8. Gauer RL, Semidey MJ. Diagnosis and treatment of temporomandibular disorders. Am Fam Physician. 2015 Mar 15;91(6):378–86. PMID: 25822556.
9. Manfredini D, Ahlberg J, Aarab G, Bracci A, Durham J, Ettlin D, Gallo LM, Koutris M, Wetselaar P, Svensson P, Lobbezoo F. Towards a Standardized Tool for the Assessment of Bruxism (STAB) – Overview and general remarks of a multidimensional bruxism evaluation system. J Oral Rehabil. 2020 May;47(5):549–556. doi: 10.1111/joor.12938. Epub 2020 Feb 17. PMID: 31999846.
10. Manfredini D, Lombardo L, Siciliani G. Temporomandibular disorders and dental occlusion. A systematic review of association studies: end of an era?. Journal of Oral Rehabilitation. 2017; 44:908-923. DOI: 10.1111/joor.12531. PMID: 28600812.
11. Okeson J, Porto FB, Furquim BD, Feu D, Sato F, Cardinal L. An interview with Jeffrey Okeson. Dental Press J Orthod. 2018 Nov – Dec; 23(6):30–39. doi: 10.1590/2177–6709.23.6.030–039.int. PMID: 30672983; PMCID: PMC6340200.

Стаття надійшла 15.07.2020 р.

DOI 10.26724/2079-8334-2021-3-77-116-120
UDC 616.31: [616.831-008.6-02

D.S. Mankovskiy
SI "Heart Institute of the Ministry of Health of Ukraine", Kyiv

PERSONIFICATION OF THE RISK OF HYPOXIC-ISCHEMIC BRAIN INJURY IN THE SYSTEM OF NEUROLOGICAL MONITORING OF CARDIAC SURGERY PATIENTS

e-mail: mds.anest7777@gmail.com

The study aimed to develop a screening algorithm for assessing the personalized risk of hypoxic-ischemic brain injuries in the preoperative period of cardiac surgery using artificial circulation. A comparative analysis of the frequency, prognostic value and diagnostic value of 26 clinical and anamnestic factors was performed in two groups of patients formed by the method of paired-comparison: 340 people with and 340 people without hypoxic-ischemic brain injuries. The most prognostically valuable factors were identified: the presence of manifestations of encephalopathy in the preoperative period – in 62.4 %, arterial hypertension – in 57.9 %, a history of closed traumatic brain injury – in 46.5 %, disorders of cerebral autoregulation – in 33.5 %, comorbid diabetes mellitus – in 34.2 %, a decrease in the left ventricular ejection fraction less than 30.0 % – in 23.7 %, and others. Prognostically unfavorable syndromes were identified and the screening tabular algorithm of risk personification of hypoxic-ischemic brain injuries based on risk assessments was substantiated.

Key words: neurological monitoring, cardiac surgery, risk assessment, cerebrovascular disorders.

Д.С. Маньковський

ПЕРСОНІФІКАЦІЯ РИЗИКУ ГІПОКСИЧНО-ІШЕМІЧНИХ УРАЖЕНЬ ГОЛОВНОГО МОЗКУ В СИСТЕМІ НЕВРОЛОГІЧНОГО СУПРОВОДУ КАРДІОХІРУРГІЧНИХ ПАЦІЄНТІВ

Автором статті було поставлено за мету розробку скринінгового алгоритму оцінювання персоніфікованого ризику гіпоксично-ішемічних уражень головного мозку в доопераційному періоді кардіохірургічних втручань з використанням штучного кровообігу. Виконано порівняльний аналіз частоти, прогностичної цінності та діагностичного значення 26 клініко-анамнестичних факторів в двох групах пацієнтів, сформованих за методом копі-пара: 340 осіб з та 340 осіб – без гіпоксично-ішемічних ураженнь головного мозку. Встановлено найбільш прогностично цінні фактори: наявність у доопераційному періоді проявів енцефалопатії – у 62,4 %, артеріальної гіпертензії – у 57,9 %, закритої черепно-мозкової травми в анамнезі – у 46,5 %, порушення церебральної ауторегуляції – у 33,5 %, комор бідний цукровий діабет – у 34,2 %, зниження фракції викиду лівого шлуночка серця менше 30,0 % – у 23,7 % та інші. Виділено прогностично несприятливі синдроми та, на основі ризикометричних оцінок, обгрунтовано скринінговий табличний алгоритм персоніфікації ризику гіпоксично-ішемічних уражень головного мозку.

Ключові слова: неврологічний супровід, хірургія серця, оцінка ризику, цереброваскулярні порушення.

The study is a fragment of research project "To study the clinical and pathogenetic mechanisms of cerebrovascular disorders formation in patients after cardiac surgery", state registration No. 0116U000009.

Modern technologies of cardiac surgery (CS) can significantly influence the structure of mortality, disability, and quality of life in patients with critical ischemic disease, valvular heart disease, cardiomyopathies [3, 4]. At the same time, neurological complications can significantly affect the course of the postoperative period and turn off the technically high-quality CS performance [10]. In recent years, the overall mortality after CS using artificial circulation (AC) is characterized by 20–25 % decrease, while the frequency of hypoxic-ischemic brain injuries (HIBI) is almost unchanged and even in older age groups increases [9, 11]. Cerebral stroke, postoperative encephalopathy and severe cognitive dysfunction, in some cases, remain a delayed problem of CS [12], which highlights the need to develop a system of intraoperative neurological monitoring. Recently, risk-solving approaches and risk-based personalization techniques have been used to address this problem, such as atherosclerosis of the aorta, arterial hypertension [5-7, 14] and brachiocephalic arteries [8, 13], atrial fibrillation [10, 11, 14], concomitant diabetes mellitus [14, 15], overweight and obesity [13], smoking and others [8, 15]. That is why cardiac surgery centers of expert level focus on the implementation of preoperative personalized screening in the selection of the type and tactics of CS and rehabilitation programs for patients [14].

The purpose of the study was to develop a screening algorithm for assessing the personalized risk of hypoxic-ischemic brain injuries in the preoperative period of cardiac surgery using artificial circulation.

Materials and methods. The study was performed on the clinical basis of the SI "Heart Institute of the Ministry of Health of Ukraine", using primary materials on CS with AC for 2015–2020; there were involved two groups of patients formed by the method of paired-comparison (according to the signs: age, gender, type of CS): in the first (n_1=340 people) – patients with HIBI after CS, in the second (n_2=340 people) – without HIBI. The study used the results of routine neurological, instrumental and laboratory examinations at the stages of CS with the completion of a special "Card of expert assessment of neurological monitoring in a CS patient". Postoperative assessment of neurological status, including diagnosis of possible HIBIs, was performed according to clinical protocols. In the course of the study we performed an analysis of clinicaland anamnestic factors (CAF) that are most often analyzed in specialized publications: the level of peripheral blood hemoglobin (CAF_1), the presence of history of closed traumatic brain injuries (cTBI, CAF_2), the value of the heart left ventricular ejection fraction EF_{LV}(CAF_3), the presence of "silent" changes in the brain according to computed tomography (CT) or magnetic resonance imaging (MRI, CAF_4), a history of artificial lung ventilation (CAF_5), the presence of arterial hypertension (AH, CAF_6), carotid artery stenosis (CAF_7), impaired cerebral autoregulation (CAF_8), the presence of encephalopathy of any genesis (CAF_9), atheromatosis of the ascending aortic arch (CAF_{10}), vertebro-basilar insufficiency (CAF_{11}), smoking (CAF_{12}), chronic kidney disease (CAF_{13}), asymmetries of cerebral blood filling (CAF_{14}), overweight (CAF_{15}), varicose veins (CAF_{16}), diabetes mellitus (CAF_{17}), a history of cerebral stroke (CAF_{18}), atrial fibrillation (CAF_{19}), somatotype abnormalities (CAF_{20}), previously suffered CS (CAF_{21}), infectious endocarditis (CAF_{22}), preoperative level of cerebral oxygenation (CAF_{23}), chronic lung diseases (CAF_{24}), a history of cardiogenic shock (CAF_{25}), mild and moderate manifestations of cognitive impairment (CAF_{26}). Known methods of medical statistics and clinical informatics are applied, in particular: variation statistics (P±m is a factor frequency index and its mean error), probabilistic distribution of clinical and instrumental laboratory data with subsequent assessment of the reliability of results' (p is the reliability of differences between groups; according to the Student's t-test) comparison between groups [1, 2]. As the basic criteria for assessing the diagnostic value and prognostic value of CAF, we used indicators: frequency, strength of influence of the factor (n^2, %), its overall information content (I; bit) and the corresponding prognostic coefficients (PC, pat), calculated according to the standard technique using the software adapted to "EXCEL" [1, 2].

Results of the study and their discussion. The comparative intergroup analysis revealed reliable ($p<0.001$) CAFs, their ranking according to the indicator of general informativeness (table 1) and the 10 most informative of them are included in the prognostic algorithm.

Thus, it was found that the presence of SE is a significant ($p<0.001$) risk factor (first ranked place); a significantly higher frequency of SE was recorded in Group n_1, compared to patients in Group n_2 (62.4±2.6 % and 14.8±1.9 %, respectively). General information content of CAF_9 is I=2.324 bits, while the force of influence of the factor is η^2 = 24.0 %, and PC: in the presence of PC^+ = +6.2 pat, in the absence of PC^- = - 3.5 pat.

It was found that the presence of hypertension in the preoperative period is a significant ($p<0.001$) risk factor for the HIBI formation; a significantly higher frequency of hypertension was recorded in Group n_1, compared to patients in Group n_2 (57.9±2.7 % and 22.7±2.3 %, respectively). The informativeness of this feature is I = 1.177 bits, while the force of influence of the factor – η^2 = 13.0 %, and PC: in the presence of AH – PC^+ =+4.1 pat, in the absence of PC^- =-2.6 pat.

A history of cTBI was recorded significantly ($p<0.001$) and three times more often in Group n_1 than in Group n_2 (46.5±2.7 % and 14.1±1.9 %, respectively); information content of the CAF_2 – I = 1.169 bits, while the force of influence is η^2= 12.0 %, and PC: if there is a cTBI – PC^+=+5.5 pat, if not – PC =-2.0 pat.

In the preoperative period, the presence of non-severe cognitive impairment was reliably diagnosed ($p<0.001$) and twice as often in Group n_1 than in Group n_2 (63.1±2.6 % and 29.1±2.5 %, respectively); overall information content of CAF_{26} – I = 1.054 bits, while the force of influence of the factor is η^2 = 12.0 %, and PC: if there is a factor – PC^+ = +3.3 pat, in the absence of-PC = 2.8 pat.

The presence of impaired cerebral autoregulation (CAF_8) in the preoperative period is also a significant ($p<0.001$) factor; thus, a significantly higher frequency of its disorders was registered in Group n_1, compared to patients in Group n_2 (33.8±2.6 % and 10.9±1.7 %, respectively). The total information content of the feature is I = 0.713 bits, while the force of the factor influence is N^2 = 7.0 %, and PC: in the presence of impaired cerebral autoregulation – PC^+ = + 4.9 pat, in the absence of violations – PC = -1.3 pat.

Table 1

Frequency, diagnostic and prognostic CAF value in the formation of HIBI risk in the postoperative period of CS with AC

CAF in the order of decreasing informativeness and their gradation			Cardiac surgery patients				PC, pat	I, bit
			n_1=340 people		n_2=340 people			
			abs.	(P±m)%	abs.	(P±m)%		
CAF_9	Encephalopathy	yes	212	62.4±2.6	50	14.8±1.9	+6.2	1.481
		no	128	37.6±2.6	287	85.2±1.9	-3.5	0.842
CAF_6	Arterial hypertension	yes	197	57.9±2.7	77	22.7±2.3	+4.1	0.713
		no	143	42.1±2.7	263	77.3±2.3	-2.6	0.464
CAF_2	History of cTBI	yes	158	46.5±2.7	48	14.1±1.9	+5.2	0.837
		no	182	53.5±2.7	292	85.9±1.9	-2.0	0.332
CAF_{26}	Mild cognitive impairment	yes	215	63.1±2.6	99	29.1±2.5	+3.3	0.571
		no	125	36.9±2.6	241	70.9±2.5	-2.8	0.483
CAF_8	Disorders of cerebral autoregulation	yes	115	33.8±2.6	37	10.9±1.7	+4.9	0.565
		no	225	66.2±2.6	303	89.1±1.7	-1.3	0.148
CAF_{17}	Type II diabetes mellitus	yes	113	34.2±2.6	39	11.5±1.7	+4.8	0.541
		no	217	65.8±2.6	301	88.5±1.7	-1.3	0.147
CAF_3	Left ventricular ejection fraction of the heart, %	< 30	83	23.7±2.3	31	9.1±1.6	+4.1	0.303
		30-40	111	31.7±2.5	74	21.8±2.2	+1.6	0.081
		>40	156	44.6±2.7	235	69.1±2.5	-1.9	0.234
CAF_4	"Silent" cerebral changes: neuroimaging	yes	114	33.5±2.6	41	12.1±1.8	+4.4	0.477
		no	226	66.5±2.6	299	87.9±1.8	-1.2	0.131
CAF_1	Peripheral blood hemoglobin level	Norm	161	47.4±2.7	236	69.4±2.5	-1.6	0.183
		-10 %	108	31.8±2.5	79	23.2±2.3	+1.4	0.058
		<-10 %	71	20.9±2.2	25	7.4±1.4	+4.5	0.307
CAF_{18}	Cerebral stroke/infarction in the anamnesis	yes	57	16.8±2.0	12	3.5±1.0	+6.7	0.448
		no	283	83.2±2.0	328	96.5±1.0	-0.6	0.042

The presence of diabetes mellitus (DM) in the anamnesis was registered significantly ($p<0.001$) and three times more often in Group n_1 than in Group n_2 (34.2±2.6 % and 11.5±1.7 %, respectively); overall information content of the CAF_{17} – I = 0.688 bits, while the force of the factor influence is η^2 = 7.0 %, and PC: if there is a DM – PC^+ = +4.8 pat, in the absence of a PC – 1.3 pat. It was found that the rate of EF_{LV} (CAF_3) in the preoperative period is a significant ($p<0.001$) risk factor; thus, a significantly higher frequency of people with EF_{LV} less than 30.0 % in Group n_1, compared to patients in Group n_2 (23.7±2.3 % and 9.1±1.6 % of people, respectively). In addition, similarly, among patients in Group n_1 there were significantly more people with EF_{LV} within 30.0 ÷ 40.0 %. At the same time, among patients of Group n_2, compared to Group n_1, patients with EF_{LV} prevailed ($p<0.001$) more than 40.0 % (69.1±2.5 % and 44.6±2.7 % of people, respectively). The total information content of this feature is I = 0.618 bits, while the force of the factor influence is η^2 = 7.0 %, and PC: if there is a reduced EF_{LV} less than 30.0 %, PC^+ = + 4.1 pat, if there is an EF_{LV} more than 40.0 %, PC^- =–1.9 pat.

During instrumental routine examination (CT, MRI), "silent" brain changes (CAF_4) were diagnosed in the preoperative period significantly ($p<0.001$) more often in Group n_1 than among patients in Group n_2 (33.5±2.6 % and 12.1±1.8 % of people, respectively). General information content of the CAF_4 is I = 0.608 bits, whereas η^2 = 6.0 %, and PC: if available PC^+ = +4.4 pat, in the absence PC^- = –1.2 pat.

At the same time, the anamnestic indication of a previous cerebral stroke was also informative: significantly ($p<0.001$) more often among patients of Group n_1 than Group n_2 (16.8±2.0 % and 3.5±1.0 % of people, respectively). General information content of the CAF_{18} was I= 0.490 bits, while the force of the factor influence is η^2 = 5.0 %, and PC: if there is a CAF_{18} PC^+ = +6.7 pat, in the absence, PC^-= –0.6 pat.

A pattern of increased risk depending on the level of peripheral blood hemoglobin in the preoperative period was revealed. Thus, in the case of its compliance with the reference value (in Group n_1 – in 47.4±2.7 %, in Group n_2 – among 69.4±2.5 % of people, $p<0.001$); we have a PC^+ = –1.6 pat, while the risk of HIBI formation increases with a decrease in hemoglobin levels. The total information content of this feature is I = 0.548 bits, the force of the factor influence is η^2=6.0 %.

Thus, the availability of reliable information on the prognostic value of CAF allowed us to justify the sequence of the procedure for personalized risk assessment HIBI and create an appropriate tabular algorithm (table 2), in which, in order of decreasing information content, the most prognostically valuable features and corresponding PCs are entered.

Table 2

Algorithm of personification of HIBI risk when performing CS with AC

I, bit	Clinical and anamnestic risk markers	Predictive coefficients	
		criteria	PC, pat
2.324	CAF_9: presence of encephalopathy	yes	+6.2
		no	-3.5
1.177	CAF_6: presence of arterial hypertension	yes	+4.1
		no	-2.6
1.169	CAF_2: verified cTBI, in the anamnesis	yes	+5.2
		no	-2.0
1.054	CAF_{26}: mild cognitive impairment	yes	+3.3
		no	-2.8
0.713	CAF_8: violation of cerebral autoregulation	yes	+4.9
		no	-1.3
0.688	CAF_{17}: diabetes mellitus	yes	+4.8
		no	-1.3
0.618	CAF_3: left ventricular ejection fraction, %	< 30	+4.1
		30-40	+1.6
		>40	-1.9
0.608	CAF_4: "Silent" cerebral changes: neuroimaging	yes	+4.4
		no	-1.2
0.524	CAF_1: peripheral blood hemoglobin level	Norm	-1.6
		-10 %	+1.4
		<-10 %	+4.5
0.490	CAF_{18}: history of stroke	yes	+6.7
		no	-0.6

It should also be noted that the predictive amounts (PA) selection provides for preliminary determination of errors of the first and second kind according to a special table, which guarantees the appropriate level of accuracy when applying the algorithm.

The expectancy technology is quite simple and involves sequentially adding the corresponding coefficients until one of the predictive amounts is reached (after assessing the presence/absence of CAF listed in the algorithm). This allows you to perform a personalized risk assessment with simultaneous distribution (correlation) of the surveyed individuals to one of the three risk groups (fig. 1).

Scale for assessing personalized expectancy results		
$PA_{min} \leq -11.0$ low risk of HIBI	$-11.0 > PA < +17.0$ uncertain risk	$PA_{max} \geq +17.0$ high risk of HIBI

Fig.1. Visual-analog scale for evaluating the personalized prediction result of HIBI in the case of performing a CS with AC

We insist that combination of certain CAF and, accordingly, risk assessment should be performed in a particular patient using the developed algorithm. This allows you to abandon some of the unwieldy and costly examination methods, "reduce" the forecasting process and, at the same time, take into account the most prognostically valuable CAFs.

Example of applying the algorithm. Patient N., 57 years old. At the stage of planning CS with AC, during the expert analysis of the medical history and according to the results of clinical and anamnestic examination, it was revealed that: patient has no manifestations of EP (PC = -3.5 pat), there is the presence of hypertension (PC = +4.1 pat; the prognostic amount (PA) is PA = -3.5 + 4.1= +0.6 pat), cTBI in the patient's anamnesis (PC = +5.2 pat; PA = 0.6+5.2=5.8 pat), mild cognitive impairment (PC = +3.3 pat: PA = 5.8+3.3=9.1 pat) and impaired cerebral autoregulation (PC = +4.9 pat: PA = 9.1+4.9=14 pat), and the presence of type II diabetes in the patient was taken into account (PC = +4.8 pat: PA = 14.0+4.8=18.8 pat). The forecasting process is suspended, as a prognostically significant amount (PA>+17.0 pat) has been reached, which allows to predict the manifestations of HIBI in the case of CS with the use of AC with a probability of at least 97.0 %.

The common risk factors for the formation of hypoxic-ischemic brain injuries in patients with cardiac surgery performed using artificial circulation were identified among the most informative factors in the postoperative period: the presence of encephalopathy manifestations in the preoperative period – in 62.4 %, arterial hypertension – in 57.9 %, a history closed traumatic brain injury – in 46.5 % of patients, etc. The obtained data correspond to the previously published results, which were performed selectively on different groups of patients [9, 12, 14], however, in our study these factors were analyzed systematically and on one group of patients.

There are three main prognostically adverse syndromes: psychoneurological (encephalopathy, hypertension, closed traumatic brain injury) – in 39.7 %; vascular dysfunction (impairment of cerebral autoregulation, decrease in the ejection fraction of the left ventricle of the heart, history of stroke) – in 16.5 %, cardiovascular disorders (atrial fibrillation, "silent" carotid artery stenosis, the presence of atheromatosis of the ascending aortic zone) – in 12.6 % of patients. Expert-level cardiac surgery centers usually use chemical, metabolic and geodynamic indicators to identify high risk in the intraoperative period [3, 12, 15], while the obtained data allow to do it at the stage of planning cardiac surgery due to a sound screening algorithm and, accordingly, to personify the tactics of treatment and rehabilitation.

Conclusions

The use of the prognostic potential of clinical and anamnestic factors to assess the risk of hypoxic-ischemic brain injuries in patients with cardiac surgery performed using artificial circulation, determines the need for a detailed neurological examination at the planning stage of interventions. Neurological monitoring of cardiac surgery patients should include clinical and anamnestic testing using a sound algorithm or at least a syndromal analysis for the presence of psychoneurological, vascular dysfunction, cardiovascular disorders.

Prospects for further research are to study the prognostic potential of CAF in assessing the personalized risk of certain nosologically outlined manifestations of HIBI in the postoperative period of CS with AC: stroke, encephalopathy, severe cognitive dysfunction.

References

1. Hubler EV. Klynycheskaia patoinformatika v meditsine y pediyatrii. Meditsina, 2002. 211-211 [in Russian]
2. Rebrova OIu. Statystycheskiy analiz meditsinskikh dannykh. Primenenie paketa prikladnykh prohramm STATISTICA. MedyaSfera, 2002: 312 [in Russian]
3. Berisavac I, Jovanovic D, Padjen V, Ercegovac M, Stanarcevic P, Budimkic-Stefanovic M et al. How to recognize and treat metabolic encephalopathy in neurology intensive care unit. Neurol India. 2017; 65(1): 123–128. doi: 10.4103/0028-3886.198192.
4. Costa M, Gauer M, Gomes R, Schafranski M. Risk factors for perioperative ischemic stroke in cardiac surgery. Rev Bras Cir Cardiovasc. 2015; 30(3): 365–372. doi: 10.5935/1678-9741.20150032.
5. Demikhov O, Dehtyarova I, Demikhova N, Rud O, Cherkashyna L. Arterial hypertension prevention as an actual medical and social problem. Bangladesh Jurnal of Medical Science. 2020; 19 (4): 722–729. doi: 10.3329/bjms.v19i4.46632.
6. Demikhov O, Dehtyarova I, Demikhova N. Actual aspects of public health policy formation on the example of Ukraine. Bangladesh Journal of Medical Science 2020; 19 (3): 358–364. doi: 10.3329/bjms.v19i3.45850.
7. Demikhov O, Demikhova N, Zakharchenko M, Bumeister L. Dynamic of endothelial dysfunction factors during treatment in renal hypertensive. Atherosclerosis. 2019; 287: 260. doi: 10.1016/j.atherosclerosis.2019.06.802.
8. Feigin V, Roth G, Naghavi M. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global burden of disease study. Lancet Neurol. 2016; 15: 913–924. doi: 10.1016/S1474-4422(16)30073-4.
9. Feigin V. Anthology of stroke epidemiology in the 20th and 21st centuries: Assessing the past, the present, and envisioning the future. Intern. Journal of Stroke. 2019; 14(3): 223–237. doi: 10.1177/1747493019832996.
10. Gopagondanahalli K, Li J, Fahey M, Hunt R, Jenkin G, Miller S et al. Preterm hypoxic–ischemic encephalopathy. Front Pediatr. 2016; 4: 114. doi: 10.3389/fped.2016.00114.
11. Hahne K, Monning G, Samol A. Atrial fibrillation and silent stroke: links, risks, and challenges. Vascular Health & Risk Management. 2016; 12: 65–74. doi: 10.2147/VHRM.S81807.
12. Jauch E, Saver J, Adams H, Askiel B, Connors B, Demaerschalk B et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association / American Stroke Association. Stroke. 2013; 44(3): 870–947. doi: 10.1161/STR.0b013e318284056a.
13. Johnson W, Onuma O, Owolabi M. Stroke: a global response is needed. Bull. WHO. 2016; 94: 634–634. doi: 10.2471/BLT.16.181636.
14. O'Neal J, Billings F, Liu X, Shotwell M, Liang Y, Shah A et al. Risk factors for delirium after cardiac surgery: an historical cohort study outlining the influence of cardiopulmonary bypass. Can J Anaesth. 2017; 64(11): 1129–1137. doi: 10.1007/s12630-017-0938-5.
15. Zerna C, Thomalla G, Campbell B, Rha J, Hill M. Current practice and future directions in the diagnosis and acute treatment of ischaemic stroke. Lancet. 2018; 392(10154): 1247–1256. doi: 10.1016/S0140-6736(18)31874-9.

Стаття надійшла 29.07.2020 р.