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ALGORITHMS FOR THE PREVENTION AND TREATMENT OF SUPRAVENTRICULAR TACHYCARDIA IN PATIENTS WITH IMPLANTED PACEMAKERS: CASE SERIES

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Two clinical cases of prevention and relief of supraventricular tachycardia using modern algorithms in pacemakers of the latest generation in patients with bradyarrhythmia and paroxysmal atrial fibrillation (AF) are presented. In the first clinical case, the patient did not have an episode of AF for six months. In the second clinical case, the patient for 2 years did not have an episode of AF lasting more than 1 minute. Episodes sinus rhythm restoration by antitachypacing algorithms were recorded. These clinical cases demonstrate the effectiveness of modern algorithms in pacemakers of the latest generation for the AF prevention and sinus rhythm restoration.

Key words: bradycardia; atrial fibrillation; supraventricular tachycardia; pacemaker; antitachypacing

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Atrial fibrillation (AF) is not only the most common arrhythmia in the population, but also frequently occurs in patients with implanted cardiac devices, particularly pacemakers [1-4]. According to the Framingham study, patients with AF have an approximately 2-fold increased risk of all-cause mortality and 5-fold increased risk of stroke [5]. Several studies have demonstrated an increased risk of cardiovascular disease and mortality in patients with AF [6-8]. These data certainly favor treatment and control of arrhythmias. Analysis of data accumulated in implanted pacemakers has shown that the occurrence of AF episodes was preceded by atrial extrasystole in 69% of cases, in 27% of cases the onset was sudden without any specific preceding event, in 4% the AF episode was an early recurrence, within 5 minutes of the end of the previous AF episode [9]. It is also well known that with regular atrial pacing in patients with sinus node dysfunction, the frequency of AF attacks can be reduced. Prolonged pause, premature atrial contraction and sinus bradycardia can provoke AF. Modern pacemakers have various algorithms to prevent and treat supraventricular tachyarrhythmias. In Medtronic (MN, USA) devices, algorithms that prevent the development of atrial tachyarrhythmias include:

- Atrial Preference Pacing (APP) is designed to maintain the pacing rate above the native sinus rhythm;
- Atrial Rate Stabilization (ARS) is designed to avoid short-to-long pauses after an unscheduled atrial contraction;
- Post-mode switch overdrive pacing (PMOP) is designed to inhibit early recurrence of atrial fibrillation after paroxysmal AF by prolonging pacing in DDIR mode.

Atrial antitachycardia pacing (ATP) can be performed using two protocols, Ramp and Burst+ (Fig. 1), each with a programmable number of pulse sequences. Each Burst+ sequence consists of a programmed number of initial pulses, followed by 2 additional pulses with a shortened coupling interval, if parameters for these pulses are programmed to be enabled. Pacing intervals for the first Burst+ sequence and additional pulses are defined as a percentage of the atrial tachycardia cycle time. If atrial tachycardia is detected again after ineffective pacing using the sequence, the device performs another sequence using the Burst+ protocol with shorter pacing intervals.

With the Ramp protocol, each pulse sequence consists of a programmable number of stimuli (from 1 to 25). In each sequence, the first pulse is applied at a pacing interval whose value is programmed between 28% and 97% of the patient's atrial tachycardia cycle time. The remaining pulses in the sequence are applied with progressively shorter pacing intervals. If atrial tachycardia retreats after ineffective pacing with the sequence, the device changes the programmed value of the first pulse parameter as a percentage of the new atrial tachycardia cycle to determine the initial pacing interval for the next sequence. Each sequence contains one additional stimulus pulse compared to the previous sequence. The interval reduction step of each subsequent stimulus in the Ramp protocol, including each additional stimulus, is programmable in the range from 0 ms to 40 ms.

Recent models of implantable cardiac devices feature Reactive ATP, which allows the device to repeat programmed atrial antitachycardia therapy during prolonged episodes of atrial tachycardia/AF. The sequence of programmed atrial ATPs automatically restarts when: the atrial rhythm cycle regularity changes and/or the programmed time interval expires.

According to the latest European Society of Cardiology 2020 guidelines for the diagnosis and management of atrial fibrillation (ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)), the burden of AF (especially of ≥24 hours) should be monitored and reduced [10]. For example, in a large retrospective cohort study assessing the daily burden of AF using remote monitoring data, there was significant variation in the practice of initiating therapy with oral anticoagulants. The strongest association of oral anticoagulant prescribing with a reduction in stroke rate was observed among patients with detectable episodes of AF with implantable cardiac devices (implantable cardiac monitors, pacemakers, cardioverter-defibrillators, etc.) lasting >24 hours. AF burden in patients with implanted devices is defined as the total time spent in AHRE (atrial high rate episodes/subclinical AF during a defined period). Clearly, the burden of AHRE/subclinical AF is not static, and can change daily, hence needs to be reassessed regularly - the greater the burden of AHRE/subclinical AF at diagnosis, the greater the risk of subsequent progression to more prolonged arrhythmic episodes [10]. Currently, the diagnostic capabilities of implanted pacemakers can be used to assess AF burden over a period of up to 14 months and, by using remote monitoring technology, obtain data at appropriate time intervals. At the same time, existing algorithms to prevent the development of supraventricular tachycardia (SVT) and antitachycardia pacing can provide interventional AF burden reduction in patients with implanted cardiac devices.

The aim of this presentation is to demonstrate the potential of current algorithms to prevent and manage SVT in the latest generation of cardiac pacemakers in patients with bradyarrhythmias.

Between 2018 and 2022 we implanted 35 latest generation pacemakers with AF prophylaxis functions (APP, ARS, PMOP) together with a new antitachycardia pacingalgorithm Reactive ATP and an algorithm to minimise ventricular pacing (MVP) at the clinic of Tver State Medical University, Ministry of Healthcare of Russia: Medtronic Advisa DR MRI - 20 patients, Medtronic Astra XT DR MRI - 15. We have observed quite effective algorithms for prevention and management of SVT, as evidenced by the following examples.

Clinical case 1

Patient A., 75 years old, was admitted to the Clinic of Tver State Medical University with the diagnosis sick sinus node syndrome on August 2, 2021. Paroxysmal form of AF. Transient sinoatrial block. Morgania-Adams-Stokes syndrome. The patient has a history of radiofrequency ablation (RFA) for paroxysmal AF in 2006. Paroxysms of AF persisted, their frequency increased to several times a month. Sinus rhythm was restored independently or after administration of amiodarone by the ambulance team. Cardioversion therapy was given three times (2019, 2019, 2020) with restoration of sinus rhythm. The patient refused to undergo a second RFA. Complaints on admission: heart palpitations, transient episodes of unconsciousness, which are self-limited. Patient takes rivaroxaban, amiodarone, telmisartan, rosuvastatin.

On February 02, 2021, a Medtronic Astra XT DR MRI dual-chamber pacemaker was implanted into the patient. The right ventricular electrode is implanted in the middle third of the interventricular septum and the atrial electrode in the auricle of the right atrium. MVP pacing mode (AAI-DDD). Pacing parameters are standard, as recommended by the Therapy Guide system built into the pacemaker. AF prevention algorithms are enabled (ARR, RMOR, ARS). The Reactive ATP algorithm was not enabled, given the acute phase after implantation.

On controls (Fig. 2), ventricular pacing is less than 0.1%, indicating that the MVP mode is quite effective in reducing right ventricular pacing. Atrial pacing was 97.3%, indicating that the algorithms for prevention of AF worked according to the principle of overdrive pacing. However, the patient did not have a single episode of AF according to the programmer. The patient did not complain of heart palpitations or episodes of unconsciousness during the entire period of follow-up. Given the lack of data for AF, it was decided to abstain from performing RFA.

Clinical case 2

Patient D., 63 years old, was admitted to the Clinic of Tver State Medical University with the diagnosis of sick sinus node syndrome on August 12, 2019. Transient sinoauricular blockade. Sinus node arrest. Paroxysmal form of atrial fibrillation-tripping. CHA2DS2-VASc risk score of 3. HAS-BLED risk of bleeding of 3. Morgania-Adams-Stokes syndrome. According to daily ECG monitoring (July 10, 2019) the patient was diagnosed with sinoauricular block, paroxysmal form of AF with ventricular contractions 25-129 per minute, episodes of sinus rhythm, maximal RR interval was 5.9 sec.

The patient is known from his medical history to have suffered a cardioembolic stroke in 2019 with paroxysmal

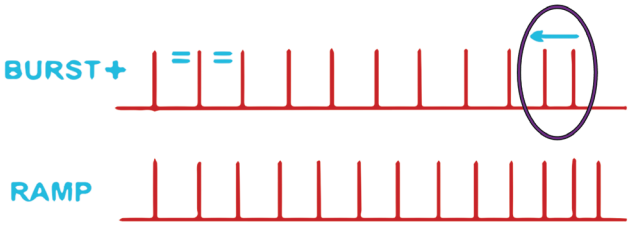

Fig. 1. Burst+ and Ramp algorithm schemes.

Окончат.: Гистограммы частоты

Устройство: **Astra XT DR MRI X2DR01** Серийный номер: **RNH667049S** Дата посещения: **14.03.2022 13:13:36**
Пациент: **A[redacted]** ID: **1738/2021** Врач: **Lukin I.B. +7-906-656-26-30**

		До последнего сеанса 23.09.2021 ... 25.11.2021 63 дн.	С посл. сеанса 25.11.2021 ... 14.03.2022 109 дн.
Время, в %	**Всего VP**	< 0,1%	< 0,1%
	Всего AP	97,3 %	97,3 %
Время, в % (без ПТ/ФП)	**AS-VS**	2,7 %	2,6 %
	AS-VP	< 0,1%	< 0,1%
	AP-VS	97,3 %	97,3 %
	AP-VP	< 0,1%	< 0,1%

Fig. 2. Patient A. Frequency histogram. Ventricular pacing <0.1%. Atrial pacing 97.3%.

AF. Patient takes rivaroxaban, atorvastatin, enalapril, metformin. Antiarrhythmic therapy was not administered due to pronounced bradycardia. It was decided to perform pacemaker implantation as the first step and to decide on RFA as the second step. Complaints on admission: frequent episodes of pre-fainting and fainting episodes.

On August 12, 2019, a Medtronic Advisa DR MRI dual-chamber pacemaker was implanted in the patient. The right ventricular electrode is implanted in the middle third of the interventricular septum and the atrial electrode in the auricle of the right atrium. MVP pacing mode (AAI-DDD). Pacing parameters are standard, as recommended by the Therapy Guide system built into the pacemaker. AF prevention algorithms are enabled (ARR, RMOR, ARS). The Reactive ATP algorithm was not enabled, given the acute phase after implantation.

On October 31, 2019 at the follow-up examination according to the electrogram recorded by the pacemaker, the patient has had frequent paroxysms of AF for 70 days, the last episode lasting more than 7 days. No complaints of cardiac abnormalities. On October 31, 2019 electro-pulse therapy was carried out, sinus rhythm was not restored. Amiodarone 200 mg 3 times daily per os was prescribed, Reactive ATP: Rx1 Ramp, Rx2 Burst+, Rx3 Ramp enabled. After 7 days, atrial pacing with spontaneous atrial-ventricular conduction on control examination according to programmer and ECG.

After 2 years, episodes of successful operation of the Reactive ATP algorithm have been recorded according to the programmer data (Fig. 3). No episodes of AF lasting more than 1 minute were registered. AF burden <0.1%. (Fig. 4). The patient has no complaints of cardiac abnormalities or episodes of unconsciousness and has not been diagnosed with an acute cerebral circulation disorder. Given the absence of data for significant episodes of AF, it was decided to abstain from RFA.

DISCUSSION

Supraventricular tachycardia is a complex and unresolved problem for patients with implanted pacemakers [1-4], which increases the risk of adverse cardiovascular events [5-8]. This is complicated by the fact that right ventricular pacing itself is a predictor of the development of AF. Today, various algorithms for prevention (APP, ARS, PMOP) and management of AF (ATP), as well as algorithms for reduction of right ventricular stimulation (MVP), have been developed to address this problem. However, these algorithms are currently poorly understood. Small clinical trials aimed at clarifying the effectiveness of such algorithms have reported mixed results, with a number of studies showing no effect in reducing the AF burden [11-13] and the ADOPT [14], PAF-PACE Study [15] showing a clear benefit in reducing the AF burden. Most studies have investigated the effect of only one algorithm on the reduction of AF burden [11-15]. In our clinical cases, we have demonstrated rather high efficiency of the above algorithms. In doing so, we considered the combined effect of all the algorithms listed, without highlighting the contribution of a particular algorithm in preventing the development of persistent AF.

In 2014, data from the MINERVA multicenter randomized clinical trial was published, which investigated three algorithms to prevent the development of SVT, together with the new Reactive ATP antitachycardia pacing algorithm and the algorithm to minimize right ventricular pacing (MVP, managed ventricular pacing). In the study, 1166 patients with bradycardia and episodes of AF were randomized into three groups:

- control group - DDDR (n=385, MVP - off, Reactive ATP - off, developmental prevention algorithms (APP, ARS, PMOP) - off)

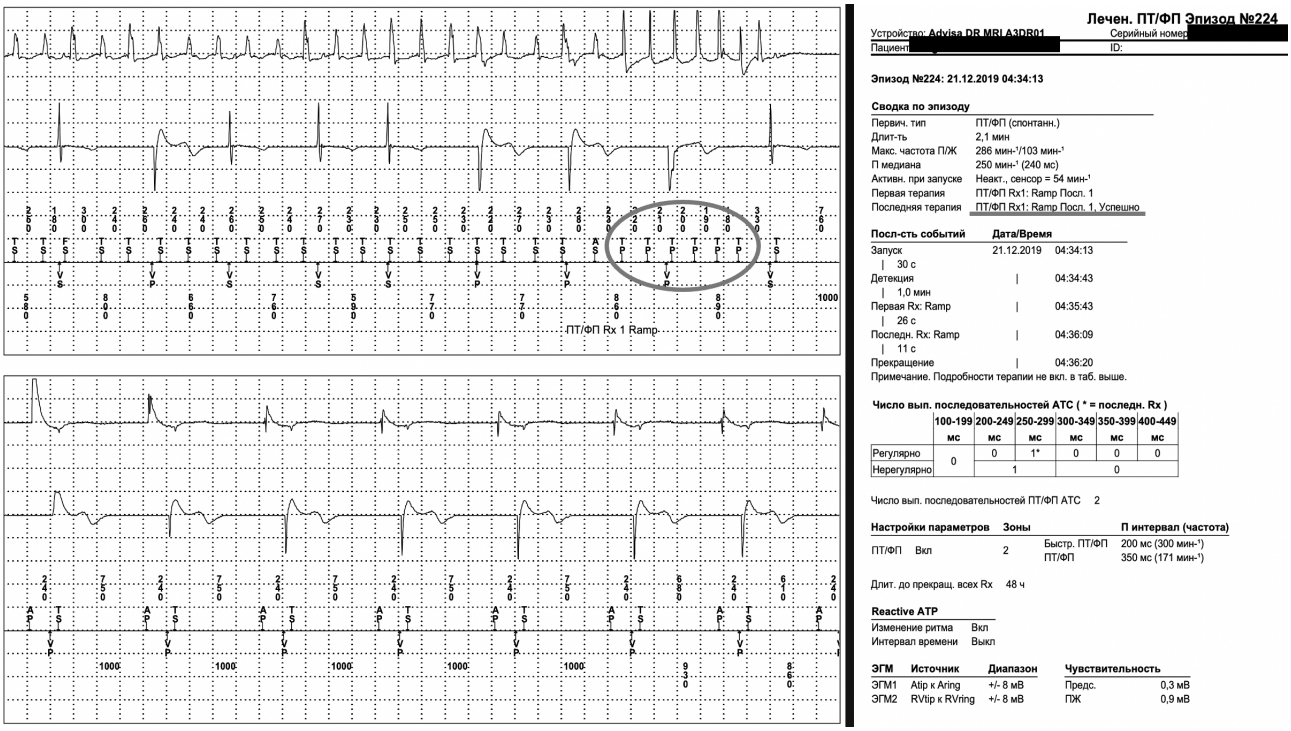

Fig. 3. Example of successful Reactive ATP algorithm by Ramp protocol with restoration of sinus rhythm and transition to Overdrive atrial pacing.

• DDDRP+MVP (n=383, MVP on, Reactive ATP on, algorithms to prevent VTE on)
• MVP (n=398, MVP - on, Reactive ATP - off, algorithms to prevent development of VTE - off)

Over the follow-up period, the risk of AF lasting more than 1 day, 7 days and persistent AF was significantly lower in the DDDRP+MVP group than in the DDDR and MVP groups. In addition, the risk of AF lasting longer than 2 and 30 days was significantly lower in the DDDRP+MVP group than in the DDDR and MVP groups. At the same time, there was no statistically significant difference in the risk of AF of 5 min, 1 hour and 6 hours in all three groups. In our observation, we did not record a single episode of AF lasting more than 1 minute when all algorithms for prevention and cessation of AF were on.

In the MINERVA study, after 2 years of follow-up, the incidence of persistent or persistent AF was 26% in the DDDR group, 25% in the MVP group and 15% in the DDDRP+MVP group [16]. The generalized estimated equation-adjusted efficacy of Reactive ATP was 44.4% (95%; confidence interval 41.3%-47.6%). Multivariate modeling revealed high efficacy of Reactive ATP function (>44.4%) as a significant predictor of reduced risk of persistent and persistent AF (hazard ratio 0.32; 95%; confidence interval 0.13-0.781; p=0.012).

In patients with bradycardia, the combination of algorithms to prevent SVT, Reactive ATP and MVP (DDDRP+MVP) reduces the risk of progression of AF, as confirmed by the MINERVA trial and our data. In addition, Reactive ATP function is an independent predictor of a reduction in permanent or persistent AF [16]. The combination of algorithms for prevention (APP, ARS, PMOP) and treatment (Reactive ATP) of AF in combination with the MVP pacing regimen has been reported to be highly effective in our study. However, in patient D. failure to enable the Reactive ATP algorithm led to the development of a prolonged episode of AF. Enabling of all algorithms has shown high efficiency.

The MINERVA study in 2021 is reflected in the European Society of Cardiology guidelines on cardiac pacing and cardiac resynchronisation therapy. Class IIb, level of evidence B: brady-tachy variant sinus node weakness syndrome patients may be considered for atrial antitachycardia programming [17].

The controversial attitude to the efficacy of ATP in AF stems from the traditional view of the mechanisms of arrhythmia onset and maintenance. As a multivariate analysis by G. Boriani et al (2005) has shown, there are predictors of ATP efficacy: atrial arrhythmia cycle, device programming and drug therapy [18]. The duration of the atrial tachycardia cycle at the start of an episode and the time before therapy are the main factors determining the efficacy of ATP. Programming of arrhythmia detection zones affects the effectiveness of ATP: selecting a 220 ms limit for ATP delivery allows selection of atrial tachycardia episodes that are most likely to arrest. These three factors are important in determining the appropriate programming for a device.

The Reactive ATP function allows applying multiple cycles of ATP when the device detects a change in rhythm regularity or the duration of the arrhythmia cycle. This leads to additional attempts of antitachycardia therapy to stop prolonged episodes of atrial tachycardia or AF. Standard antitachycardia pacing therapy fails to take advantage of rhythm changes and cannot stop prolonged atrial tachyarrhythmia. Reactive ATP monitors the atrial rhythm, monitors for changes in frequency or regularity, and applies therapy when an episode lends itself to termination by pacing. Reactive ATP prevents prolonged episodes lasting for hours or days.

CONCLUSION

Thus, algorithms for prevention of AF (APP, ARS, PMOP), antitachycardia pacing (Reactive ATP) and minimisation of right ventricular pacing (MVP) can be quite effective in a number of patients to prevent the development of persistent AF and to reduce the AF burden. However, the small number of patients, short follow-up time, and lack of comparison with proven effective treatments for AF (catheter ablation) do not allow more specific conclusions to be drawn. Furthermore detailed research into these algorithms is needed and to identify specific groups of patients who could benefit most from algorithms for the prevention and treatment of SVT.

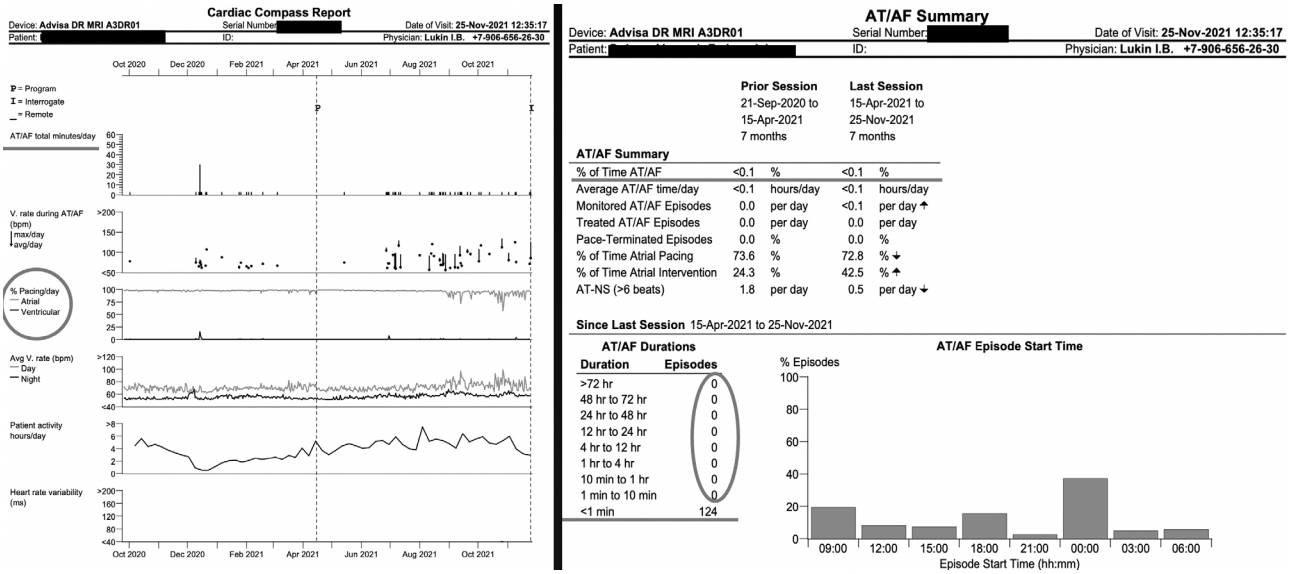

Fig. 4. Data from programmer patient D. Atrial fibrillation burden <0.1%. No episodes of atrial fibrillation longer than 1 minute.

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