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NONINVASIVE ACTIVATION MAPPING DURING THE CARDIAC CONDUCTIVE SYSTEM PACING

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Aim. To identify the features of activation of the right and left ventricles during cardiac conductive system pacing.

Methods. There are 2 groups of the study. The cardiac conductive pacing carried in patients of first group. The cardiac conductive pacing not carried in patients of second group. Before and after implantation of the pacemaker, all patients underwent ECG, noninvasive activation mapping using the Amycard software and hardware complex, the width of the QRS, the activation time of the left (LVAT) and right (RVAT) ventricles were determined initially and against the background of pacing. The parameter values are presented in the format: median and interquartile range (Me [25; 75]).

Results. The study protocol was performed in 30 patients: first group - 20 patients, second group - 10. The age of the patients was 73 [57; 81] and 71 [63; 75] years, respectively. The value of native QRS complexes in first group was 106 [100; 132] msec, in second group - 144 [109; 155] msec; LVAT 70 [60; 93] msec and 88 [75; 115] msec, respectively; RVAT 62 [50; 74] msec and 85 [67; 117] msec, respectively. There were no statistically significant differences between the groups ($p > 0.05$) in age, values of native QRS, LVAT, RVAT. The implantable electrode model is identical in both groups. The value of the QRS complex during pacing in first group was 117 [109; 125] msec and 160 [145; 173] msec in second group; LVATp 76 [65; 89] msec and 129 [119; 148] msec, respectively; RVAT 67 [60; 80] msec and 108 [90; 128] msec, respectively. The study revealed statistically significant differences between the two groups of all evaluated parameters against the background of pacing: QRS ($p = 0.01$), LVAT (p = < 0.01), RVAT ($p < 0.01$). It should be noted that the initial values and values against the background of pacing of the QRS, LVAT, RVAT complex in patients of group No. 1 did not differ ($p > 0.05$); in patients of the second group, the values of the QRS, LVAT, RVAT complex initially and against the background of stimulation had significant differences ($p = 0.11$, $p < 0.01$ and $p = 0.038$ respectively).

Conclusion. Cardiac conductive system pacing is a promising method of cardiac pacing, which allows to achieve activation of the myocardium of the left and right ventricles, which does not differ significantly from activation with a sinus rhythm.

Key words: cardiac conductive system pacing; noninvasive activation mapping; pacing; computed tomography

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Following the implementation of transvenous electrodes for permanent pacing in the 1950s, the apex of the right ventricle (RV) served as the predominant target area for ventricular electrode implantation for an extended period. This choice was influenced by the characteristics of the electrodes, particularly the absence of an active fixation mechanism [1]. However, by the 1990s, it was substantiated that the stimulation of the apex region of the RV induces a negative inotropic effect, attributed to the phenomenon of dyssynchrony [2]. In the year 2000, it was demonstrated that continuous selective stimulation of the bundle branch (BB) could be feasibly performed in patients with atrial fibrillation and normal QRS complex width [3]. BB stimulation has shown advantages relative to RV stimulation [4].

Cardiac Conduction System (CCS) stimulation emerges as a promising method of cardiac stimulation due to its capability to replicate physiological stimulation in the most natural manner. Presently, for this form of stimulation, the electrode is typically implanted in the bundle branch (BB) region or in the proximal portions of the left bundle branch (LBB). It is noteworthy that in an intact CCS,the implantation of an electrode in the bundle branch (BB) region results in action potential propagation along both legs of the BB, representing a potential alternative to biventricular stimulation [4-10].

The technique of non-invasive activation mapping is an electrocardiographic imaging method that relies on a dense matrix of electrodes positioned on the body surface around the chest. This is combined with the reconstruction of the patient's heart and body utilizing computed tomography (CT) data. This technique enables the assessment of ventricular activation characteristics under various conditions, encompassing native rhythm (including bundle branch block), as well as during stimulation [11-12]. Moreover, data acquired through non-invasive mapping demonstrates correlation with comparable data obtained through invasive mapping [12-13]. The noninvasive activation mapping method, coupled with cardiac ventricular reconstruction, facilitates the calculation of right ventricular activation time (RVAT) and left ventricular activation time (LVAT) [12-13]. This article scrutinizes the electrophysiological attributes of cardiac ventricular activation, drawing insights from our own experiences with the implantation of electrodes in the CCS.

The objective of this study was to delineate the characteristics of right and left ventricular myocardial activation during CCS pacing, compare with standard stimulation.

METHODS

This prospective, single-center, non-randomized study adhered to Good Clinical Practice standards and conformed to the principles outlined in the Declaration of Helsinki. Inclusion criteria for study participants encompassed individuals meeting the following conditions: patients with indications for cardiac pacing who underwent an attempt to implant an electrode for permanent pacing in the LBB region; provision of signed informed consent; and attainment of 18 years of age. Patients were not included in the study based on the following criteria: repeated implantation of the electrode in the CCS; coronary lesions necessitating revascularization; active inflammatory and autoimmune diseases; contraindications for the use of X-ray contrast agents; presence of psychiatric disorders; and women during pregnancy, childbirth, and breastfeeding.

Patients were excluded from the study based on the following criteria: allergic reactions to the radiographic contrast agent, refusal by the patient to participate in the study, and patient death.

Two groups were formed within the study. Patients were classified into specific groups based on the viability of intraoperative CCS stimulation. In the first group of patients, stimulation with the CCS capture is conducted, while in the second group, stimulation is performed without CCS capture. The clinical characteristics of the patients are presented in Table 1.

In adherence to the study protocol, all patients underwent preoperative assessments, including electrocardiography (ECG), noninvasive activation mapping using Amycard01C (EP Solutions SA, Switzerland), and cardiac CT an integral component of the noninvasive mapping technique. During ECG evaluation, the rhythm, QRS width, and the presence of pathology in the cardiac conduction system were assessed. During noninvasive mapping, three-dimensional models of the heart ventricles were constructed, with an evaluation of the activation time of right ventricular (RVAT) and left ventricular (LVAT) activation during their inherent rhythm and stimulation.

The implantation of the electrode into the LBB was carried out uniformly across all patients by a singular surgeon with expertise in performing this procedure. The target area for implantation is the LBB. Standard ventricular, atrial electrodes and pacemakers were implanted in all patients. The 3830 SelectSecure electrode (Medtronic, Ireland) was used for implantation in the CCS region using delivery systems (Medtronic C304, Medtronic Ireland; Medtronic C315HIS, Medtronic Ireland; Boston Scientific AcuityPro, Boston Scientific USA). Boston Scientific AcuityPro delivery system (Boston Scientific USA) was used with shape optimization. The technique of implanting a 3830 lumpless electrode into the LBB region is described in detail by Huang et al in the literature [8]. The criteria supporting the possibility of stimulation of CCS are described in detail in the literature [8, 16, 17]. It should be noted that there is no consensus on the system of differential

Table 1.

Clinical characteristics of patients

Parameter	Group 1 (n=20)	Group 2 (n=10)	p
Men, n (%)	10 (50%)	9 (90%)	> 0.05
Age, years	73 [57; 81]	71 [63; 75]	> 0.05
AF, n (%)	7 (35%)	2 (20%)	> 0.05
SND, n (%)	9 (45%)	3 (30%)	> 0.05
AVB ≥ 2 degrees, n (%)	10 (50%)	5 (50%)	> 0.05
LBBB and its branches, n (%)	6 (30%)	10 (100%)	< 0.001
Complete LBBB, n (%)	3 (15%)	3 (30%)	> 0.05
ABLBBB, n (%)	3 (15%)	7 (70 %)	< 0.05

Note: AF - atrial fibrillation; SND - sinus node dysfunction; AVB - atrioventricular blockade; LBBB and complete LBBB - left bundle branch blockade and complete blockade; LBBB - blockade of the left bundle branch, ABLBBB - blockade of the anterior branch of the LBBB.

Table 2.

Evaluated parameters

Parameter	Group 1	Group 2	p
QRS baseline, ms	106 [100; 132]	144 [109; 155]	> 0,05
LVAT baseline, ms	70 [60; 93]	88 [75; 115]	> 0,05
RVAT baseline, ms	62 [50; 74]	85 [67; 117]	> 0,05
QRS against ECS (QRSp), ms	117 [109; 125]	160 [145; 173]	0,01
LVATp on the background of ECS, ms	76 [65; 89]	129 [119; 148]	< 0,01
RVATp on the background of ECS, ms	67 [60; 80]	108 [90; 128]	< 0,01

Notes: LVAT and RVAT - left and right ventricular activation time; ECS - electrocardiostimulation.

criteria confirming the LBB stimulation [8, 15-17]. We followed ECG criteria to confirm the LBB stimulation. Upon reaching the LBB electrode during test stimulation, the W-shaped morphology of a wide QRS complex transforms into a narrow QRS complex, exhibiting the morphology of incomplete blockade of the right bundle branch on the surface ECG in lead V1. The LBB stimulation thresholds are low. In contrast to LBB stimulation, when BB stimulation is applied, the QRS complex morphology aligns entirely with that of the native complex, usually with higher stimulation thresholds compared to LBB stimulation [10].

In the postoperative period, all patients underwent repeated noninvasive activation mapping, CT, and ECG. ECG was performed both on own rhythm and on the background of cardiac stimulation. The morphology and width of the native (baseline) and stimulated QRS complex were evaluated. As per noninvasive mapping data, three-dimensional models of the heart ventricles were generated, and the activation time of the right ventricle (RVATp) and left ventricle (LVATp) during stimulation was assessed.

Statistical analysis

Statistical analysis of the indicators was performed using STATISTICA 10 software. The Shapiro-Wilk test was employed to assess the conformity of the distribution of quantitative indicators within the sample to a normal distribution, considering the constraints associated with small sample sizes. Parameters of samples exhibiting a normal distribution are expressed as mean and standard deviation in M±SD format, while parameters not conforming to a normal distribution are presented as median and interquartile range in Me [Q1;Q3] format. Considering the distribution type and the limited sample size, the Mann-Whitney Test and Student's t-test were employed to evaluate the statistical significance of differences between quantitative parameters in the sample. For qualitative (binary values) indicators, Pearson's χ^2 (Pearson's chi-squared test) was utilized, and the Wilcoxon Signed Ranks Test was applied to discern differences between dependent samples. Differences between indices were considered statistically significant at p value < 0.05.

RESULTS

The estimated parameters are presented in Table 2. According to the Shapiro-Wilk criterion, all evaluated quantitative indicators of the obtained samples do not conform to normal distribution. Based on the findings from preoperative electrocardiogram (ECG) evaluations, it was observed that 30% of patients in Group 1 and 100% of patients in Group 2 exhibited blockage of the LBBB or its branches. There were no statistically significant differences in the baseline values of native QRS complex width, LVAT and RVAT between the two groups.

Among patients of Group 1, 16 patients are carried out with non-selective stimulation of LBB, 2 - patients selective stimulation of LBB, 1 - selective stimulation of BB, 1 - non-selective stimulation of BB. No statistically significant differences were observed in the values of QRSp, LVATp, and RVATp among patients in Group 1 with different types of stimulation.

The values of QRSp width (p = 0.01), LVATp (p < 0.01), and RVATp (p < 0.01) complexes during pacingexhibit statistically significant differences between the two groups (Fig. 1). This substantiates the distinction in ventricular activation between standard stimulation and stimulation of the cardiac conduction system. Moreover, the values of native and stimulated QRS and QRSp complexes (p = 0.011), LVAT and LVATp (p < 0.01), RVAT and RVATp (p < 0.038) demonstrated statistically significant differences in the second group. In contrast, the PSS stimulation group showed no statistically significant differences (p > 0.05) from baseline for similar parameters.

According to postoperative CT in Group 1, all patients had the electrode in septal position in the projection of the CCS. In Group 2, the electrode was positioned septally in 7 patients (70%), in the region of the apex of the RV in 2 patients (20%), and in the region of the anterior wall of the RV in 1 patient (10%). At the preoperative stage, 30% of patients in Group 1 and all patients in Group 2 exhibited blockage of the LBB or its branches (Table 1).

Hence, under CCS stimulation, an activation pattern was attained where the values of QRSp, LVATp, and RVATp exhibited no statistically significant differences compared to similar parameters at the initial native sinus rhythm. However, during myocardial stimulation, the values of QRSp, LVATp, and RVATp were statistically significantly different from those during sinus rhythm.

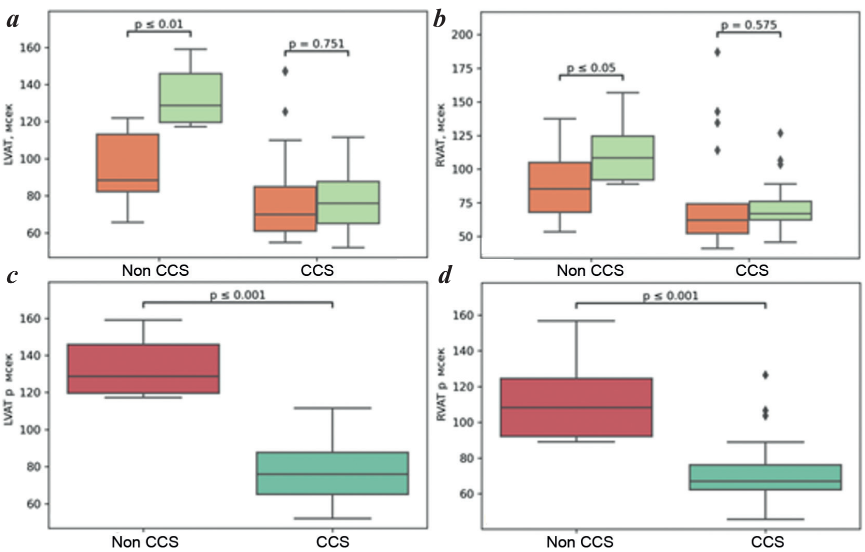

Fig. 1. Ventricular activation parameters: activation time of the left (LAVT - a) and right (RAVT - b) ventricle baseline (orange) and against stimulation (salad); activation time of the left (LAVTp - c) and right (RFVTp - d) ventricle against myocardial stimulation (non-CCS - red) and cardiac conduction system (CCS - green).

DISCUSSION

A meta-analysis by M.V.Mariani et al [14] was published in 2023. The total number of patients included in the analysis was 4,386, with 1,324 undergoing standard right ventricular stimulation, 1,032 undergoing biventricular stimulation, and 2,037 undergoing CCS stimulation (1,069 with BB stimulation and 968 with LBB stimulation). The width of the stimulated complex during the BB and LBB stimulation was notably smaller compared to standard right ventricular and biventricular stimulation ($p < 0.05$). The BB stimulation was associated with a significant increase in stimulation threshold in the remote period compared to LBB stimulation ($p < 0.05$). Electrode-related complications occurred more frequently in the groups of biventricular stimulation and BB stimulation ($p < 0.05$); in the group of patients with LBB stimulation, the results were opposite ($p = 0.4$). Thus, the most promising method of pacing, both in terms of physiologic myocardial activation and long-term results, is the LBB stimulation [14].

Evaluation of our own experience with implantation of the electrode in the LBB region confirms that this type of cardiac stimulation is a more physiologic method compared with stimulation from the interventricular septum or the apex of the RV. This is confirmed by the absence of statistically significant differences in the width of the QRS complex, left and right ventricular activation time both baseline (native rhythm) and against the background of pacing. Standard stimulation without CCS capture revealed statistically significant differences of intrinsic complexes from stimulated ones both in the width of the QRS complex and in the activation time of the left and right ventricles (Fig. 1). In addition, the three-dimensional model of left ventricular activation on its own rhythm was virtually indistinguishable from that during both selective and nonselective CCS stimulation (Fig. 2).

It should be noted that in the group with absence of CCS capture during stimulation, 100% of patients initially had complete blockade of LBB or blockade of its branches. As per the literature, the absence of CCS capture, in its pathology, may arise from both LBB pathology (distal blockade) and challenges associated with mapping of the LBB [8]. Furthermore, consensus among many authors suggests that the success of electrode implantation in the CCS is contingent on the surgeon's experience, particularly crucial in instances of CCS pathology such as blockade of the LBB and its branches. According to different authors, the so-called «learning curve» during electrode implantation in CCS ranges from 40 to 100 operations [8, 10].

Undoubtedly, the methodology of the CCS stimulation has certain peculiarities:

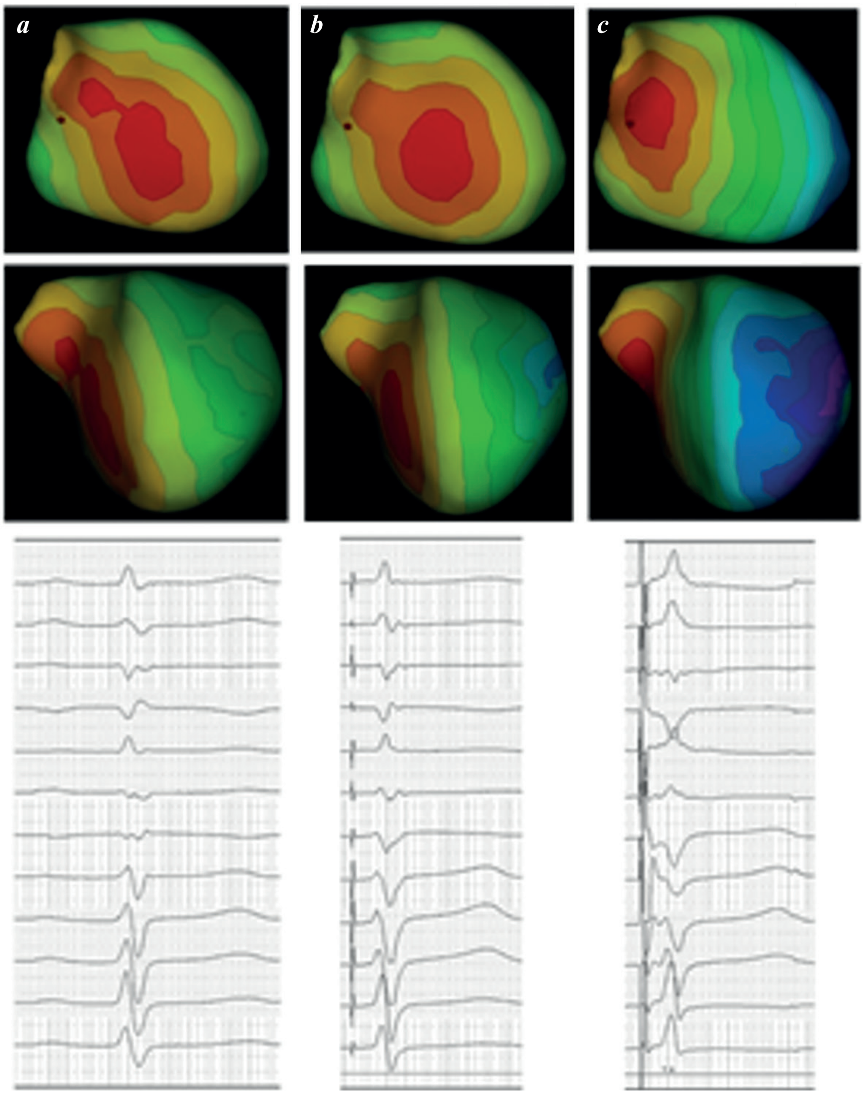

Fig. 2. Three-dimensional models of left ventricular activation and ECG at baseline sinus rhythm (a); at selective stimulation of the cardiac conduction system (b); at nonselective stimulation of the cardiac conduction system (c).

- complexity of implantation with a rather long learning curve; need to utilize a delivery system;
- longer operation duration and radiation exposure compared to standard stimulation;
- possibility of complications such as perforation of the interventricular septum, perforation of the RV wall;
- increase in stimulation thresholds in the remote period (BB);
- lack of an adapted intraoperative imaging system; possibility of damage to the CCS [8-10].

Nevertheless, notwithstanding its technical complexity, this method of stimulation enables the attainment of ventricular myocardial activation closely resembling the activation observed during native sinus rhythm.

CONCLUSION

Hence, by employing the method of noninvasive activation mapping with cardiac ventricular reconstruction, it becomes feasible to calculate RVAT and LVAT while analyzing the electrophysiological features of cardiac ventricular activation during the implantation of electrodes in the CCS. The CCS stimulation emerges as a promising method to achieve activation of the left and right ventricular myocardium, exhibiting no significant differences compared to that of the native rhythm with normal QRS width. A further clinical study of the method of direct stimulation of the CCS is imperative for its widespread integration into routine medical practice.

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