



THE USEFULNESS OF B NATRIURETIC PEPTIDE IN THE ANESTHETIC PERIOPERATIVE EVALUATION

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Abstract. Cardiac failure is a frequently associated pathology in surgical diseases, both as emergency or as programmed surgery, which requires a particular approach to anesthesia, from the commencement of the anamnesis and the clinical examination. Assessment of the brain natriuretic peptide can be useful as diagnosis marker but also as prognostic element of cardiac failure, in particular of left ventricular distress; it also conveys a significant input in the differential diagnosis with acute pulmonary dyspneic pathology. An early detection of perioperative myocardial ischemia is essential to the syndrome's therapeutic approach.

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Cardiac failure is a frequently associated pathology in surgical diseases, both as emergency or as programmed surgery, which requires a particular approach to anesthesia, from the commencement of the anamnesis and the clinical examination. Assessment of the brain natriuretic peptide can be useful as diagnosis marker but also as prognostic element of cardiac failure, in particular of left ventricular distress; it also conveys a significant input in the differential diagnosis with acute pulmonary *dyspneic* pathology. An early detection of perioperative myocardial ischemia is essential to the syndrome's therapeutic approach.

Cardiac complications are cause for perioperative mortality and morbidity and are either pro-

duced by prolonged myocardial ischemia (caused by either heightened myocardial oxygen demand, or decreased oxygen supply) or by the rupture of a coronary atheroma with secondary arterial occlusion. The determining factors for heightened myocardial oxygen demand are hypertension and tachycardia induced by surgical stress, postoperative pain, the cut-off of a preexisting beta-blocking treatment or exaggerated use of inotrope-vasopressor substances. On the other hand, decreased oxygen supply is due to hypotension, vasospasm, anemia or coronary artery occlusion. Consequently we must first evaluate the preoperative myocardial function and further choose a highly effective test out of the cardiac function exploration cluster (biochemical markers of myocardial lesion, electrocardiography, myocardial perfusion scintigraphy, radionuclid ventriculography, cardiac echography). We must concomitantly address the fact that early diagnosis of perioperative cardiac complications is influenced by the use of sedatives and analgesics which have the potential of masking coronary symptomatology or inducing false positive increased values of certain

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enzymatic markers (creatinkinase and its fraction, muscle-brain creatinkinase) in the context of surgical lesion of striate muscles. The most commonly used biochemical indicators of myocardial ischiemolesion are: cardiac troponins I and T, CK, CK-MB, lactate dehydrogenase and, a recent addition, BNP (brain natriuretic peptide). BNP has gained leverage in the evaluation of prolonged perioperative myocardial ischemia because, along with its prognostic factor, the increase of its serum concentration is prompter compared to troponin dynamics. Several other studies have shown that the BNP level raises both in the occurrence of acute cardiac failure and in the right isolated cardiac failure (especially when correlated to pulmonary embolism).

B natriuretic peptide is an acid aminopeptide with hormonal role, initially detected in pig brain, in 1988, which conferred its „*cerebral natriuretic peptide*” name which is cause for confusion since this peptide plays no role whatsoever in cerebral physiopathology. It is mainly produced in the myocytes of cardiac ventricles, particularly in the left ventricle, as inactive precursor called prepro-BNP which consists of 134 aminoacids. The pro-BNP segment of 108 aminoacids is then cleaved followed by a signal peptide (26 aminoacids). In case of cardiac volume or pressure overload, pro-BNP is cleaved into BNP (32 aminoacids) which represents the C-terminal strand and is physiologically active at the time of its passing into circulation, and into an inactive peptide, NT pro-BNP (the N-terminal strand) consisting of 76 aminoacids. BNP has a double ring (circular) structure, configured by 17 aminoacids per ring and a connecting bond between two cysteine residues.

There are 3 types of natriuretic peptides, A, B and C, all of them involved in the mechanisms for maintaining volemia and sodium homeostasis.

The type A natriuretic peptide (ANP) has a similar structure to that of BNP and is mainly produced in the atriums.

BNP has the following traits:

- molecular weight 3,5 kD;
- the gene for synthesis is situated on chromosome 1's short arm;
- plasmatic half life of 20 minutes;
- it is stocked for short period of times, as opposed to ANP;
- the produced quantity increases as the organism ages, probably secondary to physiological left ventricle hypertrophy in elderly individuals. Therefore, between 55 – 64 years, the median

concentration of BNP is 26 ± 2 pg/ml and for the age group > 75 years, 64 ± 6 pg/ml. This increase has been shown to be considerably more present in women.

- BNP acts through receptor neuropeptides type A, B or C which are present in target tissues (blood vessels, heart, kidneys, cerebral tissue).
- its elimination is done through endocytosis, a process controlled by type C receptors (elimination is ensured by attachment to transmembrane receptors) and through proteolysis, a mechanism catalyzed by an endopeptidase which is present in higher concentrations in lungs and kidneys. The dual action of C neuropeptide is noticed both in degrading BNP and in the control of concentration and respective effect of BNP.
- the secondary messenger of BNP's action is GMPc – as for ANP – produced under the action of a specific guanilcyclase – the neuropeptidic receptor A.
- recent studies have revealed a diversity of molecular shapes of plasmatic BNP in patients diagnosed with cardiac failure, among which we mention the α – BNP and γ – BNP compounds. It has been established that γ – BNP is the prevailing form in patients with cardiac failure and ventricular overload, while α – BNP is the predominant form in patients with cardiac failure and atrial overload.
- The C natriuretic peptide (CNP) was later on discovered, in 1990, in the central nervous system, but is found in larger amounts in the circulatory system, precisely in the vascular endothelium where it actually originates. It has a major venous vasodilator effect but it is less natriuretic, compared to BNP.

BNP counteracts the activation of the renin – angiotensin – aldosterone system, producing inhibition of the sympathetic tonus (respectively vasodilation), increase of diuresis and implicitly, natriuresis.

Inhibition of the renin – angiotensin – aldosterone system is acquired through three mechanisms: decrease of renin release, suppression of the activity of the conversion enzyme for agiotensin and blockage of aldosterone release.

BNP also blocks the synthesis of several vasoconstrictor substances: catecholamines, angiotensin II, endothelin 1. Its vasodilating effects determine the decrease in arterial pressure, particularly in hypervolemic context; concomitantly, it increases

the rate of glomerular filtration and therefore it increases the renal excretion of sodium. BNP also has antiproliferative effect on myocytes and on smooth muscle cells. Recent studies consider BNP as part of the endogen cytoprotector mediators released in conditions of myocardial ischemia considering its intimate action mechanism to be the activation of mitochondrial potassium ATP dependent channels through GMPc dependent kinases.

Under normal or pathologic conditions, the BNP secretion is almost exclusively provided by the left ventricle since it contains a larger muscular mass than the right ventricle. BNP is released into systemic circulation through the coronary sinus. Stimulation of the secretion is made through the tensing of the left ventricle's wall. Numerous studies have shown the existence of a correlation between the New York Heart Association classification degree (NYHA) and BNP seric concentration for evaluating the symptomatology and prognostic for cardiac failure. This reveals the importance of BNP value ascertaining in the condition of perioperative assessment of cardiac function. We can thus say that, as BNP concentration raises, cardiac failure is assessed as more severe. Here are some other correlations between BNP and the left ventricle functionality indicators:

- BNP raises in acute diastolic cardiac failure but more moderately than in acute systolic cardiac failure
- there is an inverse proportionality relation between the ejection fraction and BNP value
- BNP is correlated with left ventricle telediastolic pressure, with pulmonary artery occlusion pressure and with these parameters' variation under vasodilating and diuretic treatment.

A BNP cut-off value of *100 pg/ml* (Triage™ BNP Test) was recommended by Food and Drug Administration for the ascertaining of patients with cardiac failure.

As BNP value assessment methods, we mention:

- the "warm" – radio-immunologic – method (Shionoria BNP® - CIS Diagnostics, Gif-sur-Yvette, France). This is the election method in France although it requires approximately 20 hours of incubation, thus limiting its use in urgent diagnosis cases
- the „cold" – immunofluorescent – method (Triage™ BNP Test) provides BNP value assessment in approximately 30 minutes.

There currently are several indications for BNP

value assessment, all related to its use as marker for cardiac dysfunction:

- the early detection of cardiac failure, particularly under urgent conditions, in the emergency room, where there is need for differential diagnosis with other syndromes with display of acute dyspnea, (thus permitting the differentiation of cardiac grounds for dyspnea from the pulmonary ones). The assessment of plasmatic BNP concentration, associated with clinic and radiological exams, may allow diagnosis of cardiac failure when the value is > 500 pg/ml; in the conditions of a value under 100 pg/ml, cardiac failure can be outruled; lastly, values between 100 – 500 pg/ml allow for several diagnoses which is why complementary exams are required (cardiac echo Doppler).
- outruling marked ventricle dysfunction
- treatment follow-up in patients with cardiac decompensation; measuring BNP between the first and 4th day post acute myocardial infarction ensures prognostic information, BNP value >80pg/ml is associated to high possibility of mortality or apparition of a new cardiac decompensation episode.
- the prognostic of sudden death in cardiac failure.
- determining the severity of left ventricular hypertrophy and systolic dysfunction.
- detection of asymptomatic cardiac failure.

Based on the characteristics of BNP, we can consider that its use as marker for perioperative myocardial decompensation ensures the benefit of a quick diagnosis in the context of acutely installed dyspnea. Still, it must be used in association with clinic elements and with other diagnosis methods, among which we stress the role of cardiac echography. The prognostic value of BNP is also noteworthy.

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