Left Ventricular Global Strain Analysis by Two-Dimensional Speckle-Tracking Echocardiography: The Learning Curve

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Background: The application of left ventricular (LV) global strain by speckle-tracking is becoming more widespread, with the potential for incorporation into routine clinical echocardiography in selected patients. There are no guidelines or recommendations for the training requirements to achieve competency. The aim of this study was to determine the learning curve for global strain analysis and determine the number of studies that are required for independent reporting.

Methods: Three groups of novice observers (cardiology fellows, cardiac sonographers, medical students) received the same standardized training module prior to undertaking retrospective global strain analysis on 100 patients over a period of 3 months. To assess the effect of learning, quartiles of 25 patients were read successively by each blinded observer, and the results were compared to expert for correlation.

Results: Global longitudinal strain (GLS) had uniform learning curves and was the easiest to learn, requiring a minimum of 50 patients to achieve expert competency (intraclass correlation coefficient > 0.9) in all three groups over a period of 3 months. Prior background knowledge in echocardiography is an influential factor affecting the learning for interobserver reproducibility and time efficiency. Short-axis strain analysis using global circumferential stain and global radial strain did not yield a comprehensive learning curve, and expert level was not achieved by the end of the study.

Conclusions: There is a significant learning curve associated with LV strain analysis. We recommend a minimum of 50 studies for training to achieve competency in GLS analysis. (J Am Soc Echocardiogr 2017;30:1081-90.)

Keywords: Strain, Speckle-tracking echocardiography, Learning curve

Strain imaging by noninvasive speckle-tracking echocardiography has become an important quantitative tool in the assessment of left ventricular (LV) function with increasing clinical applications. Global longitudinal strain (GLS) is the most important measurement and has been shown to be superior to ejection fraction (EF) in the detection of early subclinical myocardial dysfunction with improved prognostic implications.[1] The use of GLS has recently been incorporated in the latest American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) chamber quantification guidelines as one of the standard parameters of LV systolic function assessment.[2] Recently, a Joint ASE/EACVI industry taskforce has been formed to standardize strain across the vendors to improve compatibility for increased clinical use.[3] GLS is particularly important in the evaluation of chemotherapy-induced cardiotoxicity with an

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Abbreviations

2D = Two-dimensional

AFI = Automated function imaging

ASE = American Society of Echocardiography

AVC = Aortic valve closure

EACVI = European Association of Cardiovascular Imaging

EF = Ejection fraction

GCS = Global circumferential strain

GLS = Global longitudinal strain

GRS = Global radial strain

ICC = Intraclass correlation coefficient

LOA = Limits of agreements

LV = Left ventricular

LVEF = Left ventricular ejection fraction

PD = Percentage difference

ROI = Region of interest

expert consensus statement published with proposed clinical diagnostic algorithms.[4] GLS has also been shown to have superior prognostic value in valvular heart disease and various cardiomyopathies.[5,6] There are other types of global strain parameters in other axes of motion including global circumferential strain (GCS), global radial strain (GRS), and torsion that remain predominantly for research use.

Previous studies have published learning curves for stress echocardiography interpretation and visual estimation of EF to guide clinical training.[7,8] However, the determination of the specific training requirements for accurate strain analysis have not yet been established. This is crucial and should be established before the widespread clinical use of strain echocardiography in the community. The aim of this study is to determine the learning curve in different groups of observers for global strain analysis (GLS, GCS, and GRS) and to evaluate the number of studies that are required to achieve competency with equivalence to an expert. We also aimed to determine whether there is a differential learning curve between different groups of observers: cardiologists versus cardiac sonographers versus medical students; and whether there will be a difference in their training requirements to achieve competency.

METHODS

Study Design

This is a longitudinal study in which myocardial strain was retrospectively analyzed in 100 patients. All patients had good image quality with fewer than two uninterpretable segments by visual analysis. There were four groups of observers who undertook offline postprocessing strain analysis on the same 100 patients in the exact same order of sequence over a period of 3 months from April to June 2016. The four groups of observers were (1) experts, (2) cardiology fellows, (3) cardiac sonographers, and (4) medical students. Each group had two observers for interobserver validation and standardization within each group. By definition, the expert group I (J.C. and K.S.) was considered as the reference standard for development of the learning curve. The experts have experience equivalent to Level III ASE competency in echocardiography with greater than 3 years of extensive clinical and research experience in strain analysis and previous publications in the field of strain imaging.[9-11] The remaining groups of novice observers have different backgrounds and levels of previous exposure to echocardiography, but none have had any previous experience in strain analysis. Group 2 comprised two cardiology fellows (N.G.O. and J.H.) who are currently undergoing a cardiology training program and have achieved the equivalence of at least Level II ASE competency in echocardiography. Group 3 comprised two accredited cardiac sonographers (R.C. and A.S.) who are competent in echocardiography acquisition with more than 2 years of experience from their postgraduate professional qualifications and certification in echocardiography. Group 4 comprised two medical students (I.S. and W.S.) undergoing their first M.D. postgraduate medical degree studies. The observers were independent, and the results were blinded to each observer. The study was approved by the ethics committee of the local institution.

Training Protocol

At baseline, apart from the experts, all observers had no previous experience in strain analysis. In the beginning, all three groups of novice observers were subject to an identical standardized training module prior to commencement of strain analysis. The permission for publication of results had been obtained from each observer. The training module was presented by the expert (J.C.) and consisted of a standard tutorial in addition to supervised practical hands-on training. The standard tutorial covered topics including (1) principles and fundamentals of strain imaging, (2) standard echocardiographic views with reference to basic cardiac anatomy, (3) strain analysis workflow with specific buttonology for offline analysis using vendor-specific software EchoPAC BT13 (GE, Horten, Norway), and (4) tips and pitfalls in strain analysis similar to protocol published by Negishi *et al.*[12] After the tutorial, each observer was given the opportunity to perform hands-on offline strain analysis on three consecutive patients under the supervision and guidance of the expert. After formal standardized training, the observers undertook independent blinded strain analysis on a cohort of 100 patients in the same order of sequence over a defined period of 3 months.

Study Population

We retrospectively performed offline strain analysis on 100 patients. The study population consisted of patients who underwent two-dimensional (2D) echocardiography with clinical indications that included dobutamine stress echocardiography, assessment of chest complaint, known ischemic heart disease, valvular heart disease, other cardiomyopathies, and pericarditis. Only patients with good image quality were included with fewer than two segments uninterpretable by visual assessment. Other exclusion criteria not suitable for strain analysis were arrhythmias and pacemaker implants.

Echocardiography

Standard 2D echocardiography was performed with the patient in the left lateral decubitus position using a commercially available system (Vivid E9, General Electric Vingmed, Milwaukee, WI) equipped with a 3.5-MHz transducer. Standard 2D images triggered to the QRS complex and were saved in cineloop digital format. LV end-systolic and end-diastolic volumes were assessed, and LVEF was calculated from the apical four- and two-chamber views using Simpson's biplane method.[2] For the assessment of GLS, apical four-chamber, two-chamber, and long-axis views were acquired with a frame rate between 50 and 80 frames/sec. For the assessment of short-axis strain (GCS and GRS), images were acquired at parasternal short-axis views at a frame rate between 50 and 80 frames/sec of the LV at three levels: basal (level of mitral valve), mid (level of papillary muscle), and apical.

Short-axis views were acquired as circular as possible and perpendicular to the long axis of the left ventricle. The set of echocardiographic images acquired were digitally stored to enable offline strain analysis by the different groups of blinded observers.

GLS

Global LV longitudinal strain was quantified using the automated function imaging (AFI) protocol from vendor-specific offline analysis software EchoPAC BT13 (GE Healthcare, Horten, Norway). The software analyzed and enabled frame-to-frame tracking of 2D motion of speckles within the myocardium, which represented natural acoustic markers. GLS analysis required the images of three apical views (apical long-axis, four- and two-chamber). First, the end-systolic frame is defined in the apical long-axis view by closure of the aortic valve (AVC) using the automatic function to ensure consistency of AVC between observers. This AVC interval is used as a subsequent reference for the four- and two-chamber view loops. After defining the mitral annulus and LV apex with 3 index points at the end-systolic frame in each apical view, the automated algorithm traces and tracks the motion of the endocardium. If the tracking does not seem to be accurate, the region of interest (ROI) can be readjusted by correcting the endocardial border or width of ROI or by selecting a new ROI altogether. The observer then visually checked and validated the automated endocardial border tracking of each myocardial segment and repeated the process of tracking if required. The automated algorithm, using a 17-segment model, calculated the GLS, which was the weighted average of the peak systolic longitudinal strain of all segments. The processing time required from the beginning to end of the GLS analysis was recorded. The average heart rate of image acquisition was 68 ± 12 bpm. The average frame rates of image acquisition were 53 ± 5.7 Hz. Out of a total of 1,700 segments for GLS, the software was able to track 98% of segments.

Global Short-Axis Strain

The GCS and GRS were derived from images of the parasternal short-axis views at three levels (basal, mid, apical) using commercially available 2D strain offline analysis software (EchoPAC BT13, GE Healthcare). The endocardial border of each short-axis level was manually traced in the end-systolic frame defined by AVC. An ROI was then drawn to include the entire myocardium. The semiautomated 2D strain algorithm then automatically segmented the LV short axis into six equidistant segments and selected suitable speckles for tracking frame by frame in the 2D short-axis plane. The observer then visually checked and validated the tracking quality and manually readjusted the ROI if required. Regional strain curves were then analyzed at end systole to minimize observer variability. The GCS and GRS were manually calculated by taking the average of the regional peak systolic circumferential and radial strain values of all segments in all three levels, respectively. The total processing time required for short-axis analysis to obtain GCS and GRS was recorded. Among a total of 1,800 segments for three levels of short axis (apex, mid, and basal), the software was able to track with a feasibility of 93% of all segments.

Statistical Analysis

Continuous data were presented as mean values ± SD. Learning curves were derived by analyzing the data in four quartiles of 25 patients. The GLS, GCS, and GRS measurements from each group of observers were compared to those of the experts using linear regression analysis with intraclass correlation coefficients (ICCs) and Bland-Altman analysis to derive the mean bias ± 1.96 SD. Learning curves for each type of strain were plotted in a graph with ICC value on the y axis and number of patients in quartiles on the x axis. An ICC plateau of >0.90 compared to expert was considered equivalent to expert-level achievement of accuracy and competency. Interobserver measurement variability within each group of observers was determined by using Spearman's correlation, Bland-Altman analysis, and percentage difference (PD), which is defined as the absolute difference between two paired values divided by the average of the two values. It is expressed as a percentage. Interobserver variability among experts was determined in a randomly selected population of 25 patients. This forms the basis of reference standard for comparing 95% CI limits of agreements (LOA) between observers in the learning curve. When comparing continuous data such as timing between two groups, Student's *t* test was used. A *P* value of < .05 was considered significant.

Table 1 Clinical, echocardiographic characteristics and clinical indications

Clinical characteristics	
Age (years)	62 ± 16
Male (%)	60
Height (cm)	169 ± 9
Body weight (kg)	81 ± 19
Body surface area (m^2)	1.90 ± 0.22
Body mass index (kg/m^2)	28 ± 6.5
Heart rate (bpm)	68 ± 12
Echocardiographic characteristics	
EF (%)	55 ± 14
End-diastolic volume (mL)	116 ± 68
End-systolic volume (mL)	59 ± 58
Frame rate (frames/sec)	53 ± 6
Clinical indication (%)	
Dobutamine stress echocardiography for diagnosis ischemic heart disease	33
Chest complaint	26
Ischemic heart disease	20
Valvular heart diseases	11
Cardiomyopathy	8
Pericarditis	2

RESULTS

Patient Characteristics

There were 100 patients included in the study (60% male and 40% female). The overall cohort had a wide spectrum of pathologies, with a mean age of 61.8 ± 16.3 years and a wide range of EF (14%–77%; mean, 55% ± 14%) and LV systolic volume 59 ± 58 mL. The clinical and echocardiographic characteristics of the study population are listed in Table 1. Thirty-three patients performed dobutamine stress echocardiography for diagnosis of

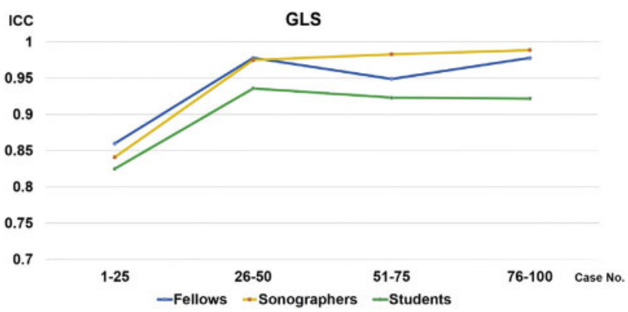

Figure 1 GLS Learning curve. ICC of each group compared with expert over consecutive quartiles of 25 cases.

ischemic heart disease, 26 patients performed echocardiography for chest complaint, 20 patients had coronary heart disease, 11 patients had valvular heart disease, eight patients had cardiomyopathy, and two patients had pericarditis.

GLS

Learning Curve. All three groups of novice independent observers (fellows, sonographers, and medical students) demonstrated similar trends and rate in their progressive improvement in consistency of GLS strain analysis. At baseline the ICCs of every novice group compared to expert were very similar for the first 25 patients (fellows: ICC, 0.86, LOA, −3.94% to 4.02%; sonographers: ICC, 0.84, LOA, −3.92% to 4.42%; students: ICC, 0.83, LOA, −3.52% to 4.72%). The consistency of every group was achieved to the level of the expert after approximately 50 cases, when the learning curves reached a plateau ICC > 0.90 for all three novice groups (Figure 1, Tables 2–4).

GLS Interobserver Reproducibility. We demonstrated the progressive improvement in interobserver reproducibility of the two blinded observers within each group. GLS analysis between experts was highly reproducible and showed excellent correlation with very narrow 95% CI LOA (r = 0.98; PD, 8% ± 19%; 95% CI LOA, −1.56% to 1.82%) in 25 randomly selected cases (Figure 2). Each novice group showed progressive improvement in their interobserver reproducibility and LOA compared with experts (Figure 2). After 50 patients, similar interobserver reproducibility correlations were achieved between the two observers within each group of fellows (r = 0.98; PD, 5% ± 4%; LOA, −2.33% to 0.97%) and sonographers (r = 0.97; PD, 5% ± 4%; LOA, −1.84% to 1.80%). However, among medical students, even though good correlation was achieved, very wide 95% CI LOA existed even after 100 patients at the end of the study (r = 0.95; PD, 45% ± 51%; LOA, −0.43% to 7.57%).

GCS

Learning Curve. By the end of the study of 100 patients, the learning curves of fellows, sonographers, and students showed nonsignificant nonlinear trend of marginal improvement for GCS (Figure 3). The learning curve failed to achieve the target plateau ICC cutoff of 0.90 at the end of the study, and no group was able to achieve competency equivalent to that of expert (fellows: ICC, 0.83, LOA, −1.75% to 7.73%; sonographers: ICC, 0.84, LOA, −0.89% to 7.19%; students: ICC 0.77, LOA, −3.55% to 10.45%; Tables 2–4).

GCS Interobserver Reproducibility. Result of GCS analysis between experts showed good interobserver correlation but wide 95% CI LOA (r = 0.81; PD, 18% ± 16%; LOA, −4.45% to 10.17%) in randomly selected 25 patients. Interobserver agreements between fellows (r = 0.90; PD, 19% ± 10%; LOA, −4.38% to 7.06%) and sonographers (r = 0.98; PD, 15% ± 39%; LOA, −2.48% to 1.88%) were similar to experts from beginning to end of the study. Student progress was comparatively suboptimal and failed to achieve reliable interobserver reproducibility, with persistent wide 95% CI LOAs by the end of the study of 100 patients (r = 0.76; PD, 60% ± 42%; LOA, −4.49% to 16.57%; Figure 4).

GRS

Learning Curve. All three novice groups demonstrated a significant improvement in GRS analysis in the first 50 cases but failed to continue to improve thereafter. The overall learning curves are inconsistent and did not demonstrate progressive improvement in consistency (Figure 5). By the end of the study, expert competency level could not be achieved (fellows: ICC, 0.75, LOA, −20.87% to 13.19%; sonographers: ICC, 0.69, LOA, −25.29% to 13.79%; students: ICC, 0.87, LOA, −13.65% to 11.83%; Tables 2–4).

GRS Interobserver Reproducibility. Interobserver agreement of GRS between experts showed only modest correlation with very wide 95% CI LOA (r = 0.75; PD, 24% ± 27%; 95% CI LOA, −19.53 to 13.87%). Interobserver reproducibility of the novice groups was comparatively suboptimal and tended to be variable with large 95% CI LOA (Figure 6). Sonographers were the only group who showed better correlation at the end of study (r = 0.92), but LOA were still too wide to be acceptable (−12.48% to 11.42%).

Comparison of Analysis Time

Average analysis time for GLS analysis of all novice groups improved progressively toward a total of 100 patients. By the end of the study, average analysis time of sonographers (68 ± 18 sec) was similar to that of the expert (64 ± 24 sec, P = .44), but fellows (77 ± 15 sec, P < .0001) and especially medical students (98 ± 16 sec, P < .0001) were still significantly slower at the end of the study after 100 cases (Figure 7).

Average analysis time for short-axis strain analysis (GCS and GRS) in all novice groups demonstrated a trend toward increased efficiency with significant improvement just after analysis of 25 patients in the first quartile. However, by the end of the study, the average analysis time of experts (118 ± 21 sec) was still significantly faster (P < .0005) than any other groups (fellows: 168 ± 18 sec; sonographers: 140 ± 11 sec; students: 151 ± 25 sec; Figure 8).

DISCUSSION

Strain imaging has evolved over the last 15 years together with the improvement in ultrasound technology with enhanced resolution in image quality, more efficient acquisition, increased accuracy, and more user-friendly postprocessing software. This development has paralleled the increasing accumulation of research evidence that demonstrated the incremental benefit of strain to detect early subclinical myocardial dysfunction beyond the conventional parameter

Table 2 Analysis of intergroup correlation (experts vs fellows)

	Cases	Experts	Fellows	*P* value	*R* value	PD	Bias	LOA	ICC (95% CI)
GLS	1–25	16.4 ± 3.9	16.4 ± 3.6	.92	0.86	7 ± 12	0.04	−3.94 to 4.02	0.86 (0.71–0.94)
	26–50	15.4 ± 3.7	15.2 ± 3.6	.27	0.98	4 ± 3	0.17	−1.30 to 1.64	0.98 (0.95–0.99)
	51–75	15.0 ± 5.2	14.3 ± 4.6	.02	0.96	6 ± 7	0.71	−2.13 to 3.55	0.95 (0.87–0.98)
	76–100	14.2 ± 6.5	13.3 ± 6.2	.0001	0.99	12 ± 13	0.93	−1.03 to 2.89	0.98 (0.85–0.99)
GCS	1–25	19.3 ± 6.0	17.1 ± 4.7	.0007	0.88	16 ± 11	2.25	−3.39 to 7.89	0.79 (0.38–0.92)
	26–50	18.7 ± 4.6	15.3 ± 4.2	<.0001	0.90	21 ± 11	3.42	−0.42 to 7.26	0.69 (−0.08 to 0.91)
	51–75	17.7 ± 6.9	14.3 ± 5.4	<.0001	0.94	21 ± 12	3.39	−1.63 to 8.41	0.80 (0.03–0.94)
	76–100	16.4 ± 6.8	13.5 ± 5.6	<.0001	0.94	22 ± 9	2.99	−1.75 to 7.73	0.83 (0.11–0.95)
GRS	1–25	24.4 ± 9.4	27.0 ± 7.8	.15	0.51	28 ± 28	−2.56	−19.40 to 14.28	0.49 (0.14–0.74)
	26–50	27.9 ± 13.8	27.8 ± 11.9	.96	0.85	20 ± 16	0.08	−14.07 to 14.23	0.85 (0.68–0.93)
	51–75	24.2 ± 13.7	29.9 ± 14.9	.01	0.77	34 ± 31	−5.73	−24.76 to 13.30	0.72 (0.38–0.88)
	76–100	23.1 ± 12.9	27.0 ± 13.1	.04	0.78	30 ± 24	−3.84	−20.87 to 13.19	0.75 (0.49–0.86)

Table 3 Analysis of intergroup correlation (experts vs sonographers)

	Cases	Experts	Sonographers	*P* value	*R* value	PD	Bias	LOA	ICC (95% CI)
GLS	1–25	16.4 ± 3.9	16.2 ± 3.6	.56	0.84	8 ± 12	0.25	−3.92 to 4.42	0.84 (0.67–0.93)
	26–50	15.4 ± 3.7	15.2 ± 3.5	.16	0.98	4 ± 3	0.23	−1.30 to 1.76	0.98 (0.94–0.99)
	51–75	15.0 ± 5.2	15.0 ± 5.1	.97	0.98	4 ± 4	0.01	−1.89 to 1.91	0.98 (0.96–0.99)
	76–100	14.2 ± 6.5	13.9 ± 6.5	.13	0.99	8 ± 12	0.30	−1.56 to 2.16	0.99 (0.97–1.00)
GCS	1–25	19.3 ± 6.0	17.1 ± 4.1	.001	0.88	18 ± 11	2.27	−3.79 to 8.33	0.75 (0.34–0.90)
	26–50	18.7 ± 4.6	15.6 ± 3.8	<.0001	0.91	18 ± 10	3.14	−0.58 to 6.86	0.70 (−0.08 to 0.91)
	51–75	17.7 ± 6.9	14.9 ± 6.1	<.0001	0.95	18 ± 11	2.74	−1.71 to 7.19	0.86 (0.19–0.96)
	76–100	16.4 ± 6.8	13.3 ± 5.8	<.0001	0.96	23 ± 16	3.15	−0.89 to 7.19	0.84 (0.01–0.96)
GRS	1–25	24.4 ± 9.4	28.6 ± 8.4	.002	0.54	32 ± 32	−4.24	−21.02 to 12.54	0.49 (0.13–0.74)
	26–50	27.9 ± 13.8	31.2 ± 11.5	.02	0.87	21 ± 19	−3.35	−16.80 to 10.10	0.83 (0.62–0.92)
	51–75	24.2 ± 13.7	30.4 ± 13.2	.0004	0.84	30 ± 23	−6.17	−20.89 to 8.55	0.77 (0.30–0.91)
	76–100	23.1 ± 12.9	28.9 ± 14.7	.008	0.75	31 ± 22	−5.75	−25.29 to 13.79	0.69 (0.35–0.86)

Table 4 Analysis of intergroup correlation (experts vs medical students)

	Cases	Experts	Medical students	*P* value	*R* value	PD	Bias	LOA	ICC (95% CI)
GLS	1–25	16.4 ± 3.9	15.8 ± 3.3	.17	0.84	8 ± 11	0.60	−3.52 to 4.72	0.83 (0.65–0.92)
	26–50	15.4 ± 3.7	14.5 ± 3.4	<.0001	0.97	7 ± 5	0.93	−0.83 to 2.69	0.94 (0.55–0.98)
	51–75	15.0 ± 5.2	13.9 ± 4.8	.004	0.95	11 ± 9	1.07	−2.26 to 4.40	0.92 (0.77–0.97)
	76–100	14.2 ± 6.5	12.3 ± 5.8	<.0001	0.97	18 ± 20	1.94	−1.16 to 5.04	0.92 (0.33–0.98)
GCS	1–25	19.3 ± 6.0	18.6 ± 5.1	.39	0.77	16 ± 13	0.68	−6.83 to 8.19	0.77 (0.54–0.89)
	26–50	18.7 ± 4.6	17.3 ± 5.5	.007	0.91	13 ± 11	1.35	−3.18 to 5.88	0.87 (0.66–0.95)
	51–75	17.7 ± 6.9	14.7 ± 5.6	.0006	0.84	24 ± 13	2.95	−4.36 to 10.26	0.75 (0.29–0.90)
	76–100	16.4 ± 6.8	13.0 ± 6.8	<.0001	0.86	33 ± 22	3.45	−3.55 to 10.45	0.77 (0.19–0.92)
GRS	1–25	24.4 ± 9.4	22.2 ± 5.9	.18	0.55	30 ± 27	2.19	−13.27 to 17.65	0.49 (0.13–0.73)
	26–50	27.9 ± 13.8	28.1 ± 11.1	.87	0.89	17 ± 16	−0.20	−12.53 to 12.13	0.88 (0.74–0.94)
	51–75	24.2 ± 13.7	25.2 ± 11.0	.56	0.79	28 ± 19	−0.99	−17.38 to 15.40	0.78 (0.56–0.90)
	76–100	23.1 ± 12.9	24.0 ± 12.1	.49	0.87	23 ± 18	−0.91	−13.65 to 11.83	0.87 (0.72–0.94)

of EF.[1] In particular, GLS has been recommended to be incorporated into routine clinical echocardiographic evaluation in a specific patient population for detection of chemotherapy-related cardiotoxicity.[4] In the latest ASE/EACVI guidelines for chamber quantification, GLS has also been recommended as one of the new parameters in the evaluation of LV systolic function.[2] However, there are no established guidelines or published studies to date that specify how much training is required to achieve competency in the use of strain imaging. This is crucial for quality control, especially if strain imaging is increasing in its clinical use. Inaccurate

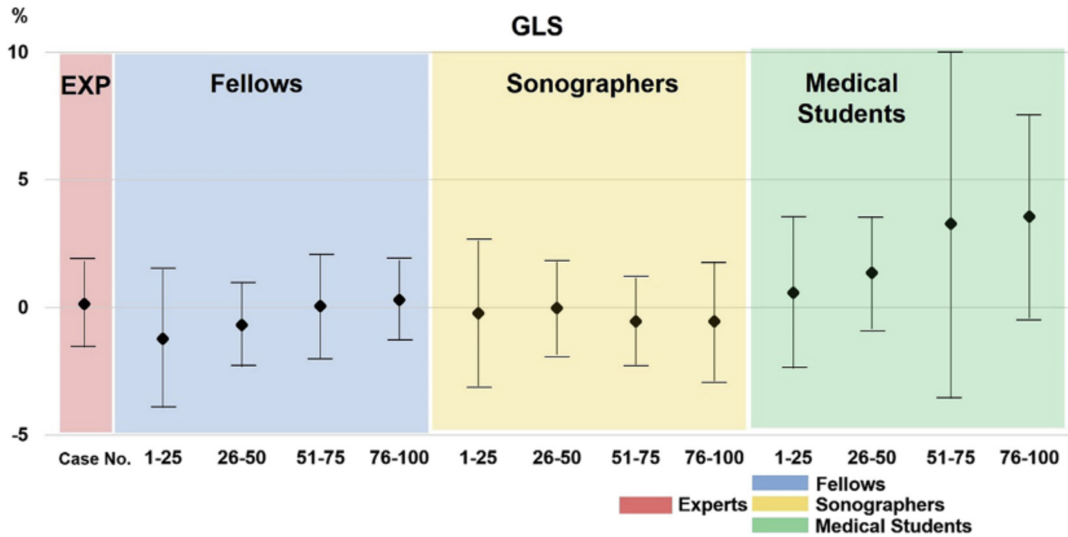

Figure 2 Comparison of GLS interobserver agreement by groups. Interobserver reproducibility data within each group presented as LOA and percentage error bars (mean bias ± 1.96 SD).

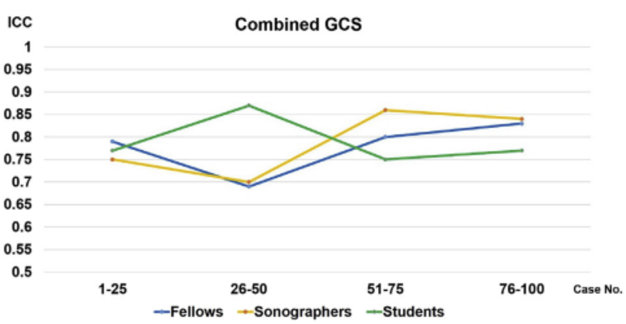

Figure 3 GCS Learning curve. ICC of each group compared with expert over consecutive quartiles of 25 cases.

analysis may lead to adverse clinical management especially in cardio-oncology patients and subsequent decisions on altering chemotherapy. The other questions are who should be performing strain analysis, is there a difference in learning curve between different groups of observers, and what is the difference in learning curves between different types of strain?

This is the first study to determine learning curves for different types of strain analyses using 100 patients with a wide range of systolic function and cardiac pathologies. We have further differentiated these learning curves among different groups of novice observers with different medical backgrounds including cardiology fellows, cardiac sonographers, and medical students. Our study found that GLS was superior to all other types of short-axis strain (GCS and GRS) with learning curves that showed the earliest achievement of competency and consistency comparable to that of experts. Regardless of the types of observers, all three groups demonstrated a similar rate of progress in improvement in accuracy in the first 50 patients. After 50 patients, the diagnostic consistency of the learning curves reached plateau with ICC > 0.90, and competency comparable to expert level could be achieved in all three groups. In comparison, previous published studies have determined the learning curves for other echocardiographic measurements. For example, Akinboboye *et al.* have determined the learning curve for visual estimation of EF to be 20 patients,[8] and Picano *et al.* have determined the learning curve for wall motion interpretation during stress echocardiography to be 100 patients.[7]

All three groups of observers were novice with no previous experience in strain analysis, but they came from different medical knowledge backgrounds and different experience with echocardiography. All underwent an identical training module in strain analysis, and they did not demonstrate any significant difference in their learning curves. It was unexpected that even the medical student group, who had no previous exposure to echocardiography, was able to achieve a similar rate of learning progress compared to that of cardiology fellows and sonographers. This may be a reflection that the latest version of postprocessing strain software is user friendly and easy to use. Possible explanations include the automation of the AFI algorithm with reasonably accurate endocardial border delineation requiring minimal manual adjustments. The buttonology and step-by-step workflow process of using the software is simplified and requires little echocardiographic knowledge to operate.

However, an important finding from the medical student group is that the GLS interobserver reproducibility within this group is suboptimal, with much wider 95% CI LOA compared with the other groups, and cannot achieve the reproducibility results comparable to those of the experts even at the end of the study after 100 patients (Figure 2). On the other hand, the sonographers and fellows were able to achieve much better interobserver reproducibility comparable to the experts by the end of the study. Our GLS interobserver reproducibility results were similar to previously published data from our authors in another study using a different group of patients undergoing dobutamine stress echocardiography.[9] Barbier *et al.* have also demonstrated similar excellent interobserver reproducibility of GLS using the same AFI software analysis algorithm.[13]

The medical student group also significantly fell short of achieving the time efficiency in GLS analysis compared with the other groups, even though there was an improvement throughout the learning curve. Luis *et al.*[10] previously reported that the average GLS analysis time was approximately 1.6 ± 0.4 min, which was similar to the average GLS analysis time performed by our experts of 64 ± 24 sec. The interobserver reproducibility of medical students is unacceptably high even for GLS measurements (PD, 45%). Based on our observations on consistency, reproducibility, and timing,

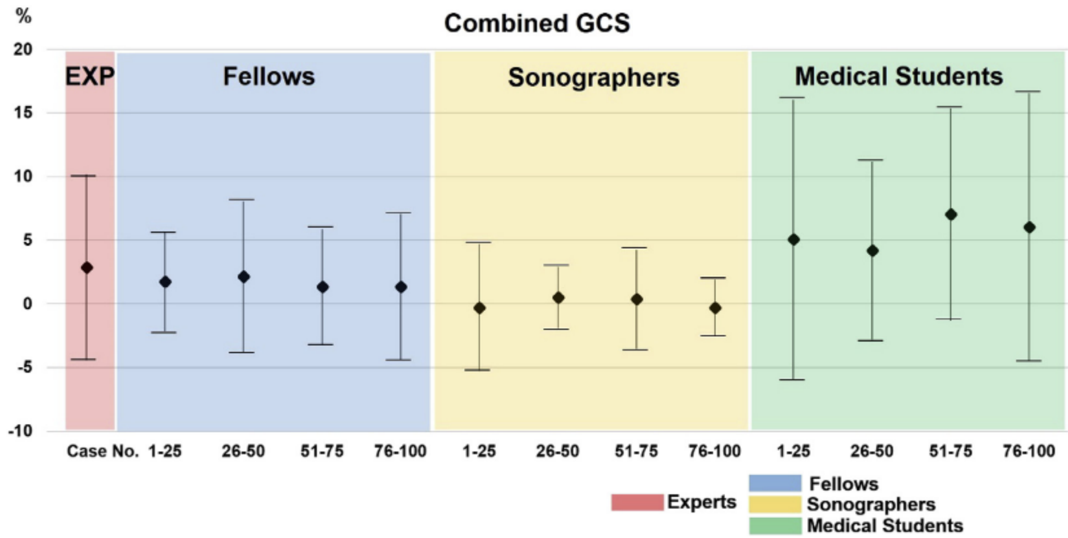

Figure 4 Comparison of GCS interobserver agreement by groups. Interobserver reproducibility data within each group presented as LOA and percentage error bars (mean bias ± 1.96 SD).

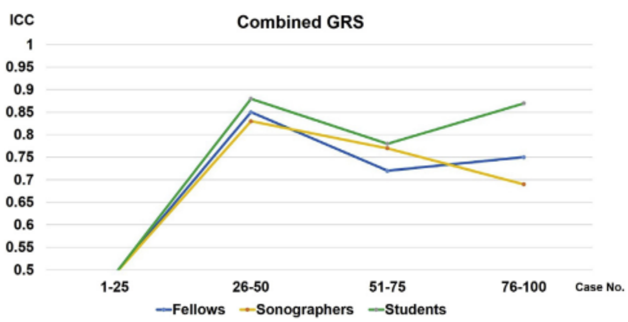

Figure 5 GRS Learning curve. ICC of each group compared with expert over consecutive quartiles of 25 cases.

we have determined the learning curve of a minimum of 50 patients to achieve competency in GLS analysis. To maintain good quality control, our recommendations cannot extend to medical students but are limited to observers who are in the practice of echocardiography or cardiology.

Short-axis strain analysis (GCS and GRS) did not yield the same favorable results as for GLS. There was marginal improvement in GCS learning curve, and expert level was not achieved by the end of the study. GRS showed significant improvement in consistency in the first 50 patients but failed to improve further after this. Expert competency and time efficiency were not achieved by the end of study. Nonexpert PDs for reproducibility between observers were unacceptably high (GCS PD, up to 60%; GRS PD, up to 47%). Even among the expert group, GRS interobserver reproducibility (PD, 24%) and GCS reproducibility (PD, 18%) remain limited and inferior compared with GLS (PD, 8%). This is not surprising for radial strain as other previous studies have also shown that the reproducibility of radial strain was the weakest in comparison with other types of strain with the least consistency in measurements.[14-16] One other possible explanation for the increased difficulty in achieving competency may lie in the technical difficulty in acquiring short-axis images that are exactly perpendicular to the long axis of the LV. Off-axis imaging may directly affect the accuracy of strain measurements. To overcome this geometric technical difficulty in image acquisition, a newer technique of three-dimensional strain imaging, which can acquire the full volume of the LV with automated standardized short-axis selection, may be helpful to ensure greater and improved consistency.

The practical implication of this study is that GLS is the preferred method and superior choice for strain analysis with respect to learning curves. We recommend a minimum of 50 studies to achieve expert consistency in GLS analysis because beyond this number, the learning curve demonstrated a plateau, with the ICC consistently >0.9 for comparisons between the expert group and the study groups. We cannot recommend a specific time frame because our study has predetermined an arbitrary period of 3 months to completion. There are more research data in the literature that support the use of GLS than the other types of strain in its clinical applicability. Our findings are consistent and support this trend of GLS superiority. The skills required for GLS analysis are easier to attain than with other types of strain, with a well-defined learning curve to achieve competency. GLS analysis is more time efficient and has superior interobserver reproducibility, which can be acquired during the learning process. These findings are important for the potential integration of GLS into routine clinical echocardiography exams. A specific learning process for this technology with minimum requirements is achievable and needs to be considered to maintain quality control. Our study could not identify specific learning requirements for GCS and GRS, which may be best limited to predominant research use and further development.

Limitations

First, this study was a retrospective analysis, which may predispose the study to selection bias and issues with missing data.

Second, our study only included patients with good image quality with good endocardial border definition for speckle-tracking. Any studies not suitable for strain analysis with more than two poorly visualized myocardial segments were excluded. This is the one of the major limitations of strain imaging, and learning curves are deemed to be very different, so strain analysis should not be recommended in the setting of suboptimal image quality. Similarly, we failed to assess

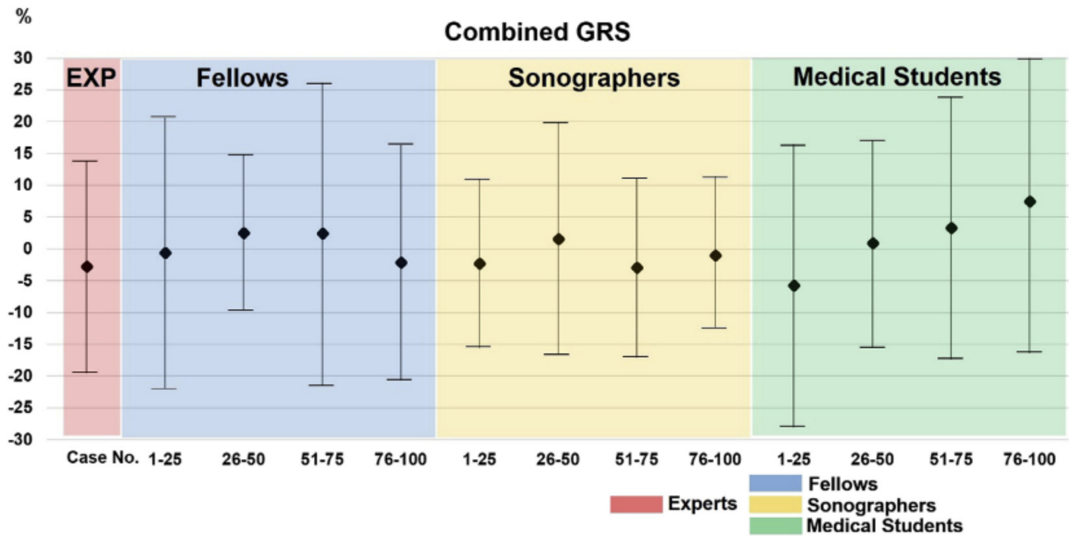

Figure 6 Comparison of GRS interobserver agreement by groups. Interobserver reproducibility data within each group presented as LOA and percentage error bars (mean bias ± 1.96 SD).

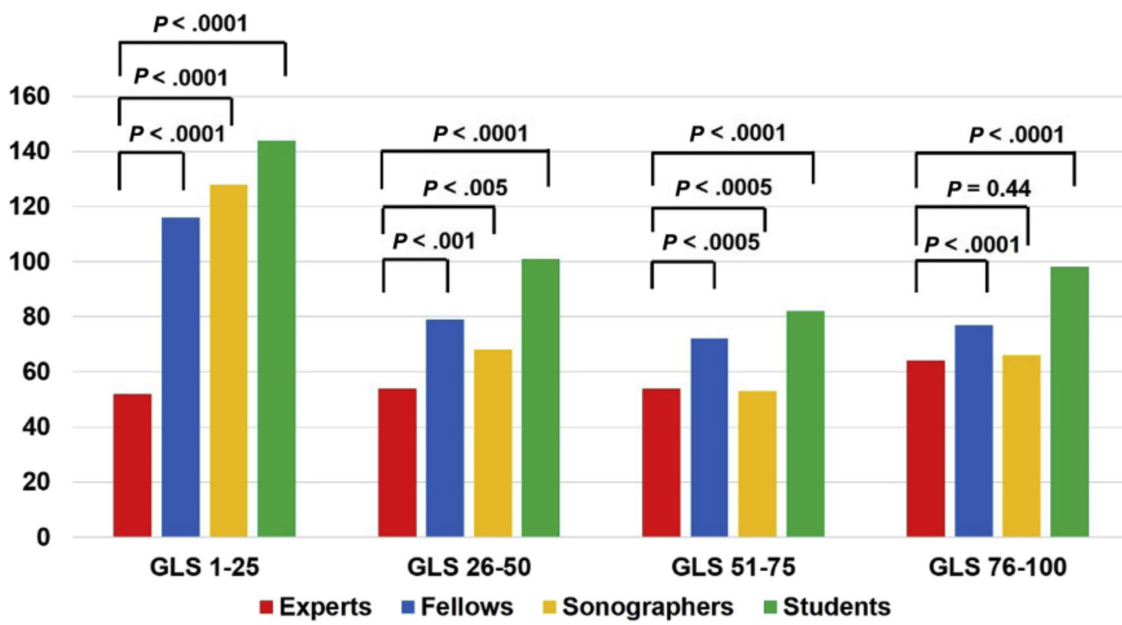

Figure 7 Comparison of analysis time for GLS by groups. Analysis time for GLS analysis (seconds) of all observers in quartiles of 25 cases.

true feasibility as strain analysis was only performed in selected studies with good image quality.

Third, the number of observers in each group was small in this study. Therefore, we made efforts to involve pairs of observers who had similar backgrounds with interobserver correlations to minimize bias. The sample size in the subgroup of patients with coronary artery disease and wall motion abnormalities was too small to extrapolate our findings. The learning curve derived from this study may not be applicable to patients with multiple regional wall motion abnormalities.

Fourth, we limited our evaluation to LV global systolic strain, which is most commonly used in clinical practice. Our study did not incorporate evaluation of other kinds of strain such as left atrial strain, rotation, torsion, diastolic strain, or right ventricular strain.

Intervendor incompatibility has been recognized, and a joint ASE/EACVI taskforce has been formed with industry partners as an ongoing effort to standardize strain measurements.[3] Although recent studies by Shiino *et al.* and Yang *et al.* have already shown marked improvement in intervendor agreement with the latest improved software,[11,17] more work is still needed to achieve intervendor consistency. We need to bear this in mind when we extrapolate our learning curve results to other vendors and other versions of analysis software, which may have different requirements in competency training.

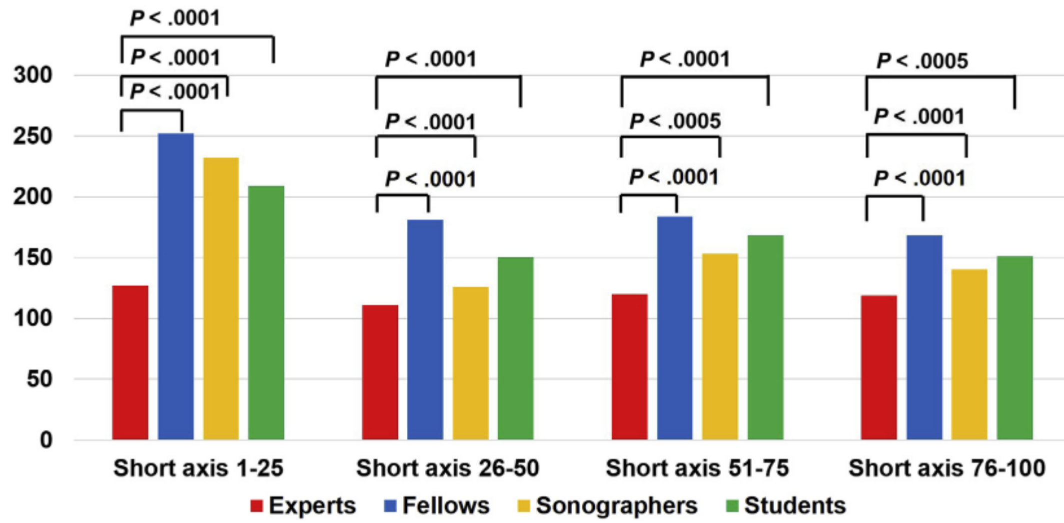

Figure 8 Comparison of analysis time for short-axis strain (GCS and GRS) by groups. Analysis time for short-axis strain analysis (seconds) of all observers in quartiles of 25 cases.

Fifth, the PDs for interobserver reproducibility for GCS and GRS were unacceptably high even among experts, and this was another reason we could not determine learning curves for GCS and GRS.

Finally, we did not have separate timing data for GCS and GRS, but this was combined as a single timing measurement for short-axis strain. This was necessary because GCS and GRS were performed simultaneously in the same algorithm to generate both results.

CONCLUSIONS

This is the first study to demonstrate that learning curves exist for LV global strain analyses. GLS is easy to learn, but if there is no previous experience, a training period is required. For those who have background training in echocardiography, we recommend a minimum of 50 GLS studies to achieve competency in diagnostic consistency, time efficiency, and reproducibility to the level of expert. Our recommendations cannot extend to medical students but are limited to observers who are in the practice of echocardiography or cardiology. We were not able to make recommendations for GCS and GRS, which had more difficult learning curves that did not reach plateau of expert diagnostic consistency.

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