Endocardial Electrophysiological Study in Clinical Practice in Patients with Bradysystole and Conduction Rhythm Disorders: a review

Andrey V. Ardashev, Evgeny G. Zhelyakov

Pirogov National Research University, Moscow, Russia

The article demonstrates modern diagnostic capabilities of endocardial electrophysiological examination in cardiological patients with bradysystole and conduction disturbances that allow adequate assessment of the clinical situation. We made an attempt to systematize current indications for an electrophysiological study in this category of patients based on the analysis of several current recommendations.

Keywords: endocardial electrophysiological research; conduction disorders; weakness of the sinus node; atrioventricular block; distal blockade; two-beam blockade.

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Эндокардиальное электрофизиологическое исследование в клинической практике у пациентов с брадисистолией и нарушениями ритма проводимости (обзор)

Е.Г. Желяков, А.В. Ардашев

Российский национальный исследовательский университет им. Н.И. Пирогова, Москва, Россия

В статье продемонстрированы современные диагностические возможности эндокардиального электрофизиологического исследования у пациентов кардиологического профиля с брадисистолией и нарушениями проводимости, позволяющими адекватно оценить клиническую ситуацию. Нами была сделана попытка систематизировать текущие показания к проведению электрофизиологического исследования у этой категории пациентов на основании анализа нескольких текущих рекомендаций.

Ключевые слова: эндокардиальное электрофизиологическое исследование; нарушения проводимости; слабость синусового узла; атриовентрикулярная блокада; дистальная блокада; двухпучковая блокада.

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The widespread implementation of endocardial electrophysiological studies (endoEPS) in clinical practice has made it possible to examine the pathophysiological mechanisms of the development of cardiac arrhythmias and contribute to the emergence of new technologies and highly effective treatment methods [1–3].

Nowadays, endoEPS is a routine in interventional treatment, such as radiofrequency ablation, and evaluation of its results in patients with paroxysmal supraventricular and ventricular tachyarrhythmias [4, 5].

Recent evidence revealed that endoEPS with the implementation of a programmed ventricular pacing protocol for the induction of ventricular arrhythmias is a highly sensitive and highly specific tool for the stratification of sudden cardiac death risk in certain patients, specifically those with a history of acute myocardial infarction with brady–asystolic disorders. Their pathogenesis is based on two main causes or a combination thereof, namely, an ineffective treatment methods [1–3].

The endoEPS specificity in diagnosing SAN dysfunction is high, with 75%–95%, whereas its sensitivity is only 50% [11–14]. An increase in procedural sensitivity is achieved when the indications for endoEPS in patients with SAN dysfunction and presents current indications for its execution.

Sinus node dysfunction

Bradysystolic rhythm and conduction disorders are most commonly caused by diseases and/or conditions characterized by the dysfunction of the sinoatrial node (SAN). Electrocardiogram (ECG) signs of SAN dysfunction are as follows:

- Pronounced sinus bradycardia with a heart rate of < 50 per min during wakefulness.
- Sinus arrest, which is a permanent impairment of the formation of the sinus rhythm (in contrast to sinus pauses, which are the result of a transient impairment of an impulse formation in the SAN and last for 2–3 s). Unfortunately, there is no clearer differentiation between these conditions.
- SA blockade.
- Bradycardia–tachycardia syndrome (Short–Rubinstein syndrome) represented by a combination of sinus bradycardia and paroxysms of both supraventricular and ventricular tachyarrhythmias [9, 10].
- Chronotropic incompetence.

Transient and irreversible disorders of SAN function should be distinguished. The former is a result of autonomic regulation disorders (parasympathicotonia syndrome) following exposure to chemical agents (most often medications), and electrolyte disorders and can emerge in acute myocardial ischemia or inflammatory myocardial diseases.

Various diseases can cause irreversible changes in SAN function, such as coronary heart diseases, post-inflammatory changes in the myocardium, mechanical damage to the SAN during heart surgery, and amyloidosis. Idiopathic SAN dysfunction may be caused by sclerodegenerative processes in the conduction system of the heart, decreasing the number of specialized SAN cells and their replacement with fibrous and adipose tissues [9].

If SAN dysfunction is accompanied by clinical symptoms, such as syncope, presyncope, angina pectoris, hypotension, and increase in signs of cardiac failure, this situation is usually called sick sinus syndrome (SSS).

Determining the leading pathogenetic mechanism is extremely important for the development of SSS and determining prognosis and treatment. A specific electrocardiographic type of SAN dysfunction has certain clinical signs and diagnostic and prognostic criteria. If the disease is accompanied by clinical symptoms, as a rule, implantation of a permanent electric cardiac pacemaker (ECP) is necessary.

The endoEPS specificity in diagnosing SAN dysfunction is high, with 75%–95%, whereas its sensitivity is only 50% [11–14]. An increase in procedural sensitivity is achieved when a drug autonomous blockade is employed within the protocol (0.0175 mg/kg of metoprolol or 0.02 mg/kg of propranolol + + 0.04 mg/kg of atropine all administered intravenously) [15, 16].

The main parameters used to characterize the sinus node function during endoEPS are the sinus node recovery time (SNRT) and corrected sinus node recovery time (cSNRT) (Fig. 1). Asynchronous ECP with a frequency exceeding the spontaneous rhythm by 10% is performed for 60 s to determine the above parameters from the upper lateral parts of the right atrium. After the cessation of stimulation, the duration of the post-stimulation pause is measured, i.e., the interval from the last extrastimulus to the complex following it, illustrating spontaneous activation in the upper lateral parts of the right atrium, caused by SAN depolarization (normal value, < 1500 ms). The cSNRT is calculated from the difference between the duration of the post-stimulation pause and the average length of the sinus rhythm cycle (CL) before the start of the ECP (normal value, < 500–550 ms). The ratio of SNRT to the CL should normally be < 1.5 (in percentage terms, < 150%) [17–20]. The evaluation of the sinoatrial conduction time (SACT) (normal value, < 120 ms) according to the Strauss and Narula method is also necessary [17–20].

Currently, endoEPS is rarely performed in patients suspected of SSS because the results of noninvasive research methods (i.e., ECG and Holter monitoring of ECG) are quite sufficient to establish a diagnosis. Table 1 presents the indications for endoEPS in patients with SAN dysfunction.
AV conduction disorders

Atrioventricular (AV) blockade is a disorder of the conduction of excitation from the atria to the ventricles. Therapeutic and diagnostic measures are needed in patients with impaired AV conduction, such as clinical symptoms due to the blockade of conduction and localization of the conduction blockade.

During endoEPS, the impulse conduction function is evaluated by measuring the intervals between spikes indicating the cardiac electrical activity in various parts of the myocardium. Simultaneous registration of the 12 leads of the body-surface ECG and EG (from the region of the upper lateral parts of the right atrium, atrioventricular bundle, venous coronary sinus, and right ventricle apex) based on the measurement of intervals enables the assessment of the sinus impulse conduction to various segments of the heart.

Table 2 presents the reference values of the main intervals and their electrophysiological value [9, 10].

Determining the localization of AV conduction disorders is essential. Generally, atrioventricular conduction disorders that have arisen in the proximal parts of the AV connection (supravitalian blockade) are usually not a threat to patients because the replacement rhythm of the “second-order” pacemakers located in the AV connection will provide a heart rate within 50–60 beats/min. Moreover, the block that occurs in the His–Purkinje system (infra- and infravitalian block) is considered life-threatening because “third-order” pacemakers located in the fibers of the His–Purkinje system can provide a heart rate of no more than 20–40 beats/min [9, 10].
Proximal (supraventricular) AV block. The most common mechanism for the development of proximal AV block is an increase in decremental impulse conduction in the AV node. Conduction disorders in the AV node (supraventricular block) often occur in the acute stage of myocardial infarction and active phase of the inflammatory process of the myocardium, when patients are taking drugs such as cardiac glycosides, beta-blockers, calcium antagonists, and antiarrhythmic drugs. Since the blood supply to the AV connection originates from the territory of the right coronary artery, acute coronary syndrome resulting from impaired coronary blood flow in this artery is often complicated by proximal AV block. When coronary blood flow is restored, conduction in the AV connection often resumes. However, a hemodynamically significant symptomatic bradycardia following proximal (supraventricular) AV conduction disturbances requires implantation of temporary ventricular ECP.

Distal (infra- and infraventricular) AV block. Ischemia and myocardial infarction resulting from impaired blood flow in the left anterior descending artery, which supplies blood to the His–Purkinje system, often cause a transient distal block. In addition, any inflammatory process in the myocardium may be accompanied by inflammation in the distal parts of the cardiac conduction system.

However, unlike proximal AV conduction disorders, the distal block is most believed to be often a manifestation of a chronic and progressive pathological process. The level of AV conduction disturbance cannot be determined based on the ECG analysis, and only the registration of intracardiac EG from the atrioventricular bundle region during endoEPS can finally answer this question. If P–Q interval elongation on the body-surface ECG occurs due to an increase in the A–H interval, then it is referred to supraventricular blockade (Fig. 2). With infraventricular
Fig. 3. Distal degree 1 (infrahisian) block and complete left bundle branch block. Leads I, II, III and V1 of the body-surface ECG, intracardiac endograms from the upper lateral segments of the right atrium (LRA), proximal parts of the coronary sinus (CSp), mapping electrode positioned in the area of the atrioventricular bundle (MAPp and MAPd), recorded against the sinus rhythm, are presented from top to bottom. According to the body-surface ECG, degree 1 AV block (P–Q interval of 230 ms) and left bundle branch block are diagnosed. An analysis of the intervals obtained during the registration of intracardiac ECG indicates that AV conduction disorders occur in the distal parts of the AV connection (V–H interval of 103 ms), whereas no conduction impairment is noted in the proximal parts of the AV connection (A–H interval of 80 ms).

Fig. 4. Distal block with programmed stimulation. Leads I, II, III, and V1 of the body-surface ECG, intracardiac endograms from the upper lateral parts of the right atrium (HRA), area of the atrioventricular bundle (HISp, HISm, and HISd), coronary sinus (from the proximal pair (CSp) to the distal part (CSd)), and right ventricular apex (RVA) are presented from top to bottom. Against the sinus rhythm, the P–Q interval is 186 ms, there are signs of right bundle branch block, and signs of infrahisian disorders in AV conduction are detected (H–V interval of 92 ms) (complex in the right part of the figure). During the programmed atrial ECP with a base cycle length of 500 ms and the introduction of S2 with a programmed extra stimulus delay of 410 ms, an atrioventricular conduction block is verified in the distal parts of the conduction system of the heart (after the A2 spike, the H2 spike is verified without the subsequent appearance of the V2 spike characterizing myocardial depolarization of ventricles).
blockade, AV conduction impairment occurs following an increase in the duration of the H–V interval (Fig. 3).

Generally, endoEPS is not required in the selection of the approach for the treatment of patients with obvious AV conduction disorders. However, in some cases, the patient may have clinical symptoms associated with conduction disorders, which do not correspond to the changes verified on the body-surface ECG, including during long-term ECG monitoring. In this situation, endoEPS becomes the defining diagnostic procedure.

The value of antegrade effective refractory period in the His–Purkinje system exceeding 400 ms is the next sign of latent AV conduction disorders (Fig. 4). Most electrophysiologists believe that this conduction disorder reflects a far advanced pathological process in the distal parts of the cardiac conduction system and requires a permanent ECP.

The indications for endoEPS in patients with AV conduction disorders are presented in Table 3.

### Conduction disorders along the bundle branches and intraventricular conduction impairments

Bundle branch and His–Purkinje conduction disorders tend to progress with subsequent risk of developing complete AV block. In this regard, the endoEPS protocol aims to identify the category of patients with a high risk of this scenario and subsequently making a decision on the need for ECP implantation.

The endoEPS protocol primarily evaluates the conduction function in the remaining fibers of the conduction system based on H–V interval assessment. In patients with a bifascicular block, an H–V interval of 33–55 ms indicates normal conduction through the structures of the conduction system, including during long-term ECG monitoring. In this situation, endoEPS becomes the defining diagnostic procedure.

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Table 4 presents the indications for endoEPS in patients with conduction disorders along the His bundle branch and intraventricular conduction.

In addition to determining the initial H–V interval during the endoEP protocol, pharmacological testing is performed using class IA antiarrhythmic drugs (amiodarone, disopyramide, or novocainamide) or class IC drugs (flecainide).
A significant prolongation of the H–V interval or development of a high-degree AV block during a pharmacological test may predict the development of complete AV block and is the basis for deciding on ECP implantation [27–30]. Pharmacological testing is generally used in patients with syncope and bifascicular block if the baseline H–V interval is < 70 ms or transient (paroxysmal) high-degree/complete AV block is the suspected cause of syncope [36–39].

The diagnostic value of the endoEPS protocol using pharmacological testing in relation to the risk of complete AV block is ≥80% [22]. However, a negative endoEPS result does not exclude the presence of transient (paroxysmal) high-degree/complete AV block in the suspected cause of syncope [36–39].

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Table 5. Algorithm for the use of pharmacological testing (novocainamide) during endoEPS in patients with impaired conduction along the bundle branches and impaired intraventricular conduction [5]

<table>
<thead>
<tr>
<th>Symptomatic patients (history of syncope)</th>
<th>Pharmacological testing</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>H–V = 35–55 ms</td>
<td>Pharmacological testing can be useful</td>
<td>[40]</td>
</tr>
<tr>
<td>H–V = 55–69 ms</td>
<td>Pharmacological testing can be useful</td>
<td>[40]</td>
</tr>
<tr>
<td>H–V ≥ 70 ms</td>
<td>ECP implantation without pharmacological testing</td>
<td>[26]</td>
</tr>
<tr>
<td>Asymptomatic patients (no syncope and endoEP was performed for other reasons)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H–V = 35–55 ms</td>
<td>Without further pharmacological testing</td>
<td></td>
</tr>
<tr>
<td>H–V = 55–69 ms</td>
<td>Without further pharmacological testing</td>
<td></td>
</tr>
<tr>
<td>H–V = 70–100 ms</td>
<td>Further follow-up</td>
<td>[26]</td>
</tr>
<tr>
<td>H–V &gt; 100 ms</td>
<td>ECP implantation without pharmacological testing</td>
<td>[26]</td>
</tr>
</tbody>
</table>

Table 6. Indications for endoEPS in patients with conduction disorders after TAVR [5]

<table>
<thead>
<tr>
<th>Indication class</th>
<th>Indications</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
| Class II         | 1. Recently developed bifascicular block (permanent ECP implantation is indicated if the H–V interval is ≥65 ms).  
2. Bifascicular block before TAVR (implantation of a permanent ECP is indicated if the H–V interval after TAVR increases by ≥13 ms). | [42]      |
| Class III        | Patients who develop complete AV block after TAVR (ECP implantation is indicated). |           |

Conduction disorders after transcatheter aortic valve replacement (TAVR)

After TAVR, hemodynamically significant AV conduction disorders requiring ECP implantation develop in approximately 20% of the patients [41]. In some cases, the bifascicular block is registered in some patients after TAVR, which requires clinical interpretation regarding the need for ECP implantation.

Since TAVR is a relatively new treatment method, prospective follow-up data for these patients with respect to the clinical course of emerging conduction disorders is limited. At present, questions remain regarding the need for ECP implantation in the event of an isolated bifascicular block or the emergence of bradycardia (without complete AV block) in patients with permanent atrial fibrillation. In this regard, endoEPS in cases of ECG signs of conduction impairment after TAVR appears to be of decisive importance when choosing further treatment approach.

After TAVR, an H–V interval of > 65 ms and an increase in the H–V interval by 13 ms compared with baseline values (before TAVR) have a high predictive value in relation to the development of complete AV block [42, 43].

Table 6 presents the indications for endoEPS in patients with conduction disorders after TAVR.

CONCLUSIONS

EndoEPI is a unique diagnostic method that enables identifying and determining the mechanisms of arrhythmias in patients with wide range of cardiological conditions. In some patients with symptoms of bradyarrhythmias and/or conduction disorders, endoEPS is the only diagnostic tool used to identify the hidden mechanisms of their occurrence, verify their transient nature, and determine the degree of their malignancy. Ultimately, the results of assessing the function
of SAN automation and conduction in the structures of the conduction system of the heart, obtained during endoEPS, in some cases can be decisive for an adequate clinical assessment of patients, risk stratification of sudden cardiac death, and selection of the optimal approach for further treatment.

REFERENCES


ADDITIONAL INFORMATION

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СПИСОК ЛИТЕРАТУРЫ


**AUTHORS INFO**

Evgeny G. Zhelyakov, associate professor; e-mail: zheleu@rambler.ru; ORCID: 0000-0003-1865-8102; eLibrary SPIN: 8498-4764

Andrey V. Ardashev, MD, PhD, Professor; e-mail: ardashev@yahoo.com; ORCID: 0000-0003-1908-9802; eLibrary SPIN: 9336-4712

* Corresponding author / Автор, ответственный за переписку

**ИНФОРМАЦИЯ ОБ АВТОРАХ**

Евгений Геннадьевич Желяков, доцент; e-mail: zheleu@rambler.ru; ORCID: 0000-0003-1865-8102; eLibrary SPIN: 8498-4764

Андрей Вячеславович Ардашев, д-р мед. наук, профессор; e-mail: ardashev@yahoo.com; ORCID: 0000-0003-1908-9802; eLibrary SPIN: 9336-4712