

Dynamics of the baroreflex sensitivity during combined anesthesia with sevoflurane or propofol: a randomized trial

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Динамика барорефлекса в условиях сочетанной анестезии севофлураном или пропофолом: рандомизированное исследование

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Abstract

INTRODUCTION: A significant number of complications is still a serious problem in abdominal surgery. It is known that patients with low baroreflex sensitivity are more prone to hemodynamic instability during general anesthesia, which allows them to be identified as a risk group. **OBJECTIVE:** To evaluate the dynamics of baroreflex sensitivity (BRS) during major abdominal surgery in patients with different risk of critical incidents under combined anesthesia with propofol or sevoflurane. **MATERIALS AND METHODS:** A randomized study was conducted in 160 patients (80 high-risk and 80 low-risk patients), who were randomized into subgroups according to the type of anesthesia (propofol or sevoflurane) to assess the effect of the type of anesthesia critical incidents and baroreflex dynamics. **RESULTS:** After the induction there was a trend towards a decrease in BRS, while in subgroups with initially low values of BRS, it decreased below 3 ms/mmHg. After the end of operation and 6 hours after extubation, there were no significant changes in comparison with intraoperative values. Evaluation of BRS after 24 hours showed that BRS in all subgroups was significantly higher than at previous time points, but did not return to baseline values. At 6 hours postoperatively, in low-risk patients, BRS values were below 3 ms/mmHg in 12.5% with propofol, and in 10% with sevoflurane, in high-risk patients — in 45% and 42.5% of cases, respectively. At 24 hours, in the low-risk group, only two patients in the propofol anesthesia group and one in the sevoflurane anesthesia subgroup experienced this dysfunction. **CONCLUSIONS:** Both anesthesia

Реферат

АКТУАЛЬНОСТЬ: Значительное число осложнений все еще является серьезной проблемой в абдоминальной хирургии. Известно, что пациенты с низкой чувствительностью барорефлекса более склонны к гемодинамической нестабильности во время общей анестезии, что позволяет выделить их в группу риска. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Оценить динамику чувствительности барорефлекса (ЧБР) при обширных абдоминальных операциях у пациентов с различным риском критических инцидентов в условиях сочетанной анестезии пропофолом или севофлураном. **МАТЕРИАЛЫ И МЕТОДЫ:** Проведено рандомизированное исследование у 160 пациентов (80 пациентов высокого риска и 80 пациентов низкого риска), которых рандомизировали в подгруппы по виду анестезии (сочетанная анестезия пропофолом или севофлураном) для оценки влияния вида анестезии на частоту критических инцидентов и динамику барорефлекса. **РЕЗУЛЬТАТЫ:** После индукции анестезии во всех группах наблюдалась тенденция к снижению уровня барорефлекса, при этом в подгруппах с исходно низкими значениями чувствительности барорефлекса она снижалась ниже 3 мс/мм рт. ст., что характеризуется как выраженная дисфункция. После окончания операции и через 6 ч после экстубации существенных изменений по сравнению с интраоперационными значениями не наблюдалось. Оценка ЧБР через 24 ч показала, что, хотя ЧБР во всех подгруппах была значительно выше, чем в предыдущие моменты времени, она не вернулась к исходным значениям. Через 6 ч после операции у пациентов

with propofol and anesthesia with sevoflurane lead to a decrease in the sensitivity of the arterial baroreflex, which is not fully restored 24 hours after the end of the operation. High-risk patients with initially reduced baroreflex sensitivity show more frequent postoperative baroreflex dysfunction.

KEYWORDS: baroreflex, sevoflurane, propofol, hemodynamic, anesthesia, prognosis

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низкого риска значения ЧБР были ниже 3 мс/мм рт. ст. В 12,5% случаев при анестезии пропофолом, при анестезии севофлураном — в 10%, у пациентов высокого риска — в 45 и 42,5% случаев соответственно. Через 24 ч в группе низкого риска только у двух пациентов в группе анестезии пропофолом и у одного в подгруппе анестезии севофлураном наблюдалась эта дисфункция, в группе высокого риска — 12,5 и 15% соответственно. **ВЫВОДЫ:** Анестезия как пропофолом, так и севофлураном приводит к снижению чувствительности артериального барорефлекса, которая не восстанавливается полностью через 24 ч после окончания операции. Пациенты высокого риска с исходно сниженной чувствительностью барорефлекса демонстрируют более частую послеоперационную барорефлекторную дисфункцию.

КЛЮЧЕВЫЕ СЛОВА: барорефлекс, севофлуран, пропофол, гемодинамика, анестезия, прогноз

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Introduction

Despite the great attention paid to improving the quality of anesthesia in abdominal surgery, a considerable number of complications are still a serious problem, and some of them significantly affect treatment and can lead to an unfavorable outcome [1]. Acute disorders of systemic hemodynamics, hypothermia, and metabolic disorders are among the specific complications of anesthesia. One of the most frequent disorders in abdominal surgery is arterial hypotension, which occurs in more than 50% of cases [2]. The causes of hemodynamic disorders in abdominal surgery are diverse. Firstly, the course of anesthesia de-

pends on the initial state of the patient [3]. A lot of patients have serious chronic diseases, while both the absence of adequate therapy of concomitant diseases and permanent intake of drugs significantly complicate the course of anesthesia [4]. Hypotension during major abdominal surgery disrupts organ perfusion and leads to organ dysfunction, which, in turn, leads to complications. The stability of hemodynamic parameters depends not so much on the presence or absence of chronic cardiac diseases, but rather on how much the functional reserves of the cardiorespiratory system are decreased, that is, how much this system is able to withstand the factors arising and affecting it during anesthesia.

A functionally unified cardiorespiratory system is a mechanism responsible for the adaptation of the body to changes in homeostasis [5]. This is the first system that reacts to changes, thereby determining the body’s ability to respond to changing conditions. The systemic level of blood gases and blood pressure control is provided by the reflex regulation of this system, the main elements of which are chemoreflex and baroreflex. Chemoreflex sensitivity is a parameter reflecting the degree of response of the respiratory system to blood gases changes. It is a marker of impairment in reflex regulation of the cardiorespiratory system in patients with the progression of chronic diseases [6]. Impairment of chemoreflex sensitivity leads to an increase in sympathetic activity [7] and a decrease in the sensitivity of the arterial baroreflex [8] that is particularly important for maintaining blood pressure in response to its changes [9].

The patients with high sensitivity of chemoreflex are known to be more prone to hemodynamic instability during general anesthesia that allows us to allocate them to the risk group [10]. However, the dynamics of baroreflex in conditions of different types of anesthesia in patients with high and low risk of critical incidents according to the sensitivity of the peripheral chemoreflex has not been studied before.

Objective: To evaluate the dynamics of baroreflex during major abdominal surgery in patients with different risks of critical incidents under combined anesthesia with propofol or sevoflurane.

Materials and methods

The study was carried out in the Regional Clinical Hospital No 2. All patients underwent combined anesthesia for upper abdominal surgery. The selection of patients to participate in the study was conducted from March 2018 to May 2019. The protocol of the study was approved by the local Ethics Committee of the Kuban State Medical University (February 20, 2017, Protocol No 48).

A randomized study was conducted in 160 patients (80 high-risk and 80 low-risk patients) who were divided into subgroups according to the type of anesthesia (combined anesthesia with propofol or sevoflurane) with the aim

to assess the effect of different types of anesthesia on the dynamics of arterial baroreflex and the frequency of critical incidents (CI). Randomization into the sevoflurane or propofol anesthesia subgroups, using a random number table in blocks of 10 patients, was performed in both groups (high and low risk). Comparison in the frequency of outcomes was performed in the treatment and comparison subgroups within each group. A total of 80 high-risk and 80 low-risk patients were included according to the critical incident prediction scale [10]. The scale is presented in Table 1. In the presence of three or more points, the risk was recognized as high.

Criteria for non-inclusion in the study: chronic cardiac arrhythmias; alcohol and drug abuse; neurological and mental diseases, patients with morbid obesity and chronic obstructive pulmonary disease stages 3–4.

Exclusion criteria: inability to perform one of the tests, failure at any stage of the study, data loss.

Assessment of baroreflex sensitivity by the pharmacological method was carried out at the following stages:

- (T1) Initially, ms/mm Hg
- (T2) After induction of anesthesia, ms/mm Hg
- (T3) 1 hour after induction
- (T4) At the end of the operation, ms/mm Hg
- (T5) 6 hours after extubation, ms/mm Hg.
- (T6) 24 hours after extubation, ms/mm Hg

Assessment of baroreflex sensitivity

Blood pressure was recorded in the supine position through a catheter inserted into the radial artery (BBraun 20G, id = 0.6 mm) connected to a pressure sensor and a Life Scope TR BSM-6301 monitor (Nihon Kohden, Japan). After the connection, the measurement was calibrated by atmospheric pressure. Blood pressure was recorded simultaneously with a continuous recording of an electrocardiogram on the adjacent channel of the same monitor. A saline solution test (10 ml) was conducted in the steady state after a 10-minute break. In the absence of blood pressure and heart rate (HR) response, a test dose of phenylephrine was administered at a dose of 25 mcg. Then at least two bolus injections of phenylephrine (100–200 micrograms) diluted in 10 ml of saline solution were injected into the cubital vein. The agent was administered before the rise of systolic blood pressure in the range from 20 to 40 mm Hg. Injections

Table 1. Predictive risk model for critical incidents

Factor	Number of points
Duration of breath-holding < 34 sec	2
ASA class ≥ III	1
Congestive chronic heart failure	1
Elderly (over 65 years old)	1

were administered every five minutes. The results obtained from the beginning of the pressure rise to the beginning of the fall were analyzed. The sensitivity of the baroreflex (BRS) was calculated by the ratio of each RR interval against each previous systolic blood pressure. Using a computer program, a linear regression line was constructed for the obtained points. The slope of the regression curve was taken as the sensitivity of the baroreflex and expressed in ms/mm Hg. The study was carried out three times at 20-minute intervals with the calculation of the average value.

Breath-holding test

The breath-holding test was performed as follows. The duration of a voluntary apnea was assessed thrice at 10-minute intervals. After inhalation of a volume equal to approximately two-thirds of the vital capacity of the lungs, the patients were asked to hold the breath. The duration of a voluntary apnea was measured from the beginning of the test until the appearance of reflex contractions of the diaphragm. The arithmetic mean of the duration of three tests was calculated.

Spirometry

Respiratory function was assessed in all patients included into the study prior to all other measurements with the help of a spirograph EasyOnePro, Ultrasound Spirometry Lab (Switzerland). Forced expiratory volume in 1st second and forced volume vital capacity were evaluated.

Anesthesia

Surgical intervention was performed in all patients under combined general anesthesia and epidural analgesia (the catheter was inserted at the level of Th 8–Th 9, perioperative analgesia was provided by the administration of a solution of ropivacaine at a concentration of 2 mg/ml).

Induction of anesthesia was provided by intravenous administration of propofol (50 mg) to achieve a hypnotic effect and fentanyl (2–3 mcg/kg), muscle relaxation was achieved by intravenous administration of rocuronium (0.6 mg/kg). Anesthesia was maintained by intravenous administration of propofol or inhalation of sevoflurane with a target level of the bispectral index between 40 and 60.

Mechanical ventilation was performed on Datex Ohmeda S/5 AESPIRE (GE, USA), in all cases the respiratory volume was 6–7 ml/kg of predicted body weight, the respiratory rate was determined by the end-tidal carbon dioxide level (normoventilation was maintained).

Monitoring used:

- Electrocardiography with assessment of heart rate and R-R interval
- Invasive arterial blood pressure
- Parameters of central hemodynamics by a noninvasive method of estimating the rate of pulse wave rise

- Pulse oximetry with pulse rate recording
- Capnometry
- Arterial blood sampling and gas analysis
- Central and peripheral thermometry
- The depth of anesthesia by registering the bispectral index
- Neuromuscular conduction was determined using a train-of-four stimulation device.

Primary key-point

Comparative assessment of the baroreflex sensitivity between different types of anesthetics used.

Secondary key-points

Critical incidents:

- a) hemodynamic incidents: hypotension (decrease in systolic blood pressure (SBP) by 20% below the baseline or less than 90 mm Hg); hypertension (rise in SBP by 20% above the baseline or more than 160 mm Hg); bradycardia (decrease in heart rate by more than 20% from the baseline or less than 50 min⁻¹); arrhythmia and tachycardia (increased heart rate by more than 20% of the initial or more than 100 min⁻¹ and all cases of cardiac arrhythmia);
- b) respiratory incidents: hypoxemia (SpO₂ less than 95%); hypercapnia (PaCO₂ more than 45 mm Hg or PetCO₂ more than 40 mm Hg);
- c) metabolic: delayed recovery of consciousness, delayed recovery of muscle tone, hypothermia.

Statistical analysis

Statistical data processing was carried out on a MacBook computer using MedCalc version 19.1.3 (MedCalc Software Ltd).

The Shapiro–Wilk criterion was used to check the hypothesis of the correct distribution of data for all variables. Data with a normal distribution is presented as an average value ± standard deviation, data with a different from normal distribution is presented as a median (25–75th percentiles).

The initial characteristics of patients in different groups and outcomes were compared using the χ^2 criterion for dichotomous variables and a paired *t*-test for continuing variables. Variance analysis was used for repeated measurements to compare one variable at different stages of the study. In all cases, the *p*-level of less than 0.05 was considered statistically significant.

Results

The initial characteristics in the subgroups are presented in Table 2.

Table 2. Preoperative parameters in the sevoflurane (S) or propofol (P) anesthesia groups according to the risk of critical incidents

Parameter	Low risk		High risk	
	P	S	P	S
Age, years	44.6* ± 4.4	45.3* ± 3.1	58.9 ± 5.4	57.1 ± 6.4
Body weight, kg	79.6 ± 4.0	75.7 ± 7.2	76.5 ± 5.1	74.5 ± 6.1
Height, cm	1.76 ± 0.06	1.75 ± 0.09	1.72 ± 0.09	1.71 ± 0.05
Body mass index, kg/m ²	25 ± 2.5	23 ± 1.5	24 ± 2.8	23 ± 2.3
Breath-holding duration, sec	41.8* ± 11	43.5* ± 10	28.4 ± 8	27.8 ± 9
Baroreflex sensitivity, ms/mm Hg	8.65* ± 1.78	7.57* ± 1.41	4.56 ± 1.38	4.41 ± 1.27
Gender (male), %	60	55	55	57.5
HR, min ⁻¹	86 ± 10	83 ± 10	87 ± 12	79 ± 10
SBP, mm Hg	141 ± 23	132 ± 18	140 ± 21	134 ± 21
DBP, mm Hg	87 ± 14	83 ± 10	84 ± 13	85 ± 11
SpO ₂ , %	98.2 ± 1.1	98.3 ± 0.9	98.5 ± 1.0	94.6 ± 0.9
PaCO ₂ , mm Hg	32.8 ± 1.5	33.4 ± 1.3	35.4 ± 1.3	32.5 ± 1.2
PaO ₂ , mm Hg	86.7 ± 4.5	84.8 ± 3.7	86.8 ± 4.7	86.3 ± 4.2
FVC, % from normal values	94.0 ± 2.6	92.0 ± 3.4	96.0 ± 2.2	92.0 ± 5.6
FEV1, from normal values	93.0 ± 3.3	93.0 ± 2.8	95.0 ± 2.3	94.0 ± 3.3
FEV1/FVC, from normal ratio	0.98 ± 0.05	0.94 ± 0.06	0.94 ± 0.05	0.94 ± 0.04
Respiratory rate, min ⁻¹	11.3 ± 2.1	12.3 ± 2.1	15.3 ± 3.1	15.3 ± 2.1

* *p* < 0.05 compared to high risk.
 Note: DBP — diastolic blood pressure; FEV1 — forced expiratory volume over first second; FVC — forced vital capacity; HR — heart rate; PaCO₂ — partial pressure of carbon dioxide in arterial blood; PaO₂ — partial pressure of oxygen in arterial blood; SBP — systolic blood pressure; SpO₂ — oxygen saturation.

Naturally, the high-risk patients were older and the duration of breath-holding in such patients was higher, as well as the sensitivity of baroreflex. There were no significant differences in parameters in the subgroups by the type of anesthesia. According to the initial structure of concomitant diseases the subgroups were comparable (Table 3).

Initially, the average level of baroreflex activity was significantly higher in the low-risk group, while the statistical significance was shown at all stages of the study (Table 4). After induction of anesthesia, there was a tendency to BRS decrease in all groups, while in subgroups with initially low values (that is, in high-risk patients), it decreased below 3 ms/mm Hg, which is considered as a prominent dysfunction of the baroreflex. After the end of the operation and in 6 hours after extubation, no significant changes were observed compared to intraoperative values. The assessment performed 24 hours after the operation showed that despite a significant increase in BRS in all subgroups compared to the previous stages, its values did not reach the baseline.

The values of BRS were below 3 ms/mm Hg in 12.5% of low-risk patients with propofol anesthesia and in 10% of patients with sevoflurane anesthesia (*p* = 0.72) 6 hours

after the operation. In high-risk patients, these values were noted in 45% and 42.5% of cases, respectively (*p* = 0.82). After 24 hours, only two low-risk patients in the propofol anesthesia group and one in the sevoflurane anesthesia subgroup had this dysfunction (*p* = 1.00). In the high-risk group it was noted in 12.5% and 15%, respectively (*p* = 1.00). As for the type of anesthesia, there were no significant differences between the subgroups in the dynamics of BRS.

When comparing the frequency of critical incidents in high-risk patients, there were no significant differences between the types of anesthesia (Table 5).

Similar results were obtained in the subgroups of low-risk patients. The type of anesthesia did not affect the risk of critical incidents (Table 6).

The obtained data indicate that in patients with a high risk of critical incidents the sensitivity of the arterial baroreflex is significantly lower. Both propofol anesthesia and sevoflurane anesthesia are accompanied by a further decrease in baroreflex function, while a substantial proportion of high-risk patients demonstrate significant (below 3 ms/mm Hg) baroreflex dysfunction. In some patients it is preserved for 24 hours after the end of anesthesia.

Table 3. Characteristics of concomitant diseases in the sevoflurane (S) or propofol (P) anesthesia groups according to the risk of critical incidents

Parameter	Number of patients, %			
	Low risk		High risk	
	P	S	P	S
Concomitant diseases				
Chronic heart failure	5	7.5	15	17.5
Coronary heart disease	20	15	27.5	30
Hypertension	35	30	45	47.5
Chronic obstructive pulmonary disease	2.5	0	12.5	15
Diabetes mellitus	5	5	10	12.5
Other diseases	5	5	15	10
Medications taken				
Beta blockers	2.5	5	25	20
Angiotensin converting enzyme inhibitors or angiotensin receptor blockers	2.5	2.5	30	35
Diuretics	2.5	0	10	12.5
Nitrates	0	0	5	5
Ca channel blockers	0	2.5	12.5	10
Insulin	2.5	2.5	7.5	10
P — propofol anesthesia group; S — sevoflurane anesthesia group.				

Table 4. Dynamics of baroreflex sensitivity during the perioperative period in patients with high and low risk of critical incidents, depending on the type of anesthesia

Stage	Low risk		High risk	
	P	S	P	S
(T1) Initially, ms/mm Hg	7.57 ± 1.41 [®]	8.65 ± 1.78 [®]	4.41 ± 1.27	4.56 ± 1.38
(T2) After induction of anesthesia, ms/mm Hg	4.71 ± 1.23 ^{*,®}	4.91 ± 1.37 ^{*,®}	2.34 ± 0.56 [*]	2.76 ± 0.81 [*]
(T3) 1 hour after induction	4.41 ± 1.46 ^{*,®}	4.51 ± 1.36 ^{*,®}	2.43 ± 0.83 [*]	2.68 ± 0.72 [*]
(T4) At the end of the operation, ms/mm Hg	4.18 ± 1.26 ^{*,®}	4.23 ± 1.39 ^{*,®}	2.68 ± 0.72 [*]	2.98 ± 0.58 [*]
(T5) 6 hours after extubation, ms/mm Hg	4.31 ± 1.13 ^{*,®}	4.30 ± 1.02 ^{*,®}	3.11 ± 0.34 [*]	3.02 ± 0.49 [*]
(T6) 24 hours after extubation, ms/mm Hg	5.56 ± 1.28 ^{*,®}	5.98 ± 1.39 ^{*,#®,}	3.42 ± 0.65 ^{*,#}	3.35 ± 0.57 ^{*,#}
[®] $p < 0.05$ compared to low risk. [*] $p < 0.05$ compared to the initial value. [#] $p < 0.05$ compared to T2, T3, T4, T5. P — propofol anesthesia group; S — sevoflurane anesthesia group.				

Table 5. The number and frequency of critical incidents in high-risk patients depending on the type of anesthesia

Critical incidents	S		P		p-value
	N	%	N	%	
	34	85	33	82.5	
Hemodynamic	30	75	28	70	0.8
Hypotension	22	55	23	57.5	1.0
Hypertension	1	2.5	1	2.5	1.0
Bradycardia	5	12.5	4	10	1.0
Arrhythmia	4	10	3	7.5	1.0
Respiratory	9	22.5	10	25	1.0
Hypoxia	7	17.5	6	15	0.77
Hypercapnia	2	5	2	5	1.0
Prolonged mechanical ventilation	2	5	3	7.5	1.0
Metabolic	5	12.5	6	15	1.0
Hypothermia	0	0	2	5	0.49
Delayed recovery of neuromuscular conductivity	3	7.5	3	7.5	1.0
Delayed postoperative awakening	2	5	2	5	1.0

P — propofol anesthesia group; S — sevoflurane anesthesia group.

Table 6. The number and frequency of critical incidents in low-risk patients depending on the type of anesthesia

Critical incidents	S		P		p-value
	N	%	N	%	
	21	55	22	55	
Hemodynamic	14	37.5	16	40	0.81
Hypotension	11	27.5	13	32.5	0.8
Hypertension	1	2.5	1	2.5	1.0
Bradycardia	2	5	2	5	1.0
Arrhythmia	2	5	2	5	1.0
Respiratory	4	10	5	12.5	1.0
Hypoxia	1	2.5	2	5	1.0
Hypercapnia	2	5	1	2.5	1.0
Prolonged mechanical ventilation	2	5	1	2.5	1.0
Metabolic	2	5	3	7.5	1.0
Hypothermia	1	2.5	1	2.5	1.0
Delayed recovery of neuromuscular conductivity	1	2.5	2	5	1.0
Delayed postoperative awakening	0	0	2	5	0.49

P — propofol anesthesia group; S — sevoflurane anesthesia group.

Discussion

The main conclusion of our study is that the sensitivity of the arterial baroreflex decreases during anesthesia, and its recovery to the initial level occurs on the second postoperative day. At the same time, the type of anesthetic used to maintain anesthesia does not significantly affect the dynamics of BRS.

The baseline level of BRS was lower in the group of patients with a high risk of hemodynamic incidents, which is not surprising. Our studies have shown that the progression of cardiovascular diseases leads to activation of peripheral chemoreceptors and increased activity of the sympathetic nervous system, which is a vicious circle for many chronic diseases [11, 12]. Moreover, these changes impair the baroreflex control of the cardiovascular system. It is known that the decrease in BRS is inversely proportional to the sensitivity of the peripheral chemoreflex in patients with chronic heart failure [7], and this pattern remains unchanged when treating patients with drugs affecting the renin-angiotensin system [13].

Induction of anesthesia led to a decrease in the level of baroreflex activity in both groups, but the absolute value of BRS was lower in the high-risk group. The obtained dynamics correlated with the results of earlier studies, which showed a decrease in baroreflex function during anesthesia with propofol [14, 15]. As shown by J. Sellgren et al. [16], propofol is a powerful inhibitor of sympathetic activity and it inhibits the baroreflex sensitivity. In another study, it was found that the sensitivity of baroreceptors decreased when propofol was administered during general anesthesia and its low level preserved for 60 minutes after discontinuation of propofol infusion in 13 healthy individuals [17]. It is known that endotracheal intubation is a sympathetic stimulus, and therefore it should be expected that it will increase blood pressure and heart rate. However, in high-risk patients, the opposite trend for a further decrease in blood pressure was observed, which is probably due to the impairment of cardiorespiratory regulation. A more pronounced drop in blood pressure is associated with a lower level of baroreflex control in the high-risk group. Hypersensitivity of peripheral chemoreflex (what is typical for this group of patients) is often associated with high sympathetic activity, and this condition can affect centrally mediated blood pressure control [7, 18]. The above-described decrease in the level of BRS was preserved throughout the entire period of anesthesia that led to hemodynamic instability. It was more prominent in the high-risk group with both types of anesthesia. This is confirmed by a greater need for infusion and a greater frequency of vasopressors.

Baroreceptor heart rate control depends on the integrative role of the parasympathetic and sympathetic nervous systems. This balance is disrupted when the sympathetic innervation of the heart is blocked by high thoracic epidural anesthesia. Numerous studies have shown that the sensitivity of the baroreflex alters during medicamentous sympathec-

tomy in patients with cervical-thoracic epidural anesthesia [19–24]. However, in some studies, thoracic epidural anesthesia attenuated a decrease in heart rate after an increase in blood pressure (a pressor test) without an increase in heart rate in response to a decrease in pressure (a depressor test) [19–21], while others demonstrated the opposite [22, 23]. In another study, it is reported that cervical, but not lumbar epidural anesthesia significantly reduces the sensitivity of the baroreflex [24], however, in this study, an analysis of spontaneously occurring fluctuations in blood pressure and heart rate was used as a method of assessing baroreflex function, which was criticized. Conflicting data may be a consequence of differences in design. Age differences between the studied populations may also have contributed to a contradictory assessment of the effect of thoracic epidural anesthesia on baroreflex control. It has been suggested that life-threatening paradoxical bradycardia in hypotensive patients undergoing spinal and epidural anesthesia is associated with a weakening of baroreflex control followed by unmasking of the Bainbridge or Bezold—Yarish reflex [25–28].

As already mentioned, the decrease in BRS was present throughout the entire anesthesia, but one of the important results of our work was the observation that the function of the arterial baroreflex was not restored immediately after the restoration of consciousness. This correlates with the data of A. Toner et al [29], who showed in their study that the BRS remains below normal values even 6 hours after the end of anesthesia in patients with low baseline values. Our data showed that some patients, especially in the high-risk group, need more than a day to restore the initial value. Long-term baroreflex dysfunction can lead to an increase in the frequency of complications particularly hemodynamic ones. An impairment of baroreflex function can occur, starting with afferent neurons transmitting information from baroreceptors to neurons of the brainstem or the parasympathetic efferent part of the reflex arc [30]. Experiments on laboratory models have shown that the loss of parasympathetic activity leads to systemic inflammation in organs through immuno-neuromodulation of nicotine receptors on macrophages located in tissues [31]. In addition, increased vagal innervation contributes to persistent inflammation through the inability to regulate the resolution of inflammation [32]. It is well known that inflammation, oxidative stress, and RBS disorders are responsible for cardiometabolic syndrome [33]. In healthy rats, loss of baroreflex function prevents the attenuation of peripheral inflammation mediated by sympathetic stimulation [34]. Thus, acute inflammation, coupled with a lack of baroreflex “reserve”, can have an even more detrimental effect on the work of the body’s anti-inflammatory system, which subsequently leads to a violation of homeostasis [35]. These changes lead to a functional predisposition to postoperative complications, which we have revealed in high-risk patients. Given the fact that the impairment of baroreflex function in patients with initially low values persists for several

days after surgery, the risk of complications is especially high in the early postoperative period.

Conclusion

Both propofol anesthesia and sevoflurane anesthesia lead to a decrease in the sensitivity of the arterial baroreflex. It was revealed that restoration of the arterial baroreflex sensitivity is not complete even 24 hours after the end of the operation, while the type of anesthetic used does not affect the dynamics of changes in the level of baroreflex. High-risk patients show more frequent postoperative baroreflex dysfunction, which may be associated with a higher frequency of critical incidents. The impairment of the reflex regulation of the cardiorespiratory system, which develops after induc-

tion of anesthesia and preserves in the postoperative period, may play a significant role in the development of postoperative complications and it continues to be an active research topic.

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