ORIGINAL ARTICLE

Prognostic value of NT-proBNP levels in patients undergoing permanent pacemaker implantation

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KEY WORDS

cardiovascular events, heart failure, implantable cardiac pacemaker, NT-proBNP

ABSTRACT

INTRODUCTION Several reports confirmed the prognostic value of the N-terminal fragment of B-type natriuretic peptide prohormone (NT-proBT) in various patient populations. Patients with medical indications for implantation of an artificial cardiac pacemaker are at high risk of cardiovascular events. There is limited data assessing the prognostic value of NT-proBNP in this group.

OBJECTIVES The aim of the study was to establish the prognostic value of NT-proBNP in patients scheduled for the implantation of a cardiac stimulator.

PATIENTS AND METHODS The study included 59 patients (average age 79.8 ±6.3 years) with indications for implantation of a permanent pacemaker. NT-proBNP was measured in each patient on admission and 46 patients had their NT-proBNP measured 1 month after implantation. All patients were followed up for 4 years. We examined the incidence of cardiovascular events as endpoints. Finally, we analyzed the relationship between the initial concentration of NT-proBNP measured on admission and at 1 month and the risk of the occurrence of the endpoint (analysis in the group in whom events occurred vs. group without the endpoint).

RESULTS NT-proBNP values at baseline and at 1 month ($NT\text{-}proBNP_{1month}$) were significantly higher in patients who experienced cardiovascular events than in those who were free of such events (NT-proBNP: 2310.6 ±2657.7 pg/ml vs. 1177.6 ±1364.6 pg/ml, $P < 0.2$; $NT\text{-}proBNP_{1month}$: 2538 ±3341.4 pg/ml vs. 1139.4 ±1294.1 pg/ml, $P < 0.03$, respectively). A cut-off point of the initial NT-proBNP value of 577 pg/ml was estimated as the most accurate prognostic risk factor for cardiovascular events within a 4-year follow-up (sensitivity 77%, specificity 52%).

CONCLUSIONS The level of NT-proBNP prior to as well as 1 month after cardiac pacemaker implantation can be useful in identifying patients with higher risk of future cardiovascular events. We suggest using the baseline NT-proBNP concentration of 577 pg/ml as a cut-off value for assessing the risk for such events.

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Received: January 29, 2010.
Revision accepted: March 23, 2010.
Conflict of interests: none declared.
Pol Arch Med Wewn. 2010; 120 (4): 120-126
Translated by Anna Kalińska, MD

INTRODUCTION Permanent cardiac stimulation is a method commonly used in modern cardiology. The available data show that approximately 18,000 of pacing devices are implanted each year in Poland (a mean of 471 per 1 million of inhabitants).[1]

Patients who require permanent heart stimulation are at high risk of subsequent cardiovascular events. It is usually related to their advanced age, coexistence of atrial fibrillation or heart failure, to prior myocardial infarction, and to the stimulation itself.

Identification of patients who are at risk for developing cardiovascular complications would certainly allow for intensifying pharmacological treatment and optimizing the parameters of heart stimulation.

B-type natriuretic peptide (BNP) and the N-terminal fragment of BNP prohormone (NT-proBNP) have been established as predictors

of cardiovascular events in patients with heart failure, after an episode of acute coronary syndrome, in patients with stable coronary heart disease, and in asymptomatic individuals.[2-4] In contrast, data concerning such prognostic value of natriuretic peptide in patients with permanent artificial heart stimulation is still limited. Results obtained in individuals without permanent heart stimulation should not, by any means, be extrapolated to the pacemaker population. Heart stimulation induces the release of BNP by triggering hemodynamic changes leading to disturbance in intraventricular synchronicity. Moreover, nonphysiological single chamber pacing such as VVI may disturb the proper sequence of contractions of atria and ventricles, which will result in impaired influx of blood into the left ventricle and consequential increase in BNP.[5,6]

The aim of this study was to test the prognostic value of serum NT-proBNP concentration in a population of patients after implantation of a permanent pacemaker.

PATIENTS AND METHODS The current study included 59 patients scheduled for the pacemaker implantation. Detailed medical records were collected and all patients underwent a physical examination. The extent of heart failure in each patient was classified according to the New York Heart Association Functional Classification (NYHA). On the last day of hospitalization, echocardiogram was performed in each case (Vivid46E machine). Left ventricular ejection fraction (EF) was estimated using biplane Simpson's analysis. The test was performed according to the guidelines of the Polish Society of Cardiology.[7]

Serum was collected from all patients on the day of the implantation procedure. NT-proBNP levels were measured by an electrochemiluminescence immunoassay using Elecsys 2010 system (Roche Diagnostics). All tests were performed in Synevo Laboratories, LLC, Łódź, Poland. The method had sensitivity of 5 pg/ml. Forty-six patients were tested again at the 1-month routine follow-up visit ($NT\text{-}proBNP_{1month}$). The remaining 13 patients did not attend their 1-month follow-up visit. No pacemaker adjustments were necessary during first month in any of the 59 participating patients.

Pacemaker was implanted through the left subclavian artery under local anesthesia. Ventricular electrode was placed in the right ventricle apex, while in case of dual chamber pacing device, atrial lead was introduced into the right atrial appendage. Pacemakers and electrodes used in this study were manufactured by Biotronik, Inc. (Berlin, Germany) and Medtronic, Inc. (Minneapolis, United States).

Patients were monitored for a period of 4 years after the implantation, particularly for the occurrence of cardiovascular episodes. Every 6 months, performance of the implanted device was assessed in each participant during routine check-up visits. Patients who missed scheduled visits were contacted by mail or phone.

The following cardiovascular events were analyzed in this study: cardiac death, acute coronary syndrome (myocardial infarction or unstable angina), acute decompensated heart failure, and stroke.

Patients were divided into 2 groups and 2 additional subgroups: group 1 (n = 30) included patients who experienced a cardiovascular event; group 2 (n = 29) comprised patients who did not experience a cardiovascular event; subgroup 1 (n = 23) with patients who experienced cardiovascular event and who had NT-proBNP levels measured 1 month after implantation; and subgroup 2 (n = 23) with patients who did not experience cardiovascular event and who had NT-proBNP levels measured 1 month after implantation.

We analyzed the relationship between NT-proBNP measured at the day of the procedure and 1 month after implantation and a risk of achieving the endpoint (analysis in the group with an endpoint vs. group without any endpoint).

Statistical analysis Values were expressed as mean values ± standard deviation. Proportions were given as the number/percentage of persons. Comparison of mean values obtained in 2 groups was performed using the Student's t-test for independent samples. The Shapiro-Wilk test was used to confirm normal distribution of data within the group.

Comparison of mean values within the same group (e.g., NT-proBNP concentration at baseline and at 1 month) was performed using the Student's t-test for related samples. Linear dependence between constant variables was estimated using the Pearson's correlation coefficient (Pearson's r). Correlation coefficient test was also used to verify statistical significance of an r-value.

The χ^2 test for 2×2 contingency table with Yates' correction for continuity was used to evaluate the independence of variables. $P < 0.05$ was considered statistically significant.

The discriminating NT-proBNP variables were plotted against their accuracy of predicting the occurrence of an endpoint in receiver operating characteristic (ROC) curve analysis. The value of 577 pg/ml was selected as the one providing the highest accuracy level. Subsequently, the area under the ROC curve (AUROC) was calculated as an indication of diagnostic value of the test – in this case, NT-proBNP as an endpoint indicator. Confidence interval (CI) for AUROC was 95%.

Next, we constructed Kaplan-Meier survival curves reflecting the relationship between the time of follow-up and probability of survival without reaching the endpoint. Survival curves for NT-proBNP values below and above 577 pg/ml were compared.

We assessed sensitivity, specificity, positive predictive value (PPV), and negative predictive

TABLE 1 Patient characteristics

Variable	Group 1 (n = 30)	Group 2 (n = 29)	*P*
age (years)	82 ±6	77.6 ±5.8	<0.003
men/women, n	21/9	12/17	<0.03
high blood pressure	25 (80%)	25 (86%)	NS
type 2 diabetes	6 (21%)	2 (7%)	NS
CAD	29 (97%)	24 (86%)	NS
stroke	4 (13%)	5 (17%)	NS
myocardial infarction	9 (30%)	3 (10%)	NS
heart failure	26 (87%)	24 (83%)	NS
NYHA			
I	10 (33%)	17 (59%)	NS
II	11 (37%)	5 (17%)	NS
III	4 (13%)	2 (7%)	NS
IV	1 (3%)	0 (0%)	NS
indications for implantation			
AV block (II/III)	12 (4%)	9 (32%)	NS
SSS	13 (43%)	13 (46%)	NS
AF-bradycardia	5 (17%)	7 (25%)	NS
clinical indications for implantation			
syncope	13 (43%)	12 (41%)	NS
presyncopal syndrome	13 (43%)	13 (45%)	NS
bradycardia	1 (3%)	0 (0%)	NS
prophylaxis	3 (10%)	4 (14%)	NS
stimulation device			
single chamber VVIR	18 (60%)	16 (55%)	NS
dual chamber DDDR	12 (40%)	13 (45%)	NS
EF (%)	49.4 ±11	59.6 ±8.9	<0.01

Data are given as mean ± standard deviation or number/percentage of individuals.

Abbreviations: AF – atrial fibrillation, AV – atrioventricular, CAD – coronary artery disease, EF – ejection fraction, NS – nonsignificant, NYHA – New York Heart Association, SSS – sick sinus syndrome

value (NPV) for different discriminating variables of NT-proBNP.

All calculations were performed using statistical analysis packets available in Excel 2007 templates and in MedCalc 11 computer program. Differences that did not reach statistical significance ($P > 0.05$) were considered as nonsignificant.

RESULTS **Characteristics of the patients** A total of 59 patients (26 women, 33 men) with indications for implantation of a pacemaker were included in this study. The average age of the patients was 79.8 ±6.3 years. Characteristics of the patients are presented in TABLE 1.

Heart stimulation procedures Two main studied groups did not differ in respect to electrocardiographic and clinical indications for pacemaker implantation. In both groups similar percentage of patients underwent VVIR and DDDR stimulation.

Percentage of right ventricle stimulation during a 4-year follow-up did not differ in both groups (TABLE 2).

TABLE 2 Comparison of right ventricle stimulation within the study groups

Stimulation mode	% right ventricular stimulation		*P*
	group 1 (n = 30)	group 2 (n = 29)	
VVIR	69 ±33.2	50 ±30.8	NS
DDDR	66.7 ±56.9	83.1 ±19.7	NS

Abbreviations: see TABLE 1

NT-proBNP A mean concentration of NT-proBNP in serum before the implantation procedure (NT-proBNP) in the whole patient population (n = 59) was 1753.7 ±2181 pg/ml, while a mean concentration of NT-proBNP measured 1 month after the procedure ($NT\text{-}proBNP_{1month}$) in a subgroup of 46 patients was 1839 ±2603 pg/ml.

The obtained values of NT-proBNP and $NT\text{-}proBNP_{1month}$ did not differ significantly between men and women (NT-proBNP: 1522.8 ±2253.9 pg/ml vs. 2046.7 ±2105.1 pg/ml, $P = 0.18$ and $NT\text{-}proBNP_{1month}$: 1592 ±1194 pg/ml vs. 2189 ±3829 pg/ml, $P = 0.52$, respectively). These values were also comparable in patients with impaired (<50%) and normal (≥50%) left ventricular EF (NT-proBNP: 2439.3 ±3571.2 pg/ml vs. 1571 ±1787.1 pg/ml, $P = 0.22$ and $NT\text{-}proBNP_{1month}$: 1619 ±1037 pg/ml vs. 1668 ±2864 pg/ml, $P = 0.93$). There was no difference in NT-proBNP levels between patients with single and dual chamber stimulation (1616 ±1347 pg/ml vs. 1507 ±2849 pg/ml, $P = 0.86$); however, $NT\text{-}proBNP_{1month}$ was significantly higher in patients with VVIR stimulation as compared with DDDR subgroup (2564 ±3184 pg/ml vs. 896 ±1029 pg/ml, $P < 0.01$).

NT-proBNP and cardiovascular events During a 4-year follow-up, 30 out of 59 patients experienced a cardiovascular event (patients identified as group 1), 15 patients died (cardiac death), while 22 were hospitalized as a result of acute coronary syndrome (11 patients), stroke (3 patients), and acute decompensating heart failure (8 patients).

Patients assigned to group 1 were characterized by significantly higher values of initial NT-proBNP as compared with group 2 (2310.6 ±2657.7 pg/ml vs. 1177.6 ±1364.6 pg/ml, $P < 0.02$).

$NT\text{-}proBNP_{1month}$ levels were also significantly higher in subgroup 1 as compared to subgroup 2 (2538 ±3341.4 pg/ml vs. 1139.4 ±1294.1 pg/ml, $P < 0.03$).

All obtained measurements are detailed in TABLES 3 and 4.

Analysis of ROC curve (FIGURE 1) indicated that the cut-off point for initial concentration of NT-proBNP that is most accurate in predicting the future cardiovascular events is 577 pg/ml (with test sensitivity of 77% and specificity of 52%). PPV was calculated at 62%, while NPV at 68%. AUROC value was 0.656 (CI = 0.521–0.775). Results obtained in ROC curve were subsequently used to plot Kaplan-Meier curves for initial value

TABLE 3 Comparison of NT-proBNP values obtained in the study groups

Parameter	Mean value ± standard deviation		*P*
NT-proBNP (pg/ml)	women (n = 26)	men (n = 33)	
	2046.7 ±2105.1	1522.8 ±2253.9	NS
	EF <50% (n = 14)	EF ≥50% (n = 45)	
	2439.3 ±3571.2	1571 ±1787.1	NS
	single chamber stimulation VVIR (n = 34)	dual chamber stimulation DDDR (n = 25)	
	1616 ±1347	1507 ±2849	NS
	group 1 (n = 30)	group 2 (n = 29)	
	2310.6 ±2657.7	1177.6 ±1364.6	<0.02

Abbreviations: NT-proBNP – N-terminal fragment of B-type natriuretic peptide prohormone at baseline, others – see TABLE 1

TABLE 4 Comparison of NT-proBNP$_{1month}$ values obtained in the study groups

Parameter	Mean value ± standard deviation		*P*
NT-proBNP$_{1month}$ (pg/ml)	women (n = 19)	men (n = 27)	
	2189 ±3829	1592 ±1194	NS
	EF <50% (n = 9)	EF ≥50% (n = 37)	
	1619 ±1037	1668 ±2864	NS
	single chamber stimulation VVIR (n = 26)	dual chamber stimulation DDDR (n = 20)	
	2564 ±3184	896 ±1029	<0.01
	subgroup 1 (n = 23)	subgroup 2 (n = 23)	
	2538 ±3341.4	1139.4 ±1294.1	<0.03

Abbreviations: NT-proBNP$_{1month}$ – N-terminal fragment of B-type natriuretic peptide prohormone at 1 month, others – see TABLE 1

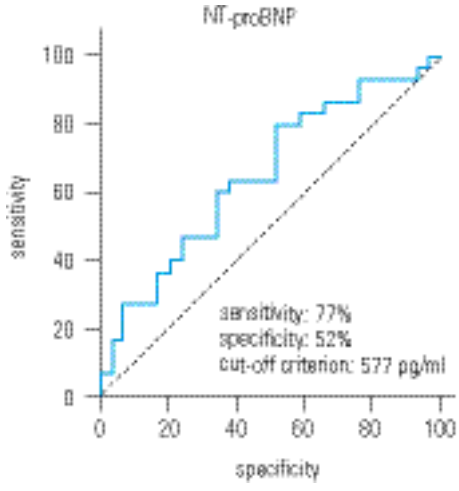

FIGURE 1 Receiver operating characteristic curve for NT-proBNP value in predicting cardiovascular events
Abbreviations: NPV – negative predictive value, PPV – positive predictive value, others – see TABLE 3

NT-proBNP (pg/ml)	sensitivity (%)	specificity (%)	PPV (%)	NPV (%)
427	80	48	62	70
527	77	48	61	67
577	77	52	62	68
721	70	52	61	65
873	70	55	60	63

of NT-proBNP below and above 577 pg/ml. As seen in FIGURE 2, the 2 curves begin to diverge after a few months of follow-up. The observed difference is statistically significant (P = 0.03).

Changes in NT-proBNP during the first month of follow-up No significant changes in NT-proBNP levels were observed during the first month after implantation. Neither stimulation mode nor varying indications for the procedure influenced NT-proBNP values (TABLES 5 and 6).

DISCUSSION Natriuretic peptide was discovered over 20 years ago when Sudoh et al.[8] isolated it for the first time from the porcine brain. Three years later, it was reported that it was also produced by ventricular myocardium.[9] An active form of the hormone (BNP) is released into the circulation with N-terminal fragment of the prohormone (NT-proBNP). Blood concentration levels of the latter are more stable than those of BNP itself.

Increased serum BNP concentrations are one of compensatory mechanisms triggered by heart failure. Main effects of BNP include natriuresis, diuresis, vasodilatation, as well as blocking the renin-angiotensin-aldosterone cascade and sympathetic nervous system. They all constitute a counterbalance for neurohormonal mechanisms typical for progressive heart failure.

Nowadays, assessment of serum concentration levels of both BNP and NT-proBNP is a common clinical practice, and current international guidelines emphasize its value in the diagnostic evaluation of heart failure.[10,11]

Several scientific reports demonstrated the essential role of BNP and NT-proBNP measurement as a prognostic factor in patients suffering from heart failure, acute coronary syndrome, stable coronary artery disease, as well as in asymptomatic individuals.[2,3,12] BNP was also established as a valuable marker of myocardial asynchrony.[13,14]

In recent years, serum BNP levels became useful in monitoring the population of patients with permanent heart stimulation. It was demonstrated that BNP could be of value in screening for heart failure or a prognostic factor of developing heart failure in patients after pacemaker implantation.[15,16] Moreover, BNP was able to predict chronic atrial fibrillation after VVIR pacemaker in patients with sick sinus syndrome (SSS).[17] In 2000, when the abovementioned study was published, the unfavorable effects of VVIR stimulation were not yet fully understood. Currently, rather than VVIR, SSS patients are receiving AAIR and DDDR pacemakers.

The effect of pacemaker implantation on serum concentrations of atrial natriuretic peptide was examined before.[18]

To our knowledge, little is known regarding the use of NT-proBNP in predicting the occurrence of cardiovascular events in patients receiving implantable pacemakers. This is in contrast to the population without permanent pacing devices,

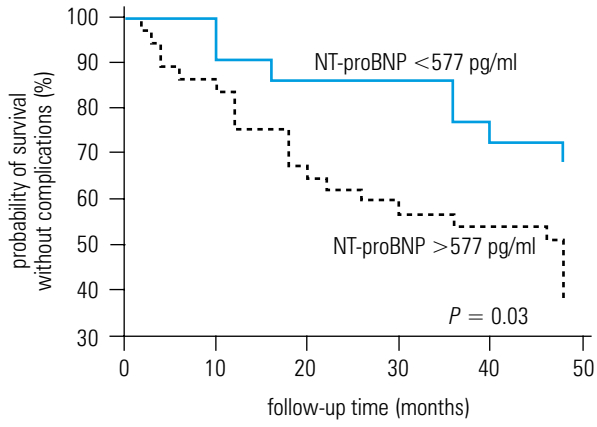

FIGURE 2 Kaplan-Meier curves reflect a probability of survival without cardiovascular event within time (months). Two curves: for NT-proBNP above and below 577 pg/ml are compared in this figure. Abbreviations: see TABLE 3

in whom such prognostic value of BNP cannot be denied.

The current study demonstrated the prognostic value of NT-proBNP in predicting cardiovascular events in patients after the implantation of cardiac pacemaker. The initial concentration of NT-proBNP was higher in individuals who later experienced a cardiovascular event. The cut-off value of the greatest accuracy in predicting such events was found at 577 pg/ml. The value of AUROC for NT-proBNP calculated in this study was significantly smaller (0.656) as compared with the values published for other populations, e.g., with heart failure (0.888).[4] This could suggest a lower discriminating value of NT-proBNP in patients with permanent pacemaker as compared to other patient populations. Nevertheless, it seems that NT-proBNP can ultimately become a useful tool in identifying permanent pacemaker patients who require more intense follow-up and prophylaxis. Some of the previously published studies confirmed this hypothesis. For example, it was shown that increased levels of BNP could be helpful in screening pacemaker patients who are at risk of developing heart failure. Indeed, among patients with BNP >151 pg/ml, 80% develop severe heart failure during a 6-year follow-up.[16]

Importantly, the mode of stimulation itself has an impact on the future occurrence of cardiovascular events. Saccomanno et al.[19] reported higher rate of such events in VVI mode as compared with DDD stimulation. Horie et al.[17] observed that the level of BNP predicts chronic atrial fibrillation in patients with VVI stimulation mode. In this case, prognostic value was only established for the BNP measured a few months after the implantation procedure. BNP levels measured prior to the procedure did not show a significant prognostic potential.

Our study clearly demonstrated prognostic value of both initial and post-implantation NT-proBNP measurements. However, in contrast to the study cited above, our assessment focused on the risk of cardiovascular events; the risk of chronic atrial fibrillation was beyond the scope of our study. Therefore, we cannot reliably compare the results of these 2 studies.

The choice of the mode of stimulation, as well as the percentage of ventricular simulation directly affects the levels of natriuretic peptides. Wu et al.[20] observed higher values of BNP in VVIR mode than in DDDR mode. Ichiki et al.[21] confirmed this observation in patients whose ventricular stimulation was above 50%. The patient groups analyzed in our study were comparable with respect to VVIR and DDDR stimulation and percentage of ventricular stimulation in each group. However, the NT-proBNP concentration measured 1 month after the procedure was significantly higher in patients with VVIR stimulation mode; moreover, during a 1-month follow-up, we observed an increase of NT-proBNP in VVIR and a decrease in DDDR population. Such results are in agreement with previously published data.[22] The differences observed in our study did not, however, reach statistical significance, possibly due to the small sample size.

Our study has several limitations. For example, the studied population sample was small, and the groups were not homogenous in respect to age, gender, and left ventricular EF, which could possibly lead to higher than expected NT-proBNP levels. Similarly, several medications that were taken by the patients are able to influence both the level of NT-proBNP as well as the prognosis, but were not analyzed in this study.

TABLE 5 Changes in NT-proBNP levels in groups with different modes of stimulation during a 1-month follow-up

Stimulation mode	Mean value ± standard deviation		*P*
	NT-proBNP (pg/ml)	$NT\text{-}proBNP_{1month}$ (pg/ml)	
VVIR (n = 26)	1616 ±1347	2564 ±3184	NS
DDDR (n = 20)	1507 ±2849	896 ±1029	NS

Abbreviations: see TABLES 1, 3, and 4.

TABLE 6 Changes of NT-proBNP levels in groups with different indications for the pacemaker implantation during a 1-month follow-up

Indications	Mean value ± standard deviation		*P*
	NT-proBNP (pg/ml)	$NT\text{-}proBNP_{1month}$ (pg/ml)	
AV block (n = 18)	2142 ±3015	2086 ±3816	NS
SSS (n = 18)	939 ±895	1294 ±1150	NS
AF-bradycardia (n = 10)	1668 ±1433	2374 ±1687	NS

Abbreviations: see TABLES 1, 3, and 4.

Clinical implications Despite some limitations, our study suggests that NT-proBNP measured prior to and after the implantation of a pacemaker can be helpful in identifying the patient population that is at an increased risk for future cardiovascular events.

Measurements of NT-proBNP before the implantation procedure and its monitoring afterwards seems to be a valuable diagnostic option in a clinical care of patients who are scheduled for this type of procedure. The cost-effectiveness ratio does not seem to be too high for this particular analytical test.

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ARTYKUŁ ORYGINALNY

Wartość rokownicza stężenia NT-proBNP u chorych poddanych zabiegowi implantacji układu stymulującego serca

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SŁOWA KLUCZOWE

incydenty sercowo-naczyniowe, niewydolność serca, NT-proBNP, rozrusznik serca

STRESZCZENIE

WPROWADZENIE W licznych pracach wykazano, że N-końcowy fragment peptydu natriuretycznego typu B (NT-proBNP) ma wartość rokowniczą w różnych populacjach chorych. Pacjenci ze wskazaniami do implantacji rozrusznika serca są obciążeni dużym ryzykiem wystąpienia incydentów sercowo-naczyniowych. Dotychczas powstało niewiele prac oceniających wartość rokowniczą NT-proBNP w tej grupie pacjentów.

CELE W niniejszym badaniu podjęto próbę wykazania znaczenia rokowniczego stężenia NT-proBNP w grupie osób zakwalifikowanych do zabiegu implantacji kardiostymulatora.

PACJENCI I METODY Badaniem objęto 59 pacjentów w wieku 79,8 ±6,3 roku ze wskazaniami do implantacji kardiostymulatora. U każdego pacjenta w dniu przyjęcia dokonywano pomiaru stężenia NT-proBNP, a w podgrupie 46 pacjentów oznaczano również stężenie NT-proBNP po miesiącu od zabiegu. Osoby badane poddano 4-letniej obserwacji. Oceniano występowanie incydentów sercowo-naczyniowych (punktu końcowego). Następnie zbadano zależność między wyjściowym stężeniem NT-proBNP i stężeniem NT-proBNP uzyskanym po miesiącu a ryzykiem wystąpienia punktu końcowego (grupa osób z punktem końcowym *vs* grupa bez punktu końcowego).

WYNIKI U pacjentów, u których wystąpił incydent sercowo-naczyniowy, wyjściowe stężenie NT-proBNP i wartość NT-proBNP uzyskana po miesiącu od zabiegu (NT-proBNP$_{1msc}$) była istotnie większa w porównaniu z pacjentami, u których nie obserwowano punktu końcowego (odpowiednio, NT-proBNP: 2310,6 ±2657,7 pg/ml *vs* 1177,6 ±1364,6 pg/ml; p<0,02; NT-proBNP$_{1msc}$: 2538 ±3341,4 pg/ml *vs* 1139,4 ±1294,1 pg/ml; p <0,03). Wyjściowe stężenie NT-proBNP wynoszące 577 pg/ml charakteryzowało się największą trafnością w przewidywaniu wystąpienia incydentów sercowo-naczyniowych w trakcie 4-letniej obserwacji (czułość 77% i swoistość 52%).

WNIOSKI Stężenie NT-proBNP oznaczone w dniu zabiegu i miesiąc po zabiegu implantacji rozrusznika serca może być pomocne w identyfikacji pacjentów zagrożonych większym ryzykiem wystąpienia incydentu sercowo-naczyniowego w przyszłości. Stężenie wyjściowe NT-proBNP 577 pg/ml wydaje się dobrym punktem odcięcia dla prognozowania tych incydentów.

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Praca wpłynęła: 29.01.2010.
Przyjęta do druku: 23.03.2010.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2010; 120 (4): 120-126