RELATIONSHIP BETWEEN NT-proBNP AND THE EJECTION FRACTION DURING INTENSIVE CARE VARIETY IN POLYTRAUMA PATIENTS WITH CONCOMITANT CARDIAC DISORDER

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Abstract

The aim. To research the impact of chronic heart failure within different origin in case of polytrauma without myocardial injury.

Materials and methods. The study the analyzed results of intensive care in 95 patients with polytrauma between the ages of 25 and 83. All patients were divided into 3 groups. Group C included 29 patients without chronic heart failure (CHF), groups C - 33 patients with CHF, the presence which was confirmed by the level of NT-proBNP more than 100 pg/ml, group E - 33 patients with CHF. Patients of groups K and C received standard
intensive care, patients of group E additionally received ethylmethylhydroxypyridine succinate (EMGPS). The study was carried out at three stages: during admission to the hospital, at the 3rd and 7th day. During admission, the level of Th I was determined in order to exclude traumatic or other acute myocardial lesions. At a concentration of Tn I more than 0.3 ng/ml, patients were not included in the study.

**Results.** During admission, NT-proBNP level in all K-group patients did not exceed 87 pg/ml throughout the study. The ejection fraction (EF) was averaged 53.7±3.4%. The NT-proBNP dynamics were as followed by 116.4±7.0, 114.4±7.4, 109.1±8.5 pg/ml. The NT-proBNP and EF correlation coefficient was according to the stages -0.84±0.06, -0.74±0.08, -0.68±0.09. The value of the EF at hospitalization in group C was 47.9±4.7%, on the 3rd day 52.2±5.2% (p < 0.001), and by 7th - until 56.8±6.9% (p < 0.001). NT-proBNP level in E patients: 119.2±10.8, 113.2±8.1 (p= 0.02), 65.2±23.3 (p < 0.0001). At stage 1 and 2, a strong negative correlation effect was observed (-0.78±0.07 and -0.77±0.07, accordingly), at the 3 stage the communication disappeared (0.07±0.17). Within admission EF level was 47.5±6.9%.

**Conclusions.** The level of NT-proBNP authentically reflects the relationship with chronic heart failure. There is also a strong correlation between NT-proBNP and EF. Therefore, it is clear from the study that NT-proBNP has not undergone changes in group K (87 pg/ml), in contrast to patients of groups C (116.4±7.0,114.4±7.4, 109.1±8.5 pg/ml) and E (119.2±10.8, 113.2±8.1 (p =0.02), 65.2±23.3 (p < 0.0001) who had concomitant disorder such as chronic heart failure.

**Key words:** polytrauma; heart failure; NT-proBNP; ejection fraction.

**Introduction**

Trauma is the main cause of the most important medical and social problems in the world. In the economy, injuries take the third place after oncological and cardiovascular diseases. Most deaths occur at working age [1]. According to WHO, up to 12 million people die per year from injury. In 70% of cases, the main cause of death is severe combined trauma, exceeding mortality from cardiovascular and cancer in general [2]. Recently, the mortality rate from injuries has been progressively increasing, in Ukraine at least 40 thousand people die annually as a result of injuries, and 250,000 become disabled [3]. Cardiac pathology seriously affects the course of other pathological processes, complicating diagnosis and violating reparations processes, which, in turn, reduces the effectiveness of treatment and can make it untimely [ 4]. In such conditions, of course, among injured patients, a significant role
is persons with cardiac history. Thus, according to various data, coronary heart disease, hypertension, arrhythmia, heart failure are found in 44-62% of those affected in our country. In the structures of road transport, industrial and domestic traumatism, a significant proportion is occupied by combined injuries. Among which polysystem damage with the development of shock conditions is characterized by a particularly severe course, including patients with a provoked cardiovascular system [5]

The aim

To study the impact of chronic heart failure within different origin in case of polytrauma without myocardial injury.

Materials and methods

The study analyzed the results of intensive care in 95 patients with polytrauma between the ages of 25 and 83 (the average was 60±6±9.3 years). Group C included 29 patients without CHF aged 58.7±9.4 years, group C - 33 patients with CHF, the presence of which was confirmed by the level of NT-proBNP more than 100 pg/ml, aged 60.0±9.6 years, group E - 33 patients with CHF aged 62.8±8.8 years. Patients of groups K and C received standard intensive care, patients of group E for optimization the myocardium metabolism additionally received ethylmethylhydroxyppyridine succinate.

The study was carried out at three stages: during admission to the hospital, on the 3rd and 7th day. Within admission, the level of Th I was determined in order to exclude traumatic or other acute myocardial lesions. Patients were not included in the study at a concentration of Tn I more than 0.3 ng/ml. At all stages, the following indicators were measured: concentration NT-proBNP, final diastolic volume (FDV), final systolic volume (FSV), heart rate (HR), systolic and diastolic blood pressure (BPs and BPd), central venous pressure (CVP), oxygen saturation of hemoglobin of arterial and venous blood (SaO2 and SvO2), oxygen tension in arterial and venous blood (pAO2 and pVO2), concentration of hemoglobin and hematocrit, lactate level.

Based on the obtained results, the following indicators were calculated: stroke index (SI), ejection fraction (EF) of the left ventricle, cardiac index (CI), systemic perfusion pressure (SPP), specific peripheral vascular resistance (SPVR), blood flow capacity (BFC), oxygen content in arterial and venous blood (CaO2 and CvO2), transport and oxygen consumption (To2 and Vo2), oxygen extraction coefficient (EO2), tissue-consumed power (TCP), oxygen reserve (OR), circulation reserve (CR).
According to demographic indicators, the groups of patients did not differ from each other. With regard to anthropometric indicators, small but authentically differences affected only the body mass index (BMI). It was less in patients of group K ($p < 0.02$), which is probably due to absence of CHF. When comparing groups C and E (i.e., patients with CHF), there were no differences in BMI ($p = 0.9$).

The absence of traumatic or other acute myocardial injury was confirmed upon admission to the polytrauma department with a Tn I level, which in all patients included in the study did not exceed 0.3 ng/ml.

The presence of CHF, in addition to anamnestic data, was confirmed by the level of NT-proBNP more than 100 pg/ml, its absence - the level of NT-proBNP less than 90 pg/ml, patients in whom the concentration of NT-proBNP was in the range from 90 to 100 pg/ml, were excluded from the study, since this boundary level did not allow the possibility unequivocally confirm or exclude the presence of CHF.

Body mass index (BMI), was calculated in a generally accepted way according to Quetelet (1835) as the ratio of body weight per kg to a growth square in m.
The volume of the heart chambers was determined using the ULTIMA PA ultrasonic apparatus using wide-band sensors 3.5/2.7 MHz, S4, S8. Used standard projections: parasternally along the long and short axis, apically — 2, 4 and 5 chamber positions.

The level of NT-proBNP with the help of the "Brain Study Kit Natriuretic Propeptide" of the company "Roche", France.

Blood pressure (BP) was measured in a routine way, by means of "Membrane meter of common use modernized BP" IADM-OPMM No. 80897, the frequency of heat rate – by means of stopwatch, the central venous pressure - Waldman direct method (1947) through the cava catheter.

By means of the measured indicators, the following were calculated: SI, EF, CI and SPVR - routine methods;

**Results**

Kinetic indicators of blood circulation of group K.

End diastolic index (EDI) within the admission of group K patients was 45.8±6.9 ml/m², which corresponds to the lower limit of reference values and is due to primary hypovolemia. On the 3rd day of being in the polytrauma department on the background of normalization of the circulating blood volume (CBV), the EDI authentically increased to 54.9±6.1 ml/m² (p <0.001), here and further in the text - M±σ), and on the 7th day - to 61.5±5.8 ml/m² (p <0.001).

End systolic index ESI during admission was 21.1±2.6 ml/m², which corresponds to the reference values and means the preservation of the myocardial contractile ability (MCA). In the future, the ESI did not change significantly, reaching by the end of the study a level of 22.4±3.6 ml/m² (p > 0.7).

Stroke index (SI) at the stages of the study in most patients was reduced. During admission - 24.7±4.8 ml/m², then, on the 3rd day, it authentically increased to 32.8±5.0 ml/m², (p <0.001), and on the 7th day - to 39.1±6.0 ml/m², (p <0.001).

EF, the most informative reflection of the (MCA), fluctuated within admission in wide limits and averaged 53.7±3.4%. In the future, the EF authentically increased, reaching 59.6±5.2% by the 3rd day (p < 0.001) and 63.3±6.4% by the 7th (p < 0.01).

When cardiac index (CI) was reduced during admission, being at the level of 2.26±0.35 l/min · m², on the 3rd day it authentically increased to 2.73±0.37 l/min · m² (p < 0.001), and by the end of the study – to 3.08±0.40 l/min · m² (p < 0.001).
Table III

Kinetic indicators of blood circulation in patients of group K (M±σ)

| Index | Study stages |       |       |       |
|-------|--------------|-------|-------|-------|
|       | Admission    | 3rd day | 7-th day |
| EDI, ml/m² | 45,8±6,9 | 54,9±6,1 † | 61,5±5,8 †‡ |
| ESI, ml/m² | 21,1±2,6 | 22,1±3,1 | 22,4±3,6 |
| SI, ml/m² | 24,7±4,8 | 32,8±5,0 † | 39,1±6,0 †‡ |
| EF, % | 53,7±3,4 | 59,6±5,2 † | 63,3±6,4 †‡ |
| CI, l/min·m² | 2,26±0,35 | 2,73±0,37 † | 3,08±0,40 †‡ |

Here and below: † — p <0,05 compared to the previous stage
‡ — p <0,05 compared to baseline

Throughout the study, the level of NT-proBNP did not exceed 87 pg/ml (Fig.1), its changes were not authentically significant, their correlations with other studied indicators were not found.

Fig.1. Dynamics of NT-proBNP in patients of group K.

Kinetic indicators of blood circulation of group C.

EDI during admission in patients of group C was 48.0±7.4 ml/m², which is within the reference values, although closer to the lower boundary, which can be associated with acute hypovolemia. On the 3rd day of intensive care aimed at normalizing the CBV, the EDI
authentically increased to 51.3±5.8 ml/m² (p <0.05), and on the 7th day - to 61.1±6.8 ml/m² (p < 0.001).

ESI in group C upon admission was at the level of 25.1±4.9 ml/m², then it did not change authentically: 24.4±3.0 and 26.4±5.9 ml/m², accordingly, on the 3rd and 7th day after admission (p > 0.09).

SI within admission was significantly reduced, amounting to 22.9±3.7 ml/m², on the 3rd day authentically increased to 26.9±4.7 ml m² (p < 0.001), and on the7th day - up to 34.6±5.5 ml/m² (p < 0.001).

Similar dynamics were observed with regard to EF. Its value for admission in group C was 47.9±4.7%, on the 3rd day it increased to 52.2±5.2% (p <0.001), and on the 7th - to 56.8±6.9% (p <0.001).

The main kinetic indicator - CI - at admission was 1.99±0.39 l/min · m², on the 3rd day its increase to 2.22±0.31 l/min · m² (p < 0.02) was noted, on the 7th - up to 2.67±0.33 l/min · m² (p < 0.001).

The concentration of NT-proBNP by the 3rd day did not authentically change, its minimum exceeded 95 pg/ml (Fig.2). By the 7th day, this indicator reliably, but slightly, decreased, exceeding 90 pg/ml.

Correlation relationships were found between the level of NT-proBNP and some other studied indicators. The particular interest are the relationships of the NT-proBNP level with EDI and EF as indicators reflecting the degree of CHF. The NT-proBNP level and EDI had no significant relationship (Fig.2), but the relationship with EF was substantial. The absence of relationship between the level of NT-proBNP and EDI upon admission can be explained by the acute development of hypovolemia, while the level of NT-proBNP as a sedentary

| Index | Study stage | 3-rd day | 7-th day |
|-------|-------------|----------|---------|
| EDI, ml/m² | Admission | 48,0±7,4 | 51,3±5,8 † | 61,1±6,8 †‡ |
| ESI, ml/m² | 25,1±4,9 | 24,4±3,0 | 26,4±5,9 |
| SI, ml/m² | 22,9±3,7 | 26,9±4,7 † | 34,6±5,5 †‡ |
| EF, % | 47,9±4,7 | 52,2±5,2 † | 56,8±6,9 †‡ |
| CI, l/min·m² | 1,99±0,39 | 2,22±0,31 † | 2,67±0,33 †‡ |

The concentration of NT-proBNP by the 3rd day did not authentically change, its minimum exceeded 95 pg/ml (Fig.2). By the 7th day, this indicator reliably, but slightly, decreased, exceeding 90 pg/ml.

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indicator did not managed to change. However, with the elimination of hypovolemia, the relationship between these indicators became negative, but weakly expressed.

The relationship of the of NT-proBNP level with EF throughout the study was pronounced and negative: within admission $r = -0.84\pm0.05$, on the 3rd day $r = -0.74\pm0.08$, on the 7th $r = -0.68\pm0.09$. This allows us to consider the level of EF as an indicator of the severity of CHF.

Kinetic indicators of blood circulation of group E.

EDI during the admission of group E patients was 50.6±11.2 $ml/m^2$, which is within the reference values, but closer to their lower boundary, which is associated with the initial hypovolemia. With the elimination of hypovolemia on the 3rd day, the EDI practically did not change ($50.5\pm7.2 \ ml/m^2$, $p > 0.9$), but on the 7th day it authentically increased to $60.5\pm6.9 \ ml/m^2$ ($p < 0.001$).

ESI within admitted of group E was 27.2±9.3 $ml/m^2$, then it showed a tendency to decrease, although it was unreliable. On the 3rd day, it decreased to 24.5±6.1 $ml/m^2$ ($p > 0.1$), and by the 7th - to 23.7±6.5 $ml/m^2$ ($p > 0.6$, compared with the baseline $p = 0.08$).

SI admitted patients of group E was significantly reduced, amounting to 23.4±2.7 $ml/m^2$, on the 3rd day it slightly, but authentically increased to 26.1±1.5 $ml/m^2$ ($p < 0.01$), and on the 7th - to 36.8±2.2 ($p < 0.01$), and only in 3 (9.1±5.0%) it was below 40 $ml/m^2$. 

Fig.2. Dynamics of NT-proBNP in patients of group C
EF admitted patients of group E was also reduced, being at the level of 47.5±6.9%. On the 3rd day, EF authentically increased to 52.3±5.3% (p < 0.003), and on the 7th day - to 61.5±6.4% (p <0.001).

SI and EF have undergone significant positive changes, which confirms the un informativeness of using 2-3 indicators to assess the state of the organism and predict the outcome. In addition, this suggests that the mechanisms of regulation of myocardial activity are very complex and the ultimate aim is adequate energy supply to tissues.

The integral kinetic index of CI when, during admission, group E was at a low level -2.0±0.38 l/min · m². By the 3rd day, it did not change significantly - 2.06±0.30 l/min · m² (p > 0.4), but on the 7th it reached 2.97±0.32 l/min · m² (p <0.001).

The concentration of NT-proBNP by the 3rd day changed slightly, but authentically, the minimum level was 100 pg/ml (Fig. 5.1). On the 7th day there was a significant descent in the concentration of NT-proBNP and the level 100 pg/ml became the maximum.

Fig.3. The relationship of the NT-proBNP level and EF at the stages of the study in group C.
Table V

Kinetic indicators of blood circulation in patients of group E (M±σ)

| Index   | Study stages | Admission | 3-rd day | 7-th day |
|---------|--------------|-----------|----------|----------|
| EDI, ml/m² | 50,6±11,2   | 50,5±7,2  | 60,5±6,9 |
| ESI, ml/m² | 27,2±9,3    | 24,5±6,1  | 23,7±6,5 |
| SI, ml/m²  | 23,4±2,7    | 26,1±1,5  | 36,8±2,2 |
| EF, %      | 47,5±6,9    | 52,3±5,3  | 61,5±6,4 |
| CI, l/min/m² | 2,00±0,38  | 2,06±0,30 | 2,97±0,32 |

NT-proBNP level.

![NT-proBNP level](image)

**Fig. 4. Dynamics of NT-proBNP in patients of group E**

An indicative correlation between the level of NT-proBNP and EF was found (Fig.5). Within admission, the correlation coefficient of this dependence was significant and negative (-0.78±0.07), on the 3rd day the situation did not change significantly (-0.77±0.07). The situation radically changed on the 7th day on the background of a significant decrease in the level of NT-proBNP. The relationship between EF and the concentration of NT-proBNP disappeared, which can be explained by the improvement of MCA on the background of EMHPS therapy.
Fig. 5. The relationship of the levels of NT-proBNP and EF at the stages of the study in group E.
Discussion

Within the study, the category of patients has a combination of at least two types of circulatory failure: chronic cardiac and acute hypovolemic. At the same time, even in the absence of traumatic myocardial injury, polytrauma deteriorates the condition of a healthy myocardium, not to mention chronically disorder [6]. The leading role in myocardial injury during polytrauma in the absence of myocardial trauma is played by oxidative stress with activation of the mechanisms of apoptosis and/or cell necrosis [7]. To distinguish chronic myocardial injury from acute at the present stage is not serious difficult due to the ability to control the level of markers of acute myocardial disorder, one of which is troponin I.

Another important biochemical marker of the state of the myocardium is the brain natriuretic peptide BNP, the level of which can be judged by the concentration of areas of prohormone NT-proBNP. The level of BNP increases with excessive stretching of the ventricles, which increases natriuresis.

Regardless of the state of the myocardium, polytrauma leads to a general energy deficiency of the body, including the myocardium, and the myocardium loses the ability to transfer the chemical energy of the substrates into the mechanical energy of contractions at a sufficient rate, that is, there is a decrease in MCA [8]. This means a violation of the subordination of the myocardium to the Frank-Starling law, that is, a decrease in the pumping function of the heart. The pumping function of the heart is to create a pressure difference between the exit from the left ventricle and the entrance to the right atrium, this difference determines the volumetric blood flow, that is, cardiac output CO. However, CO is equally dependent on the SPVR, the control mechanisms of which are very complex and various, but
with any circulatory disorders, with the exception of acute vascular insufficiency, due to the vasoconstrictor reaction of the SPVR increases. In this case, CO is determined by the ratio of MCA and SPVR, and the more the MCA decreases, the greater the probability of increasing the SPVR [9]. The aggravation of this situation leads to shock, which is a consequence of not satisfying the energy needs of tissues.

Oxidative stress reduces the antioxidant capacity of cells, including cardiomyocytes. Knowledge of this pathogenesis mechanism justifies the usage of antioxidant drugs for polytrauma, optimizing the metabolism of cardiomyocytes and preventing the development of irreversible processes in the myocardium [10]. These drugs include ethylmethylhydroxypyridine succinate (EMGPS). Many studies prove the effectiveness of EMGGs in increasing MCA in CHF.

In this regard, we decided to study the effect of EMHPS on the course of circulatory failure after polytraumatic influence in patients with CHF without myocardial injury. The severity of the circulatory failure process was assessed by us on the basis of studying the energy efficiency of blood circulation.

**Conclusions**

The NT-proBNP level in chronic heart failure in patients with polytrauma without acute myocardial injury is highly correlated with the effectiveness of the myocardium pumping function, primarily with EF (r = -0.84±0.05).

Acute hypovolemia of the polytrauma background without biochemical signs of acute myocardial injury (increased level of troponin I) and without biochemical signs of chronic heart failure (increased level of NT-proBNP) is accompanied only by hemodynamic signs of hypovolemia. Elimination of hypovolemia normalizes blood circulation completely. This is evidenced by the normalization already on the 3rd day after polytrauma CI (2.73±0.37 l/min · m²), FV (59.6±5.2%) and blood flow power (BFP) (511±91 mW/m²), and on the 7th - oxygen reserve (OR) (0.68±0.16) and circulatory reserve (CR) (403±116 mW/m²).

Ethylmethylhydroxypridine succinate (EMGPS) optimizes the energy efficiency of blood circulation in patients with chronic heart failure during polytrauma without acute myocardial injury. Such an action develops slowly, in the course of a week, but is authentically, so the inclusion of EMGPS in the intensive care regimen in this category of patients is advisable.
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