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Comparative Assessment of the Cardiodepressive Effect in Traditional and Modified Induction Schemes of Anesthesia in Elderly Patients with Ischemic Heart Disease

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Abstract: *most anesthetic drugs have a cardiodepressant action, which in elderly patients leads to a greater inhibition of the contractile functions of cardiomyocytes. Reducing the cardiodepressant action during the induction of anesthesia in elderly patients can reduce the incidence of peri- and postoperative complications and improve the safety of anesthesia in this category of patients. The aim of the study was to improve the safety of anesthesia in elderly patients with ischemic heart disease (IHD) by determining and applying an induction scheme with minimal cardiodepressant action. We examined 40 patients over 60 (in group 1, propofol and fentanyl were used for induction; in group 2, propofol, fentanyl, ketamine). Hemodynamic parameters were recorded at the following stages: 1) upon delivery of the patient to the operating room; 2) after administration of induction drugs; 3) after intubation; 4) 25 minutes after tracheal intubation. The echocardiography data were used to calculate the stroke volume index (SVI) and cardiac index (CI).*

It was found that upon delivery of patients to the operating room, the values of hemodynamic parameters indicated the stability of the overall health status of patients (SVI was 31.99 ± 3.91 ml/m² for group 1 and 32.19 ± 4.29 ml/m² for group 2; CI was 2.49 ± 0.32 l/min/m² for group 1 and 2.44 ± 0.39 l/min/m² for group 2). After the administration of drugs for induction, a decrease in the indicators characterizing the contractility of the myocardium was recorded compared with the baseline: SVI was 90.7 ± 3.71% for group 1, 89.9 ± 5.86% for group 2, CI was 81.5 ± 6.6% for group 1, 85.63 ± 10.17% for group 2. There were no statistically significant differences in these indicators between the groups. After insertion of the intubation tube, a significant difference ($p < 0.05$) between the groups was noted in the indicators of SVI (99.91 ± 2.5% for group 1, 109.6 ± 8.16% for group 2 of the initial values) and CI (96.63 ± 11.8% for group 1, 110.38 ± 12.37% for group 2 of the initial values). In 25 minutes after intubation, statistically significant differences between the groups were observed in the parameters of SVI (87.09 ± 5.3% for group 1, 108.21 ± 8.32% for group 2; CI (79.59 ± 10.11% for group 1, 108.29 ± 9.95% for group 2). Thus, it has been demonstrated that the addition of ketamine to the combination of propofol + fentanyl prevents a decrease in myocardial contractility during induction into anesthesia in patients of the older age group.

Keywords: Coronary Artery Disease; Anesthesia; Propofol; Fentanyl; Ketamine; Heart.

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Introduction

A feature of the normal aging process is a physiological decrease in the functional reserves of organs and systems after 40 (Griffiths, R. et al, 2014). According to global studies, the risk of ischemic heart disease (IHD) (Virani, S. S. et al, 2021) also increases with age. Myocardial remodeling and general vascular atherosclerosis are observed in geriatric patients (Lakatta E. G., 2003). As a consequence of IHD, which leads to impaired blood supply, cardiac fibrosis occurs. Age-related hypertrophy and decreased myocardial contractility lead to a decrease in ejection fraction and cardiac index.

Most anesthetic drugs have a cardiodepressant action, which in the case of elderly patients with IHD leads to a greater inhibition of the contractile functions of cardiomyocytes (Reich, D. L. et al, 2005; Südfeld, S. et al, 2017; Jor, O. et al, 2018; Bijker, J. B. et al, 2009). According to the literature, propofol, due to its relatively rapid metabolism, directly reduces myocardial contractility (van Klarenbosch et al, 2001) and also inhibits Ca^{2+} influx into cardiomyocytes, disrupting its metabolic processes (Fassl, J. et al, 2011). As a result, hypotension, which occurs due to vasodilation and a direct negative inotropic effect on the left ventricle, is a common side effect of the cardiovascular system during induction of anesthesia.

The search for and deployment of methods aimed at reducing the cardiodepressant action during induction of anesthesia in elderly patients will reduce the percentage of peri- and postoperative complications, as well as improve safety of anesthesia in this category of patients (Schonberger, R. B. et al, 2022).

Aim

The aim is to improve the safety of anesthesia in elderly patients with IHD by identifying and applying an induction scheme with minimal cardiodepressant action.

Materials and methods

The paper is based on the data that were identified in elderly patients who underwent coronary artery bypass grafting during a beating heart without the use of artificial circulation at the State Institution Amosov National Institute of Cardiovascular Surgery of the National Academy of Medical Sciences of Ukraine.

The presented study included 40 patients, in particular, 33 men (82.5%) and 7 women (17.5%). According to the ASA physical status classification system, all patients were classified as Class III-IV. According to the Mallampati Score (Classification), only patients of Classes I-II were included in the study

The values of arterial and venous pressure were recorded by invasive measurement, intracardiac hemodynamics were recorded using EchoCG.

The mean age of the persons under study was 67.00 ± 5.79 (60-85 years old). The average number of coronary artery bypass grafts was 3.14 ± 1.03 (from 2 to 5). All patients were divided into 4 NYHA classes (number of patients and percent of the total population): FC I – 2 patients (5.0%); FC II – 19 patients (47.5%); FC III – 18 patients (45.0%); FC IV – 1 patient (2.5%). Among the most common comorbidities, arterial hypertension prevailed in 35 cases (87.5%) and type 2 diabetes mellitus (13 patients, 32.5%).

For the purpose of premedication, each patient was administered diazepam (0.25 mg/kg).

Using a computer program (randomization method), patients were divided into 2 groups. Induction of anesthesia in group 1 was performed with propofol (2 mg/kg), fentanyl (2.0 μg/kg), pipecuronium bromide (0.1 mg/kg); and in group 2 – propofol (2 mg/kg), fentanyl (2.0 μg/kg), ketamine (0.5 mg/kg), pipecuronium bromide (0.1 mg/kg). Anesthesia for both groups was maintained by intravenous injection of propofol (4 mg/kg/h) and fentanyl (2.0 μg/kg/h).

Hemodynamic parameters were recorded at four stages: Stage 1 – upon arrival of the patient in the operating room; Stage 2 – after administration of drugs for induction of anesthesia; Stage 3 – after intubation; Stage 4 – 25 minutes after successful intubation and fixation of the intubation tube. During these 25 minutes, additional vascular catheterization, patient warming, and extended transesophageal echocardiographic examinations were performed to more accurately determine the strategy for cardiac surgical intervention and enhance patient safety.

For better understanding, we show the deviation from the baseline in percentages at each stage during the text.

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Results

During the first stage of the study, the overall physical and psychological health status of the patients was assessed as stable. The results of the examination of patients at this stage are summarized in Table 1.

As can be seen from Table 1, the indicators characterizing the contractility (end- systolic volume index – ESVI, end-diastolic volume index – EDVI, stroke volume index – SVI, ejection fraction – EF, cardiac index – CI) of the heart were within the expected range for age and corresponded to the data of the preoperative examination. There was no statistically significant difference between the parameters of groups 1 and 2 (in all cases, $p > 0.05$), which made it possible to further conduct a reliable study of the effect of changes in the pharmacological factor on myocardial contractility.

After the administration of drugs for induction according to the study design, the data were re-registered and summarized in Table 2.

ESVI in group 1 was 102.9 ± 2.15% of the initial state, but in group 2 this parameter was recorded below the initial state (98.9 ± 3.1%). However, comparing absolute values, this difference in indicators did not have statistically significant differences ($p = 0.75$). In both cases, the EDVI decreased relative to the previous stage (96.9 ± 1.01% for group 1and 94.5 ± 3.84% for group 2 of the baseline data), *p* was 0.765 between groups. The values of SVI after the administration of drugs for induction in both cases decreased by almost 10% (90.7 ± 3.71% for group 1, 89.9 ± 5.86% for group 2, Fig. 1). A similar trend was noted in the values of EF, which was 93.6 ± 3.32% for group 1, 95.01± 3.05% for group 2. The EF was recorded higher in the group in combination with ketamine (1.4% higher), but this difference was not statistically significant ($p = 0.7$). After induction of anesthesia, the CI also decreased and amounted to 81.5 ± 6.6% for group 1 and 85.63 ± 10.17% for group 2 of the baseline value (*p* between groups = 0.555, Fig. 2).

After the intubation tube was inserted and securely fixed, the data were recorded again and summarized in Table 3.

Table 1. Hemodynamic parameters of patients in groups 1 and 2 at the time of delivery to the operating room

Parameters	Group 1 (n = 20)	Group 2 (n = 20)	"p"
ESVI (ml/m^2)	33.42 ± 9.06	33.65 ± 10.46	0.9403
EDVI (ml/m^2)	65.4 ± 10.53	65.84 ± 12.55	0.9062
SVI (ml/m^2)	31.99 ± 3.91	32.19 ± 4.29	0.8775
EF (%)	49.55 ± 6.31	49.68 ± 6.61	0.9486
CI (l/min/m^2)	2.49 ± 0.32	2.44 ± 0.39	0.6746

The analysis of the data presented in the table indicates that the groups were statistically homogeneous.

Table 2. Hemodynamic parameters of patients of groups 1 and 2 after administration of drugs for induction into anesthesia

Parameters	Group 1(n = 20)		Group 2 (n = 20)		"p"
ESVI (ml/m^2)	34.37 ± 9.36	102.9 ± 2.15%	33.36±10.6	98.9 ± 3.1%	0.7520
EDVI (ml/m^2)	63.4 ± 10.29	96.9 ± 1.01%	62.31±12.43	94.5 ± .84%	0.7650
SVI (ml/m^2)	29.03 ± 3.91	90.7 ± 3.71%	28.95±4.38	89.9 ± .86%	0.9516
EF (%)	46.46 ± 6.78	93.6 ± 3.32%	47.29±6.97	95.01±3.05%	0.7043
CI (l/min/m^2)	2.02 ± 0.25	81.5 ± 6.6%	2.08 ± 0.35	85.63 ± 10.17%	0.5550

*Additionally, the percentage deviation of the indicator from baseline values was noted.

The analysis of the data presented in the table suggests that immediately after drug administration, no statistically significant changes in cardiac contractility indicators were observed between the groups.

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Table 3. Hemodynamic parameters of patients in groups 1 and 2 after intubation

Parameters	Group 1(n = 20)		Group 2 (n = 20)		"p"
ESVI (ml/m^2)	34.55 ± 9.23	103.6 ± 4.04%	32.68 ± 9.97	97.47 ± 6.58%	0.5436
EDVI (ml/m^2)	66.51 ± 10.36	101.8 ± 2.39%	67.84 ± 12.72	103.2 ± 4.27%	0.7177
SVI (ml/m2)	31.96 ± 4.07	99.91 ± 2.5%	35.16 ± 4.52	109.6 ± 8.16%	0.0241
EF (%)	48.68 ± 6.56	98.2 ± 2.53%	52.57 ± 5.95	106.23 ± 6.11%	0.0564
CI (l/min/m^2)	2.39 ± 0.3	96.63 ± 11.8%	2.69 ± 0.45	110.38 ± 12.37%	0.0209

*Additionally, the percentage deviation of the indicator from baseline values was noted.

The analysis of the data that presented in the table indicates that statistically significant changes after intubation were observed in the indicators SVI and CI.

As can be seen from Table 3, the trend of the dynamics of the ESVI continued in accordance with the previous stage with an increase in group 1 and a decrease in group 2 (group 1 = 103.6 ± 4.04% and group 2 = 97.47 ± 6.58%, p = 0.54). At this stage, the EDVI was registered above the baseline values in both groups (101.8 ± 2.39% for group 1, 103.2 ± 4.27% for group 2 of the baseline data, p = 0.72). The SVI in group 1 almost reached the baseline level (99.91 ± 2.5%), and in group 2 this indicator was registered above the baseline values, 109.6 ± 8.16% (Fig. 1). The statistically significant difference between the indicators was confirmed by "p" and amounted to 0.024. When registering the EF, it was found that for group 1 this indicator was 98.2 ± 2.53% of the baseline data, and for group 2 – 106.23 ± 6.11%, but the reliability of the difference between the values was not statistically confirmed (p = 0.056). The CI differed between groups at this stage, with a predominance of the index in the group with the addition of ketamine (group 1 = 96.63 ± 11.8%, group 2 = 110.38 ± 12.37%, Fig. 2). This difference was confirmed statistically, p = 0.02.

At the final stage of the study, 25 minutes after intubation, the hemodynamic parameters that were recorded are shown in Table 4.

According to Table 4, at the final stage of the study, most of the hemodynamic parameters had a statistically significant difference between the groups, which confirmed the effect of adding ketamine to the combination of propofol + fentanyl. The ESVI in group 1 was higher than the baseline level (110.13 ± 4.24%), in group 2 – lower than the baseline level (95.04 ± 7.01%), "p" between groups = 0.109. The EDVI in both groups almost reached the level of baseline values, and amounted to 98.62 ± 2.77% for group 1 and 101.21 ± 4.72% for group 2, "p" between groups = 0.565. The SVI was significantly different: group 1 = 87.09 ± 5.3% of the baseline values, group 2 = 108.21 ± 8.32% of the baseline data (Fig. 1). The significance of this difference was confirmed statistically ($p < 0.001$). A similar trend was observed in the value of EF, which was 88.3 ± 3.58% in group 1 and 106.89 ± 6.22% in group 2 of the baseline values. This difference of 18.63% between the groups was significant (p value was confirmed to be <0.001).

Table 4. Hemodynamic parameters of patients in groups 1 and 2 25 minutes after intubation

Parameters	Group 1(n = 20)		Group 2 (n = 20)		"p"
ESVI (ml/m^2)	36.57 ± 9.05	110.13 ± 4.24%	31.78 ± 9.39	95.04 ± 7.01%	0.1090
EDVI (ml/m^2)	64.4 ± 9.91	98.62 ± 2.77%	66.4 ± 11.76	101.21 ± 4.72%	0.5650
SVI (ml/m^2)	27.83 ± 3.70	87.09 ± 5.3%	34.61 ± 3.73	108.21 ± 8.32%	<0.0001
EF (%)	43.78 ± 6.18	88.3 ± 3.58%	52.86 ± 5.78	106.89 ± 6.22%	<0.0001
CI (l/min/m^2)	1.97 ± 0.3	79.59 ± 10.11%	2.63 ± 0.34	108.29 ± 9.95%	<0.0001

*Additionally, the percentage deviation of the indicator from baseline values was noted.

The analysis of the data presented in the table indicates that 25 minutes after intubation, statistically significant changes were observed in three indicators: SVI, EF and CI.

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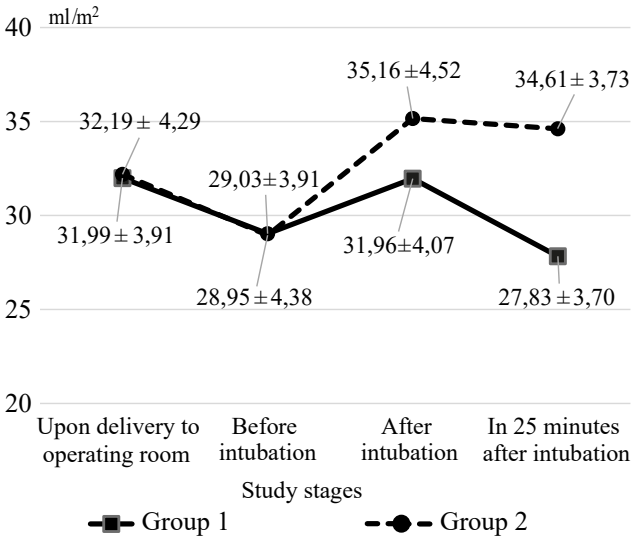

Fig. 1. Dynamics of the SVI (ml/m²) in group 1 (n = 20) and group 2 (n = 20) at the stages of the study

A significant difference between the groups was also recorded in the CI, which was recorded at 79.59 ± 10.11% for group 1 and 108.29 ± 9.95% for group 2 ("p" between groups < 0.001, Fig. 2).

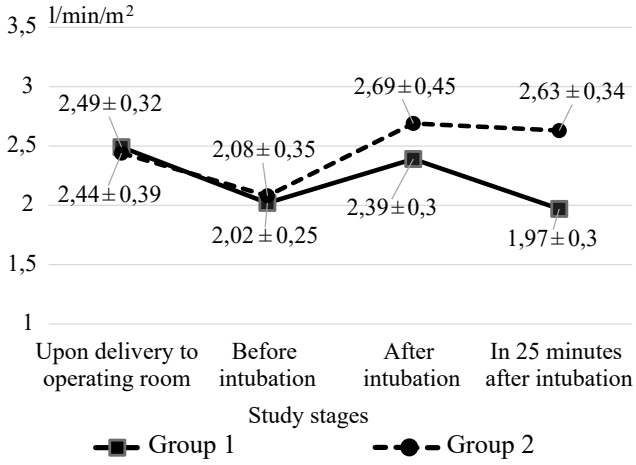

Fig. 2. Dynamics of the CI (l/min/m2) in group 1 (**n** = 20) and group 2 (n = 20) at the stages of the study

Discussion

When analyzing the data obtained, it should be noted that there is a general trend in changes in hemodynamic parameters such as EF, CI. The use of the classical combination of propofol + fentanyl leads to a cardiodepressant action, as a result of which cardiac contractility decreases. However, with the addition of ketamine, it is possible to avoid significant fluctuations in hemodynamics and maintain cardiac contractility within the range closer to the baseline values.

It was found no difference in changes in ESVI and EDVI at stages 2-3 between the observation groups (after the administration of drugs for induction, the p-value for ESVI was 0.7520 between the groups, for EDVI - 0.7650; after intubation, ESVI was 0.5436, and EDVI – 0.7177). However, integral indices such as SVI and EF, based on the values of ESVI and EDVI, showed statistically significant differences between the groups. Thus, it was found that insignificant differences in changes in ESVI and EDVI in total lead to a significant difference in the integral indices of myocardial contractility. This likely occurred because ketamine is a sympathomimetic agent that stimulates the release of endogenous catecholamines, particularly norepinephrine, which increases myocardial contractility and supports hemodynamic stability [Zhou, N. et al, 2022]. At the stage after the intubation tube placement, the p-value between the groups for the SI was 0.0241, and for the CI – 0.0209. It is important to note that in the classical induction scheme, the short-term recovery of the EF immediately after intubation (presumably due to the release of its own catecholamines at the stage of intubation) subsequently has a steady downward trend. At the same time, in group 2 (with the addition of ketamine), the increase in the EF immediately after intubation leads to an excess of baseline values, and subsequently has a steady upward trend. This fact is of significant clinical importance in patients of the older age group with IHD.

This may indicate that, depending on the chosen induction scheme, classical or modified, there will be a different effect on the myocardium. When ketamine is added to the classical anesthesia induction scheme, a lesser cardiodepressant action is observed after intubation and 25 minutes afterwards.

Our data have been confirmed by the results of global studies. It should be noted that these scientific papers investigated the hemodynamics of patients of a younger age group, as well as the physiological status according to ASA I - II. Our results have expanded the data on the effect of drugs for induction of anesthesia with the use of ketamine on the hemodynamic parameters of patients with IHD of the older age group with ASA Groups III and IV.

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Similar results of fluctuations in the EF and CI were obtained by Trimmel H et al. [Trimmel, H. et al, 2018], Tu W et al. [Tu, W. et al, 2021], Zhou N et al. [Zhou, N. et al, 2022], in which higher myocardial contractility and less fluctuation in hemodynamic parameters were recorded with ketamine. Our results complement previous studies on the evaluation of these parameters by including patients with high perioperative risk, such as elderly patients with IHD.

Conclusion

The use of traditional induction drugs, such as propofol and fentanyl, leads to a cardiodepressant action, which is manifested in a decrease in the SVI and EF by 15% from the baseline in the peri-induction period. Together with the negative vasodilating effect of analgesic drugs, this phenomenon leads to a decrease in blood pressure (BP). This is dangerous in elderly patients with IHD, as a decrease in perfusion pressure in atherosclerotic coronary arteries can lead to zonal myocardial ischemia and life-threatening arrhythmias.

The addition of ketamine to the combination of propofol + fentanyl prevents a decrease in myocardial contractility during induction of anesthesia, which is an important component of maintaining a stable blood pressure level in the peri- intubation period. The use of a combination of drugs together with ketamine can improve the safety of anesthesia in elderly patients with IHD, as it reduces the risk of cardiac depression due to the action of propofol and fentanyl.

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Conflict of interest

The author declares no conflict of interest.

Consent to publish

Consent to publish this paper was obtained from all patients who participated in the study.

In accordance with the provisions of the Committee on Publication Ethics (COPE)

ORCID ID and authors contribution

0000-0003-3282-6539 (A, B, C, D, E, F) Andrii Vitovskyi

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

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Порівняльна оцінка кардіодепресивного ефекту при традиційній та модифікованій схемах індукції в анестезію у пацієнтів з ішемічною хворобою серця старшої вікової групи

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Анотація: *більшість анестезіологічних препаратів мають кардіодепресивний ефект, що у пацієнтів старшого віку призводить до більшого пригнічення скоротливої функції кардіоміоцитів. Зменшення кардіодепресивного впливу під час індукції анестезії у пацієнтів старшої вікової групи може знизити частоту пери- та післяопераційних ускладнень і підвищити безпеку проведення анестезії в даній категорії хворих. Метою роботи стало підвищення безпеки проведення анестезії у пацієнтів старшої вікової групи з ІХС шляхом визначення та застосування схеми індукції в анестезію з мінімальним кардіодепресивним ефектом. Було обстежено 40 пацієнтів старше 60 років (в гр. 1 застосовувались препарати для індукції пропофол та фентаніл; у гр. 2 з використанням препаратів пропофол, фентаніл, кетамін). Гемодинамічні показники реєструвались на наступних етапах: 1) при доставленні пацієнта в операційну; 2) після введення індукційних препаратів; 3) після інтубації; 4) через 25 хвилин після інтубації трахеї. За даними ЕхоКГ розраховували ударний індекс (УІ) та серцевий індекс (СІ).*

Встановлено, що при доставленні пацієнтів до операційної значення гемодинамічних показників свідчили про стабільність загального стану пацієнтів (УІ для гр.1 становив – 31,99±3,91 мл/м², для гр.2 – 32,19±4,29 мл/м2, СІ для гр.1 – 2,49±0,32 л/хв/м², для гр.2 – 2,44±0,39 л/хв/м²). Після введення препаратів для індукції, зареєстровано зниження показників, що характеризують

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скоротливу здатність міокарда в порівнянні з вихідним рівнем: УІ становив для гр.1 – 90,7±3,71%, для гр.2 – 89,9±5,86%, СІ для гр.1 – 81,5±6,6%, для гр.2 – 85,63±10,17%. Статистично значущої відмінності по цім показникам між групами не спостерігались. Після встановлення інтубаційної трубки достовірна відмінність (p<0,05) між групами була відмічена в показниках УІ (для гр.1 – 99,91±2,5%, для гр.2 – 109,6±8,16% вихідних значень) та СІ (для 1 групи – 96,63±11,8%, для 2 групи – 110,38±12,37% від вихідних значень). Через 25 хвилин після інтубації статистично значущі відмінності між групами спостерігались у параметрах УІ (гр.1 – 87,09±5,3%, для гр.2 – 108,21±8,32%;, СІ (гр.1 – 79,59±10,11%, гр.2 – 108,29±9,95%). Таким чином продемонстровано, що додавання препарату кетамін до комбінації пропофол+фентаніл запобігає зниженню показників скоротливості міокарду під час індукції в анестезію у пацієнтів старшої вікової групи.

Ключові слова: ішемічна хвороба серця, анестезія, пропофол, фентаніл, кетамін, серце.