

Flow disturbances in carotid and vertebral arteries in symptomatic patients referred for pacemaker implantation

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Abstract

Background: Electrocardiographic abnormalities and clinical symptoms are used as indications for cardiac pacing. Syncope, faints and other neurological symptoms are of multi-factorial origin and are due to reduced brain perfusion.

Aim: To examine the carotid and vertebral artery blood flow and to assess whether stenosis of these arteries is associated with symptoms of cerebral hypoperfusion in patients undergoing pacemaker implantation.

Methods: In 152 consecutive patients (84 men, age 70.6 ± 10 years), admitted for pacemaker implantation from January 2003 to June 2004, ultrasonographic and colour Doppler examinations of the carotid and vertebral arteries were performed. The patient's medical history and symptoms, conduction disturbances, and modes of pacing were evaluated using a uniform questionnaire. Clinical manifestations of atherosclerosis were present in 21% (remote myocardial infarction) and 8% (stroke) of patients. Patients were divided into 2 groups: asymptomatic subjects (25%) and those with symptoms of cerebral hypoperfusion (75%).

Results: There were no significant differences in indications and modes of pacing between the groups; only second degree atrioventricular block was significantly more frequent in patients without symptoms ($p = 0.0163$). Prevalence of either common or internal carotid artery stenosis $> 50\%$ was higher in symptomatic than asymptomatic patients (32 vs. 16, $p < 0.05$). Multivariate analysis revealed a 3.5 times higher probability of Stokes-Adams attacks and syncope in patients with confirmed atherosclerotic lesions (OR 3.5, 95% CI 1.2-13.4; $p = 0.0351$). Blood flow disturbances in vertebral arteries were more frequent in symptomatic patients: 26 vs. 11%, $p = 0.0438$. The lowest risk of loss of consciousness was observed in patients with second degree atrioventricular block, with no atherosclerotic lesions: (OR 0.2; 95% CI 0.03-0.06; $p = 0.0102$).

Conclusions: Prevalence of atherosclerotic lesions in carotid and vertebral arteries is higher in symptomatic patients referred for pacemaker implantation. The lowest risk of symptoms was found in patients with a second degree atrioventricular block and no atherosclerotic lesions. Ultrasonographic examination of carotid and vertebral arteries should be considered in all symptomatic patients with indications for pacemaker implantation.

Key words: pacemaker implantation, carotid arteries flow disturbances, syncope

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Introduction

Syncope or Morgagni-Adams-Stokes (MAS) attacks are caused by brain ischaemia following inadequate brain perfusion. One of the precipitating factors of syncope may be transient heart rhythm abnormalities – asystole, severe bradycardia or arrhythmias. Syncope in patients with conduction or automaticity disorders is an indication for permanent cardiac pacing [1]. This form of therapy is indicated in patients with symptomatic, chronic or paroxysmal complete atrioventricular (AV) block, advanced symptomatic AV block, trifascicular or bifascicular block

with second degree AV block, symptomatic sinus bradycardia (including drug-provoked), sinus node dysfunction or carotid sinus hypersensitivity with fainting spells [2-5]. Patients from these groups frequently suffer from several other different symptoms such as motor or sensory disorders, transient speech or visual disorders which may also suggest a pathology of the brain-supplying arteries.

The aim of the study was to assess the prevalence of atherosclerotic flow disturbances in the brain-supplying arteries in patients with syncope, selected for pacemaker

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(PM) implantation, and to assess the severity of atherosclerosis.

Methods

Study group

The study group consisted of 152 patients (84 men, 68 women), mean age 70.6 ± 10 years, admitted for pacemaker implantation between January 2003 and June 2004. Patients were divided into 2 groups: those without syncope (25% of the study group) and those with syncope (75% of the study group). Qualification for pacemaker implantation was conducted independently from the ultrasonographic assessment according to current guidelines [5]. It was mainly determined by the presence of conduction and automaticity disorders or clinical symptoms. Clinical documentation, study results and indications for pacemaker implantation were assessed and entered into the database by independent physicians. Medical history data and symptoms present during the physical examination such as syncope, fainting spells, dizziness, fatigue or tiredness were assessed using a unified questionnaire.

Ultrasonographic examination

Ultrasonographic examination of the brain-supplying arteries was performed with the Doppler method (SONOS 5500 with linear array scan head 7.5 MHz H-P) irrespective of the presence of symptoms indicative of possible flow disturbances [6]. During ultrasonographic examination atherosclerotic changes were assessed in the common, internal and external carotid arteries, and vertebral arteries. Haemodynamically significant stenosis was defined as lumen narrowing of 50-70% or more. Sensitivity of ultrasonographic examination in the detection of significant narrowing of the internal carotid artery has been reported as 75-94%, and specificity as 86-90%, according to different authors. Examination included assessment of the arteries in 2D presentation, in longitudinal and transverse projection with determination of stenosis degree and atherosclerotic plaque echogenicity, as well as flow velocity spectrum analysis by pulsatile Doppler with calculation of maximal systolic and end-diastolic velocity in the common and internal carotid artery and image analysis using colour Doppler. Stenosis assessment was based on the Bluth (1998) and Robinson criteria. Artery narrowing of more than 60% was diagnosed in the presence of systolic velocity (PSV) > 130 cm/s and end-diastolic velocity (EDV) > 40 cm/s after adjustment for the ratio of PSV in the internal and common carotid arteries > 1.8 and analogically for EDV ratio > 2.4 . To diagnose stenosis of 80% or above significant values of systolic and diastolic velocities were set at > 250 cm/s and > 100 cm/s, respectively, according to guidelines. For these stenoses significant reduction of the arterial lumen in

transverse projection was higher than 70%. Additional assessment included arterial diameter measurement in the locus of maximal narrowing in relation to the post-stenotic vessel diameter in the longitudinal projection according to the following formula: $(1 - \text{diameter at stenosis} / \text{post-stenotic diameter of the internal carotid artery}) \times 100\%$ [7-10]. Flow disturbances in the vertebral arteries were defined by PSV > 120 cm/s and EDV > 40 cm/s, flow asymmetry exceeding 15% between right and left artery and lower post-stenotic velocities (< 25 cm/s) [10]. Low flow velocity was defined as < 25 cm/s. Studies were registered on video tape. There was no angiographic verification of atherosclerotic changes found on ultrasonographic examination. Patients with significant changes were further diagnosed and treated in the reference centres. The study was registered with the ID 3.4/IV/03. Local Bioethical Committee permission was obtained for the conduction of the study (registration number 813, decision IK-NP-0021-14/813/04).

Statistical analysis

Statistical analysis was performed using the SAS 8.2 package. Results are presented as means \pm SD and as numbers and percentages. Chi-square test with Yates correction or Fisher's exact test (for the number of expected observations below 5 per cell) were used for the assessment of patients with presented symptoms and risk factors who had been divided into two groups according to the flow characteristics in the brain-supplying arteries. Multivariable analysis was performed with means of backward stepwise logistic regression. The null model included all variables correlating with the dependent variable at the statistical significance level of at least 0.1 ($p < 0.01$). Independent variables correlating with each other were analysed in separate models. Goodness-of-fit for the presented model and observed data was checked using the Hosmer and Lemeshow test. Null hypotheses were verified at the level of statistical significance lower than 0.05.

Results

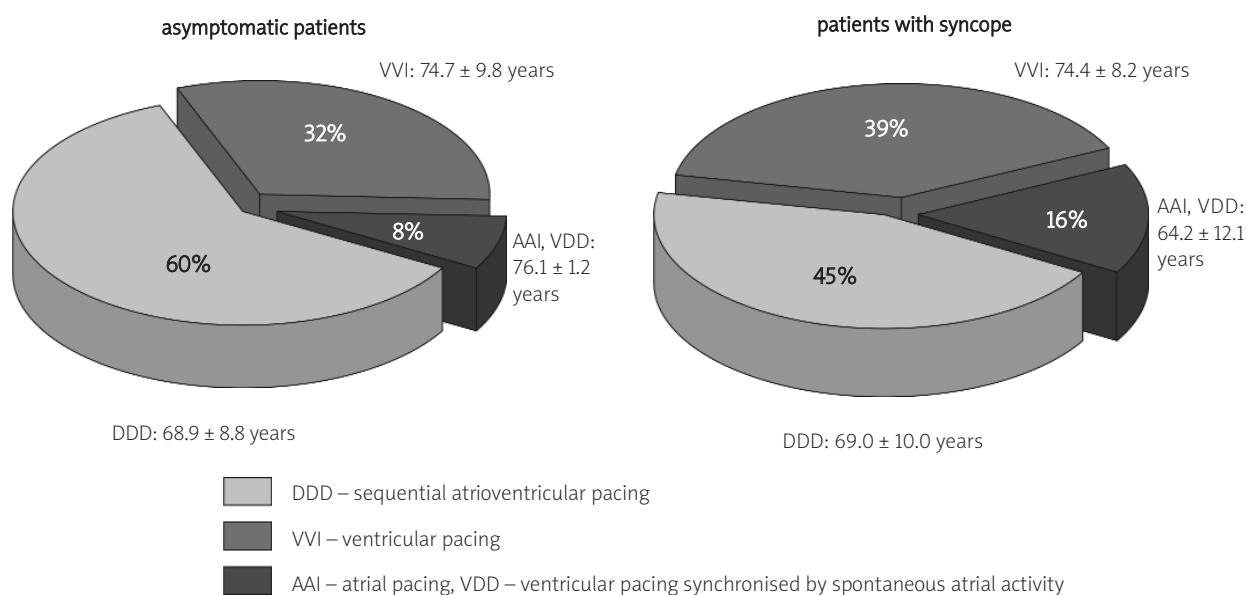
Baseline characteristics of the studied groups including asymptomatic patients and patients with syncope are presented in Table I. There was no significant difference in the prevalence of coronary artery disease, myocardial infarction, atrial fibrillation, stroke or transient ischaemic attack (TIA) between the groups. However, symptomatic patients had significantly higher prevalence of atherosclerotic changes in carotid arteries reducing the arterial lumen $> 50\%$. There was a predominance of hard uniform atherosclerotic plaques. Flow disturbances in the vertebral arteries were also significantly more frequent in symptomatic patients. The study included 75 patients (49%) with atrial fibrillation. Paroxysmal/persistent or chronic atrial fibrillation was present in both studied groups with similar frequency (Table I).

Table I. Baseline characteristics of patients

	All n = 152	Asymptomatic patients n = 38 (25%)	Patients with syncope n = 114 (75%)	P
Age [years], mean \pm SD	70.6 \pm 10.0	71.3 \pm 9.1	70.4 \pm 10.3	NS
Male gender, n (%)	84 (55)	21 (55)	63 (55)	NS
Coronary artery disease, n (%)	63 (42)	20 (53)	43 (38)	NS
Prior myocardial infarction, n (%)	32 (21)	11 (29)	21 (18)	NS
Atrial fibrillation (all), n (%)	75 (50)	19 (50)	56 (49)	NS
Paroxysmal, n (%)	33 (22)	9 (24)	24 (21)	NS
Chronic, n (%)	42 (28)	10 (26)	32 (28)	NS
Stroke + TIA, n (%)	18 (12)	3 (8)	15 (13)	NS
Stroke, n (%)	12 (8)	2 (5)	10 (9)	NS
TIA, n (%)	6 (4)	1 (2.6)	5 (4.4)	NS
Changes in the carotid arteries > 50%, n (%)	43 (28)	6 (16)	37 (32)	< 0.05
Slow flow in the arteries, n (%)	51 (33)	8 (21)	43 (38)	0.0595
Flow disturbances in the vertebral arteries, n (%)	34 (22)	4 (11)	30 (26)	0.0438

Table II. Comparison of electrocardiographic abnormalities in patients with or without syncope

	All n = 152	Asymptomatic patients n = 38 (25%)	Patients with syncope n = 114 (75%)	P
Automaticity dysfunction, n (%)	31 (20)	8 (21)	23 (20)	NS
Tachycardia-bradycardia syndrome, n (%)	31 (20)	4 (10)	27 (24)	NS
Second degree AV block, n (%)	10 (7)	6 (16)	4 (3.5)	0.0163
Advanced AV block (in the presence of chronic atrial fibrillation), n (%)	24 (16)	7 (18)	17 (15)	NS
Third degree AV block, n (%)	21 (14)	3 (8)	18 (16)	NS
Third degree AV block + advanced AV block (combined), n (%)	45 (30)	10 (26)	35 (31)	NS

**Figure 1.** Pacing type in asymptomatic and symptomatic patients adjusted for age

Except for more frequent occurrence of second degree AV block in asymptomatic patients there was no difference in ECG indications for pacemaker implantation (Table II). There was no significant difference in the percentage of various pacing types used between the groups. Patients with syncope who underwent a VVI type pacemaker implantation were older than other patients from this group (Figure 1).

Medical history oriented on neurological symptoms was analysed. The percentage of patients with motor, sensory or visual disorders did not differ significantly between the analysed groups. Symptomatic patients more often reported episodes of syncope and fainting spells, which was related to the initial qualification. Headaches and equilibrium disorders were present with similar frequency in both groups. However, symptomatic patients had a tendency towards more frequent prevalence of memory disorders (Table III).

There was a relationship between changes in the carotid arteries > 50% and motor, sensory and visual disorders. Patients with atherosclerotic changes were significantly more likely to have motor disorders such as paresis of extremities, or sensory disorders such as paraesthesia of extremities. They were also more likely to have visual disorders including blurred vision and visual field deficits (Figure 2).

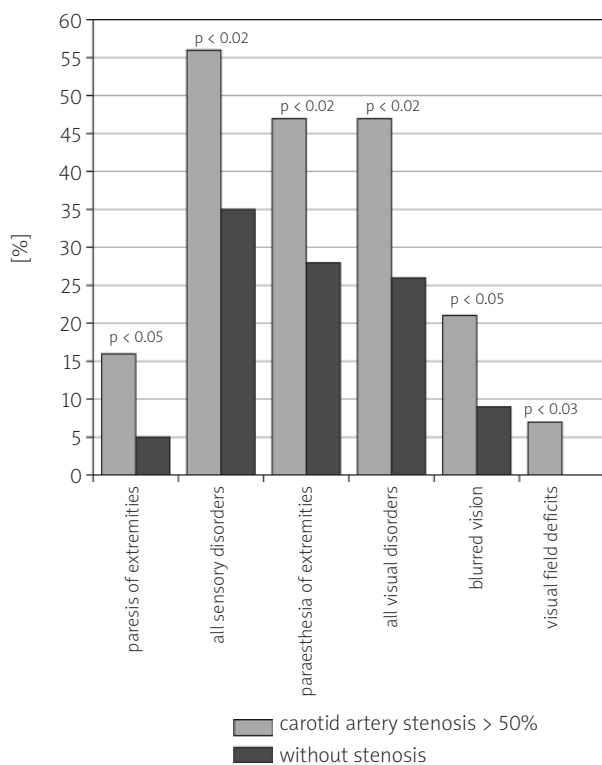


Figure 2. Frequency of neurological symptoms in patients with carotid artery stenosis > 50% and without stenosis

Some of those neurological disorders were more frequently found in patients with flow disturbances in the vertebral arteries. They included paraesthesia of extremities, blurred vision and visual field deficits (Figure 3). Furthermore, a tendency towards more frequent prevalence of paraesthesia in patients with flow disturbances in the vertebral arteries was found.

There was no relationship between slow flow in the arteries (< 25 cm/s) and the analysed neurological symptoms. Visual disorders were more frequently present in patients with coronary artery disease than in patients without this diagnosis: visual disorders: 43 vs. 24%, p < 0.02, blurred vision: 19 vs. 8%, p < 0.05, black spots in the eyes 35 vs. 18%, p < 0.02.

Multivariable analysis using logistic regression demonstrated that flow disturbances in the carotid arteries and II° AV block were the only independent predictors of syncope among all analysed variables. Adjusted odds ratio for the first predictor equal to 3.5 (95% CI 1.2-13.4; p = 0.0351) signifies a 3.5-fold higher probability of syncope in an individual with carotid artery stenosis. On the other hand, odds ratio for the second variable equal to 0.2 (0.03-0.06; p = 0.0102) shows a significantly lower risk of syncope (1 : 5) in patients with II° AV block. Despite good fit of the presented model and observed data (statistically insignificant result of the Hosmer and Lemeshow test), its accuracy was 76.3%.

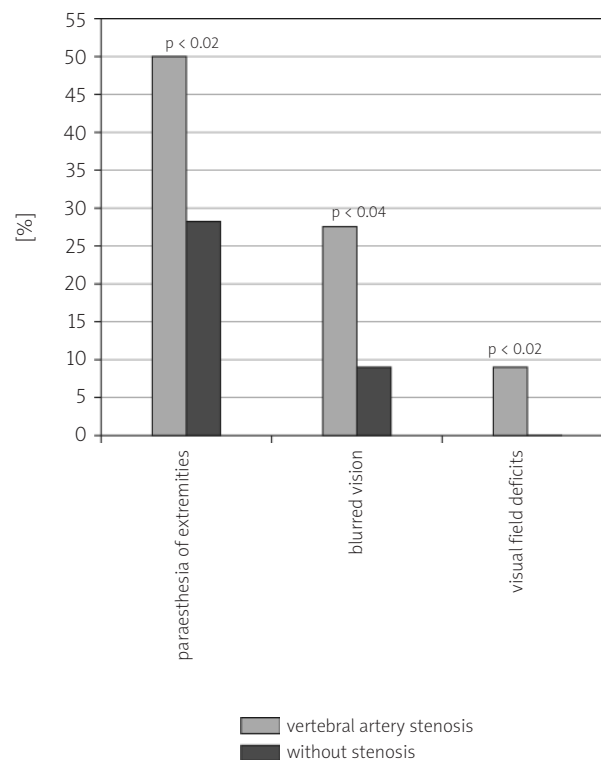


Figure 3. Comparison between the frequency of neurological symptoms in patients with vertebral artery stenosis

Table III. Neurological disorders in the studied groups

	All n = 152	Asymptomatic patients n = 38 (25%)	Patients with syncope n = 114 (75%)	p
Motor disorders				
paresis, n (%)	13 (9)	3 (8)	10 (9)	NS
paralysis, n (%)	8 (5.3)	2 (5.3)	6 (5.3)	NS
all motor disorders, n (%)	13 (9)	3 (8)	10 (9)	NS
Sensory disorders				
numbness, n (%)	50 (33)	10 (26)	40 (35)	NS
paraesthesia, n (%)	44 (30)	7 (18)	37 (32)	NS
sensory loss, n (%)	4 (2.6)	2 (5.3)	2 (1.8)	NS
hyperaesthesia, n (%)	1 (0.7)	1 (2.6)	0	NS
all sensory disorders, n (%)	62 (41)	13 (34)	49 (43)	NS
Visual disorders				
black spots, n (%)	38 (25)	8 (21)	30 (26)	NS
blurred vision, n (%)	19 (13)	2 (5.3)	17 (15)	NS
visual field deficits, n (%)	3 (2.0)	0	3 (2.6)	NS
all visual disorders, n (%)	48 (32)	8 (21)	40 (35)	NS
Other				
headache, n (%)	77 (51)	17 (45)	60 (53)	NS
equilibrium disorders, n (%)	76 (50)	18 (47)	58 (51)	NS
syncope, n (%)	53 (35)	0	53 (46)	< 0.0001
fainting spells, n (%)	82 (54)	0	82 (72)	< 0.0001
memory disorders, n (%)	37 (24)	5 (13)	32 (28)	0.0636

Discussion

The present study sought to determine the role of ultrasonographic examination of the brain-supplying arteries in patients selected for pacemaker implantation. This problem has a multidisciplinary character. Taking into account the advanced age of many patients and frequent prevalence of other risk factors of atherosclerosis it is likely that atherosclerotic changes and flow disturbances in the carotid arteries play a role in the occurrence of consciousness abnormalities. Apart from patients referred for those examinations because of prior stroke, TIA episode, presence of bruit over the carotid artery, headache and dizziness, visual disorders, equilibrium disorders or syncope, there is a group of asymptomatic patients with an estimated stroke risk of 7-10%.

Ischaemic strokes account for 75-80% of all strokes and 20% of them are caused by disorders of the extracranial arteries. The most frequent aetiology of brain and/or retinal ischaemia symptoms in patients with atherosclerotic changes in the internal carotid artery is an embolism caused by thrombi or atherosclerotic plaque fragments. Haemodynamic flow disturbances in this group of patients are responsible for retinal and brain ischaemia in around 10% of cases [11, 12]. These patients remain at risk of neurological disorders despite pacemaker implantation. Coexistence of atherosclerotic changes and

symptoms was assessed in a prospective, open study of 2590 patients referred for ultrasonographic examination of the brain-supplying arteries. Symptoms were present in one-half of patients (51.6%) with significant changes in the carotid arteries, most frequently 80-99% stenosis, $p < 0.0001$. Stenosis of 80-99% was present in 151 (4.7%) asymptomatic patients and in 120 (3.7%) patients one of the arteries was closed [12].

There are situations when symptoms are caused only by the narrowing of carotid arteries, while conduction or automaticity disorders remain asymptomatic. These situations may include paresis, paralysis, numbness, paraesthesia, hyperesthesia of skin, motor, sensory or mixed aphasia and visual disorders such as black spots in the eyes, hemi- or quadrant-amblyopia, blurred or dim vision up to sudden monocular blindness (amaurosis fugax).

Symptoms caused by changes in the internal carotid artery may vary, which is related to the individual and interpersonally changeable collateral flow competence [11]. It is interesting that a common indication for pacemaker implantation such as II° AV block has a low causal relationship with consciousness abnormalities. Some patients with implanted pacemaker are disappointed because they hoped for resolution of symptoms after the procedure. One of the studies analysed causes of syncope

in 46 patients with implanted VVI type pacemaker. Vasovagal syndrome was diagnosed in 36.9% of patients, orthostatic hypotension in 8.6% and stenosis of the carotid arteries in 6.5% of patients [13].

A separate issue is to document the relationship between carotid artery stenosis and carotid sinus hypersensitivity. Under normal conditions during asystole or significant hypotension brain hypoperfusion is compensated by autoregulatory mechanisms. In one of the studies it was shown that 15 out of 18 patients with carotid sinus hypersensitivity and recurrent TIA episodes had a significant unilateral stenosis of the common or internal carotid artery and 3 had bilateral changes. Pacemaker implantation was necessary in 14 cases [14]. Perhaps these patients or patients with symptoms of atherosclerosis should undergo a routine carotid flow assessment, which may allow a more comprehensive understanding of mechanisms of consciousness abnormalities. This will also help to determine the percentage of patients who should undergo a procedure on the carotid artery.

Atrial fibrillation is often present in patients with sinus node dysfunction and conduction disorders leading to haemodynamic flow changes in the central nervous system in response to 20-30% decrease of cardiac output. This factor increases the risk of syncope in patients with organic or functional changes of brain-supplying arteries. In the analysed groups various forms of arrhythmia were present in a similar percentage of patients. The analysis of NASCET and SPAF I, II and III trials disclosed that symptoms of retinal ischaemia are more representative of carotid artery stenosis than of atrial fibrillation, where ischaemia includes the brain and has a larger extent [15].

Taking into account the advanced age of patients it is hard to exclude that the occurrence and severity of syncope is determined by the organic changes and anatomical predispositions of the brain-supplying arteries. The relationship between consciousness abnormalities in the presence of conduction disorders and flow disturbances in the carotid arteries caused by atherosclerotic changes is an argument for more comprehensive assessment of consciousness abnormalities in patients selected for pacemaker implantation.

Study limitations

Angiographic verification of ultrasonographic examination results and follow-up of patients were not performed. Indications for cardiac pacing in the aspect of concomitant diseases or pharmacotherapy were not analysed. Another study limitation may be the subjective nature of neurological symptoms presented by patients, which are often difficult to precisely define.

Conclusions

Patients with syncope are more likely to have atherosclerotic changes in the carotid or vertebral arteries. Ultrasonographic examination of carotid and vertebral arteries should be considered in all symptomatic patients with indications for pacemaker implantation.

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Zaburzenia przepływów w tętnicach dogłowych u chorych z objawami zakwalifikowanych do wszczepienia układu stymulującego serce

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Streszczenie

Wstęp: Objawy kliniczne oraz typ zaburzeń automatyzmu i przewodzenia determinują tryb stymulacji serca. Omdlenia, zasłabnięcia, objawy neurologiczne czy pełnoobjawowe zespoły MAS (ang. *Morgagni-Adams-Stokes syndrome*) wynikają głównie z zaburzeń perfuzji ośrodkowego układu nerwowego, natomiast mechanizmy ich powstawania mogą być złożone.

Cel: Ocena przepływów w tętnicach szyjnych i kręgowych oraz zmian miażdżycowych u chorych zakwalifikowanych do wszczepienia układu stymulującego serce (USS).

Metody: U 152 chorych (84 mężczyzn, 68 kobiet, średni wiek $70,6 \pm 10$ lat), przyjętych do ośrodka w celu wszczepienia USS od stycznia 2003 r. do czerwca 2004 r., przeprowadzono badania metodą USG tętnic dogłowych z oceną przepływów metodą Dopplera (aparatus SONOS 5500 z głowicą liniową 7,5 MHz H-P). Analizowano niezależnie dane z historii choroby oraz objawy z zastosowaniem jednolitego kwestionariusza. Określono typ zaburzeń przewodzenia, tryb stymulacji, objawy, przepływy w tętnicach szyjnych i kręgowych oraz inne dane kliniczne. Kliniczne objawy miażdżycy występowały u 21% (zawał serca) i u 8% (przebyty udar) chorych. Chorych podzielono na 2 grupy: bez poronnych i pełnoobjawowych zespołów MAS (25%) oraz z zespołami MAS (75%).

Wyniki: Przyczyny wszczepienia USS oraz rodzaje stymulacji nie różniły się istotnie w badanych grupach, z wyjątkiem częstszego występowania bloku przedsionkowo-komorowego II stopnia w grupie chorych bez objawów ($p = 0,0163$). Występowanie zmian miażdżycowych zawężających światło tętnicy $> 50\%$ stwierdzono istotnie częściej w grupie z zaburzeniami przytomności: 32 vs 16% ($p < 0,05$). W analizie wieloczynnikowej wykazano 3,5-krotnie większe prawdopodobieństwo utrat przytomności u osób z potwierdzonymi zaburzeniami przepływu (OR 3,5; 95% CI 1,2–13,4; $p = 0,0351$). Zaburzenia przepływu w tętnicach kręgowych także występowały częściej w grupie chorych z objawami: 26 vs 11%, $p = 0,0438$. Najniższe ryzyko wystąpienia zespołu MAS stwierdzono u chorych z blokiem II stopnia, bez zmian naczyniowych (OR 0,2; 95% CI 0,03–0,06; $p = 0,0102$).

Wnioski: U chorych z objawami, z poronnymi i pełnoobjawowymi zespołami MAS, kwalifikowanych do wszczepienia USS częściej występują zmiany miażdżycowe w tętnicach szyjnych niż u chorych bez objawów. Analiza wieloczynnikowa wykazała najniższą wartość predykcyjną bloku przedsionkowo-komorowego II stopnia jako potencjalnej przyczyny zaburzeń przytomności u chorych bez zmian miażdżycowych. Ocena ultrasonograficzna tętnic szyjnych powinna być rozważana u wszystkich chorych z objawami kwalifikowanych do wszczepienia USS, pomimo niskiego ryzyka sercowo-naczyniowego.

Słowa kluczowe: stymulacja serca, zaburzenia przepływów dogłowych, zespoły MAS

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