Machine Learning-Enabled Fully Automated Assessment of Left Ventricular Volume, Ejection Fraction and Strain: Experience in Pediatric and Young Adult Echocardiography

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Abstract

Background: Left ventricular (LV) volumes, ejection fraction (EF), and myocardial strain have been shown to be predictive of clinical and subclinical heart disease. Automation of LV functional assessment overcomes difficult technical challenges and complexities, potentially decreasing inter-observer and inter-center variability, reducing analysis times and improving echocardiography laboratory throughput and efficiency. We sought to assess whether a fully automated assessment of LV function could be reliably used in children and young adults. **Methods:** Fifty normal volunteers (22/28, female/male) were prospectively recruited for clinical research echocardiography. LV volumes, EF, and strain were measured both manually and automatically. An experienced sonographer performed all the manual analysis and recorded the analysis timing. The fully automated analyses were accomplished by 5 groups of observers with different knowledge and medical background (experienced sonographer, high school students, college students, medical students and pediatric cardiologists). AutoLV and AutoSTRAIN (TomTec) were employed for the fully automated LV analysis. The LV volumes, EF, strain, and analysis time were compared between manual and automated methods, and among the 5 groups of observers. **Results:** Software-determined endocardial border detection was achievable in all subjects. Image quality did not affect the ability of automated programs to record measurements. The analysis times of the experienced sonographer were significantly shorter for AutoLV than biplane Simpson's method and AutoSTRAIN than manual strain analyses ($p<0.001$). Strong correlations were seen between conventional EF and AutoLV ($r=0.8373$), and between conventional three view global longitudinal strain (GLS) and AutoSTRAIN ($r=0.9766$). The volumes from AutoLV and three view GLS from AutoSTRAIN had strong correlations among different observers regardless of level of expertise. EF from AutoLV analysis had moderately strong correlations among different observers. **Conclusion:** Automated pediatric LV analysis is feasible in normal hearts. Machine learning-enabled image analysis saves time and produces results that are comparable to traditional methods.

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Running Head: Automated assessment of left ventricle in pediatrics and young adult

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ABSTRACT

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Methods: Fifty normal volunteers (22/28, female/male) were prospectively recruited for clinical research echocardiography. LV volumes, EF, and strain were measured both manually and automatically. An experienced sonographer performed all the manual analysis and recorded the analysis timing. The fully automated analyses were accomplished by 5 groups of observers with different knowledge and medical background (experienced sonographer, high school students, college students, medical students and pediatric cardiologists). AutoLV and AutoSTRAIN (TomTec) were employed for the fully automated LV analysis. The LV volumes, EF, strain, and analysis time were compared between manual and automated methods, and among the 5 groups of observers.

Results: Software-determined endocardial border detection was achievable in all subjects. Image quality did not affect the ability of automated programs to record measurements. The analysis times of the experienced sonographer were significantly shorter for AutoLV than biplane Simpson's method and AutoSTRAIN than manual strain analyses ($p<0.001$). Strong correlations were seen between conventional EF and AutoLV ($r=0.8373$), and between conventional three view global longitudinal strain (GLS) and AutoSTRAIN ($r=0.9766$). The volumes from AutoLV and three view GLS from AutoSTRAIN had strong correlations among different observers regardless of level of expertise. EF from AutoLV analysis had moderately strong correlations among different observers.

Conclusion: Automated pediatric LV analysis is feasible in normal hearts. Machine learning-enabled image analysis saves time and produces results that are comparable to traditional methods.

Keywords: machine learning, fully automated assessment, left ventricular function, pediatric echocardiography

Abbreviations

LV: left ventricular

EF: ejection fraction

GLS: global longitudinal strain

2DE: 2-dimensional echocardiography

BSA: body surface area

CPA: cardiac performance analysis

EDV: end-diastolic volume

ESV: end-systolic volume

SV: stroke volume

ICCs: intraclass correlation coefficients

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INTRODUCTION

The quantitative evaluation of left ventricular (LV) size, geometry, and function is an indispensable component of routine clinical cardiology practice and is crucial for patient evaluation and management[1,2]. Various imaging techniques including 2-dimensional echocardiography (2DE), real time 3-dimensional echocardiography, cardiac computed tomography, and magnetic resonance imaging have been extensively studied and applied in clinical decision making by measuring LV volumes, ejection fractions (EFs), and deformation indexes[3–6]. For decades, 2DE has been the main noninvasive imaging modality used to evaluate LV size and function in clinical practice due to its accessibility and low cost.

Visual LVEF assessment by 2DE involves no time-consuming measurements or computations, and is commonly used in busy echocardiographic laboratories, but it is reader-dependent and requires imaging expertise[7,8]. The most utilized quantitative method for 2DE volume and EF calculations is the biplane method of disk summation (modified Simpson's rule)[9]. Despite wide application, the method can be limited by errors in calculation due to LV apical foreshortening, endocardial dropout, and inconsistencies in manual tracing of the endocardial borders[9,10]. Myocardial deformation indices, including strain and strain rate have been shown to detect subtle ventricular dysfunction when conventional measurements of function such as EF and shortening fraction are normal[11]. Technical challenges, measurement complexities, and the time-consuming nature of these methods are recognized barriers to routine use. Automated assessment of LV size and function is considered a more robust, less operator dependent means of providing rapid and reproducible assessment of LV performance capable of improving echocardiography laboratory throughput and efficiency[10,12–15]. Several groups have studied automated LVEF measurements in adult (>35 years old) populations[10,14,16]. However, the impact of automation of LVEF and strain measurements in pediatric and young adult subjects is not well known.

The aim of this study was to test the accuracy and time required for using a novel machine learning-enabled, fully automated assessment of LV volumes, EF and strain in a pediatric and young adult cohort. We hypothesized that LVEF and strain measurements by fully automated analysis would be comparable to that of a manual tracking method, and that the fully automated evaluation of the LV would not be dependent on the medical imaging experience of the user.

MATERIAL AND METHODS

Study Patients

This was a single center IRB approved prospective investigation from October 2014 to January 2020. Healthy volunteer children and young adults were recruited for research echocardiograms. Inclusion criteria were (1) age 0–35 years, (2) no previous history of any heart disease, hypertension or any other systemic disease, and (3) the provision of informed consent. Demographic data was collected, including gender, date of birth, height, weight, heart rate and blood pressure. Body surface area (BSA) was calculated using the Haycock formula[17].

Echocardiography

All recruited subjects underwent complete 2DE examination in a non-sedated state utilizing commercially available ultrasound systems (iE33, Philips, Amsterdam, Netherlands; Vivid E9, GE Health Care, Milwaukee, USA; Aplio i900, Canon Medical Systems, USA) according to the recommendations of the American Society of Echocardiography[9]. Images were optimized for gain, compression, depth, and sector width according to subjects' body size with the aim of achieving the highest imaging frame rate while retaining image quality adequate for accurate measurement. 3-5 beat captures in LV focused four-chamber, two-chamber and long-axis view were acquired consistently during quiet respiration. All data was stored digitally for subsequent analysis. All subjects had structurally and functionally normal hearts.

The image loop with the best visualization of the myocardium without foreshortening was chosen for analysis. End-diastole was defined at the peak of the electrocardiographic R-wave and/or the frame of mitral valve closure. End-systole was defined at one frame before mitral valve opening.

Manual EF and Strain Analyses

An experienced sonographer measured LV volumes and EF using the conventional biplane Simpson's method. The volume measurements were performed at both end-diastole and end-systole by manually delineating the endocardial border (blood-tissue interface) in apical four- and two-chamber views with the papillary muscles and trabeculae included. At the mitral valve level, the contour was closed by connecting the two opposite sections of the mitral ring with a straight line. LVEF was calculated according to the biplane method of disks summation[9]. The measurement process was timed beginning when selected images were loaded into respective observing windows to be analyzed. Timing was stopped once the end-diastole and systole borders had been traced.

The sonographer then performed the manual LV strain analyses by employing offline 2D CPA 1.4 (Cardiac Performance Analysis) (TomTec Imaging Systems, Unterschleissheim, Germany). The endocardial border was manually traced at end-systole in the apical four-, three-, and two-chamber views. Tracking of the endocardial border was confirmed by visual inspection and was manually adjusted if necessary. The cardiac cycle with the best tracking was selected for analysis. The semi-automated quantification of LV longitudinal strain measurements of all three views were generated by the software. Timing began when optimal images were loaded into 2D CPA to be analyzed and was stopped when the longitudinal strain had been generated.

Observers for Fully Automated Analysis

There were 5 groups of observers who participated in this study: (i) a sonographer with more than 30-years of clinical echocardiographic experience and more than 1 year AutoLV and AutoSTRAIN experience whose measurements served as the standard of comparison for the purposes of this study, (ii) two high school students, (iii) two college students, (iv) one medical student, and (v) two pediatric cardiologists who subspecialized in areas other than cardiac imaging. The sonographer educated high school students, college students, and medical students on the basic cardiac anatomy and recognition of standard echocardiographic views. The sonographer gave a one-hour AutoLV and AutoSTRAIN training to the other four group observers. Each observer practiced AutoLV and AutoSTRAIN analysis on at least 10 good image quality normal echocardiograms. Then each observer performed a timed fully automated LV analysis on all recruited subjects' echocardiography.

Fully Automated Analysis

All observers performed the fully automated LV analysis with offline AutoLV and AutoSTRAIN (TomTec Imaging Systems, Unterschleissheim, Germany). AutoLV provides automated LV measurements using Simpson's biplane method of disk summation[9] by applying a machine-learning algorithm for DICOM images[10]. With clip selection of apical four- and two-chamber views of LV by the observer, the software automatically provides initial contouring of the LV in end-diastole and end-systole (**Figure 1**). LV volumes and EF are visualized for immediate assessment of left ventricular function and manually adjusted if necessary. Timing of the automated process began when optimal images were loaded into AutoLV to be analyzed. Timing was stopped when the volumes and EF had been produced.

AutoSTRAIN utilizes speckle tracking to automatically detect the endocardial border of the LV and assess cardiac motion over the cardiac cycle and also applies a machine-learning algorithm for DICOM images. With clip selection of apical four-, two-chamber and long axis views of LV by observer, the longitudinal strain results as well as time-to-peak longitudinal strain values were automatically visualized at a glance in a bull's-eye view. End-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and EF are computed according to a triplane approach, and endocardial global longitudinal strain (GLS) is given as the average endocardial GLS of all views (**Figure 1**). Timing began when optimal images were loaded into AutoSTRAIN to be analyzed. Timing was stopped when the strain values had been generated.

Statistical Analysis

Distribution normality of continuous variables was confirmed before further analysis. Continuous variables were presented as mean±SD and categorical variables were presented as n (%). The paired Student t test and one-way ANOVA were used to compare the mean values between analysis methods and among observer types. Agreement between various measures was evaluated using intraclass correlation coefficients (ICCs) and Bland-Altman analysis. For all statistical tests, a 2-tailed p value <0.05 was considered statistically significant. Statistical analysis was performed using Minitab 19.2.0 (Minitab Inc, State College, PA, US) and MedCalc 19.1.6 (MedCalc Software Ltd, Ostend, Belgium).

RESULTS

Feasibility

Fifty normal volunteers (22/28, female/male) were recruited. Their age was 15.9±11.7 years, body surface area was 1.4±0.7 m^2, body mass index was 22.2± 5.3 kg/m2and heart rate was 84.5±23.4 beat/minute. Software-determined endocardial border detection was achievable in all subjects. Echocardiographic images were graded a priori by an experienced sonographer as Good, Fair, and Poor using the following definitions: (i) Good- all segments with clear endocardial definition; (ii)Fair - 1-2 segments with suboptimal endocardial definition; (iii) Poor - more than 2 segments, but less than 4 segments with suboptimal endocardial definition. There were 26 cases with good image quality, 20 with fair, and 4 with poor. No images were excluded from analysis. Image quality did not affect the ability of automated programs to record measurements. **Table 1** summarizes volumes, EF, and strain measurements of all study subjects by all methods with all observers.

Manual analyses vs. fully automated analyses

The analysis times of the experienced sonographer were significantly shorter for AutoLV than for standard biplane Simpson's method (111.9±35.7 sec vs. 155.2±37.6 sec, $p<0.001$), and significantly shorter for AutoSTRAIN than with manual strain analyses (71.8±23.2 sec vs. 317.5±188.1 sec, $p<0.001$) (**Figure 2**). Based on ICC analysis, strong correlations were seen between all conventional volumes and AutoLV (EDV r=0.9935; ESV r=0.9887; SV r=0.9044), between conventional three view GLS and AutoSTRAIN (r=0.9766), between conventional EF and AutoLV (r=0.8373), and between conventional 4 chamber, 2 chamber, 3 chamber GLS and AutoSTRAIN (4 chamber r=0.7310; 2 chamber r=0.8195; 3 chamber r=0.8561) (**Figure 3**). Bland-Altman analysis showed good agreement between all conventional volumes, EF and AutoLV, and the bias and limits of agreement of conventional strain and AutoSTRAIN were lower with three view GLS than with separated 4 chamber, 2 chamber and 3 chamber GLS (**Figure 4**).

Automated methods with different observers

The average training time for these 5 groups of observers was 3.5±1.5 hours with trainees performing test measurements on at least 10 different echocardiograms prior to study analysis. High school students took the longest time to perform AutoLV analysis whereas pediatric cardiologists and medical students performed the AutoLV analysis as quickly as the experienced sonographer (**Figure 5**). The volumes, including EDV, ESV and SV from AutoLV had strong correlations among different observers regardless of level of expertise (r=0.907, 0.903, 0.906). Even when volumes were used in combination to produce EF, the AutoLV analysis still had moderately good correlations among different observers. The three view GLS from AutoSTRAIN had strong correlations among different observers which provided the most consistent results across operators. Four, two and three chamber GLS varied widely between different observers (**Figure 3**).

DISCUSSION

We demonstrate the utility of AutoLV and AutoSTRAIN for rapid and reliable measurement of LV indices in a pediatric and young adult population. Previous attempts with automated EF measurement in 2DE using artificial intelligence-learned pattern recognition and database-guided segmentation programming have been confounded by difficulties with inconsistent endocardial border tracking throughout the cardiac cycle and by dependence on gain settings[18]. AutoLV utilizes new algorithms that rely primarily on speckle tracking and artificial intelligence to follow endocardial borders throughout the cardiac cycle even with frames that may have endocardial dropout[19]. We have demonstrated that AutoLV can overcome these obstacles to allow rapid, accurate calculation of LV size and EF. AutoSTRAIN uses the similar algorithms as AutoLV plus LV longitudinal strain analysis of apical long axis views. Thus, we have validated AutoSTRAIN in pediatric populations.

Multiple studies have shown AutoLV is not significantly affected by poor image quality, unlike visual assessment and Simpson's biplane method[5,10,20,21]. In our study, image quality did not affect the ability of both AutoLV and AutoSTRAIN to record measurements, which allows application in patients with less than optimal echocardiographic windows. This feature has important clinical implications in pediatric cardiology, especially in young children, when optimal echocardiographic images are sometimes unavailable from uncooperative patients.

Currently 2DE EF with visual assessment and Simpson's biplane method are the most accepted standards to evaluate cardiac function. Visual measurement is a time-efficient practice, but the inter- and intra-observer variability remains higher than computer assisted methods[19,21,22]. It requires considerable expertise, often acquired over years of echocardiographic practice, before it becomes comparable with the accepted standard of comparison, MRI[5,13,23]. The Simpson's biplane method requires manual tracing of endocardial borders and demands operator experience and sufficient image quality to accurately define the endocardial outline. It is a time inefficient method which ultimately leads practitioners to abandon it in favor of using visual EF estimation alone. Even though myocardial strain provides additional prognostic value over EF alone[24], the image quality requirement, measurement complexities, and its time-consuming nature have limited myocardial strain analysis in routine clinical use. We have demonstrated a strong correlation between Simpson's biplane method and AutoLV as well as between manual strain analysis and AutoSTRAIN when performed by an experienced sonographer and demonstrated that automated imaging is much less time-consuming. The agreement between conventional EF and AutoLV, and between conventional three view GLS and AutoSTRAIN were good, indicating these methods provide reliable measurements.

Variability is a particularly important issue for manual EF and strain and is an even greater concern with visual EF because of the subjective nature of the assessment[10]. In our study, the comparison of automated analysis among 5 groups of observers, demonstrated that automated imaging can reduce variability and is less operator dependent than conventional manual methods. This finding has valuable clinical implications for single and multi- center longitudinal studies. Declining in EF and GLS over time can be used to identify high-risk patients who need closer follow-up and may benefit from specific therapies to improve their outcome. GLS can also be used to track subclinical changes in LV function over time with serial echocardiographic examinations[25]. Automated imaging can help maintain consistency and quality of EF and GLS measurements among the different operators over time.

LIMITATIONS

Although it is likely that the results will translate to actual practical application in busy clinical echocardiography laboratories, it is beyond the scope of the investigation to demonstrate this. Furthermore, the investigation is limited to normal hearts, so cannot directly address the application of AutoLV and AutoSTRAIN in dysfunctional and structurally abnormal hearts.

CONCLUSIONS

Automated pediatric LV analysis is feasible in normal hearts. Machine learning-enabled image analysis saves time and produces results that are comparable to traditional methods. Clinical implications of machine learning-enabled automated assessment include longitudinal follow-up of pediatric patients, with potentially less operator-dependency and improved echocardiography workflow.

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FIGURES

Figure-1

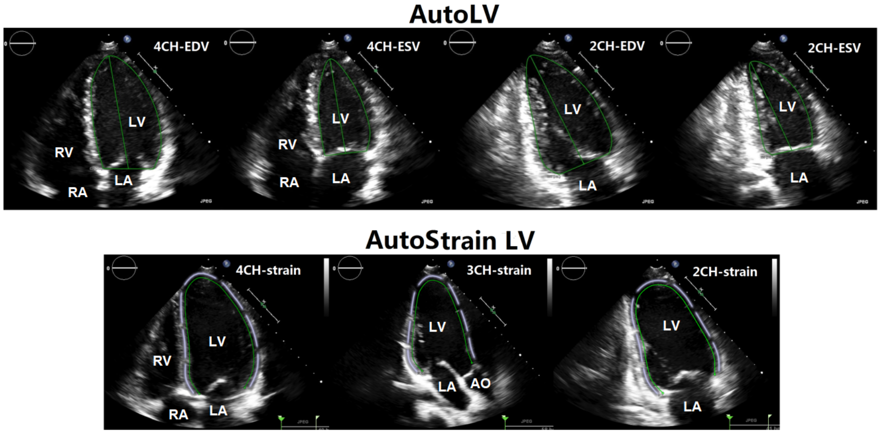

Figure 1: AutoLV and AutoSTRAIN tracking. Top panels show the LV endocardial tracking in apical 4-chamber and 2-chamber views at end-diastole and end-systole by AutoLV. Bottom panels show the LV strain tracking in apical 4-chamber, 3-chamber and 2-chamber views by AutoSTRAIN.

Figure-2

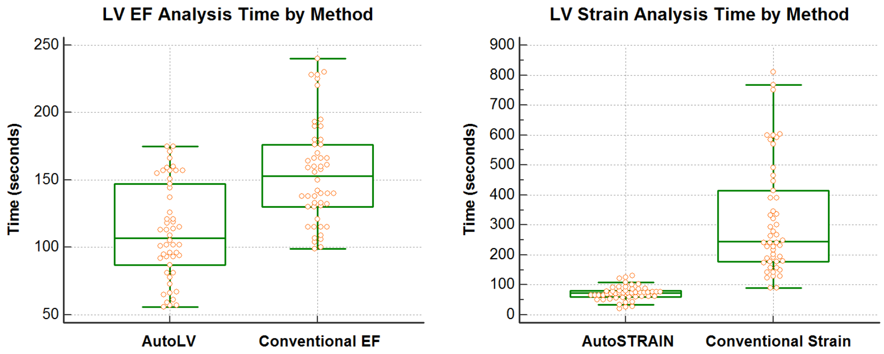

Figure 2: The box plots compare the experienced sonographer's analysis times using automated and conventional methods.

Figure-3

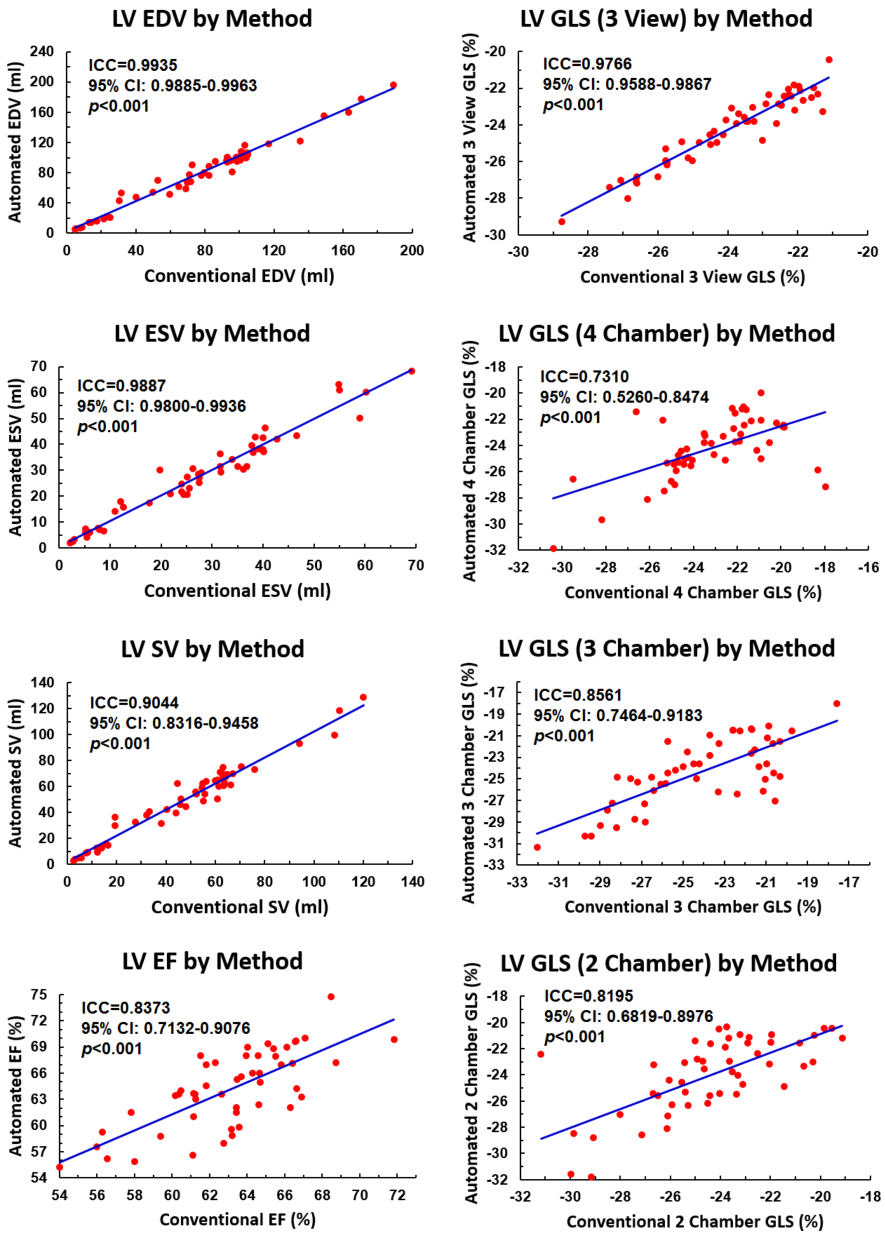

Figure 3: Regressions of measurements of experienced sonographer by automated vs conventional method with ICC analysis information.

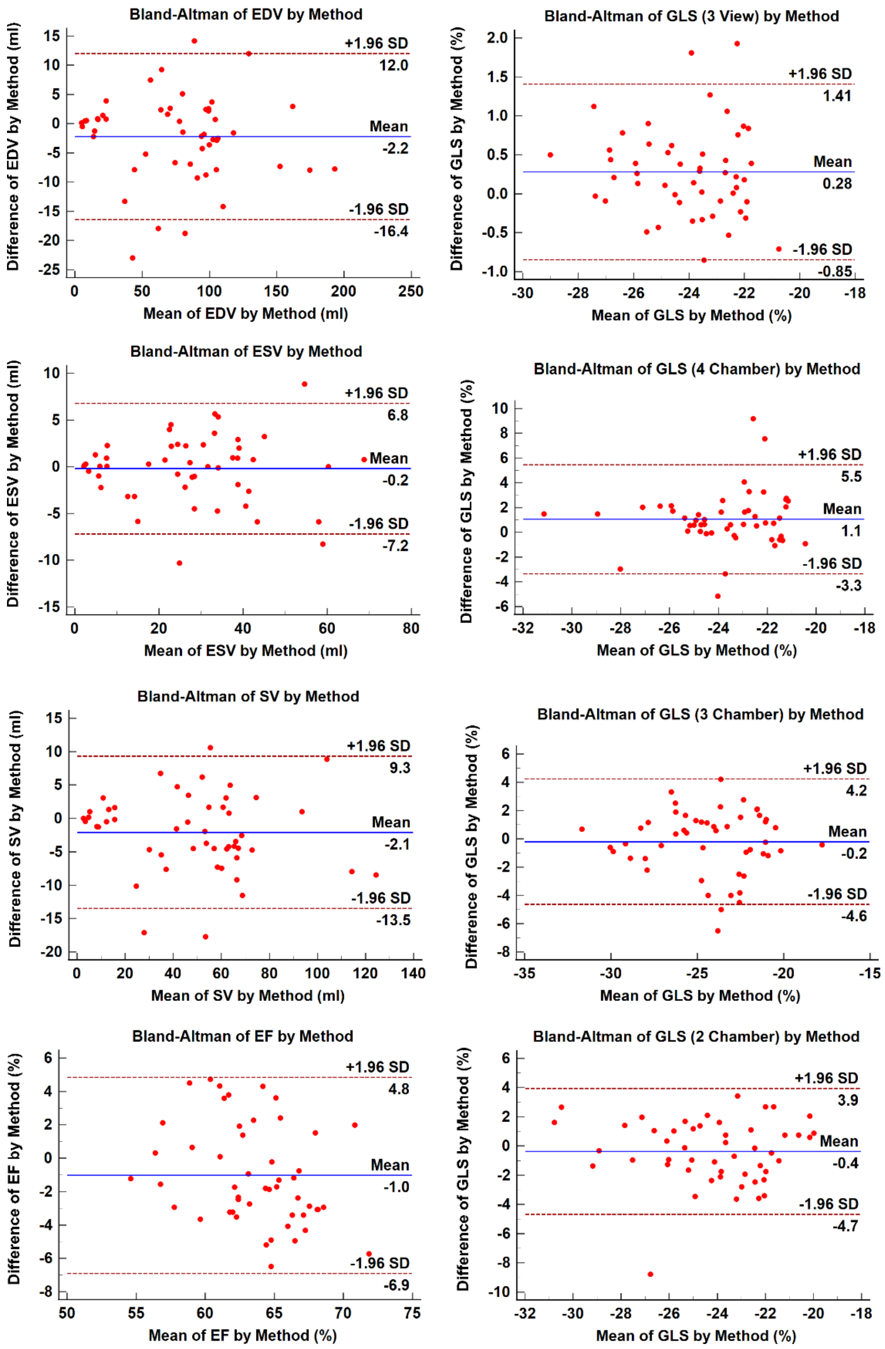

Figure-4

Figure 4: Bland-Altman analysis of experienced sonographer by automated vs conventional method.

Figure-5

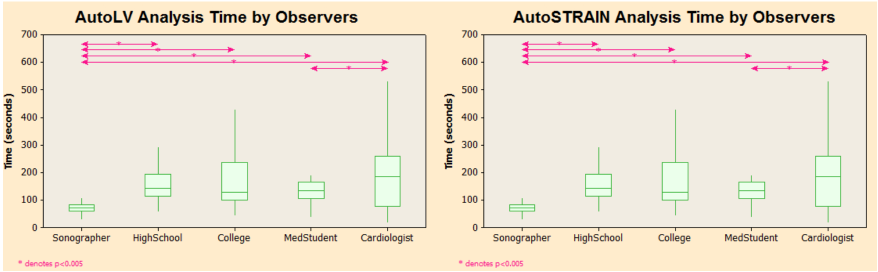

Figure 5: The box plots compare analysis time among the 5 types of observers.

Table 1

Measurements	Sonographer (N=1)	High School Student (N=2)	College Student (N=2)	Medical Student (N=1)	Pediatric Cardiologist (N=2)
AutoLV-EDV (ml)	77.5±45.4	78.0±46.4	86.5±50.5	78.6±45.5	81.0±47.2
AutoLV-ESV (ml)	27.7±16.9	32.8±20.3	35.8±22.2	33.2±20.0	33.9±21.1
AutoLV-SV (ml)	49.8±29.0	45.2±26.9	50.7±29.1	45.4±26.2	47.2±26.6
Auto LV-EF (%)	64.2±4.4	57.9±5.4	59.0±4.6	58.3±4.8	59.3±4.6
Analysis Time AutoLV (seconds)	114±36	209±69	160±82	107±41	107±45
AutoSTRAIN-3 view GLS (%)	-24.2±1.9	-22.3±2.6	-20.8±3.3	-22.1±2.6	-22.0±3.1
AutoSTRAIN-4CH (%)	-24.2±2.3	-22.2±2.8	-20.3±7.5	-22.2±2.8	-23.1±3.5
AutoSTRAIN-2CH (%)	-24.0±2.9	-22.8±3.5	-20.8±7.3	-22.6±3.4	-22.7±3.9
AutoSTRAIN-3CH (%)	-24.4±3.1	-21.9±3.5	-20.0±7.8	-22.1±3.6	-21.4±7.9
Analysis Time AutoSTRAIN (seconds)	72±23	160±81	188±142	139±49	204±156

EDV: end-diastolic volume; ESV: end-systolic volume; SV: stroke volume; EF: ejection fraction; 4CH: four chamber view; 3CH: three chamber view; 2CH: two chamber view; LV: left ventricle

Data expressed as means + standard deviation