COMPUTERIZED TOMOGRAPHY ANGIOGRAPHY CONTRAST EXTRAVASATION ("SPOT SIGN") IN PRIMARY ACUTE INTRACEREBRAL HEMORRHAGE

M. Gavriliuc*, M. Arion, T. Plescan,
Department of Neuroradiology, Republican Institute of Neurology and Neurosurgery
2, Korolenko Street, Chisinau, Republic of Moldova
plescan.t@gmail.com. 079706280

Summary

Intracerebral hemorrhage (ICH) is a devastating condition associated with significant mortality due to ongoing hemorrhage and hematoma expansion. Hematoma expansion is highly predictive of neurological deterioration, poor functional outcome, and mortality. The identification and prevention of hematoma expansion are targets in ICH management as such. The CT angiography (CTA) "spot sign" has emerged in recent years as a potent predictor of hematoma expansion, and a potential tool in guiding therapies in both research and clinical care. This clinical case presentation demonstrates that we can with high accuracy visualize the contrast extravasation (so-called "spot sign"), ongoing hemorrhage and predict hematoma expansion in hyper-acute phase of intracerebral bleeding – even in 1 hour after the onset of the symptoms, using computerized angiographic tomography investigation.

Key words: computed tomography angiography, spot sign, contrast extravasation, intracerebral hemorrhage (ICH), hematoma growth

Rezumat. Extravazarea substanței de contrast („spot sign”) la Angiografie prin Computer Tomografie în hemoragie intracerebrală acută primară

Hemoragie intracerebrală (HIC) este o condiție devastatoare şi este asociată cu mortalitate semnificativă, mai ales în cazul hemoragiei active şi extpansiei ulterioare a hematomului. Ca atare, identificarea şi prevenirea extinderii hematomului sunt ținte în managementul HIC. CT angiografic (CTA) ,,spot sign” (semn de punct) a apărut în ultimii ani ca un predictor puternic de expansiune a hematomului, precum şi un instrument potențial în ghidarea tratamentului, în cercetare şi strategie clinică. Cazul clinic prezentat demonstrează, că CTA este un instrument, care ne dă posibilitatea de a vizualiza cu înaltă acuratețe extravazarea contrastului (aşa-numit ,,spot sign”) şi de a prognoza expansiunea hematomului în faza hiperacută a hemoragiei intracerebrale – chiar şi peste o oră după apariția simptomelor.

Резюме. Экстравазация контрастного вещества („spot sign”) на Компьютерно-Томографической Ангиографии при остром первичном внутримозговом кровоизлиянии

Внутримозговое кровоизлияние (ВМК) является угрожающей жизни патологией и связано со значительной смертностью, особенно в случае продолжающегося кровотечения и увеличения гематомы. Таким образом, выявление и предотвращение увеличения гематомы является одной из важнейших целей в стратегии ведения пациентов с ВМК. В последние годы появилось понятие «spot sign» на КТ-ангиографии (КТА), которое является мощным инструментом прогнозирования увеличения гематомы, и обладает потенциалом для менеджмента лечения в исследовательской и клинической практике. Представленный клинический случай демонстрирует, что мы с помощью КТА можем с высокой точностью визуализировать экстравазацию контраста (так называемый “spot sign”), активное кровотечение и прогнозировать увеличение гематомы в острейшей фазе ВМК – даже спустя 1 час от начала симптомов.

Introduction

Cerebral Hemorrhage is the most deadly and disabling form of stroke. The 1-month mortality is 30%–50%, with half of these deaths occurring within the first 48 hours [1]. Intracerebral hemorrhage accounts for 8-13% of all strokes and results from a wide spectrum of disorders. The etiology of hemorrhage is classified as either primary or secondary. Primary ICH usually occurs in older patients and is often associated with hypertension or Cerebral Amyloid angiopathy. Secondary ICH may be caused by the underlying vascular lesion (arterio-venous malformation, cavernous malformation, ruptured aneurysm and other), venous sinus thrombosis, anticoagulation and neoplasm. Timely and accurate identification of patients with secondary ICH is important because therapeutic options and rates of rehemorrhage are substantially different from primary ICH [2].

MDCTA is rapidly becoming the favored diagnostic examination in the initial evaluation of patients presented with ICH in medical centers all around the world. Native MDCT and contrast MDCTA had shown (versus MRI and interventional digital subtraction angiography -DSA) the wide availability, low cost, easy effectuation and rapid scan times, compatibility with emergency and anesthetic equipment, high sensitivity and noninvasive character with low-grade risk of complications. In our hospital non-contrast emergency cerebral MDCT is routinely used to evaluate all patients with suspected stroke of any type, especially when there is a possible risk of ICH. Equipment which is used at the moment corresponds to the latest technology in radiology – multidetector CT 64 slices “VCT select”, manufacturer – General Electric, equipped with power injector with 2 syringe – “Nemoto”. Some patients, especially when underlying vascular lesion or other probable cause of secondary ICH is suspected, undergo the MDCTA procedure.

One of the most important factor is early hematoma growth, which is associated with high rate of massive functional deterioration and increased mortality.

Early neurological deterioration frequently results from hematoma expansion, occurring in 30% of patients with ICH within 3 hours of symptom onset. Secondary lesions also have a higher rebleed rate, impacting patient outcomes. The risk of early rebleed in aneurysmal SAH is 12%, with significant morbidity and mortality rate. Rehemorrhage risk from AVM is 7% in the first year, thereafter reducing to 2%–4% annual risk [3]. Recently, the presence of contrast extravasation (“spot sign”) on CTA has been associated with increased risk of hematoma expansion and poor outcome in both retrospective and prospective studies. Identification of vascular lesions and patients at risk for early hematoma expansion may improve outcome by allowing directed clinical decision-making [4].

Definition - First described in 1999 [5], the CTA spot sign has evolved in its definition from the broader concept of contrast extravasation (contrast leakage from the vessels into hematoma), comprising high-density material or contrast leakage within hematoma, to encompass foci of enhancement within hematoma on CTA source images [4]. In 2009, a spot sign score was developed, incorporating the number, maximum attenuation (in Hounsfield units), and maximum dimension of spot signs [6].

Multiple retrospective single-center cohort studies have confirmed that contrast extravasation and the spot sign are potent, independent predictors of hematoma expansion. All studies show a robust association of the CTA spot sign with both functional outcome and mortality. Similarly, the spot sign score has shown to be associated with both in-hospital mortality and poor clinical outcome at 3 months. In the PREDICT study, the 3-month mortality hazard ratio was 2.4 (95% CI, 1.4–4.0) for spot sign–positive patients compared to spot sign–negative patients [7].

Risk Factors - several (clinical) risk factors for the spot sign have been identified. In addition to early presentation, anticoagulation, and apolipoprotein E ε2; large baseline hematoma volume, low Glasgow Coma Scale score on presentation, mean arterial blood pressure of >120 mm Hg, and the presence of intraventricular hemorrhage have been associated with risk of spot sign [5, 6, 8].

There is a potential role for the spot sign as a selection tool in research studies on possible new treatment strategies for patients with ICH. With the spot sign as strong predictor of hematoma expansion, it may be possible to identify ICH patients who are most likely to have poor outcomes and treat them aggressively. Ongoing clinical trials including Spot Sign for Predicting and Treating ICH Growth (STOP-IT) (ClinicalTrials.gov NCT00810888) and Spot Sign Selection of Intracerebral Hemorrhage to Guide Hemostatic Therapy (SPOTLIGHT) (ClinicalTrials.gov NCT01359202) are using the spot sign to select patients for treatment with recombinant VIIa factor. Aggressive blood pressure lowering, as currently tested in nonselected patients by Second Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT2) [9] and Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH-II) [10], may also be guided by spot sign status. The ancillary study of ATACH-II, the Spot Sign Score in Restricting ICH Growth (SCORE-IT, National Institutes of Health—National Institute of Neurological Disorders and Stroke [NIH–NINDS] R01NS073344) study, is currently testing the hypothesis that patients with the highest spot sign scores benefit most from aggressive antihypertensive treatment.

Thus, in conclusion to all data studied from literature, we can make a conclusion that the presence of contrast extravasation on MDCTA in patients with ICH is an independent and strong predictor of poor outcome. NCCT and MDCTA, especially in the acute stage may be used as a tool for early stratification of patients with primary ICH into those at high risk of poor clinical outcome and therefore optimize their therapies early. Intensified monitoring and treatment should be provided to patients not only with larger hematoma or presence of IVH, but also to those with signs of contrast extravasation. In addition, MDCTA is a very qualitative tool for the assessment of ICH etiology, which directly effects the treatment strategy for those patients, especially when the underlying vascular etiology is present.

Results and discussion

We present a clinical case of a 57-year-old woman, who was urgently transported by ambulance and admitted to the Republican Institute of Neurology and Neurosurgery at 03.50. Verbal contact is difficult, the patient is unconscious, in an actual comatose state, the level of consciousness was assessed as coma I. Basic medical information was obtained from relatives (son) – he informed on sudden onset of consciousness disorders and motor failures at about 03.00. The patient has a history of hypertension (gr III) and hyperlipidemia, for most of her adult life. She takes aspirin every morning in addition to her other medications (antihypertensive). While being transported to the hospital, the physician on duty performed a neurologic screening scale - Hunt-Hess III-IV. They also obtained an initial set of vital signs, which revealed the patient to be hypertensive, and the cardiac monitor showed a normal sinus rhythm.

Objective exam revealed: somato-visceral conditions: general state is severe; 165 cm height, 75 kg weight, T 36.6°C; Skin and mucous status: pale pink; respiratory frequency 18 / min; respiration- spontaneous, rough; auscultation - bilateral coarse breath; cardiovascular: AT- 240 systolic and 130 diastolic mm Hg, Ps -78/min; cardiac noises are rhythmic; abdomen is palpatory soft; urogenital functions of pelvic organs: urinary incontinence.

Neurological assessment: coma I, intact cranial nerves, osteo-tendinous reflexes are missing on the left, deep left hemiparesis, positive pathological reflex Babinski bilateral, negative elongation maneuvers, pathological meningeal signs are negative; sphincter functions: incontinence. Sensitivity, motility, cerebellum functions – assessment is impossible, because of comatose state of consciousness.

Preventive clinical diagnosis was established as Cerebro-Vascular Disease, essential hypertension with medium risk of complications NYHA grade I-II, deep left hemiparesis, progressive intracranial hypertension syndrome, coma I, the emergency medical service personnel suspect a stroke. Emergency multidetector computer tomography (MDCT) was performed 01.04.2014 at 04:08 (1 hour from the onset of symptoms) with following scan parameters: scan type – axial, tube rotation speed – 1 sec, axial thickness – 5 mm, whole detector coverage for small field

of view, mA range – minimum= 100 and maximum =550 (with automatic mA regulation), kV =120, reconstruction thickness = 0.625 mm.

Non-contrast multiplanar CT native slices and 3D volume-rendering reconstructions of craniocerebral region, revealed (fig 1): acute massive intracerebral hemorrhage with temporo- parietal hematoma on the right. Maximal hematoma dimensions are: antero-posterior 7.0 cm, transversal 3.7 cm, cranio-caudal 6.8 cm. There is evidence of local edema with approximate 1 cm hypodense zone surrounding the hematoma, 15 mm contralateral shift of the median brain structures, compression of the right lateral ventricle. Intraventricular eruption of hemorrhage with integral blood invasion of right lateral ventricle and blood-fluid horizontal level 1,2 cm in posterior horn of left lateral ventricle; evidence of blood presence in ventricle IV. There is no imaging signs of subarachnoid hemorrhage or traumatic cranio-cerebral injuries, or expansive process.

Considering data of NCCT, necessity to identify possible primary vascular pathology (arterio-venous malformation), short period from the symptoms onset (possible ongoing hemorrhage) was made decision to perform CT angiography. Emergency multidetector computer tomography angiography (MDCTA) was performed at 04:12 (1 hour from the onset of symptoms) following scan parameters: scan type – helical with full detector active area, tube rotation speed – 0.5 sec, slice thickness – 0.625 mm, pitch = 0.531:1, speed = 10,62 mm per rotation, coverage speed = 21.24 mm/sec, whole detector coverage for small field of view, mA range –minimum= 200 and maximum = 700 (with automatic mA regulation), kV =120, reconstruction thickness = 0.625 mm. Routinely bolus intravenous injection via the power injector is used: with injection rate of 5 ml / sec is introduced the contrast agent Visipaque (international name – iodixanol, 320 mg Iodine/ml) in the volume of about 0.8-1 ml/kg (patient body weight for the adults) but not less then 60 ml, followed by administration of 40 ml saline solution.

MDCTA revealed (fig. 2): Pathology of cerebral blood vessels and related conditions such as: injury,

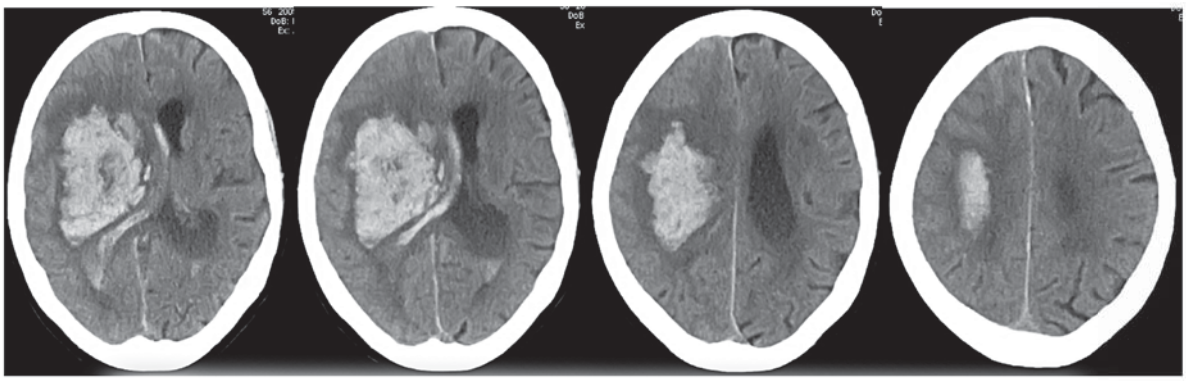

Fig. 1. NCCT. *Acute massive intracerebral hemorrhage with intraventricular eruption*

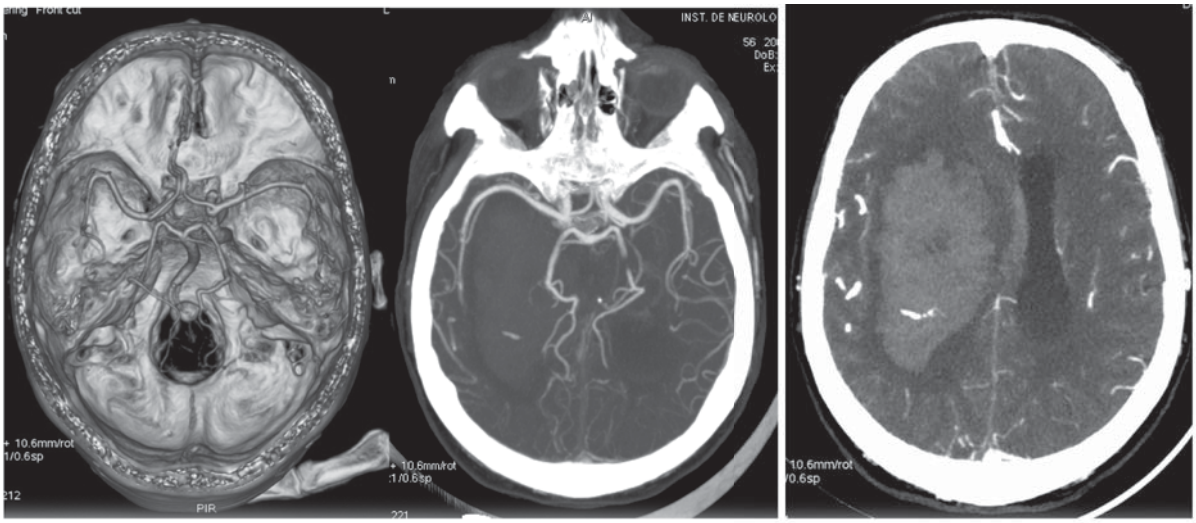

Fig. 2. *MDCTA. A-3D volume rendering, Absence of underlying vascular pathology of HIC, variant of the circle of Willis – aplasia of both right and left posterior communicating artery. B, C – MIP circle of Willis with massive ICH and ,,spot sign" (arrow) - unifocal filiform contrast enhancement within an acute primary intracerebral hemorrhage and discontinuous from adjacent normal blood vessels.*

aneurysms, obstruction, neovascularization, congenital anomalies, was not found, confirming the primary etiology of the hematoma. Middle cerebral artery is displaced laterally and anteriorly by hematoma. On CTA source images is visible unifocal filiform hyperdense (+300 Hounsfield Units) contrast enhancement (14 x 3 mm) within an acute primary intracerebral hemorrhage and discontinuous from adjacent normal blood vessels, which is not present on pre-contrast images – so-called spot sign.

Considering the NCCT, MDCTA and clinical data, presence of intraventricular, major vital risk for the large surgery, was performed emergency surgery: external ventricular drainage type Arendt. Post-surgery the patient presents severe general state, neurological positive dynamics, spontaneous breathing through endotracheal tube, but with somatic unstable blood pressure jumps up to 220-240 / 20 mmHg, which is not relieved by medication, afebrile; unconscious, coma-II, pupils are D = S and narrow, photoreaction is diminished, reacts to manipulations by grimaces, movements in right hand are present. Alimentation is performed by nasogastric tube. Objective examination: Skin is pale. Artificial respiration with oxygen support. Monitoring SPO2 96%. Unstable hemodynamics: rhythmic heart sounds, systolic murmur at the apex, the heart rate - 70 /min., AP 205/110 mm Hg. T 36,3C. Abdomen is soft, diuresis is adequate. From the ventricular drainage was excreted 100 ml of sanguineous CSF.

02.04.2014 at 12:30 control brain CT was performed (fig. 3), which revealed the negative imaging dynamics: enlargement of hematoma volume. Maximal hematoma dimensions are: antero-posterior 8.3 cm, transversal 5.3 cm, cranio-caudal 7.2 cm. There is evidence of diffuse lobar cerebral edema with approximate 4 cm hypodense zone surrounding the hematoma, 21 mm contralateral shift of the median brain structures, compression of the both lateral ventricle. Is detected the drainage tube, installed in posterior horn of left lateral ventricle; there is no signs of blood presence in ventricle IV.

04.4.14. 13:00 The general state of the patient is extremely severe, consciousness level is 5 points by the Glasgow coma scale, pupils are dilated with absence of photoreaction. Objective examination: Skin is cyanotic. Artificial respiration with oxygen support, patient is febrile 39.0 °C. Respiratory rate = 12 / min, SpO2 80%, AP 100/60 mm / Hg; heart rate= 120 / min. At 17:00 in spite of active maintenance therapy cardiac stop occurred and clinical death of the organism. Despite the resuscitation measures by external cardiac massage, adrenomimetic administration, anticholinesterases, calcium substances, corticosteroids, rheological solutions, there was no positive effect. At 19.30 biological death was confirmed.

Cause of death: acute cardiorespiratory failure on the background of cerebro-vascular disease, hemorrhagic stroke, hematoma with ventricular eruption. State after surgery - external ventricular drainage type Arendt. Malign cerebral edema with intracranial hypertension and brain stem compression; cardiorespiratory failure.

Conclusions

Intracerebral hemorrhage (ICH) is a devastating condition and is associated with significant mortality due to ongoing hemorrhage and hematoma expansion. Hematoma expansion is highly predictive of neurological deterioration, poor functional outcome, and mortality. The identification and prevention of hematoma expansion are targets in ICH management as such. The CT angiography (CTA) “spot sign” has emerged in recent years as a potent predictor of hematoma expansion, and a potential tool in guiding therapies in both research and clinical care. This clinical case presentation demonstrates that we can with high accuracy visualize the ongoing hemorrhage and predict hematoma expansion in hyper-acute faze of intracerebral bleeding – even in 1 hour after the symptom onset, using computer tomography angiography investigation. CTA reveals additional information in the assessment of harboring an underlying vascular etiology, which directly effects the strategy of treatment for such patients.

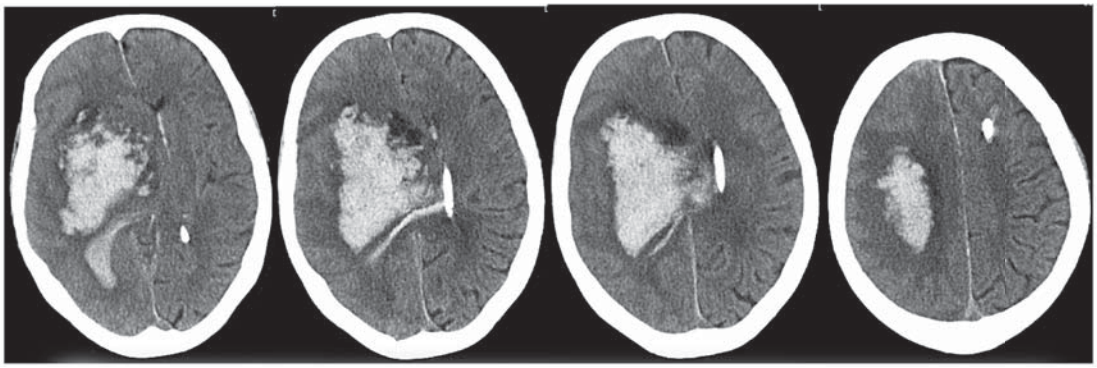

Fig. 3. *Control brain NCCT- enlargement of hematoma volume, increased cerebral edema*

There is a potential role for the spot sign as a selection tool in research studies on possible new treatment strategies for patients with ICH, to identify ICH patients who are most likely to have poor outcomes and treat them aggressively - hemostatic therapy with intravenous recombinant VIIa (rFVIIa) factor or aggressive blood pressure lowering (ongoing trials all over the world).

CTA (versus MRI and interventional digital subtraction angiography -DSA) represents the wide availability, low cost, easy implementation and rapid scan times, high sensitivity and low-risk of noninvasive tool. In conclusion of the above data, we propose:

1) to initiate a large-scale trial of "spot-sign" phenomenon,

2) to list the MDCTA in routine management algorithm of ICH patients.

References

1. H. Khosravani, S.A. Mayer, et al. Emergency Noninvasive Angiography for Acute Intracerebral Hemorrhage. American Journal of Neuroradiology. 01.11. 2012; 10.3174.

2. Badjatia N., Rosand J. Intracerebral hemorrhage. Neurologist 2005;11:311–24.

3. Li N., Wang Y., Wang W. et al. Contrast extravasation on computed tomography angiography predicts clinical outcome in primary intracerebral hemorrhage: a prospective study of 139 cases. Stroke 2011;42:3441–46.

4. Wada R., Aviv R.I., Fox A.J. et al. CT angiography „spot sign" predicts hematoma expansion in acute intracerebral hemorrhage. Stroke. 2007;38:1257–1262.

5. Becker K.J., Baxter A.B., Bybee H.M., Tirschwell D.L., Abouelsaad T., Cohen W.A. Extravasation of radiographic contrast is an independent predictor of death in primary intracerebral hemorrhage. Stroke. 1999;30:2025–2032.

6. Delgado Almandoz J.E., Yoo A.J., Stone M.J., Schaefer P.W., Oleinik A., Brouwers H.B., Goldstein J.N., Rosand J., Lev M.H., Gonzalez R.G., Romero J.M. The spot sign score in primary intracerebral hemorrhage identifies patients at highest risk of in-hospital mortality and poor outcome among survivors. Stroke. 2010;41:54–60.

7. Demchuk A.M., Dowlatshahi D., Rodriguez-Luna D., Molina C.A., Blas Y.S., Dzialowski I., Kobayashi A., Boulanger J.M., Lum C., Gubitz G., Padma V., Roy J., Kase C.S., Kosior J., Bhatia R., Tymchuk S., Subramaniam S., Gladstone D.J., Hill M.D., Aviv R.I. PREDICT/Sunnybrook ICH CTA study group. Prediction of haematoma growth and outcome in patients with intracerebral haemorrhage using the CT-angiography spot sign (PREDICT): a prospective observational study. Lancet Neurol. 2012;11:307–314.

8. Goldstein J.N., Fazen L.E., Snider R., Schwab K., Greenberg S.M., Smith E.E., Lev M.H., Rosand J. Contrast extravasation on CT angiography predicts hematoma expansion in intracerebral hemorrhage. Neurology. 2007;68:889–894.

9. Delcourt C., Huang Y., Wang J., Heeley E., Lindley R., Stapf C., Tzourio C., Arima H., Parsons M., Sun J., Neal B., Chalmers J., Anderson C. INTERACT2 Investigators. The second (main) phase of an open, randomised, multicentre study to investigate the effectiveness of an intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT2). Int J Stroke. 2010;5:110–116.

10. Qureshi A.I., Palesch Y.Y. Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) II: design, methods, and rationale. Neurocrit Care. 2011;15:559–576.