INTRODUCTION
Stroke is a big social problem [1]. Despite the high risk of complications in the postoperative period among patients with acute ischemic neurological symptoms, the feasibility of surgical treatment is justified as the chances for complete recovery of the neurological deficit increase [2].

The topicality of the determination for terms of carotid endarterectomy (CEA) in patients with carotid stenosis after postoperative neurological deficit with the least risk of developing a re-stroke is uncertain. The risks and timing of the development of repeat neurological deficits in patients with atherosclerotic lesions of the carotid arteries are still controversial. Therefore, today there is no unanimous opinion when CEA is the safest. Depending on the duration of the marker event and the surgical intervention, CEA is divided into urgent, early, delayed and scheduled (or late). Urgent CEA is an operation performed up to 48 hours after the marker event, early CEA - up to 14 days after the transient neurological deficit, delayed - from 14 to 30 days and scheduled (late) CEA - after 30 days [3, 4, 5].

A meta-analysis of two studies comparing CEA and the treatment of symptomatic carotid stenoses showed that the short term from the last neurological symptom to surgical re-vascularization contributes to a better recovery of the patient [6]. However, a clear time interval is not defined and the possible frequency of life-threatening complications in the urgent and early CEA.

THE AIM
To analyze available sources of scientific information on the terms of surgical treatment of patients with acute neurological deficit and to determine the safest time for the implementation of CEA with the lowest risk of developing repeated cerebral circulation disorder.

MATERIALS AND METHODS
It was analyzed 41 English-language publications in PubMed for 5 years from 2012 to 2017, with the CEA words “urgent carotid endarterectomy” and “early carotid endarterectomy”. Five articles were devoted to the problem of organization of urgent CEA, 5 - discussion letters of the editorial boards of professional editions. Another 5 publications compared the results of different regimens of disaggregation therapy among symptomatic patients after early CEA. In one publication, the authors described a clinical case. In 7 articles, the results of early CEA in symptomatic patients were based on the analysis of less than 100 operations. Among the 12 scientific papers, the clinical sample was from 143 to 989 patients after a neurological deficit. Six studies have analyzed the complications that have arisen in more than 1000 symptomatic patients after CEA. In most reports patients brain revascularization after developing a stable or regressive neurological deficit, and in four studies CEA results were compared among patients undergoing crescendo transient ischemic attacks (cTIA) and a stroke-in-evolution.

REVIEW AND DISCUSSION
The analysis of the sources of scientific reports was based on information of the risk of re-stroke after marker event, the influence of the terms of surgical treatment on the risk
of developing a new neurological deficiency, on the feature of the organization of medical care in different countries, influencing the timing of hospitalization and treatment of patients in specialized clinics, the results of CEA, depending on the type of ischemic lesion of the brain.

In reports E. Johansson et al. (2013) and M. Marnane et al. (2014) the risk of re-development of the neurological deficiency is 5% during the first 48 hours, and according to M. Mono et al. (2013), the risk of a re-marker event during the first 72 hours is only 4% [7, 8, 9].

S. Strömberg (2015) in his study notes that in patients with stenosis 70% of the ipsilateral internal carotid artery, the risk of recurrent ischemic stroke increases, but only after 3 weeks after the postponed marker event is more than 6% [10].

According to the results of these publications, the risk of recurrent acute ischemic lesion of the brain with conservative treatment is less than 6%, which calls into question the expediency of urgent surgical treatment of carotid stenosis to prevent the development of a repeated ischemic stroke.

However, the results of D. Bonifatiet. al (2011) are controversial and indicate that the risk of recurrent ischemic stroke or TIA in the first 2 days is higher and is 8% [11]. Also, the high risk of early recurrent ischemic lesions of the brain was reported by Ois et al. (2009). According to the study, the risk of recurrent ischemic stroke or TIA in the first 3 days is higher than 17% and increases to 25% on the 14th day [12].

Themeta-analysis of publications from 1950 to 2015 collected data from 2,634 patients. The authors show quite wide limits of the risk of recurrent stroke or TIA: within the first three days - 2.0-17.2%; during the first week - 0-22.1%; within 2 weeks - 0-29.6%. Interestingly, the risk of a repeat marker event, according to this meta-analysis, is reduced to 11.1% on 30 day [13].

Guided by the information of these studies, which are based on sufficiently large clinical material, urgent and early revascularization of the brain is appropriate.

According to the European management of atherosclerotic carotid and vertebral artery disease in symptomatic patients with stenosis of 50-99%, revascularization is required within 14 days after the onset of the neurological deficiency (class of evidence I, level A), and in case of an increase in the neurological deficit, preference is given to the urgent CEA in the first day (class of evidence IIa, level C). To reduce the risk of postoperative intracranial hemorrhage in patients with ischemic lesions of more than 1/3 of the cerebral hemisphere, with a disturbance in consciousness and severity of neurological disorders greater than 3 points on the modified Rankin score, revascularization should be delayed (class of evidence of class I, level C) [14].

Several publications concerned the organization of urgent CEA. So in a joint work of scientists from London and Ontario (Erin Dyer et al., 2013), attention was drawn to the “circle of hell” that should be addressed to the patient after the development of a neurological deficiency before being hospitalized for surgical treatment. This undoubtedly influenced the fact that urgent CEA were performed only in a small number of patients, since from the onset of the neurological event to the operation, on average, it ranged from 82 to 111 days [15].

That is why in Denmark, according to Saeid Shahidi (2013), no patient was operated in the first two days after the development of an ischemic stroke or TIA, and only 17% of patients were operated within 2 days of onset of hospitalization. Most (28%) of brain revascularisations, among patients with acute neurological deficiency, was performed only on the 8th-14th day after the postponed marker event [16].

The same author in 2016 repeatedly conducted a study on the timing of the implementation of CEA in symptomatic patients. The results did not differ from the previous 2013 study. So, no patient was operated in the first two days after the development of neurological deficiency.

Most patients were operated on the 8th-14th day, and the proportion of such patients increased to 38%. The article states that aggressive drug therapy allows to refrain from performing urgent CEA without increasing the risk of recurrent stroke [17].

Statistic in Sweden is similar, where only 3% of CEA [5] and in the United Kingdom 3% follow the first two days after the development of the neurological deficit [1]. Some higher rates of such operations are in Germany - 9%, but it is also not optimal [18].

Analyzing the causes of deferral of CEA in the University Hospital, Lester, M. Ali et al. (2013) found that the main factors were the development of a marker event during the weekend (44%) and a lack of free space in the schedule of operations (24%) [19].

Several countries have developed special stroke centers that increase patients chances of developing neurological deficits to receive the earliest surgical help for brain revascularization [2, 20, 21].

In the analysis of the New England (USA) registry from 2003 to 2014, it was found that in this region the number of early CEA in symptomatic patients is gradually increasing. In 2014, the percentage of early CEA is about 68%, and planned - 32%, respectively. According to the authors, the increase in the proportion of early CEA is a modern trend in carotid artery surgery [2].

The ESVS European management 2017 reports the results of three studies on urgent CEA to prevent recurrent ischemic stroke in symptomatic patients. These are publications from Sweden, Great Britain and Germany [14].

In Sweden, according to investigation in 2012, the frequency of postoperation neurological events among patients with atherosclerosis of carotid arteries, operated in the first two days, was 11.5%. In other patients who were operated later, the incidence of ischemic lesions in the brain was less than 6% [5]. Studies from the United Kingdom (2016) and Germany (2016) also indicate the highest risk of recurrent neurological deficits among patients operated in the first two days, but did not exceed 6% and amounted to 3.7% and 3.0% respectively [1, 18].

Therefore, in studies referring to the authors of the ESVS management, the highest risk of recurrence of stroke was
in patients who were operated in the first two days after the first ischemic attack, therefore urgent operating CEA are not appropriate. However, there are significant differences in the frequency of this complication after urgent CEA. This is also observed in other publications.

L.M. Loftus with co-authors in 2016, analyzed the results of 33,194 CEA that were included in the UK’s national registry and concluded that the highest risk of post-surgical stroke and death was experienced by patients who had experienced CEA in the first two days after the onset of symptoms, which was 3.7%. The frequency of complications in patients who were operated later did not exceed 2.6% [1].

An article from Göteborg S. Strömberg with co-authors (2015) reported the results of the treatment of 321 patients who had undergone CEA. The incidence of recurrent stroke in patients who were operated during the first 2 days was 20%, and among those who were operated 2 days after the postmarked event - 5%. However, it should be noted that in the first group the number of patients was only 15 patients, in contrast to the second group included 297 patients [10].

In the publications of 2017, Efthymios D. Avgelinos and his collaborators from the United States and A. Nordanstig from Göteborg there were analyzed the results of CEA in 989 and 418 symptomatic patients with atherosclerotic lesions of the carotid arteries. The frequency of an early postoperative stroke in a group of patients who underwent CEA in the first two days after the transmitted neurological deficiency was 7.3-8%. It is statistically significantly higher than in patients who were operated 2-14 days after a neurological deficiency, in which the incidence of ischemic stroke did not exceed 4% [2, 21].

These findings correlate with the results of the analysis of the Paola De Rango conducted in 2015. According to their data, the highest risk of post-surgical stroke or death in patients undergoing CEA in the first 2 days is 8.44%. Among the patients operated later from the moment of neurological deficiency, the given risk decreases. In general, the risk of postoperative ischemia or death among patients who had an early CEA was 3.77% [22].

In 2013, in Switzerland, Mono M. et al. compared the results of the surgical treatment of 94 patients: 85 of them suffered from CEA, and 9 - stenting. For the duration of the surgical intervention, patients were divided into 3 groups: in the first 3 days, within 3-7 days and from the week to two after the transmitted neurological deficiency. As a result, the incidence of repeat cerebrovascular events was the lowest in patients who operated for 3-7 days and amounted to 2.4%. These rates in groups of operated patients in the first 72 hours and from the 7th to 14th day after the marker event were 11.4% and 7.9% respectively [9].

Similar conclusions were made by Austrian researchers who analyzed the results of the treatment of 761 patients with symptoms of neurological deficiency. Most often, stroke and death were observed in patients who performed CEA from the 8th-14th days after the transient neurological deficiency, and at least from 3rd-7th day [23].

So, Swiss and Austrian surgeons consider that it is most appropriate to perform surgical interventions in the period from 3rd to 7th day after the onset of an ischemic attack, which is an early CEA in the first week.

In Croatian clinics from 2008 to 2014, 69 early CEA were performed in symptomatic patients in the first 14 days after the development of neurological deficits. Postoperative stroke arose at 5.79% [24]. This indicator is high enough, but below 6%, and is acceptable in accordance with the European guidelines for the treatment of atherosclerosis of the carotid and vertebral arteries.

James F. Meschia, with a group of contributors from the United States, Canada and England, compared the results of early, delayed, and planned CEA treatments. The work showed the safety of CEA in symptomatic patients, regardless of the duration of the operation after the primary neurological deficiency. Among 597 patients, the risk of postoperative stroke or death after CEA in the first two weeks was 2.6%, from 15 days to 60 days - 2.3%, in 2 months - 2.8% [25].

In 2017, Barbara Rantner and colleagues conducted a goal analysis of 4 randomized trials. According to his results, the frequency of postoperative stroke is lower after CEA, which was performed by symptomatic patients during the first week after the marker event, than in the operated symptomatic patients after 7 days (1.3% vs. 3.6% respectively) [26].

In the publication of Emiliano Chisc with co-authors of 2015, the results of surgical treatment of 322 patients with acute neurological deficiency within 30 days have been analyzed. In 3 (10%) patients who were operated during the first two days, an early postoperative ischemic stroke developed. Among patients in other groups, the incidence of postoperative stroke was the highest in the group of patients who were operated from 15th-30th day after the primary neurological deficiency and amounted to 0.4% [27].

In favor of early CEA, there is information from Thierry Merlini et al. (2014) that analyzed the results of early CEA in 91 patients operated in two centers in France from 2011 to 2013. Neurological deficiency after the operation developed in only 1 patient in 27 patients with TIA and 1 in 64 patients after acute ischemic stroke. The most frequent complication after such operations, the authors consider postoperative hematomas - 7.7% [28].

In 2014, the work of Tsivgoulis et al., which analyzed the results of urgent CEA among patients with acute neurological deficiency, developed after carotid stenting (CAS). The sample included 165 patients from 5 centers. In 70% of patients afterCAS, an ischemic stroke was developed, and in 30% - TIA, of which 6% is crescendo TIA. 20 patients were operated in the first 2 days after the development of neurological deficiency, the remaining 145 - in the range of 3 to 14 days. So in the first group the recurrent stroke was diagnosed in 2 patients (10%), and in the second group - 6 (4.1%) [29].

Active surgical tactics is recommended by Samuel Bruls et al, who in 2013 published a 5-year experience of urgent CEA in patients with carotid stenosis and brain ischemia at the University of Liege Hospital. Despite a small sam-
ple (30 patients in total), there was no re-stroke or TIA, 1 (3.3%) died of a primary stroke, and in 5 (17%) - the clinical picture did not improve. The authors specify that when neuroimaging in patients, the diameter of the center of ischemia of the brain did not exceed 1.5 cm [20].

Authors from Turin, under the guidance of Emanuele Ferrero (2014), emphasize that in order to correctly comparison of the frequency of complications after CEA, apart from the spread of the focus of brain ischemia, the clinical course of TIA should be taken into account. The researchers analyzed the results of CEA performed for 48 hours in 176 patients with acute neurological deficiency. 55 of them had a classical TIA, 55 - an increasing TIA, 60 - a progressive brain infarction. The percentage of postoperative ischemic stroke and death was the highest in the group with progressive ischemic stroke of the brain and amounted to 7.6% [30].

Similar findings were made by Rodolfo Pini with co-authors (2017) from the University Hospital in Bologna. Thus, after urgent CEA, a cerebral infarction among the 87 patients with an increasing TIA occurred in 5.5%, and among 56 patients with classical TIA - only 1.6%. In total, the incidence of cerebral infarction and death was also higher among patients with unstable TIA - 6% and 2.2% respectively [31].

Some other results were received by Iacopo Barbetta with co-authors from Milan. In a study of 90 post-KE patients with acute cerebral ischemia, which were evenly divided into 2 groups (operated for 48 hours and later), the risk of postoperative re-stroke, regardless of the type and stability of the neurological deficiency, was higher in 6% in the second group and amounted to 8.8% [32].

A small study of CEA results from the 3rd to 10th days after a neurological event in 2012 was conducted by Georgios Tsivgoulis. According to the design of the study, all patients from the onset of neurological deficiency received dual disaggregation therapy - aspirin and clopidogrel. None of the 11 patients experienced severe complications within 30 days after surgery [33].

The 2013 Leicester study (475 patients) has shown that the risk of recurrent stroke and death after CO in patients with a recent neurological deficiency decreases over time from marker events and does not exceed 3%. In the first two days, this risk is 2.4%, in 3rd-7th day - 1.8%, 8th-14th and in two weeks - 0.8% [34].

In the scientific article of the authors from Germany in 2016 under the direction of Pavlos Tsantilas, the results of surgical treatment of 56,336 patients with neurological deficiency that were conducted within 180 days after the development of the neurological deficiency were highlighted. The patients were divided into four groups: operated in the first two days, from the 3rd-7th day, in the interval from the 8th-14th day and 15th-180th day. Most often, recurrent ischemic deficiency - 3.0% occurred in patients who were operated in the first two days. Its risk was reduced to 2.3% in patients who had been exposed to CEA within 15 to 180 days after the marker event [18].

In 2015, Charmoille E. et al. analyzed the results of treatment of patients with acute neurological deficiency that were operated before and after two weeks after the marker event. In total, 149 CEA were performed, 62 of them - within the first 2 weeks after the development of neurological deficits, 87 - after 14 days. The authors did not find a statistically significant difference in the results of treatment depending on the terms of CEA [3].

A group of authors led by Suman Annambothla from the University of Chicago studied the direct and delayed follow-up of 10 years of treatment of 312 patients depending on the duration of CO after the development of neurological deficits. Despite the fact that among the analyzed intervals the highest incidence of postoperative ischemic stroke was 6% in the group operated from 8 to 14, it was in this group that the lowest frequency of cerebral infarction was 10 years after CEA. In general, according to the results of this study, CEA within the first 30 days, after the development of an ischemic disaster of the brain, is a safe operation [4].

CONCLUSIONS

So, there is unanimous opinion that when choosing a treatment method and terms for performing a CEA, it is necessary to take into account the prevalence of ischemic focal area of the brain, the severity of the patient's condition and the severity of the course of the disease. Organizational and paramedical factors should not be influenced by the timing of surgical care for patients with ischemic lesions of the brain. In the classic course of ischemic stroke or TIA, the best treatment results are obtained when the CEA is performed from the 3rd-7th day after the marker event. With crescendo TIA or stroke-in-evolution, despite the fact that the risk of complications and disability after surgical treatment may be higher than 6%, CEA should be performed as soon as possible to restore brain revascularization and prevent the fatal progression of neurological deficiency.

REFERENCES


Conflict of interest:
The Author declare no conflict of interest.