## Circadian index in the acute period of concomitant severe traumatic brain injury

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**Abstract.** Fluctuations of the circadian index occurred in the range of 0.9-1.1, which characterized the pronounced rigidity of the heart rate during the acute period of CSTBI. The baseline heart rate indicators corresponded to the age norm. In dynamics in group 1 on days 8 - 15, an increase in the mesor of the HR circadian rhythm by an average of 16% was revealed. In the 3rd group during the indicated period, the mesor of the circadian rhythm HR remained less than in the 1st group by an average of 11%. Hourly heart rate in the circadian rhythm in the acute period of CSTBI for 25 days in the light and dark hours of the day in patients of group 3 were lower than in groups 1 and 2. Throughout the observation, strong direct correlations between the heart rate and the indicators of myocardial oxygen demand in all injured were revealed.

Keywords: circadian index, combined severe traumatic brain injury

Relevance. In practical medicine, deviations of the circadian index are observed both upward and downward. The norm of the circadian index in adult men and women should be in the range of 1.24-1.44. The indicator is not affected by either the age or gender of the subject. a normal circadian profile indicates a stable autonomic organization of the circadian rhythm. If the CI is elevated, this is a sign of high sensitivity of the myocardium to sympathetic stimulation. In some cases, an enhanced circadian profile is an individual norm of a person accustomed to intense physical activity. A decrease in the index is considered an indicator of cardiovascular disorders. A decrease in CI is an unfavorable symptom indicating autonomic denervation of the heart. This means that the sympathetic and parasympathetic divisions of the ANS do not properly regulate myocardial contractions. With a persistent deviation of the indicator to the lower side, we can say that the contractility of the myocardium has decreased, and the patient has developed irreversible changes in the myocardium and chronic heart failure. A drop in the circadian index to 1.2 is a sign of heart failure with a probability of death. HR rigidity during treatment is a poor prognostic sign, an increase in the upward direction is a guarantee of the adequacy of the prescribed therapy. However, there is not enough information in the literature about the features of CI HR changes in CSTBI, which prompted us to study this issue [1-4].

**Purpose of the work.** Circadian index in the acute period of combined severe traumatic brain injury

**Material and research methods.** The indicators of a comprehensive examination of 30 patients with concomitant severe traumatic brain injury (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. Continuous hourly monitoring of heart rate (HR), circadian index (CI), oxygen saturation (OS), 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) were performed within 25 days after CSTBI. Mechanical respiratory support (MRS) started with artificial lung ventilation (ALV) for a short time with subsequent transfer to SIMV. ALV was performed in the mode of normoventilation or moderate hyperventilation (pCO2 - 30–35 mmHg) with an air – oxygen mixture of 30–50%. At low pO2 in arterial blood, ALV was performed with constant positive pressure. However, the end-expiratory pressure did not exceed 5-7 cm aq., since higher pressure could impede the outflow of blood from the brain and increase ICP.

The assessment of the severity of the condition was carried out using scoring methods according to the scales for assessing the severity of concomitant 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). The division into groups was dictated by the well-known features inherent in each age group, described in detail in the literature. The calculation was carried out according to the formula: CI = Average HR in the daytime (from 8.00 to 22.00)/Average HR at night (from 23.00 to 7.00).

## **Results and discussion.**

#### Table 1.

|      |           | <b>J</b>  | , I       |  |  |
|------|-----------|-----------|-----------|--|--|
| days | group 1   | group 2   | group 3   |  |  |
| 1    | 78.8±4.8  | 97.4±11.4 | 83.6±6.1  |  |  |
| 2    | 75.7±2.4  | 88.5±2.9  | 76.3±4.3  |  |  |
| 3    | 81.8±3.2  | 85.8±4.5  | 77.9±2.0  |  |  |
| 4    | 83.5±1.7  | 82.7±6.0  | 82.6±1.6  |  |  |
| 5    | 85.8±1.7  | 90.1±4.5  | 82.6±5.0  |  |  |
| 6    | 88.7±2.3  | 90.7±2.1  | 79.7±2.0  |  |  |
| 7    | 86.7±2.8  | 92.4±2.7  | 77.1±2.8‴ |  |  |
| 8    | 90.1±2.1* | 88.4±2.4  | 83.4±3.5‴ |  |  |
| 9    | 91.7±1.7* | 88.9±2.5  | 79.9±4.0‴ |  |  |
| 10   | 93.1±3.5* | 87.2±1.7  | 81.1±2.5‴ |  |  |

Dynamics of the mesor of the circadian rhythm, heart rate, beats per minute

| 11 | 93.1±2.6* | 92.4±3.3 | 84.9±2.9‴ |
|----|-----------|----------|-----------|
| 12 | 97.2±2.9* | 86.7±1.9 | 82.6±2.6‴ |
| 13 | 92.3±3.3* | 90.4±2.4 | 79.9±2.1‴ |
| 14 | 89.0±2.1* | 86.5±4.0 | 83.3±3.5‴ |
| 15 | 90.5±3.8* | 88.2±3.3 | 82.9±1.7‴ |
| 16 | 88.3±3.4  | 85.9±2.8 | 84.6±2.2  |
| 17 | 85.9±2.6  | 87.8±3.3 | 78.0±4.4  |
| 18 | 85.6±2.3  | 92.9±2.2 | 79.2±2.5  |
| 19 | 83.8±2.5  | 91.4±2.3 | 79.6±4.1  |
| 20 | 83.5±2.2  | 90.2±3.7 | 79.1±1.9  |
| 21 | 84.0±2.9  | 90.5±4.2 | 80.7±3.3  |
| 22 | 90.1±3.0  | 91.3±5.0 | 73.7±3.2  |
| 23 | 84.9±2.2  | 90.9±3.4 | 77.6±1.6  |
| 24 | 87.6±2.9  | 94.5±1.9 | 78.1±4.7  |
| 25 | 85.7±2.6  | 90.2±5.1 | 87.7±5.5  |

\*the difference is significant relative to the indicator in 1 day

" the difference is significant relative to the indicator in group 1

The baseline values corresponded to the age norm. However, the dynamics revealed a reliably significant increase in the HR mesor in group 1 on days 8-15 of the acute period by 14%, 16%, 18%, 18%, 23%, 17%, 12%, 15% (p <0.05, respectively). In groups 2 and 3, in the dynamics of significant changes in the mesor of the circadian rhythm HR was not observed, which is most likely due to the large spread of the average deviation of the indicator in 1 day. In group 3, on days 7-15, significantly lower HR indicators were found relative to the HR mesor in group 1 by 11%, 7%, 12%, 13%, 8%, 15%, 13%, 7%, 8% (p < 0.05, respectively).

Thus, in group 1, the most significant increase in the mesor of the circadian rhythm HR was revealed in the second week, in group 3 during the indicated period, the mesor of the circadian rhythm HR remained less than in group 1, on average by 11% (fig. 1).

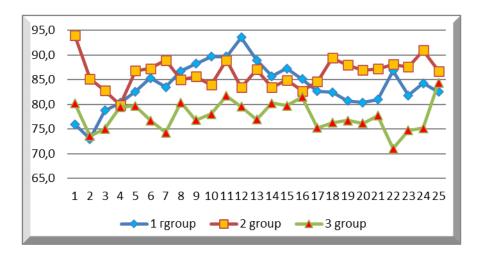


Fig. 1. Dynamics of the mesor of the circadian rhythm HR in the acute period of CSTBI

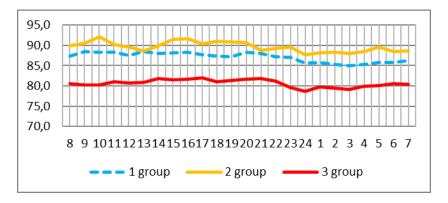


Fig. 2. Hourly heart rate in circadian rhythm in the acute period, beats per minute

Hourly heart rate indicators in the circadian rhythm in the acute period of CSTBI for 25 days (fig. 2) of patients of group 3 were lower than in groups 1 and 2 during the day (at night and daytime).

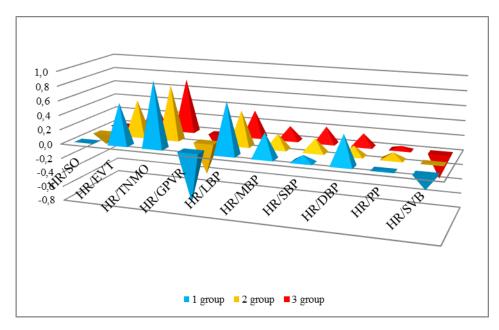


Fig. 3. HR correlations in the acute period of CSTBI

The revealed strong direct correlations between heart rate and TNMO indices in all injured patients (fig. 3) indicate that even with normal HR in the early post-traumatic period, the tendency to increase myocardial oxygen consumption persisted. In the previous work, an increase in the mesor of the circadian rhythm of TNMO in group 1 on days 3-15 was revealed, with a tendency to 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 the indicator in the 1st group.

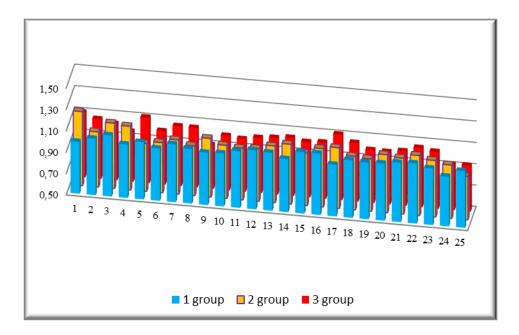


Fig. 4. Changes in the circadian index in the first 25 days of the acute period of CSTBI

Fluctuations in the circadian index occurred in the range of 0.9-1.1, which characterized the rigidity of the heart rhythm (fig. 4). In the first week, you can see fluctuations with a period of 3-4 days.

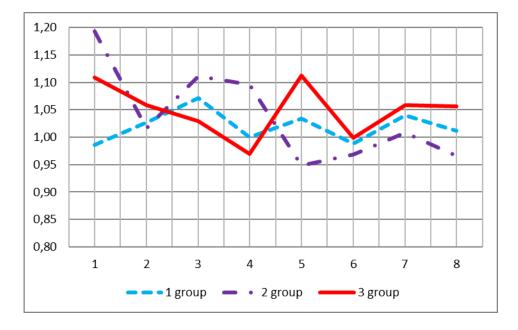


Fig. 5. Changes in the circadian index in the acute period of CSTBI from 1 to 8 days

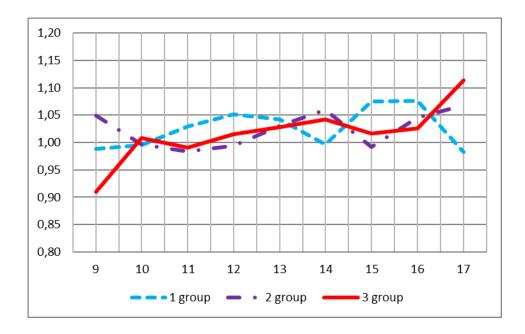


Fig. 6. Dynamics of the circadian index on days 9-17

In the second week, the amplitude of CI fluctuations decreased (fig. 6). On the 18-25th day (fig. 7) the amplitude and wavelength of the CI did not change with signs of an increase in the rigidity of the heart rate on the 22-25th day of intensive therapy. After 20 days in the dynamics of CI, changes appeared indicating cardiovascular disorders caused by autonomic denervation of the heart, a decrease in myocardial contractility, which confirmed the development of irreversible changes in the myocardium and chronic heart failure in patients.

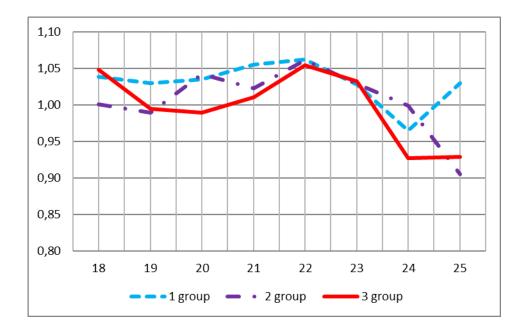


Fig. 7. Change in circadian index for 18-25 days

## Table 2

Correlation relationships between HR and hemodynamic parameters in the weekly biorhythm

|                      | group 1 |      |       | group 2 |      | group 3 |      |        |           |
|----------------------|---------|------|-------|---------|------|---------|------|--------|-----------|
| Days                 | 1-8     | 9-17 | 18-25 | 1-8     | 9-17 | 18-25   | 1-8  | 9 - 17 | 18-25 day |
| HR/oxygen saturation | 0.3     | 0.4  | -0.1  | 0.1     | -0.2 | -0.2    | -0.6 | -0.3   | -0.2      |
| HR/EAT               | 0.9     | 0.9  | 0.7   | 0.4     | 0.9  | -0.1    | 0.4  | 0.0    | 0.6       |
| HR/TNMO              | 1.0     | 0.9  | 0.9   | 0.9     | 0.9  | 0.2     | 0.8  | 0.8    | 0.8       |
| HR/GPVR              | -0.6    | -0.7 | -0.7  | -0.8    | -0.7 | 0.0     | -0.1 | -0.3   | -0.3      |
| HR/CO                | 0.6     | 0.7  | 0.8   | 0.6     | 0.7  | -0.1    | 0.2  | 0.1    | 0.6       |
| HR/MBP               | 0.7     | 0.6  | 0.6   | -0.5    | 0.5  | -0.1    | 0.5  | 0.0    | 0.2       |
| HR/SBP               | 0.3     | 0.6  | 0.7   | -0.5    | 0.3  | 0.0     | 0.6  | 0.0    | 0.2       |
| HR/DBP               | 0.8     | 0.5  | 0.3   | -0.5    | 0.2  | 0.0     | 0.4  | 0.2    | 0.1       |
| HR/PP                | 0.0     | 0.7  | 0.6   | -0.6    | 0.6  | -0.4    | 0.1  | -0.1   | 0.0       |
| HR/SVB               | -0.4    | 0.0  | 0.5   | -0.4    | 0.3  | -0.3    | -0.3 | -0.5   | -0.2      |

As shown in Table 2, in the 1st group of patients throughout the observation there was a strong direct correlation between the heart rate and autonomic tone, that is, sympathotonia was accompanied by a tendency to increase the heart rate. In group 2, a strong direct relationship between HR and EAT was found only in the second week of intensive therapy (0.9). In group 3, a certain trend in the influence of sympathetic activity on HR was observed only on days 18-25 (0.6). Direct dependence of myocardial oxygen demand on HR was observed in all patients, except for 18-25 days in group 2 (0.2). That is, in the majority of injured patients, increased heart rate was accompanied by an increase in oxygen demand. In this regard, in the acute period of CSTBI, it is advisable to maintain HR within the age norm. However, knowing that tachycardia is a compensatory mechanism aimed at restoring the increased needs of the brain tissue for oxygen, then, apparently, it is necessary to search for additional methods to effectively combat oxygen starvation, brain hypoxia in other ways. One of them is MRS, which proved to be

insufficiently effective in our patients. Therefore, it is necessary to develop additional methods to combat post-traumatic brain hypoxia.

The inverse correlation turned out to be inconsistent, so in group 1 the inverse correlation of HR and GPVR was small in the first week (-0.6), it became significant at 2-3 weeks of treatment, amounting to -0.7; -0.7, respectively. In group 2, the increase in heart rate with a decrease in peripheral resistance in the first two weeks was -0.8; -0.7. However, the compensatory response to a decrease in peripheral vascular tone completely disappeared at 3 weeks of intensive therapy. Group 3 differed from the first two in that the dependence of the heart rate on GPVR was completely absent throughout the acute period of CSTBI. That is, the age-related difference in group 3 patients was the absence of a compensatory reaction of the sinus node in response to changes in peripheral hemodynamics. The latter is most likely associated with a change in the trophism of the sinus node, vascular walls, the adequacy of the functional response of the brain caused by STBI against the background of age-related chronic oxygen deficiency.

Direct strong correlation characterized the adequate compensatory reaction of blood circulation in response to stress tachycardia in group 1 0.6; 0.7; 0.8. While in group 2, a strong direct correlation between HR and CO in the first 17 days after injury, on days 18-25 practically disappeared (-0.1). In group 3, the correlation between CO and HR was absent until the 17th day, appearing on the 18-25th day (it became 0.6). Interestingly, correlations between HR and SVB, as well as with SBP, DBP, PP, were not revealed in almost all patients. Only group 1 showed a direct correlation between HR and MBP in the acute period of CSTBI. In groups 2 and 3, the relationship between cardiac function and MBP level was not revealed. Thus, the study of the correlations between HR and other circulatory parameters in the peri-weekly biorhythm made it possible to obtain additional diagnostic information that would allow timely or prophylactic correction of metabolic changes in the circulatory system in order to optimize intensive therapy and increase the viability of organs and tissues in the acute period of CSTBI.

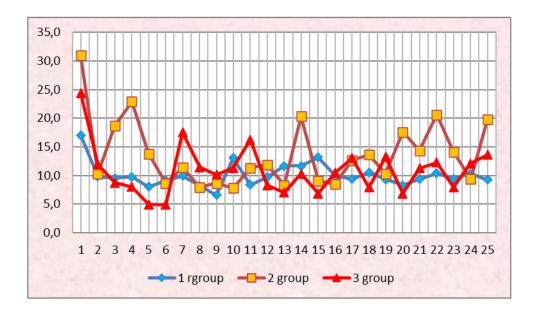


Fig. 8. Dynamics of the amplitude of the circadian rhythm HR, beats per minute

As shown in fig. 8, the greatest amplitude of daily fluctuations was observed on day 1 in group 2 (30 beats per minute), the smallest in group 3 (17 beats per minute). On the following days, the amplitude of the HR circadian rhythm turned out to be greater in group 2 at 4,14,22,25 days.

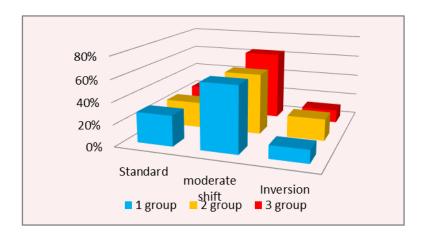


Fig. 9. The duration and degree of shifts in the acrophase of the circadian rhythm of the heart rate

The most prolonged inversion of the HR circadian rhythm was also found in patients of group 2 than in groups 1 and 3.

**Conclusion.** Fluctuations of the circadian index occurred in the range of 0.9-1.1, which characterized the pronounced rigidity of the heart rate during the acute period of CSTBI. The baseline heart rate indicators corresponded to the age norm. In dynamics, in group 1 on days 8 - 15, an increase in the mesor of the HR circadian rhythm by an average of 16% was revealed. In group 3, during the indicated period, the mesor of the circadian rhythm HR remained less than in

group 1 by an average of 11%. Hourly heart rate in the circadian rhythm in the acute period of CSTBI for 25 days in the light and dark hours of the day in patients of group 3 were lower than in groups 1 and 2. Throughout the observation, strong direct correlations between the heart rate and the indicators of myocardial oxygen demand in all injured were revealed.

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