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Original Article

Comparison of Left Ventricular Ejection Fraction Measurements by Echocardiography and Contrast Ventriculography: A Study on a Large Hospitalized Population

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ABSTRACT

Background: The evaluation of the left ventricular ejection fraction (LVEF) is important for predicting mortality and identifying high-risk patients. We aimed to identify factors affecting the variation in the LVEF measurement via echocardiography and contrast left ventriculography (CVG).

Methods: A total of 4422 patients (mean age=59.0±10.52 y, range=22–88) who underwent echocardiography and CVG within the same hospitalization period (0- to 14-day intervals) were included. Data were obtained from the Echocardiography Data Bank and the Coronary Angiography Data Bank in Tehran Heart Center.

Results: The correlation between the estimation of the EF by echocardiography and CVG was good (r=0.716); however, there was no point-by-point agreement. In 21.5% of the patients, echocardiography and CVG estimated the EF equally, and a difference greater than 20% was found in 1.8% of the patients. The differences between the 2 measurements were remarkable either in the patients with EFs greater than 50% or in those with EFs of 50% or less by CVG (59.71±3.72 by CVG vs 55.96±7.57% by echocardiography in EFs>50% and 40.69±8.96 by CVG vs 43.90±10.71% by echocardiography in EFs≤50%). By linear regression analysis, the presence of pathologic Q wave, atrial fibrillation and left bundle branch block, moderate and severe mitral regurgitation, increased LV size, and increased interventricular septal diameter resulted in a higher EF value via CVG, whereas in those with EFs of 50% or less, the EF by echocardiography was higher. No effect of time gap between the measurements was found.

Conclusions: According to our study, the EF measurements obtained by echocardiography and CVG varied on an individual basis. The level of the EF was the most important factor correlating with the difference between the measurements by the methods. ***(Iranian heart Journal 2018; 19(2): 27-35)***

KEYWORDS: Echocardiography, Contrast ventriculography, Ejection fraction

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The evaluation of the left ventricular ejection fraction (LVEF) is important for predicting mortality due to cardiac disease and has been used to identify high-risk patients willing to enroll in primary treatment trials.[1-4] Measuring the EF is essential in evaluating the level of the cardiac function, management of medical treatment, and selection for procedures like replacement of an automated implantable cardioverter-defibrillator.

Different surveys have compared the measurements of the EF by invasive and noninvasive modalities such as contrast left ventriculography (CVG), radionuclide ventriculography, single-photon emission computed tomography, and echocardiography.[4-10] Some clinical situations may necessitate the application of one method, so it is important for the clinician to know whether the estimates of the EF are comparable between the available methods. If these methods can be used interchangeably, this could reduce the need for multiple tests and the cost for patients.

The correlation between ventriculography and echocardiography in most of the studies conducted hitherto has been good, although the concordance between them is varied.[4,11] Moreover, concordance between these methods may vary on account of the fact that the methods are equipped with advanced technology and new studies may, therefore, yield different results. Therefore, we aimed to compare the EF measurements via echocardiography and CVG in a single hospitalization period amongst a large patient population.

METHODS

In a retrospective design, between January 2010 and January 2015, a total of 4264 patients who underwent echocardiography and CVG within the same hospitalization period were included in the study. The number of hospitalized patients for coronary angiography in the above period of time was 28 168 and among them 4422 patients had echocardiography at the same hospitalization. Of the 4422 patients, a total of 4264 patients had complete data for analysis and were subsequently included in the study.

All the data regarding past medical history, coronary artery risk factors, sign and symptoms at admission time, ECG changes, and drug history were prepared using the angiography database, in which the information was obtained through a comprehensive interview and examination by cardiologists prior to angiography. A trained nurse was responsible for taking blood pressure (using a mercury device), height, and weight of each patient. The definition of the variables in the data bank was published previously.[12]

Echocardiography

Standard 2D echocardiography was performed for all the study subjects by experienced echocardiography specialists. The measurements were taken according to the guidelines of the American Society of Echocardiography.[13] The LVEF images were acquired from the apical long-axis, 2-, and 4-chamber views and evaluations were based on eyeball estimation using the biplane Simpson rule.[14] The LV size was categorized as follows: 1) normal and 2) dilated (mild, moderate, and severe). Diastolic dysfunction was categorized as: 1) normal and 2) abnormal.[15] The severity of the regurgitation of the mitral and tricuspid valves was graded as normal, mild, moderate, and severe[16] and was categorized as: 1) none, 2) mild, 3) and moderate or higher for the present study.

Contrast Ventriculography

CVG was performed via the single-plane method with a Philips device (Version H 3000) using the right anterior oblique projections at a film rate of 12.5 frames/s. Injections of 20 to 30 cc of nonionic contrast (Visipaque TM) using an automated injector were done, and the EF was estimated visually according to the current guidelines. The patients with atrial fibrillation underwent the catheterization process after their heart rate was reduced to fewer than 80 bpm. Therefore, the EF estimation for this group of patients was performed in the same manner as that for the patients with normal sinus rhythms.

Intraobserver variability for CVG was assessed via the assessment of 18 randomly selected patients by 1 observer twice at an interval of 6 months. These patients were assessed by a second observer to obtain interobserver reproducibility of the same set of measurements. Inter- and intraobserver variabilities for echocardiography were determined by the random selection of 10 echocardiograms for analysis at least 6 months later by the same echocardiographer. These 10 echocardiograms were independently analyzed by the second blinded observer. Inter- and intraobserver variabilities were calculated via dividing the mean difference between the observations by their average measurement.[17,18]

Statistical Analysis

The results are presented as means ± standard deviations (SDs) for the numerical variables or by absolute frequencies and percentages for the categorical variables. The continuous variables were compared using the Student *t*-test or the nonparametric Mann–Whitney *U* test whenever the data did not appear to have normal distributions, while the categorical variables were compared using the χ^2 or Fisher exact test—as required. Paired sample *t*-tests were conducted to determine significant differences between the values measured by the 2 tests. The Difference between the 2 methods was obtained by subtracting the echo measurements from the CVG measurements (CVG EF – Echo EF). Furthermore, the patients were divided into 2 groups according to the evaluation across the quintiles of the EF by CVG: EFs greater than 50% and EFs equal to or less than 50%.

The correlation between the 2 methods was assessed using the Pearson correlation coefficient (*r*), and a 95% confidence interval (CI) was also obtained. The correlations were considered poor if *r* was less than 0.25, fair if *r* was greater than 0.25 but less than 0.50, moderate to good if *r* was greater than 0.50 but less than 0.75, and good to excellent if *r* was greater than 0.75.

A linear regression analysis was performed for to examine the factors significantly associated with the difference between the 2 modalities. The variables included in this analysis were comprised of age, gender, absolute time gap between the 2 clinical measurements, LV size, mitral regurgitation severity, interventricular septal diameter (IVSd), EF level, existence of diastolic dysfunction, and existence of left bundle branch block (LBBB) and right bundle branch block (RBBB).

Only those patients with complete data of the mentioned variables were entered into the analysis. For the statistical analysis, the statistical software SPSS, version 15.0, for Windows (SPSS Inc, Chicago, IL) was utilized. All the *P* values were 2-tailed, with statistical significance of equal to or less than 0.05.

RESULTS

The mean age of the study population (66.9% male), was 59.04±10.52 years, ranging between 22 and 88 years. The baseline characteristics of the patients are depicted in Table 1. Overall, there was no significant difference between the mean EF estimated by echocardiography and that by CVG (49.18±1.20% vs 49.02±11.84%, respectively; *P*=0.226). In addition, there was a good correlation between the EF values measured by these 2 methods (*r*=0.716; *P*<0.001). The mean differences between the EF measurements with respect to the EF quintile are shown in Table 2. (Due to the importance of low EFs, the first quintile was divided into 2 categories.)

Table 1. Patients' characteristics (N= 4422)

Demographic		Number	Valid Percent
Medical history			
	Hypertension	2230	51.3%
	Congestive heart failure	456	10.3%
	Diabetes	1380	31.8%
	Stroke	154	3.6%
	Hypertriglyceridemia	994	24.5%
	Hypercholesterolemia	1446	35.3%
	Positive family history	992	23.2%
	Current cigarette smoking	1108	25.5%
	Chronic lung disease	126	3.1%
Admission presentation			
	Stable angina	1108	25.6%
	Unstable angina	1030	23.8%
ECG			
	Q wave	1547	35.9%
	Atrial fibrillation	96	2.2%
	Right bundle branch block	50	2.1%
	Left bundle branch block	87	3.5%
Drug history			
	ACEI	2525	58.3%
	ASA	3958	91.4%
	Beta-blocker	3631	83.9%
	Thrombolytic agent	420	9.7%
Physiologic date		mean ± standard deviation	
	Systolic blood pressure (mm Hg)	127.50 ± 21.24	
	Diastolic blood pressure (mm Hg)	82.68 ± 14.59	
	Body mass index (kg/m^2)	27.21 ± 4.59	

ECG, Surface electrocardiography; ACEI, Angiotensin-converting enzyme inhibitor

Table 2. Mean differences between the EF measurements via echocardiography and ventriculography according to the EF quintile

Quintile	EF (%) By CVG	EF Difference (EF echo – CVG)
1	≤ 40	-4.74 ± 8.12
2	40-50	-1.58 ± 7.84
3	51-55	1.93 ± 6.55
4	55-60	3.24 ± 7.85
5	> 60	10.09 ± 6.65

EF, Ejection fraction; CVG, Contrast left ventriculography

When the patients were divided into 2 categories in terms of the EF values by CVG, the differences between the 2 measurements were statistically significant in each category as follows: echocardiography showed lower values of the EF in the patients with EFs above 50% by CVG, while it demonstrated higher values in the patients with EFs of 50% or less by CVG (59.71±3.72 by CVG vs 55.96±7.57% by echocardiography in EFs>50% and 40.69±8.96 by CVG vs 43.90±10.71% by echocardiography in EFs≤50%). The related scatter plot is illustrated in Figure 1. The reference line is 45° and the points laid on the line are those which were equally estimated by the 2 modalities. Despite the good correlation found across the 2 methods, their agreement was not point by point. The actual and absolute mean differences between the EF measurements were -0.16±8.71% and 6.55±5.74%, respectively. According to Figure 2, the histogram of the differences between the 2 methods was normally distributed. In 21.5% of the patients, echocardiography and CVG estimated the EF equally. In 41.0% of the patients, the difference between the EF measurements via echocardiography and CVG was up to 5%. A difference of greater than 5% and 10% or less was found in 22.8%, a difference of greater than 10% and 20% or less in 13.0%, and a difference of greater than 20% in 1.8% of the patients.

Figure 3 shows the Bland and Altman plot, indicating the level of agreement between the methods. Using an average difference of -0.16 and an SD of 8.71 points, we found that the limits of agreement between the methods (95% CI) ranged from a lower limit of -17.24 to an upper limit of 17.56. With respect to these limits of agreement, the agreement between echocardiography and CVG reached 94.5%.

The mean time interval between the 2 modalities was 2.99±2.62 days (range= 0–14 d). Regarding the sequence of the modalities, in 55.2% of the patients, CVG was the first modality and in 36.5% echocardiography was done prior to CVG. Measurement by the 2 methods was performed in 8.3% of the cases (386 patients) on the same day. The difference between the 2 measurements was not correlated with the sequence of the methods in the univariate analysis. All the analyses were repeated for the subgroup of patients in whom CVG and echocardiography were performed on the same day. The results were similar to those obtained from the whole population.

By linear regression analysis, the variation between the methods was correlated with the patient-related characteristics. According to Table 3, CVG was more likely to report the EF values higher than echocardiography in the presence of pathologic Q wave, atrial fibrillation and LBBB, diastolic dysfunction, moderate or severe mitral regurgitation, increased LV size, and IVSd; whereas in EFs equal to or less than 50%, the value by echocardiography was higher. No effect of absolute time gap was observed.

Table 3. Result of the multivariable linear regression analysis with respect to the factors which potentially could correlate with the variation between echocardiography and contrast ventriculography

Variable	β Coefficient	95% CI	*P* value
Age	-0.014	-0.038 , 0.010	0.265
Gender	0.184	-0.715 , 0.347	0.497
Presence of pathologic Q wave	1.561	1.033 , 2.090	<0.001
Presence of atrial fibrillation	2.756	1.212 , 4.301	<0.001
Interventricular septal diameter	0.092	0.016 , 0.169	0.018
Diastolic dysfunction	2.457	1.923 , 2.991	<0.001
Left ventricular dilation	2.539	1.820 , 3.258	<0.001
Mild mitral regurgitation	0.249	-0.283 , 0.780	0.359
Moderate and severe mitral regurgitation	0.832	0.001 , 1.663	0.050
Right bundle branch block	-1.316	-3.007 , 0.376	0.127
Left bundle branch block	2.888	1.555 , 4.221	<0.001
Ejection fraction ≤50% by angiography	-8.361	-8.896 , 7.826	<0.001
Absolute time gap	0.070	-0.023 , 0.163	0.139

R square=20.4% CI, Confidence interval

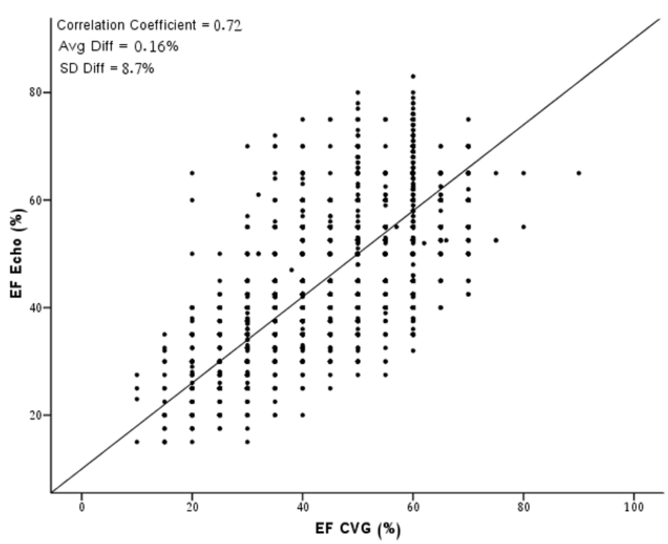

Figure 1. Scatter plot for the ejection fraction measurements by echocardiography and angiography

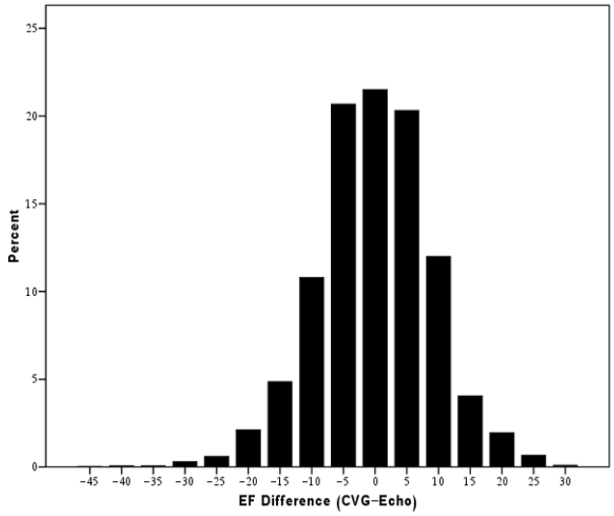

Figure 2. Distribution of the differences in the left ventricular ejection fraction estimation between echocardiography (Echo) and contrast ventriculography (CVG)

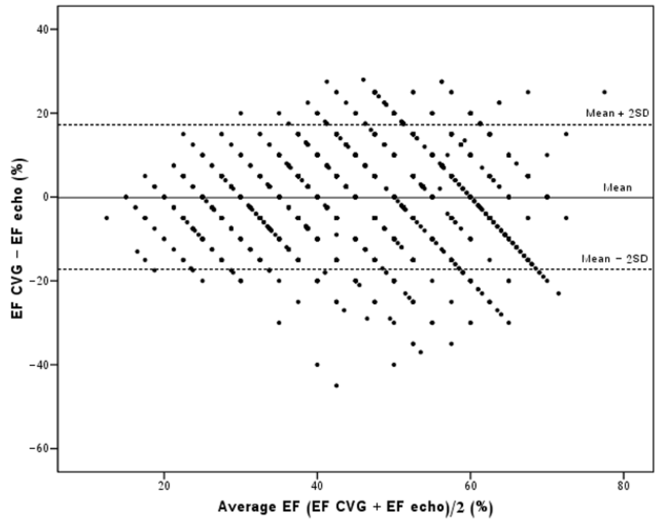

Figure 3. Bland-Altman plot of agreement between echocardiographic (Echo) and contrast vetriculographic (CVG) left ventricular ejection fraction. The dotted lines indicate 95% confidence intervals for the difference

Inter- and Intraobserver Variabilities

For echocardiography, the mean difference of the EF values was 3.89±1.81% between the first and the second measurements by 1 observer and 2.06±1.40% between the 2 distinct observers. For CVG, the inter- and intraobserver variabilities were 3.25±3.73% and 1.50±6.30%, respectively.

DISCUSSION

The present study on patients who had various indications for coronary angiography showed that despite a good correlation between echocardiography and angiography in the measurement of the EF, there was no point-by-point agreement between these modalities. This variation was influenced by patient-associated characteristics. Increased IVSd and LV size; severity of mitral regurgitation; and presence of pathologic Q wave, atrial fibrillation, and LBBB resulted in higher EFs by CVG. In the EFs of 50% or less, echocardiography reported higher values than did angiography.

The main advantage of the present study over previous studies is the inclusion of a large sample size of patients, in whom both tests were performed within a single hospitalization period using state-of-the-art diagnostic equipment. The most similar study to ours is a multicenter one evaluating 741 patients after myocardial infarction. In that study, the test results in 1 index hospital admission are compared. [5] The present study is a single-center one, evaluating 4422 patients (of about 6 fold) with different indications for angiography within the same hospitalization period.

Previous studies have reported that the difference between the mean values of the EF by echocardiography and CVG is not significant and that there is a good linear correlation between cross-sectional echocardiography and CVG methods. [5,8-10] The present study also demonstrated no remarkable difference between the mean EF by the 2 methods and found a good correlation between them (r=0.716; P<0.001). Joffe et al [5] reported Bland-Altman 95% confidence limits, ranging from -20 to +20 points. This figure in our study was narrower and ranged between -17.24 and +17.56 points; this means that the variation between the methods ranged between 0 and about 34 points.

Recent guidelines recommend the quantitative estimation of echocardiograms instead of "eyeball" methods which is more useful owing to such factors as speed, economy, and feasibility. A systematic review of 43 published studies showed that on average, echocardiographic methods (Simpson rule and subjective visual assessment) do not systematically under- or overestimate the EF to any major extent. [11] Because the EF parameter is an important guide for patient management, the guidelines almost have special recommendations with respect to the EF level. Whereas the variability in diagnostic procedures is of less importance in normal ranges of the EF, treatment decision is important in lower ranges of the value. A recent study on patients with acute myocardial infarction concluded that the variation between the EF measurements by echocardiography and ventriculography was not caused by the level of the EF. [5] Nonetheless, echocardiography in that study yielded slightly higher values for the EF at low EF levels and slightly lower values at high EF levels and these small differences were not statistically significant. In our study, the impact of the level of EF was more prominent than that of the other factors. We observed that in the patients with low EFs, the mean difference between the 2 modalities was significant compared to those with a high EF level. In the EFs greater than 50%, echocardiography estimated the value lower than CVG, while in the EFs equal to or less than 50% the echocardiographic estimation was higher than that of CVG. After adjustment for the other factors, this effect was significant. A possible explanation for this finding may be due to dye effect on the LV contractility, which is obvious in low EFs. [19]

The present study also found that in addition to the level of the EF, some other patient-related factors such as the presence of Q wave, atrial fibrillation, LBBB, LV dilation, moderate or severe mitral regurgitation, diastolic dysfunction, and increased IVSd were correlated with the amount of difference between the 2 measurements. The mechanisms of these observations, however, need to be clarified in future studies.

According to a previous study, the presence of atrial fibrillation may render the assessment of the LV ventricular systolic function by any method less accurate. [11] McGowan et al [11] in their review on studies including a small number of subjects with atrial fibrillation concluded that for the EF determination, the presence of atrial fibrillation might have contributed to a poor agreement between the visual assessment by echocardiography and the measurement by CVG. Similarly, the present study found that the presence of atrial fibrillation significantly correlated with the difference between these methods.

Via the same method, Joffe et al [5] reported that the contemporariness and the small time gap between the diagnostic modalities showed that the variation in the EF estimation was not related to a time interval between the tests. Our study, with a larger study population, confirms this conclusion.

CONCLUSIONS

The present data set showed that the EF measurements obtained by echocardiography and CVG varied on an individual basis and this variation was influenced by patient-associated characteristics. The level of the EF was the most important factor affecting the measurement by the 2 methods.

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REFERENCES

1. Goldberg RJ, Spencer FA, Yarzebski J, Lessard D, Gore JM, Alpert JS, Dalen JE. A 25-year perspective into the changing landscape of patients hospitalized with acute myocardial infarction (the Worcester Heart Attack Study). Am J Cardiol 2004; 94:1373–1378.

2. The American College of Cardiology/ American Heart Association Task Force. ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. J Am Coll Cardiol 2004;44:E1–E212.

3. Sadeghian H, Salarifar M, Karimi AA, Marzban M, Abbasi K, Lotfi-Tokaldany M, et al. Coronary Artery Bypass Surgery versus Medical Treatment in Patients with Low Ejection Fraction and Coronary Artery Disease. J Teh Univ Heart Ctr 2008; 3: 145-150

4. Gula LJ, Klein GJ, Hellkamp AS, Massel D, Krahn AD, Skanes AC, Yee R, Anderson J, Johnson GW, Poole JE, Mark DB, Lee KL, Bardy GH. Ejection fraction Assessment and Survival: An Analysis of the sudden cardiac Death in Heart Failure Trial (SCD-HeFT). Am Heart J 2008; 156:1196-200.

5. Joffe SW, Ferrara J, Chalian A, Tighe DA, Aurigemma GP, Goldberg RJ. Are ejection fraction measurement by echocardiography and left ventriculography equivalent? Am Heart J 2009;158:496-502.

6. Godkar D, Bachu k, Dave B, Megna R, Niranjan S and Khanna A. Comparison and CO-Relation of Invasive and Noninvasive Methods of Ejection Fraction Measurement. J Natl Med Assoc 2007; 99:1227-8, 1231-4.

7. Nosir YF, Fioretti PM, Vletter WB, Boersma E, Salustri A, Postma JT, Reijs AE, Ten Cate FJ, Roelandt JR. Accurate measurement of left ventricular ejection fraction by three-dimensional echocardiography. A comparison with radionuclide angiography. Circulation 1996;94:460-466.

8. Mohan HK, Livieratos L, Gallagher S, Bailey DL, Chambers J, Fogelman I. Comparison of myocardial gated single photon emission computerized tomography, planar radionuclide ventriculography and echocardiography in evaluating left ventricular ejection fraction, wall thickening and wall motion. Int J clin pract 2004; 58: 1120-6.

9. Bernard Y, Meneveau N, Boucher S, Magnin D, Anguenot T, Schiele F, Vuillemenot A and Bessand JP. Lack of agreement between left ventricular volumes and ejection fraction determined by two-dimensional echocardiography and contrast cineangiography in postinfarction patients. Echocardiography 2001;18:113-22.

10. Naik MM, Diamond GA, Pai T, Soffer A and Siegel RJ. Correspondence of left ventricular ejection fraction determinations from two-dimensional Echocardiography, Radionuclide angiography and Contrast Cineangiography. J Am Coll Cardiol 1995; 25:937-42.

11. McGowan, Cleland JG. Reliability of reporting left ventricular systolic function by echocardiography: A systematic review of 3 methods. Am Heart J 2003; 146:380-382.

12. Sadeghian S, Karimi AA, Salarifar M, Lotfi Tokaldany M, Hakki Kazzazi M, Sheikh Fathollahi M. Using Workload to Predict Left Main Coronary Artery Stenosis in Candidates for Coronary Angiography. J Teh Univ Heart 2007; 3: 145-150

13. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. European Association of Echocardiography. J Am Soc Echocardiogr 2005; 18:1440-63.

14. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. J Am Soc Echocardiogr 2002; 15:167-84.

15. Connolly HM. Oh JK. Echocardiography. In Libby P, Bonow PO, Mann DL, Zipes DP and Brawnwald E (eds): Brounwald's heart disease; a text book of cardiovascular medicine 8th international ed, Saunders Elsevier publishing Co, Philadelphia, 2008.p.227-325.

16. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, et al. American Society of Echocardiography. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777-802.

17. Dagianti A, Vitarelli A, Conde Y, et al: Assessment of regional left ventricular function during exercise test with pulsed tissue Doppler imaging. Am J Cardiol 2000;86(Suppl):30G–32G.

18. Sadeghian H, Majidi S, Lotfi-Tokaldany M, Nikdoust F, Sheikhfathollahi M, Abbasi SH. Evaluation of longitudinal tissue velocity and deformation imaging in akinetic nonviable inferobasal segments of left ventricular myocardium by dobutamine stress echocardiography. Echocardiography 2009;26:801-6.

19. Popma JJ. Coronary arteriography and intravascular imaging. In Libby P, Bonow PO, Mann DL, Zipes DP and Brawnwald E (eds): Brounwald's heart disease; a text book of cardiovascular medicine 8th international ed, Saunders Elsevier publishing Co, Philadelphia, 2008. p. 465-508.