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Arterial hypertension in acute stroke. Current therapeutical indications

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ABSTRACT

Acute stroke (the first hours after its onset) is accompanied in over 70% of cases by rapid and significant increases in blood pressure, above normal values. The acute or reactive hypertensive response occurs both in patients with a history of hypertension and in normotensive patients. The greatly increased BP values, not controlled therapeutically, can befollowed by the increase in the volume of the cerebral infarct and hemorrhagic transformation or thee xpansion of the hematoma and the increase in intracerebral pressure, respectively in ischemic or hemorrhagic stroke.

This paper especially refers to the therapeutic control of hypertension in various situations (conditions): 1. Laboratory emergencies; 2. Hospital treatment with out thrombolytics or thrombolysis; 3. Endovascular treatment in acute stroke; 4. BP control in hemorrhagic stroke; 5. Continuation or discontinuation of antihypertensive treatement.

The updated recommendations for the treatment of HTN in acute stroke result from clinical studies and recommendations of the recent ESO and AHA/ASA Guidelines.

Keywords: reactive hypertension, acute stroke, vasoactive treatment

GENERAL ASPECTS

Acute stroke (in the first hours) is accompanied in more than 75% of cases by rapid BP increas above normal values (≥ 140/80 mmHg). Increases in arterial pressure occur both in patients without a history of hypertension and in patients with known treated or incompletely treated hypertension. This type of increase in blood pressure values is defined as acute hypertensive response (1) or hypertensive reaction and is found in both acute ischemic stroke and acute hemorrhagic stroke (intracerebral hemorrhage – ICH). The greatly increased (excessive) therapeutically uncontrolled BP values can befollowed by the increase in the volume of the cerebral infarction possibly of hemorrhagic transformation (in case of ischemic stroke); by the expansion of the hematoma and possibly by the increase in intracerebral pressure (in case of hemorrhagic stroke), conditions that mark the worsening of the neurological condition and possibly the evolution towards death.

The prevalence of the hypertensive response in stroke is known. In a statement by the ISH, BP values ≥ 140/90 mmHg, during or immediately after Stroke, the acute hypertensive response was recorded in 75% of cases in ischemic Stroke and ≥ 80% of cases in Hemorrhagic Stroke [2]. Similarly, in a large US follow-up of 563,704 stroke patients, SBP ≥ 140 mmHg was recorded in 63% of cases, DBP ≥ 90 mmHg in 28% and mean arterial pressure (MBP) in 38% [3].

The constantly increasing prevalence in the population of cerebrovascular diseases, arterial hypertension (HT) – with the main major risk factor for Stroke, as well as the extent of the incidence of the hypertensive response in acute Stroke and its negative prognosis, are current topics. These are of interest to multiple specialties: neurology, cardiology, intensive care, neuroimaging and interventional neurologists [4].

The treatment of the hypertensive response is oriented by the type of stroke (ischemic or hemor-

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rhagic) and the dynamics of the BP level – conditions that require differentiated pharmacological treatment. BP control is only one chapter of Stroke Management, which largely includes general measures, BP control, treatment of Stroke complications and comorbidities, and the secondary prevention.

ANTIHYPERTENSIVE TREATMENT IN ACUTE STROKE IN AMBULATORY EMERGENCY CONDITIONS

Stroke diagnosis and treatment is a major emergency: diagnosis and treatment through the establishment of early optimal therapy leads to saving the brain injury. Recognizing stroke and eventually starting prehospital treatmentis an important goal in stroke management.

The suspicion of an acute vascular accident is often formulated on site, at the patient's home, by the family or by the medical or paramedical personnel from the ambulance service. The monitoring of vital functions and the evaluation of BP values represent minimum measures in prehospital conditions [5].

The increase in BP values is very common at the onset of Stroke and BP control is a main element that rapidly influences the evolution of Stroke. High or very high BP values can precipitate hematoma expansion or hemorrhage in the developing infarct. However, the antihypertensive medication administered in the ambulance can have negative effects by reducing the perfusion pressure in the affected cerebral area, especially in the penumbra area in the ischemic stroke (6].

Studies using nitrates in emergency blood pressure lowering showed no difference in mortality and functional improvement (mRS) [7].

The ESO 2021 guideline does not recommend routinely BP lowering in patients with suspected stroke, in pre-hospital conditions [6]. Lowering very high blood pressure values (≥ 220/120 mmHg) may be necessary in specific conditions (such as acute pulmonary edema, acute coronary syndrome, suspected ruptured aortic aneurysm) [6,8].

The current guidelines regarding the management of acute stroke and the treatment of the hypertensive response could be modified based on the results obtained in the Mobile Stroke Units (MSU). They have medical staff, brain CT machine and the possibility of communication with a hospital unit specialized in acute stroke management. In such conditions, time can be gained for thrombolysis with alteplase or the decision to refer to a specialized unit with modern methods of acute stroke treatment [9].

The studies conducted on the benefits and risks of MSU report gratifyin gresults [10]. A meta-analysis published results for approx. 3000 patients to whom the MSU model was applied - in diagnosis and treatment. Thus, in patients with acute ischemic stroke, prehospital treatment in the MSU increases the rate of thrombolysis with rtPA, achieves the administration of alteplase in a period closer to the onset of the stroke, improves the functional evolution of the patients. In addition, MSU can select patients who need Stroke management in tertiary units and to which they urgently refer patients [11].

In 2021, ESO developed and published an extensive Guide that analyzes the experience of prehospital management through MSU and formulated recommendations for clinicians and the health system [9].

ANTIHYPERTENSIVE TREATMENT TARGETS IN CONVENTIONALLY TREATED ACUTE STROKE

The majority of patients presented to the Emergency Service or admitted to the hospital with a high probability of acute stroke can not benefit from modern treatment methods (thrombolysis, endovascular therapy) and are cared for „conventionally" based on the guideline recommendations. The causes that delay confirming of the diagnosis of acute - ischemic or hemorrhagic stroke and the establishment of an optimal therapeutic course are multiple. Among these we mention: late recognition, by the patient or family, of the probability of a stroke; late request for medical help and thus late hospitalization (> 4.5hours); the time in which the diagnosis of stroke and its type is defined in the hospital, and which can be approximately one hour (neurological or multidisciplinary team consultation, brain imaging evaluation); treatment decision of the medical team: „conservative" with all components of stroke management or eligibility for timely thrombolytic treatment (<4.5 hours); possibly emergency transport to a specialized (tertiary) stroke treatment unit. The length of time between the patient's arrival at the emergency service and the effective start of treatment measures the efficiency of medical services that take care of major cerebrovascular emergencies.

The development of a hypertensive response in acute stroke occurs in the first hours in at least 70-80% of patients, either with a history of hypertension or patients considered non-hypertensive. The pathophysiological mechanisms that determine the hypertensive response (reactive hypertension) are partly known. Briefly formulated are: stress and sympathoadrenergic hyperstimulation (with its cardiovascular effects and on the Renin-Angiotensin-Aldosterone RAAS system [12]; vagal sympathetic imbalance and altered sensitivity of baroreceptors [13]; intracranial hypertension and cerebral compression [14]; injury to brain are as involved in cardiovascular regulation and blood pressure (BP) [1].

The management of hospitalized patients with acute stroke who cannot benefit from thrombolysis for various reasons, presumes a conventional treatment for the acute period based on the current guideline recommendations: vital functions control, rehydration, assessment of pathological conditions associated with stroke and which need urgent treatment (such as heart disease etc.). The patient with acute stroke, regardless of its type (atherothrombotic, cardio embolic or hemorrhagic), urgently needs an accurate control of reactive hypertension in a differentiated way, in relation to the BP values, the type of stroke, the severity of the neurological deficit, the brain immaging appearance and the general conditions of the patient. The control of high BP levels in acute stroke represents only one of the management directions of acute stroke.

European (ESO) and US (AHA/ASC) guidelines suggest caution in treating BP with values <220/110 mmHg and not to routinely intervene with pharmacological treatment for at least 24 hours [6,8]. Exception from the previous recommendation concerns situations of maximum emergency, such as acute pulmonary edema, acute coronary syndrome, aortic dissection. Over a 24-hour period, BP tends to decrease spontaneously with neurological stabilization or improvement.

For patients with acute stroke and with BP values >220/120 mmHg, it is necessary to carefully and progressively (by 10-20%) reduce pressure values using preferably vasoactive agents – with immediate action: labetalol, nicardipine, clavipine or enalapril [6]. Similary visions can be found in the 2018 ESC/EHA Guideline, for the management of hypertension for patients with acute ischemic stroke [15].

The most frequently used vasoactive agents for the control of severe hypertension in acute stroke are:

- Labetalol – 10-20 mg/minute, in i.v. infusion, the dose can be repeated 1-2 times, until the blood pressure decreases and stabilizes.
- Nicardipine – 5 mg i.v., titrated up to 2.5 mg every 10-15 min; maximum 15 mg/hour.
- Clavipin – 1-2 mg i.v., titrated by doubling the dose every 2-5 min, upto max. 20 mg/hour, until the desired BP is obtained.

Severe and rapid lowering of BP with vasoactive i.v. medication. And uncontrolled by permanent monitoring reduces the blood flow in the penumbra area, with the extension of the cerebral infarction.

Numerous studies shave investigated whether reducing BP to values between 140-220 mmHg, using other pharmacological agents, would not have positive effects on functional evolution and mortality in acute ischemic stroke.

Thus the Scandinavian study (SCAST) used candesartan vs placebo in acute ischemic stroke with BP >140 mmHg [16]. The ENOS study used transdermal nitroglycerin 48 hours after the onset of stroke and BP between 140-220 mmHG [17]. The Chinese CATIS study used ACE-I, calcium-channel blockers, diuretics in patients with acute ischemic stroke and BP between 140-220 mmHg [18].

All studies reported, after treatment, small reductions in the SBP levels (-5, -2; -7, -3) and similar, non-significant overall results.

ANTIHYPERTENSIVE TREATMENT IN THROMBOLYZED STROKE PATIENTS

Thrombolysis through the administration of intravenous alteplase (rtPA) is the most frequently used therapeutic method for the recanalization of the obstructed cerebral vessel from the cerebral circulation, which represents the direct cause of acute ischemic stroke. Vascular recanalization avoids the establishment and further extension of cerebral infarction, a better functional evolution (reduction of dependence) and decrease of mortality.

The success of thrombolysis is conditioned, in the eligible patient, by the early administration of alteplase compared to the onset of the stroke (<4.5 hours), but also by the rigorous control of arterial pressure, before and during thrombolysis [19].

An acute hypertensive response is often transient and with variability in BP values and frequently resolves after recanalization of the obstructed vessel [20,21].

Studies from the era of use of streptokinase for thrombolysis showed that elevated BP values before thrombolysis were associated with an increase in the risk of bleeding by approx. 25% in patients with acute ischemic stroke [22]. The observations regarding the risk of cerebral bleeding in correlation with BP values were also confirmed in thrombolysis with alteplase. Increases in SBP values by 10 mmHg were associated with a 10% increased risk of intracranial bleeding [23]. The classic results of the NINDS, with the administration of alteplase, have become the directions of studies for thrombolysis, including BP control in the acute phase of stroke [24]. BP control has become a central element in thrombolysis.

The decision to undergo thrombolysisis made urgently after evaluating the duration of at least 3-4.5 hours from the onset of the Stroke on neurological signs and mandatory after brain immaging exploration and exclusion of contraindications for thrombolysis. Mobile stroke units, with a doctor, CT machine and communication possibilities with a cerebrovascular emergency center shorten the time from the institution of thrombolysis.

BP values at stroke onset are an indicator for thrombolysis. BP values >185/110 mmHg exclude thrombolysis, except for stabilization of BP values at

<180/105 mmHg by vasoactive medication (e.g. labetalol or nicardipine). If stabilization of BP values <180/105 mmHg is not achieved using antihypertensives, then thrombolysis cannot be performed [25, 26].

BP values <180/105 mmHg are currently recommended as eligibility parameters for thrombolysis with rtPA regardless of the patient's age [6,21].

Treatment with alteplase is carried out according to a standard scheme: 0.9 mg/kg i.v. infusion. Lasting one hour; 1/10 of alteplase is administered as a bolus over 1-3 minutes. It is mandatory to administer alteplase as soon as possible, preferably within the first hour after the onset of the stroke, but practically between 3-4.5 hours [27].

Studies with tenecteplase 0.25 mg bolusi.v. did not prove their superiority [28]. The ESO 2021 guideline suggests thrombolysis with alteplase (rtPA) in acute ischemic stroke over tenecteplase [6].

Treatment with alteplase requires BP monitoring: every 15 min in the firs thour; every 30 min up to 6 hours, then once an hour for a minimum of 24 hours. BP values <180/105 mmHg are maintained during alteplase infusion for the next 24 hours/possibly 48 hours.

Achieving revascularization by thrombolysis (approx. 1/3 of occlusions in the large cerebral arteries) can cause a severe drop in BP, requiring vasopressor medication [29]. It is estimated that the aggressive lowering of BP can reduce perfusion in the viable penumbra area, with infarct expansion and neurological degradation [30,31].

A severe complication of thrombolytic treatment in acute ischemic stroke is cranial bleeding. The risk of intracranial bleeding is observed at 6-7% with thrombolysis with alteplase, but the risk increases with the severity of the stroke [6,25].

Reducing the risk of cerebral bleeding at lower BP values, compared to the target value (< 180/105 mmHg), was the premise of the ENCHANGED study with 2196 patients with acute ischemic stroke [32]. A group of patients with values ≥150 mmHg and ≤ 180/105 mmHg were compared with a group (intensive) with BP values between 130-140 mmHg. Functional evolution at 90 days was not different between the two groups. In intensive group patients compared to the group with standard BP values – intracerebral bleeding was less frequent (14.8% vs 18.7%), p = 0.01. The results from the ENCHANGED study were useful in the development of the ESO Guidelines for the treatment of HTN in acute ischemic stroke.

The ESO 2021 guideline presents recommendations or suggestions for BP control in acute ischemic stroke [6]. In patients with acute ischemic stroke with i.v. thrombolytic treatment, with or without thrombolectomy, it is suggested that SBP values < 180 mmHg before the bolus and 24 hours after the alteplase infusion. In addition, it is suggested against a target BP of 130-140 mmHg, compared to values <180 mmHg, for 72 hours after the onset of the stroke.

The results obtained by thrombolysis with alteplase can be optimized by endovascular therapy.

ARTERIAL HYPERTENSION AND ENDOVASCULAR THERAPY IN ACUTE STROKE

Endovascular therapy for the interventional treatment of acute ischemic stroke has established itself as a treatment standard, due to its reperfusion efficiency in the cerebral ischemic area [33]. Recanalization and reperfusion of the occluded vessel is obtained in 70-80% of cases, compared to thrombolysis (30%). Endovascular recanalization therapy refers primarily to the obstruction of large intracerebral vessels of the anterior circulation, where the best results are obtained [34]. Endovascular therapy in ischemic stroke with occlusion of the vessels of the posterior circulation (basal artery, vertebral artery, posterior artery) is still being studied in clinical trials [36].

Achieving mechanical recanalization (or mechanical thrombectomy) is achieved by thromboaspiration catheter or optimally bys tenting.

The problems of cerebral vessel recanalization through endovascular therapy are related to the reperfusion of the cerebral ischemic area and its consequences. The MR CLEAN study showed that reperfusion can be complicated by reperfusion injury or parenchymal hemorrhage dependent on the baseline BP level [37]. In the ischemic area, self-regulation is practically abolished and the perfusion is dependent on the arterial pressure level: at high BP values, the ischemic area tends to become hemorrhagic, symptomatic or asymptomatic, through the disruption of theblood-brainbarrier; at low BP values with low perfusion pressure, ischemic injury tends to extend in to the ischemic penumbra.

Endovascular therapy in acute ischemic stroke is reserved for patients eligible for thrombolysis. The optimal recanalization method in acute ischemic stroke includes initial thrombolysis performed with maximum urgency (<4.5 hours) followed by mechanical thrombectomy 6-24 hours after the onset of the neurological accident (bridge therapy) [38]. The success of the recanalization and the reduction or stopping of the evolution of the ischemic are depending on the precocity of both procedures [39]. Thrombolysis or mechanical thrombectomy - alone - are inferior in terms of immediate and long-term results to „bridge therapy". The advantages, at least theoretically, of i.v. thrombolysis before mechanical thrombectomy results from the partial or complete

lysis of the thrombus from the large cerebral vessels, but also from the lysis of distal emboli, conditions for improving cerebral perfusion in the ischemic area.

The selection of patients for endovascular therapy includes not only the eligibility for thrombolysis, but also the cerebral immaging evaluation (angiography, CT angio, MRI angio) which identifies the location of the occlusive lesion in the large cerebral vessels, possibly the composition of the thromboembolic material and excludes the presence of a large or hemorrhagic cerebral infarction [6].

The recanalization technique of the occluded vessel uses various devices, thrombo aspiration catheter and/or stenting, thrombolysis with stenting representing the current standard of treatment in acute ischemic stroke. According to the experience of the interventional neurosurgeons, periprocedural antithrombotic agents should be used – aspirin and unfractionated heparin. Studies have shown that the use of antithrombotic agents, especially unfractionated heparin (lowdoses), was associated with a better clinical outcome and lower risk of intracerebral hemorrhage [40,41].

A recent study – MR CLEAN MED (2022) investigated the safety and effectiveness of i.v. aspirin, UFH, both or only one, during endovascular therapy in patients with intracerebral large vessel occlusion. The conclusions of the study show that both antithrombotic agents are associated with an increased risk of symptomatic ICH and without evidence of good functional evolution [42].

The BP and perfusion pressure values after recanalization of the obstructed vessel are an important element in the evolution of cerebral ischemic injury, both for thrombolysis and for mechanical thrombectomy. High or low BP values and their variability can lead to cerebral hemorrhage, respectively the extension of cerebral ischemic damage. Establishing an "optimal" mode of BP in endovascular therapy is a widely debated topic in the management of acute intracerebral ischemic stroke [43,37,44,45,46]. Thrombolysis with alteplase (rtPA) in acute stroke, brought information about the optimal BP leveland in endovascular therapy.

BP values >185/110 mmHg contraindicate immediate thrombolysis, and similarly mechanical thrombectomy. BP control with vasoactive agents (labetalol, nicardipine) at values < 180/105 mmHg allows thrombolysis and endovascular therapy. Two international guidelines recommend values of TAS < 180 mmHg pre- and post-intervention for the first 24 hours after the end of the procedure [5,8].

Numerous studies have investigated the association between BP with various levels on vascular recanalization and the functional evolution of patients [44, 46]. Sudden 10% drop in BP during mechanical thrombectomy for stroke has been associated with severe neurological outcome [48]. The study by Petersen et al. also analyzed the effects of reduced BP before recanalization; the decrease in BP during thrombectomy was associated with the development of large-volume infarcts and severe functional evolution [49].

Observational studies have investigated whether lower levels of SBP (<130, 140 – 159) would not lead to better results in mechanical thrombectomy.

The BP-TARGET study (1324 patients) compared the results of 2 groups: the group with SBP between 100-129 mmHg compared to the group with standard SBP (130-180 mmHg). The primary objective was HIC (on Radiological examination) 24-36 hours post-procedural. The BP-TARGET trial provides evidence that reducing the „target" BP of 100-129 mmHg after vascular endotherapy does not reduce cerebral hemorrhage (for 24-36 hours) compared to standard BP. The study also reports BP variability during the procedure, and sudden drop in BP worsens the prognosis [50].

Overall, there is no consensus on the intensity of BP reduction during and after thrombectomy in the large vessels of the anterior cerebral circulation. The ESO 2021 guideline recommends a level of SBP <180 mmHg and DBP <105 mmHg in the first 24 hours after thrombectomy, similar to the BP values in thrombolysis. Such levels would avoid reperfusion hemorrhage. Other opinions, however, suggest maintaining TAS ≥140 mmHg and >70 mmHg for TAM, before recanalization and maintaining TAS values ≥ 140-180 mmHg post intervention for 24 hours. For severe stenoses in the anterior cerebral circulation, relatively higher BP values are required.

In the recent ESO Guide (2021), 3 recommendations are provided - suggestions for BP values in patients with acute ischemic stroke due to occlusion of large cerebral vessels, in which thrombectomy is performed - with or without prior thrombolysis [6]:

- It is suggested to keep BP <180/105 mmHg during and 24 hours after thrombectomy.
- It is suggested not to reduce SBP ≤130 mmHg for 24 hours after a successful procedure.
- Sudden (severe) drop in BP during thrombectomy should be avoided.

ARTERIAL HYPERTENSION IN HEMORRHAGIC STROKE

Intracerebral hemorrhage represents approximately 10% of all acute strokes. It is less common than acute ischemic stroke, but has a greater severity in terms of mortality and morbidity.

Patients who develop cerebral hemorrhage are most frequently hypertensive, incompletely treated or without a history of hypertension. In addition, patients with intracerebral hemorrhage (ICH) devel-

op (80% of cases) a reactive hypertensive response, in the firs thours after the onset of symptoms. The risks of high BP values are related to the expansion of the hematoma, the recurrence of bleeding and the evolution towards increased intracranial pressure. Hematoma growth is the major determinant of mortality and severe evolution after intracranial hemorrhage [51]. The evolution of the intracerebral hematoma is related to the increased BP values, the reduction of the perilesional perfusion and possibly the cerebral edema.

The control of elevated BP values is an essential component of the management of ICH, after confirmation of the clinical diagnosis and cerebral imaging and the control of vital functions [52].

American (AHA/ASA) and European (ESI) recommendations, from 2010, stipulated the need to lower and maintain BP in patients with ICH, at values below< 180 mmHg for SBP [53,54]. The data obtained in neurological practice and a multicenter clinical study indicated the possibility of a more aggressive treatment of hypertension in patients with acute intracerebral hemorrhage [55]. A study from 2010 also reported the effects of lowering SBP (140, 150, or 160 mmHg) on hematoma expansion. The hematoma expansion rate was 9% in patients with SBP <150 mmHg, 30% in patients maintaining SBP <160 mmHg [56].

Subsequent studies have confirmed that achieving lower BP levels in ICH is possible, under safe conditions, without being able to specify the optimal target level to achieve.

The ATACH-2 study comparatively analyzed the results obtained in the evolution of HIC in relation to the BP level, in 2 groups of patients: 500 patients with standard treatment (149-179 mmHg) and intensive treatment (110-139 mmHg). Death, disability and evolution in the short-medium term were pursued as major end-points. No difference in results was noted between the intensive group vs the standard treatment group. Adverse effects of lowering SBP levels were similar, with the exception of renal adverse events in the intensive treatment group. The study concludes that intensive treatment in ICH (BP between 110-139 mmHg) does not lead to a lower death rate than standard therapy (140-179 mmHg) [57]. The INTERACT study (2839 patients) included a group of patients with ICH, who had SBP between 150-220 mmHg 6 hours after the onset of symptoms, compared to a group treated with BP reduction <140 mmHg. The rate of death and disability was lower in patients with lower BP values (limit of significance) than in the group of patients with standard treatment. In evolution, at 90 days, a significant decrease in the functional mRS stroke was also found [58,59].

The results from the ATACH and INTERACT Study are partially different, but they confirm the need for more important BP reductions in hemorrhagic stroke.

The recent ESO (European Stroke Organization) Guide 2021, based on the analysis of all the publications on blood pressure control in hemorrhagic stroke, formulated recommendations and suggestions regarding the targets of SBP values in ICH, the efficiency and risks of low blood pressure values.

The ESO 2021 Guide recommends[6]:

- In patients with ICH, there are uncertainties regarding the benefit and risks of intensive BP-lowering therapy, on the functional evolution in ICH.
- In patients with ICH of <6 hours from the onset of symptoms, it is suggested to lower the BP <140 mmHg and with care to maintain the level> 110 mmHg – to reduce the expansion of the hematoma.

The guide also mentions the observations of specialists. Antihypertensive treatment should be initiated as early as possible – ideally <2 hours after onset; it is suggested that the BP decrease be maintained for at least 24 hours – upto 72 hours, to reduce the expansion of the hematoma.

The control of high BP values is carried out by administering i.v. of nicardipine or labetalol; nitrates are contraindicated and increase intracranial pressure.

Stopping intracerebral bleeding and thus decreasing hematoma expansion has been studied with agents that block the coagulation cascade at a certain level.

The use of rF VII (recombined F VII) which intervenes in the extrinsic coagulation cascade, initially provided favorable results (h) in the EAST study, the administration of rF VII 4 hours after the onset of symptoms resulted in substantial reduction of growth (expansion) of the hematoma, but not the reduction in death [60]. The administration of rF VII has a thromboembolic risk, as e.g. myocardial infarction, cerebral infarction.

In conclusion, the tendency of specialists to reduce BP early, in ICH, to values <140 mmHg for a period of at least 24 hours, with BP monitoring, clinical, biological and immaging, is evident. The reduction of BP values must be done gradually; low values can be accompanied by cerebral and renal hypoperfusion.

CONTINUATION OR INTERRUPTION OF THE ANTIHYPERTENSIVE TREATMENT

BP lowering and control therapy according to the „targets" established by the guidelines (< 140/90 mmHg) is the most important step in primary and secondary prevention of stroke, but also of other cardiovascular conditions. Approx. 50% hospital-

ized acute stroke patients develop the neurological event under conditions of regular antihypertensive treatment.

Stopping or continuing antihypertensive therapy immediately after the acute stroke is a decision that can improve or worsen the immediate evolution of the stroke [61]. Several COSSACS and ENOS clinical studies investigated the neurological effects of continuing or stopping antihypertensive therapy in acute ischemic stroke. The COSSACS study reported benefits in terms of death or dependence at 3 months (mRS ≥3) in the group with continuous treatment versus the group with discontinuation of therapy [62].

Data from the studies were included in a meta-analysis – continuation or discontinuation of BP-lowering antihypertensive therapy. At the final analysis, no significant difference was found between the continuation or stopping of the previous BP, or the lowering the BP, on mortality (p = 0.07) [63].

The ESO 2021 stroke treatment guideline emphasizes that there are uncertainties between benefits and risks (disadvantages) in continuing or stopping antihypertensive therapy followed by patients [6].

In known and treated patients with ischemic stroke and hypertension, the choice is between stopping the therapy and continuing the therapy. It is preferable to stop the therapy for 24-48 hours, a critical period for the evolution of the ischemic lesion. After 24-48 hours from the onset of the stroke, the previous antihypertensive therapy can be resumed, possibly supplemented with another pharmacological agent – in order to obtain the target BP (≤ 140/90 mmHg) underconditions of neurological stability and favorable imaging evolution of the cerebral lesion.

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