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NATRIURETIC PEPTIDES-GUIDED THERAPY IN CHRONIC HEART FAILURE: RELEVANCE TO OUTCOMES AND SURVIVAL

The review is devoted to a discussion of modern strategy of guided chronic heart failure therapy and possible prospects for improved survival of patients through the timely correction of pharmacotherapy depends on the dynamics of the circulating levels of brain natriuretic peptides. The prospects of using serial measurements of circulating levels of both brain natriuretic peptide (BNP) and NT-pro-BNP to assess the immediate and long-term prognosis for patients with chronic heart failure, including outpatients and those admitted for urgent indications of different age groups. The possible advantages and limitations for the cardiovascular system arising from the functional activation of natriuretic peptides in CHF patients are also discussed. The results of randomized clinical trials and meta-analyzes that devoted guided therapy of chronic heart failure are discussed.

Keywords: heart failure, cardiovascular risk, brain natriuretic peptides, guided therapy, outcomes.

Chronic heart failure (CHF) represents the leading cause of cardiovascular morbidity and mortality in worldwide [26]. The possibility of timely diagnosis and modern treatment allow significantly improve both immediate and long-term prognosis of this disease [16]. However, five-year survival among patients with symptomatic heart failure remains low, despite all the advances in modern medicine [32]. Even getting of optimal CHF therapy is not guarantee from the occurrence of acute decompensated CHF, sudden cardiac death, fatal arrhythmias, urgent hospitalization due to CHF or other cardiovascular reasons [29]. Understanding of CHF has progressed from the concept of a purely hemodynamic disorder to that of a syndrome that results from dysfunction in interconnected molecular pathways [18]. As a result, the focus of research investigations and clinical care has shifted to measurement and modification of maladaptive molecular processes [3]. In this regard, significant efforts to identify biological markers that reflected several edges of biochemical processes and the risk of clinical outcomes in CHF patients were used. The review is dedicated discussion for an overview of biomarker-guided clinical trial results, and consideration of the therapeutic potential of a natriuretic peptides-based strategy in CHF.

The natriuretic peptides and heart failure

Atrial natriuretic peptide (ANP) and brain (or B-type) natriuretic peptide (BNP) are neurohormones secreted predominantly from cardiomyocytes in response to atrial or ventricular wall stretch and intracardiac volume loading [4]. The natriuretic peptides have a fundamental role in

cardiovascular remodeling, volume homeostasis, and the response to myocardial injury. BNP is considered a counterregulatory hormone to angiotensin II, norepinephrine, and endothelin, having vasodilatory and diuretic effects [34]. The precursor of BNP is pro-BNP, stored in secretory granules in myocytes. Pro-BNP is split by a protease enzyme into BNP and N-terminal pro-BNP (NT-pro-BNP) [6]. It has investigated that BNP can easily be measured in plasma. It has suggested that the compensatory activity of the cardiac natriuretic peptide system is attenuated as mortality increases in chronic CHF patients with high plasma levels of ANP and BNP [20]. However, BNP and NT-pro-BNP are more useful than ANP for diagnosis and management of acute decompensated CHF [38]. Among patients with CHF, concentrations of natriuretic peptides are strongly linked to the presence and severity of structural heart disease and are strongly prognostic in this setting [24, 35]. The current guidelines for CHF management indicate that evidence supports the use of natriuretic peptides for the diagnosis, staging, making hospitalization and / or discharge decisions, and identifying patients at risk for clinical events [21, 40]. Because about 50% of individuals with left ventricular systolic dysfunction are asymptomatic, BNP level has been evaluated for this purpose [7]. At current time measurement of plasma concentrations of B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) is useful to rule-out diagnosis and to predict prognosis of CHF patients [37]. The evidence for their use in monitoring and adjusting drug therapy is less clearly established [36].

The principles of the natriuretic peptides-guided therapy in chronic heart failure

Standard CHF care has substantial opportunity for improvement outcomes in patients affected by the disorder. Unfortunately, physical signs and symptoms of heart failure lack diagnostic sensitivity and specificity, and medication doses proven to improve mortality in clinical trials are often not achieved [27]. Natriuretic peptide-guided CHF therapy has recently been given a recommendation in USA CHF guidelines to achieve guideline-directed medical therapy (Class IIa) and possibly improve outcome (Class IIb), while other clinical practice guidelines (including those from the European Society of Cardiology) await results from emerging clinical trial data [21, 40]. Experience gained in biomarker-guided CHF trials suggests that the approach results in improvement in the quality of care without an excess of adverse events related to more aggressive management [1]. Additionally, favorable reduction in the concentration of BNP and NT-pro-BNP may be seen during treatment of CHF, with parallel improvement in short- and long-term prognosis. Given these issues, there is increasing interest in harnessing cardiovascular biomarkers for clinical application to more effectively guide diagnosis, risk stratification, and further therapy [11]. It may be possible to realize an era of personalized medicine for CHF care in which therapy is optimized and costs are controlled and, probably, reduced [3].

Serial natriuretic peptide measurements as a useful predictive tool in chronic heart failure management

Recently it has been found that the natriuretic peptides are important tools to establish diagnosis and prognosis in CHF. With application of therapies for CHF, changes in both BNP and NT-pro-BNP parallel the benefits of the CHF therapy might be applied [33]. Overall, it has been asserted that serial measurements of natriuretic peptides could help modulate more accurately the intensity of drug treatment in patients with CHF [13]. Short-term therapeutic studies of inpatients have largely resulted in a statistically significant decline in BNP and NT-pro-BNP with clinical evidence of patient improvements [39]. In contrast, many therapeutic studies involving long-term outpatient monitoring have produced changes in BNP/NT-pro-BNP that do not exceed the biologic variances. Nevertheless, strategy of monitoring NT-pro-BNP and BNP to guide therapy cannot be universally advocated because there are still several open questions about the presumed role of natriuretic peptides-guided pharmacologic adjustment as a valuable strategy in this setting [10, 22].

Results of the most important clinical trials devoted BNP-guided therapy

The use of plasma levels of natriuretic peptides to guide treatment of patients with CHF has been investigated in a number of randomized controlled and retrospective clinical trials, however, results of them were closely controversial and the benefits have been high variable. It has found that BNP-guided therapy was not better than expert's clinical assessment for beta-blocker titration in CHF patients [5]. In a retrospective study, O'Neill J. O., Bott-Silverman C. E., McRae A. T. 3rd. et al. (2005) analyzed serial BNP levels in patients receiving hemodynamically guided therapy for severe CHF [25]. Authors concluded that in patients with severe heart failure, BNP levels do not accurately predict serial hemodynamic changes. In the recent Pro-BNP Outpatient Tailored Chronic Heart Failure Therapy (PROTECT) study, patients treated with biomarker-guided care also had improved quality of life and significantly better reverse remodeling on echocardiography compared with patients who received standard care [12]. A multicenter randomized pilot trial STARBRITE was tested whether outpatient diuretic management guided by BNP and clinical assessment resulted in more days alive and not hospitalized over 90 days compared with clinical assessment alone [30]. There was no significant difference in number of days alive and not hospitalized (hazard ratio=0.72; 95% confidence interval [CI]=0.41–1.27; P=0.25), change in serum creatinine, or change in systolic blood pressure. BNP strategy was associated with a trend toward a lower blood urea nitrogen (24 mg/dL versus 29 mg/dL; P=0.07); BNP strategy patients received significantly more angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and the combination of ACE inhibitor or angiotensin receptor blocker plus beta-blockers [30]. Karlström P., Alehagen U., Boman K., Dahlström U. (2011) did not confirm improving morbidity and mortality in CHF patients by treatment guided by BNP levels [15]. However, in the study authors found that BNP responders had a significantly better clinical outcome than non-responders.

The long-term prognostic impact of a therapeutic strategy using plasma brain natriuretic peptide levels was evaluated in STARS-BNP Multicenter Study [14]. A total of 220 New York Heart Association functional class II to III patients considered optimally treated with ACE inhibitors, beta-blockers, and diuretics by CHF specialists were randomized to medical treatment according to either current guidelines (clinical group) or a goal of decreasing BNP plasma levels <100 pg/ml (BNP group). The primary combined end point was CHF-related death or hospital stay for CHF. During follow-up (median 15 months), significantly fewer patients reached the combined end point in the BNP group (24%

versus 52%, $p < 0.001$) [14]. Noted, that the result mentioned above was mainly obtained through an increase in ACE inhibitors and beta-blocker dosages. Later in TIME-CHF trial was found that in contrast to CHF with reduced left ventricular ejection fraction (LVEF), NT-pro-BNP-guided therapy may not be beneficial in CHF with preserved LVEF [19].

Results of the retrospective case-control study presented by De Vecchis R. et al (2013) have showed that a fall in BNP on the fifth day after admission was found to be a predictor of a decreased risk of the composite endpoint «death or new hospitalization, CHF-related» (hazard ratio=0.1508; 95% CI: 0.049 to 0.463; $P=0.001$). On the other hand, low glomerular filtration rate at admission (<60 mL/min/1.73 m²) was associated with increased risk of the abovementioned endpoint (hazard ratio=7.1785; 95% CI: 1.574 to 32.725; $P=0.0113$). On the contrary, BNP-guided therapy was associated with a similar risk of death and/or CHF-related hospitalization, compared to the conventional clinical approach. Authors concluded that among the outpatients with previous ADHF, a substantial improvement in cardiovascular event rates could not be demonstrated in those treated with BNP-guided therapy compared with those undergoing usual, symptom-guided treatment.

There are several meta-analysis devoted an assessment of efficacy of natriuretic peptides-guided therapy of CHF. Li P., Luo Y., Chen Y. M. (2013) included 11 randomized clinical trials with a total of 2414 patients and with a mean duration of 12 months (range=3–36 months) in the meta-analysis [18]. Authors found that there was a significantly decreased risk of all-cause mortality (relative risk [RR]=0.83; 95% CI=0.69–0.99; $P=0.035$) and CHF rehospitalisation (RR=0.75; 95% CI, 0.62–0.91; $P=0.004$) in the BNP-guided therapy group. Age, baseline BNP are the major dominants of CHF rehospitalization when analyzed using meta-regression. In the subgroup analysis, CHF rehospitalization was significantly decreased in the patients younger than 70 years (RR=0.45; 95% CI=0.33–0.61; $P=0.001$), or with baseline higher BNP (≥ 2114 pg/mL) (RR=0.53; 95% CI=0.39–0.72; $P=0.001$). Thus, compared with usual clinical care, B-type natriuretic peptide-guided therapy reduces all-cause mortality and HF rehospitalization, especially in patients younger than 70 years or with higher baseline BNP.

Meta-analysis to assess the influence of natriuretic peptide-guided therapy, compared to clinically-guided therapy on clinical outcomes was performed by Savarese G. et al. (2013) [28]. Twelve trials enrolling 2,686 participants were included. Natriuretic peptide-guided therapy (either BNP- or NT-pro-BNP-guided therapy) significantly reduced all-cause mortality (Odds Ratio [OR]=0.738; 95% CI=0.596–0.913; $p=0.005$) and HF-related hospitalization (OR=0.554; 95% CI=0.399–

0.769; $p=0.001$), but not all-cause hospitalization (OR=0.803; 95% CI=0.629–1.024; $p=0.077$). When separately assessed, NT-pro-BNP-guided therapy significantly reduced all-cause mortality (OR=0.717; 95% CI=0.563–0.914; $p=0.007$) and CHF-related hospitalization (OR=0.531; 95% CI=0.347–0.811; $p=0.003$), but not all-cause hospitalization (OR=0.779; 95% CI=0.414–1.465; $p=0.438$), whereas BNP-guided therapy did not significantly reduce all-cause mortality (OR=0.814; 95% CI=0.518–1.279; $p=0.371$), HF-related hospitalization (OR=0.599; 95% CI=0.303–1.187; $p=0.142$) or all-cause hospitalization (OR=0.726; 95% CI=0.609–0.964; $p=0.077$). Thus, BNP-guided therapy did not significantly reduce both mortality and morbidity. On the other hand, improved all-cause mortality and CHF-related hospitalization rate were found in BNP-guided therapy cohorts.

Cost-effectiveness of natriuretic peptides-guided therapy of CHF

Chronic heart failure management strategies have been shown to reduce re-hospitalizations and mortality, but the costs of treatment may provoke concern in the current cost-conscious clinical setting. Recent studies showed that an introduction of BNP measurement in CHF management may be cost-effective [23, 31]. It was found that the optimal use of NT-pro-BNP guidance could reduce the use of echocardiography by up to 58%, prevent 13% of initial hospitalizations, and reduce hospital days by 12% [31]. Moreover, NT-pro-BNP-guided assessment was associated with a 1.6% relative reduction of serious adverse event risk and a 9.4% reduction in costs, translating into savings of \$474 per patient, compared with standard clinical assessment. Adlbrecht C., Huelsmann M., Berger R. et al. (2011) from Vienna (Austria) investigated a new disease management comparing usual care to home-based nurse care and a home-based nurse care group in which decision-making was based on natriuretic peptides levels [2]. Using a cost-effectiveness model authors concluded that NT-BNP-guided CHF specialist care in addition to home-based nurse care is cost effective and cheaper than standard care, whereas home-based nurse care is cost neutral. Thus, BNP-guided CHF therapy may considered high effective strategy to minimize expenditures of health care system for patients with heart failure.

Limitations of the natriuretic peptides-guided therapy of CHF

Although the pooling of data derived from the clinical trials demonstrates an overall effect of slightly significant improvement in clinical outcomes with the natriuretic peptide-guided approach, there are some relatively large stud-

ies that failed to document a significant clinical improvement in terms of mortality and morbidity using natriuretic peptide-guided strategy [9]. On the other hand, compared with standard management, biomarker-guided care appears cost effective, may improve patient quality of life, and may promote reverse ventricular remodeling. However, there is exist between randomized clinical trials and real-world practice affected implementation of natriuretic peptides guided therapy. The limitation of standard care strategies is evident from the suboptimal uptake and application of proven therapies documented in CHF registries [12, 13]. There are certain subgroups such as the elderly and subjects at low-to-moderate cardiovascular risk that may respond in a less vigorous manner to the approach of natriuretic peptides guided strategy. In certain studies patients treated with biomarker-guided care had superior outcomes when compared with standard heart failure management alone, particularly in younger study populations, in patients with left ventricular systolic dysfunction, and particularly when substantial reductions in natriuretic peptides were achieved in association with biomarker-guided care [8]. This may reflect the effects of age on

CHF therapy. Therefore, subjects at different cardiovascular risk may distinguish in responses of natriuretic peptides guided therapy. Overall, novel approach, based on biomarker serial measurements, is required serious adaptation in real clinical practice.

Conclusion

Recent studies suggested that a strategy of standard-of-care management together with a goal to suppress BNP or NT-pro-BNP concentrations leads to greater application of guideline-derived medical therapy and is well tolerated. Apart from them, a variety of novel (fibroblast-growth factor) or already used (high sensitive C-reactive protein, ST-2 protein, galectin-3) biomarkers, have been tested by small trials for heart failure management, without managing to dominate in every day care. Larger and better randomized clinical trials with high statistical power addressing the unresolved issues of natriuretic peptide-guided therapy in CHF should be provided in the future. However, it might believe that heart failure management will probably involve an algorithm using clinical assessment and a biomarker-guided approach.

References

1. Adams K.F. Jr., Felker G.M., Fraij G. et al. Biomarker guided therapy for heart failure: focus on natriuretic peptides // *Heart Fail Rev.* – 2010. – Vol. 15 (4). – P. 351–370.
2. Adlbrecht C., Huelsmann M., Berger R. et al. Cost analysis and cost-effectiveness of NT-proBNP-guided heart failure specialist care in addition to home-based nurse care // *Eur. J. Clin. Invest.* – 2011. – Vol. 41 (3). – P. 315–322.
3. Ahmad T., O'Connor C.M. Therapeutic implications of biomarkers in chronic heart failure // *Clin. Pharmacol. Ther.* – 2013. – Vol. 94(4). – P. 468–479.
4. Ancona R., Limongelli G., Pacileo G. et al. The role of natriuretic peptides in heart failure // *Minerva Med.* – 2007. – Vol. 98 (5). – P. 591–602.
5. Beck-da-Silva L., de Bold A., Fraser M. et al. BNP-guided therapy not better than expert's clinical assessment for beta-blocker titration in patients with heart failure // *Congest Heart Fail.* – 2005. – Vol. 11(5). – P. 248–253.
6. Chen H. H., Burnett J. C. Natriuretic peptides in the pathophysiology of congestive heart failure // *Curr. Cardiol Rep.* – 2000. – Vol. 2 (3). – P. 198–205.
7. Costello-Boerrigter L. C., Boerrigter G., Redfield M. M. et al. Amino-terminal pro-B-type natriuretic peptide and B-type natriuretic peptide in the general community: determinants and detection of left ventricular dysfunction // *J. Am. Coll. Cardiol.* – 2006. – Vol. 47 (2). – P. 345–353.
8. De Beradinis B., Januzzi J. L. Jr. Use of biomarkers to guide outpatient therapy of heart failure // *Curr Opin Cardiol.* – 2012. – Vol. 27 (6). – P. 661–668.
9. De Vecchis R., Esposito C., Cantatrione S. Natriuretic peptide-guided therapy: further research required for still-unresolved issues // *Herz.* – 2013. – Vol. 38 (6). – P. 618–628.
10. De Vecchis R., Esposito C., Di Biase G., Ariano C. B-type natriuretic peptide. Guided vs. conventional care in outpatients with chronic heart failure: a retrospective study // *Minerva Cardioangiol.* – 2013. – Vol. 61 (4). – P. 437–449.
11. Fiuzat M., O'Connor C. M., Gueyffier F. et al. Biomarker-guided therapies in heart failure: a forum for unified strategies // *J. Card. Fail.* – 2013. – Vol. 19 (8). – P. 592–599.
12. Januzzi J. L. Jr. The role of natriuretic peptide testing in guiding chronic heart failure management: review of available data and recommendations for use // *Arch. Cardiovasc. Dis* – 2012. – Vol. 105 (1). – P. 40–50.
13. Januzzi J. L., Troughton R. Are serial BNP measurements useful in heart failure management? Serial natriuretic peptide measurements are useful in heart failure management // *Circulation.* – 2013. – Vol. 127 (4). – P. 500–507.
14. Jourdain P., Jondeau G., Funck F et al. Plasma brain natriuretic peptide-guided therapy to improve outcome in heart failure: the STARS-BNP Multicenter Study // *J. Am. Coll. Cardiol.* – 2007. – Vol. 49 (16). – P. 1733–1739.
15. Karlström P., Alehagen U., Boman K., Dahlström U.; UPSTEP-study group. Brain natriuretic peptide-guided treatment does not improve morbidity and mortality in extensively treated patients with chronic heart failure: responders to treatment have a significantly better outcome // *Eur. J. Heart Fail.* – 2011. – Vol. 13 (10). – P. 1096–103.
16. Komajda M., Lapuerta P., Hermans N. et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey // *Eur. Heart J.* – 2005. – Vol. 26. – P. 1653–1659.
17. Li P., Luo Y., Chen Y. M. B-type natriuretic peptide-

- guided chronic heart failure therapy: a meta-analysis of 11 randomized controlled trials // *Heart Lung Circ.* – 2013. – Vol. 22 (10). – P. 852–860.
18. Liu L., Eisen H. J. Epidemiology of heart failure and scope of the problem // *Cardiol. Clin.* – 2014. Vol. 32 (1). – P. 1–8.
 19. Maeder M. T., Rickenbacher P., Rickli H. et al.; TIME-CHF Investigators. N-terminal pro brain natriuretic peptide-guided management in patients with heart failure and preserved ejection fraction: findings from the Trial of Intensified versus standard Medical therapy in Elderly patients with Congestive Heart Failure (TIME-CHF) // *Eur. J. Heart Fail.* – 2013. – Vol. 15 (10). – P. 1148–1156.
 20. Mant D., Hobbs F. R., Glasziou P. et al. Identification and guided treatment of ventricular dysfunction in general practice using blood B-type natriuretic peptide // *Br. J. Gen. Pract.* – 2008. – Vol. 58 (551). – P. 393–399.
 21. McMurray J. J., Adamopoulos S., Anker S. D. et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC // *Eur. J. Heart Fail.* – 2012. Vol. 14 (8). – P. 803–869.
 22. Miller W. L., Hartman K. A., Burritt M. F. et al. Biomarker responses during and after treatment with nesiritide infusion in patients with decompensated chronic heart failure // *Clin. Chem.* – 2005. – Vol. 51 (3). – P. 569–577.
 23. Morimoto T., Hayashino Y., Shimbo T. et al. Is B-type natriuretic peptide-guided heart failure management cost-effective? // *Int. J. Cardiol.* – 2004. – Vol. 96 (2). – P. 177–181.
 24. Nishikimi T. Clinical significance of BNP as a biomarker for cardiac disease--from a viewpoint of basic science and clinical aspect // *Nihon Rinsho.* – 2012. – Vol. 70 (5). – P. 774–784.
 25. O'Neill J. O., Bott-Silverman C. E., McRae A.T. 3rd. et al. B-type natriuretic peptide levels are not a surrogate marker for invasive hemodynamics during management of patients with severe heart failure // *Am. Heart J.* – 2005. – Vol. 149(2). – P. 363–369.
 26. Santulli G. Epidemiology of cardiovascular disease in the 21st century: updated numbers and updated facts // *J Cardiovasc. Disease.* – 2013. Vol. 1(1). – P. 1–2.
 27. Saremi A., Gopal D., Maisel A. S. Brain natriuretic peptide-guided therapy in the inpatient management of decompensated heart failure // *Expert Rev. Cardiovasc. Ther.* – 2012. – Vol. 10 (2). – P. 191–203.
 28. Savarese G., Trimarco B., DelleGrottaglie S. et al. Natriuretic peptide-guided therapy in chronic heart failure: a meta-analysis of 2,686 patients in 12 randomized trials // *PLoS One.* – 2013. – Vol. 8 (3). – P. e58287.
 29. Schou M., Gustafsson F., Videbaek L. et al.; North-Star Investigators, all members of The Danish Heart Failure Clinics Network. Extended heart failure clinic follow-up in low-risk patients: a randomized clinical trial (NorthStar) // *Eur. Heart J.* – 2013. – Vol. 34 (6). – P. 432–442.
 30. Shah M. R., Califf R. M., Nohria A. et al. The STARBRITE trial: a randomized, pilot study of B-type natriuretic peptide-guided therapy in patients with advanced heart failure // *J. Card. Fail.* – 2011. – Vol. 17(8). – P. 613–621.
 31. Siebert U., Januzzi J. L Jr., Beinfeld M. T. et al. Cost-effectiveness of using N-terminal pro-brain natriuretic peptide to guide the diagnostic assessment and management of dyspneic patients in the emergency department // *Am. J. Cardiol.* – 2006. – Vol. 98 (6). – P. 800–805.
 32. Stewart S., MacIntyre K., Hole D.J., Capewell S., McMurray J. J. More 'malignant' than cancer? Five-year survival following a first admission for heart failure // *Eur. J. Heart Fail.* – 2001. – Vol. 3. – P. 315–322.
 33. Troughton R., Michael Felker G., Januzzi J. L. Jr. Natriuretic peptide-guided heart failure management // *Eur Heart J.* – 2013. [Epub ahead of print].
 34. Tsutamoto T., Horie M. Brain natriuretic peptide // *Rinsho Byori.* – 2004. – Vol. 52 (8). – P. 655–668.
 35. Valle R., Aspromonte N., Giovinazzo P. et al. B-type natriuretic Peptide-guided treatment for predicting outcome in patients hospitalized in sub-intensive care unit with acute heart failure // *J. Card. Fail.* – 2008. – Vol. 14 (3). – P. 219–224.
 36. Vavuranakis M., Kariori M. G., Kalogeras K. I. et al. Biomarkers as a guide of medical treatment in cardiovascular diseases // *Curr. Med. Chem.* – 2012. – Vol. 19 (16). – P. 2485–2496.
 37. Wang T. J., Larson M. G., Levy D. et al. Plasma natriuretic peptide levels and the risk of cardiovascular events and death // *N. Engl. J. Med.* – 2004. – Vol. 350 (7). – P. 655–663.
 38. Worster A., Balion C. M., Hill S. A. et al. Diagnostic accuracy of BNP and NT-pro-BNP in patients presenting to acute care settings with dyspnea: a systematic review // *Clin. Biochem.* – 2008. – Vol. 41 (4–5). – P. 250–259.
 39. Wu A. H. Serial testing of B-type natriuretic peptide and NT-pro-BNP for monitoring therapy of heart failure: the role of biologic variation in the interpretation of results // *Am. Heart J.* – 2006. – Vol. 152 (5). – P. 828–834.
 40. Yancy C.W., Jessup M., Bozkurt B. et al.; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines // *J. Am. Coll. Cardiol.* – 2013. – Vol. 62 (16). – P. e147–239.

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ЛІКУВАННЯ ХРОНІЧНОЇ СЕРЦЕВОЇ НЕДОСТАТНОСТІ ПІД КОНТРОЛЕМ РІВНЯ ЦИРКУЛЮЮЧОГО НАТРІЙУРЕТИЧНОГО ПЕПТИДУ: ВПЛИВ НА КЛІНІЧНІ НАСЛІДКИ ТА ВИЖИВАНІСТЬ (огляд літератури)

Огляд присвячений обговоренню сучасної стратегії терапії хронічної серцевої недостатності під контролем серійного вимірювання циркулюючого мозкового натрійуретичного пептиду та перспективам поліпшення виживання пацієнтів шляхом своєчасної корекції фармакотерапії цього захворювання. Обговорюються перспективи використання серійних вимірювань циркулюючого рівня мозкового натрійуретичного пептиду (МНУП) і NT-pro-МНУП з метою оцінки найближчого і віддаленого прогнозу для пацієнтів з хронічною серцевою недостатністю, а саме: амбулаторних хворих та осіб, госпіталізованих за ургентними показаннями різних вікових груп. Наводяться результати основних клінічних досліджень і мета-аналізів, присвячених оцінці ефективності терапії хронічної серцевої недостатності, що проводиться під контролем вимірювання циркулюючого рівня натрійуретичних пептидів.

Ключові слова: серцева недостатність, кардіоваскулярний ризик, мозковий натрійуретичний пептид, цільова терапія, клінічні наслідки.

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ЛЕЧЕНИЕ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ ПОД КОНТРОЛЕМ УРОВНЯ ЦИРКУЛИРУЮЩИХ НАТРИЙУРЕТИЧЕСКИХ ПЕПТИДОВ: ВЛИЯНИЕ НА КЛИНИЧЕСКИЕ ИСХОДЫ И ВЫЖИВАЕМОСТЬ (обзор литературы)

Настоящий обзор посвящен обсуждению современной стратегии «целевой» терапии хронической сердечной недостаточности и возможным перспективам улучшения выживаемости пациентов путем своевременной коррекции фармакотерапии, зависящей от динамики циркулирующего уровня мозговых натрийуретических пептидов. Обсуждаются перспективы использования серийных измерений циркулирующего уровня мозгового натрийуретического пептида (МНУП) и NT-pro-МНУП с целью оценки ближайшего и отдаленного прогноза для пациентов с хронической сердечной недостаточностью, включая амбулаторных больных и лиц, госпитализированных по ургентным показаниям различных возрастных групп. Приводятся результаты основных клинических исследований и мета-анализов, посвященных оценке эффективности терапии хронической сердечной недостаточности под контролем измерения циркулирующего уровня мозгового натрийуретического пептида.

Ключевые слова: сердечная недостаточность, кардиоваскулярный риск, мозговой натрийуретический пептид, целевая терапия, клинические исходы.