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PREVENTION OF PATHOLOGICAL EFFECT OF ISCHEMIA-REPERFUSION IN LIVER RESECTION BY SEVOFLURANE PRECONDITIONING

Background. The intermittent Pringle maneuver remains the major technique for controlling hemorrhage during liver surgery. Nevertheless, this procedure involves a risk of triggering a cascade of pathological changes resulting in the ischemia-reperfusion injury (I/R) effect. The pharmacological prevention of this I/R injury represents a promising approach. The aim of the study was to compare the effects of pharmacological preconditioning with sevoflurane and propofol-based intravenous anesthesia on the postoperative function of the liver as the primary end-point. **Materials and Methods.** A prospective cohort study includes the analysis of the data of 73 patients who underwent liver surgery. In the study group (n = 41), preconditioning with sevoflurane inhalation was provided 30 minutes prior to liver resection. In the control group (n = 32), sevoflurane preconditioning was not provided. The primary endpoints were blood lactate concentration shortly after the surgery and one day later; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities on postoperative Days 1, 3, and 5 as markers of hepatocyte damage. **Results.** On postoperative Day 1, in patients of the study group, lactate decreased to preoperative levels, while in the control group, lactate content increased as compared to both preoperative levels and the levels immediately after liver resection. A significant difference in AST activity levels between the groups was registered on Day 5, although this difference was not clinically relevant. The decrease in the prothrombin index in the study group on Day 3 was superior to that in the control group. The multiple regression analysis demonstrated a moderate positive association between the number of resected liver segments and the markers of the functional state of the liver in the study group while in the control group, such association was not significant. **Conclusion.** The protective effect of sevoflurane on the postoperative function of the liver is manifested by the lower level of blood lactate and the stable level of transaminase activity.

Keywords: colorectal cancer, liver metastasis, ischemia-reperfusion injury, sevoflurane preconditioning.

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Liver resections in patients with metastatic colorectal cancer (CRC) have been a treatment standard for more than three decades [1]. Among the key factors affecting the control of the blood loss in the resection are the technique of parenchyma transection and the vascular control of the blood inflow/outflow. Although the intermittent Pringle maneuver (PM) remains the major technique for controlling hemorrhage in surgical manipulations during liver surgery, performing this manipulation involves a risk of triggering the changes in the cascade of the mitochondrial respiratory chain known as the pathological effect of ischemia-reperfusion (I/R) [2]. The activation of cytokine production and the complement system, the accumulation of free radicals, and the exhaustion of the antioxidant systems due to I/R are triggers of apoptosis and necrosis of hepatocytes.

Ischemia of the liver parenchyma results in the inhibition of aerobic metabolism due to the shortage of oxygen. Since the initiation of reperfusion, the oxidative injury of cells increases with the accruing generation of the free radicals of oxygen and nitrogen oxide. Upon reperfusion, the activated cells of the immune system (neutrophils and macrophages) enter the ischemic areas with blood flow and generate the release of cytokines. While the mechanisms of autophagy, apoptosis, and necrosis in hepatocytes are well studied upon normoxia, much less is known about the mechanisms of their activation in the I/R setting [3]. In a randomized study in 2003, Clavien et al. [4] analyzed how to prevent the effects of ischemia in the clinical setting. The prevention of I/R envisaged the limitation of the blood inflow via the portal vein system for 10 min and the reperfusion of the same duration. The postoperative decrease in the serum level of the transaminase activity and the reduction of the apoptotic death of parenchyma cells were registered following such ischemic preconditioning in most patients with moderate hepatic steatosis. This effect was lost in patients older than 60 years of age while in younger patients the ischemic preconditioning demonstrated increased benefits. In addition, this study proved that the most pronounced cytoprotective effect was attained with ischemia for 40 min and longer. Other similar studies also demonstrated the postoperative decrease in the transaminase level and markers of apoptosis and inflammation [5]. Nevertheless, most studies did not demonstrate any association between the machine perfusion (MP) used in liver transplantation and the viability of liver graft [6]. In one study, the negative outcome of MP was revealed resulting in increased graft injury [7].

The most promising approach to the pharmacological correction of I/R seems to consist in combining pharmaceuticals intended for the different stages of the cascade of molecular pathways of the activated pathological process. The optimal is the combination of sevoflurane, steroids, and caspase inhibitors.

The aim of the study was to compare the effects of pharmacological preconditioning with sevoflurane on the postoperative function of the liver as the primary end-point.

Materials and Methods

Design of the study. This prospective cohort study was performed at the National Cancer Institute in Kyiv in 2020—2022. The design of the study was approved by the Ethics Committee of the Institute. Within the framework of the clinical study, all patients signed an informed consent. The patients were examined comprehensively. The examination work-up comprised general clinical examination (general physicals and the assessment of the form, stage, severity, and the metastatic pattern of cancer), laboratory tests (complete blood cell count and blood biochemistry, coagulogram, urine analysis), diagnostic imaging (echography, CT of three regions with contrasting, MRI of the abdomen

and pelvic organs with contrasting if indicated, 3D reconstruction of DICOM images, segmental volumetry, metastatic foci mapping), instrumental methods (colonoscopy, esophagogastroscopy, ECG), biophysical methods (EPR spectroscopy, zymography), and histological study (immunohistochemistry).

In total, 82 patients treated for metastatic liver lesions of colorectal cancer (CRC) or primary liver cancer at the National Institute of Cancer were enrolled in the study and randomized in the control and study groups, 41 patients per group. However, later 9 patients were excluded from the control group (4 — due to peritoneal carcinomatosis found during the surgery and 5 — due to the voluntary drop-out). So, the data of 73 patients were analyzed: the study group (Group 1 n = 41) and the control group (Group 2 n = 32).

The patients of both groups were comparable by age, sex, body weight, and the presence of concomitant diseases (Table 1).

In most patients with CRC, the depth of invasion in primary tumors was T3 (59.6%), and regional lymph nodes were unaffected (pN0, 0.9%). Metachronous metastases in the liver were found in 83.4% of patients. The concurrent resection of the rectum and liver was provided in 2.4% of patients of Group 1 and 9.4% of patients of Group 2. According to histopathological findings, the status of the liver margin was R0 and R1v in 94.7% and 5.3%, respectively. In both groups, the patients had three chemotherapy cycles on average. To control the blood loss during transection of liver parenchyma, the intermittent PM (20 min ischemia, 5 min reperfusion) was performed in its classic variant.

The inclusion criteria: patients eligible for liver resection (≥ 30% of the apparently intact liver parenchyma could be spared).

The exclusion criteria: > 3 metastatic foci in the lungs and/or peritoneal carcinomatosis, age below 18, urgent situations when the obturation of the liver inflow could not be overcome by pharmacological methods, the need for the extracorporeal blood circulation, severe cardiopulmonary pathology, myocardial infarction within the last 6 months, chronic obstructive lung diseases (PaO_2 < 60 mm Hg), and the neuropsychiatric disorders.

Anesthesia protocol. In case of emotional stability, the patients were not premedicated (opioids, hypnotics) the day before surgery or directly prior to surgery. Prior to the general anesthesia, the epidural catheter was installed

Table 1. **Characteristics of patients**

Characteristics	Group 1 (n = 41)	Group 2 (n = 32)	*p*
Age, years	58 ± 6.4 (30—72)	58 ± 7.4 (38—72)	0.53
Sex (males/females)	25/16	15/17	0.55
Body weight, kg	79.4 ± 15 (45—100)	74.9 ± 13 (50—103)	0.11
Metastases of CRC, n (%)	33 (80.5)	29 (90.6)	0.86
Hepatocellular carcinoma, n (%)	2 (4.9)	1 (3.1)	0.38
Cholangiocarcinoma, n (%)	4 (9.8)	2 (6.3)	0.69
Other malignancies, n (%)	2 (4.9)	0 (0)	0.5
ASA status			
II	36 (85.7)	29 (90.6)	1.0
III	5 (12.2)	3 (9.4)	1.0

at the Th7/Th8 or Th8/Th9 level, and 10—12 ml of 0.125% bupivacaine combined with 200 μg fentanyl was administered epidurally. The upper and lower sensor levels of anesthesia were assessed prior to anesthesia. The patients were randomized into two groups depending on the method of general anesthesia.

Prospectively, two groups of patients were delineated. In Group 1 (sevoflurane preconditioning), the induction of anesthesia was achieved with atracurium 0.5 mg/kg, fentanyl 1—2 μg/kg, and propofol 2 mg/kg. Preconditioning was provided 30 min prior to liver resection with sevoflurane inhalation (1.5—2 v/v% for 25—30 min). The propofol infusion was stopped during sevoflurane inhalation and was restored afterward. In Group 2 (control), the induction of anesthesia was achieved with propofol 2 mg/kg i/v atracurium 0.5 mg/kg, and fentanyl 1—2 μg/kg. Following trachea intubation, propofol infusion was continued at a dose sufficient for maintaining the bispectral index (BIS) at the level of 40—60. When AP and cardiac rate exceeded preoperative values by 20%, an additional dose of fentanyl (1 μg/kg) was administered. Atracurium (0.2 mg/kg) was added when electromyography indices exceeded 30.

During the surgery, ECG, BP, heart rate (HR), and exhaled CO_2 were monitored. The restrictive mode of infusion therapy was provided (2—3 ml/kg/h with crystalloid solutions). The mean BP was maintained at the level of not below 65 mm Hg. In case of BP reduction below this level, noradrenaline infusion (0.2—0.4 μg/kg/min) was initiated. Arterial hypotension was defined as BP decrease by at least 20% relative to the initial values, while BP increase by at least 20% was defined as arterial hypertension. The cardiac rate increase/decrease by 20% was considered tachy-/bradycardia.

End-points of the study. The primary endpoints were lactate concentration in the arterial blood shortly after the surgery and on postoperative day (POD) 1; alanine aminotransferase (ALT), bilirubin, and aspartate aminotransferase (AST) activities on POD 1 3 and 5 as markers of hepatocyte damage. Taking into account the active role of the liver in the production of blood coagulation factors, the changes in coagulograms (fibrinogen, prothrombin index) were also assessed pre- and postoperatively. The acid-base balance in the arterial blood was assessed preoperatively, shortly after the surgery, and one day later.

The hemodynamic parameters (BP and HR) were registered prior to the surgery, before resection, and then every 10 min until the end of the surgery.

Statistical analysis. The sample size was calculated based on the maximal lactate concentration (as primary end-point) in 30 min following liver resection. In our previous study, the mean difference between the control and study groups was 1.1 with a standard deviation of 1.45. For the statistical significance of 0.05 and statistical power of 0.8 the calculated sample size was 28. Therefore, at least 64 patients should be included in the study to compensate for the probable dropout of 15%.

The data obtained were processed with "STATISTICA 8.0" software (StatSoft. Inc., 2008). The distribution of the continuous data was assessed by distribution diagrams as well as the Kolmogorov — Smirnov test. Accounting for the normal distribution in the groups, non-parametric methods were used. The descriptive statistics comprised the calculation of the mean with standard error and 95% confidence interval (CI), standard deviation, as well as median and 25—75 percentile range. The difference in the continuous data between the groups was assessed by the Mann — Whitney test, and dichotomous variables were analyzed using a two-sided Fisher's exact test. Spearman's rank correlation was calculated. The threshold for sta tistical significance was set at $p < 0.05$.

Results

The intraoperative blood loss and the volume of diuresis in Group 1 and Group 2 did not differ significantly (288 ± 137 ml vs. 275 ± 199 ml and 362 ± 159 ml vs. 307 ± 190 ml, respectively). The extent of the infusion therapy in both groups was not different; the use of the frozen plasma during the surgery was not required.

The PM was employed in 27 (65.9%) patients of Group 1 and 13 (40.6%) patients of Group 2 (the difference was not significant; $p = 0.2347$, Fisher's exact test). The duration of inflow occlusion did not differ between the groups (45 ± 17 min vs. 31 ± 15 min, $p = 0.186$). The extensive resection (≥3 anatomical segments) was performed in 22.5% of patients of Group 1 and 9.7% of patients of Group 2. In 77.5% of patients of Group 1 and 90.3% of patients of Group 2, the parenchyma-sparing surgery was provided.

The changes in hemodynamics parameters, namely the mean arterial blood pressure (MAP) and heart rate (HR), in the course of anesthesia are represented in Figs. 1 and 2. HR decreased moderately throughout the surgery with a slight increase shortly before the end of the anesthesia. MAP also decreased moderately keeping at the reduced level up to the end of anesthesia. The values of MAP and HR did not differ significantly between the two groups.

The preoperative ALT levels did not differ between the groups (Table 2). On POD 1, a 7-fold increase in ALT was registered in both groups. The elevated ALT remained on POD 3 and started to decrease on POD 5. The difference between the groups was not significant. The same dynamics was evident for AST. On POD 5, a significant difference between the groups was registered although this difference was not clinically relevant.

The preoperative lactate blood content was similar in both groups. After resection, the lactate increased although the difference was not significant. Postoperative patterns for lactate concentration were different in the groups. On POD 1, in patients of Group 1 lactate decreased to preoperative levels, while in Group 2 lactate content increased as compared to both preoperative levels and the levels immediately after liver resection (Table 2).

Albumin concentration in blood decreased beginning from POD 1. The decrease pattern was similar in both groups. On POD 3, the decrease in albumin content was more significant in Group 2.

Blood bilirubin in Group 1 increased on POD 1 and remained at the same level up to Day 5. Nevertheless, such an increase (20%) was not clinically relevant being within reference values. In Group 2 bilirubin content increased by 56% on POD 1 followed by its decrease restoring to the preoperative values on POD 5.

The changes in the prothrombin index (moderate decrease on POD 1 and 3 followed by restoration of the preoperative values on POD 5) were not clinically relevant in both groups. Its decrease in Group 1 on POD 3 was superior to that in Group 2.

The levels of fibrinogen in both groups fluctuated at different time points with the increase on POD 5 which was not clinically relevant.

The multiple regression analysis demonstrated a moderate positive association between the inflow occlusion duration and the markers of the functional state of the liver (ALT, AST, fibrinogen, prothrombin index, blood lactate) in Group 1 ($R^2 = 0.6178$; $p = 0.0333$) and Group 2 ($R^2 = 0.6401$; $p = 0.0085$). In addition, the association between the occlusion duration and lactate level on a day following liver resection was evident both in Group 1 ($p = 0.0203$) and Group 2 ($p = 0.0049$).

Furthermore, the multiple regression analysis demonstrated a moderate positive association between the number of the resected liver segments and the markers of the functional state of the liver in Group 1 ($R^2 = 0.8428$; $p = 0.0207$), while in Group 2 such an association was not significant ($R^2 = 0.5535$; $p = 0.1394$).

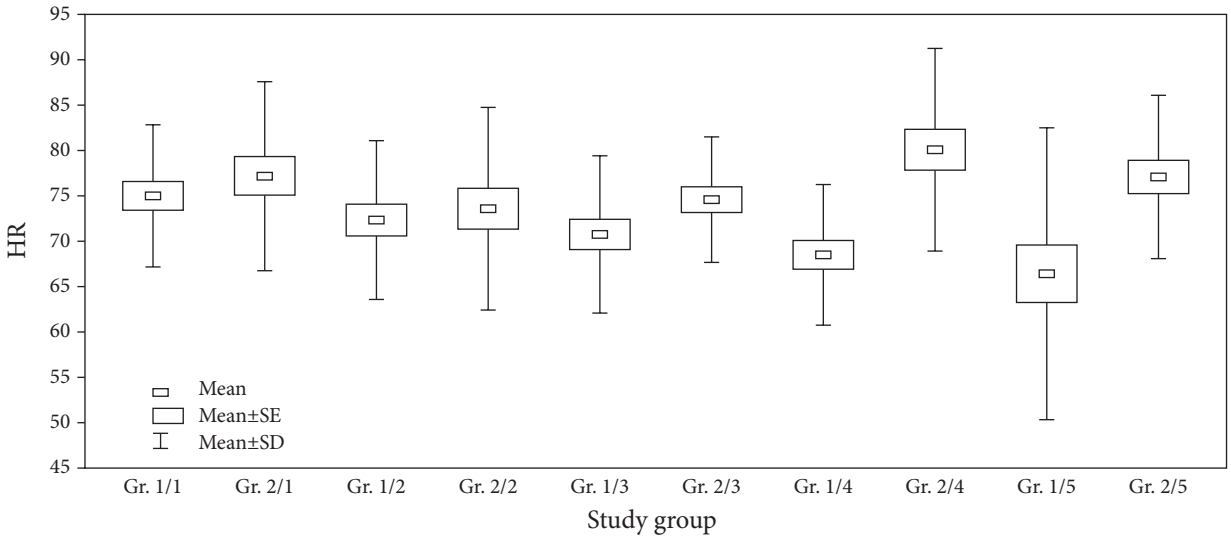

Fig. 1. HR in the groups of patients during anesthesia: Gr.1/1 and Gr.2/1 — prior to surgery, Gr.1/2 and Gr.2/2 — in 30 min, Gr.1/3 and Gr.2/3 — in 60 min, Gr.1/4 and Gr.2/4 — in 90 min, Gr.1/5 and Gr.2/5 — in 120 min from the beginning of the surgery

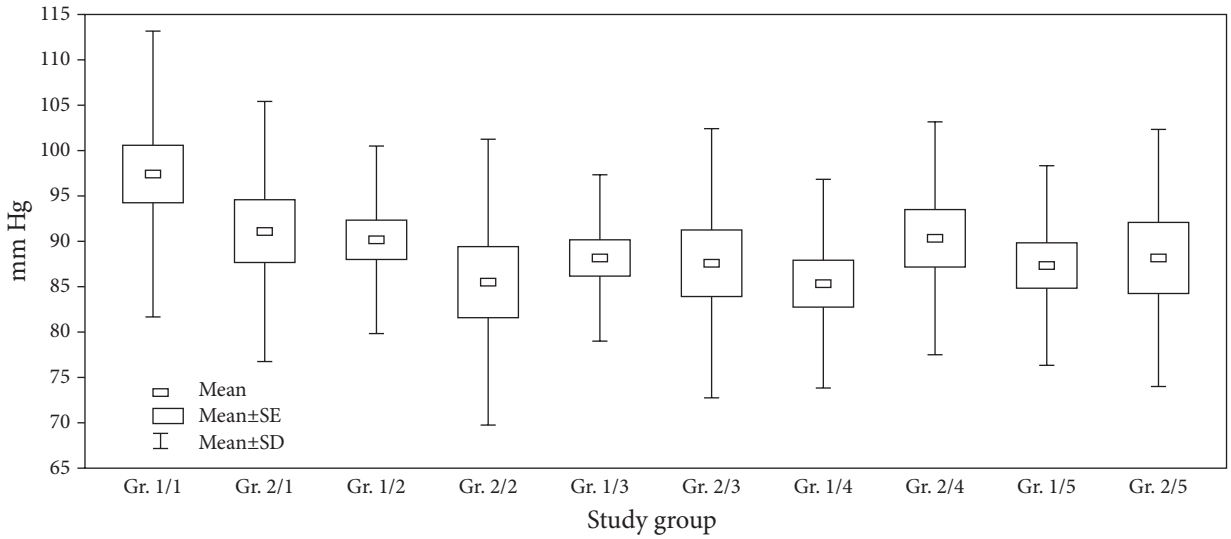

Fig. 2. MAP in the groups of patients during anesthesia: Gr.1/1 and Gr.2/1 — prior to surgery, Gr.1/2 and Gr.2/2 — in 30 min, Gr.1/3 and Gr.2/3 — in 60 min, Gr.1/4 and Gr.2/4 — in 90 min, Gr.1/5 and Gr.2/5 — in 120 min from the beginning of the surgery

Discussion

The present study was aimed at assessing the efficacy of pharmacological preconditioning with sevoflurane during liver resection and PM. The levels of transaminase and blood lactate, which are considered markers of hepatocyte damage, were followed. Moreover, the functional state of the liver was assessed by its protein-synthesizing (proteins of the blood coagulation system) and excretory (bilirubin) functions. These parameters analyzed in our study may be affected not

Table 1. **The comparison of the perioperative parameters in the groups of patients**

Parameters		Group 1	Group 2	p^1
ALT, U/l	Preoperative	31.6 ± 20	34.2 ± 21	0.63
	POD 1	276.6 ± 101.7	216.1 ± 79.1	0.0046
	POD 3	284.8 ± 186.4	253 ± 128.4	0.99
	POD 5	151.6 ± 77.6	138.7 ± 56.1	0.4
	p^2	0.0001	0.0001	
AST, U/l	Preoperative	33.6 ± 15.9	36.6 ± 16.9	0.58
	POD 1	329.2 ± 106.3	309.9 ± 99.4	0.22
	POD 3	227.2 ± 116.9	184.0 ± 99.4	0.13
	POD 5	100.6 ± 63.2	63.8 ± 23.6	0.0006
	p^2	0.0001	0.0001	
Bilirubin, μM	Preoperative	12.9 ± 6.9	14.4 ± 11.1	0.974
	POD 1	15.7 ± 7.1	22.5 ± 11.9	0.0013
	POD 3	15.6 ± 7.9	18.2 ± 12.7	0.897
	POD 5	15.6 ± 6.0	12.5 ± 6.5	0.0006
	p^2	0.002	0.0001	
Lactate, mM	Preoperative	1.55 ± 0.6	1.55 ± 0.7	0.93
	After resection	2.0 ± 0.6	2.02 ± 0.7	0.78
	POD 1	1.62 ± 0.4	2.24 ± 0.8	0.0007
	p^2	0.0007	0.0001	
Albumin, g/l	Preoperative	42.1 ± 3.0	43.2 ± 1.9	0.054
	POD 1	33.4 ± 2.8	34.2 ± 2.4	0.064
	POD 3	31.8 ± 2.1	27.2 ± 2.0	0.0001
	POD 5	31.1 ± 2.1	32.1 ± 1.6	0.0116
	p^2	0.0001	0.0001	
Prothrombin index, %	Preoperative	92.1 ± 16.2	88.8 ± 17.8	0.186
	POD 1	79.9 ± 5.1	84.2 ± 5.2	0.0002
	POD 3	83.1 ± 7.4	82.7 ± 8.0	0.87
	POD 5	93.2 ± 3.4	89.2 ± 11.1	0.097
	p^2	0.0009	0.216	
Fibrinogen, g/l	Preoperative	3.89 ± 1.1	4.18 ± 2.9	0.317
	POD 1	3.97 ± 2.6	4.43 ± 1.2	0.0019
	POD 3	3.52 ± 0.84	4.53 ± 0.6	0.0002
	POD 5	4.74 ± 0.77	4.25 ± 0.66	0.077
	p^2	0.0001	0.0012	
Blood loss, ml	—	288 ± 137 (30—600)	275 ± 199 (50—700)	0.44
Ischemia duration, min	—	45 ± 17 (12—81)	31 ± 15 (10—55)	0.11
Diuresis during surgery, ml	—	362 ± 159 (100—800)	307 ± 190 (20—800)	0.18
Simultaneous resection of rectum and liver, n (%)	—	1 (2.4)	3 (9.4)	0.3
Extensive liver resection, n (%)	—	11 (26)	5 (15.6)	0.41

Notes: [1] Mann-Whitney U test; [2] Friedman ANOVA and Kendall coefficient.

only by anesthesia methods with sevoflurane preconditioning but also by the duration of ischemia (PM), the number of the resected liver segments, the postoperative functional capability of the liver, as well as other factors being out of the scope of the study. The impact of PM on the functional state of the liver remaining after resection was analyzed by the multiple linear regression analysis.

For ALT, the significant increase in the activity was registered only on POD 1 while for AST — on POD 5. The increase in the activity of transaminases was evident in both groups of patients. Contrary to transaminases, lactate decreased to the preoperative levels on POD 1 in patients of Group 1 while in Group 2 lactate increased as compared to both preoperative levels and the levels immediately after liver resection. Such an effect may be associated with preconditioning. It should be noted that the level of transaminase activity in the peripheral blood does not seem to reflect solely the real damage of hepatocytes but could be also affected by various perioperative factors [8]. According to the literature data, the levels of transaminase activity may correlate with the surgery duration and intraoperative liver injury [9—13].

The experimental studies demonstrated that sevoflurane diminishes myocardial dysfunction and reduces the alterations of cardiomyocytes in reperfusion following ischemia [14, 15]. Some other experiments have shown that isoflurane preconditioning prior to liver ischemia resulted in a decrease in the AST and ALT activities as compared to preconditioning without isoflurane. Sevoflurane preconditioning also significantly decreased the elevated liver enzyme activity following liver resection when the blood inflow occlusion was employed. Several mechanisms of hepatocyte protection by pharmacological preconditioning have been proposed. The role of nitrogen oxide in mediating such protection has been suggested in [16]. Barrier et al. [17] demonstrated a modulation of gene expression, in particular inducible nitric-oxide synthase (iNOS), resulting from the ischemic preconditioning. The increased iNOS level confirms the association of the preconditioning with NO generation. NO is also a key signal component involved in the preconditioning caused by the inhalation of anesthetics in the myocytes by the activation of the protein kinase C with the following activation of KATP channels in sarcolemma and mitochondria [18]. Nevertheless, there are certain doubts as to the pharmacological preconditioning since both intravenous and inhalation anesthetics possess similar anti-inflammatory modulating effects manifested in inhibition or enhancement of the control of NO synthesis [19, 20]. Figueira et al. [21] demonstrated that preconditioning with sevoflurane reduces hepatocellular damage and acid-base imbalance in the setting of liver ischemia. In addition, sevoflurane postconditioning facilitates the systemic restoration of hemodynamics with the accompanying decrease in the inflammatory response.

Our study demonstrated that the decrease in the prothrombin index on POD 1 was more pronounced in Group 1. The decrease in the coagulation markers and the blood clotting factors such as prothrombin time/prothrombin index ratio, international normalized ratio, and factor V are common indicators of the state following hepatectomy that correlate with the extent of the liver resection. Furthermore, the damage to the liver is accompanied by the increased consumption of blood coagulation factors and the reduced synthetic function of the remaining liver [22—24]. Nguyen et al. [22] demonstrated that the increase in prothrombin time and factor V points to the improvement of the synthetic function of the liver. Therefore, the prothrombin time and prothrombin index could be considered markers of liver dysfunction following its resection. In our study, the fibrinogen level decreased similarly in both groups of patients while the decrease in the pro-

thrombin index on POD 1 and 3 was more pronounced in Group 1.

The changes in the parameters under study in both groups may be in principle associated with different PM durations in the surgery. Nevertheless, PM duration in Group 1 and Group 2 did not differ significantly. Up to the present, the dose—effect of the pharmacological preconditioning has not been defined [22, 24, 25]. Obal et al. [27] have demonstrated in the experiment that the pharmacological preconditioning with sevoflurane at a dose of 1 MAC provides more protection from infrared heart damage than 0.75 MAC while the dose increase above 1 MAC is not accompanied by further growth of this protective effect. This conclusion was also confirmed in other studies although it was stated that the duration of the use of inhalation anesthetics could also contribute to the outcome [28, 29].

To sum up, the pharmacological preconditioning with sevoflurane for preventing ischemia/reperfusion injury of the liver in patients following liver resection has demonstrated a protective effect on the functional state of the remaining liver. Further studies with the enrollment of a larger number of patients are required to confirm our observations.

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ПОПЕРЕДЖЕННЯ ПАТОЛОГІЧНОГО ЕФЕКТУ
ІШЕМІЇ-РЕПЕРФУЗІЇ ПРИ РЕЗЕКЦІЇ ПЕЧІНКИ ШЛЯХОМ
ПОПЕРЕДНЬОГО КОНДИЦІЮВАННЯ СЕВОФЛУРАНОМ

Актуальність. Інтермітований маневр Прінгла залишається основним методом контролю крововтрати під час резекцій печінки. Такий підхід пов'язаний з ризиком запуску каскаду патологічних змін, що призводять до ефекту ішемічно-реперфузійного пошкодження (I/P). Вважається, що перспективним методом корекції

I/P є фармакологічне попередження. **Мета.** Оцінити вплив фармакологічного прекондиціювання севофлюраном на післяопераційну функцію печінки. **Матеріали та методи.** Проспективне когортне дослідження включає аналіз даних 73 пацієнтів, що перенесли резекцію печінки. В основній групі за 30 хв. до резекції печінки проводили прекондиціювання інгаляцією севофлурану. У контрольній групі прекондиціювання севофлураном не проводили. Первинними кінцевими точками були концентрація лактату в крові після операції та через 1 добу; активність аланінамінотрансферази (АЛТ) і аспартатамінотрансферази (АСТ) на 1, 3 і 5-й післяопераційні дні. **Результати.** На 1-шу післяопераційну добу у пацієнтів групи прекондиціювання севофлураном вміст лактату знизився до передопераційного рівня, тоді як у контрольній групі він підвищився порівняно як з передопераційним рівнем, так і з рівнем одразу після резекції печінки. Достовірну різницю в рівнях АСТ між групами було зареєстровано на 5-й день, і вона не була клінічно значущою. Зниження протромбінового індексу в групі прекондиціювання севофлураном на 3-й день було вищим, ніж у контрольній групі. Множинний регресійний аналіз продемонстрував помірний позитивний зв'язок між кількістю резектованих сегментів печінки та маркерами функціонального стану печінки в групі прекондиціювання севофлураном, тоді як у контрольній групі такий зв'язок не був значущим. **Висновки.** Протекторний вплив севофлурану на післяопераційну функцію печінки проявляється зниженням рівня лактату крові та стабільним рівнем трансаміназ.

Ключові слова: колоректальний рак, метастази в печінку, ішемічно-реперфузійне ушкодження, прекондиціювання севофлураном.