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THE CLINICAL OUTCOME AND THE INCIDENCE OF PACEMAKER SYNDROME IN VVIR PACED PATIENTS

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Abstract: *Pacemaker therapy has become an important therapeutic option for patients with heart rhythm conditions worldwide. In Romania in the last decade pacing is playing an increasingly important role in the management of cardiac disease.*
A few years after the introduction of pacing therapies, the general practitioners and cardiologists realized that despite of the relief of life-threatening arrhythmias in paced patients, the changes in the hemodynamic and humor status may influence the clinical outcome, prognosis and the quality of life after cardio stimulation and be followed by a deterioration of the patients' condition.
This study evaluates the clinical outcome and the incidence and predictors of the pacemaker syndrome in 547 patients with ventricular-based (VVIR) pacing, implanted in "Sf. Ioan" Hospital, Bucharest, over a period of 7 years.

Key words: *right ventricular pacing; AV dyssynchrony syndrome; pacemaker syndrome; VVI = ventricular-based pacing; VVIR = rate modulated ventricular-based pacing*

1. Introduction

Numerous international multicenter studies, already published, or in progress, trie to compare the benefits of the two types of cardiac pacing devices – mono and bicameral - on life quality, incidence of complications and mortality.

Study	Nr. of pts.	Pacing mode tested
CTOPP[2]	2450	VVI(R) *versus* AAI(R) si DDD(R)
UKPACE[3]	2021	VVIR *versus* DDDR
MOST[4]	2010	VVI sau VVI(R) *versus* DDD

Pacemaker syndrome, or intolerance to VVIR pacing, consists of a number of cardiovascular signs and symptoms induced by the right ventricular pacing. Erbel was the first to name the pacemaker syndrome in 1979. He described a patient in whom ventricular pacing was associated with an episodic, highly symptomatic decline of peripheral arterial pressure when there was a loss of synchrony between atrial and ventricular contraction.

Since then the definition of the pacemaker syndrome has gone through several stages of evolution. The question of improvement in the quality of life by single chamber right ventricular pacing has not been thoroughly examined.

The expectation that the hemodynamic benefits of atrioventricular synchrony would lead to a reduction in cardiac mortality, a reduced risk of heart failure, and a better quality of life were not proven by all the clinical trials. The MOST study which followed for three years the cardiovascular mortality and morbidity in patients with DDDR cardio stimulation toward patients with VVIR cardio stimulation showed no statistical differences between the two groups. In exchange, concerning the heart failure episodes and the quality of life, the study proved the superiority of the DDDR stimulation.

Since heart failure is one of the most important complications after cardiostimulation and it is accompanied by high level of invalidity and mortality the aim of many clinical studies was to asses the real incidence of the pacemaker syndrome. According to statistical dates 70% of the men and 63% of the women which develop heart failure symptoms die in the first 6 years. The high morbidity and mortality due to this post implant complication justifies detailed clinical and fundamental research in order to accurate stratify the risk patients.

2. Methods

The study included 547 patients, men and women, who needed permanent pacing according to the guidelines ACC/AHA/NASPE 2002 (Guideline Update for Implantation of Cardiac Pacemakers anti arrhythmia devices).

Patients who refused to sign the written consent and those with serious (severe) coagulation disorders, chronic patients with dialysis or with cancer in terminal stages were excluded.

The follow up after the implant was made at 1 month, 3 month and 12 month.

Patients were evaluated before implant by a complete clinical examination. Cardiac risk factors, cardiac and associated non cardiac pathology were identified and concomitant medication was recorded.

For a proper evaluation of heart failure a special attention was given to include the patients in different NYHA classes according with their symptoms. The symptom screening, prior to the clinical examination and echocardiogram was made by the physician by asking the same questions in order to evaluate symptoms of heart failure.

The real effort capacity was estimated by standard 6 minutes walking test.

Before and after the implant, the end systolic and end diastolic volumes of the left ventricle and the ejection fraction (Simpson method in two and four chambers incidence) were measured.

Echocardiographic measurements were made in M mode and two-dimensional echocardiography (2DE). Measurements of left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and EF were obtained using the software installed on

the ultrasound equipment, with LVEDV measurements at the time of mitral valve closure and LVESV measured on the image with the smallest LV cavity. The papillary muscles were excluded from the volumes. Biplane Simpson's rule volumes were obtained from the apical four- and two-chamber views.

Mode parameters were measured according to the American Society of Cardiology. The quality of life before and after the implant was also assessed by using CDC HRQOL-14 Module which included the *Healthy Days Core Module* (4 questions). *Activity Limitations Module* (5 questions) and the *Healthy Days Symptoms Module* (5 questions).

We also used the MLHFQ score, an 21 question test which was developed at the University of Minnesota, Minneapolis USA, as an independent scale for the outcome of the patients with heart failure. The questionnaire is scored by summating the responses to all 21 questions (score 105 meaning severe limitation and score 0 meaning no limitation).

We defined a pacemaker syndrome when a patient with single-chamber VVIR pacing developed after the implant either congestive signs and symptoms associated with retrograde conduction during VVIR pacing, or a ≥20 mm Hg reduction of systolic blood pressure during VVIR pacing, associated with reproducible symptoms of weakness, lightheadedness, or syncope.

3. Results

The study included 547 patients with ventricular-based (VVIR) pacing, implanted in "Sf. Ioan" Hospital, Bucharest, between 2000 and 2007. All includend patients did sign the informed consent. The male sex was preponderant (62,24%). The mean age was 73 ± 12 years, with 21,9% of the patients aged over 85 years.

The highest incidence between the risk factors was hypertension (63%) in the female group and history of smoking in the male group (66%). Other risk factors were equally prevalent in the male and female group. 24% of the female group and 44,1% of the male group had evidence of ischaemic heart disease. ($p<0,001$)

Regarding the follow up after the implant - at 1 month, 3 month and 12 month, at the end of the study only 29 (5,30%) patients were lost from the follow up.

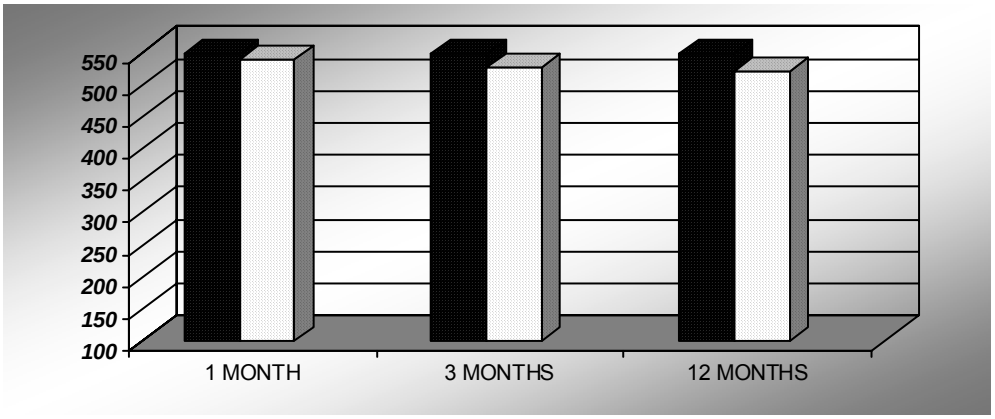

Figure 1. Patient's follow up

Prior to the clinical examination, at each follow up each patient was asked a number of questions in order to evaluate the symptoms.

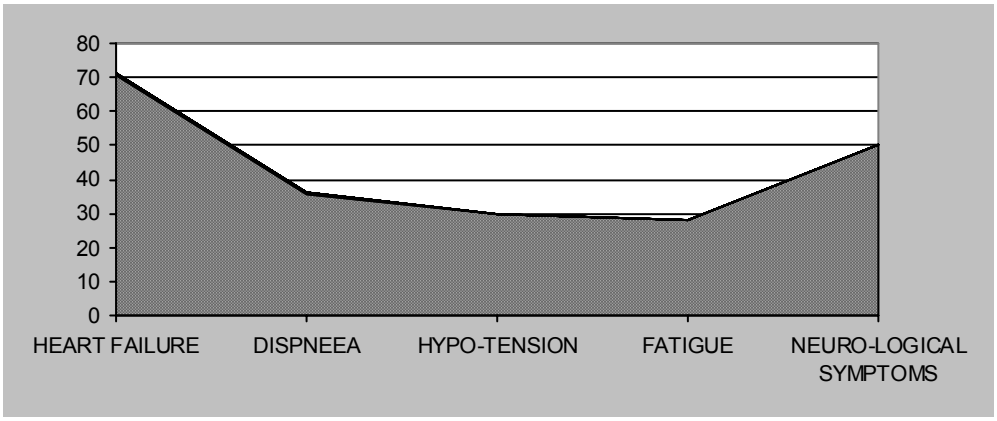

Figure 2. Symptom burden (%)

In order to assess the exercise capacity, a standardized six minutes walk test was performed. Patients which were noncompliant (5,11%), or incapable of performing the test due to immobility (3,47%) were excluded from the test.

The echocardiographic findings showed at baseline (before the pacemaker implant) that 455 patients (13,8%) of the patients had EF>50% and no symptoms of heart failure.

147 patients (16,8%) had symptoms correlated with NYHA class II – IV and a LVEF between 35 - 40% and 28 patients had the same symptoms but had a LVREF < 35%.

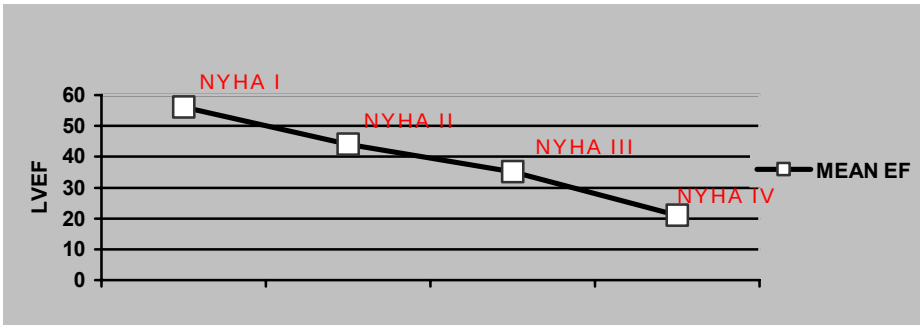

Figure 3. Mean LVEF for each NYHA class

Prevalence of heart failure showed to increase steeply with age in the patient group at baseline (prior to stimulation), so that while around 4% of the patients aged under 65 had heart failure, this increased to between 25 and 28% of those aged 75 to 84 and to 55,8% of those aged 85 and over.

AGE	Number of patients	Number with heart failure	Number without heart failure
≤ 65	25	2	23
65-74	220	55	165
75-84	182	51	131
≥ 85	120	67	53
Total	**547**	**175**	**372**

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he incidence of atrial fibrillation was increasing during the study from 63,43% to 77,41%.

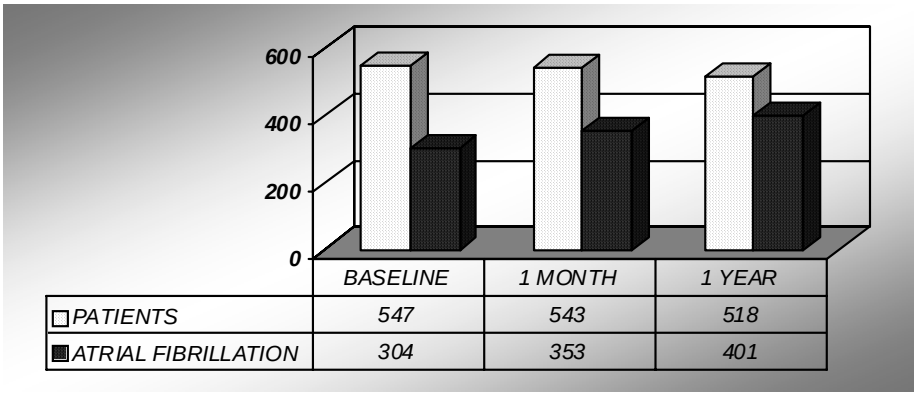

Figure 4. The incidence of atrial fibrillation

The scores on the specific activity scale varied as follows:

Score on Specific Activity Scale	BASELINE	1 MONTH	3 MONTHS
1 (best)	185	195	190
2	125	116	115
3	180	179	180
4 (worst)	10	10	15
P VALUE		0.71	0.22

MLHFQ	BASELINE	1 YEAR	P VALUE
	21,7 ± 2,5	18,7 ± 3,0	0,0284

After cardiostimulation the pacemaker syndrome as defined in our study occurred at 23 patients (4,2%).

4. Discussions and Conclusions

The global incidence of the pacemaker syndrome in our group of patients was lower (4,20%) than in the TRAVILL STUDY (20%), and much lower than in the HELDMAN STUDY (83%).

The incidence of the pacemaker syndrome was similar in the male group (4.9%) and the female group (4,06%) ($p<0,0001$).

The relation between VVIR pacing and the development of the pacemaker syndrome is likely to be complex. Age, comorbidity and haemodinamic status before pacing are factors that influence the appearance of the pacemaker syndrome.

The patient group over 85 years had a higher incidence of worsening heart failure than the other age groups.

The patients with EF> 40% before pacing had a better outcome than those with impaired left ventricular systolic function.

The data of our study show that VVIR pacing may not induce directly heart failure but may increase the risk of developing atrial fibrillation, an important precipitant of heart failure.

One limitation of the study is the fail to study the relationship paced beats/ nonpaced beats in our patients. It might be a direct relationship between the percentage of VVI paced beats and the occurrence of the pacemaker syndrome.

The echocardiographic measurement of the LVEF was a better predictor for developing heart failure than the 6 minutes walk test.

Pacemaker implantation resulted in substantial improvement in almost all QOL measures. Subjects 75 years or older experienced significantly less improvement in functional status and physical scores than did younger patients.

The aethiology of heart failure and of the pacemaker syndrome in VVIR paced patients is variate and may only partial be induced by the right ventricular pacing.

Further studies are required in order to evaluate the impact of VVIR on clinical outcome and its relationship with QOL coefficients.

Pacemaker syndrome incidence was much lower in our study, comparing to other clinical studies.

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