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The value of diagnostic procedures for essential hypertension control after an early recovery period of hemorrhagic stroke (literature review)

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Abstract: hemorrhagic stroke is the most severe type of stroke, which is more likely to lead to death and severe disability. Although there are many causes and risk factors for hemorrhagic stroke – both congenital and acquired, and mostly their combination – essential hypertension is the most common and leading cause of intracranial hemorrhage. This study aimed to make a comprehensive overview on the value of diagnostic procedures for essential hypertension control after an early recovery period of hemorrhagic stroke. The analyzed data were observed on PubMed and Ukrainian scientific sources concerning essential hypertension course in post-hemorrhagic stroke patients in relation to further prophylaxis in stable phase. All the observed manuscripts were published within the period 2014-2024. The focus of attention was made predominantly on the essential hypertension as the key factor for hemorrhagic stroke development. From the literature review, it could be concluded that the problem of essential hypertension control after hemorrhagic stroke is relevant today and needs a thorough solution to prevent the re-occurrence of cerebrovascular events. For a rational approach to the management of hypertensive patients with hemorrhagic stroke medical history, it would be necessary to perform a set of diagnostic procedures, which would include ultrasound examination of the major cervical arteries, echocardiography, 24-hour ambulatory blood pressure and electrocardiogram monitoring, determination of plasma cholesterol panel indices and blood coagulation tests.

Keywords: [Essential Hypertension](#); [Hemorrhagic Stroke](#); [Blood Pressure Monitoring](#); [Ambulatory](#); [Carotid Arteries](#); [Cholesterol](#); [Blood Coagulation Tests](#).

Introduction

Today, cardiovascular diseases (CVD) are the leading causes of death worldwide. High blood pressure (BP) – $\geq 140/90$ mm Hg – leads to target organs damage, particularly the brain. Globally, stroke is the second-leading cause of mortality and the third-leading reason of death and disability combined (Feigin et al., 2022). Hypertension has been reported to be the commonest risk factor for HS (Kitagawa K., 2022).

There are sparse data on how essential hypertension progresses and what changes occur in the cardiovascular system (CS) after an early recovery period from a HS – > 6 months since its onset. Simultaneously, patients who have suffered a HS as a complication of essential hypertension have an increased risk of further complications and death (Sirenko, Radchenko & Mishchenko, 2018), which necessitates an improvement of diagnostic measures for timely detection and correction of

risk factors. It is noted that most patients with previous intracerebral hemorrhage (ICH) continue to have elevated BP, and therefore need an adequate antihypertensive treatment regimen after HS – when the acute condition has been eliminated and comprehensive rescue care has been provided to the patient (Van Matre, Cook, Shah, Rydz & Smetana, 2019). Therefore, it is extremely important to adequately control BP to prevent recurrence of CVD (Gorelick et al., 2020).

There are conflicting data on the feasibility and safety of correction of lipid profile in patients who have suffered a HS, which is justified by the increased risk of re-bleeding (Gong et al., 2022) due to thrombin formation inhibition by statin (Orsi et al., 2019). Accordingly, there is a need to study the coagulogram indices in this category of patients due to the high degree of comorbidity of essential hypertension and atherosclerosis.

Aim

Aim of the study was to make a comprehensive overview on the value of diagnostic procedures for essential hypertension control after an early recovery period of HS.

Materials and methods

The data were observed on PubMed and Ukrainian scientific sources concerning essential hypertension course in patients with the complication of HS from the point of view of further prophylaxis in the stable phase. All the observed manuscripts were published within the period 2014-2024. The literature overview includes 49 scientific sources. The focus of the attention is made predominantly on the essential hypertension as the key factor for HS development.

Review and discussion

1. Etiology, pathogenesis, risk factors for HS as a complication of essential hypertension

There are evidence-based data that the increase in BP by 20/10 mm Hg doubles the risk of cardiovascular complications (Karmali & Lloyd-Jones, 2017). The most common cause of cerebral hemorrhage is chronic BP elevation (Magid-Bernstein et al., 2022), as well as hypertensive crisis (Cantone et al., 2021), the pathogenesis of which is autoregulation failure (Varounis et al., 2017). Autoregulation of the brain involves active changes in vascular resistance to maintain a constant blood flow in a relatively wide range of mean BP –

usually 50-150 mm Hg (Avolio et al., 2018). The mechanisms in which the central nervous system is involved begin to work in the first seconds after the onset of receptor excitation. They act as a buffer, functioning continuously, and are designed to minimize fluctuations in BP when one changes body position or undergoes psycho-emotional and physical stress, i.e. they adapt the CS to the constantly changing environmental conditions (Візір, Деміденко, Гончаров & Школович, 2019). Accordingly, not only the influence of BP is important, but also the initial state of autoregulation of the brain's vascular network.

As for subarachnoid hemorrhage (SAH) of aneurysmal genesis – the initiation of the formation of a cerebral artery aneurysm has congenital and acquired components. Hypertension is an important cause of aneurysms development (Kim et al., 2021). According to Jung-Laplace law, the increased area increases the tension of the aneurysmal wall, which causes its expansion. The increase in the size of the aneurysm is due to the thinning of the artery walls under the influence of many factors, including hemodynamic – increase in intravascular pressure due to systemic BP and permanent/temporary change of laminar blood flow to turbulent. The combined effect of hemodynamic factors has the most negative impact on arterial branches, which in most cases causes the formation of aneurysms at the bifurcations of cerebral vessels (Gao et al., 2022). The causes of aneurysms are high BP, atherosclerosis, acquired traumas, heredity and abnormal blood flow at the junction where the arteries meet (Wedro, 2022; Veeturi et al., 2021).

2. Diagnostic value of ultrasound examination of the major cervical arteries and heart

When essential hypertension led to damage of one of the sections of the cerebrovascular arterial network with its rupture, it would seem appropriate to check the condition of the origin of this network – the major cervical arteries, which would also be exposed to high BP. However, there is lack of data on the assessment of the diameter of the major cervical arteries in patients who have suffered HS, although the features of essential hypertension, which led to rupture of a smaller diameter artery, probably have contributed to the dilation of larger

vessels. With increasing BP there is an increasing damage to the vessel walls due to its repeated impregnation with plasma and loss of the muscular skeleton, which at some stage can not provide an autoregulatory response. The above-mentioned leads to a “shift” of autoregulation failure to distal arteries (Боев, Доценко, Герасименко, Шехунова & Яценко, 2017), which have a thinner wall and, accordingly, are more prone to rupture.

Ultrasound examination of the major cervical arteries with the assessment of the carotid intima-media thickness (IMT) is a non-invasive, safe, fast, well-reproducible method for determining subclinical atherosclerosis and evaluation of cardiovascular and cerebrovascular risk (Nakanishi et al., 2020). In essential hypertension, there is an increase in the thickness of the common carotid artery. The carotid IMT may be a potential predictor of aneurysm rupture (Lundervik et al., 2014). In patients with essential hypertension, stage II, with uncontrolled BP levels, there are increased values of the IMT of the common carotid artery (Боев et al., 2017). In the study of post-aneurysmal SAH without selection of only hypertensive subjects, the major cervical arteries IMT was found to be slightly increased in patients with ruptured and non-ruptured cerebral aneurysms – 0,79 and 0,65 mm, respectively (Lundervik et al., 2014). The increase of the IMT by every 0,1 mm significantly increased the risk of rupture of cerebral artery aneurysms (Lundervik et al., 2014).

However, it is noted that the value of ultrasound carotid IMT for risk stratification is contradictory, and the developers of new guidelines should also take into account the presence and features of atherosclerotic plaques, and hemodynamic parameters (Li et al., 2021). An association between extracranial atherosclerosis and the number of intracranial atherosclerotic plaques has been reported, leading to an increased recurrence of HS (Che et al., 2022). Atherosclerotic changes of cerebral vessels and the presence of cerebral artery aneurysms cause the risk of recurrent intracranial hemorrhage (Lu et al., 2024). Thus, the study of major cervical arteries may indirectly indicate the state of the arterial network of the brain in patients with essential hypertension, complicated by HS.

In addition, given the reported rates of left ventricular hypertrophy, diastolic dysfunction and

left ventricular systolic dysfunction in patients with ICH of non-traumatic origin, echocardiography (ECHO) may play an important role. Thus, further investigations might be reasonable (Palleesen et al., 2020). A number of studies have been conducted on the results of ECHO in patients with HS in the first two periods after its occurrence (acutest, acute) (Malik, Gross, Rosalind Lai, Moses & Du, 2015; Cinotti et al., 2016), but data on the corresponding examinations in later periods (> 6 months after the onset of HS, i.e. in the late recovery period and the period of residual effects), as in the case of ultrasound examination of the major cervical arteries, are also currently limited.

3. Diagnostic value of 24-h ambulatory BP monitoring (ABPM) and electrocardiogram (ECG) monitoring

Prevention of cardiovascular complications of essential hypertension once the acute state of HS is over is a significant problem in modern cardiology. It remains an indisputable fact that the most important in preventing those complications is BP control, and its assessment should not be limited to measuring office BP, but should be based on data from daily monitoring, home self-monitoring and assessment of central BP (Townsend, 2020). ABPM is a method that allows to perform the most complete chronobiological analysis of the BP profile in the normal daily activity of the patient (Huang et al., 2021), including white coat, masked and nocturnal hypertension (Dadlani et al., 2019), all of which lead to an increased risk of recurrent HS since the cerebrovascular system, still compromised by previous HS may not have time to adapt to sudden, abrupt, and short-term systolic BP changes.

To get a complete picture of the course of essential hypertension in patients after HS, it is necessary to take into account fluctuations in office BP over a period of time (during one visit, or several visits, or days) (Радченко, 2015), which is not always possible due to high level of disability of such patients with subsequent restriction of mobility and/or impaired cognitive function (Donkor, 2018). Given all the above features of this category of patients (including a low level of adherence to BP control post-stroke) (Biffi et al., 2021), there is a need to obtain as much information as possible on BP during a

single visit to the doctor, which is attainable with 24-h ABPM.

Low adherence to treatment is the most common factor leading to hypertensive crisis, and a common immediate cause is the sudden cessation of antihypertensive drugs usage (Yousuf et al., 2023). According to recent studies, 24-h ABPM procedure helps to ensure better compliance: only 37% of patients with essential hypertension controlled BP when measuring it randomly, while this figure has increased up to 54% after 24-h ABPM (O'Brien, White, Parati & Dolan, 2018).

Numerous studies have shown that 24-h ABPM is a more sensitive predictor of the risk of cerebrovascular events and death than office BP (Dadlani et al., 2019), which is also reflected in the new European guidelines for the management of arterial hypertension (Mancia et al., 2023).

Therefore, when performing 24-h ABPM, it is possible to timely select the appropriate treatment with correction of BP variability ranges and prevent further complications, including in the already compromised vascular system of the brain.

It is also noted that the percentage of “non-dippers” in patients with essential hypertension has been roughly estimated at 25%, with autonomic dysfunction being strongly associated with non-dipping BP profile and nocturnal hypertension (Huart et al., 2023). Given the signs of impaired regulation of BP, the passage of an electrical impulse through the ventricular myocardium should be considered. To assess the presence of autonomic imbalance, the 24-h ECG monitoring data are analyzed, namely: QT interval and its variance (Singh & Rabkin, 2021).

In review studies, the material was analyzed for the negative impact on the prognosis of CVD with increased QTc dispersion (Kaur & Dhoat, 2022). QTc interval studies are already available in patients with HS in the early periods (Hira et al., 2022; Guerra, Carrera & Schenone, 2021). However, there are still limited data on 24-h ABPM and ECG in patients after HS starting from the late rehabilitation period. Therefore, there is a lack of knowledge about the features of the further course of hypertension in such patients to contribute to a better treatment outcome, and the necessary data should be obtained.

4. Diagnostic value of changes in lipid metabolism and its relationship with the coagulation hemostasis

Today there are two main pathogenetic mechanisms of development and formation of atherosclerosis: the damage response and the lipid-infiltration hypothesis, which do not contradict but rather largely complement each other in developing atherosclerosis (Jebari-Benslaiman et al., 2022). Another well-known fact is the comorbidity between essential hypertension and atherosclerotic vascular lesions (Tian et al., 2024). In atherosclerosis, it has been shown that lowering of the elevated total cholesterol level and low-density lipoprotein (LDL) level reduces the risk of cardiovascular events and death from any cause (Peng et al., 2022). However, there are conflicting data on the feasibility and safety of correction of lipid profile in patients who have had HS, due to the increased risk of re-bleeding. In particular, statins inhibit thrombin production, which can be dangerous for recurrence of hemorrhage in patients after HS (Bétrisey et al., 2024). However, there is very limited information on a subgroup of patients with HS, associated primarily with essential hypertension, for whom the problem of atherosclerosis is especially relevant, given the above-mentioned comorbidity. In addition, almost all studies relate to the first 3 periods of HS, but not to the late rehabilitation period and the period of residual effects.

Several retrospective meta-analyses and database studies have shown a reduction in mortality and improved functional outcomes with statin therapy after HS (Lin et al., 2021). However, none of the analyzes clearly defined the timing of initiation of statin treatment after HS, so the window of opportunity to start statin therapy is wide, which requires a reasonable specification of the time frame in further studies.

In a recent trial sequential analysis, despite the increased risk of HS with treatment duration, statin therapy in patients with previous stroke could still be recommended, as the net composite endpoints, including ischemic stroke, HS, transient ischemic attack, and myocardial infarction are still significantly reduced (Teoh et al., 2019). Furthermore, a population-based, propensity score-matched cohort study reached the conclusion that

the risk of ICH has been similar for statin users and nonusers when evaluated among those with prior ICH, and it has been reduced by half in those with prior ischemic stroke (Ribe et al., 2020).

Summarizing the above-mentioned, the high levels of LDL lead to weakening of the compromised vascular wall with an increased risk of its rupture, but aggressive tactics to reduce LDL levels are accompanied by more pronounced pleiotropic effects of statins with slowing of coagulation processes (Siniscalchi et al., 2023). At both extremes, an increased risk of cerebrovascular hemorrhagic events appears to be present that requires to find out a “golden mean” in the category of post-HS survivals. Given the previously established evidence of a certain risk of hemorrhagic events when prescribing statins to patients after HS and data on fibrin deposition in vascular wall injury due to significant fluctuations in BP (Harvey et al., 2016), it is appropriate to check such patients for coagulation hemostasis indices.

Conclusions

From the literature review, it may be concluded that the problem of essential hypertension control after hemorrhagic stroke is relevant today and needs a thorough solution to prevent the

occurrence of subsequent cerebrovascular events. For a rational approach to the treatment of patients with hypertension complicated by hemorrhagic stroke, it is necessary to conduct a set of diagnostic procedures, which includes ultrasound investigation of the major cervical arteries, ECHO, 24-h ABPM and ECG monitoring, determination of plasma lipid panel indices and coagulation hemostasis panel parameters.

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Conflict of interests

The authors declares that there is no conflict of interest in the preparation of this article.

Consent to publication

The authors read the text of the manuscript and agreed with its publication.

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Значення діагностичних заходів для контролю гіпертонічної хвороби після раннього відновного періоду геморагічного інсульту (огляд літератури)

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Анотація: геморагічний інсульт – найважчий вид інсульту, який частіше призводить до смерті та важкої інвалідизації. Хоча існує багато причин і факторів ризику геморагічного інсульту – як вроджених, так і набутих, а здебільшого їх поєднання, – гіпертонічна хвороба є найпоширенішою та основною причиною внутрішньочерепних крововиливів. Метою дослідження було зробити комплексний огляд цінності діагностичних процедур для контролю перебігу гіпертонічної хвороби після раннього відновного періоду геморагічного інсульту. Проаналізовано дані PubMed та українських наукових джерел щодо перебігу гіпертонічної хвороби у пацієнтів з ускладненням у вигляді геморагічного інсульту з точки зору профілактики подальших ускладнень серед хворих, які перебувають у стабільній фазі. Усі досліджувані наукові праці були опубліковані між 2014 та 2024 рр. У даній роботі акцентовано увагу переважно на гіпертонічній хворобі як ключовому факторі розвитку геморагічного інсульту. З огляду літератури можна зробити висновок, що проблема контролю гіпертонічної хвороби після геморагічного інсульту є актуальною на сьогоднішній день і потребує ґрунтовного вирішення для запобігання виникненню подальших цереброваскулярних подій. Для раціонального підходу до ведення хворих на гіпертонічну хворобу, ускладнену геморагічним інсультом, необхідно проводити комплекс діагностичних заходів, що включає ультразвукове дослідження магістральних артерій шиї, ехокардіографію, добове моніторування артеріального тиску та електрокардіограми, визначення показників ліпідограми та коагуляційного гемостазу.

Ключові слова: есенціальна артеріальна гіпертензія, геморагічний інсульт, амбулаторне моніторування артеріального тиску, сонні артерії, холестерин, дослідження згортання крові.



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