Původní sdělení | Original research article

NT-proBNP as predictive factor for the conversion of paroxysmal atrial fibrillation of heart to sinus rhythm in non-diabetic and diabetic populations

Jarmila Harvanová[a], Roman Beňačka[b], Alexander Hudák[c]

[a] *I. Internal Clinic, University Hospital L. Pasteur Košice, Košice, Slovak Republic*
[b] *Institute of Pathological Physiology, Faculty of Medicine, P.J. Šafarik, University in Košice, Košice, Slovak Republic*
[c] *Department of Chemistry, Biochemistry and Biophysics,University of Veterinary Medicine and Pharmacy in Košice, Košice, Slovak Republic*

ARTICLE INFO

Article history:
Received: 2. 12. 2018
Accepted: 2. 3. 2019
Available online: 24. 7. 2019

Kľúčové slová:
Diabetik
Fibrilácia predsiení
Hodnota NT-proBNP
Konverzia rytmu

SÚHRN

Úvod: Fibrilácia predsiení je dnes považovaná za najčastejšie sa vyskytujúcu arytmiu. Hodnota NT-proBNP je preukázateľne zvýšená u pacientov s fibriláciou predsiení, a to aj bez dokumentovaného srdcového zlyhávania. Asociácia medzi výškou koncentrácie NT-proBNP a konverziou fibrilácie predsiení na sínusový rytmus nebola doteraz preukázaná a nie je jasné, či takáto súvislosť vôbec existuje.
Cieľ: Cieľom štúdie je analyzovať spojitosť medzi výškou koncentrácie NT-proBNP a konverziou fibrilácie predsiení a poukázať na možnú prediktívnu hodnotu tohto markera v súvislosti s konverziou rytmu.
Materiál a metodika: V súbore bolo sledovaných celkovo 96 pacientov (50 % diabetikov) bez dokumentovaného srdcového zlyhávania, s paroxyzmom fibrilácie predsiení v trvaní do 24 hodín. U všetkých pacientov bol realizovaný odber venóznej krvi na stanovenie výšky koncentrácie NT-proBNP. Následne boli rozdelení do dvoch skupín (diabetici a pacienti bez diabetu), v každej skupine boli zaznamenané priemerné hodnoty NT-proBNP, pri ktorých došlo ku konverzii rytmu. V ďalšom sledovaní boli zhodnotení všetci účastníci štúdie, bez ohľadu na prítomnosť diabetu.
Výsledky: Nízke hodnoty NT-proBNP majú pozitívnu prediktívnu hodnotu v predikcii konverzie rytmu (priemerná hodnota 678,8 ± 936,6 ng/l pri úspešnej konverzii) a ďalší nárast NT-proBNP je spojený s nižšou pravdepodobnosťou konverzie (priemerná hodnota 2 597,5 ± 2 300,4 ng/l pri neúspešnej konverzii). U 45 pacientov bola zaznamenaná spontánna konverzia na sínusový rytmus, u 51 pacientov ku konverzii rytmu nedošlo. V tomto sledovaní sme dosiahli štatistickú významnosť v predikcii konverzie na základe hodnôt NT-proBNP ($p < 0,001$). U diabetikov nebola zaznamenaná priekazná závislosť medzi koncentráciou NT-proBNP a konverziou rytmu. 37,5 % diabetikov s priemernou hodnotou NT-proBNP 824,1 ± 1 338,0 ng/l dosiahlo konverziu rytmu, u 62,5 % diabetikov s priemernou hodnotou 1 807,3 ± 1 875,3 ng/l pretrvávala fibrilácia predsiení ($p = 0,149$).
Záver: Dosiahnuté výsledky poukazujú na potenciálne prognostické hľadisko koncentrácie NT-proBNP na konverziu rytmu u pacientov s paroxyzmálnou fibriláciou predsiení. Sú však potrebné ďalšie štúdie, ktoré by bližšie objasnili mechanizmy uvedených javov a našli ďalšie využitie v klinickom výskume.

ABSTRACT

Introduction: Atrial fibrillation is considered today as the most common arrhythmia. The NT-proBNP level is provably elevated in patients with atrial fibrillation in atrium of heart, even without documented heart failure. The association between NT-proBNP level and the conversion of atrial fibrillation to sinus rhythm has not been proved so far, and it is unclear whether such a link exists at all.
Objective: The aim of the study is to analyze the relationship between NT-proBNP levels and the conversion of atrial fibrillation and to point to the possible predictive value of this marker in relation to rhythm conversion.
Material and methods: A total number of 96 patients (50% of diabetics) with no documented cardiac failure, with paroxysmal atrial fibrillation lasting up to 24 hours, were monitored. In all patients, venous blood was collected to determine the level of NT-proBNP. Subsequently, the patients were divided into two groups (diabetics and non-diabetic patients), with mean NT-proBNP values recorded in each group in which the rhythm conversion occurred. In the follow-up examination all participants of the study were evaluated, regardless of the presence of diabetes.

Address: MUDr. Jarmila Harvanová, I. Internal Clinic, University Hospital L. Pasteur Košice, Rastislavova 43, 040 01 Košice, Slovak Republic, e-mail: jarka.harvanova@gmail.com
DOI: 10.33678/cor.2019.044

Please cite this article as: Harvanová J, Beňačka R, Hudák A. NT-proBNP as predictive factor for the conversion of paroxysmal atrial fibrillation of heart to sinus rhythm in non-diabetic and diabetic populations. Cor Vasa 2019;61:e397–e402.

Results: Low NT-proBNP values have a positive predictive value in rhythm conversion prediction (mean value of 678.8 ± 936.6 ng/l in successful conversion), and a further increase in NT-proBNP is associated with a lower probability of conversion (mean value 2 597.5 ± 2 300.4 ng/l in unsuccessful conversion). In 45 patients spontaneous conversion to sinus rhythm was recorded, in 51 patients there was no rhythm conversion. In this observation, we achieved statistical significance in the prediction of conversion based on NT-proBNP values ($p < 0.001$). There was no evidence of dependence between NT-proBNP level and rhythm conversion in diabetics. In 37.5% of patients suffering from diabetes with the mean value of NT-proBNP 824.1 ± 1 338.0 ng/l rhythm conversion occurred, in 62.5% of patients-diabetics with an average value of 1 807.3 ± 1 875.3 ng/l atrial fibrillation in atrium of heart persisted ($p = 0.149$).
Conclusion: The results indicate the potential prognostic aspect of NT-proBNP levels for rhythm conversion in patients with paroxysmal atrial fibrillation. However, further studies are needed to clarify the mechanisms of these phenomena and to find further use in clinical research.

Keywords:
Atrial fibrillation
Diabetic
NT-proBNP value
Rhythm conversion

Introduction

Atrial fibrillation (AF), commonly occurring arrhythmia, has been the subject of increased interest and intense research in recent years. Since its first description in 1909 it has had more than a century of history, and therefore it is one of the oldest known arrhythmias.[1,2] The association of atrial fibrillation with cardiac and non-cardiac diseases is known, but it is unclear whether arterial hypertension, ischemic heart disease, diabetes mellitus and other diseases are really associated with atrial fibrillation or there is just their coincidence. The relationship between atrial fibrillation and diabetes mellitus alone has not been investigated adequately. Some authors consider diabetes mellitus to be a separate "cardiovascular disease" that is rapidly rising globally.[3,4]

The risks resulting from late diagnosis and inadequate treatment of AF are alarming, with a diabetic population particularly at risk, in which as a result of autonomic dysfunction, is an oligosymptomatic or asymptomatic course of arrhythmia. Therefore, there is a need for timely identification and targeted treatment of risk individuals. For this purpose, various peptides with endocrine, paracrine, and autocrine effects are also being investigated which would provide diagnostic value, but research in this field is in the beginning, and there is a lack of evidence from randomized studies, but lesser observational studies are already available.[5] N-terminal fragment of the pro-brain natriuretic peptide (NT-proBNP) is one of the foregoing biomarkers with a predictive and stratification value, nowadays easily available in basic laboratory diagnostics.[6,7]

The use of natriuretic peptides in the risk stratification of some cardiovascular diseases is widespread worldwide – their contribution to the prognosis of patients with heart failure is clearly demonstrated.[8] Today, there is an interest in studies whose role is to clarify the possible stratification value of NT-proBNP in acute coronary syndromes, valvular diseases and atrial fibrillation. However, these indications have not yet become valid recommendations.[9,10]

The aim of our work is to define whether the value of NT-proBNP in patients admitted to hospital ward rooms with paroxysmal fibrillation of known duration (up to 24 hours) may be a predictor of conversion to sinus rhythm (SR) in the non-diabetic population as well as in patients with type 2 diabetes without another documented serious cardiovascular disease. On the basis of the results thus obtained, our intention is to choose and individualize without delay the patient's treatment strategy (rhythm control vs. frequency control). AF is a benign arrhythmia, but it is associated with an increased risk of death, especially due to cardiovascular causes, due to stroke, left ventricular dysfunction and heart failure and, last but not least, cognitive functions decline and vascular dementia.[11,12] The results of our published work can contribute to the early and effective management of arrhythmia as such, and to a large extent avoid the above-mentioned complications.

Material and methods

The study included 96 patients from the 1st Internal Clinic of UNLP in Košice in the reference period from 1.7.2014 to 31.12.2015. Of the total number of patients, there were 52 women and 44 men. In this group, there were 48 patients with type 2 diabetes – diabetes compensation such as diet, oral antidiabetic drugs or insulin were disregarded. Table 1 shows the baseline demographic data and associated diagnoses in each patient group, Table 2 shows the baseline echocardiographic morphometric parameters of heart in the patients enrolled in the study. Data were collected prospectively – all patients who were admitted and hospitalized at the time in the First Internal Clinic with known paroxysm of atrial fibrillation in duration up to 24 hours, were enrolled in the study.

Patients with severe cardiovascular comorbidities that could affect NT-proBNP levels such as acute coronary syndrome, chronic heart failure with left ventricular systolic dysfunction, severe heart valve disease, patients with documented pulmonary hypertension, as well as patients with chronic obstructive pulmonary disease and malignant diseases were excluded from our study. Tables 3 and 4 show known cardiovascular and extracardial comorbidities affecting NT-proBNP level.

The group included patients with primomanifestation of AF, as well as patients with already documented recurrent paroxysmal form of AF in long-term antiarrhythmic treatment, with heart rate at arrhythmia having to be at least 110/min on admission – the patient met the criteria for AF with a rapid chambers response. In acute pre-hospital care he was not treated with an antiarrhythmic and bradycardiac treatment and he required hospitalization in a department providing intensive health care with continuous monitoring of vital functions.

Table 1 – Basic demographics and comorbidities of study participants	
Male/female	44/52
Patients with DM/patients without DM	48/48
Age (men/women)	71.8 ± 10.54 (67 ± 10.57/74.53 ± 9.6)
Normal blood pressure/hypertension	6/90
IHD without HF/without IHD	8/88
Obesity with BMI above 30/BMI below 30	44/52

BMI – body mass index; DM – diabetes mellitus; HF – heart failure; IHD – ischemic heart disease.

Table 2 – Echocardiographic parameters of study participants	
LV systolic function	55.5 ± 4.7%
LV with myocardial hypertrophy/without myocardial hypertrophy	81/15
Left AoH size	42.6 ± 36 mm

AoH – atrium of heart; LV – left ventricle.

Table 3 – NT-proBNP positivity for cardiovascular diseases
1. Differential diagnosis of dyspnea – cardiac versus non-cardiac etiology
2. Stratification of risk in patients with heart failure, IHD (acute and chronic forms)
3. Early diagnosis of cardiotoxicity (chemotherapy, radiotherapy)
4. Monitoring the effect of treatment of heart failure
5. Diastolic dysfunction of LV and RV
6. Heart disease – hypertrophic cardiomyopathy, infiltrating myocardial diseases (amyloidosis), myocarditis
7. Valve diseases – aortic and mitral stenosis, regurgitation
8. Rhythm disorders – atrial fibrillation, flutter

IHD – ischemic heart disease; LV – left ventricle; RV – right ventricle.

Table 4 – NT-proBNP positivity in non-cardiac diseases
1. Critical conditions – bacterial sepsis (G-), burns, ARDS
2. Ischemic stroke
3. Anemia
4. Pulmonary diseases – sleep apnea, pulmonary embolism, pulmonary hypertension, asthma, pneumonia, lung cancer, COPD
5. Diabetes mellitus type 1 and type 2

ARDS – acute respiratory distress syndrome; COPD – chronic obstructive pulmonary disease.

Table 5 – Cut-off value of NT-proBNP in standard laboratory conditions	
Norm of NT-proBNP A: female B: male	5–125 ng/l < 150 ng/l < 100 ng/l
To confirm the diagnosis of heart failure A: age < 50 years B: age 50–75 years C: age > 75 years	from 450 ng/l to 35 000 ng/l > 450 ng/l > 900 ng/l > 1 800 ng/l

In patients who met the inclusion criteria, venous blood sampling was performed immediately upon admission to the hospital to determine the baseline biochemical parameters and NT-proBNP cut-off levels in Table 5 (we also took into account the level of potassium as a potential trigger and its possible contribution to the conversion of arrhythmia – the parameter, however, did not reach statistical significance in the monitored group). The patients were placed on the beds of the intensive care unit for continuous bedside rhythm monitoring with the possibility of accurately recording the time of eventual conversion to sinus rhythm. The medication administered to the patient in the monitored group included bradycardia treatment (beta-blocker, digoxin, or their combination), anticoagulation therapy, in case of need potassium-surrogate treatment and chronic therapy used by the patient – most commonly hypotensive, antidiabetic drugs, and hypolipidemics. During the follow-up monitoring, no antiarrhythmic drugs were administered to patients for 48 hours. After this time interval, the monitoring was terminated, the success rate of conversion to sinus rhythm was recorded in each patient, and if necessary, an acute pharmacological or electrical cardioversion was performed, or a delayed strategy of rhythm control was selected – elective cardioversion after prior treatment with antiarrhythmic drug in long-term suitable anticoagulant therapy (only if in the patient in whom the attempt for acute cardioversion was unsuccessful).

Statistical analysis and results

The arithmetic mean and standard deviation (SD) were used for data analysis. To test the differences in quantity variations the chí-kvadrat test was used, for testing the differences of quantitative variables the Student T-test was used. The result was considered statistically significant at p-value ≤ 0.05.

In this group, 96 patients with a paroxysmal form of AF were evaluated of known duration up to 24 hours, of which 52 were women aged 74.5 ± 9.6 years and 44 men aged 67 ± 10.6 years. Of the total number of patients, 50% were diabetics, type 2. For each patient, an NT-proBNP level was recorded, determined from venous blood immediately at the time of admission into the hospital, with an average level of 1 698.1 ± 2 029.3 ng/l. In the diabetic group (DM patients), the mean value NT-proBNP was 1 430.8 ± 1 742.3 ng/l, in the non-diabetic population 1 954.5 ± 2 029.3 ng/l (Fig. 1).

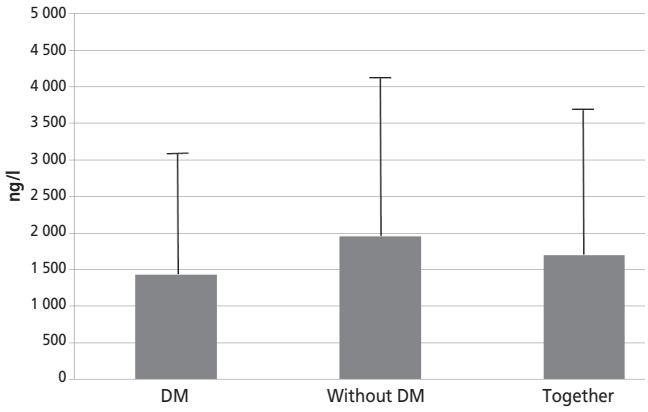

Fig. 1 – Graphic representation of mean NT-proBNP values in ng/l in each subgroup of the group. Patients with DM (diabetes mellitus) with NT-proBNP 1 430.8 ± 1 742.3 ng/l, patients without DM with NT-proBNP 1 954.5 ± 2 029.3 ng/l, mean NT-proBNP in the whole patient population 1 698.1 ± 2 029.3 ng/l.

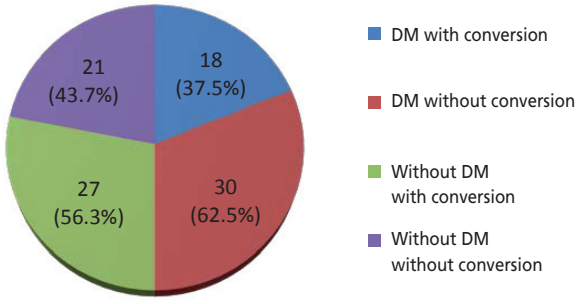

Fig. 2 – The success of rhythm conversion in individual file groups. In each section of the graph the numbers of patients, expressed in percentage values, are shown.

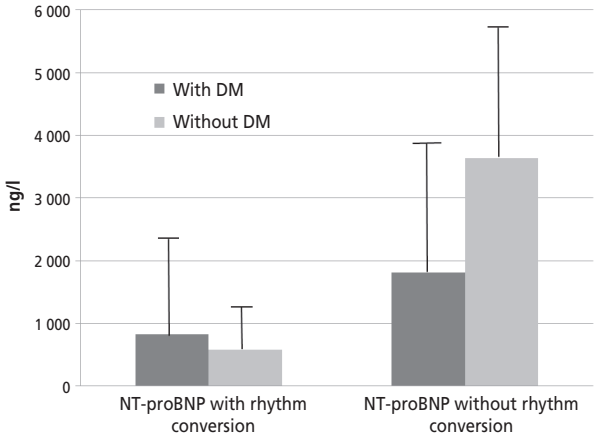

Fig. 3 – Rate of rhythm conversion dependence on the level of NT-proBNP. Patients without DM with achieved rhythm conversion, with the mean value of NT-proBNP of 581.9 ± 538.2 ng/l, patients without DM, without rhythm conversion with an average NT-proBNP of 3 639.1 ± 2 431.5 ng/l. DM patients with achieved rhythm conversion with mean value NT-proBNP of 824.1 ± 1 338.0 ng/l, DM patients without rhythm conversion with an average value of NT-proBNP of 1 807.3 ± 1 875.3 ng/l.

Patients were monitored for successful conversion to sinus rhythm, correlated with the measured value of NT-proBNP. After a statistical evaluation of the results, we noted in the first step that in 45 patients with an average NT-proBNP value of 678.8 ± 936.6 ng/l conversion to the sinus rhythm occurred. AF persisted in 51 patients with an average value of NT-proBNP 2 597.5 ± 2 300.4 ng/l, regardless of the presence of diabetes. The level of statistical significance reached the value of $p < 0.001$. From the above results it can be concluded that low NT-proBNP levels at the time of AF paroxysm duration have a significant predictive value of conversion to sinus rhythm, and the increasing NT-proBNP value reduces this probability.

In the second step, we have statistically analyzed the success rate of rhythm conversion in particular in diabetic and non-diabetic populations. In this group, successful rhythm conversion was recorded in 37.5% of diabetics with an average NT-proBNP value of 824.1 ± 1 338.0 ng/l, while in 62.5% of diabetics with an average value of NT-proBNP 1 807.3 ± 1 875.3 ng/l AF continued.

In the nondiabetic group, a rhythm conversion occurred in 56.3% of patients with an average NT-proBNP of 581.9 ± 538.2 ng/l and AF persisted in 43.7% of patients with an average value of NT-proBNP of 3 639.1 ± 2 431.5 ng/l (Figs 2, 3). In this part of the analyzed population, the result did not reach a statistically significant predictive value ($p = 0.149$), and therefore it can be concluded that in the subpopulation of diabetics alone the level of NT-proBNP does not significantly affect the success rate of AF conversion to sinus rhythm. It follows from this that the presence of diabetes as risk comorbidity does not improve the predictive effect of NT-proBNP in rhythm conversion.

Discussion

Several studies have recently been carried out that have shown significant increases in NT-proBNP also in cardiac compensated atrial fibrillation patients, with its average values around 800–1 100 ng/l.[13,14] After the sinus rhythm resumes its level is rapidly decreasing. The decrease in NT-proBNP levels after the version to sinus rhythm cannot be attributed to a fall in heart rate because the correlation between heart rate and NT-proBNP level before and after the conversion was not observed. In the study by Dogan et al. NT-proBNP levels were compared in patients with paroxysmal, persistent, and permanent AF, the authors conclude that the duration of arrhythmia had an effect on NT-proBNP levels, i.e., patients with persistent and permanent atrial fibrillation had higher NT-proBNP levels than patients with paroxysmal form. However, they also point to another published study in which the NT-proBNP levels were comparable in all of the above-mentioned forms of arrhythmia.[15,16]

Only patients with a paroxysmal form of AF with a known duration of 24 hours were included in our group, with NT-proBNP levels reaching a relatively large numerical range (1 698.1 ± 2 029.3 ng/l), which is related to laboratory variation of values of this parameter in the range of several thousand ng/l (max. measurable value is 35 000 ng/l in laboratory conditions), but without significant impact on the clinical manifestations of the patient. At the same

time, the difference in mean values of NT-proBNP between diabetic and non-diabetic patients (1 430.8 ± 1 742.3 ng/l vs. 1 954.5 ± 2 029.3 ng/l) was observed despite the fact that several retrospective observations, which were performed in the diabetic population, in which were monitored values of NT-proBNP in the group without AF as well as in diabetic patients with documented arrhythmia, pointed to elevated levels of NT-proBNP in diabetics.[17,18]

We can explain the above results to some extent on the principle of gradually progressive structural remodeling of atriums of heart in diabetics. Hyperglycemia contributes to excessive formation of reactive oxygen radicals (superoxide, peroxynitrate and others) due to increased glucose oxidation in the insulin resistance environment.

Likewise, hyperglycemia-supported protein glycation and the formation of AGEs (Advanced Glycation End-products) also promote the onset and development of inflammation in the myocardium, thereby stimulating further accumulation of fibrosis in myocardial interstitium. Such a fibrotically altered left atrium cannot promptly respond to changing hemodynamic conditions, i.e., transient volumetric and pressure overload of the atrium in the resulting AF, which present a stimulus to the secretion of natriuretic peptides.

Therefore, the increase in NT-proBNP level in AF on the diabetic heart is slower and reaches quantitatively lower values than in non-diabetic patients. NT-proBNP values in diabetics in our group achieved smaller numerical dispersion and therefore did not appear to be a suitable conversion marker in this population. Healthy myocardium of the left atrium reacts to short-term overload with "watch and wait", meaning that it has well-developed compensation mechanisms, and does not activate NT-proBNP synthesis, or is synthesized only in small amounts. Consequently, the AF conversion on a healthy atrium takes place without the need of more complex pharmacotherapy, and the sinus rhythm is more stable. In our group there are patients with a relatively low mean NT-proBNP level. However, in patients with paroxysmal form of AF without diabetes, due to structural remodeling of the myocardium of left atrium, progressive fibrosis may also occur, but its myocardium does not cope with the complications described above, caused by hyperglycemia.

The rate of fibrosis and its progression is therefore lower in non-diabetics. Such a structurally altered atrium responds to volume and pressure overload in acute attack by AF – synthesis of NT-proBNP measurable in high-values but with respect to the altered atrial myocardium there is already a conversion with the need for pharmacological intervention.

In other words, we could divide the patients involved in our study, into three groups:

1. Without predicted structural damage to the left atrial myocardium, with good adaptability to overload, those, who have low NT-proBNP values in AF paroxysm with a tendency to spontaneous rhythm conversion.
2. With onset or moderate involvement of left atrium myocardium which, due to sufficient functional reserve of atrial cardiomyocytes, synthesizes NT-proBNP at high levels, while for rhythm conversion a therapeutic intervention is required.
3. With more progressive changes in atrial myocardium, whose ability to react to overload is limited to a certain degree, which in laboratory condition appears as measurement of NT-proBNP in the so-called gray zone – without significant variability from very low to very high values, without the possibility of unambiguous determination of the success of rhythm conversion (there is an interference with NT-proBNP measurements with patients in the first and second groups).

Conclusion

Natriuretic peptides affect the function of cardiovascular system due to multiple endocrine paracrine and autocrine effects and belong to the markers with high diagnostic and prognostic potential from all, up to now monitored, laboratory indicators of myocardial function.[19] Each introduction of a new biomarker into practice brings the temptation to use it as much as possible, either as a marker to eliminate certain condition (a rule-out diagnostics, use of a negative predictive value of a test), for confirmation of a diagnosis (rule-in diagnostics, use of a positive predictive test value) and to monitor the clinical status or success of the therapy.[20] The advantage of NT-proBNP over BNP is, in addition to longer biological half-life, a lesser influence by physical activity and lower intra-individual variability, i.e., level fluctuations in the individual, allowing to obtain stable results in his evaluation.

Our study pointed to the possibility of using NT-proBNP monitoring as a marker of possible AF conversion to sinus rhythm. In conclusion we can state that in patients without a more serious cardiovascular comorbidity and low NT-proBNP level (on average 678.8 ± 936.6 ng/l), we register that spontaneous conversion of AF to sinus rhythm is more frequent than in patients with high NT-proBNP (on average 2 597.5 ± 2 300.4 ng/l) ($p < 0.001$), with the difference in this laboratory parameter beginning to be significant with a distinction normally of several thousand ng/l. Statistically significant results were not recorded in this respect in the diabetic group ($p = 0.149$), therefore the very presence of this diagnosis is not considered to be indicative of predicting the success of rhythm conversion.

In our treatment group, patients with a lower value of NT-proBNP were clinically highly presumed to convert AF to sinus rhythm with a high probability of its maintenance, and a low risk of recurrent arrhythmia. From our results, it is possible to assume that patients with paroxysmal AF, whose measured values of NT-proBNP were higher, do not achieve spontaneous rhythm conversion, there is a higher risk of recurrent arrhythmia and its transition to persistent or permanent form. These patients require targeted and long-term antiarrhythmic treatment, potent thromboprophylaxis therapy, and rigorous dispensary care to detect the recurrence of a symptomatic, eventually asymptomatic form of AF early on.

The limitation of our study is a relatively small number of participants, as well as an insufficient characterization and fragmentation of patients with AF. In spite of this, we consider the results we achieved a significant contribution for everyday clinical practice, e.g. "Triage" of patients

in that, on the basis of the evaluation of one biochemical parameter, the AF treatment strategy can be determined without delay and so to define the patients with a high risk of persistence or recurrence of arrhythmias.

In the clinical context, we can make the therapeutic options for influencing AF more effective – to choose an effective antiarrhythmics, timely optimize the need for dose-uptitration, bradycardia treatment, eventually initiate early and effective anticoagulation therapy in the prevention of thromboembolic complications of AF.

Finally, we would like to emphasize that despite the limitations of our study, we have pointed out to some new and interesting facts related to the potential use of the marker – which has long been considered a selective indicator of heart failure, which presents further possibilities for clinical use and especially space and perspectives in further research.

Conflict of interest
None.

Funding body
None.

Ethical statement
The authors state that the publication was made in accordance with ethical standards.

References

1. Samol A, Masin M, Gellner R. Prevalence of unknown atrial fibrillation in patients with risk factors. Europace 2013;15:657–662.
2. Táborský M. Fibrilace síní. Praha: Mladá fronta, 2012:300.
3. Chlup R, Navrátilová L, Řehořová J, et al. Programová léčba diabetu. Praha: Galén, 1996:196.
4. Murín J. Diabetes a srdcové zlyhávanie. Cardiology Lett 2012;21:493–501.
5. Govindan M, Borgulya G, Kiotsekoglou A, et al. Prognostic value of left atrial expansion index and exercise-induced change in atrial natriuretic peptide as long-term predictors of atrial fibrillation recurrence. Eur Heart J 2012;14:1302–1310.
6. Bálková O. Mezinárodní panel expertů: stanovení NT-proBNP v klinické praxi. Labor Aktuell 2008;2:18–25.
7. Pudil R. 5th International symposium on NT-proBNP. Labor Aktuell 2007;3:20–22.
8. Murín J. Nátriuretické peptidy a srdcové zlyhávanie. Interná med 2016;16:199–202.
9. Lesný P, Goncalvesová E, Význam BNP a NT-proBNP pri predikcii kardiovaskulárneho rizika. Kardiol Prax 2007;5:185–188.
10. Murín J, Pernický M, Compagnon R. Srdcové zlyhávanie a predsieňová fibrilácia – častá a nedobrá kombinácia ochorení. Interná med 2016;16:258–261.
11. Griffin WF, Salahuddin T, O'Neal WT, et al. Peripheral arterial disease is associated with an increased risk of atrial fibrillation in the elderly. Europace 2016;18:794–798.
12. Yubi L, Hairui L, Xianwu L, et al. Mechanism of and therapeutic strategy for atrial fibrillation associated with diabetes mellitus. The Scientific World Journal 2013;1:31–36.
13. Pokorná V, Jurkovičová O, Kalužay J, et al. Zmeny hladín NT--proBNP u pacientov s fibriláciou predsiení v súvislosti s verziou na sínusový rytmus. Cardiology Lett 2011;20:396–401.
14. Richards M, Di Somma S, Mueller C, et al. Atrial fibrillation impairs the diagnostic performance of cardiac natriuretic peptides in dyspneic patients. JACC Heart Fail 2013;1:192–199.
15. Hailong C, Lei X, Yanhu W, et al. Natriuretic peptides and right atrial fibrosis in patients with paroxysmal versus persistent atrial fibrillation. Peptides 2010;31:1531–1539.
16. Dogan A, Gedikli O, Ozaydin M, et al. Plasma renin activity and pro-B-type natriuretic peptide levels in different atrial fibrillation types. Anadolu Kardiyol Derg 2010;10:317–322.
17. Pfister R, Sharp S, Luben R, et al. Mendelian Randomization study of B-type natriuretic peptide and type 2 diabetes: Evidence of casual association from population studies. PLoS Medicine 2011;8:1–11.
18. Sahu A, Gupta T, Kavishwar A, et al. Diagnostic role of NT-proBNP in diabetes type 2 patients associated with cardiovascular disease risk, a study from Central India. J Medicine 2010;11:33–38.
19. Murín J, Rajecová O, Daňová K. Natriuretic peptides and heart failure – useful in early diagnosis. Cardiology Lett 2014;23:348–352.
20. Jabor A. Natriuretické peptidy: méně tradiční úvahy o roli NT-proBNP (a BNP) v kontextu klinického stavu pacienta. Labor Aktuell 2012;1:18–23.