

## **Age features of the circadian rhythm of myocardial oxygen demand in concomitant severe traumatic brain injury**

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### **Abstract**

Only those injured under the age of 40 (group 1) showed normal values of the mesor of the circadian rhythm TNMO on day 1, while in groups 2 and 3 there was a tendency to increase. During the first 25 days in group 1, there was an increase in TNMO on days 3-15 with a tendency to normalization of the indicator on the following days of intensive therapy. The highest values of the amplitude of the circadian rhythm TNMO were revealed on day 1, amounting to 20% in group 1, 55% in group 2, and 65% in group 3. Such abrupt changes in myocardial metabolism on the first day significantly increased the risk of complications from heart function, which suggests that it is advisable to start the earliest (in the first hours) active coronary artery disease and metabolite therapy, especially in patients over 41 years of age. Compensatory mobilization of blood circulation in favor of maintaining intracranial capillary perfusion in patients over the age of 41 is fraught with aggravation of the existing coronary insufficiency.

Keywords: circadian rhythm, myocardial oxygen demand, combined severe traumatic brain injury

**Relevance.** In the structure of mortality, multiple injuries in combination with TBI account for 48%. According to the literature, vasospasm may be one of the factors determining the outcome of TBI. P. Macpherson and D. Graham found vasospasm on angiograms in 41% of patients who died due to TBI. Cerebral ischemia was detected in 51% of patients with vasospasm and only 32% of cases were without vasospasm. It has been established that changes in myocardial trophism remain for 3-4 weeks after the elimination of the manifestations of diencephalic syndrome [1,2,3]. Due to the lack of information on the state of myocardial oxygen demand (TNMO), one of the leading causes of possible complications from heart function, we made an attempt to study the features of TNMO changes in the acute period of CSTBI.

**Purpose of the work.** To study the circadian rhythm of myocardial oxygen demand in concomitant severe traumatic brain injury.

**Material and research methods.** The indicators of a comprehensive examination of 30 patients with concomitant severe craniocerebral trauma (CSTBI) who were admitted to the ICU of the neurosurgical department of RSCEMA in the first hours after an accident - 28, catatrauma of 2 patients were studied. According to indications, 29 patients were started on admission to invasive mechanical respiratory support (MRS). Monitoring was carried out by complex hourly registration of hemodynamic parameters: stroke volume of blood (SVB), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), pulse pressure (PP), cardiac output (CO), general peripheral vascular resistance (GPVR), estimation of autonomic tone (EAT), the need of myocardium in oxygen (TNMO). Mechanical respiratory support was initiated with artificial lung ventilation (ALV) for a short time followed by switching to SIMV. The severity of the condition was assessed by scoring methods according to the scales for assessing the severity of combined injuries - the CRAMS scale, the assessment of the severity of injuries according to the ISS scale. On admission, impaired consciousness in 29 injured patients was assessed on the Glasgow Coma Scale (GS) 8 points or less. Patients were considered in three age groups: group 1 - 19-40 years old (13), group 2 - 41-60 years old (9), 3 - 61-84 years old (8 patients). In 28 patients, the clinic was dominated by the diencephalic and mesencephalo-bulbar forms, which, due to a critical disorder of the vital systems (respiratory and cardiovascular), required urgent intensive therapy, and sometimes resuscitation. Complex intensive therapy consisted in identifying and timely correction of deviations: MRS, after removing from shock

anesthetic, anti-inflammatory, antibacterial, infusion therapy, correction of protein and water-electrolyte balance disorders, surgical early correction to the extent possible, stress-protective therapy.

## Result and discussion.

Table 1

Dynamics of the mesor of the circadian rhythm of myocardial oxygen demand

Days	Group 1	Group 2	Group 3
1	99±6	117±20	112±16
2	94±3	113±4	96±6
3	105±5*	107±6	99±4
4	111±3*	107±6	104±3
5	111±3*	115±8	108±6
6	117±5*	116±4	104±4
7	114±6*	119±4	98±4'''
8	115±4*	113±4	100±7'''
9	117±3*	113±6	100±5'''
10	122±7*	110±3	102±6'''
11	117±4*	118±6	103±7'''
12	124±4*	107±4'''	105±5'''
13	117±5*	111±5	92±4'''
14	114±5*	106±6	104±7
15	115±6*	108±4	104±
16	110±7	104±5	107±5
17	105±5	106±6	88±6
18	105±6	123±7	93±5
19	100±5	118±6	96±7
20	102±4	113±6	98±5
21	108±6	119±8	100±6
22	116±6	121±12	95±8
23	106±7	115±5	95±6
24	108±6	121±4	102±7
25	106±8	127±12	113±8

\* - reliable relative to the indicator in 1 day

''' - reliable relative to the indicator in group 1

As presented in tab. 1, on day 1 only the injured group 1 showed normal values of the mesor of the circadian rhythm TNMO, while in groups 2 and 3 there was a tendency to increase. During the first 25 days in group 1, an increase in TNMO was noted, starting from the third day to 15 days, inclusive, with a tendency towards normalization of the indicator on the following days of intensive therapy. In group 2, TNMO on day 12 turned out to be less than in group 1. In traumatized patients of the 3rd group, on the 7th - 13th day, the mesor of the circadian rhythm TNMO was significantly less than in the 1st group, which was most likely due to the more active coronary artery therapy in patients over 61 years of age due to concomitant cardiovascular diseases (hypertension, coronary heart disease). There were no statistically significant changes in the 25-day average hourly TNMO indices in the circadian rhythm in the acute period of CSTBI (fig. 1).

Average hourly data of TNMO in circadian rhythm in the acute period of CSTBI, in%

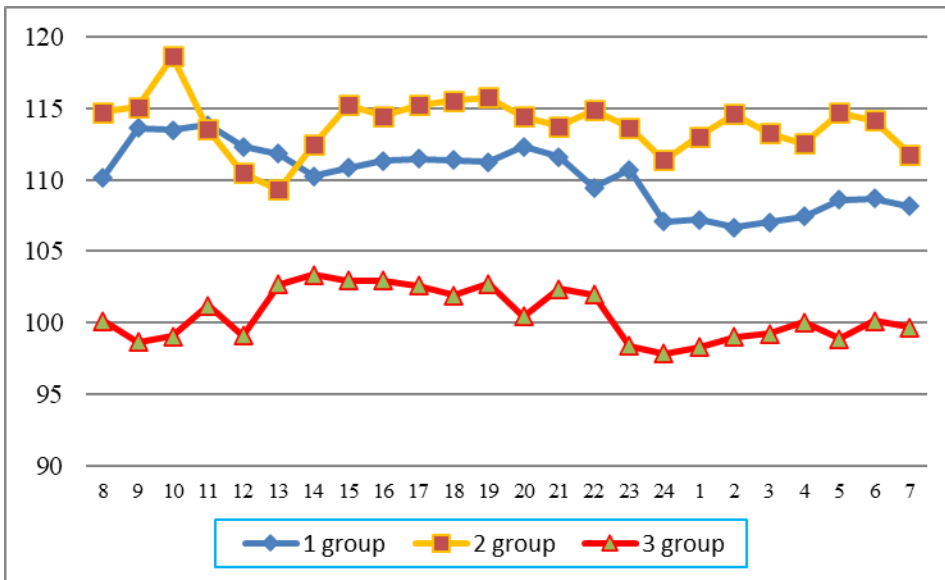


Fig.1

Dynamics of the amplitude of the TNMO circadian rhythm, in%

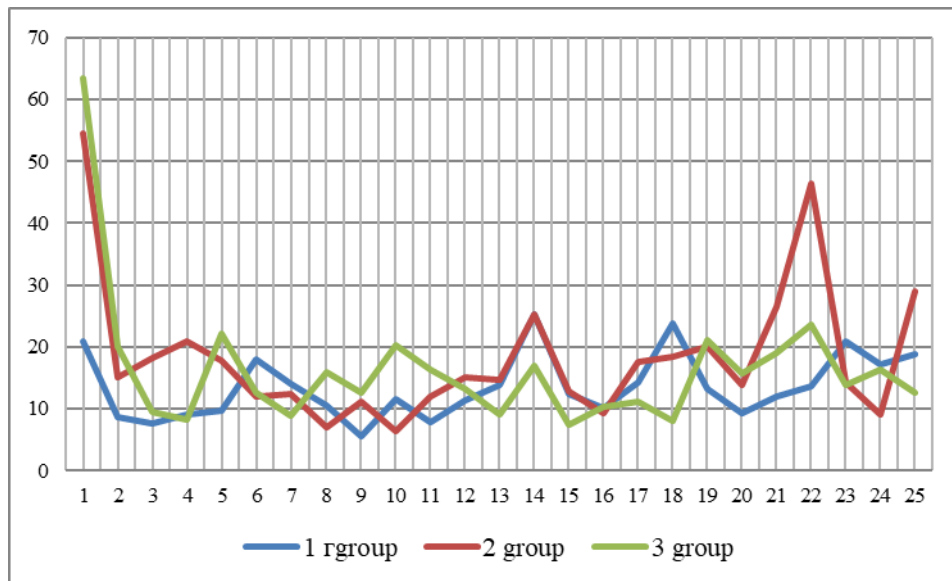


Fig.2

As shown in fig. 2, the highest values of the amplitude of the TNMO circadian rhythm were detected on day 1, amounting to 20% in group 1, 55% in group 2, and 65% in group 3. Changes in the amplitude of the TNMO circadian rhythm in the acute period were low-amplitude fluctuations with a tendency to increase up to 45% in patients of group 2 on the 22nd day.

Daily range of TNMO changes, in%

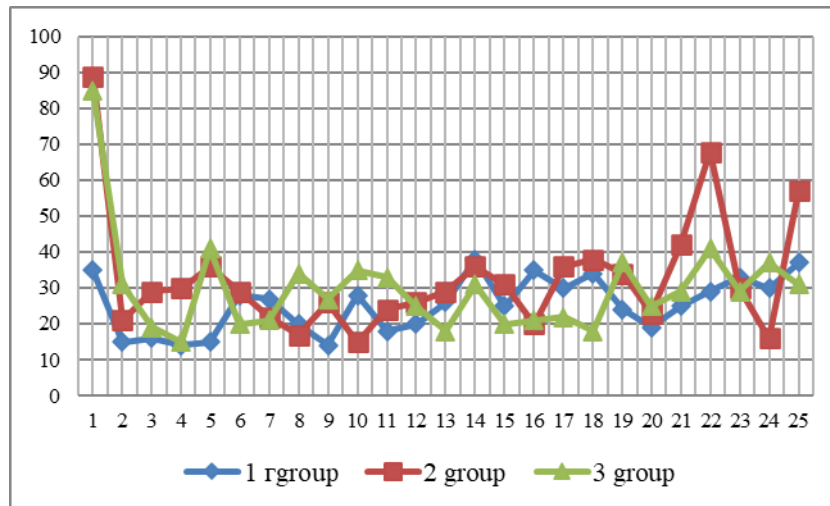


Fig.3

The maximum values of changes in the circadian rhythm of TNMO were also detected on day 1, which amounted to 35% in group 1, 88% in group 2, and 90% in group 3. It is quite understandable that such abrupt changes in myocardial metabolism in the first day significantly increased the risk of complications from heart function, such as, for example, acute tachy- or brady arrhythmia. This suggests that it is advisable to start the earliest (in the first hours) active coronary and metabolic therapy aimed at maintaining myocardial metabolism in extremely unfavorable conditions of changes in systemic hemodynamics, especially in patients over 41 years of age. Moreover, in order to maintain perfusion blood flow in the injured brain, to maintain the delivery of the required minimum of oxygen to preventative irreversible secondary changes in the brain, the load on the heart increases 7-10 times.

Circadian rhythms TNMO from 1 to 8 days, in%

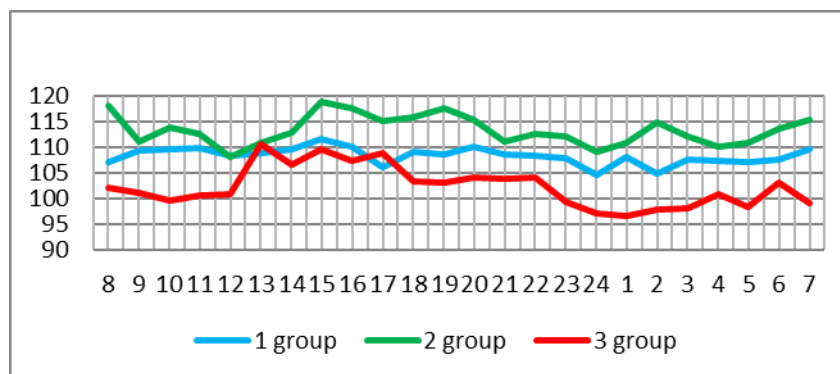


Fig.4

In the first 8 days, the average daily TNMO level in group 3 ( $102 \pm 3\%$ ) was the closest to the standard values. In group 1, TNMO was increased relative to the norm by 8%, in group 2 by

13%, and significantly higher than in group 3 in group 1 by 5% and in group 2 by 12% ( $p < 0.05$ , respectively).

Figure 5 shows the circadian rhythms of TNMO from 9 to 17 days, when in group 1 the mesor of the circadian rhythm TNMO was the highest in patients of group 3, amounting to  $120 \pm 3\%$ , in group 1 -  $116 \pm 2\%$ , in group 2 -  $109 \pm 2\%$ . Age differences in the TNMO circadian rhythm mesor indicator were significant. The highest level of the indicator in group 3 indicated an extremely unfavorable state of myocardial trophism due to an increase in the tendency to oxygen starvation against the background of prolonged intensive therapy.

As shown in fig. 6, from the 18th to the 25th day of treatment, on average per day, TNMO was found to be the closest to the normative values in group 3, averaging  $99 \pm 2\%$ . At the same time, the TNMO indicator in group 3 turned out to be significantly less relative to groups 1 and 2 by 6% and 17% ( $p < 0.05$ , respectively).

Circadian rhythms TNMO from 9 to 17 days, in%

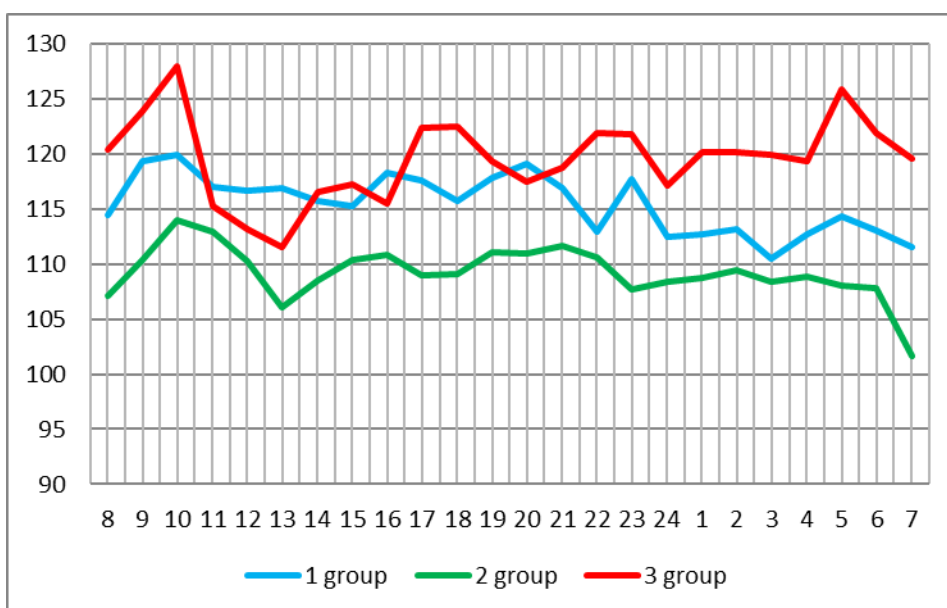


Fig.5

Circadian rhythms TNMO from 18 to 25 days, in%

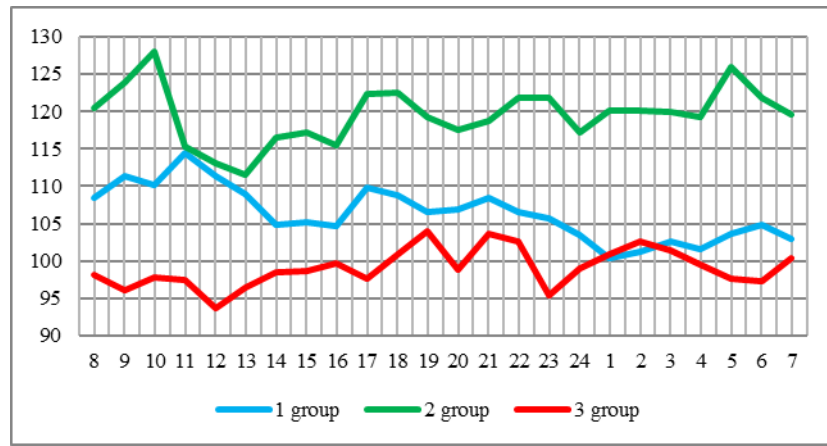


Fig.6

Correlation relationships of myocardial oxygen demand for 25 days

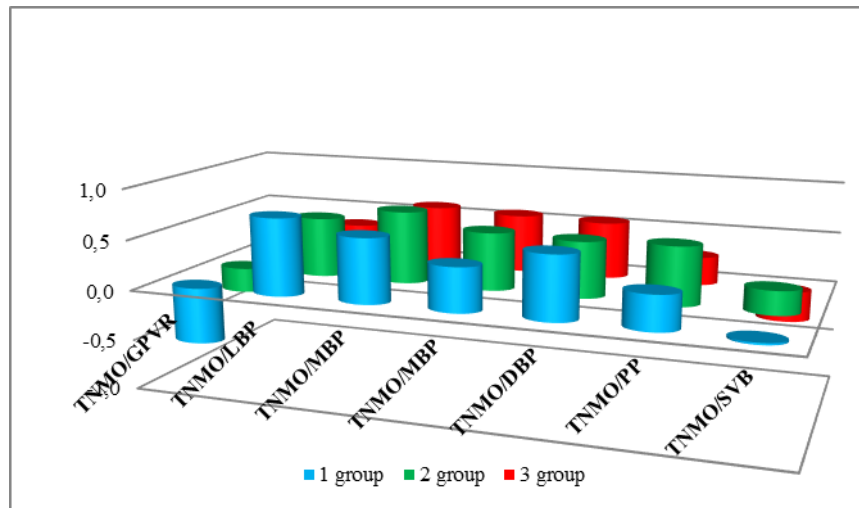


Fig.7

Significant correlations (fig. 7) of the mesors of the circadian rhythms TNMO and CO (0.8) were found only in group 1, and TNMO with MBP in group 2 (0.7) during 25 days of the acute period of SCTBI. In the first week (fig. 8) in group 1, with a strong direct correlation between the mesor of the circadian rhythm TNMO with the mesors of CO (0.7), MBP (0.8), a direct relationship with DBP (0.8) was also reliable. In group 2 from 1 to 8 days negative correlation with GPVR (-0.8), and positive with CO (0.8). And in group 3 with MBP (0.9), SBP (0.9) and DBP (0.8).

In the second week (fig. 9), patients of group 1 showed strong direct correlations of TNMO with MBP (0.8), with SBP (0.8), with DBP (0.7), with PP (0.8). In group 2, only a direct correlation was found with the MBP indicator (0.8). In group 3, connections with MBP, SBP and DBP were completely broken and practically disappeared.

Correlation links TNMO from 1 to 8 days of the acute period

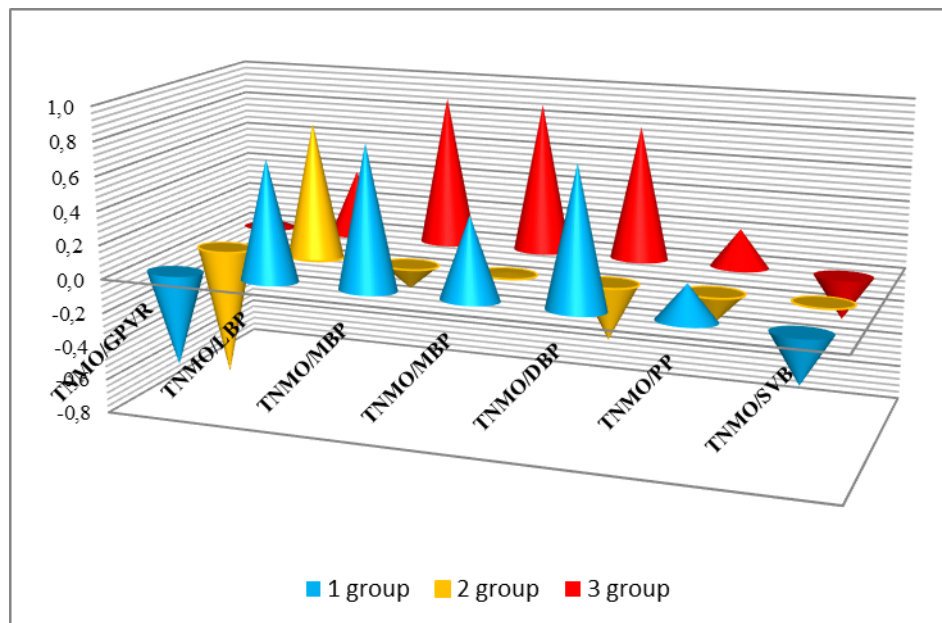


Fig.8

On the third week, from 18 to 25 days in group 1, a negative correlation was formed between TNMO and GPVR (-0.7), direct correlation with CO (0.9), with MBP (0.7), with SBP (0.9), with PP (0.8) and SV (0.7). From the results obtained, it can be imagined that in order to reduce myocardial oxygen demand on days 18-25 in group 1, it is necessary to maintain GPVR at the level of  $1342 \pm 71$ , a decrease in TNMO less than  $106 \pm 3.2\%$  can lead to a decrease in CO less than  $5 \pm 0.3$  l/min, decrease in SBP less than  $121 \pm 3.9$  mmHg, decrease in PP to  $50 \pm 2.5$  mmHg and SV of the heart to  $57 \pm 2.5$  ml with an average level of the mesor of the circadian rhythm PP  $106 \pm 3.2\%$ .

In group 2, from 18 to 25 days (fig. 10), a strong direct relationship was found between the mesor of the circadian rhythm TNMO at the TNMO level ( $120 \pm 3.2\%$ ) with MBP (0.9) and DBP (0.7). That is, an increase in MBP above  $95 \pm 2.4$  mmHg, DBP above  $77 \pm 2.3$  mmHg will be accompanied by an increase in TNMO of more than 120%. In group 3, a direct correlation was observed between the PP and CO mesor (0.7) and SBP (0.7). That is, an increase in the mesor of the circadian rhythm of CO above  $5 \pm 0.2$  l/min and an increase in SBP above  $125 \pm 3.6$  mmHg will be accompanied by an increase in TNMO of more than  $99 \pm 4.5\%$ . Thus, the most vulnerable in terms of the likelihood of increased coronary hypoxia was the 2nd age group, in which, in the third week of intensive complex therapy, myocardial oxygen demand remained increased by 20%. From this we can conclude. That compensatory mobilization of blood circulation in favor of maintaining intracranial capillary perfusion in patients aged 41 to 60 years is fraught with aggravation of the existing coronary insufficiency with the ensuing consequences and complications.



Correlation links TNMO from 9 to 17 days

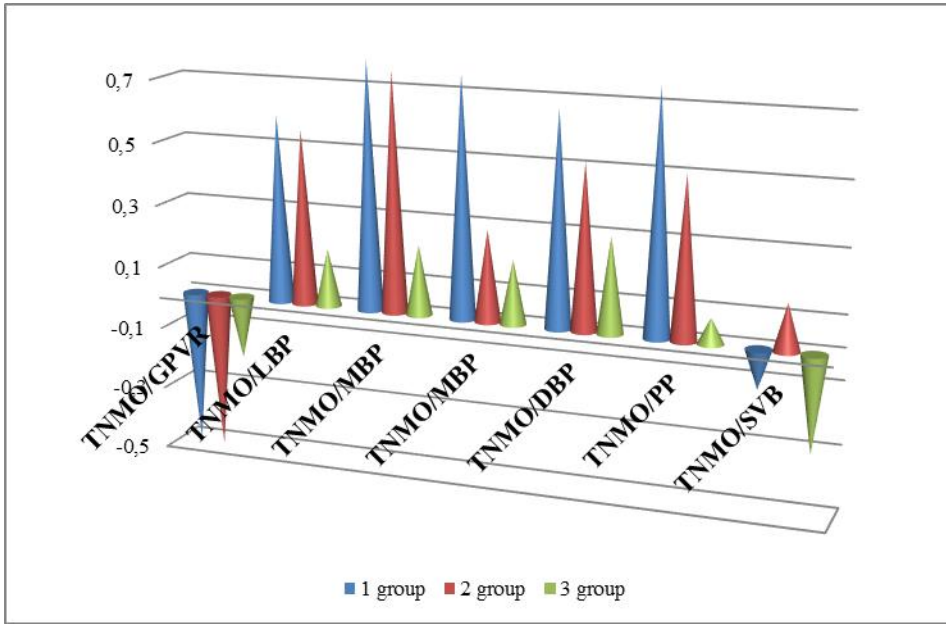


Fig.9

Correlation links TNMO from 18 to 25 days

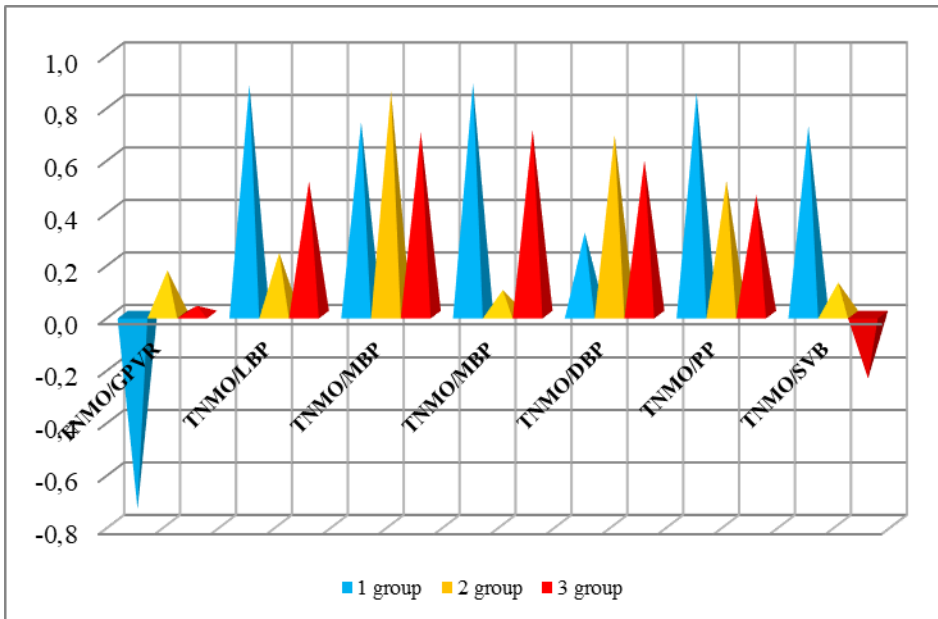


Fig.10

Duration of TNMO acrophase displacement in the acute period of CSTBI

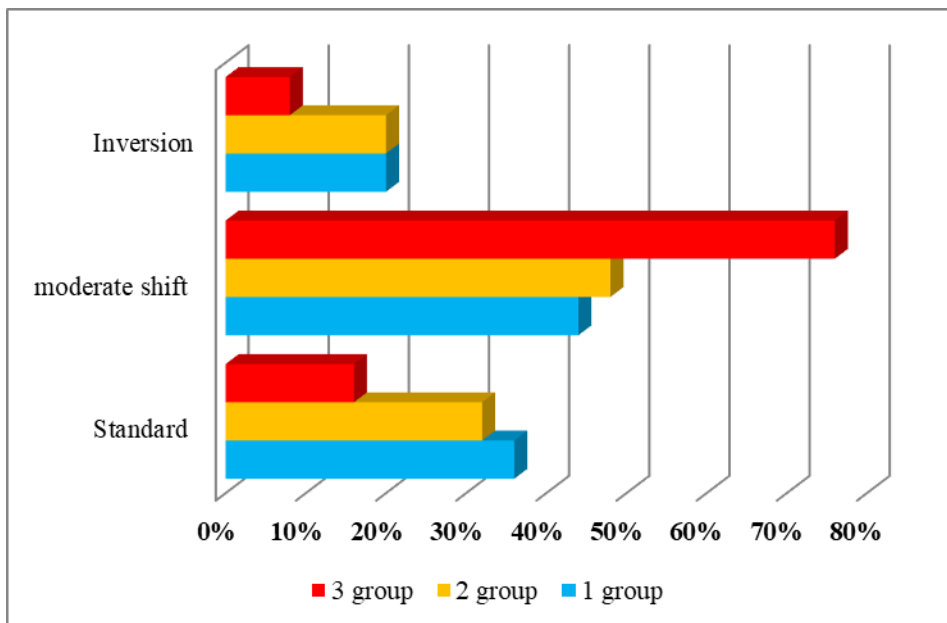


Fig.11

During the acute period of CSTBI, a moderate shift in the acrophase peak prevailed over 75% in group 3, 45% in group 2, and 42% in group 1 during intensive care in the ICU (fig. 11).

**Conclusions.** Only those injured under the age of 40 (group 1) showed normal values of the mesor of the circadian rhythm TNMO on day 1, while in groups 2 and 3 there was a tendency to increase. During the first 25 days in group 1, there was an increase in TNMO on days 3-15 with a tendency to normalize the indicator on the following days of intensive therapy. The highest values of the amplitude of the TNMO circadian rhythm were revealed on day 1, amounting to 20% in group 1, 55% in group 2, and 65% in group 3. Such abrupt changes in myocardial metabolism on the first day significantly increased the risk of complications from the heart function, which suggests that it is advisable to start the earliest (in the first hours) active coronary and metabolic therapy, especially in patients over 41 years of age.

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