45) GLS is a predictor of HF-related acute hospitalisation and cardiovascular death (OR: 1.47; 95% CI, 1.33 to 1.62, p < 0.000, 1cut-off −14% ± 3.3%) (7).

The table above summarises the main applications of (only) global longitudinal strain of left ventricle in diagnostic or prognostic evaluations of heart failure and/or ischaemic heart disease. Readers may find many other implementations for other indices of speckle tracking echocardiography used for the same purposes and same pathologies in other publications which may not be listed above

ACS – acute coronary syndrome, AMI – acute myocardial infarction, CI – confidence interval, ECHO – echocardiography, GLS – global longitudinal strain, HF – heart failure, HFpEF – heart failure with preserved ejection fraction, HFrEF – heart failure with reduced ejection fraction, HR – hazard ratio, IHD – ischaemic heart disease, LV – left ventricle, LV-GLS – left ventricular global longitudinal strain, NSTEMI – non-ST segment elevation myocardial infarction, OR – odds ratio, PCI – percutaneous coronary intervention, STEMI – ST segment elevation myocardial infarction, VHD – valvular heart disease.

associated with better clinical outcomes after edge-to--edge mitral valve repair and guideline-directed medical treatment (23).

For patients with HFpEF, a significant decrease in LV-GLS in the presence of aortic valvular disease (stenosis/regurgitation) has been documented (24). It is assumed that GLS is more sensitive to the pressure overload caused by aortic valvular disease than EF (4, 13, 24). Nagata et al. investigated the prognostic value of GLS (2D and 3D) in the prediction of major adverse cardiac events in asymptomatic patients with severe aortic stenosis and preserved EF (14). They documented that baseline 2D and 3D GLS values were significantly lower in patients who developed such events (14). Hence, they argued that GLS can be used in the stratification of asymptomatic patients with preserved EF and severe aortic stenosis (14).

For some clinical or diagnostic evaluations of HF or heart failure-related treatments, the GLS value alone might not be informative enough, and there will be a need to examine other data obtained from performing the LV-LS STE, such as the regional deformation changes, changes in peak systolic shortening time, area change rate, and so on. Below, we present two examples of published applications of other LS indices proposed for the diagnostic improvement or treatment selection of patients with HF.

Despite efforts in the evaluation of diastolic function and STE, the exact correlations of GLS results with clinical presentations have not been determined (25). A decreased GLS has been documented in patients with decreased diastolic function and decreased EF. For patients with preserved EF, the currently available conventional methods have been shown to have good sensitivity with no specific inferiority to GLS (25). Nonetheless, by using other indices of 3D-STE, such as the area change rate (ACR), new applications for speckle tracking in the diagnosis of diastolic dysfunction have been proposed. For instance, Tatsumi et al. claimed that E/E-ACR can diagnose increased LV filling pressure in patients with reduced EF where the use of conventional early diastolic mitral inflow and annulus velocity ratio, known as (E/e’), is limited (25). They demonstrated that, in a cohort of 125 patients who underwent pulmonary capillary wedge pressure (PCWP) and echocardiographic evaluation (conventional parameters and STE), E/E-ACR was a better predictor of elevated PCWP and more accurate than E/e’ (25). They concluded that this index is dependent on LV relaxion and is a powerful predictor of LV filling pressure regardless of EF (25).

Cardiac resynchronisation therapy (CRT) has emerged as an important treatment for patients with advanced HF (26). It works by improving the pattern of myocardial contraction through biventricular pacing (26). The biggest problem with this treatment modality is the absence of response to CRT post-implantation in as many as one-third of patients (26). The selection of optimal candidates using echocardiographic assessment with standard M-mode, pulse wave Doppler, and/or TDI showed mixed results in predicting the CRT response (26). Due to the ability of STE to demonstrate the specific status of each myocardial segment during the cardiac cycle in HF patients, it was proposed that this method could improve the analysis of ventricular mechanical desynchrony, and thereby the selection of patients suitable for CRT implantation. In a study published in the *Journal of Cardiovascular Ultrasound*, the authors assessed myocardial synchrony through the slope and coefficient of determination (R^2-S/D) to evaluate the value of the strain volume loops in order to predict the CRT response (26). They demonstrated that mid-septal (R^2-S/D) coupling at baseline is an independent predictor of the CRT response, with a cut-off value of 0.55, sensitivity of 89%, and specificity of 77% (26).

Ischaemic heart disease

Since GLS provides information about regional myocardial function and wall motion, the application of this method for detection of wall motion abnormalities has been suggested. The cost–risk vs. benefit in comparison to the current gold standard methods is very promising (27). Catheter coronary angiography (CCA) is currently the gold standard method for the diagnosis of coronary artery diseases (CADs); however, despite its widespread clinical application, CCA remains limited due to its relative operational risk, technical dependency, and cost (28). Moreover, one-third of males and two-thirds of females with stable angina pectoris demonstrate no obstructive CAD (28). The conventional transthoracic echocardiography (TTE) evaluation of IHD relies on the determination of EF and macroscopic wall motion abnormalities detectable by the examiner’s eye during the procedure. In about 50% of patients with IHD, such wall motion abnormalities are not detectable via TTE (29). LV-LS STE can determine the regional wall motion abnormality using a bullseye map of LV, or by the assessment of LS curves and the presence of post-systolic shortening (**Figure 2-3**). GLS provides information about the early impact on the subendocardial fibres, and bullseye maps provide a demographic regional evaluation of LV abnormalities according to coronary vascularisation territories in the three-layer analysis (**Figure 3**).

Chronic setting

To determine the applications of GLS in IHD, we need to first look at its ability to diagnose CAD. To date, stable chronic CAD has been the major focus of investigation for STE and LV-GLS (27). Several studies have demonstrated that GLS is significantly correlated with the presence of obstructive CAD in both symptomatic and asymptomatic patients with chronic IHD (27, 30, 31). These studies showed that the GLS value is significantly lower in patients with obstructive CAD with at least one stenosis of >50% or ≥70% luminal area reduction (30, 31). Furthermore, the published results argue that GLS values at rest have diagnostic accuracy in predicting significant CAD and reduced exercise capacity (30, 31). Although the measure of accuracy (moderate or high) of GLS remains under debate, the ability of the method to diagnose such changes has been clearly demonstrated (30-32). The cut-off value of GLS for diagnosis is not completely clear; however, the accumulated evidence suggests that borderline to abnormal GLS values (-17% and less) are sensitive (86%) and specific (73%) enough for this purpose (30-32). For example, in a meta-analysis studying the accuracy of LV-GLS in the detection of CAD in a cohort of 1385 patients, the mean value of GLS in patients with CAD was -16.5% (95% confidence interval (CI): -15.8% to -17.3%), with a sensitivity of 74.4% in the detection of moderate to severe CAD (33). It is important to note that although these studies argued that decreased GLS values correlate with the presence of obstructive CAD, they also reported that normal GLS values or normal wall motion in STE do not rule out the presence of IHD (32).

Moreover, GLS STE can be performed in stress echocardiographic examinations to assess subtle myocardial damage or myocardial viability if the conventional stress test results are in doubt (27). The *American Heart Journal* published an article comparing the accuracy of GLS to other indices of STE in the detection of CAD in patients undergoing stress echocardiography. They argued that GLS had a higher diagnostic accuracy than GCS or GRS, and its results were “comparable to the wall motion score index (WMSI) for the detection of significant CAD” (34). They recommended that the combination of both GLS and WMSI results in a “significant incremental increase” in diagnostic accuracy (**Table 1**) (34).

Acute setting

Due to the accumulation of a comprehensive body of evidence regarding the diagnostic capability of GLS in the detection of CAD, the ESC, in their 2023 guidelines for the diagnosis and management of acute/chronic coronary syndrome (ACS/CCS), suggested the use of LV-GLS to support diagnosis in patients with clinical suspicion of IHD and an absence of visual wall motion abnormalities, as assessed by conventional methods (in a chronic setting) or in patients with the presence of chest pain and inconclusive echocardiographic/blood test results (in an acute setting) (**Table 1**) (5, 27, 35). This recommendation is in accordance with the results of a multivariate analysis comparing GLS and GRACE ACS risk scores in symptomatic CAD patients with positive/inconclusive cardiac biomarkers, presenting GLS as an independent predictor of CAD (GLS: OR 0.51, $p < 0.001$, GRACE score: OR = 0.938, $p = 0.007$) (36).

It has been documented that LV regional LS can identify epicardial coronary lesions in ACS (in correlation with CCA), and its measurement after revascularisation can predict the extension of myocardial necrosis (37, 38). A meta-analysis of 11 studies with a cohort of more than 700 patients comparing the accuracy of LV-GLS to late gadolinium enhancement as a reference method demonstrated that the pooled estimates of GLS had a specificity of 77% and sensitivity of 86% for the assessment of the myocardial infarction area (39).

Moreover, post-revascularisation GLS can predict the extent of LV remodelling, along with post-procedural short-term and long-term complications such as HF and/or re-hospitalisation (**Table 1**) (17, 40). Since STE has been shown to be a marker of myocardial fibrosis, it can be utilised in the assessment of myocardial post-

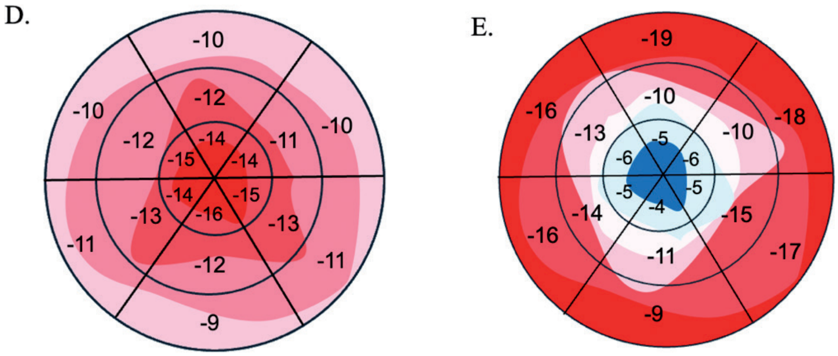

Figure 4 Example of polar maps of bullseye plots of the left ventricle, obtained by speckle tracking
The idea behind polar mapping is to visualise the extent of deformation (contraction) of a given segment beyond the numerical value presented. This map provides an understanding of the amplitude of abnormalities in relation to other segments, and as a whole for the chamber. The redder the colour, the more negative the value, representing normal contraction of the segment. The polar mapping of some pathologies gives a pattern of similarity that can be used in identification or differential diagnosis. For example, pattern D is typically seen in patients with cardiac amyloidosis, known as the "cherry on the top pattern", while pattern E is consistent with "typical" takotsubo cardiomyopathy with akinesis of the apex and normal to near-normal contraction of the base.

-ischaemic scars (27). Ersbøll et al., in a study assessing the predictors of all-cause mortality and HF in patients after acute myocardial infarction (AMI), reported that an LV-GLS value of >-14% was a predictor of increased likelihood of admission for acute HF and increased cardiovascular death (**Table 1**) (41).

LV torsion changes (as another index of STE) should also be noted with regard to the early detection of subclinical ischaemia and post-revascularisation changes as a diagnostic index and prognostic tool for non-favourable cardiac events (27).

In addition to the GLS value, bullseye/polar maps of LV have been considered promising to provide an easy assessment method for the regional distribution of myocardial injury in a segmented manner (from apex to base), according to the affected coronary artery (**Figure 3C**) (27). The possibility of the application of wall motion abnormalities in bullseye maps for differential diagnosis between Takotsubo cardiomyopathy, acute myocarditis, and ACS is of even greater interest (**Figure 4**). Some authors have claimed that the analysis of segmental LS for the evaluation of such abnormalities is less reliable due to large inter-observer and inter-vendor variabilities, as well as limitations such as echocardiographic acquisition during tachycardia, a poor acoustic window (typical in acute settings), and a lack of optimal ECG tracing (27, 42). These authors suggested that it is reasonable to limit the use of regional strain abnormalities and evaluation of numerical segment-specific strain values to the overall assessment of typical patterns, and to "guide" the diagnosis (27). One of the better known and more widely used regional LS applications is post-systolic shortening. Post-systolic shortening (PSS) is the myocardial shortening that occurs after end systole, observed during isovolumic relaxation (16, 27, 43). The regional contraction of the myocardium depends not only on its inherent contractility, but also on the tension from the surrounding myocardia (16). During a decrease in contractility due to ischaemia, the amplitude of shortening during the ejection time decreases, causing PSS (**Figure 2**) (43). Since PSS represents ischaemic dysfunction of the myocardium, some authors have considered the measurement of PSS in patients with CAD as equally important as LV-GLS (43). In some cases, especially when macroscopic, visual regional wall motion abnormalities are not seen during conventional echocardiography, an analysis of LV strain curves may show the presence of PSS. This abnormal finding may be seen as late peaking of the regional LS curve of a myocardial segment that appears after aortic valve closure. The more commonly used value for the evaluation of ischaemic changes in myocardial abnormal shortening is the post-systolic index (PSI), calculated using the formula (peak strain – end systolic strain / peak strain), with a normal value of ≤ 20% (27). The echocardiographer should carefully consider the limitations of this examination and the results obtained, especially in the case of poor acoustic quality, and evaluate the results in accordance with the individual patient's clinical symptoms and results from other available indices.

In conclusion, LV-GLS in echocardiography is an important index of LV function and its physiologic contractility, providing incremental prognostic/diagnostic information about HF or IHD. It can be implemented as a reliable stratification tool for treatment/patient selection and can be used as a post-procedural follow-up method for the estimation of short/long-term cardiac adverse events.

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