ORIGINAL ARTICLE

Decoding electrocardiographic predictors of left ventricular mechanical remodeling in patients with left bundle branch block

Oana Andrei[1], Florin Barbu[1], Liliana Anghel[1], Carmen Ginghina[1,2], Radu Ciudin[1,2]

Abstract: **Introduction –** Left bundle branch block (LBBB) occurrence is uncommon in the general population (~1-3%), but is more prevalent among patients with congestive heart failure (~30%), and portends worse prognosis[1-3]. The impact of LBBB on left ventricular (LV) systolic function can range from minimal to dramatic reduction of ejection fraction. The delay in electrical activation subsequently triggers dyssynchronous contraction of the LV opposing walls, leading to ventricular remodeling and elevated LV filling pressures[6,7]. This is turn results in electrical and mechanical left atrium (LA) remodeling. The left ventricular activation time (LVAT) and P-wave terminal force in lead V1 (PTFV1) have been correlated with cardiac resynchronization response. However, the relationship between these electrocardiographic markers and LV mechanical remodeling has not been evaluated. **Aims –** The aim of this study is to investigate the relationship between LVAT and PTFV1 recorded on ECG and the LV mechanical remodeling evaluated by the left ventricular end-diastolic diameter (LVEDd) in patients with LBBB. **Methods –** We have conducted a retrospective, observational study on 155 consecutive patients diagnosed with LBBB admitted in our clinic between January 2017 and December 2019 with NYHA class I-IV, regardless of the left ventricle ejection fraction (LVEF). Biventricular electrical activation in LBBB was performed by measuring the right and left ventricular activation times (RVAT, LVAT) and electrical activation of the LA was analyzed by measuring P-wave terminal force in lead V1 (PTFV1). **Results –** In our cohort, LVEDd is statistically significantly correlated with LVAT and PTFV1, with a higher Pearson correlation coefficient for LVAT compared to PTFV1. In multivariate analysis LVAT and PTFV1 are independent predictors of LVEDd. **Conclusion –** This study suggests that LV mechanical remodeling in patients with LBBB can be predicted by the delayed electrical activation of the LV and the magnitude of P-wave negative terminal forces in V1.
Keywords: left bundle branch block, electrocardiography, P - wave terminal forces in V1, left ventricular remodeling.

Rezumat: **Introducere –** Blocul complet de ramură stângă (BRS) este rar în populaţia generală (~5%), dar relativ frecvent în rândul pacienţilor cu insuficienţă cardiacă, agravându-le prognosticul. Impactul BRSc asupra funcţiei mecanice cardiace variază de la efecte minime la reducerea marcată a funcţiei sistolice a ventriculului stâng (VS). Activarea electrică asincronă urmată de contracţia regională necoordonată a VS declanşează iniţial remodelarea negativă a VS şi ulterior prin creşterea persistentă a presiunii de umplere a VS, remodelarea electrică şi mecanică a atriului stâng (AS). Până acum nu a fost studiată relaţia dintre aceşti parametrii EKG şi remodelarea mecanică a VS. **Scop –** Scopul studiului este investigarea, la pacienţii cu BRS, a relaţiei dintre activarea electrică a VS şi AS evaluată electrocardiografic şi remodelarea mecanică a VS evaluată ecocardiografic. **Metode şi rezultate –** Am realizat un studiu retrospectiv, observaţional, nerandomizat pe un eşantion de 155 de pacienţi diagnosticaţi BRS, consecutiv internaţi în clinică între ianuarie 2017 şi decembrie 2019, în clasa funcţională NYHA I-IV, disfuncţia sistolică a VS nu a fost criteriu de includere sau excludere. Activarea electrică ventriculară a fost evaluate prin măsurarea timpului de activare a ventriculului drept şi stâng (LVAT, RVAT), iar activarea electrică a AS prin măsurarea forţelor terminale ale undei P in V1 (PTFV1). DTDVS se corelează semnificativ statistic cu TAVS şi FTPV1, coeficientul de corelaţie Pearson este mai mare pentru LVAT comparativ cu PTFV1. LVAT şi PTFV1 sunt predictori independenţi ai remodelării mecanice a VS. **Concluzii –** Acest studiu demonstrează că remodelarea mecanică a VS la pacienţii cu BRS poate fi prezisă parţial de activarea electrică întârziată la nivelul VS şi de forţele terminale negative ale undei P în V1.
Cuvinte cheie: bloc complet de ramură stângă, electrocardiografie, forţe terminale ale undei P în V1, remodelare ventriculară.

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INTRODUCTION

Left bundle branch block (LBBB) occurrence is uncommon in the general population (~1-3%), but is more prevalent among patients with congestive heart failure (~30%), and portends worse prognosis[1-3]. LBBB is of major clinical importance[4], being associated with a 3 to 4-fold increased risk of cardiovascular death in general population. LBBB is an electrophysiological abnormality affecting dromotropism of the conduction tissue, and electrocardiogram (ECG) is a simple and essential tool used to evaluate this type of conduction abnormality. The impact of LBBB on the left ventricular (LV) systolic function can range from minimal to dramatic reduction in left ventricular ejection fraction (LVEF). This variability is related to the left bundle branch anatomy, different levels and extent of the bundle block, different left ventricular breakthrough sites and different ranges of intrinsic myocardium contractility impairment[5-8]. The negative effect of LBBB on the LV systolic function consists of delay in electrical activation which subsequently triggers dyssynchronous contraction of the LV opposing walls, leading to a loss or diminished contribution of the interventricular septum to the LV systolic function with a transfer of an excessive workload on the lateral LV wall. This is the main mechanism that triggers cardiac remodeling, promoting ventricular dilation, alteration of the heart's pumping function and elevated LV filling pressure[6,7]. The left atrium (LA) and the left ventricle are functionally and anatomically interconnected, the LA being seen as a barometer of the LV filling pressures. An elevation of the LV filling pressures will directly result in elevation of the LA filling pressures, which in turn will dilate in order to help maintain the cardiac output, according to the Frank-Starling principle[9-12]. Structural and functional alterations of the heart chambers are reflected on their electrophysiological properties. The ECG contains relevant information about these electric properties of the cardiac chambers. Left ventricular activation time (LVAT) has proven to be a great marker for degree of reverse remodeling in patients with resynchronization therapies[13] as it was the P-wave terminal force in V1 (PTFV1)[14]. However the relationship between these markers and mechanical remodeling as evaluated by left ventricular end-diastolic diameter (LVEDd) in patients with preserved and decreased LVEF has not been evaluated.

The aim of this study is to investigate the relationship between electric activation of left ventricular and left atrium, registered on the ECG and the mechanical remodeling evaluated by echocardiography in patients with LBBB.

MATERIAL AND METHODS

Study population

We have conducted a retrospective, observational study on 155 consecutive patients with LBBB admitted in our clinic between January 2017 and December 2019 with NYHA class I-IV heart failure, regardless of the left ventricle ejection fraction (LVEF). The LBBB was diagnosed using conventional definition criteria[15,16]: QRSd ≥120ms, QS or rS complexes in V1, wide R wave – often with a notch - in DI, aVL, V5, V6, absent Q wave in V5, V6). Patients with atrial fibrillation, right bundle branch block (RBBB), RV pacing, valvular heart disease worse than mild or patients with a history of acute coronary syndrome in the last 3 months were excluded.

The standard 12-lead ECG (25 mm/s, 10 mm/mV) was performed with the patient lying in supine position, during hospitalization. All ECGs were analyzed by a cardiologist blinded to echocardiographic data. All measurements were performed manually using a caliper and image zoom of at least 200%.

Ventricular electric activation in LBBB was performed by measuring the right and left ventricular activation times (RVAT, LVAT). Notches that occurred in the first 40 ms of the S wave in V1 and V2 leads were excluded, as they suggest ventricular scar tissue. RVAT, counting right ventricular activation time and transseptal activation time, was measured as time between QRS onset and first notch of R wave in 2 or more adjacent leads (Figure 1). LVAT was calculated as the difference between QRSd and RVAT[13,17]. The notches in QRS were identified in all the ECGs, the longest LVAT in any lead was considered for the analyses (Figure 1).

Electrical activation of the LA was analyzed by measuring P-wave terminal force in V1 (PTFV1), which was calculated as the product of the duration (in milliseconds) and amplitude (in mV) of the negative terminal deflection of the P-wave in V1 (Figure 2).

All patients were evaluated by echocardiography during hospitalization and standard parameters were recorded[18]. Echocardiographic images were obtained using cardiology ultrasound machines – Vivid E9 and E95 (GE Healthcare, Horten, Norway. Echocardiography images were acquired using protocols in accordance with actual recommendations. Standard echocardiographic views were obtained using harmo-
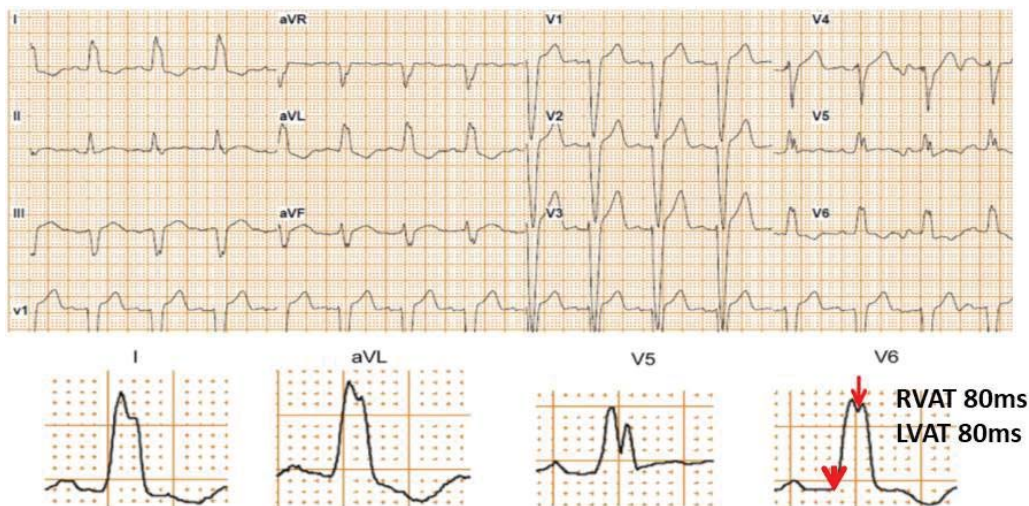
Figure 1. Determination of RVAT with the use of QRS notching. Time between QRS onset (first arrow) and notch nadir (second arrow) is RVAT. LVAT is QRSd (160 msec) – 80 msec = 80 msec. (RVAT, right ventricular activation time; LVAT, left ventricular activation time, QRSd, duration of QRS interval).
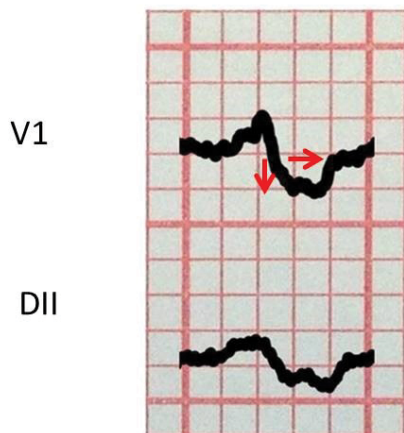

Figure 2. Measurement of PTFV1 the duration of negative terminal deflection of P wave is multiplied by amplitude of negative terminal deflection of P wave. (PTFV1, terminal forces of P wave in V1).

nic imaging, adjusting the frequency of the ultrasound transducer, the depth and the width of the sector in order to optimize the frame rate (60-80 fps for 2D echography).

LV size and function

LV size, systolic and diastolic functions were evaluated in accordance with actual recommendations:

- LV end-systolic and end-diastolic diameters (LVESd, LVEDd) and the end-systolic and end-diastolic thickness of the interventricular septum and the LV posterior wall (parasternal long-axis view – 2D guided measurements)
- LV volumes and ejection fraction – measured on images obtain in apical 4 chamber view and apical 2 chamber view, using the modified Simpson biplane method. LV volumes were indexed to body surface area (BSA).

The primary endpoint of this study was determination of LV mechanical remodelling, as evaluated by LV end-diastolic diameter (LVEDd).

This study was conducted in accordance with Declaration of Helsinki regarding ethical principles for medical research involving human subjects.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, while variables with skewed distribution were expressed as median or percentiles. Variables were compared using Student t test. A Pearson correlation was used to evaluate the relationships of LVAT and PTFV1 with LVEDd, severity of LVEF and NYHA class.

A multivariate analysis was performed with the statistically significant univariate ECG characteristics. LVEDd was the dependent variable, while the ECG parameters recorded in this study were the predictors.

To assess the comparative accuracy of different electrocardiographic variables in identifying LV remodelling, receiver operating characteristic (ROC) curves and the respective area under the curve were calculated for every parameters. Predictors of LV remodelling in patients with LBBB were assessed using binary logistic analysis. The P values below 0.05 were considered statistically significant.

Statistical analysis was computed using the R software, version 4.0.2 (2020-06-22), (Copyright (C) 2020 The R Foundation for Statistical Computing, R

Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org).

RESULTS

The study cohort included 155 patients with a mean age of 63.14±11.5 years, 62.58% were of males, 57% in NYHA class II, 27% in NYHA class III and the mean LVEF was 39.25±14.15% (Table 1). The mean QRSd was 152.69±19.08 ms, maximum LVAT measured was in V5 and its mean was 105.68±17.38 ms, the mean negative terminal force of P wave in V1 was 40.3±9.16 mm*ms and the mean LVEDd was 59.46±11.6 mm.

Relationship of electrocardiographic parameters with left ventricular ejection fraction

The LVAT and PTFV1 was significantly different between patients with LVEF ≤35% and those with LVEF >35% (LVAT 112.12±18.689 ms vs 101.82±15.396 ms, p<0,001; PTFV1 53.1818±29.94400 ms*mV vs 34.5909±18.38343 ms*mV, p<0.001). In patients with severe systolic dysfunction (LVEF ≤ 35%) the electrical activation was more delayed and the P-wave terminal forces in V1 were more negative.

In patients with LVEF ≤35%, PTFV1 was significantly corelated with LVEDd, but not in those with LVEF >35% (Table 2). The relationship of PTFV1 with LVEDd depending on LVEF, highlights the succession of the physio-pathological events induced by the delayed electrical activation of the LV in patients with LBBB, as LV remodeling and systolic dysfunction precede electrical and haemodynamic alterations in the LA.

Association between electrocardiographic parameters and left ventricular mechanical remodeling in left bundle branch block patients

In order to analyze the relationship between LV mechanical remodeling and electrical dyssynchrony we used univariate and then multivariate linear regression, the dependent variable being the LVEDd (Table 3). The predictors were ECG parameters known to be associated with LV electrical dyssynchrony.

Multivariate linear regression only included significant parameters identified in the univariate linear regression, using the backward selection algorithm (the regression model found in the (Table 4); the multiple regression model included only ECG parameters.

The multiple regression model identified only 2 independent parameters out of 10 (LVAT and PTFV1), showing significant collinearity of the predictors identified in the simple regression (Table 4). The R^2 (R-square) in the model was 0.352, the two ECG parameters explaining slightly more than 1/3 of the LVEDd

Table 2. Correlations of LVAT, PTFV1 with LVEDd depending on LVEF in left bundle branch block patients

	LVEF ≤35%	LVEF >35%
Predictors	LVEDd r Pearson (p Value)	LVEDd r Pearson (p Value)
PTFV1	0.46 (0.0004)	-0.16 (0.1209)
LVAT	0.49 (0.0001)	0.33 (0.0012)

LVAT, left ventricular activation tim; LVEF left ventricular ejection fraction; LVEDd, left ventricular end diastolic diameter; PTFV1, terminal forces of P wave in V1.

Table 1. Characteristics of studied population

Variable	Study group (n=155 pts)
Age, years ± s.d.	63.14 ± 11.50
Gender M, n (%)	97 (62.58%)
F, n (%)	58 (37.42%)
NYHA class I, n (%)	8 (5.16%)
II, n (%)	72 (46.45%)
III, n (%)	55 (35.48%)
IV, n (%)	19 (12.25%)
Coronary Present, n(%)	23 (14.84%)
disease Absent, n (%)	132 (85.16 %)
QRSd below 150 ms, n (%)	52 (33.54 %)
above 150 ms, n (%)	103 (66.46 %)
LVEF (%) below 35%, n (%)	78 (50.32 %)
above 35%, n (%)	77 (49.68 %)
LVEF ≤ 35% dilated CMP n (%)	63 (83.11%)
ischemic CMP n (%)	15 (16.89%)
Mean LVEDd ± s.d.	59.84 ± 11.73 mm

QRSd, QRS duration; LVEF, left ventricular ejection fraction; CMP, cardiomyopathy; LVEDd, left ventricular end-diastolic diameter.

Table 3. Relationship of ECG parameters with LVEDd

Predictor	T-statistic	p-value	Coefficient [IC95%]
PR interval	-0.476	0.6340	-0.007 [-0.03 to 0.02]
Pa-_V1	2.451	0.0154	5.68 [1.10 to 10.26]
Pd-_V1	2.114	0.0361	0.06 [0.01 to 0.13]
Pdt_V1	2.083	0.0389	0.10 [0.005 to 0.20]
PTFV1	4.276	< 0.0001	0.13 [0.07 to 0.19]
QRS axis	-2.367	0.0192	-0.06 [-0.12 to -0.01]
QTc	2.295	0.0230	0.04 [0.006 to 0.08]
QRSd	5.040	< 0.0001	0.23 [0.14 to 0.32]
LVAT	6.489	< 0.0001	0.32 [0.22 to 0.42]
T_d	1.810	0.0722	0.06 [-0.005 to 0.12]
RVAT	0.79	0.431	0.9 [-0.066 to 0.12]
PT_FT/QTc	0.814	0.4170	21.19 [-30.42 to 73.01]

Pa-_V1, amplitude of negative P wave in V1 lead; Pd-_V1, duration of negative Pwave in V1 lead; PTFV1, negative terminal force of P wave in V1; QRSd, QRS duration; LVAT_V, left ventricular activation time in V5 lead; QTd, QT interval duration; T_d, duration of T wave, PT_FT/QTc, the ratio between the time from the peak of the T wave to the end of the T wave and QTc interval duration; RVAT, right ventricular activation time.

Table 4. ECG parameters predictors of LV mechanical remodeling

Predictor	T-statistic	p-value	Coefficient [IC95%]
PTFV1	3.570	0.0004	0.09 [0.04 to 0.15]
LVAT	6.169	< 0.0001	0.28 [0.19 to 0.37]

LVAT, left ventricular activation time; PTFV1, terminal forces of P wave in V1;

Table 5. R-squared - the strength of the relationship between PTFV1, LVAT and LVEDd

Model	R	R Square	Change Statistics		
			R Square Change	F Change	Sig. F Change
1	.577[a]	.352	.352	41.590	.000

[a] Predictors: (constant) PTFV1, LVAT

variation (Table 5). The important collinearity of the predictors is demonstrated by the statistically significant correlations between them.

The analysis of the correlation between LVEDd, LVAT and PTFV1 showed a higher Pearson correlation coefficient for LVAT compared to PTFV1 (Figure 3).

Binary logistic regression, with dependent variable LVEDd greater than 55 mm for male and 53 mm for female (yes/no) and predictors categories of LVAT and PTFV1 (determined with a ROC analysis), show that LV significant dilatation is predicted by LVAT higher than 105ms with 50% specificity and 75% sensitivity and by PTFV1 greater than 65 ms*mV with 86% specificity and 25% sensitivity. Therefore, mechanical LV remodelling is accurately identified by PFTV1 higher than 65ms*mV (Table 6, Figure 4).

DISCUSSIONS

This study indicates that LV mechanical remodeling, as evaluated by LVEDd, in patients with LBBB can be predicted by the delayed electrical activation of the LV and the P-wave negative terminal forces in V1, which reflects high LV filling pressures, with a significant correlation with LVEDd.

Left bundle branch block is a complex electrical disease that causes a block in the conduction of the electrical impulse at different anatomical levels and leads to its abnormal propagation in the LV myocardium. In 2004 Aurichio et al. described the LV electrical activation pattern during LBBB using 3D contact and non-contact mapping[6,19]. They showed that electric impulse propagation in the left ventricular myocardium originates in RV, followed by a transseptal propagation to the LV septal endocardium, from mid to apex. In a heart with normal conduction system, transseptal conduction requires about 20 ms, but in patients with LBBB it requires more than 40 ms, indicating slow, myocardial to myocardial cell conduction. Afterwards, the wave front continue to spread from mid or apical septal LV endocardium to the posterolateral LV wall through the apex and inferior wall. This
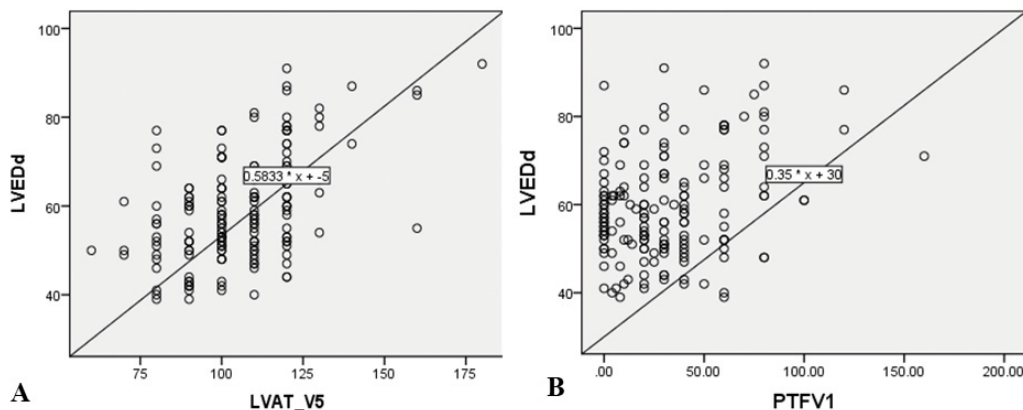

Figure 3. LVEDd plotted as a function of LVAT (A) and PTFV1 (B). This figure demonstrate the higher correlation for LVAT compared to PTFV1. LVAT, left ventricular activation time; LVEDd, left ventricular end diastolic diameter; PTFV1, terminal forces of P wave in V1.

Table 6. PTFV1 > 65ms*mV and LVAT > 105ms predict accurately LV dilatation

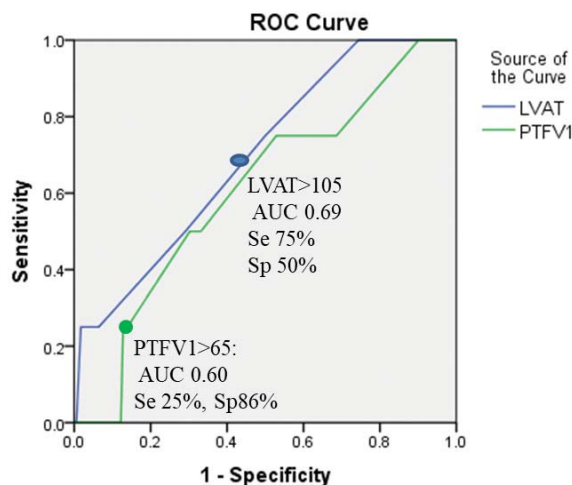| Predictor	Coefficient	p Value	OR [IC95%]
PTFV1 >65		0.0158	6.42 [1.73 to 41.69]
LVAT >105	1.15	0.0009	3.17 [1.61 to 6.40]
LVAT, left ventricular activation tim; PTFV1, terminal forces of P wave in V1.			

Figure 4. ROC curves for LVEd vs LVAT and PTFV1. LVAT, left ventricular activation time; LVEDd, left ventricular end diastolic diameter; PTFV1, terminal forces of P wave in V1.

Figure 5. "U" shaped pattern of electrical activation caused by wavefront propagation around the apex due to line of functional block, explaining the presence of notching on the ECG (adapted from Kanawati et al.[20]).

"*U*-shaped" electro-mechanical activation pattern is caused by lines of functional conduction block (Figure 5) described during electrophysiology studies. Lines of functional block are located in the anterior, lateral and inferior LV wall. The transseptal delay and the sites of LV breakthrough are the major determinants of the location of the lines of functional block and the QRS duration, in LBBB. Therefore, patients with apical LV septal breakthrough site have a line of functional block located in the anterior wall, and are related to more severe interventricular and intraventricular electrical dyssynchrony compared to patients with other LV breakthrough sites. The anterior location of block line will cause electro-mechanic activation of the septum to propagate along the apex and the inferior wall, toward the lateral or posterior wall, without directly passing through the anterior wall, as would happen in the healthy heart. Therefore, the last segment to activate is the basal region of the lateral or posterolateral wall, adjacent to the mitral annulus[6,17,19-21].

Electrical depolarization initiates myocardial mechanical contraction. This sequential electro-mechanic activation of the myocardium causes the dyssynchronous contract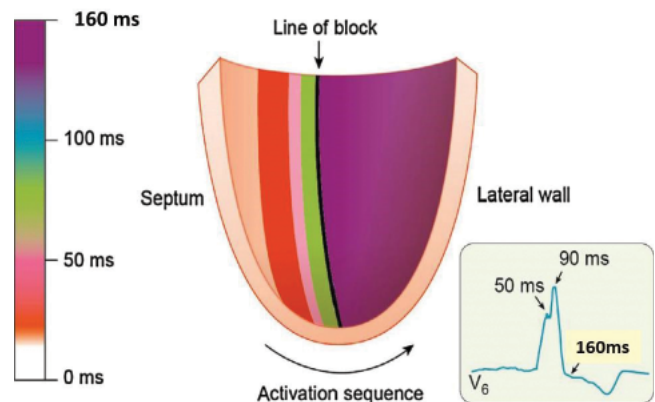ions of opposing walls of the LV. As a consequence of in-coordinated contractions, the shortening of the first electrical activated walls will induce stretching of the opposing myocardial walls, which are electrical activated later[22]. The mechanical stretching of the myocardium further delays the propagation of the electric impulse, as a result of the molecular alterations in the connexin 43 and the calcium channels[6,21]. In LBBB, the septum is the first segment of the LV myocardium to contract, and its contraction begins before the opening of the aortic valve, occurring during isovolumetric contraction period, against low pressures before opening of the aortic valve. Hence, it doesn't contribute to the cardiac output. This way the septal workload is wasted, causing lateral wall stretching and increasing its workload. According to the Frank-Starling law, the pre-stretched lateral wall has a vigorous contraction that determines increasing intraventricular pressure, causing opening of the aortic valve and ejection of blood, along with stretching and left-to-right movement of the septum. Since the septum is a third of the LV mass, the important septal workload waste causes lateral wall overload, triggering the harmful LV mechanical remodeling, which consists of asymmetrical hypertrophy of the lateral wall and LV dilation, along with an increase in the LV filling pressures[2,6,7,22-24]. Hemodynamic alterations in the LV directly and rapidly affect the electromechanical function of the LA, which is considered a "barometer" of dias-

tolic burden of the LV[9-12]. Therefore, LA anatomical and functional changes mirror the cumulative effects of LV filling pressures over time, comparable to the role of hemoglobin A1c in diabetes[11,12]. Consequently, LA electro-anatomic remodeling provides more sensitive and probably more accurate markers of diastolic dysfunction severity than the usual LV diastolic function parameters, that are highly variable and related to hemodynamic status at the time of examination[23-27]. In a recent review, regarding LA importance in patients with LBBB and LV systolic disfunction which were candidates for CRT, Camelli et al showed that LA structural and functional parameters are independent predictors of outcome, in these patients[9].

The relationship between LBBB and LV remodeling is supported by numerous experimental and clinical studies. In 2018, Auffret et al. reviewed data and concluded that LBBB promotes structural remodeling and LV systolic dysfunction[28].

The ECG records the abnormal electrical activation and its consequences. The ECG image of the activation wavefront reaching the endocardium of the LV septum is the first R wave notch, while the second R wave notch represents the beginning of depolarization of the epicardium of the LV lateral wall. QRS morphology is insignificantly changed between these two notches due to the fact that the direction and magnitude of the mean electrical vector is constant, as the depolarization occurs in the LV myocardial wall[29]. Total electrical activation time in LBBB patients is 80-150 ms longer than in normal conduction[29]. The duration and morphology of QRS complexes represent a crude image of the asynchronous intramyocardial electrical activation, that is based both on the electrical asynchrony caused by abnormal conduction tissue and the mechanical asynchrony caused by intrinsic myocardial alterations (such as overload, hypertrophy, fibrosis, scar tissue)[22,30]. In order to aid identification of patients with QRS morphology predominantly resulting from altered conduction tissue, Strauss et al introduced a novel electrocardiographic definition of complete LBBB, emphasizing that criteria for LBBB should include the presence of the two R wave notches in at least two contiguous lateral leads[29]. Sweneey et al analyzed the relationship between the electrical activation of the LV as recorded on the ECG and the structural changes of the LV, and showed that LVAT is an independent predictor of mechanical remodeling of the LV and of CRT response[13]. Our study showed the statistically significant correlation between mecha-

nical LV remodeling assessed by LVEDd and LVAT in patients with LBBB.

ECG signs of LA overload are determined by a leftward and posterior shift of the electrical vectors of P wave in the horizontal plane, causing a predominantly negative component of the P wave in V1[27]. In a study assessing the structure and function of the LV and LA by cardiac MRI, Tiffany et al revealed the underlying mechanisms of the electrocardiographic indices of the P wave. They indicated that electrical alterations caused by LA overload, assessed by PTFV1, are independent predictors of fibrosis in the LV before structural and functional changes of the LA[27]. Baturova et al showed, in a sub-study of the MADIT-CRT trial, that the electrical LA abnormality expressed as PTFV1 on ECG was a sign of electrophysiological LA changes caused by LV remodeling. PTFV1 had an additive prognostic insight for LBBB patients. Normal PTFV1 is an independent predictor of better prognosis regardless of LA volume[23]. The P wave morphology is in part influenced by LA volume, but it is unlikely to be the sole determinant[24]. Left atrial remodeling includes structural, ultrastructural, ionic and electrical remodeling. The electrical remodeling is considered to be induced by alterations of expression and function of ion channels and gap junctions in the cardiac myocyte[25].

The relationship between LV remodeling and mechanical dyssynchrony was analyzed by Tayal et al., who showed that significant negative remodeling of the LV, quantified as LVEDv is a negative predictor of CRT response. They highlight the fact that severe dilation of LV involves both electromechanical asynchrony and severe remodeling, which further increase the fibrotic burden of the LV myocardium[31]. Bernard-Brunet et al demonstrated high predictive value of a score for CRT response, in which LV mechanical remodeling was assessed by LVEDd[32]. In a review, Vernooy et al analyzing the factors related to favorable response to cardiac resynchronization therapy, found that increased LVEDv was an independent predictor of the absence of LV reverse remodeling after CRT[32]. The results of several studies emphasized the prognostic significance of LVED diameter and volume. Severe LV dilation predicted lack of response to CRT[34]. Instead, moderate remodeling predicted a favourable response to CRT[29]. In patients with LBBB and moderate LV systolic dysfunction, LVEDv predicted progression to severe LV dysfunction[35].

The results of our study highlighted the interrelationship between electrical LV asynchrony and elec-

trical LA changes and mechanical LV remodeling in patients with LBBB. LV dilation is partially predicted by the duration of LV electrical activation and by the abnormal electrical forces of the left atrium. LVEDd better correlated with LVAT than with PTFV1, even though both correlations were statistically significant.

CLINICAL IMPLICATIONS

ECG decoding of patients with cLBBB should include not only a rigorous analysis of the QRS complex, but also a careful characterization of the atrial depolarization, by assessing the P wave morphology. Thorough understanding of cardiac electrical activity, well-integrated in clinical context, may improve optimal treatment strategy for each patient.

LIMITATIONS

This represented the experience of a single center. A first limitation of this study was the retrospective nature of it, as electrocardiographic and echocardiographic evaluations were performed in conventional settings. For this reason, the chosen parameter for evaluating mechanical remodeling was LVEDd and not LVEDv. Data demonstrating the significance of this parameter support our choice. Another limitation of our study was that all ECG measurements were carried out manually, enlarging the image by at least 200%.

CONCLUSION

In patients with LBBB on ECG, LVAT and PTFV1 were significant correlated with left ventricular remodeling as demonstrated by LVEDd.

The heart's electric signature can be a subtle indicator of cardiac function and anatomy, providing valuable prognostic and therapeutic clues.

Conflict of interests: none declared.

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