CARDIONEUROABLATION FOR RECURRENT VASOVAGAL SYNCOPE AND FUNCTIONAL SINUS BRADYCARDIA: A CASE SERIES

T. Shalganov¹, M. Stoyanov¹, I. Bayraktarova², L. Bardarska³

¹Department of invasive electrophysiology, ²Department of non-invasive diagnostics, Cardiology clinic, National Heart Hospital – Sofia ³Department of pediatric cardiology, National Heart Hospital – Sofia

Abstract.

Patients with recurrent vasovagal syncope with cardioinhibitory or mixed mechanism, or with symptomatic functional sinus bradycardia or AV block can be treated with cardioneuroablation. Material and methods: A case series of 5 patients is presented – four with recurrent syncope and/or symptomatic sinus bradycardia, and one with paroxysmal atrial fibrillation and recurrent syncope. After a confirmation of the syncope mechanism with tilt-test table, and after positive atropine test, radiofrequency catheter cardioneuroablation was performed (this was adjunctive procedure for the patient with atrial fibrillation who received pulmonary vein isolation). During short-term follow-up none of the patients had syncopal recurrence. Conclusion: Catheter neuromodulation provided very good short-term results and lack of serious complications in this first case series in Bulgaria.

Key words:
syncope; sinus bradycardia; neuromodulation; atrial fibrillation

Address
Prof. Tchavdar Shalganov, MD, PhD, Cardiology Department, National Heart Hospital, 65 Konyovitsa St., BG – 1309 Sofia, tel: +359-2-9211-411; e-mail: icd@hearthospital.bg
**Introduction**

Syncope is defined as short transitory self-terminating loss of consciousness caused by global cerebral hypoperfusion [1]. One of the most common subtypes of the reflex (neurally mediated) syncope is vasovagal syncope (VVS). VVS can recur and impair seriously the quality of life. Syncope is classified according to its mechanism as cardioinhibitory, mixed, and vasodepressor. Current European Society of Cardiology guidelines recommend implantation of a permanent pacemaker DDD(R) (with closed-loop stimulation or rate-drop response) for decreasing syncopal recurrences [2]. The indication for pacing includes patients > 40 years, with severe recurrent syncope without prodromes and documented spontaneous pauses > 3 sec. or asymptomatic pauses > 6 sec. due to sinus arrest or AV block, or with cardioinhibitory carotid sinus syndrome, or with tilt-induced asystolic syncope. The indication for pacing is rated class IA in the Guidelines for cardiac pacing [2] and class IIaB in the Guidelines for management of syncope [1]. However, in patients ≤40 years there is no viable guideline-directed therapeutic alternative.

In recent years, the possibility of eliminating or reducing syncopal recurrences by radiofrequency catheter neuromodulation (cardioneuroablation) of the epicardial ganglionated plexi (GP) in patients with VVS, functional AV block and functional sinus bradycardia has been intensively investigated [3-8].

**Material and methods**

Consecutive patients with VVS and/or functional sinus bradycardia who underwent radiofrequency catheter neuromodulation, are reported here. All patients had signed informed consent for the procedure after discussion on the alternative treatment options. The preprocedural preparation and the ablation were done following a protocol approved by the local Ethics committee and consisted of cardiac imaging by contrast-enhanced multidetector computed tomography, tilt-table test (only for patients with syncope), and atropine test. The tilt test was deemed positive if syncope with cardioinhibitory or mixed mechanism was induced. Atropine test was deemed positive if the baseline heart rate increased by at least 25%. The procedure itself consisted of electroanatomic mapping using EnSite Precision system and irrigat-
EnSite Precision and irrigated ablation in the left and/or right atrium at sites defined by anatomical landmarks. Radiofrequency energy was delivered with a power of 35-50W and duration of up to 30 seconds. The superior left and the anterior right GPs were targeted always, while the remaining GPs were ablated only at the discretion of the physician. The ablation of the left-sided GPs aimed to elicit and abolish vagal reflex, while the ablation of the right-sided GPs aimed to increase durably the heart rate (and improve the AV conduction if deemed necessary). The procedure is completed when the heart rate attains 75% of the peak heart rate during the atropine test. The follow-up consists of a clinical visit, ECG and Holter-ECG, and when possible – repeat tilt-test.

**Results**

All patients with positive tilt table test had a syncope induced with a mechanism defined according to the modified VASIS classification [9]. In all patients with an atropine test performed, it was positive. Several preprocedural characteristics and test results of the patients are shown on Table 1. Additional details are presented below for each patient.

**Case 1**

A 15-year-old girl with recurrent syncope (a total of 9 episodes during the last year, of which 3 in the last two months), euthyroid, with normal neurological status and electroencephalogram. The heart was structurally normal. The ECG in sinus rhythm and ambulatory Holter-ECG were completely normal. There was no family history for arrhythmias or sudden death. During

<p>| Table 1. Предел процедурните характеристики на пациентите // Table 1. Preprocedural characteristics of the patients |
|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age (years)</th>
<th>Indication for ablation</th>
<th>Tilt test, type of response</th>
<th>Change of HR during atropine test (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ж/15 F/15</td>
<td>Синкоп</td>
<td>(+), 1</td>
<td>+65</td>
</tr>
<tr>
<td>2</td>
<td>Ж/43 F/43</td>
<td>Синкоп</td>
<td>(+), 2В</td>
<td>+50</td>
</tr>
<tr>
<td>3</td>
<td>Ж/38 F/38</td>
<td>Синкоп, синусова брадикардия</td>
<td>(+), 1</td>
<td>+60</td>
</tr>
<tr>
<td>4</td>
<td>Ж/49 F/49</td>
<td>Синусова брадикардия</td>
<td>NA</td>
<td>+60</td>
</tr>
<tr>
<td>5</td>
<td>М/76</td>
<td>Предсърдно мъждене</td>
<td>(+), 3</td>
<td>NA</td>
</tr>
</tbody>
</table>

СЧ – сърдечна честота; Ж – жени; М – мъже; (+) - положителен; NA – не е правен.
HR – heart rate; F – female; M – male; (+) – positive; NA – not done.
Случай 2

Жена на 43 г., с 3 синкопални епизода без продроми (последният е постмикцион, с травма на главата при падането). Сърцето е структурно здраво. ЕКГ и холтер-ЕКГ не показват отклонения. Електроенцефалограмата също е в норма. При тилт-теста се индуцира кардиовагален синкоп с асистолия с продължителност 17.8 секунди. При ЕФИ синусовата честота беше 86 уд./мин на фоната на венозна аналгоседация с фентанил и мидазолам. Един месец по-късно съобщава за интермитентно усещане за ускорен пулс и леко замайване при рязко изправяне, но няма синкопални рецидиви при телефонен контакт 6 месеца след абляцията също няма синкопални рецидиви.

A 43-year-old woman with 3 syncopal recurrences without prodromes (the last one was micturition syncope with head trauma after the fall). The heart was structurally normal. The ECG and ambulatory Holter-ECG were also normal, as was the electroencephalogram. The tilt-table test induced cardioinhibitory syncope with asystole of 17.8 sec. At EP study the heart rate was 60 bpm, the AH interval was prolonged to 130 ms, the ERPAV was also prolonged to 470 ms, while the Wenckebach point was decreased to 520 ms. Ablation of the superior left and of the right-sided GPs was done (Fig. 1). The ablation of the superior left GP induced a brady-cardiac vagal reflex without asystole, followed by increase of the heart rate to 90 bpm. The ablation of the anterior right GP caused additional increase of the sinus rate to 107 bpm. After the ablation of the inferior right GP the ERPAV became normal, and the Wenckebach point increased. The final heart rate was 83 bpm under i.v. analgesia/sedation with fentanyl and midazolam. One month later she is feeling faster pulse in the evening at rest, which is not limiting her. The follow-up Holter-ECG showed a heart rate of 74 to 125 bpm, with an average heart rate of 89 bpm at daytime and 80 bpm at night. The follow-up tilt-test done 45 days after the ablation induced a pure vasodepressor syncope after sublingual nitroglycerin challenge – the lowest heart rate was 95 bpm even during the syncope. The patient was given recommendations for liberal fluid intake and avoidance of long periods of immobile upright standing, and she also showed the physical counter-pressure maneuvers.

Case 2

A 43-year-old woman with 3 syncopal recurrences without prodromes (the last one was micturition syncope with head trauma after the fall). The heart was structurally normal. The ECG and ambulatory Holter-ECG were also normal, as was the electroencephalogram. The tilt-table test induced cardioinhibitory syncope with asystole of 17.8 sec. At EP study the heart rate was 60 bpm, the AH interval was prolonged to 130 ms, the ERPAV was also prolonged to 470 ms, while the Wenckebach point was decreased to 520 ms. Ablation of the superior left and of the right-sided GPs was done (Fig. 1). The ablation of the superior left GP induced a brady-cardiac vagal reflex without asystole, followed by increase of the heart rate to 90 bpm. The ablation of the anterior right GP caused additional increase of the sinus rate to 107 bpm. After the ablation of the inferior right GP the ERPAV became normal, and the Wenckebach point increased. The final heart rate was 83 bpm under i.v. analgesia/sedation with fentanyl and midazolam. One month later she is feeling faster pulse in the evening at rest, which is not limiting her. The follow-up Holter-ECG showed a heart rate of 74 to 125 bpm, with an average heart rate of 89 bpm at daytime and 80 bpm at night. The follow-up tilt-test done 45 days after the ablation induced a pure vasodepressor syncope after sublingual nitroglycerin challenge – the lowest heart rate was 95 bpm even during the syncope. The patient was given recommendations for liberal fluid intake and avoidance of long periods of immobile upright standing, and she also showed the physical counter-pressure maneuvers.
Case 3

A 38-year-old woman with medically compensated mild hypothyroidism and history of recurrent syncope between 18 and 32-year-old age. In the following years she had persistent sinus bradycardia (38-40 bpm during daytime), adynamia, severely compromised physical capacity, daytime sleepiness, chronic fatigue. The heart was structurally normal. On Holter-ECG the heart rate fluctuated between 40 and 92 bpm. At the EP study the sinus node recovery time (SNRT) and the corrected SNRT were very prolonged – 3115 and 1685 ms respectively. The AV conduction parameters were also abnormal with a Wenckebach point of 840 ms and ERP AV 540 ms. Cardioneuroablation of the left-sided and the anterior right GPs was done (Fig. 2). During the ablation of the left-sided GPs a severe asystolic reflex was induced with subsequent sinus bradycardia of 28-32 bpm. The reflex was abolished by repeat radiofrequency applications. During the ablation of the anterior right GP a sudden increase of the sinus rate ensued – initially up to 72 bpm, and later on – up to 90 bpm. Wenckebach point also increased without reaching normal values, so the inferior right GP was also ablated. The final sinus rate was 84 bpm (Fig. 3). The parameters of the sinus node function and the AV conduction completely normalized – SNRT shortened to 1275 ms, corrected SNRT – to 485 ms, Wenckebach point increased to 380 ms, the ERP AV shortened to 340 ms. At the follow-up visit one month later she was in highly improved clinical condition, without adynamia or sleepiness, with improved physical capacity in daily activi-
капацитет в ежедневните дейности. Холтер-ЕКГ показва синусов ритъм с фр. 62-113 уд./мин, средна честота през деня 88 уд./мин, през нощта 70 уд./мин, без брадикардии или паузи, без ектопия. Контрол-

ties. The follow-up Holter-ECG showed sinus rhythm at a rate of 62 to 113 bpm, average heart rate of 88 bpm at daytime and 70 bpm at night, without bradycardia, pauses or ectopy. The follow-up tilt test was
ният тилт-тест е негативен, вкл. след провокация с нитрат – не се предизвиква синкопална/пресинкопална симптоматика, няма брадикардии или паузи.

**Случай 4**

Жена на 49 г., с пресинкопи, хронична умора и адинамия при отдавна известен „бавен пулс“. Преди една година е установена мономорфна камера ексстрастиолия при структурно здраво сърце, за която е предписан бисепролол 2.5 mg дн., но независимо от това в различни холтер-ЕКГ записи броят на ексстрастиолите варира от 7000 до 20 000/24 часа. ЕКГ е нормална, с изключение на синусова брадикардия до 41 bpm. Придружаващите заболявания са артериална хипертония, автоимуен тиреоидит (eutireoидна при заместително лечение с левотироксин 50 mcg дневно), преболедувана Covid-19 инфекция, хроничен копит и нефролитиаза. Първоначалното предположение беше, че „бавният пулс вероятно е резултат от пулсов дефицит при камера ектомия, но впоследствие установихме, че оплакванията от отпадналост и умора са постоянни, вкл. през дълги периоди без никаква ектопична активност. Синусовата брадикардия също се оказа постоянна – дори след прекратяване на лечението с бета-блокер синусовата честота не надхвърли 48-53 уд./мин. След положителен атропинов тест беше планирана за катетърна аблация на ектопичното огнище и невромодулация. По време на ЕФИ синусовият базален цикъл варираше от 1240 до 1440 ms (фр. 48-42 уд./мин). При предсърдна стимулация се установиха силно удължени ВВСВ (4307 ms) и коригирано ВВСВ (2540 ms), с изява на дълги периоди на заместителен нодален ритъм с цикъл 1100-1520 ms (фр. 54-39 уд./мин.). Поради изключително редки камерни ексстрастиоли, вкл. след фармакологично потенциране с хексопреналин и електрическа стимулация, се извършиха усилия за невромодулация на термичното огнище и включване на нодалния ритъм възстановена синусовата честота до 900 ms (фр. 67 уд./мин.) и епизодите на нодален ритъм изчезнаха напълно. След маркиране на хода на френикусиевия нерв бяха нанесени допълнителни лезии на предната десен ГП на страната на дясното предсърдие и горната празна вена, при което синусовият цикъл се съкъс допълнително и се задържа на 850 ms. ВВСВ и коригираното ВВСВ се нормализираха, съответно на 1205 ms и 355 ms, без никакви паузи, нито заместителен нодален ритъм или дори единични нодални съкращения. След процедурата с олакване на преходна болка и подуване на корема, преодолявания със спазмолитик. Един месец negative, incl. after nitrate challenge – no syncope/ presyncope was provoked, there were not bradycardia nor pauses.

**Case 4**

A 49-year-old woman with recurrent presyncope, chronic fatigue and adynia together with known for many years “slow pulse rate”. One year earlier monomorphic ventricular premature beats were detected in structurally normal heart and bisoprolol was started at a daily dose 2.5 mg. Nevertheless, at several Holter recordings the number of premature beats varied between 7000 and 20000/24 hours. The ECG was normal except for sinus bradycardia of 41 bpm. She had also arterial hypertension, autoimmune thyroiditis (she was euthyroid while substituted with 50 mcg levothyroxine daily), previous Covid-19 infection, chronic colitis and nephrolithiasis. Our initial suspicion was that the “slow pulse rate” was due to pulse deficiency during ventricular premature beats. However, subsequently we found that the complaints of exhaustion and fatigue were constant, incl. during long periods without any ectopic activity. Sinus bradycardia also proved constant – even after stopping the beta-blocker treatment the sinus rate did not exceed 48-53 bpm. After a positive atropine test she was scheduled for catheter ablation of the ectopic focus and concomitant neuromodulation. At the time of the EP study the sinus cycle length varied between 1240 and 1440 ms (48-42 bpm). During atrial pacing we found severely prolonged SNRT of 4307 ms and corrected SNRT of 2540 ms, with long periods of escape nodal rhythm at a cycle length of 1100-1520 ms (54-39 bpm). The ventricular premature beats were exceedingly rare and not potentiated by infusion of hexoprenaline and pacing, so only neuromodulation of the superior left and anterior right GPs was performed. Radiofrequency applications at the superior left GP provoked a vagal reflex with pauses of 2 seconds which was abolished. The applications at the anterior right GP persistently shortened the sinus cycle length to 900 ms (67 bpm), while the nodal rhythm completely disappeared. After tagging the phrenic nerve additional lesions were delivered on the right atrial aspect and within the superior caval vein, thus decreasing and stabilizing the sinus cycle length to 850 ms. SNRT and corrected SNRT became normal – 1205 and 355 ms respectively, and there were neither pauses, nor escape nodal rhythm or even single nodal beats. After the procedure she complained of transient abdominal pain and distension, resolved with spasmylic drug treatment. One
последните 6 месеца няма рецидив на предсърдно мъждене, нито синкопи или пресинкопи.

Таблица 2 показва някои параметри непосредствено преди и веднага след невромодулацията, както и целите места за аблация при всички пациенти.

Обсъждане

За разбиране на теоретичната основа и ефектите на кардионевроаблацията е добре да се припомни анатомията на автономната нервна система на сърцето и механизмът на неврално медиран синкоп. Собствената автономна нервна система на сърцето включва симпатикусова и вагална инервация. Симпатикусовата инервация се осъществява директно от торакалните паравертебрални симпатикусови ганглии посредством дълги постганглийни

Case 5

A 76-year-old male patient with recurrent paroxysmal atrial fibrillation, frequent atrial ectopic beats, and recurrent syncope (2 episodes during the last month) and presyncope occurring just before the arrhythmia bouts. The atrial fibrillation recurred usually at the evenings, at rest, after meals, and was preceded by feeling of bloating, belching and flatulence. One year earlier a vasodepressor syncope was induced during tilt-test. The patient had also arterial hypertension, type 2 diabetes mellitus, mild anemia after sigmoidal polypectomy, and chronic gastritis. He had no significant coronary or carotid disease. A pulmonary vein isolation was done, followed by ablation of the ectopic focus located on the left atrial floor posteroseptally, just over the proximal part of the coronary sinus. The sinus rate increased from 57 to 74 bpm, the Wenckebach point – from 480 to 360 ms, while ERP AV shortened from 410 to 340 ms. One month later the Holter-ECG showed sinus rhythm with a heart rate of 48 to 109 bpm, and average heart rate of 61 bpm at daytime and 59 bpm at night. Six months later there were neither recurrences of atrial fibrillation, nor syncope or presyncope.

Table 2 shows some parameters just before and immediately after the neuromodulation, as well as the targeted sites in all patients.

Discussion

To understand the rationale and effects of cardioneuroablation, it is necessary to recall the anatomy of the autonomic nervous system of the heart and the mechanism of neurally mediated syncope. The intrinsic autonomic nervous system of the heart includes sympathetic and vagal innervation. Sympathetic innervation is effectuated directly from the thoracic paravertebral sympathetic ganglia by means of long postganglionic axons that form a
Таблица 2. Някои процедурни параметри непосредствено преди и след абляцията, и прицелни места

<table>
<thead>
<tr>
<th>Пациент</th>
<th>СЧ преди/след (уд./мин.)</th>
<th>СЧ след (% от пикова СЧ при атропиновия тест)</th>
<th>Точка на Венкебах преди/след (мс)</th>
<th>ЕРП AV преди/след (мс)</th>
<th>Прицелни ГП</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58/86</td>
<td>60</td>
<td>400/400</td>
<td>340/330</td>
<td>ЛГ, ДП, LS, RA</td>
</tr>
<tr>
<td>2</td>
<td>60/83</td>
<td>88</td>
<td>520/460</td>
<td>470/300</td>
<td>ЛГ, ДП, ДД, LS, RA, RI</td>
</tr>
<tr>
<td>3</td>
<td>42-51'/84</td>
<td>104</td>
<td>840/380</td>
<td>540/340</td>
<td>ЛГ, ЛД, ДП, ДД, LS, LI, RA, RI</td>
</tr>
<tr>
<td>4</td>
<td>41-48'/70</td>
<td>86</td>
<td>400/380</td>
<td>360/320</td>
<td>ЛГ, ДП, LS, RA</td>
</tr>
<tr>
<td>5</td>
<td>57/74</td>
<td>-</td>
<td>480/360</td>
<td>410/340</td>
<td>ДП, ДД, RA, RI</td>
</tr>
</tbody>
</table>

* Изходно синусовата честота показва големи спонтани вариации. СЧ – сърдечна честота; ЕРП AV – ефективен рефрактерен период на AV възела, ЛГ – горен ляв ГП, ДД – долен десен ГП. *The baseline sinus heart rate showed large spontaneous variations. HR – heart rate; ERP AV – effective refractory period of the AV node, LS – superior left GP, LI – inferior left GP, RA – anterior right GP.*
QTc-интервалите, съкъсвайки на ВВСВ и на ЕРП AV, увеличаване на точката на Венкебах, а от клинична гледна точка – значимо намаление на рецидивите на синкоп и пресинкоп [5-8, 13, 14].

С тази серия случаи представяме за пръв път в България прилагането на кардионевроаблация при пациенти с рецидивиращ синкоп или симптомна функционална синусова брадикардия. Предпредложение на подготовката и самата абляция при пациенти 1-4 бяха осъществени по протокол, изготвен от нас и утвърден от местната Комисия по етика. Задължителните предпредуредни изследвания включват образна диагностика на сърцето, тилт-тест за изявяване на механизма на синкопа и атропинов тест за оценка на потенциалния ефект от абляция. Кардионевроаблацията имитира ваголитичните ефекти на атропина и се извършва само при положителен атропинов тест. Пациенти с вазодепресорен синкоп, синкоп с неизяснен механизъм или негативен атропинов тест не подлежат на абляция. Тестът се прави поне 24 часа преди самата абляция, за да е сигурно, че медикаментозният ефект е напълно изчерпан и няма да маскира ефекта на кардионевроаблацията.

Освен много добрите непосредствени резултати по отношение на параметрите на синусовата функция и AV провеждането, краткосрочно проследяване при описаните пациенти също е много окуражително. При всички има отчетливо клинично подобряние, изразяващо се в липса на синкопални рецидиви и/или в значително подобрение на физическия капацитет. При пациент 2 при контролния тилт-тест се индуцира синкоп, въпреки изцяло вазодепресорен механизм. Вероятно още при първия тилт-тест индуцираният синкоп е бил със смесен механизъм, който поради дългата асистолична пауза е бил интерпретиран като изцяло кардиоинхибиторен. В такива случаи няма смисъл от повторна абляция, нито от имплантация на постоянен пейсмейкър, тъй като кардиоинхибиторната компонента е елиминирана. Необходимо е на пациентите да се дадат препоръки за поведение и лечение като за изолиран вазодепресорен синкоп. За отбелязване е, че в съвременско поведение и лечение като за изолиран вазодепресорен синкоп, вкл. при пациенти с изходен асистоличен тилт-индуциран синкоп, но много ниска честота на клинично изявени симптоми – само при два от 17 пациенти [15]. Следователно тилт-индуцираният вазодепресорен синкоп след кардионевроаблация може би не предсказва клиничен рецидив и дори в тези случаи прогнозата изглежда е благоприятна.

Извършваме невромодулация на анатомичен принцип, защото независимо от използваните методи QTC intervals, shortening of the SNRT and the ERP AV, an increase in Wenckebach point, and from a clinical point of view – a significant decrease of syncope and presyncope recurrences [5-8, 13, 14].

With this case series, we report for the first time in Bulgaria the implementation of cardioneuroablation in patients with recurrent syncope or symptomatic functional sinus bradycardia. The pre-procedural preparation and the ablation in patients 1-4 were carried out following a protocol designed by us and approved by the local Ethics Committee. Mandatory preprocedural investigations include cardiac imaging, a tilt table test to elucidate the mechanism of syncope, and an atropine test to evaluate the potential effect of ablation. Cardioneuroablation mimics the vagolytic effects of atropine and is performed only after a positive atropine test. Patients with vasodepressor syncope, syncope with an unclear mechanism, or a negative atropine test are not eligible for ablation. The test is done at least 24 hours before the ablation to be sure that the drug effect has completely worn off and will not mask the effect of the cardioneuroablation.

Besides the very good acute results regarding the sinus node function and AV conduction parameters, the short-term follow-up in these patients is also very encouraging. In all of them, there was a manifest clinical improvement, as demonstrated by the absence of syncopal recurrences and/or in a significant improvement of the physical capacity. In patient 2, the follow-up tilt test induced a syncope, now with a pure vasodepressor mechanism. Probably already during the preprocedural tilt-test the induced syncope had a mixed mechanism, which was interpreted as cardion inhibitory due to the long asystolic pause. In such cases, there is no point in repeat ablation, nor in implantation of a permanent pacemaker, since the cardion inhibitory component is eliminated. It is necessary the patients to receive recommendations for management as for isolated vasodepressor syncope. Of note, in a very recent study with a median follow-up of 8 months, a relatively high incidence of tilt-induced vasodepressor syncope after cardioneuroablation was reported, incl. in patients with baseline asystolic tilt-induced syncope, but at the same time the incidence of clinically apparent symptoms was very low – in only two of 17 patients [15]. Therefore, tilt-induced vasodepressor syncope after cardioneuroablation may not predict clinical recurrence, and even in these cases the prognosis seems to be favourable.

We perform the neuromodulation on an anatomical basis, because, regardless of the method used...
for localization on GPs difference in the end points [14], however, the duration of the procedure is shortened with this approach. Our initial impression is that ablation of the superior left GP induces and then abolishes vagal reflex with a subsequent short-lived and transient increase of the heart rate, whereas ablation of the anterior right GP produces an immediate and sustained increase of the heart rate. When possible, we prefer a more limited ablation directed to the superior GPs, because the influence of the autonomic nervous system on the sinus node is mainly carried out by them – from the anterior right GP directly and from the superior left GP mediated through the anterior right GP. The same two GPs also influence the AV conduction through the inferior right GP [10].

Case 5 is interesting in that his atrial fibrillation had signs of the so-called “vagal” fibrillation [10] and neuromodulation was actually done primarily to reduce the risk of arrhythmia recurrence, especially since the tilt-induced symptoms were interpreted as the result of a vasodepressor mechanism. Probably, in a mixed mechanism with a very pronounced predominance of one component, it is difficult to detect the “minor” component and the interpretation may be incorrect, as in case 2. However, in patient 5, the clinical outcome was excellent not only with respect to the paroxysmal arrhythmia but also with respect to syncopal recurrences. Interestingly, in the above-cited ELEGANCE study one of the patients undergoing cardineuroablation had vasodepressor tilt-induced syncope at baseline, but the repeat tilt test after ablation was negative [15].

One of the patients had abdominal pain and distension a few hours after the procedure. Complications related to vascular access and surgical abdominal emergency were excluded. Symptoms were managed conservatively, and subsequently during hospitalization in a gastroenterology department, a diagnosis of “exacerbated chronic colitis” was made. It is not clear whether there was a causal relation to the ablation.

Other complications were not registered. Potential risks are common to any catheter intervention and are associated with vascular and transseptal access. In terms of the neuromodulation itself, the procedure appears to be safe, and most publications report only transient inappropriate sinus tachycardia in a minority of patients [14]. In a small clinical series, there was also one case of transient gastroparesis after cardineuroablation [16].

In this case series the follow-up is short and with some limitations. A significant part of the patients
пациентите са от други населени места и контролните холтер-ЕКГ се правят от амбулаторни кардио- 
лози, които представят в заключенията различни параметри по неуточнени начин. Това не позво-
лява да се направи валидно сравнение на амбула-
торното мониториране преди и след абляцията при всички пациенти. Контролен тилт-тест също създа-
пи и функционална синусова брадикардия е първата 
томите, свързани със синусова брадикардия.

**ЗАКЛЮЧЕНИЕ**

Настоящата серия от случаи на катетърна невро-
ромодулиация при рецидивиращи вазовагални синко-
пи и функционална синусова брадикардия е първата 
докладвана в България и показва много добри крат-
косрочни резултати след необходимата предвари-
телна подготовка, и липса на сериозни усложнения.

Не е деклариран конфликт на интереси

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**CONCLUSION**

This case series of catheter neuromodulation in 
recurrent vasovagal syncope and functional sinus bradycardia is the first reported in Bulgaria and dem-
strated very good short-term results after appropriate 
preparation, and lack of serious complications.

No conflict of interest was declared