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Diagnostic criteria for proximal left bundle branch block and their significance in predicting the success of cardiac resynchronization therapy

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Aim. To develop diagnostic criteria for proximal left bundle branch block (LBBB) based on non-invasive methods and to determine the significance of these criteria in predicting the effect of cardiac resynchronization therapy (CRT).

Material and methods. To develop criteria, 58 patients (21 men, mean age, 76.1±7.1 years) with LBBB occurred immediately after transcatheter aortic valve implantation (TAVI) were included. To assess the significance of the developed criteria, the second group included 22 patients (11 men, mean age, 57.9±9.3 years) with dilated cardiomyopathy (DCM), who had indications for CRT. The effectiveness of CRT was assessed by echocardiography 6 months after implantation. All patients in the DCM group and 15 patients in the TAVI group underwent superficial epi- and endocardial non-invasive mapping using Amycard 01C EP Lab (EP Solutions SA, Switzerland). Patients in the DCM group underwent contrast-enhanced cardiac magnetic resonance imaging (MRI) before device implantation.

Results. The criteria for proximal LBBB included 3 electrocardiographic features: QRS complex >130 ms in women and 140 ms in men, QS- or rS-configuration in V_1 lead, notch in two or more lateral leads (I, avL, V_5, V_6), and 2 mapping criteria: characteristic location of block line and delayed activation site. In the DCM group, the criteria were positive in 13 of 22 patients (59%). The developed criteria for proximal LBBB showed a relatively strong, significant relationship with the positive effect of CRT (chi-square test =5.46, p=0.02, Cramer test =0.5, odds ratio (OR) =15,0, 95% confidence interval (CI), 1.32-169.9, p=0.002). An additional analysis showed that both the criteria for proximal block and CRT effect are associated with myocardial fibrosis according to MRI. In particular, intramural stria-shaped contrast accumulation in the interventricular septum leads to a change in characteristic of proximal block mapping phenomena — displacement of delayed activation site (chi-square test =13.9, p<0.001, Cramer test =0.79) and displacement or absence of conduction block lines (chi-square test =6.92, p=0.009, Cramer test =0.56) and prevents the CRT effect (OR=8.67, 95% CI, 1.05-71.57 p=0.03).

Conclusion. Proximal LBBB is only one of the factors determining the effectiveness of CRT. Proximal LBBB may mask significant myocardial structural changes that prevent the CRT success.

Keywords: left bundle branch block, proximal left bundle branch block, non-invasive mapping, dilated cardiomyopathy, heart failure, cardiac resynchronization therapy, contrast-enhanced cardiac magnetic resonance, myocardial fibrosis, transcatheter aortic valve implantation.

Relationships and Activities: none.

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Key messages

- Based on ECG analysis and non-invasive mapping in patients with left bundle branch block (LBBB) after transcatheter aortic valve implantation, criteria for proximal LBBB were developed.
- The significance of the developed criteria in predicting the success of cardiac resynchronization therapy (CRT) in patients with dilated cardiomyopathy was assessed.
- Proximal LBBB may mask significant myocardial structural changes that prevent CRT success.

In recent years, there has been a growing interest in the left bundle branch block (LBBB) mainly due to the widely appreciated efficacy of cardiac resynchronization therapy (CRT) in the treatment of chronic heart failure (CHF). This method can result in the complete elimination of CHF manifestations and normalization of left ventricular (LV) ejection fraction (EF). But such complete reverse cardiac remodeling in CRT (super-response) cannot be achieved in all patients. This initiated numerous studies aimed at finding predictors of CRT effectiveness. A key element was the analysis of ECG criteria for LBBB. In 2011, Strauss DG et al. formulated ECG criteria for LBBB that most closely corresponded to non-invasive cardiac activation mapping (NIAM) for LBBB [2]. These criteria,

according to foreign [3] and Russian studies [4, 5], have demonstrated high sensitivity and specificity in predicting reverse LV remodeling in CRT. However, papers on His bundle pacing as a method of alternative CRT for HF and LBBB showed that the Strauss DG criteria alone are not enough to predict the effect of these techniques. There was a need to characterize the electrophysiological performance of LBBB depending on the block site in His-Purkinje system. Thus, LBBB was divided into a proximal type (site of block located at the level of the left His bundle and in the proximal left bundle branch at left conduction system) and the distal type with intact Purkinje activation [6]. Moreover, it was shown that the proximal LBBB predicts the normalization of QRS complex during CCP and possibly the effectiveness of classic CRT. However, the electrophysiological criteria for various LBBB levels were obtained using complex invasive techniques and are not applicable in routine practice. In this regard, we aimed to develop diagnostic criteria for proximal LBBB based on non-invasive methods and determine its value in predicting CRT effectiveness.

Material and methods

Object of research: To develop criteria for proximal LBBB, the first group (transcatheter aortic valve implantation (TAVI) group) included 58 patients (21 men and 37 women, mean age 76.1±7.1 years) with a prior proximal LBBB. In all these cases, the appearance of LBBB was preceded by TAVI, performed due to severe aortic stenosis (Figure 1). LBBB in such interventions results from the mechanical effect of implanted valve frame on the proximal conduction structures, primarily on the atrioventricular junction and the left bundle branch, which are anatomically close to the aortic valve. The preoperative QRS duration in all these patients was 97.7±12.1 ms. Nine (15.5%) patients initially had left anterior fascicular block. In most cases (n=49, 85%), ECG signs of newly diagnosed LBBB were recorded on the first day after the operation. On the second day, LBBB was registered in 2 (3%) patients, on the third — in 4 (7%) and on the fifth day — in 3 (5%) patients. The QRS duration in newly diagnosed LBBB in this group was 153.5±14.5 ms.

The second group (dilated cardiomyopathy (DCM) group) included 22 patients (11 men, 11 women, mean age 57.9±9.3 years), which had clinical and instrumental signs of DCM. Echocardiography in patients in this group confirmed a significant dilation of heart chambers, mainly the LV (LV end-diastolic volume — 242 [171; 344] ml, LV end-systolic volume — 171 [131; 262] ml), a significant decrease global contractility (LVEF — 30 [25; 32]%). Ischemic origin of the disease was excluded due to intact coronary arteries according to angiography. All patients in this group had NYHA class II-IV HF, despite optimal 3-month therapy and signs of LBBB (QRS duration — 177.8±20.4 ms), which determined the indications for CRT and biventricular implantable cardioverter defibrillator was implanted. In all of them, optimal posterolateral lead position was achieved. For atrioventricular delay selection, automatic adjustment algorithms recommended by device manufacturer were used; intraventricular delay was not optimized; basal settings (0 ms) were used [7]. The effectiveness of CRT was assessed 6 months after device implantation according to transthoracic echocardiography. In this case, the criterion for reverse LV remodeling and a positive response to CRT was a decrease in LV end-systolic volume by no less than 15% of the initial value [8]. All included patients had 95-100% biventricular pacing by 6 months of follow-up.

Investigations. Twelve-lead ECG. ECG was recorded using an Easy ECG system (ATES MEDICA, Russia) with paper speed of 25 and 50 mm/s and amplitude of 10 mm/mV.

Non-invasive activation mapping (NIAM). All patients in the DCM group, as well as 15 patients in the TAVI group, underwent superficial epi- and endocardial non-invasive mapping using the Amycard 01C EP Lab system (EP Solutions SA, Switzerland), as previously described [9, 10]. Based on individual three-dimensional heart anatomy obtained by tomography, we analyzed various activation maps with an assessment of right ventricular (RV) and LV activation time (AT) on the endocardial and epicardial surface and AT difference between them in milliseconds. In addition, the isochrone map was used for LV marker division into 17 segments according to Cerqueira MD [11] for determination the site of latest LV activation (LAS). Isochrone maps were also used to assess the presence of conduction block line and its topography according to Ploux S technique [12]. The conduction block line is required for U-shaped type of electric signal propagation along the LV myocardium, specific for LBBB. This conventional border is represented by electrically-inexcitable myocardium located along the long LV axis, parallel to the interventricular septum (IVS) and directed from the LV base to the apex. The presence of a conduction block line was confirmed when the difference in myocardial AT on both sides of this line is more than 50 ms.

Contrast-enhanced magnetic resonance imaging (MRI). All patients in the DCM group underwent cardiac MRI on a Magnetom Avanto superconducting system (Siemens, Germany) with a field of 1.5 Tesla, with a surface radiofrequency chest coil and synchronized with an ECG. A gadolinium-based contrast media (gadoversetamide) was administered intravenously at a dose of 0.15 mmol (0.3 ml) per 1 kg of patient body weight. Obtained images were assessed for morphology, cardiac function, as well as the presence and location of late gadolinium enhancement (LGE) 10-15 minutes after the contrast agent intravenous administration.

First, based on the ECG and NIAM data, criteria for proximal LBBB were formulated. Then, the significance

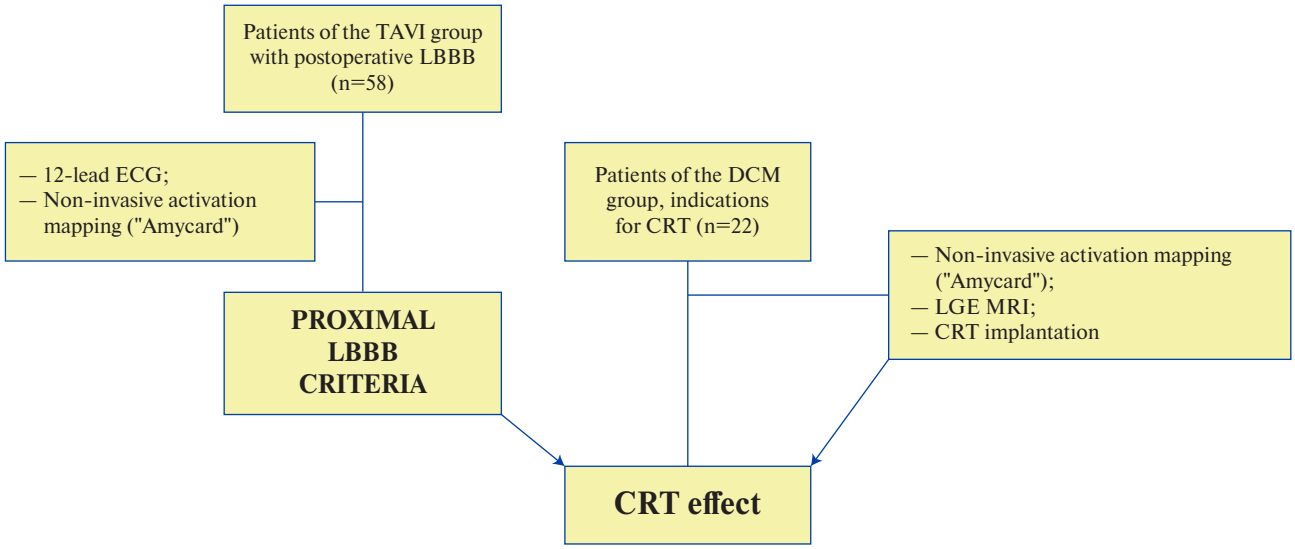

Figure 1. Study design.
Abbreviations: LBBB — left bundle branch block, DCM — dilated cardiomyopathy, MRI — magnetic resonance imaging, CRT — cardiac resynchronization therapy, ECG — electrocardiography, TAVI — transcatheter aortic valve implantation.

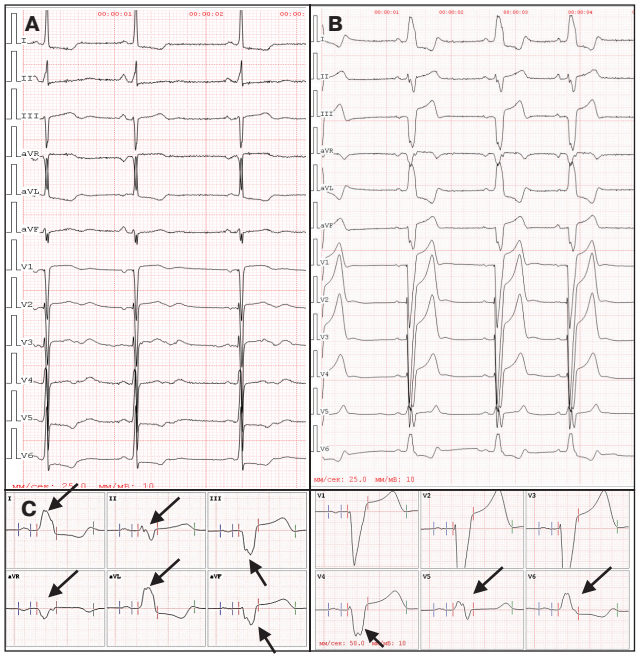

Figure 2. An example of LBBB on the ECG in an 82-year-old patient after TAVI. **A** — Presurgical ECG of the patient. QRS complex duration is 92 ms. **B**, **C** — ECG of the patient, at the first day after surgery. **C** — separate image of the morphology of QRS complex in each of the 12 ECG leads in LBBB. The arrows indicate the notched QRS complex in leads I, II, III, avR, avL, avF, V4-V6.

of these criteria were evaluated in predicting the CRT effect. The study design is presented in Figure 1.

Statistical analysis. Statistical analysis included calculation of means, standard deviations (SD), medians (Me), lower and upper quartiles (Q1 — Q3) depending on the distribution normality. The normality of distribution was assessed using the Kolmogorov-Smirnov test (n>50) or the Shapiro-Wilk test (n<50). Group comparisons were made using the Mann-Whitney U test, Student t test, and Wilcoxon T test. The analysis of nominal variables was carried out with the Pearson chi-square test and Fisher's exact test. Cramer's V was used to assess the association between nominal variables. The interpretation of Cramer's V was carried out according to Rea & Parker guidelines (0.2-<0.4 — moderate relationship, 0.4-<0.6 — relatively strong relationship, 0.6-<0.8 — strong relationship, 0.8-1.0 — very strong relationship). The correlation coefficient between a continuous and a dichotomous value was estimated using point-biserial correlation. To assess the significance of binary values, the odds ratio (OR) was used. In addition, sensitivity and specificity was calculated. Differences were considered significant at p<0.05. Data

Table 1

Initial parameters of RV and LV activation in DCM and TAVI patients

	DCM group (n=22)	TAVI group (n=15)	P-value
QRS complex duration, ms	177.8±20.4	153.5±14.5	0.03*
RV AT (epi), ms	83 [66; 102]	80 [74; 85]	0.32
RV AT (endo), ms	90 [73; 105]	82 [65; 89]	0.31
LV AT (epi), ms	93 [88; 106]	72 [64; 79]	0.006*
LV AT (endo), ms	117 [93; 133]	93 [73; 101]	0.008*
AT difference	51 [39; 59]	44 [20; 52]	0.37

Notes: data are presented as n — absolute number of cases, % — relative number of cases, means ± SD or medians (Me) and lower and upper quartiles [Q1 ; Q3], * — statistical significance at p value <0,05.

Abbreviations: AT — activation time, DCM — dilated cardiomyopathy, LV — left ventricle, RV — right ventricle, epi — epicardial surface, endo — endocardial surface, TAVI — transcatheter aortic valve implantation.

Figure 3. Detection rate of notched QRS complex in patients included in the study. **A** — TAVI group, **B** — DCM group.

entry, editing and statistical analysis was carried out using statistical packages Statistics 8, SPSS 20.

The study was performed in accordance with the Good Clinical Practice and the Declaration of Helsinki standards. The study protocol was approved by the Independent Ethics Committee for Clinical Research of the E. I. Chazov National Medical Research Center for Cardiology. Before inclusion in the study, written informed consent was obtained from all participants.

Results

1. Twelve-lead ECG analysis

Analysis of 12-lead ECG found that LBBB met the Strauss DG criteria [2] in all (100%) patients of the TAVI group: the QRS complex duration exceeded 130 ms in women, 140 ms in men; the QRS morphology in lead V1 was QS or rS; and QRS complex was notched or slurred in ⩾2 lateral leads including I, avL, V5-V6 (Figure 2, 3 A), while a notch in the septal leads was a single finding. At the same time, notched QRS complex in the inferior leads was revealed as often as in lateral leads: in lead II — in 74.1% of patients, in lead III — in 84.5% of patients, in lead avF — 67.2% (Figure 3). Notched QRS complex in ⩾2 inferior leads was found in 79.3% of patients in the TAVI group and its presence was associated with the QRS duration (r=0.59).

Since the LBBB developed after acutely TAVI surgery is a result of the mechanical impact of the aortic valve frame on the upper conduction system, the ECG signs of LBBB proposed by Strauss DG and found in TAVI group patients (100%) were considered to be the diagnostic criteria for the proximal LBBB.

In all patients in the DCM group, the QRS complex duration on the ECG exceeded 130 ms for women and 140 ms for men, while the QRS morphology in V1 was QS or rS. At the same time, the other Strauss DG LBBB criteria were detected less frequently than in the TAVI group (Figure 3B). Notched or slurred QRS in ⩾2 leads lateral (I, avL, V5-V6) was observed in 18 (81.8%) patients. The presence of notched QRS complex in the inferior leads was recorded with the same frequency as in the lateral leads (17 (77.2%) cases for lead II, 18 (81.8%) for lead III and 16 (72.7%) in lead avF). In septal leads V1 and V2, notched QRS was detected in only 2 (9.1%) patients. Thus, among

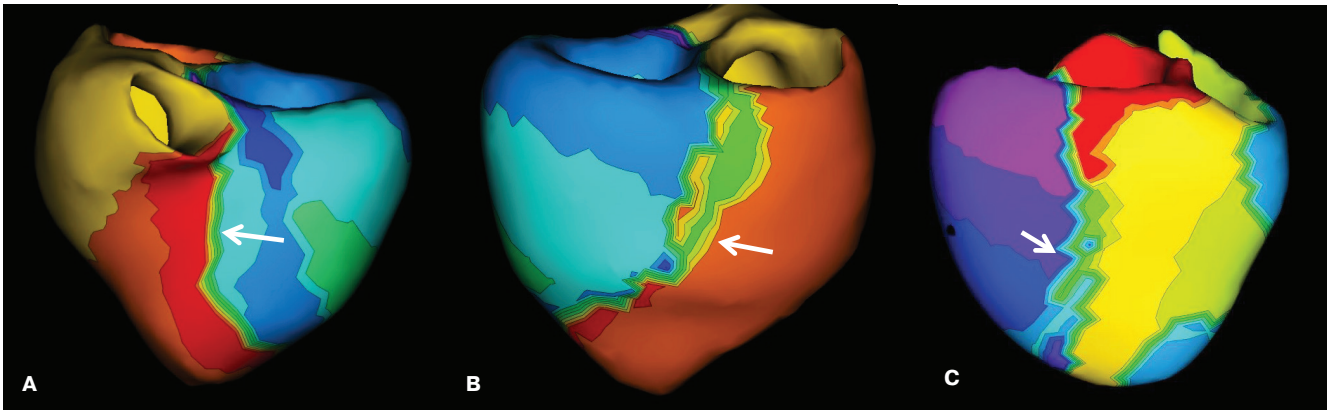

Figure 4. Localization of conduction block lines (indicated by an arrow) in patients of the examined groups according to NIAM using Amycard system. **A** — anterior septal line of the conduction block in a TAVI patient, **B** — posterolateral line of the conduction block in a TAVI patient, **C** — lateral localization of the conduction block line in a DCM patient.

patients in the DCM group, positive Strauss DG criteria [2] as a sign of proximal LBBB were identified in only 18 (81.8%) of this group. This means that the remaining 4 patients could have other conduction disorders along the left bundle branch.

2. Results of NIAM

Analysis of electrical propagation was performed in 15 TAVI group patients and in all (n=22) DCM patients. When analyzing epi- and endocardial cardiac models of DCM and TAVI patients, no significant differences were found in the parameters of RV activation, but significant differences in LV AT were identified (Table 1). DCM patients had significantly greater than in the TAVI group LV AT in both epicardial and endocardial models (93 [88; 106] ms vs 72 [64; 79] ms, p=0,006 and 117 [93; 133] vs 93 [73; 101] ms in the TAVI group, p=0.008). This finding corresponds to longer QRS duration in DCM group (177.8±20.4 ms) than in patients in the TAVI group (153.5±14.5 ms, p=0.03) and could be explained by the greater myocardial mass, contributing to delayed LV in the DCM patients. However, LV myocardial hypertrophy in patients of the TAVI group due to long-existing aortic valve disease makes this assumption doubtful. A possible reason for the longer QRS duration in DCM patients may be the diffuse changes in LV myocardium, leading to disrupted intercellular coupling, and additionally contributing to delayed electrical propagation.

During the analysis of the wave propagation along the LV myocardium, conduction block lines were revealed on isochrone maps in all TAVI group patients. The localisation of the conduction block line was anteroseptal in 5 (33%) patients (Figure 4 A) and posterolateral in 9 (60%) patients (Figure 4 B). The combination of the anteroseptal and posterolateral conduction block lines was determined in another 1 (7%) TAVI patient.

When assessing the location of conduction block lines in DCM group, more heterogeneous results were obtained. In addition to anteroseptal and posterolateral lines in 8 (36.4%) and 7 (31.8%) patients, respectively, which were recently identified in the TAVI group, in some DCM patients the conduction block line was localized in the lateral LV part (n=3, 13.6% of patients, Figure 4 B). In 2 cases (9.1%), the block line was completely absent. A combination of anteroseptal and posterolateral lines was identified in 2 (9.1%) patients.

Determining the location of myocardial LASs was another part of this work. When analyzing isochrone maps of 15 TAVI group patients, the same localization of LV LAS was revealed. In 14 (93%) TAVI group patients, LASs were in a zone consisting of 4 segments: basal posterior or lateral or mid posterior and lateral (segments 5, 6, 11, 12 are marked with blue-violet in Figure 5 A, B). And only in 1 (7%) patient of the TAVI group the LAPs was displaced to the mid anterior and anteroseptal LV segments (segments 7, 8 are marked with beige in Figure 2 B). It should be noted that only this patient in TAVI group had a long-term coronary artery disease, including a previous myocardial infarction resulted in impaired local contractility in inferior and posterolateral LV walls.

As it was shown in the TAVI group, in 14 of 22 (64%) patients in the DCM group, LASs were most often detected in the posterolateral zone (posterolateral segments 5, 6, 11, 12 are marked with blue-violet in Figure 5 B, G). In other 8 (36%) cases, the LAS was displaced from the most typical, posterolateral zone. Among these patients, 2 (9%) had LASs localized in the mid inferior segment (segment 10 with Figure 5 D) and there was one case (4.5%) for each of following segments: mid anterior, the apical inferior, anterior and lateral and apex (7, 13, 15, 16, 17 segments, indicated with different colors in Figure 5 D).

The results of NIAM obtained in the TAVI group indicate that the propagation of electrical excitation in patients with the proximal LBBB can be described by main features: 1) conduction block line in the anteroseptal and posterolateral zones; 2) LaSs in the posterolateral segments at the basal and mid levels.

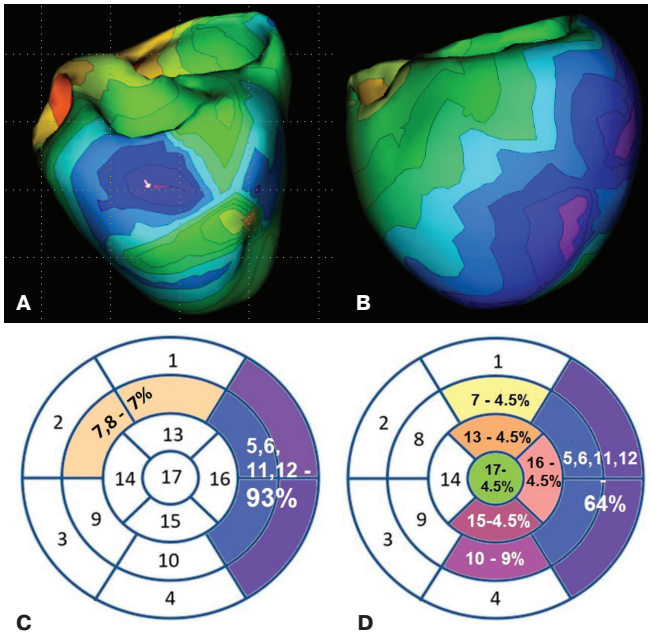

Figure 5. A, **B** — 3D isochrone maps, obtained with NIAM "Amycard", demonstrated LAS localization (indicated with blue-violet) at basal and mid segments of posterolateral wall in TAVI patient (**A**) and DCM patient (**B**). **C, D** — LAS distribution in all TAVI patients (**C**) and DCM patients (**D**).

Notes: segments 5, 6, 11, 12 indicated with blue-violet (basal lateral, mid lateral, basal posterior, mid posterior) with most frequent LAS localization. Other colors indicate more rare localization of LAS (data presented as segment number according to Cerqueira M. D. [10] and percent of patients with LAS localized in this segment).

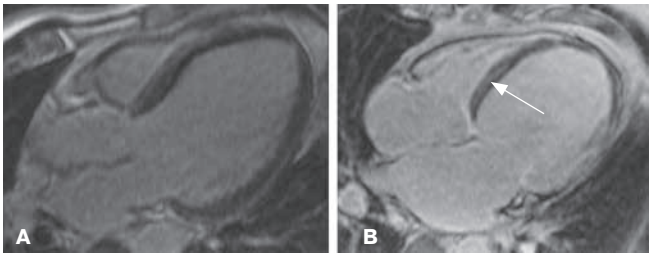

Figure 6. LGE-MRI images in DCM patients. **A** — absence of LGE, **B** — intramural LGE in interventricular septum ("striae", indicated with an arrow).

Table 2

Comparison of initial clinical and instrumental data in CRT responders and non-responders

	CRT responders (n=16, 73%)	CRT non-responders (n=6, 27%)	P-value
Women, n (%)	8 (50)	2 (33.3)	0.23
Age, years	59±7	53±13	0.077
QRS complex duration, ms	182±18	1721±28	0.25
Initial EDV, ml	227 [170; 336]	318 [264; 341]	0.21
Initial ESV, ml	151 [117; 251]	231 [178; 280]	0.15
Initial LVEF, %	30.1 [25.8; 32.5]	27.4 [20; 29.5]	0.29

Notes: data are presented as n — absolute number of cases, % — relative number of cases, means ± SD or medians (Me) and lower and upper quartiles [Q1 ; Q3], * — statistical significance at p value <0,05.

Abbreviations: EDV — end-diastolic volume, ESV — end-systolic volume, CRT — cardiac resynchronization therapy, LVEF — left ventricular ejection fraction.

3. General results of 12-lead ECG and NIAM. Development of criteria for proximal LBBB

A cumulative analysis of standard 12-lead ECG and NIAM data made it possible to identify signs that can be considered as diagnostic criteria for proximal LBBB. The first group was formed by three ECG criteria proposed by Strauss DG:

(1) QRS duration >130 ms in women and 140 ms in men;

(2) QS or rS in lead V1 QRS complex morphology;

(3) Notching or slurring in ⩾2 lateral (I, avL, V5, V6) leads.

The NIAM results formed 2 additional criteria:

(4) Conduction block line in the anteroseptal or posterolateral zone;

(5) LAS located at the basal or mid level of LV posterolateral wall.

We tested 5 developed criteria in the DCM group and confirmed the proximal LBBB in 13 (59%) out of 22 patients. It should be noted once again that myocardial scar, even in a patient with the proximal LBBB of the TAVI group (presented above), modifies the propagation picture. This fact, as well as the heterogeneity of LAS and conduction block line localization in DCM patients, allows a\us a relationship between the nature of electrical propagation, on the one hand, and the nature of LV structure in this category of patients, on the other. To test this hypothesis, all 22 patients in the DCM group underwent contrast-enhanced cardiac MRI.

4. Results of LGE-MRI in patients of the DCM group and comparison with NIAM

According to cardiac MRI, in 13 of 22 (59.0%) patients in the DCM group, there were no LGE zones (Figure 6 A). At the same time, in 9 (40.9%) cases, LGE areas were detected, including intramural, subepicardial, and transmural. It should be noted that in 6 out of 9 patients with LGE, intramural "striae" in the IVS (midwall fibrosis) was detected, which is typical for DCM (Figure 6 B) [13].

Despite the fact that the conduction block line is currently considered as a functional barrier to electrical propagation, we compared the NIAM data of the DCM patients with data on LV structure according to LGE-MRI. We found that the conduction block line in LV lateral region or its absence is associated with intramural LGE ("striae") in IVS according to MRI data (Chi-square test =6.92, p=0.009, Cramer's V =0.56). Thus, our study confirmed that in DCM patients there is association between presence of conduction block lines and their location with structural myocardial changes, as it was already suggested in earlier studies [14].

Table 3

Diagnostic value of criteria in predicting the CRT effect

	OR	95% CI	P-value	Sensitivity, %	Specificity, %
No LGE according to MRI	4.4	0.66-32.5	0.28	68.8	66.7
No intramural fibrosis ("striae") in the interventricular septum according to MRI	8.67	1.05-71.57*	0.03	81.3	66.7
Typical LAS loclization according to NIAM	30.0	2.14-421.14*	0.0001	93.8	66.7
Typical localization of conduction block lines according to NIAM	4.3	0,56-33.13	0.38	81.3	50.0
Positive three Strauss DG criteria	3.5	0.37-33.0	0.32	87.5	33.3
Positive 5 original criteria for proximal LBBB	15.0	1.32-169.9*	0.002	75	83.3

Note: * — signs are indicated that have a significant effect on CRT response.

Abbreviations: CI — confidence interval, MRI — magnetic resonance imaging, OR — odds ratio, LGE — late gadolinium enhancement, LAS — latest activation site, NIAM — non-invasive activation mapping.

Comparison of LAS localization and MRI data also demonstrated that LAS displacement is associated with both LGE presence (Chi-squared test =9.35, p=0.003, Cramer's test =0.65), and particularly, with intramural LGE lesions in IVS (Chi-square test =13.9, p<0.001, Cramer test =0.79).

Thus, our study indicate that LV fibrosis disrupt electrical propagation along the ventricular myocardium, shifting the localization of LASs and conduction block lines.

5. The contribution of ECG criteria for LBBB and NIAM data to the CRT effect

We compared the LBBB type defined with originally developed criteria with the CRT effectiveness in DCM patients. Six months after device implantation, the positive effect of CRT was detected in 16 (73%) patients in the DCM group. All these patients had a significant decrease in LV end-systolic volume by at least 15% from baseline (151 [117.8; 253.3] ml initially and 72.3 [56.3; 100.8] ml later 6 months of CRT, p=0.0035) and a significant increase in LVEF (from 30,1 [26.4; 32.5]% to 45,9 [42.3; 51.4]% after 6-month therapy , p=0.0002). A comparison of the main initial clinical and instrumental parameters in the subgroups of CRT responders and non-responders did not reveal any significant differences (Table 2).

The analysis revealed a moderate association between proximal LBBB in accordance with the original criteria and CRT response (Chi-square test =5.6, p=0.02, Cramer's V =0.5). Along with this, another, namely the typical for DCM patients LAS localization in the posterolateral segments, was more important for CRT effect (Chi-squared test =9.1, p=0.003, Cramer's V =0.64). An additional analysis demonstrated the significance of the proposed criteria for proximal LBBB in predicting the CRT effect (OR =15.0, 95% confidence interval (CI): 1.32-169.9, p=0.002) and a favorable ratio of sensitivity and specificity (75 and 83,3%, respectively) (Table 3). In addition, the typical LAS localization in the posterolateral segments was also significant for predicting the CRT response (OR =30.0, 95% CI: 2.14-421.14, p=0,0001, sensitivity 93.8, specificity 66.7%), while the localization of conduction block lines and Strauss DG ECG criteria for LBBB turned out to be less important. This analysis also revealed a close relationship between CRT effect and the absence of intramural LGE lesions in IVS ("striae") according to MRI (OR =8.67, 95% CI: 1.05-71.57, p=0.03; sensitivity 81.3%, specificity 66.7%) (Table 4).

Table 4

Detection rate of the studied phenomena in the TAVI and DCM groups

	TAVI patinets (n=15)	DCM patients (n=22)
Typical LAS localization according to NIAM	14 (93%)	14 (64%)
Typical (anteroseptal and/or posterolateral) localization of conduction block lines according to NIAM	15 (100%)	17 (77%)
Positive Strauss DG criteria for LBBB	15 (100%)	18 (81.8%)
Positive 5 original criteria for proximal LBBB	14 (93%)	13 (59%)

Notes: data are presented as n — absolute number of cases, % — relative number of cases.

Abbreviations: LBBB — left bundle branch block, DCM — dilated cardiomyopathy, LAS — latest activation site, NIAM — non-invasive activation mapping, TAVI — trans-catheter aortic valve implantation.

Discussion

Increasing the percentage of CRT responders remains to be a relevant task. One of the possible solutions is improving the criteria for patient selection. Upadhyay GA, et al. [6] suggested that patients with high efficiency of CRT could be the patients with proximal LBBB. In this regard, we and others [15, 16] have attempted to develop non-invasive criteria for proximal LBBB. For the first time, patients with LBBB developed after TAVI were examined in the study conducted by Calle S, et al. [15] in 2021. Having analyzed the 12-lead ECG data, the researchers formulated 4 main and 1 auxiliary criteria for proximal LBBB, which included a QRS complex duration >120 ms, the QRS morphology of QS or rS in lead V1, absence of Q wave in V5-V6 leads, and notched or slurred

QRS complex in ⩾2 lateral leads. In 2022, the other researchers made another attempt to develop ECG criteria for proximal LBBB in patients underwent septal myectomy due to obstructive hypertrophic cardiomyopathy. The authors proposed the notched/slurred QRS complex in at least two of leads I, aVL, V1-V2, V5-V6, absence of a Q wave in leads V5-V6 and a discordant T wave in at least two of leads I, aVL, V5, V6, as well as the QRS complex duration ⩾120 ms for proximal block criteria [16]. However, neither the first nor the second group of researchers assessed the significance of the proposed criteria for CRT response. In addition, the QRS complex duration exceeding 120 ms, formulated in both criteria [15, 16], are doubtful in its prediction value for CRT effectiveness, since large studies [3] indicated the maximal CRT response in patients with QRS complex duration ⩾150 ms. Based on the ECG and NIAM data obtained in patients with LBBB developed after TAVI, we proposed our original criteria for proximal LBBB. According to our data, in 100% of TAVI group patients, the Strauss DG ECG criteria for LBBB [2] were identified, which made it possible to include them in original criteria. In addition to ECG data, our criteria included following characteristic signs found in these patients in NIAM: conduction block line in the anteroseptal or posterolateral region and LAS localization at the basal or mid level of posterolateral LV wall. The analysis of the diagnostic value of developed criteria for proximal LBBB on a relatively small group of patients with CRT demonstrated a good ratio of sensitivity and specificity (75 and 83.3%, respectively). Along with this, possible predictors of CRT effect were the individual characteristic location of LAPs in the posterolateral segments (sensitivity 93.8%, specificity 66.7%) and no LGE (intramural fibrosis — "striae") in the IVS according to MRI (sensitivity 81.3%, specificity 66.7%). The obtained results can be explained based on the fact that in addition to the proximal LBBB, a necessary condition for reverse cardiac remodeling is sufficient viable myocardium volume. It is well known that location and volume of fibrous tissue are important determinants of CRT effectiveness [17]. Our previous study indicates that in patients with non-ischemic DCM, the effectiveness of CRT is directly related to fibrous mass content [18]. The heterogeneity of LV myocardial tissue, resulting from scar changes of any etiology, can distort the nature of electrical propagation, which was convincingly demonstrated by our study. Thus, LAS displacement in one patient of the TAVI group (7%) and 8 (36%) patients of the DCM group, as well as displacement or complete absence of conduction block lines in 5 (23%) patients of the DCM group turned out to be directly related to the intramural IVS fibrosis. At the same time, fibrosis-related LAS displacement from the target lead position in the posterolateral zone predetermines the CRT failure [10, 19].

Study limitations. The assessment of the sensitivity and specificity of the developed criteria for proximal block in this study was carried out on a small group of patients with non-ischemic DCM and CRT, which limits the study power. Studying the diagnostic significance of the proximal LBBB criteria in a larger population of patients with CRT would allow to determine their sensitivity and specificity more accurately and to reveal the interaction with other factors of CRT effect.

Conclusion

Based on the analysis of ECG and NIAM data in patients with LBBB after TAVI, diagnostic criteria for proximal LBBB were developed. These criteria have demonstrated a strong association with CRT response. However, our study indicates that the proximal LBBB is only one of the factors determining the CRT effectiveness. In addition, to our mind, it is not entirely correct to consider the CRT effectiveness only from the viewpoint of LBBB types. True, typical, or proximal LBBB on the ECG can mask significant structural changes, which, in turn, can modify the electrical propagation in the myocardium and, thus, hinder the success of CRT.

Relationships and Activities: none.

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