THE COURSE OF COMPLICATED INJURY OF THE CERVICAL SPINE WITH THE DEVELOPMENT OF NEUROGENIC SHOCK

M.N. Lebedeva, I.A. Statsenko, A.V. Palmash, E.Yu. Ivanova, V.V. Rerikh
Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, Novosibirsk, Russia

Objective. To establish the effect of neurogenic shock (NS) on the course of acute complicated injury of the cervical spine.
Material and Methods. The retrospective study included 96 patients with acute complicated injury of the cervical spine. The criteria for the presence of NS were determined as mean arterial pressure (MAP) < 70 mm Hg, and heart rate (HR) < 60 per minute. Two groups were distinguished: Group 1 included 13 patients with NS, and Group 2 – 83 patients without NS. The main characteristics of patients and the course of spinal cord injury were analyzed from the moment of admission to the 30th day of follow-up.
Results. There were no statistically significant differences between the groups in terms of gender, age, level of spinal injury, severity of spinal cord injury and comorbidity. Admission BP and HR in patients with NS were below the reference values and had statistically significant differences in comparison with similar indicators in patients of Group 2. On the first day of treatment in the intensive care unit (ICU), hemodynamic support was required for all patients of Group 1, and for 69 patients of Group 2 (83.1 %). The duration of hemodynamic support in Group 1 was 11 days [6; 15], and in Group 2 – 7 days [4; 14]; p = 0.231. Blood lactate and pH levels were consistent with reference values at all stages, with no intergroup differences. Differences in the severity of organ dysfunctions (SOFA scale) were registered only on the seventh day of treatment in the ICU (p = 0.010); there were no significant differences in the severity of the patients' condition (APACHE II scale). The presence of NS was accompanied by a statistically significant increase in the complication rate. The duration of treatment in the ICU was 28 days [22; 57] in Group 1, 23.5 days [11; 37] in Group 2 (p = 0.055), and that in the hospital – 58 days [44; 70] in Group 1 versus 41.5 [24; 59.5] in Group 2 (p < 0.025). Positive dynamics in the neurological status was noted at discharge in 15.0 % of Group 1 patients and in 19.3 % of Group 2 patients.
Conclusion. The prevalence of NS in isolated injury of the cervical spine was 13.5 %. The development of NS significantly increases the complication rate and duration of hospital stay, but does not exclude the possibility of regression of existing neurological disorders.
Key Words: complicated injury of the cervical spine, spinal cord injury, neurogenic shock, hemodynamics, complications.
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The development of neurogenic shock (NS) in complicated spinal injuries is associated with autonomic dysfunction, characterized by an acute loss of sympathetic innervation of the heart and blood vessels with complete dominance of the parasympathetic nervous system. NS can significantly affect the course of the early period of spinal cord injury and, consequently, the management of patients [1, 2]. According to American researchers [3, 4], the incidence rate of NS in isolated spinal cord injuries is 14.2 %. A significantly higher incidence rate of NS has been indicated in patients with complete spinal cord injuries and in those with injury localization above the T6 vertebra.

The leading clinical signs of NS are arterial hypotension and bradycardia, in which the perfusion of organs and tissues is critically reduced. This is not only a risk factor for the development of multiple organ system failure but also for secondary ischemic injury to the spinal cord. Moreover, the probability of recovery of neurological functions decreases [5–7]. The authors of most academic papers have already considered arterial hypotension with a systolic blood pressure (SBP) of less than 100 mm Hg and a heart rate (HR) of less than 80 per minute as a criterion for the identification of NS. Nevertheless, no widely accepted criteria for verifying the incidence of NS in individuals with spinal cord injuries have been implemented to date. The scientific literature is still divided on which hemodynamic abnormalities associated with a complicated spinal injury should be attributed to a shock. The issues of the NS incidence rate and its effect on the early period of traumatic spinal cord injury are still relevant.

The objective is to establish the effect of NS on the course of an acute complicated injury of the cervical spine.

Material and Methods

Patients

A retrospective single-center cohort study was performed, which included 96 patients who were treated at the Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan from January 2014 to March 2022.

Inclusion criteria: an acute, isolated, complicated injury of the cervical spine;

peracute, acute and early periods of injury in patients at the time of admission to the hospital; the severity of spinal cord injury of grades A, B and C according to ASIA. Exclusion criteria: severity of a spinal cord injury grade D according to ASIA.

Techniques

To evaluate the severity of spinal cord injury, the ASIA/IMSOP classifications developed by the American Spinal Injury Association and the International Medical Society of Paraplegia were used [8]. The injury period was classified according to the current clinical recommendations of the Ministry of Health of the Russian Federation, "Spinal cord and spinal cord injury in adults": the peracute period (the first 8 hours); the acute period (from 8 hours to 3 days); the early period (from 3 days to 4 weeks); the interim period (from 1 to 3 months); and the late period (more than 3 months) [9].

The clinical criteria for the NS incidence in patients were determined by the level of mean arterial pressure (MAP) < 70 mm Hg and heart rate (HR) < 60 per minute according to the generally accepted definitions of hypotension and bradycardia. The analysis was performed both for the entire sample of patients and with the distinguishing of two observation groups: Group I – patients with NS; and Group II – patients whose hemodynamics did not meet the accepted criteria of NS.

During the study, gender, age, comorbidities, time before admission to the hospital from the moment of injury, time before decompression of the spinal cord, indicators of systemic hemodynamics, severity of the condition and severity of organ dysfunction, duration of hemodynamic support, blood lactate level, ABG and acid-base balance, complications, dynamics of neurological status, duration of follow-up and treatment in the intensive care unit (ICU), duration of hospital stay, and mortality were analyzed.

Hemodynamic support aimed at ensuring an effective blood pressure (BP) level with target values of MAP not less than 85–90 mm Hg was started from the stage of preoperative examination of patients. The starting drug of choice was 0.02 % norepinephrine at a dose of 0.05–0.5 μg/kg/min.

An emergency surgery aimed at decompression of the spinal cord and stabilization of the spine was indicated to 82 (85.4 %) patients due to spinal cord compression. There were no indications for surgical treatment in 14 patients with spinal cord injuries. After the examination was completed, they were transferred to the ICU for case follow-up and treatment aimed at organ dysfunction correction.

Decompressin and stabilization surgeries were performed under inhalation anaesthetic agents with artificial ventilation and continuous hemodynamic support (sevoflurane, fentanyl, rocuronium bromide and norepinephrine). Postoperative intensive care in the ICU was aimed at providing normoxaemia, normocapnia, effective blood pressure level, and normovolemia.

The target values for artificial ventilation were as follows: oxygen saturation (SaO_2) > 96 %, partial pressure of carbon dioxide ($PaCO_2$) 35–45 mm Hg, partial pressure of oxygen (PaO_2) > 65 mm Hg, pH 7.35–7.45.

Advanced noninvasive hemodynamic monitoring was performed in the ICU using a Nicom Reliant monitor (Israel). The evaluated parameters included systolic blood pressure (SBP, mm Hg), diastolic blood pressure (DBP, mm Hg), MAP (mm Hg), HR per minute, cardiac output (CO, L/min), cardiac index (CI, L/min/m2), stroke volume (SV, ml), systolic volume index (SVI, ml/m^2), total peripheral resistance (TPR, dyn sec/cm^{-5}), and total peripheral resistance index (TPRI, dyn sec/cm^{-5}/m^2).

Hemodynamic support aimed at correcting arterial hypotension was performed under extended hemodynamic monitoring. At normal CI values and reduced TPR, the drug of choice was 0.02 % norepinephrine at a dose of 0.05–0.5 μg/kg/min or dopamine 0.5 % at a dose of 1.0–10.0 μg/kg/min. At CI values < 3.5 L/min/m2 and normal TPR values, dobutamine was used at a dose of 1.0–10.0 μg/kg/min. When registering MAP < 70 mm Hg, CI < 3.5 L/min/m^2 and TPR < 1000 dyn sec/cm^{-5}, combined administration of vasopressors and cardiotonics was used. Infusion therapy in a volume of up to 20 ml per kg of ideal body weight was a first-line treatment in order to achieve and maintain normovolemia.

The analysis of the ABG and acid-base balance (ABB) of arterial blood was performed on a Blood Gas Analyser GEM Premier 3000 (USA). Blood lactate (mmol/L), PO2 (mm Hg), and PCO2 (mm Hg) were evaluated; the oxygenation index (OI = PO2/FiO2) was calculated.

The severity of the condition and the intensity of organ dysfunction were evaluated according to the APACHE II (Acute Physiology and Chronic Health Evaluation) and SOFA (Sequential Organ Failure Assessment) scales.

The neurological status dynamics was regarded as positive when registering the fact of a transition to a milder degree of severity of spinal cord injury on the ASIA scale.

We recorded the main parameters and indicators studied at the following time points: when at admission to the emergency unit, on 1, 3, 5, 7, 10, 15, 20, 25, and the 30th day of follow-up.

The research was approved by the Committee on Biomedical Ethics of the Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan (extract 003/23 from the minutes of the meeting 001/23 dated January 17, 2023).

Statistical analysis

Statistical calculations were performed in the RStudio software (version 1.3.959 – © 2009-2020 RStudio, Inc., USA, URL: https://www.rstudio.com) in R (version 4.0.2, URL: https://www.R-project.org). Continuous indicators were checked for compliance with the law of normal distribution by the Shapiro–Wilk test. The homogeneity of the deviations of the indicators in the compared groups was studied by Fisher's exact test.

Continuous indicators were compared using nonparametric rank tests such as the Mann–Whitney U test and the Wilcoxon signed-rank test.

Descriptive statistics for continuous data are shown as a median [first quartile; third quartile]; binary data are described as the number of elements (events, complications, etc.), a percentage of the group size [lower bound 95 % CI; upper bound of 95 % CI] according to the Wilson formula; and for each level of categorical data, the number of patients at the level (percentage of the total number of patients in the group) was fulfilled.

The Wilcoxon signed-rank test was used to statistically verify hypotheses concerning the equality of sample distributions for continuous indicators at different time points.

The identification of predictors of the development of NS was performed by modeling logistic regressions.

Statistical hypotheses were checked at a critical significance value of 0.05, which means that the difference was considered statistically significant at the achieved value of $p < 0.05$.

Results

The mean age of patients in the entire sample was 39.91 ± 15.48 years old. The absolute number of injured were male patients: 89 (92.7 %). The leading causes of injuries were so-called diver's injury – 36 (37.5 %) cases, accidents – 23 (24.0%) cases, and a fall from height – 20 (20.8 %) cases. Fifty seven (59.4 %) patients were admitted to the hospital in the peracute period of the injury, 33 (34.4%) in the acute period, and 6 (6.2 %) in the early period. The mean time prior to in-patient facility admission was 6 hours [2.88; 18.75]. Sixty four (66.7 %) patients with the most severe neurological disorders related to grade A, according to ASIA, were the absolute majority. There were 22 (22.9 %) patients with grade B spinal cord injury severity according to ASIA and 10 (10.4 %) patients with grade C spinal cord injury.

Forty (41.6 %) patients had no comorbidity, whereas 56 (58.3 %) patients had a variety of comorbidities as indicated in Table 1.

According to the adopted criteria, NS was detected in 13 (13.5 %) patients at the time of admission. Out of them 8 (61.5 %) suffered the peracute injuries, and 5 (38.5 %) had injuries in the acute stage.

There was no statistically significant difference between the groups in terms of gender, age, mechanism of injury, or presence of comorbidity. The pattern of patient distribution according to the level of cervical spine cord injury in the groups is shown in Table 2.

According to the severity of spinal cord injury, patients in the distinguished groups were distributed as follows: ASIA A – 11 (84.6 %) in Group I, 54 (65.0 %) in Group II ($p = 0.533$); ASIA B – 2 (15.4 %) in Group I, 20 (24.0 %) in Group II ($p = 0.726$), and ASIA C – 9 (11.0 %) in Group II ($p > 0.999$).

There are 11 (84.6 %) patients in Group I and 71 (85.5 %) patients in Group II who underwent surgery. While comparing the main characteristics of the intraoperative period, there was no statistically significant difference in the intergroup comparison. The surgery duration was 230.0 [207.5; 250.0] min in Group I and 217.5 [195.0; 260.0] min in Group II ($p = 0.526$). The blood loss volume was 150.0 [100.0; 275.0] ml in Group I and 200.0 [100; 300] ml in Group II ($p = 0.550$).

The dynamics of BP and HR during the follow-up and treatment of patients in the ICU are given in Table 3. As can be seen from the data, the indicators of BP and HR in patients with NS at admission to the hospital were lower than the reference values and had statistically significant differences in comparison with similar indicators in patients in Group II. However, during follow-up, there were no statistically significant differences in the considered indicators at all stages of the study, including the intergroup comparison.

On the 1st day of treatment in the ICU, all patients in Group I required correction of hemodynamic parameters; in Group II, a similar situation was observed in 69 (83.1 %) patients. The drugs of choice for hemodynamic support in Group I were norepinephrine in 5 (38.5 %) cases, dobutamine in 1 (7.7 %) case, dopamine in 1 (7.7 %) case, norepinephrine + dobutamine in 3 (23.1 %) cases, and norepinephrine + dopamine in 3 (23.1 %) cases. In Group II, norepinephrine was used for hemodynamic support in 32 (38.6 %) cases, dobutamine in 8 (9.6 %) cases, dopamine in 4 (4.8 %) cases, norepinephrine + dobutamine in 13 (15.7 %) cases, and norepinephrine + dopamine in 12 (14.5 %) cases.

The CI and TPR values as the main indicators of central hemodynamics during the first week of follow-up and treatment in the ICU are shown in Table 4.

The CI and TPR indicators, which were recorded in conjunction with hemodynamic support in the ICU, did not differ considerably between groups. They were within the range of reference values at all stages of the study.

The maximum duration of hemodynamic support, which exceeded 30 days, was recorded in three patients in Group I with a long period of unstable hemodynamics and a spinal cord injury of ASIA A severity affected by the development of severe complications (pulmonogenic sepsis, PATE, and severe bilateral ventilator-associated pneumonia). In Group II, hemodynamic support, which eventually exceeded 30 days, was necessary for four patients with a spinal cord injury of ASIA A severity. The causes of a long period of unstable hemodynamics in these patients were acute Q-negative anterior myocardial infarction in one case and a severe course of bilateral nosocomial pneumonia in three cases.

The blood lactate and pH levels remained within the reference ranges throughout the study while there were no statistically significant intergroup differences (Fig. 1).

Fig. 2 shows the assessment of the severity of the patients' condition on the APACHE II scale and the severity of organ dysfunction on the SOFA scale. The severity analysis of the patients' condition during the intergroup comparison showed the absence of statistically significant differences at all stages of the study. The severity of organ dysfunction on the first day of follow-up in the groups showed no differences. By the 3rd day, the severity of organ dysfunction in Group I increased, and then it was higher in patients with NS at all stages of the study. Nevertheless, a statistically significant difference was registered only on

Table 1

Pattern of comorbidities in the entire sample of patients

Nature of the comorbidity	Patients, n (%) [95 % CI]
Arterial hypertension	25 (26) [18; 36]
Coronary heart disease	12 (12) [7; 21]
Atrial fibrillation	2 (2) [1; 7]
Cardiosclerosis	7 (7) [4; 14]
Presence of coronary artery stents	1 (1) [0; 6]
Chronic heart failure	20 (21) [14; 30]
Chronic bronchitis	15 (16) [10; 24]
Chronic obstructive pulmonary disease	9 (9) [5; 17]
Bronchial asthma	1 (1) [0; 6]
Tuberculosis	2 (2) [1; 7]
Chronic anemia	6 (6) [3; 13]
Thrombocytopenia	7 (7) [4; 14]
Chronic gastritis	15 (16) [10; 24]
Peptic ulcer disease	5 (5) [2; 12]
Ankylosing spondylitis	2 (2) [1; 7]
Diabetes mellitus	3 (3) [1; 9]
Chronic renal disease	3 (3) [1; 9]
Viral hepatitis	9 (9) [5; 17]
HIV	5 (5) [2; 12]

Table 2

Distribution of patients in groups according to the level of cervical spine injury, n (%)

Level of injury	Group I (n=13)	Group II (n=83)	Fisher's exact two-sided test (p value)
C2–C5	0 (0.0)	1 (1.2)	>0.999
C2–C7	1 (7.7)	0 (0.0)	0.137
C3–C4	0 (0.0)	3 (3.7)	>0.999
C3–C5	0 (0.0)	3 (3.7)	>0.999
C3–C6	0 (0.0)	2 (2.4)	>0.999
C3–C7	0 (0.0)	3 (3.7)	>0.999
C4	0 (0.0)	2 (2.4)	>0.999
C4–D1	0 (0.0)	1 (1.2)	>0.999
C4–C5	2 (15.4)	9 (11.0)	=0.644
C4–C5	0 (0.0)	3 (3.7)	>0.999
C4–C7	2 (15.4)	2 (2.4)	=0.089
C5	1 (7.7)	5 (6.1)	>0.999
C5–C6	2 (15.4)	8 (9.8)	=0.623
C5–C6	0 (0.0)	5 (6.1)	>0.999
C6	2 (15.4)	13 (15.9)	>0.999
C6–C7	2 (15.4)	19 (22.1)	0.729
C7	1 (7.7)	4 (4.9)	0.529
Total	13	83	–

the 7th day of follow-up and treatment in the ICU (p = 0.010).

Cases of complications from the respiratory, cardiovascular, and urinary systems, the gastrointestinal tract, as well as venous thromboembolism and trophic disturbances, were registered in both observation groups. Table 5 presents the pattern of the most common complications.

When comparing the groups, the difference in indicators of ICU stay duration approached the statistical significance value and amounted to 28.0 [22; 57] days in Group I and 23.5 [11; 37] days in Group II (p = 0.055). Meanwhile, statistically significant differences in the duration of in-patient facility were obtained: 58.0 [44; 70] days in Group I and 41.5 [24; 59.5] days in Group II (p = 0.025).

Positive trends in the neurological status at the time of discharge from the hospital were noted in two patients in Group I: one patient switched from ASIA A to ASIA B and one patient switched from ASIA B to ASIA D. In Group II, positive trends in neurological status were noted in 16 patients: the switch from ASIA A to ASIA B in three patients, from ASIA A to ASIA C in four patients, from ASIA B to ASIA C in three patients, and from ASIA C to ASIA D in six patients.

Fatal outcomes were present in both groups: 1 (7.7 %) [1.0; 33.0] in Group I; 3 (3.6 %) [2.0; 12.0] in Group II. There was no statistically significant difference in the frequency of fatal outcomes (p = 0.529).

By constructing single-factor models of logistic regression, some significant predictors of the development of NS in the entire sample of patients were revealed. It was found that the C5–C6 spinal cord injury is associated with increase in the chances of developing NS by 21.25 [1.85; 488.45] times. Multiplicative significant predictors of the NS development in the backward multivariate logistic regression model of patients have not been identified.

Discussion

The currently published data on the incidence rate of NS in complicat-

Table 3

Dynamics of blood pressure and heart rate in the observation groups

Indicator	Group I (n=13)	Group II (n=83)	Comparison with Mann—Whitney U test	
	MED [IQI]	MED [IQI]	MED [95 % CI]	p value
SBP at admission	86.50 [83.50; 95.75]	115.00 [107.00; 124.75]	-26.0 [-36.0; -19.0]	<0.001*
DBP at admission	45.00 [45.00; 50.00]	70.00 [63.25; 78.00]	-25.0 [-29.0; -19.0]	<0.001*
MAP at admission	60.30 [58.00; 63.30]	85.65 [79.30; 92.70]	-26.2 [-32.3; -20.6]	<0.001*
HR at admission	51.00 [48.00; 55.00]	68.00 [61.00; 76.00]	-17.0 [-23.0; -12.0]	<0.001*
MAP on the 1st day	89.15 [81.78; 6.45]	86.70 [80.70; 99.00]	-0.6 [-7.7; 7.4]	0.888
HR on the 1st day	66.00 [61.00; 79.75]	64.00 [60.00; 70.00]	-2.0 [-9.0; 5.0]	0.491
MAP on the 3rd day	93.70 [86.30; 100.30]	103.70 [87.70; 106.70]	5.0 [-4.0; 12.4]	0.226
HR o the 3rd day	68.00 [62.00; 74.00]	60.00 [56.00; 67.00]	-5.0 [-11.0; 2.0]	0.178
MAP on the 5th day	92.00 [83.70; 97.30]	92.30 [89.30; 101.00]	4.3 [-2.7; 13.4]	0.241
HR on the 5th day	68.00 [60.75; 75.00]	76.00 [64.00; 80.00]	5.0 [-3.0; 13.0]	0.195
MAP on the 7th day	91.70 [84.65; 97.15]	96.50 [92.00; 99.00]	4.3 [-1.0; 10.0]	0.108
HR on the 7th day	66.00 [61.00; 74.00]	69.50 [62.50; 79.25]	2.0 [-6.0; 10.0]	0.589
MAP on the 10th day	85.00 [79.50; 93.30]	83.80 [80.70; 91.35]	-0.3 [-6.6; 6.0]	0.908
HR on the 10th day	69.00 [61.00; 75.50]	66.00 [58.00; 73.50]	-3.0 [-11.0; 5.0]	0.649
MAP on the 15th day	84.30 [77.30; 92.30]	85.00 [79.08; 89.95]	-1.0 [-8.4; 6.0]	0.793
HR on the 15th day	67.00 [62.00; 73.00]	72.50 [65.50; 78.50]	5.0 [0.0; 11.0]	0.074
MAP on the 20th day	82.85 [76.05; 8.53]	83.65 [81.60; 87.30]	1.3 [-5.4; 10.6]	0.715
HR on the 20th day	68.00 [64.00; 74.00]	68.00 [63.75; 71.50]	-1.0 [-8.0; 6.0]	0.756
MAP on the 25th day	83.35 [79.25; 0.22]	74.50 [72.10; 81.40]	-7.7 [-16.6; 3.0]	0.140
HR on the 25th day	67.00 [60.00; 76.00]	70.50 [66.75; 75.75]	4.0 [-6.0; 12.0]	0.391
MAP on the 30th day	80.70 [72.70; 90.30]	83.50 [76.25; 88.72]	2.0 [-9.7; 14.0]	0.745
HR on the 30th day	67.00 [60.00; 72.00]	70.50 [65.00; 75.25]	4.0 [-6.0; 11.0]	0.467

MED — median; IQI — interquartile interval; * statistically significant differences.

ed spinal cord injury contain very different indicators, which are between 7.0 and 43.8 percent [2, 4, 10]. The presented differences can be explained by the diverse criteria for inclusion in the studies used by their authors (for example, isolated injury, combined injury, severity of spinal cord injury, hemodynamic criteria of shock, timing of NS manifestation, etc.).

In a previously performed study involving 27 patients with complicated cervical spine injury at the C4–T1 level and the spinal cord injury severity of ASIA A, where MAP < 85 mm Hg and HR < 65 per minute were accepted as criteria indicating NS in patients, the established NS incidence rate was 70.3 %. We associ-

Table 4

The values of the main indicators of central hemodynamics during the first week of treatment of patients in the ICU

Indicator	Group I (n=13)	Group II (n=83)	Comparison with Mann—Whitney U test	
	MED [IQI]	MED [IQI]	MED [95 % CI]	p value
CI on the 1st day	3.50 [3.17; 3.70]	3.40 [3.00; 3.82]	0.0 [-0.8; 0.7]	>0.999
TPR on the 1st day	1541.00 [1499.00; 1619.50]	1211.50 [858.00; 1813.50]	401.5 [-972.0; 83.0]	0.487
CI on the 3rd day	4.10 [3.00; 4.20]	3.20 [2.90; 4.00]	0.3 [-0.6; 1.5]	0.493
TPR on the 3rd day	1507.00 [1443.00; 1821.00]	1144.00 [871.00; 1303.75]	498.5 [-250.0; 1039.0]	0.085
CI on the 5th day	4.10 [3.55; 4.20]	3.35 [3.13; 3.75]	0.4 [-0.8; 1.4]	0.630
TPR on the 5th day	1311.00 [1296.00; 1621.50]	2208.00 [1271.25; 2325.00]	1138.5 [-421.0; 1782.0]	0.244
CI on the 7th day	2.50 [1.90; 3.15]	3.10 [2.80; 3.50]	-0.6 [-1.9; 0.8]	0.426
TPR on the 7th day	1511.00 [1264.00; 2316.00]	1243.00 [1013.70; 601.50]	-205.0 [-1028.0; 477.0]	0.491

CI — cardiac index (L/min/m^2); TPR — total peripheral resistance (dyn sec/cm^{-5}); MED — median; IQI — interquartile interval; * statistically significant differences.

ated such a high incidence rate of NS at hospital admission both with the severity of spinal cord injury in the patients included in the study (ASIA A) and with the small number of its participants [11].

Therefore, it was provocative to consider an isolated injury of the cervical spine with different grades of severity of spinal cord injury. It was also noteworthy to clarify the effect of NS on the course of a complicated acute cervical spine injury.

It was found that the NS incidence at the time of admission to the hospital was 13.5 %, which is quite consistent with the middle position in the recognized range of data. Most of the patients were in the peracute injury period. This fully corresponds to the published data to the effect that, in the vast majority of patients, the NS manifestations were registered already 2 hours after the injury [3, 4].

According to Tee et al. [12], patients suffering from acute spinal cord injury may experience many episodes of arterial hypotension even before admission to specialized units. Considering this circumstance, the absolute majority of patients initially need hemodynamic monitoring and support, in particular vasoconstrictor agents, to exclude secondary spinal cord hypoperfusion [5, 6, 13].

In our study, the absolute majority of patients (92.3 %) included in Group I had hemodynamic support already at the stage of transportation to the hospital. The BP and HR values registered at admission to the hospital were lower than the reference values and statistically significantly different from similar values in Group II, where hemodynamic support was performed in only 32.5 % of patients at the stage of transportation. This is certainly due to the severity of arterial hypotension that characterizes NS.

Despite the fact that the use of vasopressors to maintain hemodynamics after acute spinal cord injury is still recommended, data on the optimal target values of MAP for adequate spinal cord perfusion and the duration of administration of vasoactive agents, as well as the possible risks of this practice, are very limited. Most researchers, as well as current treatment guidelines, consider the retention of a MAP level of more than 85 mm Hg for seven days as the target value. It must be noted that none of the studies compared the outcomes of different durations of application of these guidelines [13–16].

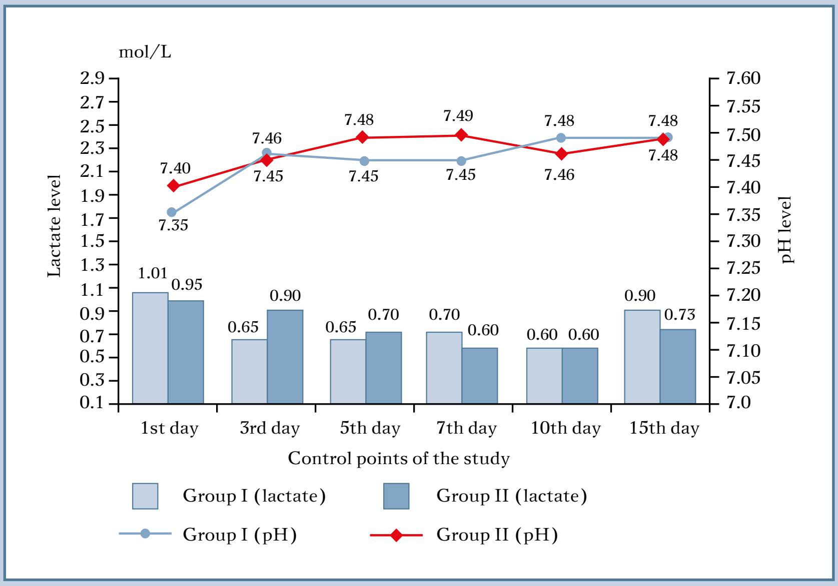

Fig. 1
Dynamics of lactate and pH levels in patients with spinal cord injury in the cervical spine

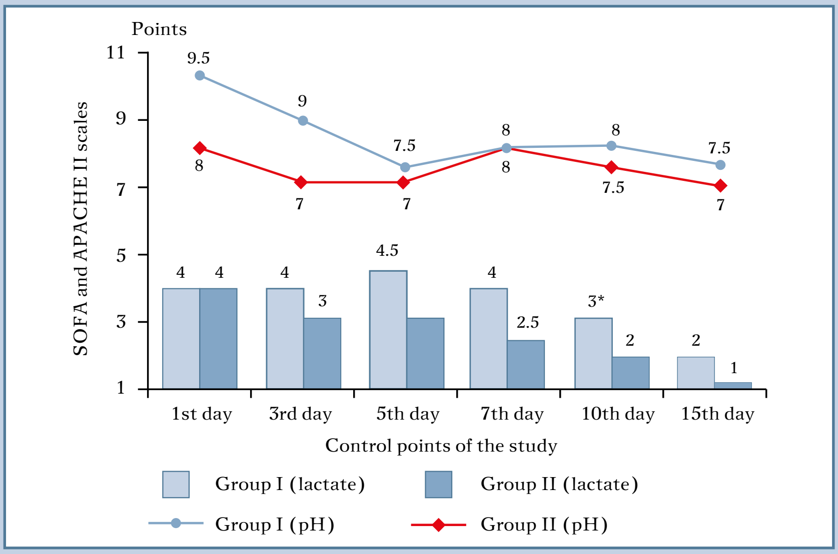

Fig. 2
Dynamics of the severity of the condition of patients with spinal cord injury to the cervical spine according to the APACHE II scale and the severity of organ dysfunctions according to the SOFA scale

Table 5

Pattern and frequency of complications in the observation groups

Nature of complications	Group I (n=13)	Group II (n=83)	Fisher's exact two-sided test	
	n (%) [95 % CI]	n (%) [95 % CI]	OR [95 % CI]	p value
Pneumonia	12 (92) [67; 99]	50 (61) [50; 71]	7.6 [1.0; 37.8]	0.030*
Purulent tracheobronchitis	11 (85) [58; 96]	64 (78) [68; 86]	1.5 [0.3; 15.6]	0.729
Acute renal failure	4 (31) [13; 58]	5 (6) [3; 13]	6.6 [1.1; 37.7]	0.019*
Cerebral salt-wasting syndrome	6 (46) [23; 71]	10 (12) [7; 21]	6.0 [1.4; 26.1]	0.008*
Pulmonogenic sepsis	1 (8) [1; 33]	3 (4) [1; 10]	2.2 [0.0; 29.7]	0.451
Deep vein thrombosis of the lower extremities	6 (46) [23; 71]	26 (32) [23; 42]	1.8 [0.5; 7.1]	0.351
Pulmonary artery thromboembolia	2 (15) [4; 42]	2 (2) [1; 8]	7.0 [0.5; 106.1]	0.089
Acute myocardial infarction	1 (8) [1; 33]	3 (4) [1; 10]	2.2 [0.0; 29.7]	0.451
Heart rhythm disturbances	2 (15) [4; 42]	4 (5) [2; 12]	3.5 [0.3; 27.8]	0.189

MED — median; IQI — interquartile interval; * statistically significant differences.

Quite interesting are the data obtained during a prospective single-center pilot study performed at the ICU of the University Hospital Bergmannsheil Bochum (Germany), which studied the indicators of systemic hemodynamics using the PiCCO system in a cohort of 30 patients with acute spinal cord injury [18]. The authors found that the systemic vascular resistance index (SVRI), central venous pressure (CVP), and the global end-diastolic volume index (GEDVI) were the indicators that diverged from the reference range, while CI, MAP, and HR were in the reference range. The authors emphasize that they conducted almost the first study using extended hemodynamic monitoring for acute spinal cord injury under the thermodilution method in patients who were mostly not affected by vasopressors and other factors affecting the cardiovascular system. The volume status of all patients was thoroughly monitored by thermodilution, and the fluid balance was corrected in accordance with volumetric measurements to achieve euvolemia. Vasoconstrictor agents were used only when the MAP was below 70 mm Hg or when the patient showed signs of decreased perfusion of organs – increased serum lactate levels, oliguria, and dizziness. It was found that in the cohort of patients with acute spinal cord injury, SVRI is always lower than the reference range. This was observed regardless of the use of vasopressors. Additionally, in cases where vasopressors were used, the study revealed a significant negative association between norepinephrine administration and MAP (83.97 vs 73.69 mm Hg; $p < 0.001$), as well as SVRI (1,463.40 vs 1,332.14 dyn sec cm^{-5} m^2; $p = 0.001$) and GEDVI (808.89 vs 759.39 ml/m^2; $p = 0.001$). In reliance on the results of the authors, the performed study provides an unbiased hemodynamic profile of patients with acute spinal cord injury [17]. Additionally, they consider the conclusions obtained by a group of scientists based on the results of a multicenter study performed in 2019 absolutely fair. They established that compliance with the target values of perfusion pressure of the spinal cord, rather than the target values of MAP, is more significant for the possibility of neurological recovery. Thus, in their opinion, MAP of 70 mm Hg is permissible for patients with acute spinal cord injury, if there are no signs of decreased perfusion of organs (increased lactate, oliguria) [18].

The opinion that spinal cord perfusion pressure is a stronger predictor of favorable outcomes is also shared by other authors, who report the need to control perfusion pressure by direct measurement of intraspinal pressure as a safe and efficient way to monitor spinal cord perfusion [19, 20].

The absolute majority of participants in our study received pharmacological support for their blood pressure levels at the recommended target values. The choice of pharmacological agents to provide the target values of MAP was based on the outcomes of noninvasive monitoring of CI and TPRI. Against the background of the correction of the existing disorders, hemodynamic parameters in the groups at all time points of the study were within the range of reference values and did not differ significantly in the intergroup comparison. The mean duration of hemodynamic support in the groups was 11 [6; 15] days in Group I and 7 [4; 14] days in Group II ($p = 0.231$). Nevertheless, it should be noted that a number of patients in both groups required longer hemodynamic support due to the continuing unstable hemodynamics associated with the development of severe complications.

The main reason for the existing requirements for the BP level was the positive correlation established in several previously performed studies between the values of MAP and neurological recovery in patients with injuries A, B, and C according to the ASIA scale [14, 21, 22]. Positive trends in neurological status at the time of discharge from the hospital were noted in both observation groups: 15.0 % of cases in Group I and 19.3 % in Group II.

We should focus on the peculiarities of the course of NS associated with the blood lactate level. Hyperlactatemia is known to be a biomarker of shock and is closely associated with a dismal prognosis. The level of lactate in shock conditions also corresponds to the indicators of acid-base balance of the blood, characterized by types of acidosis severity [23, 24]. We have long drawn attention to the fact that when considering issues related to NS in spinal injury, researchers do not evaluate the level of lactatemia. But the question arises: Why?

In earlier obtained data and in the current study, the results of which we present, in the presence of hemodynamic criteria of NS in patients, blood lactate indicators were indeed within reference values at all phases of follow-up, indicating a lack of organ and tissue hypoperfusion. This was confirmed by the acid-base balance of the blood. Perhaps the already mentioned study by the University Hospital of Bochum includes the explanation for this circumstance. Its authors concluded that in acute spinal cord injury, cardiac output increases to compensate for the loss of afterload and thereby enhance the delivery of oxygen to organs and tissues. According to the authors from the University Hospital of Bochum, the increase in cardiac output can be explained by an increase in preload. In this case, GEDVI, which was at the upper limit of the reference range, was considered a preload marker. Because of this compensatory mechanism, sufficient perfusion of organs and tissues is preserved even with reduced peripheral vascular resistance. The authors concluded that low vascular resistance is admissible from the point of view of the cardiovascular system. Consequentially, it is necessary to consider the possibility of regulating the reference values of MAP if the patient has no signs of a decrease in organ perfusion.

Despite published data on the target rates of MAP after spinal cord injury, the special pharmacological management of BP in acute traumatic spinal cord injury and the consequences of these interventions have yet to be clarified.

Undesired events in various periods of complicated cervical spine injury are considered emerging complications, which, in turn, are frequent causes of fatal outcomes. Respiratory, renal, cardiovascular, and thromboembolic complications most often develop, aggravating the hemodynamic instability of the patient, and the diagnosis of which is especially complicated in the acute injury phase associated with neurogenic shock. The data obtained on the frequency and nature of complications as well as mortality do not contradict the data from scholarly sources. All registered complications were more often observed in the group of NS patients. Nevertheless, statistically significant differences were found in the incidence of pneumonia, acute renal failure, and cerebral salt wasting syndrome, which is characterized by hyponatremia and is a typical complication for patients with traumatic injury to the spinal cord [25–27]. Undoubtedly, the development of such complications affected the duration of stay and treatment of patients with NS in the ICU and the total duration of their hospital stay.

According to univariate regression analysis, the localization of spinal injury at the C5–C6 level is a separate significant predictor of the development of NS. Nevertheless, according to the results of multivariate regression analysis, no significant predictors were identified.

The positive side of the completed study is the number of participants and the follow-up of patients in the ICU setting, that was quite sufficient to achieve the aim of the study. In our opinion, the main limitation of the study is the lack of invasive hemodynamic monitoring. The use of the latter would make it possible to optimize the duration of drug management of blood pressure levels, considering that the pharmacological effect of the drugs used is the result of increased vasoconstriction, and the consequences of such exposure have yet to be studied.

Conclusion

The use of hemodynamic criteria consistent with the generally accepted concepts of hypotension and bradycardia provided a more accurate determination of the incidence of NS in isolated cervical spinal cord injuries, which was 13.5 %. Even in the absence of adequate hemodynamic support, NS remains compensated for a long time, as evidenced by the absence of lactic acidosis. The development of neurogenic shock significantly increases the number of complications and the hospital stay duration of patients, but does not exclude the possibility of regression of existing neurological disorders.

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The authors declare that they have no conflict of interest.

The study was approved by the local ethical committee of the institution.

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Address correspondence to:

Statsenko Ivan Anatolyevich
Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan,
17 Frunze str., Novosibirsk, 630091, Russia,
Stacenco_i@mail.ru

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Maya Nikolayevna Lebedeva, DMSc, Head of Research Department of Anesthesiology and Reanimatology, Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0002-9911-8919, MLebedeva@niito.ru;

Ivan Anatolyevich Statsenko, anesthesiologist-intensivist, Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0003-2860-9566, Stacenco_i@mail.ru;

Aleksey Viktorovich Palmash, anesthesiologist-intensivist, Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0002-2454-477X, alexpslmasph@gmail.com;

Elena Yuryevna Ivanova, anesthesiologist-intensivist, Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0001-9999-9384, lenamayveeve888@mail.ru;

Viktor Viktorovich Rerikh, DMSc, Head of the Research Department of Spine Pathology, Novosibirsk Research Institute of Traumatology and Orthopaedics n.a. Ya.L. Tsivyan, 17 Frunze str., Novosibirsk, 630091, Russia, ORCID: 0000-0001-8545-0024, VRerih@niito.ru.