Abstract
Background. Although cardiac pacemakers can prevent the occurrence of heart failure secondary to low cardiac output in patients suffering from extreme bradycardia, they can also induce, in some circumstances, heart failure by decreasing the left ventricular stroke volume. In our study, we aim to describe the effect of permanent cardiac pacing on the evolution of patients with heart failure, objectively determined by the N-terminal pro b-type natriuretic peptide (NT-proBNP) dynamics. Material and methods. Complete clinical examination and determination of NT-proBNP were performed before and 5 days after pacemaker implantation. Results. We enrolled in our study 32 patients with an indication for permanent cardiac pacing in which we implanted 21 single-chamber ventricular pacemakers (VVI, 65.6%), 4 single-chamber atrial pacemakers (AAI, 12.5%) and 7 dual-chamber atrio-ventricular pacemakers (DDD, 21.9%). Patients with heart failure had an average NT-proBNP value of 2542.2±2311.12 pg/mL and patients without heart failure (control group), had an average NT-proBNP value of 190.58±98.16pg/mL. Patients in sinus rhythm that received a VVI pacemaker experienced an increase in NT-proBNP values of 103.73%, while patients in atrial fibrillation and VVI of only 0.27%. NT-proBNP values decreased in patients in sinus rhythm that received a DDD or AAI pacemaker by 20.94%. Conclusion. Permanent cardiac pacemakers are able to influence the clinical status of patients with heart failure, especially if they cause the loss of atrio-ventricular synchronism.
Key words: cardiac pacemaker, heart failure, NT-proBNP

Introduction
The number of cardiac pacemaker implantation procedures is currently increasing secondary to the aging of the global population [1]. Elderly patients often develop degenerative diseases like sick sinus syndrome or atrioventricular block, which are able to cause severe symptoms: syncope, heart failure [2].

Although cardiac pacemakers can prevent the occurrence of heart failure secondary to low cardiac output in patients suffering from extreme bradycardia [3], they can also induce, in some circumstances, heart failure [4] by decreasing the left ventricular stroke volume through two main mechanisms.

The first one consists of an artificially induces atrio-ventricular asynchronism that can be observed when a patient in sinus rhythm receives a single-chamber ventricular pacemaker (VVI). Because this type of pacemaker is able to detect only the ventricular electrical activity, it will induce ventricular depolarizations followed by contractions irrespective of the atrial activity. As a consequence, some of the atrial contractions take place simultaneously with the ventricular contractions, against closed atrioventricular valves, causing atrial volume overload, poor ventricular filling, which lead to symptoms and signs of heart failure [5].

The second mechanism is represented by interventricular asynchronism secondary to right ventricular pacing.

Because the pacemaker lead is placed in the right ventricle, this is the place were the myocardial depolarization and contraction start. The left ventricle contracts only after the right ventricular contraction, involving also the interventricular septum, ends [6].

This type of contraction pattern has lower efficiency compared to a physiological one and leads to a decrease in stroke volume and cardiac output, followed by clinical signs of heart failure [7].

N-terminal pro b-type natriuretic peptide (NT-proBNP) is a well known biological marker used for the diagnosis and follow-up of patients with heart failure. It can be used to asses the evolution of the disease and to guide the medical decisions [8, 9].

In our study we aim to describe the effect of permanent cardiac pacing on the evolution of patients with heart failure, objectively determined by the NT-proBNP dynamics.
Materials and methods

The study was conducted at the Cardiology Department of the Clinical Rehabilitation Hospital in Cluj-Napoca in 2017.

We included in our study patients with an indication for permanent cardiac pacemaker implantation for either sick sinus syndrome or atrioventricular block. The pacing indication was established by their cardiologist according to the European Society of Cardiology (ESC) Guidelines for Cardiac Pacing and Cardiac Resynchronization Therapy published in 2013 [10].

The pacemaker implanted were either single-chamber pacemakers (Medtronic Sensia SESR01 and Saint Jude Medical Sustain XL SR) or dual-chamber pacemakers (Medtronic Sensia SEDR01 and Saint Jude Medical Sustain XL DR). For the interrogation of the pacing parameters we used Medtronic Pacemaker and ICD Programmer model 2090 and St. Jude Medical Merlin Patient Care System.

Before inclusion, all patients gave their informed consent. The study was performed in accordance with the ethical standards stated by the 1964 Declaration of Helsinki and its later amendments.

The NT-proBNP was determined with the use of a Roche Cobas H232 POC system. The first blood sample for NT-proBNP determination was obtained at the moment when the pacing decision was made and the second sample 5 days after the pacemaker implantation procedure.

The diagnosis of heart failure was confirmed by using the criteria stated in the 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure [11], taking into account the initial NT-proBNP value. Patients with acute heart failure were excluded from the study.

For the statistical analysis we used Microsoft Office 2013 Excel Data Analysis module.

Results

We enrolled in our study 32 patients of which 20 males (62.5%) with a mean age of 71.7±10.3 years and 12 females (37.5%) with a mean age of 72.6±7.25 years. 22 of the patients (68.75%) were in sinus rhythm at the moment of admission and 10 patients (31.25%) were in atrial fibrillation.

We implanted 21 single-chamber ventricular pacemakers (VVI), representing 65.6% of the total devices, 4 single-chamber atrial pacemakers (AAI, 12.5%) and 7 dual-chamber atrio-ventricular pacemakers (DDD, 21.9%).

The patients were divided in two groups considering the NT-proBNP values at the moment of hospital admission: patients with heart failure, with an average value of 2542.2±2311.12 pg/mL and patients without heart failure (control group), which had an average value of 190.58±98.16pg/mL. The baseline characteristics of the two groups are described in table I. Patients with heart failure recorded an increase of the NT-proBNP after the pacing procedure by 39.65±1.23%, while the control group of 20.61±0.89%.

<table>
<thead>
<tr>
<th>Patients with HF (20)</th>
<th>Patients without HF (12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>73.8 ± 7.97</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Treatment with ACEi / ARBs</td>
<td>17 (85%)</td>
</tr>
<tr>
<td>Treatment with diuretics</td>
<td>18 (90%)</td>
</tr>
<tr>
<td>Initial NT-proBNP (pg/mL)</td>
<td>2542.2 ± 2311.12</td>
</tr>
<tr>
<td>NT-proBNP after pacing (pg/mL)</td>
<td>2938.9 ± 2500.77</td>
</tr>
<tr>
<td>Type of pacemaker implanted</td>
<td>VVI (17 (85%))</td>
</tr>
<tr>
<td></td>
<td>4 (33.33%)</td>
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<tr>
<td></td>
<td>DDD (2 (10%))</td>
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</tbody>
</table>

Table I. Baseline characteristics of the patients enrolled. HF = heart failure, ACEi = angiotensin-converting-enzyme inhibitor, ARBs = Angiotensin II receptor blockers, NT-proBNP = N-terminal pro b-type natriuretic peptide, VVI = single-chamber ventricular pacemaker, AAI = single-chamber atrial pacemaker, DDD = dual-chamber atrio-ventricular pacemaker.
Patients with heart failure were older, half of them were in atrial fibrillation and received more often diuretics. In their group, the most frequently used pacemaker programming mode was VVI, in 85% of the cases, while in the group of patients without heart failure, the DDD pacing mode was predominant (41.67%).

When we analyzed the patients taking into account the atrioventricular synchronism, we identified three groups: group A – patients in sinus rhythm with a single-chamber ventricular (VVI) pacemaker implanted, that caused an acute loss of the atrioventricular synchronism, group B – patients in sinus rhythm with either a single-chamber atrial (AAI) or a dual-chamber atrio-ventricular (DDD) pacemaker implanted, that preserved the atrioventricular synchronism and group C – patients in atrial fibrillation that already had atrioventricular asynchronism. In group A, there was an average relative increase of the NT-proBNP values by 103.73% after the pacemaker implantation compared to the baseline values, in group C there was an increase of 0.27%, while in group B, a decrease by 20.94% of the NT-proBNP values was recorded (figure 1).

**Discussion**

The pacemaker programming mode significantly influences the exercise capacity and the clinical evolution of the patients, including the ones with heart failure. Choosing an inappropriate pacing mode can induce or aggravate symptoms of heart failure [12].

The lack of atrial contractions, as in the case of patients suffering from atrial fibrillation, can determine a decrease in cardiac output of up to 25% [13]. A similar clinical situation is met in patients in sinus rhythm which receive a VVI pacemaker. This type of pacemaker induces an immediate loss of atrioventricular synchronism because the ventricles are stimulated irrespective of the timing of the atrial contractions and, as a consequence, many of these contractions are simultaneous with the ventricular systole [14, 15].

A study published in 2006 by Buob et al showed that the serum levels of NT-proBNP significantly reduce after successful conversion of patients in atrial fibrillation to sinus rhythm, even in the presence of normal left ventricular ejection fraction [16].
In our study, we observed a significant increase of the NT-proBNP levels in patients with sinus rhythm which received a VVI pacemaker.

For the patients in which the atrioventricular synchronism was preserved by implanting an AAI or DDD pacemaker or in which the synchronism was already impaired secondary to the presence of persistent atrial fibrillation, the NT-proBNP levels remained unchanged or even decreased. The decrease could probably be explained by the optimized treatment for heart failure during hospitalization.

Comprehensive evaluation of the patient’s exercise capacity after permanent cardiac pacing, preferably through cardiopulmonary exercise testing, might prove to be an useful tool in the adjustment process of the pacemaker, having as main purposes the reduction of heart failure symptoms and the improvement of the quality of life [17, 18].

In conclusion, permanent cardiac pacemakers are able to influence the clinical status of patients with heart failure, especially if they cause the loss of atrioventricular synchronism. The use of asynchronous pacing modes (VVI) should be avoided in patients in sinus rhythm as it could lead to decreased functional capacity and worsening of heart failure.

Acknowledgements. This research was financially supported by a PhD Research Grant (PCD 2016) from the “Iuliu Hatieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania.

References


