Septal Flash Relationship with LBBB and its ECG Predictors in Heart Failure Patient Population

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Abstract

Objective: Recent studies have elaborated classical echo patterns of typical LBBB, which have preliminarily shown to enhance the CRT prediction over and above ECG. This study was undertaken to understand the relationship of typical echo dyssynchrony pattern with various ECG parameters in heart failure patients with true LBBB.

Methods: Subjects with LBBB and EF ≤35% were involved. ECG parameters studied included intrinsicoid deflection duration, left ventricular activation time, mechanical deflection index along with global QRS duration. Septal flash pattern on echo was chosen to indicate true mechanical dyssynchrony due to LBBB. Standard 12 lead ECG were analyzed manually with use of digital EP calipers. Univariate comparison done with Mann–Whitney U and Chi-square test. Stepwise multivariate logistic regression analysis carried out to predict SF and receiver operating characteristic (ROC) curves constructed. Subgroup analysis done in group with QRSd 130-149ms separately. Significance was set at a probability level of < 0.05 and analysis performed using SPSS software.

Results: 220 patients were enrolled. Overall 59.5% patients demonstrated septal flash with positive correlation with QRSd and negative with ischemic etiology of heart failure. Intrinsicoid deflection duration predicted septal flash significantly in multivariate analysis (OR 1.78 for every 10ms increase). Subgroup analysis involving 130-149ms of QRSd patients too showed intrinsicoid deflection duration as only significant predictor (OR 1.9 for every 10ms increase) with ROC analysis providing optimal cut-off of 87ms.

Conclusion: Septal flash was present in significant number of patients with QRS duration between 130-149. Ischemic etiology of heart failure had lower septal flash prevalence. Intrinsicoid deflection duration and mechanical deflection index successfully predicted septal flash, even in patients with narrower QRS complex while QRS duration and left ventricular activation time added no value.

Key Words: Mechanical dyssynchrony, Septal flash, Intrinsicoid deflection, Left ventricular activation time, Mechanical deflection index.

Introduction

CRT is therapy for an electrical substrate induced mechanical dyssynchrony. However, current guideline criteria [1,2] for CRT implantation rely only on ECG, focusing on QRS duration and morphology, with approximately 30% of the patients fulfilling them not being responsive to the therapy [3]. Electrical delay as specified by current ECG criteria for CRT can be result of the result of pathological process at multiple levels, as revealed by electrophysiology studies in widely varying activation patterns in case of LBBB [4,5]. Majority of attempts for including mechanical dyssynchrony into the equation so as to increase their utility in prediction of the subset most responsive to the therapy have proved futile [6,7]. Now from almost a decade [8], typical mechanical patterns for electrical dyssynchrony in LBBB, in forms of septal flash have made resurgence and have shown to be increasingly beneficial in predicting CRT response [9]. The aim of the current study was to explore the prevalence of typical echo pattern and to study closely the various ECG parameters in relation to their ability to predict this new parameter of mechanical dyssynchrony. Specifically, prevalence of septal flash will be assessed and various ECG parameters will be analyzed to predict determinants of SF among patients with LBBB.

Methods

Study participants

12 lead standard ECG and 2D Echocardiography of patients with LBBB and LVEF ≤35% presenting to the cardiology department of SMS hospital, Jaipur were recorded between June 2018 to June 2020. Only subjects with QRS duration of ≥ 130ms were included, this was done based on the results of EchoCRT trial [7] showing no benefit among patients with smaller QRS duration. Patients with echocardiographic signs of scar, such as akinesia or dyskinesia in thin & hyperechogenic segments, associated valvular lesion other than secondary MR/TR, uncontrolled HTN, poor echo windows were excluded from the analysis.

ECG and echo measurements.

Standard 12 lead ECG were analyzed manually with use of digital EP calipers. LBBB was identified according to the according to the recent American Heart Association, American College of Cardiology Foundation and Heart Rhythm Society criteria [10]. The guidelines comment on presence of broad notched or slurred R waves in leads I, aVL, V5 and V6. This might be construed as presence in all leads and has been variably interpreted in literature however in our study we included patients with presence of this in at least 1 lead. As recommended by American Heart Association, American College of Cardiology Foundation, and the Heart Rhythm Society global QRS duration between the earliest and latest identified QRS complex in the 12 channel ECG rhythm strips. Also measured were the other ECG parameters described previously in the literature namely the left ventricular activation time and intrinsicoid deflections in the lateral leads (Figure 1). First notch in the QRS complex was taken to indicate the transition from RV to LV depolarization. LVAT was taken as the maximum single lead duration from that first notch to the end of QRS complex [11]. ID was measured in the lead having the maximum duration from the start of QRS to the peak of the R wave [12]. Both the parameters were then indexed to Global QRS durations. Septal flash was defined as rapid early systolic inward movement of septum followed by outward motion [8]. Presence of septal flash was checked in either SAX or PLAX M mode (Figure 2). All patients provided informed clinical consent and approval from institutional ethics committee was obtained.

Statisical Analysis

Continuous variables were expressed as mean ± SD or median [quartile 1; quartile 3] if not normally distributed. Categorical variables as absolute numbers with percentage. Normality of the data was assessed with Shapiro-Wilk test. Comparison of continuous variables among groups were done by independent samples t-test if normally distributed and by Mann–Whitney U test if not and categorical variables by Chi-square tests. Correlations between continuous variables were analysed using Spearman rank-order correlation coefficients. Univariate followed by stepwise multivariate logistic regression analysis were carried out to predict SF. Receiver operating characteristic (ROC) curves constructed to assess the presence of septal flash by ECG parameters. Statistical significance was set at a probability level of < 0.05. Statistical analysis was performed using SPSS software.

Results

Over the study duration period, a total of 220 patients LBBB and EF ≤ 35% underwent analysis with detailed ECG and interpretable Echo examinations. Patients were grouped into two QRS categories by cutoff of 150ms for analysis. Overall prevalence of septal flash in study cohort was 59.5%. Prevalence of SF was higher in the wider QRS group at 69% and 42% in the relatively narrower QRS duration group. Also, the median QRS duration was significantly higher in septal flash group. Characteristics at baseline stratified by presence or absence of septal flash are shown in Table 1. There were no significant differences between the two groups in demographics. LVEF was also not significantly different between the groups. Ischemic heart disease was significantly found to be associated with absence of septal flash, being present in 37% of SF group compared to 62% in those without. All the ECG parameters were significantly higher in group with septal flash.

Correlation between LVAT and ID with both QRSd were high and statistically significant with ID ($r_s = .62$, $p < .001$) as compared to LVAT ($r_s = .59$, $p < .001$).

Next stepwise multivariate logistic regression involving the ECG parameters showed that only ID correlated with presence of septal flash with achievement of correct classification of 73% by itself while both QRSd and LVAT having no significance over and above ID. Every 10ms increase in ID increased the odds of having septal flash by 78% with odds ratio of 1.78 with 95% CI ranging from 1.54-2.03 with p value <0.001 (Table 2).

Receiver operating characteristic curve (Figure 3a) for ID to predict the presence of SF for study population .797 with p value of <0.001. while for MDI was .772 (Table 3). Best cutoff for ID & MDI by Youden index were 92.5ms and .615 respectively. Sensitivity and specificity for ID cutoff values were 85% and 63% and for MDI were 80% and 66%.

Similar analysis for the narrow QRS subgroup were done. Like for the whole patient population only ID and MDI contributed significantly towards prediction of SF, with odds for every 10ms increase in ID being 1.9 with 95% CI ranging from 1.41 to 2.42 with p value of <0.001 and a correct classification of about 72% (Table 2). Likewise, LVAT and QRSd did not contribute significantly towards prediction of SF over and above ID. Next the AUC values were explored for the group with QRSd from 130 to 149 separately (Figure 3b). AUC values for ID & MDI were 0.785 and .781 respectively and were statistically significant (Table 3). Cutoff values for ID and MDI for narrow QRS for presence of mechanical dyssynchrony with regards to SF being 87ms and .625 respectively.

Table 1: Baseline characteristics with respect to presence of septal flash.

ECG Measurements	Septal Flash	P Value

		Present (n=131)	Absent(n=89)	
Age		58±10	60±9	.13
Female		38(29%)	21(24%)	.33
Ischemic Heart Disease		49(37%)	55(62%)	<.001
LVEF		25.4±6.5	26±5.4	.47
QRS (ms)	130-149	34(42.5%)	46(57.5%)	<.001
	≥150	97(69.3%)	43(30.7%)	
QRSd		162(149-170)	149(144-162)	<.001
LVAT		94(87-105)	86(76-94)	<.001
ID		109(96-120)	88(80-101)	<.001
LVATindex		.59(.55-.64)	.55(.51-.60)	<.001
MDI		.67(.62-.72)	.57(.53-.64)	<.001

Table 2: Stepwise Multivariate regression analysis of ECG parameters predicting septal flash

	Odds Ratio (for every 10ms increase) for ID	P Value
>130	1.78 (95% CI 1.54-2.03)	<0.001
130-149	1.9 (95% 1.41-2.42)	<0.001

Table 3: ROC Analysis of ECG predictors in relation to narrow versus wide QRS

Test Variable	QRSd ≥130		QRSd 130-149	
	AUC	P value	AUC	P value
ID	.797	< .001	.785	< .001
MDI	.772	<.001	.781	< .001

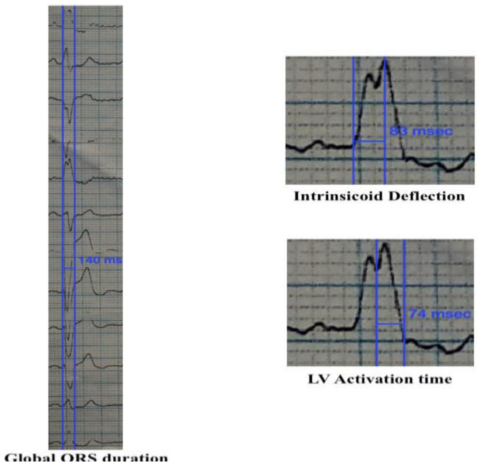


Figure 1: Example of methodology for quantification of various ECG parameters.

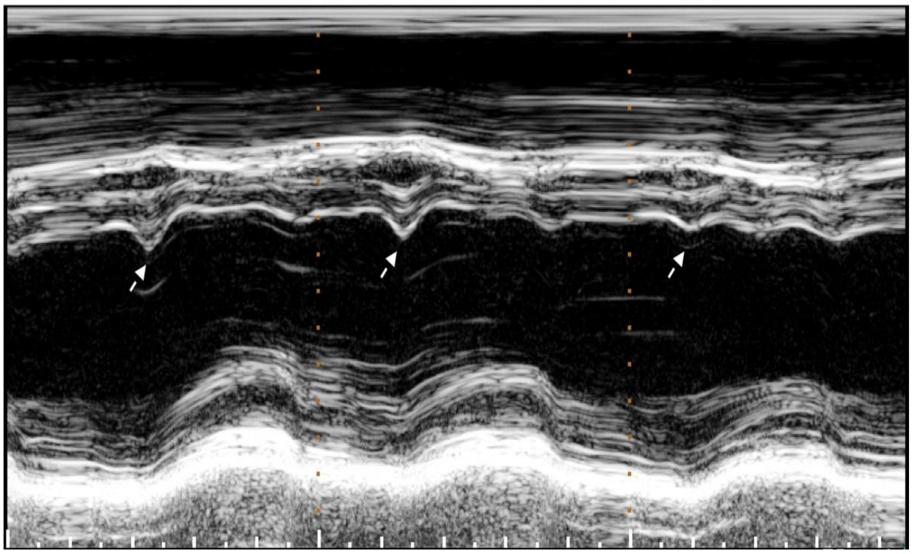
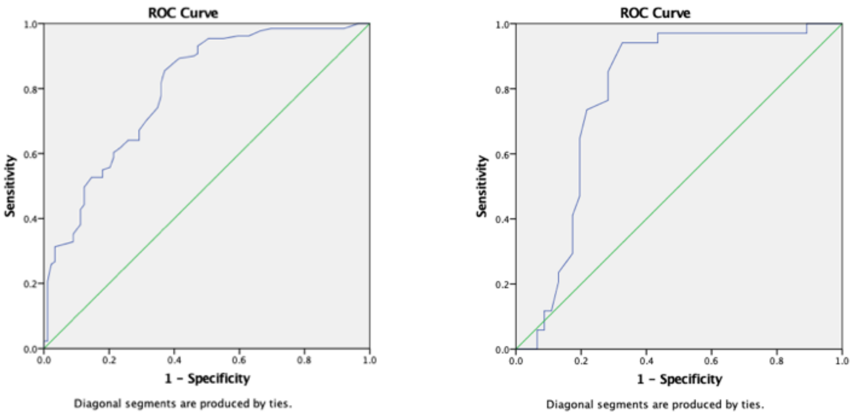


Figure 2: Septal Flash seen on M-mode image.



a **b**

Figure 3: ROC curves of ID prediction of echo evidence of mechanical dyssynchrony in a) whole group b) patients with narrower QRS

Discussion

Among the patients fulfilling the current CRT criteria approximately 40% are non-responsive to therapy [3]. Although a significant contribution could be due to RBBB and non-specific conduction defect [13,14]. These patients have also not been represented well in the landmark trials. The placement of lead on the lateral surface of heart has its root in the pathophysiology of LBBB type of conduction defect and placing leads according to latest mechanical activation has not been standardized yet for other wide ECG morphologies with recommendations of individualization of lead placement not being widely followed as a result. Moreover, it has been shown that typical LBBB as defined by current ACC, AHA, and HRS criteria have different electrical activation patterns in EP studies and furthermore those patterns cannot be reliably differentiated on surface ECG [4,5]. All the efforts of correlating the mechanical and electrical dyssynchrony have failed miserably in past because of using parameters singly or using numerical parameters with the inherent inter-user variability and even the intra-user dependency of echo being high [6,7]. Since the past decade the focus has turned to the pattern of mechanical dyssynchrony as the whole, with typical echo and strain patterns of LBBB being elicited [8,15]. These parameters have shown to be having less intra and inter user variability. Using those patterns was recently shown to be predictive of outcomes over and above the ECG parameters [9]. However, uptake in the routine of clinical parameters have been slow. Our study further examined the interplay between the typical LBBB ECG and Echo pattern. Overall prevalence of mechanical dyssynchrony by septal flash was 59.5%. Septal flash was more prevalent in the wider QRS group. Also, it was seen that ischemic LBBB subgroup have significantly lower prevalence of mechanical dyssynchrony. This could be due to the presence of fibrotic tissue preventing rapid movement needed to produce the flash. Although we did not include patients with echo evidence of scar, it well known that it is not the optimum method to do so. Next the relationship of echo dyssynchrony with the two novel ECG markers of LVAT and ID were examined. LVAT depicts the time taken by the electrical impulse to spread through the whole LV myocardium [11], whereas ID denotes the time taken for impulse to arrive at the later most part of LV to be depolarized in LBBB which the basal postero-lateral wall [12]. Earlier, LVAT has been shown to accurately predict LV reverse remodeling during CRT therapy [11]. ID also, has been shown to predict response to CRT, adjusting for baseline QRS and was shown to be better predictor of response than QRS duration parameters [12]. Cut-off values were provided. However, results for various subgroups were not explored.

Sahin et al [16] studying 144 heart failure patients with wide LBBB QRS observed QRS duration as well as MDI to be independent predictor of mechanical dyssynchrony. However, the parameter by which they studied dsysynchrony was septal-lateral delay. Their patient population also included non-strict LBBB criteria patients too. However, no cut-off were provided neither was the patient population of narrower QRSd analyzed.

Corteville et al [17] while studying a population of 104 patients without heart failure also addressed the issue of mechanical dyssynchrony prediction from ECG parameters. In their cohort the prevalence of septal flash was 45.2%. 93.3% of the patient population fulfilled the strict ECG criteria. They also observed that mechanical dyssynchrony was more prevalent the wider the patient populations's QRSd got and anterior ICMP negatively correlated with it.

Pooter et al [18] conducted a large level analysis on the electro-mechanical coupling over 545 patients. They included vectorcardiographic analysis in addition to other parameters. Prevalence of septal flash in their study was 52%. They too observed less ischemic heart disease in patients with SF. In multivariate analysis they found QRSd, LVAT to be independent predictors. However, in their study best predicting variable was from vector analysis. They concluded that overall accuracy to predict mechanical dyssynchrony by ECG analysis to be low. This difference of result from ours might have been due to the fact that they included all patients with LBBB even those with duration 120-130 and also patients without heart failure.

Because of the wide variability of QRS duration in the cohort as well as in the real life, both parameters were also explored in our study after being indexed to baseline QRSd. Whereas LVAT includes time taken from the notch, which is thought to respond LV breakthrough, to the end of QRS which includes time to reach posterolateral wall and completely activate it; ID represents time for impulse to reach the posterolateral wall and includes the time taken for LV breakthrough to happen. The difference between the two parameters behavior in narrow QRS could be due to exclusion of time to breakthrough versus inclusion of time to completely activate the posterolateral wall. First component contributes significantly in LBBB whereas second component is a major contributor when disease is causing diffuse intramyocardial delay, thereby predicting true LBBB versus delay due to LV hypertrophy and fibrosis. ID time in EP studies too have proved to be valuable marker for evaluation of true LBBB capture.

Contrary to the above-mentioned studies, Klaeboe et al [19] studying 28 post-TAVI acute LBBB patients did not find any correlation whatsoever between strict ECG criteria and mechanical dyssynchrony by evaluating classical LBBB strain pattern. Patients in their study had preserved ejection fraction. Authors were unable to provide any hypothesis regarding the same but it may be that the particular contraction pattern may be specific to chronically dilated heart of failure patients.

Limitations

The major limitation of the study was limited number of participants, single center involvement. However, we did find internal validity with similar nature of AUC in our predefined subgroup. As ours was a cross-sectional study, longitudinal follow-up data of patients with and without septal flash needs to be looked into so as to gain information regarding how these two groups progresses over time. Lastly, we did not include atypical LBBB and RV paced rhythm. Similar kind of analysis needs to be looked into in these patient populations.

Conclusion

Septal Flash was present in 60% of the LBBB population under study, with numbers being significantly higher in the group with greater QRSd. Prevalence of SF was 42% in the group with QRSd 130-149. SF was found to be significantly associated with non-ischemic subgroup among the study cohort. Only ID and MDI successfully predicted presence of mechanical dyssynchrony even over and above QRSd. Amongst patients with narrow QRS we provide cut-offs for the ECG parameter identified to predict mechanical dyssynchrony. Further work needs to be done regarding interaction between mechanical and electrical dyssynchrony.

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