Feasibility and Reproducibility of Contemporary Diastolic Parameters and Classification

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Abstract

Aims To evaluate the feasibility, time consumption, intra- and inter-observer re-test reproducibility of echocardiographic indexes and classification algorithms of diastolic function. Methods A total of 356 patients were examined prior to coronary artery by-pass grafting and/or aortic valve replacement surgery. A subgroup of 50 were examined with 3 successive echocardiograms in conditions reflecting daily clinical practice. Diastolic parameters suggested by former (2009) and current (2016) guidelines were obtained and analysed. Acquisition and analysis time, plus intra- and inter-observer variability were assessed. Results Most of the parameters' feasibility were between 93 and 99%, except the TR Vmax (65%). Mean acquisition and analysis time were highest for the left atrial volume (141±24 seconds), in contrast to other parameters which were obtained in approximately one minute. 368 and 360 seconds was in average needed to classify according to the 2009 and 2016 algorithms, respectively (NS). The overall reproducibility was moderate (CV between 10-35%), with TR Vmax having lowest (CV 9.9-12%) and E/e' the highest (CV 22-35%) variation. The 2009 algorithm resulted in higher indeterminate cases vs. the 2016 algorithm. Comparing the old and recent guidelines, 20 and 8 patients were reclassified during inter-examiner analysis, respectively. Conclusion The diastolic parameters are, in general, feasible and time efficient. Reproducibility is moderate. The 2016 guidelines algorithm seemed superior to the 2009 algorithm in terms of its feasibility and precision to classify patients in a uniform matter. Time consumption was equal. The 2016 algorithm proved more restrictive than 2009 in classifying patients with advanced stages of DD.

Title

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Introduction

Heart failure (HF) remains a rising global epidemic, with an estimated prevalence of > 37.7 million individuals globally (1, 2). Excluding sub-Saharan Africa, the rates of death from noncommunicable diseases, such as HF, are increasing worldwide (3). Left ventricular (LV) diastolic dysfunction (DD) is a recognized pathophysiologic mechanism of heart failure (4-6). Moreover, even in the absence of heart failure, DD has been shown to have independent prognostic significance (7, 8). While the gold standard for assessing diastolic dysfunction is thought to be derived from ventricular pressure volume relationships, this invasive approach is rarely used in clinical practice. Echocardiography allows indirect non-invasive evaluation of LV diastolic function (9-11). However, applicability of echocardiography for evaluations of LV filling and relaxation parameters in a clinical setting may be significantly limited if measurements of diastolic parameters are exceedingly time-consuming or affected by reduced feasibility and excessive variability. Therefore, evaluation of the time-consumption, as well as the feasibility and reproducibility, in a realistic clinical setting is important.

The majority of validations studies is reporting re-analyse reproducibility, only few report re-test reproducibility (12, 13). Recently, updated recommendations for the classification of diastolic function has been released (9). Indeed, this algorithm is based on expert consensus and on parameters in which the re-test reproducibility is unknown, stressing the need to validate it in a clinical setting. Presently, the available literature regarding the feasibility and re-test reproducibility of the latest recommended diastolic measurements and their impact on the guideline's classification algorithms are scarce.

The aim of this study was to evaluate the feasibility, time consumption, and the intra- and inter-observer re-test reproducibility of echocardiographic indexes and classification algorithms of diastolic function.

Materials and methods

Study population

This was a single centre study at Rigshospitalet, Denmark. 356 patients planned to undergo coronary artery by-pass grafting and/or aortic valve replacement were enrolled from February 2016 to March 2018. A subgroup of 50 patients, consecutively enrolled from October 2017 to January 2018, were used for the reproducibility studies. In order to reflect daily clinical practice, patients were not excluded due to poor acoustic window, dyspnoea, or obesity. The study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee for the Capital Region Copenhagen. All patients provided written informed consent.

Study design

Three experienced echocardiographers scanned the 356 patients. Two of these echocardiographers blinded to each other's recordings scanned the subgroup of 50 patients three times independently on the same day. The scans were performed consecutively, though between each scan, the echocardiographer guided and repositioned the patient as would happen in a regular clinical situation. Both echocardiographers separately analysed the diastolic function after recordings of all patients were obtained. Analyses were performed offline. Inter-observer reproducibility was defined as the reproducibility calculated by the separate recordings of the two echocardiographers. Intra-observer reproducibility was defined as the reproducibility calculated by the separate recordings of the same echocardiographer. Measurements for intra-examiner analysis were

analysed at least one week apart. In all, patients (n=50) were examined 3 times in total (echocardiographic examinations=150), apart from the remaining pool which were examined once (n=306).

Echocardiographic data acquisition

Echocardiographic images were obtained by three experienced echocardiographers using a Vivid E95 ultrasound scanner (GE Vingmed Ultrasound AS, Horten, Norway). Patients were scanned in the left lateral recumbent position.

A M5Sc-D matrix phased array transducer (1.5-4.6 MHz) was used for two-dimensional echocardiography. A focused examination to evaluate the diastolic function, including 2D and Doppler methods, was performed according to the ASE/EACVI recommendations (9). Three loops were acquired in sinus rhythm and five during atrial fibrillation. Special care was taken to produce an apical 4-chamber and 2-chamber view with a maximized left atria (LA) chamber optimal for endocardial border tracings. Sector width and depth were adjusted to include only the LA. Pulse Wave (PW) Doppler sample volume was aligned with blood flow as accurately as possible according to guidelines (9) in all relevant recordings. 3D images were acquired with a 4V-D volume phased array transducer (1.5-4 MHz). A full-volume dataset of LA consisting of 4-6 wedge-shaped subvolumes was obtained during a single breath hold. Care was taken to avoid stitching artefacts and to include the entire LA by using a nine-slice view, along with three apical views.

Echocardiographic data analysis

Examinations were transferred to an offline workstation and analysed using the EchoPAC software version 201.61 (GE Vingmed Ultrasound AS).

The LA maximum volume was assessed by the disc integration method and corrected for body surface area. The loop with the best visualization of the chamber in which the LA length and transverse diameter were maximized was chosen for analysis. In apical four- and two-chamber view, freeze frames 1-2 frames before mitral valve opening were acquired. The endocardial border in apical 4- and 2-chamber view was delineated, without including LA appendage and pulmonary veins. Peak mitral E- and A-wave velocities (including velocities during Valsalva) and pulmonary vein systolic (S) and diastolic (D) waves were labelled at the leading edge of the spectral waveform. Tissue Doppler measurements of e' and a' velocities (septal and lateral) were labelled at the leading edge of the spectral PW tissue Doppler modal band, after lowering signal gain to reduce feathering. The maximal tricuspid regurgitation velocity (TR Vmax) was acknowledged only when a convincing regurgitation jet with clear borders was obtained. The deceleration times, isovolumetric relaxation time, and pulmonal AR- and mitral A wave duration were analysed as recommend in the guidelines (9).

3D analysis of LA volumes was performed using the 4D Auto LVQ software. The endocardial border was automatically traced by speckle tracking and adjusted when necessary by adding points in either image. LA volume tracings during the entire cardiac cycle were visualized for final validation.

Feasibility of the different diastolic variables was calculated. Exclusion of Doppler images for analysis were due to reduced image quality, based on either unclear and ambiguous Doppler signals or inability to adequately represent the entire velocity jets. 3D images were excluded in cases of stitching artefacts or improper visualization of LA length and transverse diameter, resulting in images unfit for analysis.

Time analysis

Echocardiographic acquisition time and offline analysis time were recorded on 50 patients. Time recordings were performed with a digital stopwatch and with the help of a second observer during echocardiographic acquisition. The order of the acquisition time is presented in appendix. Time was started with the patient in position, with no previous apical images acquired, and thus no knowledge of apical image quality. When 2D images had been acquired, time was stopped while the echocardiographer switched to a 3D probe. Time was then recorded for 3D of the LA. 3D acquisition time included shifting to full-volume mode, adjusting number of subvolumes, and instructing the patient in breath holding.

Offline analysis time was recorded for all methods. Analysis time did not include opening of the EchoPAC software or downloading images from the server. Total time consumption was calculated.

Statistics

Continuous data are presented as mean ± SD. Agreement between methods was expressed according to the Bland-Altman method (14), including calculation of bias and 95 % limits of agreement (LoA). Examiner variability was assessed by the coefficient of variation (CV), and correlation was assessed by Pearson's correlation coefficient. Time analysis was compared by a paired t-test and $p < 0.05$ was considered significant. Data analysis was performed using R and R studio software (version 1.0.143).

Results

Baseline characteristics of the total study population are displayed in Table 1 and 2.

Feasibility of Echocardiographic Diastolic Parameters and Algorithms

Most of the 2016 parameters had feasibility above 95 %, except TR Vmax (65 %), pulmonary parameters (64-70 %), mitral valve A velocity and E/A ratio (93 %) (Table 2). Poor feasibility of TR Vmax was due to indistinct visualization of an envelope for proper labelling, the mitral valve A velocity, and as consequence E/A ratio, was mostly (73 %) due to atrial fibrillation. The remaining parameters used in the 2009 guidelines had moderate feasibility below 80 %, except the mitral valve DT (99 %) (Table 2).

The 2009 algorithm is challenged with many indeterminate cases by its assumption of a combined enlarged LA and reduced e', in order to distinguish DD from normal diastolic function (Figure 2). In our population all cases were assumed as having abnormal diastolic function, since patients were planning to undergo cardiac surgery. According to the 2009 algorithm DD was graded by allowing the majority of the five suggested parameters (E/A ratio, decrease in E/A ratio during Valsalva, time difference between the pulmonal reversal A-wave and mitral A-wave, average E/e' and mitral valve DT) decide the gradings. 85 cases (24 %) had indeterminate gradings. According to the 2016 algorithm, 39 cases (11 %) had indeterminate grading of DD; 27 with unavailable E/A ratio, 8 with two available criteria and unavailable S/D ratio and 4 with only one available criterion.

Time analysis

Most of the diastolic parameters could be acquired and analysed within 30-60 seconds. Few parameters exceeded this, as shown in table 2. The total time needed to classify according to was almost equal in the different algorithms with 8 seconds difference (NS) as shown in figure 1 and table 2. Estimation of LA volume was the most time-consuming parameter (141 +/- 24 s) and decreased (126 +/- 36 s) when accessed by 3D, p = 0,02.

Reproducibility

Intra- and inter-examiner analyses and test-retest variability are displayed in Table 3. Most of the diastolic echocardiographic parameters exhibited a moderate reproducibility with a coefficient of variation between 10 and 35 %. Nevertheless, among these, the current prevailing variables, such as the E/A ratio, e' septal, and the LA volume, showed superior reproducibility. Of note, it seemed that the reproducibility of the E/e' average was influenced by the high variation of the E/e' lateral, as this parameter was 60 % inconsistent than E/e' septal. The parameters used only in the 2009 guidelines were slightly more prone to variation than the ones used in the 2016 algorithm. Almost none of the other investigated diastolic parameters not included in any guidelines surpassed the reproducibility of parameters in use, except the LA volume acquired by 3D and e' average. Surprisingly do the most reproduceable parameter among all seemed to be the newly introduced TR Vmax (Table 3).

To test and compare the reproducibility of the diastolic classification according to the 2009 and 2016 guidelines, re-classification tables were constructed (Table 4a and 4b, appendix). The analyses showed a superiority of the 2016 algorithm, seeing as fewer patients changed diastolic function grade with respect to the intra-examiner (2009: n = 20 vs. 2016: n = 13) and inter-examiner (2009: n = 20 vs. 2016: n = 8) re-test re-classification analyses, as well as the intra-examiner re-analyze re-classification (200: n = 20 vs. 2006: n = 5).

When comparing the two diastolic classification models applied to the entire study population, a pronounced dissimilarity was observed, as 158 of the 356 cases were classified differently. Furthermore, none of the diastolic dysfunction grade 1 and 2 according to the 2009 algorithm changed to DD grade 3 in the 2016 model, whereas 44 % of the DD grade 3 in 2009 stayed as DD grade 3 according to the 2016 proposed algorithm (Table 5).

Discussion

To the best of our knowledge, the present study is the first to assess the feasibility and test-retest reproducibility of all major measurements of left ventricular diastolic function included in the former and current guidelines. The findings, acquired from patients commonly encountered, are in accordance with a true clinical scenario and thus mirror daily clinical practice. Comparing the recent guidelines from 2016 with the more ambiguous guidelines from 2009, it was exposed that the classification of diastolic function in the guidelines from 2016 was superior in terms of both feasibility and reproducibility.

Feasibility of the diastolic variables and classification algorithms

Comparing feasibility across studies is difficult due to different study populations, equipment's, software's and echocardiographic expertise. These factors may also have influenced our findings. The mitral Doppler inflow and e' is acknowledged as feasible in the 2016 guidelines (9). Interestingly, TR Vmax showed lowest feasibility, which might be a problem in light of its implementation in current guidelines (9). This is expected, considering its prevalence of 70-90 % (15, 16). Hence, it seems illogical to incorporate a parameter, that by default, is not obtainable in all – at least without allowing an alternative to estimate the pulmonary artery pressure, such as the pulmonary acceleration time. Feasibility might have improved if estimation of TR Vmax were attempted from a different view. Leg elevation or i.v. administration of agitated saline could also enhance the regurgitation envelope (17, 18); however, these techniques are seldomly conducted in clinical practice and may also yield false higher values (18). Interestingly, our populations high BMI, did not hamper feasibility.

Feasibility of 2009 and 2016 algorithm was remarkably different (Figure 2). In the 2009 guidelines, many patients were indeterminate, since the guidelines classify DD as a combination of enlarged LA and reduced e' (19). Abnormal LV relaxation is an early manifestation of DD, reliably described by mitral e', and the LA volume reflects increased LV filling pressure over time (9). It is therefore no surprise that, even with normal LA, DD may be present, indicated by a low e'. Conversely, as e' decreases with aging (9, 20), younger patients with enlarged LA may have DD, despite e' above cut-off values (21). The frequent indeterminate cases are not a problem in our study per se, as patients undergoing cardiac surgery reliably can be assumed of having diastolic dysfunction, but it might prove a weakness in other studies/cohorts.

Another major problem of the 2009 algorithm was its ambiguity in DD grading, producing indeterminate results, in contrast to a more unequivocal method proposed in the 2016 algorithm. In a systematic review, Selmeryd et al (22) reported prevalence of DDF between 12 to 84 %, depending on the 2009 algorithm interpretation. Frequency of indeterminate results by the 2016 algorithm has been reported 2 times less than the 2009 by Alekhin et al (23). Likewise, in a study of 75.650 cases, 65 % and 21 % of the subjects were indeterminate according to the 2009 and 2016 algorithm, respectively (24). Excluding normal subjects, 86 % of the cohort's cases were indeterminate, resembling our findings.

The recent simplified guidelines also use fewer measurements for the evaluation of diastolic function. While a

step at the right direction, time consumption remains unchanged (6 minutes), leaving room for improvement.

Reproducibility of the diastolic variables and classifications algorithms

Our study yielded poorer reproducibility of diastolic measurements compared to previous findings (12, 13, 26-28). One important explanation is that all previous results are based on intra-observer re-analyse reproducibility (13, 26-28), whereas we reported intra-observer re-test reproducibility. Nevertheless, even in analogous study designs reproducibility has been reported to be very good (12, 13). However, such results must be re-considered with the studies' hampered power (n=20 examinations) and healthy (vs. our clinical) population (13). In other instances, the studies are older (12, 26, 27), providing results about traditional measurements and not contemporary parameters such as E/e', LA volume, and TR Vmax.

Our populations high BMI (27.6 ± 4.6) increases variability, a phenomenon well-known (29). By averaging measurements of multiple cycles, variability can be diminished, as executed in previous studies (12, 13, 26, 27), in opposition to our analyses. Furthermore, Vinereanu et al. (30) found better reproducibility of e' in normal hearts than with coronary disease and wall motion abnormalities, also explaining our high variability. However, the aim of our study was to reflect daily clinic, in which the abovementioned limitations are inevitable. Interestingly, new indexes of diastolic function seemed more reproducible compared to traditional (TR Vmax CV = 9.9-12 % vs. MV E and A CV = 12-20 %, LA volume CV = 19-22 % and E/e' CV = 22-36 %). The overall moderate reproducibility found in our study is, however, not unique (31, 32).

The 2016 algorithm was superior at classifying patients compared to 2009 (Table 4a and 4b, appendix). This emphasises the dominance of an algorithm's influence on grading, which can partly diminish the consequences of a high variability of the individual parameters.

Through reclassification analysis of the total (n=356) population, did the 2016 algorithm proved more restrictive than 2009 in classifying patients with advanced stages of DD (table 5). Other authors have reported similar decrease in the prevalence of DD by comparing the 2009 and 2016 algorithms (23, 33, 34). Elsewhere, the 2016 algorithm have likewise been shown superior to the 2009 in its ability to correlate with clinical outcome (35-37)

It is a natural chain of reasoning that a stronger reproducibility could have yielded improved re-classification. Therefore, the re-implementation of E/e' average in the current guidelines (9) is striking in light of its considerable variability. We found the reproducibility of E/e' average, most likely, is hampered by E/e' lateral (intra- and inter-observer CV = 36 % and 45 % for E/e' lateral vs. CV = 22 % and 23 % for E/e' septal), suggesting replacement of E/e' average with E/e' septal. Further elaboration is needed for the optimal differentiation between normal and abnormal diastolic function and subsequent grading. Rather than more expert opinions there is a need for studies that relate novel classification schemes containing the most feasible, reproducible, time-efficient, and prognostic variables to clinical outcome.

Study limitations

Our study must be interpreted within the context of its potential limitations. Possible inter-vendor and inter-software differences were not investigated, nor were the impact of the operator's experience level on echocardiographic feasibility, time-consumption and reproducibility. Furthermore, traditional parameters for assessment of diastolic function are influenced by biological variation, and we sought to minimize these by repeating the study over a short time, so that main source of variation was imaging *per se* . Feasibility of TR Vmax might be higher if other projections were attempted. The majority of the patients were in sinus rhythm, which limits the generalizability of our findings to patients with arrhythmias. Our cohort were also old and overweight with suboptimal image quality. Reproducibility may be higher and time-consumption lower in a broader patient population.

Conclusion

In conclusion, the feasibility of the individual diastolic parameters was excellent, except TR Vmax and pulmonary venous flows. Overall, the algorithm in the 2016 guidelines was superior to the 2009 algorithm

in terms of its precision in classifying patients (i.e., fewer indeterminate cases) and subsequently classifying patients in a uniform matter (i.e., fewer re-classifications). The 2016 algorithm proved more restrictive than 2009 in classifying patients with advanced stages of DD.

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Text tables

Table 1. Clinical characteristics of the study population.

Male sex, n (%)	Male sex, n (%)	Ma
Age (years)	Age (years)	Ag
Body mass index (kg/m^2)	Body mass index (kg/m^2)	Bo
Body surface area (m^2)	Body surface area (m^2)	Bo
Blood pressure systolic (mmHg)	Blood pressure systolic (mmHg)	Bl
Blood pressure diastolic (mmHg)	Blood pressure diastolic (mmHg)	Bl
Heart rate (beats/min)	Heart rate (beats/min)	He
Heart rhythm, n (%)	Heart rhythm, n (%)	He
Sinus rhythm	326 (92)	32
Atrial fibrillation	24 (7)	24
Other	6 (1)	6 (
Significant valvular heart disease (more than mild), n (%)	Significant valvular heart disease (more than mild), n (%)	Sig
Pulmonary regurgitation	Pulmonary regurgitation	Pu
Mitral regurgitation	Mitral regurgitation	Mi
Mitral stenosis	Mitral stenosis	Mi
Aortic regurgitation	Aortic regurgitation	Ao
Aortic stenosis	Aortic stenosis	Ao
Tricuspid regurgitation	Tricuspid regurgitation	Tr

Male sex, n (%)	Male sex, n (%)	Ma
Planned surgical procedure, n (%)	Planned surgical procedure, n (%)	Pla
CABG	CABG	CA
AVR	AVR	AV
CABG + AVR	CABG + AVR	CA

Data are presented as numbers or mean ± standard deviation. Range in square brackets.

CABG = coronary artery by-pass grafting; AVR = aortic valve replacement.

Table 2. Echocardiographic characteristics of the study population with feasibility, acquisition, analysis and total time consumption of diastolic echocardiographic parameters used to assess left ventricular diastolic function according to the 2009 and 2016 guidelines (n = 356).

	Mean ± SD [Range]
Non-diastolic parameters	Non-diastolic parameters
LVEF (%)	53 ± 13 [6-77]
LV GLS (%)	15 ± 4 [5-25]
Pulmonary acceleration time (ms)	119 ± 25 [64-201]
Diastolic parameters used in 2009 and 2016 guidelines	Diastolic parameters used in 2009 and 2016 guid
Mitral valve E velocity (cm/s)	63 ± 24 [8-156]
Mitral valve A velocity (cm/s)	72 ± 23 [10-151]
MV E/A ratio	1.0 ± 0.6 [0.3-5.2]
e' septal (cm/s)	5.2 ± 1.9 [1.4-15.6]
e' lateral (cm/s)	7.0 ± 2.5 [2.0-16.0]
E/e' septal	13.5 ± 6.6 [1.0-43.0]
E/e' lateral	10.4 ± 5.9 [0.9-55.5]
E/e' average	11.5 ± 5.7 [1.0-47.7]
TR Vmax (m/s)	2.6 ± 0.4 [1.8-3.9]
LA max volume (ml)	60 ± 22 [21-141]
LA max volume index (ml/m^2)	30 ± 11 [12-82]
PV systolic (S) velocity (cm/s)	60 ± 15 [20-95]
PV diastolic (D) velocity (cm/s)	49 ± 15 [18-105]
Pulmonal vein S/D ratio	1.3 ± 0.5 [0.3-3.0]
Other diastolic measurements of interest	Other diastolic measurements of interest
Mitral valve DT (ms)	205 ± 71 [26-461]
Mitral valve A duration (ms)	140 ± 28 [75-332]
Pulmonal vein A duration (ms)	139 ± 26 [80-228]
Valsalva E velocity (cm/s)	52 ± 22 [17-137]
Valsalva A velocity (cm/s)	68 ± 22 [18-146]
Valsalva E/A (cm/s)	0.9 ± 0.7 [0.2-7.1]
IVRT (ms)	96 ± 26 [36-204]
e' average	6.1 ± 2.0 [1.8-15.5]
LA maximum volume 3D (ml)	51 ± 19 [15-111]
Mean total classification time according to the 2009 guidelines algorithm	Mean total classification time according to the 2
Mean total classification time according to the 2016 guidelines algorithm	Mean total classification time according to the 2

Data are presented as mean ± standard deviation. Range in square brackets.

LVEF = left ventricular ejection fraction; LV GLS = left ventricular global longitudinal peak systolic strain

(absolute values); TR Vmax = maximal tricuspid regurgitation velocity; LA max = left atria maximum; PV = pulmonary vein; DT = deceleration time; IVRT = isovolumetric relaxation time.

Table 3. Test-retest variability of various diastolic parameters.	**Table 3. Test-retest variability of various di**
	Intra-analyzer
	Mean diff (95% LoA)
Parameters used in 2009 and 2016 guidelines	Parameters used in 2009 and 2016 guidelines
Mitral valve E velocity (cm/s)	-0.9 ± (-7.3 – 5.4)
Mitral valve A velocity (cm/s)	-0.7 ± (-8.4 – 7.0)
MV E/A ratio	-0.001 ± (-0.2 – 0.2)
e' septal (cm/s)	0.3 ± (-0.3 – 1.0)
e' lateral (cm/s)	0.01 ± (-1.0 – 1.1)
E/e' septal	-0.9 ± (-4.2 – 2.3)
E/e' lateral	-0.1 ± (-1.7 – 1.9)
E/e' average	-0.3 ± (-2.7 – 2.2)
TR Vmax (m/s)	-0.04 ± (-0.2 – 0.2)
LA max volume (ml)	1.8 ± (-18.1 – 21.7)
LA max volume index (ml/m^2)	0.9 ± (-9.3 – 11.1)
PV systolic (S) velocity (cm/s)	0.9 ± (-4.6 – 6.3)
PV diastolic (D) velocity (cm/s)	0.4 ± (-7.1 – 8.0)
Pulmonal vein S/D ratio	-0.004 ± (-0.2 – 0.2)
Other diastolic measurements of interest	Other diastolic measurements of interest
Mitral valve DT (ms)	10.0 ± (-45.8 – 65.8)
Mitral valve A duration (ms)	16.4 ± (-15.5 – 48.3)
Pulmonal vein A duration (ms)	13.7 ± (-44.2 – 71.7)
Valsalva E velocity (ms)	-1.1 ± (-11.3 – 9.1)
Valsalva A velocity (ms)	0.01 ± (-13.6 – 13.6)
Valsalva E/A	-0.002 ± (-0.1 – 0.1)
IVRT (ms)	-4.5 ± (-45.7 – 36.8)
e' average	0.2 ± (-0.4 – 0.8)
LA maximum volume 3D (ml)	-1.5 ± (-20.9 – 17.8)

LoA = Limits of Agreement; CV (%) = coefficient of variation; r = Pearson's correlation coefficient TR Vmax = maximal tricuspid regurgitation velocity; LA max = left atria maximum; PV = pulmonary vein; DT = deceleration time; IVRT = isovolumetric relaxation time

Table 5. Comparison of diastolic classification models.	**Table 5. Comparison of diastolic classification models.**	**Table 5. Comparison of diastolic classification models.**	**Table 5. Comparison of diastolic classification models.**	**Table 5. Comparison of diastolic classification models.**	**Table 5. Comparison of diastolic classification models.**	**Table 5. Comparison of diastolic classification models.**	**Table 5. Comparison of diastolic classification models.**
2016 vs. 2009	**2016 vs. 2009**	**2016 vs. 2009**	**2016 vs. 2009**	**2016 vs. 2009**	**2016 vs. 2009**	**2016 vs. 2009**	**2016 vs. 2009**
	2016 2009	**DDF 1**	**DDF 2**	**DDF 3**	**N/A**	**Total**	
	DDF 1	155 (61 %)	24 (53 %)	0	4 (10 %)	183	
	DDF 2	41 (16 %)	4 (9 %)	0	5 (12 %)	49	

Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.	Table 5. Comparison of diastolic classification models.
	DDF 3	7 (3 %)	7 (16 %)	17 (100 %)	8 (20 %)	39	
	N/A	52 (20 %)	10 (22 %)	0	23 (58 %)	85	
	Total	255	45	17	39	356	