

STUDY OF SPECKLE TRACKING ECHOCARDIOGRAPHY IN ISCHEMIC AND NON ISCHEMIC LEFT BUNDLE BRANCH BLOCK

Cardiology

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ABSTRACT

Background: Speckle tracking echocardiography parameters like Global longitudinal strain (GLS) and Global circumferential strain (GCS) are developing modalities to analyze ischemia, which has the unique advantage of differentiating active contraction from passive motion. Speckle tracking echocardiography can be utilized as a non invasive technique to analyze and differentiate Left Bundle Branch Block (LBBB) caused by ischemia.

Aims & objectives: To study the 2D Echo Spectral imaging in patients presenting with symptomatic LBBB, to assess their coronary angiogram and determine the efficacy of 2D spectral imaging by sensitivity analysis

Methods: The prospective observational study was conducted in Apollo Hospitals, Chennai in the Department of Cardiology. A total of 95 patients with symptomatic LBBB were included in our study. GLS and GCS were measured followed by Coronary Angiogram. Speckle tracking echocardiography findings in ischemic and non-ischemic LBBB were correlated at our center.

Results: The mean GLS of Ischemic subgroup (N=50) patients is -10.90 ± 3.54 , whereas the mean GLS of non-ischemic subgroup (N = 45) is -14.41 ± 4.79 . On analyzing and correlating GLS between both the groups, it was found to have statistically significant differences between ischemic and non-ischemic patients with p-value = 0.001. The mean GCS of non-ischemic patients (N = 45) is -15.100 ± 5.07 . The mean GCS of Ischemic patients (N = 50) is -13.30 ± 3.48 . There are statistically significant differences in GCS between ischemic and non-ischemic patients, p-value = 0.006.

Conclusion: 2D Echo Spectral imaging parameters like GLS and GCS are useful in discriminating Ischemic and Non ischemic aetiology in the patients presenting with LBBB.

KEYWORDS

Left Bundle Branch Block, Global Longitudinal Strain, Global circumferential strain

INTRODUCTION

Isolated Left Bundle Branch Block (LBBB) refers to asymptomatic LBBB in young subjects without any structural heart disease, without any cardiovascular risk factors, has not been seen to affect those individuals and is generally associated with a good prognosis. In subjects older than 40 years of age, it has been seen that LBBB affects cardiovascular events and there by acts as a prognostic marker¹. Contrary to the right bundle branch, the left ventricular conduction system is a large, diffuse structure that typically requires a significant insult to result in widespread injury. If LBBB is present in the context of myocardial infarction, the infarction site is usually anterior or anteroseptal, and the MI usually involves a large territory of the myocardium². The most widely accepted tools to aid in diagnosing MI in the presence of LBBB are the Sgarbossa criteria, which is first introduced over 20 years ago to substantially improve the diagnostic accuracy for MI in the presence of LBBB. Notwithstanding, stress testing within sight of LBBB is complicated because of the higher paces of false-positive discoveries, regardless of whether imaging modalities are utilized. As a result of these constraints, patients with LBBB are frequently alluded to invasive Coronary angiography (CAG) to exclude Coronary artery disease (CAD).³ Speckle tracking echocardiography is one of the developing modalities to analyze ischemia, ischemic wall motion abnormalities are often associated with passive motion, such as passive expansion and recoil and tethering from adjacent segments, strain imaging has the unique advantage of differentiating active contraction from passive motion, which is visually challenging. In this manner, it can be utilized to analyze LBBB brought about by ischemia non-invasively.⁴ This obviated the need to study further the role of speckle tracking in the determination of the etiology of LBBB to prevent unnecessary invasive tests.⁵

In this study, we analyzed the 2D Echo Spectral imaging in patients

presenting with symptomatic LBBB admitted in cardiology department at Apollo Main Hospitals, Chennai. We assess coronary angiogram in patients presenting with symptomatic LBBB and determine the efficacy of 2D spectral imaging by sensitivity analysis.

MATERIAL AND METHODS

This is a prospective observational study involving 95 patients who came to Cardiology outpatient department (OPD) or Emergency department at Apollo Main Hospitals, Chennai with baseline 12 lead electrocardiography of complete LBBB (QRS 120 ms) in Sinus rhythm and presented with history of Angina on exertion – Canadian Cardiovascular Class 2/3, Acute onset chest pain, Dyspnea on exertion – NYHA class II/III, Acute onset class IV dyspnea are included in the study. The exclusion criteria involves patients with known case of Valvular Heart Diseases, CAD, ischemic and non-ischemic cardiomyopathy, Congenital heart disease, patients with poor echocardiographic window not suitable for Speckle echocardiographic analysis and patients in whom CAG could not be done

Data collection

It included baseline patient characteristics including atherosclerotic risk factors, ECG, echocardiography, routine research center work, and statistical and clinical information. The associated conditions considered in the study were hypertension, dyslipidemia, diabetes mellitus. Patients with complete LBBB with the above-mentioned symptoms were admitted for the treatment and stabilization and further classified into three groups on the basis of ejection fraction (2D Planimetry method)

1. LVEF > 50 % (Group 1)

2. LVEF 35 to 50 % (Group 2)

3. LVEF < 35 % (Group 3)

Electrocardiographic Criteria for Complete LBBB -A complete LBBB is characterized as

- QRS duration 120 ms
- Broad Notched or slurred R wave in lead 1, aVL, V5, V6
- Narrow r followed by broad and deep S waves in right precordial leads.
- R peak time >60 ms in leads V5 and V6.

Following which patients were taken for invasive coronary angiogram and were grouped into ischemic and non-ischemic LBBB accordingly. For CAG either by radial or femoral route, a 5-Fr or 6-Fr diagnostic catheter was used to specifically cannulate the ostium of the coronaries. All viewed angiographic images were analyzed and the stenosis degree was evaluated by the American Heart Association classifying framework and offline QCA. The minimal lumen diameter (MLD), distal reference, proximal reference, reference width (RD), level of measurement stenosis (% DS), and lesion length with the least foreshortening view was estimated utilizing standard procedures.

Finally speckle echocardiography was pursued to study and correlate the following parameters in the two groups.

- Global longitudinal strain (GLS)
- Global circumferential strain (GCS)

2D Echocardiographic examination-Study participants will undergo a 2D trans thoracic echocardiographic examination in the left lateral recumbent position utilizing a commercialized ultrasound scanner (Philips EPIQ 7) with electronic ultrasonic transducer(X5-1).

All participants underwent conventional 2D echocardiography and 2D speckle tracking for the counts of morphometric parameters as per the suggestions of the American Society of Echocardiography. After interfacing the ECG, two-dimensional images were acquired from the following standard views (Parasternal short axis view at basal, mid and apical level, Apical 4 chamber, Apical 3 chamber view, Apical 2chamber view) All images were taken during breath-holding and put away in three continuous heart cycles. Gain, depth, and central range were changed in accordance with ideal left ventricular border view and high rate of frame.

Left ventricular end-systolic volumes (LVESVs) and end-diastolic volumes (LVEDVs) were usually based on tracings of the interface between the compacted myocardium and the LV cavity. At the mitral valve level, the contour is closed by connecting the two opposite sections of the mitral ring with a straight line. LV length is defined as the distance between the bisector of this line and the apical point of the LV contour, which is most distant to it. The use of the longer LV length between the apical two and four chamber views recommended. LV volumes should be measured from the apical four and two chamber views. Two-dimensional echocardiographic image acquisition should aim to maximize LV areas, while avoiding foreshortening of the left ventricle, which results in volume underestimation. Acquiring LV views at a reduced depth to focus on the LV cavity will reduce the likelihood of foreshortening and minimize errors in endocardial border tracings.^{6,7}

2 D speckle tracking -2-D speckle tracking was performed via using post processing software CMQ (Version 1.5.6, PhilipsMedical Systems). For 2- D speckle tracking analysis, standard two-dimensional images were recorded to get Global longitudinal strain (GLS) utilizing apical (4, 2-chamber, and 3 chamber view). Global circumferential strain was calculated using short axis view at mid basal and apical level. All the images to be acquired at a frame rate of 50 to 80 for each second. The reference point was set toward the start of the QRS complex. Aortic valve closing and opening were characterized utilizing a pulse wave Doppler ultrasound in the LV outflow tract with a 2-mm test volume. The endocardial border was traced in end-systole and the automatically created ROI was acclimated to eradicate the pericardium. Segments with insufficient or poor tracking of the endocardial were avoided from the investigation. If there should arise an occurrence of poor tracking in at least 2 segments, the patient was excluded from investigation. All strain examination was performed blinded to results.⁷

STATISTICAL ANALYSIS:

Continuous variables were expressed as Mean Standard deviation.

Categorical data was expressed as percentage (%). Comparison of categorical variables was done by chi square test (or) Fisher's exact test. Comparison of Continuous variables was done by independent sample t test. Data analysis was carried out by IBM SPSS Statistics for windows version 25.0, Armonk: NY, IBM corp. All 'p' values <0.05 was considered as statistical significance.

RESULTS:

In the present study, we have investigated the correlation of speckle tracking echocardiography findings in ischemic and non-ischemic left bundle branch block subjects at our center.

Out of the 95 patients studied, 50 patients were stratified into ischemic group and remaining 45 were stratified into non-ischemic group.

Table 1: Baseline Characteristics

	Ischemic LBBB (N= 50)	Non ischemic LBBB (N= 45)	P value
Mean Age	64	52	0.001
Male	31	18	0.032
Female	19	27	
Hypertension	43	20	0.001
Dyslipidaemia	35	17	0.02
Diabetes Mellitus	28	8	0.001
Mean EF	41.15%	45.88%	0.01
Mean GLS	-10.90±3.54	-14.41±4.79	0.001
Mean GCS	-13.30± 3.48	-15.10± 5.07	0.006

From the 95 patients studied, Mean age in Ischemic LBBB group is 64 yrs and Mean age in Non Ischemic LBBB group is 52 yrs, there were 19 females and 31 males in the ischemic group, 20 of the patients with hypertension were non-ischemic while 43 patients were ischemic, 17 of the patients with dyslipidemia were non-ischemic while 35 were ischemic, 28 patients with Diabetes mellitus belong to ischemic subgroup and 8 of the patients with Diabetes belong to non-ischemic subgroup, the mean Ejection Fraction of non-ischemic patients was 45.88 % ± 11.59, while the mean Ejection Fraction of Ischemic patients is 41.15 % ± 8.33 (Table 1).

The mean Global Longitudinal Strain (GLS) of Ischemic subgroup patients is -10.90±3.54, whereas the mean GLS of non-ischemic subgroup (N = 45) is -14.41±4.79. On analyzing and correlating GLS between both the groups, it was found to have statistically significant differences between ischemic and non-ischemic patients with p-value = 0.001 (Table 1).

The average Global circumferential strain (GCS) of the studied patients was -13.30 ± 3.34. There are statistically significant differences in GCS between ischemic and non-ischemic patients, p-value = 0.006. The mean GCS of non-ischemic patients (N = 45) is -15.100 ± 5.07. The mean GCS of Ischemic patients (N = 50) is -13.30 ± 3.48 (Table 1).

Table 2: Categories of GLS among ischemic and non-ischemic patients

			LBBB Subgroups		Total
			Ischemic	Non Ischemic	
GLS	<-8	Count	10	5	15
	-8.1 to -12.49	Count	17	14	31
	-12.5 to -18	Count	23	13	36
	>-18	Count	0	13	13
Total		Count	50	45	95

Table 3: Categories of GCS among ischemic and non-ischemic patients

			LBBB Subgroups		Total
			Ischemic	Non ischemic	
GCS	-20	Count	0	11	11
	<-20	Count	50	34	84
Total		Count	50	45	95

It can be inferred that among the ischemic subgroup, no patient was having GLS above -18. While in non-ischemic group, 13 patients were having GLS > -18. However, patients with severely reduced GLS, i.e. less than -8 were almost double to that of non-ischemic group, i.e. 20 % (10 patients) in ischemic subgroup while 11% (5 patients) in the non-ischemic subgroup. There is almost similar number of patients in the with the GLS -8.1 to -12.49 (Table 2).

It is inferred that there was no patient in the GCS of normal value i.e. -20 in the ischemic group, while in the non-ischemic group 11 patients were having Normal GCS value which was statistically significant ($p = 0.006$). On the other hand, only 34 out of total 45 patients were having GCS value less than -20. (Table 3).

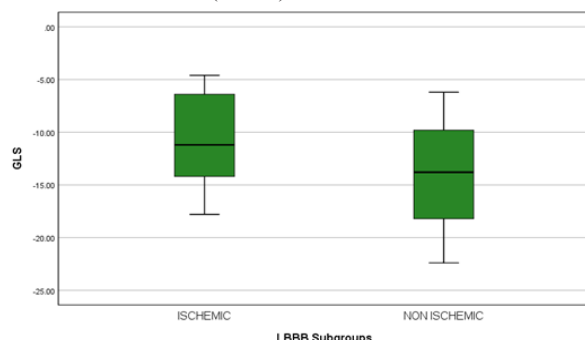


Fig.1. Box-plot showing distribution of GLS among Ischemic and Non Ischemic patients

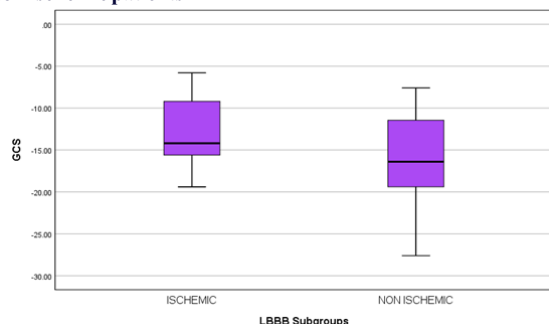


Fig.2. Box-plot showing distribution of GCS among Ischemic and Non Ischemic patients

Box-plots (Fig.1 & 2) showing the distribution of GLS and GCS between Ischemic and Non Ischemic patients. In Ischemic patients median GLS was -11.2 (-14.2 to -6.4) and in Non Ischemic patients median GLS was -13.8 (-18.2 to -9.8). Median GCS among Ischemic patients was -14.2 (-15.6 to -9.2) and in Non Ischemic patients -16.4 (-19.4 to -11.4).

DISCUSSION

Studies have estimated the prevalence of LBBB within a range of 0.1% to 0.9% in the general population and significantly higher in elderly or those with HF. About 2.2% of individuals aged 55 years, 5.7% of individuals above 80 years of age, and 25% to 30% of patients with HF⁹⁻¹⁴, were found to have LBBB. LBBB is associated with higher cardiovascular events and mortality risk, largely attributable to the fatal arrhythmias and the detrimental hemodynamic influence associated with LBBB¹⁷⁻²¹.

Accurate risk assessment and early recognition of LV dysfunction is essential in patients with LBBB, given its impact on the risk for mortality and hemodynamic deterioration. By mechanisms of delayed ventricular activation and shortened LV filling time, LBBB is associated with deterioration of LV systolic and diastolic function¹⁹⁻²¹. True LV function is underestimated in patients with LBBB as a result of dyssynchronous LV motion with earlier septal wall activation than the lateral wall, making LVEF unreliable to estimate LV function. Also, being an indirect method of LV function estimation, using geometric changes in LV dimensions rather than the intrinsic myocardial contractility, LVEF has significant limitations for this purpose in patients with LBBB. However, LV GLS measures the intrinsic myocardial contractility and is the more reliable method of LV function estimation in these patients¹⁹⁻²¹.

Apart from having prognostic influence, LBBB alone itself is considered a separate 'cardiovascular clinical entity' representing various diagnostic and management difficulties to the clinicians and cardiologists particularly in the context of CAD.⁵ Thus, the incidental finding of LBBB is currently considered a potential marker of underlying heart disease, prompting further non-invasive or invasive diagnostic procedures, particularly in individuals with high-risk

occupations. Hence, this study aims to evaluate and correlate between ischemic and non-ischemic LBBB subgroups (categorized on the basis of coronary angiography) with 2D Speckle Echo analysis. There are three different components of contraction that are generally described and studied: radial, longitudinal, and circumferential.^{22,23} Longitudinal contraction represents motion from the base to the apex. Radial contraction in the short axis is perpendicular to both long axis and epicardium and thus radial strain represents myocardial thickening and thinning. Circumferential strain is defined as the change of the radius in the short axis, perpendicular to the radial and long axes. In patients with Heart failure, myocardial global strain has been found to be a comprehensive indicator of left ventricular (LV) function and also a reliable prognostic factor with respect to cardiovascular events.²⁴⁻²⁶

In our study, it was found that impaired LV GLS and GCS, measured by 2D STE, has a significant and independent association with Ischemic LBBB. In this study on Invasive coronary angiography evaluation, 52.6% (50) of the participants were grouped into ischemic group while rest 47.3 % (45) were grouped into non-ischemic group. Among the ischemic group, it was found that 17 patients had single vessel disease with involvement of proximal LAD >80 %, 10 were having double vessel disease, again with involvement of Proximal LAD >80 %, while 20 patients had three vessel disease with involvement of Proximal LAD >80 %. Lastly three patients were found to have Distal LMCA with three vessel disease, with involvement of proximal LAD >80 %. Out of 45 non-ischemic LBBB patients, 23 patients were found to have normal coronaries, 11 patients had Minor CAD (presence of minor plaques) while 11 had non-flow limiting CAD (presence of stenosis <50 %).

The echocardiographic parameters studied among the participants were as follows

- Ejection Fraction by 2D Planimetry
- Global longitudinal strain
- Global circumferential strain

Ejection fraction by 2D planimetry, mean Ejection fraction was around 48 %. On subgroup analysis, the mean Ejection Fraction of non-ischemic patients (N = 45) was 45.88 % $\pm$ 11.59, while the mean Ejection Fraction of Ischemic patients (N = 50) is 41.15 % $\pm$ 8.33. On evaluating it shows that there are statistically significant differences between ischemic and non-ischemic patients, p -value = 0.01. Study conducted by Abrol R et al in 2006 to evaluate the association of LBBB with angiographic analysis, all risk factors was more in favor of CAD. Likewise, in the study mean EF was lower more in the patients with CAD as compared to patients without CAD similar to the present study.⁸

Among the strain imaging parameters, the first parameter evaluated was GLS. The average GLS of the patients was - 15.48 $\pm$ 5.26. The mean GLS of Ischemic subgroup patients (N = 50) is - 10.90 $\pm$ 3.54, whereas the mean GLS of non-ischemic subgroup (N = 45) is - 14.41 $\pm$ 4.79. On analyzing and correlating GLS between both the groups, it was found to have statistically significant differences between ischemic and non-ischemic patients, p -value = 0.001. GLS was further subdivided into 4 subgroups of >-18 (Normal), Mildly reduced (-12.5 to -18), Moderately reduced (-8 to -12.4) and severely reduced (<-8). On analyzing within these subgroups, it was inferred that among the ischemic subgroup, no patient was having GLS above -18 while in non-ischemic group, 28.8% of the patients (13 patients) were having GLS > -18.

However, patients with severely reduced GLS, i.e. less than -8 were almost double to that of non-ischemic group, i.e. 20 % (10 patients) in ischemic subgroup while 11% (5 patients) in the non-ischemic subgroup. On the contrary, there were almost similar number of patients with the GLS -8.1 to -12.49. A study conducted by Biering-sorensen T et al in 2014, for evaluation of GLS in patient with ischemia, it was found that GLS significantly lower in patients with CAD compared with patients without (17.1 $\pm$ 2.5% versus 18.8 $\pm$ 2.6%; $P < 0.001$) and proved to be an independent predictor of CAD.⁷ The present study also confirms these findings.

The second strain parameter we evaluated was Global circumferential strain. The average GCS of the studied patients was - 13.30 $\pm$ 3.48. There were statistically significant differences in GCS between ischemic and non-ischemic patients, p -value = 0.006. The mean GCS of non-ischemic patients (N = 45) is - 15.100 $\pm$ 5.07. The mean GCS of Ischemic patients (N = 50) is - 13.30 $\pm$ 3.48. GCS was further evaluated

with two subgroups of above -20 and less than -20. From the sub analysis, it was inferred that there was no patient in the GCS of normal value i.e. > -20 in the ischemic group while in the non-ischemic group, 11 patients were having Normal GCS value. On the other hand, only 34 out of total 45 patients in the non-ischemic were having GCS value less than -20 which was statistically significant ($p = 0.006$).

Fazio G et al in 2013, studied a total of 134 patients with dilated cardiomyopathy, among which 74 were considered as ischemic on the of coronary angiography while rest 60 were the non-ischemic one and found that the longitudinal and circumferential strains were found to be significantly reduced (P value < 0.05) in patients with ischemic etiology compared with those with the non-ischemic dilated cardiomyopathy. Our study also repeats the similar findings as the mentioned findings in the study.¹⁰

LIMITATIONS OF THE STUDY

Although results of this work were consistent with previous studies and reached statistical significance, but the population was small in number. Radial strain analysis not done. Early systolic lengthening duration, post systolic strain index not assessed.

Speckle-tracking echocardiography is dependent on frame rates, as well as image resolution. Low frame rates result in the speckle pattern changing too much from frame to frame, which prevents the precise characterization of regional myocardial motion and impacts the overall temporal resolution of the regional strain map. In contrast, increasing the frame rate reduces scan-line density, which reduces image resolution.

CONCLUSION

In the present Prospective observational study conducted in subset of patients presenting with symptomatic LBBB, we tried to correlate the relationship of speckle echocardiographic findings with ischemic and non-ischemic LBBB and the following conclusions can be drawn from it.

- There is strong inverse correlation between GLS with ischemia (p value 0.001)
- There is strong inverse correlation between GCS with ischemia (p value 0.006)
- Ischemic LBBB patients have lower EF in comparison to non-ischemic LBBB patients. (p value 0.009)
- It was noted that Ischemic LBBB patients with LVEF > 50% ($n = 5$) had Low GLS and GCS values, however subgroup analysis could not be done because of small numbers.
- Ischemic LBBB patients are more elderly as compared to non-ischemic LBBB patients.
- Ischemic LBBB patients are more associated risk factors like dyslipidaemia (p value 0.02) diabetes mellitus (p value 0.001), hypertension (p value 0.0001)

2D Echo Spectral imaging parameters like GLS and GCS are useful in discriminating Ischemic and Non ischemic aetiology in the patients presenting with LBBB. In recent years, speckle 2D echocardiography has proved to be a boon in the field of cardiology, patients presenting with LBBB can be assessed early, Non-Invasively and within less time through speckle 2D echocardiography. Moreover it also decreases patients discomfort and the need of a Invasive procedure.

RECOMMENDATIONS

- 1) GLS and GCS can be considered in patients with symptomatic LBBB for further Risk Stratification.
- 2) Further multi centre and large-scale study is Recommended to confirm these findings.
- 3) Large scale study would allow to compare GLS and GCS pattern in Low vs Normal LVEF with Ischemic LBBB.
- 4) Study of Radial Strain will probably help in further Risk Stratification.

CONFLICTS OF INTEREST: No conflicts

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REFERENCES:

1. Imanishi R, Seto S, Ichimaru S, Nakashima E, Yano K, Akahoshi M. Prognostic significance of incident complete left bundle branch block observed over a 40-year period. *The American journal of cardiology*. 2006 Sep 1;98(5):644-8.

2. Schneider JF, Thomas Jr HE, Kreger BE, McNamara PM, Kannel WB. Newly acquired left bundle-branch block: the Framingham study. *Annals of Internal Medicine*. 1979 Mar 1;90(3):303-10.
3. Rasmussen PV, Skov MW, Ghouse J, Pietersen A, Hansen SM, Torp-Pedersen C, Kober L, Haunso S, Olesen MS, Svendsen JH, Melgaard J. Clinical implications of electrocardiographic bundle branch block in primary care. *Heart*. 2019 Aug 1;105(15):1160-7.
4. Favot M, Courage C, Ehrman R, Khait L, Levy P. Strain echocardiography in acute cardiovascular diseases. *Western Journal of Emergency Medicine*. 2016 Jan;17(1):54.
5. Feigenbaum H, Mastouri R, Sawada S. A practical approach to using strain echocardiography to evaluate the left ventricle. *Circulation Journal*. 2012;76(7):1550-5.
6. Kawagishi T. Speckle tracking for assessment of cardiac motion and dyssynchrony. *Echocardiography*. 2008 Nov;25(10):1167-71.
7. Freedman RA, Alderman EL, Sheffield LT, Saporito M, Fisher LD. Bundle branch block in patients with chronic coronary artery disease: angiographic correlates and prognostic significance. *Journal of the American College of Cardiology*. 1987 Jul 1;10(1):73-80.
8. Abrol R, Trost JC, Nguyen K, Cigarroa JE, Murphy SA, McGuire DK, Hillis LD, Keeley EC. Predictors of coronary artery disease in patients with left bundle branch block undergoing coronary angiography. *The American journal of cardiology*. 2006 Nov 15;98(10):1307-10.
9. Biering-Sorensen T, Hoffmann S, Mogelvang R, Zeeberg Iversen A, Galatius S, Fritz-Hansen T, Bech J, Jensen JS. Myocardial strain analysis by 2-dimensional speckle tracking echocardiography improves diagnostics of coronary artery stenosis in stable angina pectoris. *Circulation: Cardiovascular Imaging*. 2014 Jan;7(1):58-65.
10. Fazio G, Vernuccio F, Grasseo E, Grutta G, Re GL, Midiri M. Ischemic and non-ischemic dilated cardiomyopathy. *Open Medicine*. 2014 Feb 1;9(1):15-20.
11. Baldasseroni S, Opasich C, Gorini M, Lucci D, Marchionni N, Marini M, et al. Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: a report from the Italian network on congestive heart failure. *Am Heart J*. 2002;143:398-405.
12. Eriksson P, Hansson PO, Eriksson H, Dellborg M. Bundle-branch block in a general male population: the study of men born 1913. *Circulation*. 1998;98:2494-500.
13. Kashani A, Barold SS. Significance of QRS complex duration in patients with heart failure. *J Am Coll Cardiol*. 2005;46:2183-92.
14. Huvelle E, Fay R, Alla F, Cohen Solal A, Mebazaa A, Zannad F. Left bundle branch block and mortality in patients with acute heart failure syndrome: a substudy of the EFICA cohort. *Eur J Heart Fail*. 2010;12:156-63.
15. Haataja P, Nikus K, Kahonen M, Huhtala H, Nieminen T, Jula A, et al. Prevalence of ventricular conduction blocks in the resting electrocardiogram in a general population: the Health 2000 Survey. *Int J Cardiol*. 2013;167:1953-60.
16. Pelliccia A, Culasso F, Di Paolo FM, Accettura D, Cantore R, Castagna W, et al. Prevalence of abnormal electrocardiograms in a large, unselected population undergoing pre-participation cardiovascular screening. *Eur Heart J*. 2007;28:2006-10.
17. Bijnens BH, Cikes M, Claus P, Sutherland GR. Velocity and deformation imaging for the assessment of myocardial dysfunction. *Eur J Echocardiogr*. 2009;10:216-26.
18. Ciampi G, Cortigiani L, Pratali L, Rigo F, Villari B, Picano E, et al. Left bundle branch block negatively affects coronary flow velocity reserve and myocardial contractile reserve in nonischemic dilated cardiomyopathy. *J Am Soc Echocardiogr*. 2016;29:112-8.
19. Grines CL, Bashore TM, Boudoulas H, Olson S, Shafer P, Wooley CF. Functional abnormalities in isolated left bundle branch block. The effect of interventricular asynchrony. *Circulation*. 1989;79:845-53.
20. Xiao HB, Lee CH, Gibson DG. Effect of left bundle branch block on diastolic function in dilated cardiomyopathy. *Br Heart J*. 1991;66:443-7.
21. Ozdemir K, Altunkeser BB, Danis G, Ozdemir A, Uluca Y, Tokac M, et al. Effect of the isolated left bundle branch block on systolic and diastolic functions of left ventricle. *J Am Soc Echocardiogr*. 2001;14:1075-9.
22. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28:1-39.
23. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, Pedri S, Ito Y, Abe Y, Metz S, Song JH. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *European Heart Journal-Cardiovascular Imaging*. 2015 Jan 1;16(1):1-1.
24. Cho GY, Marwick TH, Kim HS, Kim MK, Hong KS, Oh DJ. Global 2-dimensional strain as a new prognosticator in patients with heart failure. *J Am Coll Cardiol*. 2009;54:618-24.
25. Cho GY, Kim HK, Kim YJ, Choi DJ, Sohn DW, Oh BH, et al. Electrical and mechanical dyssynchrony for prediction of cardiac events in patients with systolic heart failure. *Heart*. 2010;96:1029-32.
26. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. *Circ Cardiovasc Imaging*. 2009;2:356-64.