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"IULIU HATIEGANU" UNIVERSITY
OF MEDICINE AND PHARMACY

DOCTORAL SCHOOL NEUROSCIENCE

PROGRAM

2017-2018 | SECTION 2

25 - 27 JANUARY, 2018
"MULTIMEDIA" AUDITORIUM, "IULIU HATIEGANU" UMF CLUJ-NAPOCA
8 VICTOR BABES STREET | CLUJ-NAPOCA | ROMANIA
RONEURO INSTITUTE FOR NEUROLOGICAL RESEARCH AND DIAGNOSTIC
37 MIRCEA ELIADE STREET | CLUJ-NAPOCA | ROMANIA

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President of the European Federation of NeuroRehabilitation Societies (EFNR)

Past President of the Romanian Society of Neurology

Professor of Neurology, Chairman Department of Neurosciences "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

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Department of Neurology, University of Debrecen, Hungary

Milija Mijajlovic

Neurology Clinic, Clinical Center of Serbia and School of Medicine University of Belgrade, Serbia

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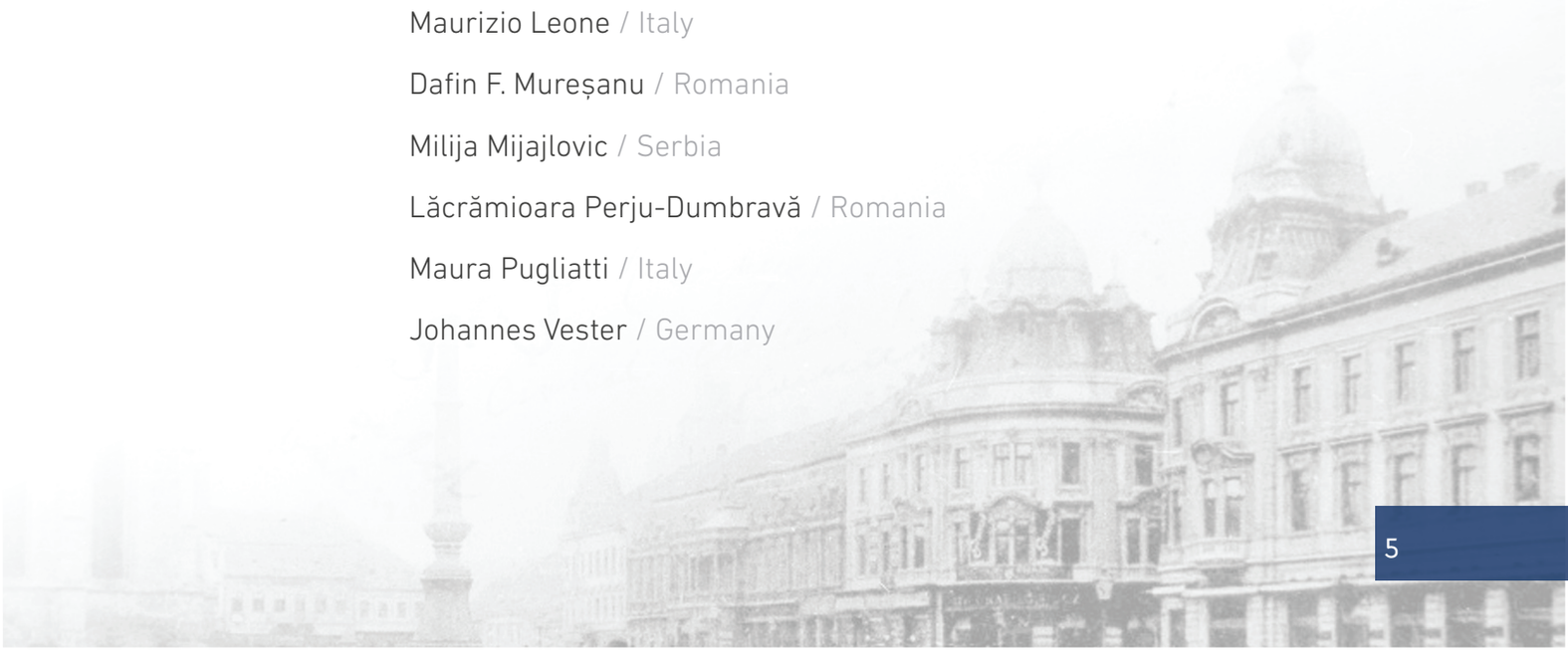

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COURSE PROGRAM

COURSE PROGRAM

JANUARY 25TH, 2018

"MULTIMEDIA" AUDITORIUM, "IULIU HATIEGANU" UMF CLUJ-NAPOCA
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09:50 – 10:00	Welcome Address
10:00 – 10:40	Milija Mijajlovic / Serbia Possibilities and our expectations from the ultrasound techniques in neurology
10:40 – 11:20	Milija Mijajlovic / Serbia Transcranial brain parenchyma sonography in neurological and psychiatric diseases
11:20 – 11:50	Coffee Break
11:50 – 12:30	Milija Mijajlovic / Serbia Ultrasound markers in dementia
12:30 – 13:10	Milija Mijajlovic / Serbia Cervical artery dissection: acute treatment and secondary prevention
13:10 – 14:40	Lunch Break
14:40 – 15:10	Milija Mijajlovic / Serbia Carotid disease: diagnosis, clinical presentation and treatment
15:10 – 15:50	Milija Mijajlovic / Serbia Cerebral non-atherosclerotic vasculopathies
15:50 – 16:30	Milija Mijajlovic / Serbia Treatment strategies for intracranial stenosis

COURSE PROGRAM

JANUARY 26TH, 2018

RONEURO INSTITUTE FOR NEUROLOGICAL
RESEARCH AND DIAGNOSTIC | 37 MIRCEA ELIADE STREET
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10:00 – 13:00 Milija Mijajlovic / Serbia
Hands-On Session

"MULTIMEDIA" AUDITORIUM, "IULIU HATIEGANU" UMF CLUJ-NAPOCA
8 VICTOR BABES STREET | CLUJ-NAPOCA | ROMANIA

14:30 – 15:10 László Csiba / Hungary
The use of ultrasound in clinical research

15:10 – 15:50 László Csiba / Hungary
Bedside differential diagnosis of acute disturbances of hypnoid type of consciousness

15:50 – 16:20 László Csiba / Hungary
Ultrasound in acute stroke. My difficult or surprising patients

JANUARY 27TH, 2018

RONEURO INSTITUTE FOR NEUROLOGICAL
RESEARCH AND DIAGNOSTIC | 37 MIRCEA ELIADE STREET
CLUJ-NAPOCA | ROMANIA

09:30 – 12:00 László Csiba / Hungary
Hands-On Session

INTERNATIONAL GUEST LECTURERS

LÁSZLÓ CSIBA
HUNGARY

Professor of the Department of Neurology at the University of Debrecen, Hungary since 1992.

- visiting scientist in the Max-Planck Institute for Neurological Research in Cologne (1981-83),
- one year in Kure City, Japan (1986)
- half year in Toulouse (INSERM, France).
- He is the founder of Hungarian Neurosonological Society (1994),
- honorary member of Austrian Stroke Society,
- visiting professor of Belgrade, Cluj/Kolozsvár, Targu Mures/Marosvásárhely, Novi Sad/Újvidék University and Israel Association of Neurology.
- Editorial board member of "International Journal of Stroke", "LAM" "Neurosonology (Japan)" "Frontiers in Stroke" (associate editor"), "Neurosonology and Cerebral Hemodynamics", "Emergency Medicine Search and Rescue Journal", "European J of Stroke"
- Past president of the Hungarian Stroke Society,
- Corresp. member of Deutsche Gesellschaft für Klinische Neurophysiologie und Funktionelle Bildgebung
- Between 2009 and 2013 he was the president of European Society of Neurosonology and Cerebral Hemodynamics.
- Since 2015 he is the president of Hungarian Neurological Society.
- Since 2016 corresponding member of Hungarian Academy of Sciences.
- He was awarded with the prize of European Stroke Conference, Eur. Neuroson. Soc. Cer. Hemodyn., Batthyány-Strattmann Prize (Ministry of Health), Francis Crick Award, Szentgyörgyi Award (Ministry of Health) and Lazarevics prize (Serbian Neurol Soc) for his activity in stroke care, education and research.
- His students elected him 7x "Teacher of the Year" and the "Faculty prize" has been donated him due to his outstanding educational activity.
- The President of Hungarian Republic awarded him the Knight's Cross of Republic (for outstanding educational and clinical work).
- His department hosted two times the Stroke Summer Course of the European Stroke Organisation.
- He has published 250 papers on stroke, stroke risk disease, neurosonology and arteriosclerosis.
- His book ("Dissect me, please") had two Hungarian editions and has been translated on German, English, Rumanian and Serbian language.

MILIJA MIJAJLOVIC
SERBIA

Dr. Milija Mijajlovic, MD, MSc, PhD is Ass.Professor of Neurology at School of Medicine University of Belgrade, Serbia. He is working as Board Certified Neurology Specialist/Angiology Subspecialist and Head of the Neurosonology Unit at the Department for Cerebrovascular Disorders of the Neurology Clinic, Clinical Center of Serbia in Belgrade. Dr. Mijajlovic is a Research Associate of the Ministry of Science and Education of Serbia. He received his Masters Degree in Neurology (Stroke) and PhD title in Neurology from School of Medicine University of Belgrade. He was trained at the Department of Neurology University of Muenster, at Neurology Clinic of the TU Dresden; at Stroke Unit of the Sackler Medical Center, Tel Aviv University; Stroke Unit of the Vall d'Hebron Hospital in Barcelona; at the Neurology Department of the University hospital in Amines in France and at Hertie Institute for clinical brain research, University Tuebingen, Germany. His research is focused on stroke, neuroangiology, neurosonology, neurodegenerative diseases and headaches/pain. Dr Mijajlovic is a member of the Executive Committee of the Neurosonology Research Group of the World Federation of Neurology as well as Neurosonology Subspecialist Panel of the European Academy of Neurology. He is also member of the Teaching course Committee of the European Academy of Neurology. Dr. Mijajlovic is Senior Editor of the Clinical Case Reports Journal and member of the Editorial Board of the Journal of Ultrasound in Medicine from which he received distinguished reviewer award in 2014. Dr. Mijajlovic serve as invited reviewer for more than 20 peer reviewed journals including Neurodegenerative Diseases, Journal of Neural Transmission, Journal of Neurology Neurosurgery and Psychiatry, Journal of Neurology, Journal of the Neurological Sciences, International Journal of Stroke etc.
Dr. Mijajlovic is author of more than 150 articles published in peer-reviewed journals, he served invited speaker at more than 60 national and international conferences, and coauthored 20 books and book chapters.

DAFIN F. MUREȘANU
ROMANIA

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Past President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), member of the Academy of Medical Sciences, Romania, secretary of its Cluj Branch. He is member of 16 scientific international societies (being member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 10 national ones, being part of the executive board of most of these societies. Professor Dafin F. Muresanu is a specialist in Leadership and Management of Research and Health Care Systems (specialization in Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998 and several international courses and training stages in Neurology, research, management and leadership). Professor Dafin F. Muresanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary Neurotraumatolgy (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 400 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (157 papers indexed on Web of Science-ISI, H-index: 17) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: the University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Faculty of Medicine, "Iuliu Hatieganu Great Award 2016" for the best educational project in the last five years; the Academy of Romanian Scientists, "Carol Davila Award for Medical Sciences / 2011", for the contribution to the Neurosurgery book "Tratat de Neurochirurgie" (vol.2), Editura Medicala, Bucuresti, 2011; the Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.

ABSTRACTS

THE USE OF ULTRASOUND IN CLINICAL RESEARCH

LÁSZLÓ CSIBA
Department of Neurology, University of Debrecen, Hungary

The measurement of carotid intima-media thickness have been used in stroke field for 25 years. The thickness of carotid IMT is influenced by numerous factors: age, hypertension, hyperlipidemia, smoking, alcohol consumption etc. By the use of new ultrasound machines the CIMT can be assessed with a sensitivity of less than one millimeter in a reproducible manner. It was proven with prospective trials, that the thickness of carotid CIMT is related to the number of risk factors and to the risk of future vascular events. Fortunately, many prospective trials also demonstrated, that the thickness of IMT could be decreased by appropriate treatment. Among others, the positive effect of statin, antihypertensive drugs and some hormone therapies have been proven. It was also observed, that the effects of different statins and antihypertensive drugs were not the same. Some could result in significant decrease of IMT thickness after one or 2 years of therapy some did not have a beneficial effect. The majority of trials observed close relationship between the reversal of IMT and vascular events. The future areas for CIMT measurements are as follow: the CIMT measurement can be useful in vascular risk stratification: a./ by measuring the effect of new drugs onto the IMT thickness, b./ the results of a CIMT trial (needs much less time than an m/m trial to complete) performed before a morbidity-mortality trial may be decisive to support or refute the start of a long-lasting and expensive morbidity trial on drugs aimed on atherosclerosis.

- The transcranial Doppler (TCD) is also an useful method for evaluation of the efficacy of pharmacotherapy not only in subarachnoidal bleeding but also in ischemic stroke risk patients. The microembolic signals could be measured only by transcranial Doppler. The microembolic signals are an accepted surrogate marker of future stroke risk and have been used to show treatment efficacy in different clinical conditions (TIA, carotid stenosis, carotid endarterectomy, coronary bypass surgery and during some intravascular interventions). The randomized trials successfully evaluated the effect of different anticoagulants (e.g. heparin vs. LMWH) or that of mono vs dual antiplatelet therapy in stroke or stroke risk patients (e.g. a significant correlation was found between the number of persisting microembolic signals and the risk of future TIA or stroke).
- With the help of continuous monitoring of cerebral blood velocity (e.g.MCA), you can evaluate the efficacy of old (e.g. t-PA) and new fibrinolytic agents in acute ischemic stroke patients.
- The impairment of dilatative capacity of brain arteriolas can be also measured noninvasively, without radiation hazard, by a transcranial Doppler. The improving or worsening effect of different pharmacotherapies on cerebral vasomotor reactivity could be also studied by TCD (statins, antihypertensives, antiparkinson drugs, NSAIDS, diuretics etc.
- Conclusion: both extra-and intracranial US methods proved their usefulness in the evaluation of pharmacological interventions. They are attractive techniques due to their low cost, non-invasive characteristics, excellent time resolution and some unique abilities (e.g. embolus detection, continuous cerebral blood velocity monitoring).

ULTRASOUND IN ACUTE STROKE. MY DIFFICULT OR SURPRISING PATIENTS

LÁSZLÓ CSIBA
Department of Neurology, University of Debrecen, Hungary

3.1. Ultrasound in acute stroke

Doppler ultrasonography is the primary non-invasive test for evaluating carotid stenosis. The sonographic characteristics of symptomatic and asymptomatic
carotid plaques are different: symptomatic plaques are more likely to be hypoechoic and highly stenotic, while asymptomatic plaques are hyperechoic and moderately stenotic. The degree of stenosis is better measured

on the basis of the waveform and spectral analysis. When no stenosis is present, blood flow is laminar. With greater stenosis, the flow becomes turbulent. An important general rule for ultrasound is the greater the degree of stenosis, the higher the velocity. Most studies consider carotid stenosis of 60% or greater to be clinically important. Commonly used methods to estimate stenosis with ultrasonography are:
Peak systolic velocities:

- Normal: ICA PSV <125 cm/s, no plaque or intimal thickening.
- <50% stenosis: ICA PSV <125 cm/s and plaque or intimal thickening.
- 50–69% stenosis: ICA PSV is 125–230 cm/s and plaque is visible.

- >70% stenosis to near occlusion: ICA PSV >230 cm/s and visible lumen narrowing.
-
- Near occlusion: a markedly narrowed lumen on c-Doppler ultrasound.
-
- Total occlusion: no detectable patent lumen is seen on grayscale ultrasound, and no flow is seen on spectral, power and color Doppler ultrasound.
-
- Ratios of the maximal systolic flow velocity within the ICA stenosis divided by the maximal systolic flow velocity within the non-affected CCA:

- 50% stenoses ICA/CCA: <2.0.
-
- 50–69% stenoses ICA/CCA:2.0–4.0.
-
- >70% stenoses ICA/CCA: >4.0.

Ratios may be particularly helpful in situations in which cardiovascular factors (e.g. poor ejection fraction) limit the increase in velocity. Velocity measurements in a stenosis (PSV and carotid ratio) alone are not sufficient to differentiate a moderate from a severe (>70% NASCET) stenosis. Additional criteria refer to the effect of a stenosis on prestenotic flow (common carotid artery), the extent of poststenotic flow disturbances, and derived velocity criteria (diastolic peak velocity and the carotid ratio).
In case of hemodynamically significant ICA stenosis or occlusion (proximal to the origin of the ophthalmic artery) a reversed (extra-intracranial) flow can be detected in the ophthalmic artery. The compression of ECA branches can identify the source of collateral circulation. Occlusion results in a complete absence of color-flow signal in ICA, and the diagnosis can be confirmed by ultrasound contrast agents. Intracranial stenosis and occlusion corresponds to approximately 8–10% of acute ischemic stroke. Transcranial color-coded duplex sonography (TCCD) combines the imaging of intracranial vessels and parenchymal structures. To penetrate the skull, TCCD uses low frequencies (1.75–3.5 MHz), which limit the spatial resolution. Some patients cannot be examined because of an insufficient acoustic window. The duplex mode of TCCD enables sampling of vessels and Doppler measurements of angle-corrected blood flow velocities. Mean velocity analysis is not enough to identify intracranial vessel abnormalities. It must be combined with other parameters such as asymmetry, segmental elevations, spectral analysis and knowledge of extracranial circulation. The use of echo-contrast enhancing agents (ECE) increases the sensitivity and specificity and with ECE the diagnostic confidence of TCCD for intracranial vessel occlusion is similar to that of magnetic resonance angiography. Recently, a practical algorithm has been published for urgent bedside neurovascular ultrasound examination.
Sonography in acute stroke of the anterior cerebral circulation:
Technical requirements: extracranial and transcranial duplex, supplemented by Doppler if necessary (e.g. for supratrochlear artery)

- Course of examination: color-coded visualization of the ipsilateral internal carotid artery and middle cerebral artery with Doppler spectrum, supported by signal enhancers if necessary. In case of a suspected proximal occlusion of the middle cerebral artery, color-coded visualization of the other ipsilateral and contralateral arteries of the cerebral circle in the same acoustic window. In case of a suspected distal occlusion of the middle cerebral artery or its branches, angle-oriented determination of the blood flow velocity in the

proximal middle cerebral artery. In case of unclear situations, also sonographic detection of the supratrochlear artery and the common carotid artery comparing the two sides. With a completely normal spectral TCD, there is less than 5% chance that an urgent angiogram will show any acute obstruction.

- TCD identifies microembolic signs (MES) in the intracranial circulation. Detection of MES can identify patients with stroke or TIA likely to be due to embolism and, in addition, acts as a predictor for new cerebral ischemic event recurrence. TCD monitoring may help to discriminate between different potential sources of embolism (i.e. artery-to-artery or cardioembolic strokes). Different types of emboli (i.e. cardiac or carotid) have different acoustic properties and ultrasonic characteristics, based on composition and size, which could permit differentiation. MES detection by TCD in CEA candidates may allow identification of a particularly high-risk group of patients who merit an early intervention or, if this is not possible, more aggressive antithrombotic therapy is necessary.
- New ultrasound contrast agents (UCAs) that can pass through the microcirculation and the development of contrast-specific imaging modalities make it possible to use ultrasound for the visualization of brain perfusion deficits. But perfusion imaging in acute stroke is still in the experimental phase.
- Ultrasound has an important prognostic role in acute stroke and

can be used to monitor thrombus dissolution during thrombolysis. The waveform changes correlate well with clinical improvement and a rapid arterial recanalization is associated with better short-term improvement, whereas slow flow improvement and dampened flow signals are less favorable prognostic signs.

- Contrast-enhanced TCD can also be used to identify patients with a patent foramen ovale.
- Midline shift measurement, arterial resistance and optical sheat measurements are useful ancillary methods for detection of increased intracranial pressure.

3.2. My most surprising or difficult cases

- 56 years old male. Previous case history without any remarkable disease.December- January. Neck pain and headache (frontal region). The patient was suspect for cervical spondylosis and MRI has been performed in March. C-IV minor disc protrusion, spondylarthrosis but suspect for space occupying disease in the cerebellum. Brain MRI multiple abscess? No neurological deficit, no fever. CSF: cell 37/3, 60% monocytes, 40% lymphocytes Protein: 2,49 g/l No bacteria, HIV: negativ, Tumor markers: negative Blood hemoculture:negative. Surprising disease course....

- 46 y male No specific disease before. In 2017 September: pneumonia, between 2017 October-November fever, CRP 165 mg/l. Thorax empyema-drainage:Stenotrophomonas maltophilia+Streptococcus mitis— AB therapy. Complete recovery, CRP normalised. No complain. During the removal of thorax drainage sudden onset of severe left sided hemiparesis with sudden onset of confusion. After CT preparation for iv. thrombolysis but stopped due to some bleeding from the thorax shunt. Surprising disease course....

- 32 y female with sudden onset of left sided hemiparesis. Right carotid bifurcation:echo free plaque, which results in 60 % stenosis. CEA is planned repeated imaging, surprising finding the CEA was cancelled...

- 76 y old ambulatory patient with transient headaches and mild vertigo. No aphasia, no double vision, he walks w/o support or device. Surprising imaging...

BEDSIDE DIFFERENTIAL DIAGNOSIS OF ACUTE DISTURBANCES OF HYPNOID TYPE OF CONSCIOUSNESS

LÁSZLÓ CSIBA
Department of Neurology, University of Debrecen, Hungary

1. Introduction
The causative diagnosis of consciousness disturbances is one of the most important and difficult clinical tasks. While an incipient renal failure can have vague symptoms, the primary (e.g. commotion) or secondary (e.g. cardiac arrest) insults of the brain provocate a quickdisturbance of consciousness, due to the significant oxygen and energy demand of the brain. Sooner or later, every practicing physician will provide emergency care for a patient suffering from disturbances of consciousness, and will meet the difficulty of the differential diagnosis, too.

2. Hypnoid types of disturbances of consciousness (HDC)

This lecure discusses the hypnoid types of disturbances of consciousness. This patient is similar to a sleeping healthy person. In everyday practice these conditions can be divided into two groups:
1. The patient becomes unconscious very suddenly (usually in seconds). Because the pathological event is transient (such as epileptic seizure or transient cardiac arhythmia), the patient regains his/her awareness quickly.

The possible causes:
a. Central nervous system
   a.a mild head injury resulting only in reversible damage in neurons and axons (concussion without structural impairment).
   a.b epilepsy
   a.c psychogenic mechanism
b. Heart: temporary dysfunction of the pump function of the heart (e.g. cardiac arrest) or transient arrhythmias.
c. Reflex vasodilation with or without the presence of "b" mechanisms.

3. The classification of the severity of hypnoid types of disturbances of consciousness (HDC).

This large group of consciousness disturbances does not involve only the coma, but it contains also the state of somnolence and stupor too. All patients suffering from any type of hypnoid unconsciousness are alike sleeping people, who are healthy otherwise. If not provoked by pain or any other stimulus, the patient is lying with his/her eyes closed.
Somnolence: the patient can be woken up easily, but sleeps away right after being left alone.
Stupor (also known as sopor): the patient seems to be sleeping abnormally deeply, but reflects with motor or verbal responses for motor or verbal stimuli.
Coma (from a greek word meaning deep sleep): The patient does not react for strong pain stimuli, but both the spontaneous breathing and circulation are intact.

In the everyday practice, the terms somnolent-stuporous and stuporo-comatose are also widely used for indicating the severity, but cannot be used for quantitative assessments. Instead, we use different coma scales to record the level of consciousness. The lowest possible scoreof Glasgow Coma scale 3, while the highest is 15 (fully awake person).

Table 1. The Glasgow Coma Scale

Eye-opening	Spontaneous	4
	In response to voice	3
	In response to painful stimuli	2
	No response	1
Motor response	Obeying command	6
	Localizing response	5
	Withdraws	4
	Abnormal flexor response	3
	Extensor posturing	2
	No response	1
Verbal response	Oriented	5
	Confused conversation	4
	Inappropriate speech	3
	Incomprehensible speech	2
	No verbal response	1

A recommendation published in 2010 compared the scales, which are commonly used to assess the disorders of consciousness. The use of Coma Recovery Scale-Revised (Table 3) is recommended with minimal limitations. The total score range is between 0-23, and the assessment takes 25 minutes.

Table 2. The most frequently used scales in the assessment of consciousness disturbances

CRS-R Coma Recovery Scale-Revised
CLOCS Comprehensive Levels of Consciousness Scale
CNC Coma/Near-Coma Scale
FOUR Full Outline of UnResponsiveness Score
GCS Glasgow Coma Scale
GLS Glasgow-Liege Coma Scale
INNS Innsbruck Coma Scale
LOEW Loewenstein Communication Scale
RLS85 Swedish Reaction Level Scale-1985
SMART Sensory Modality Assessment Technique
SSAM Sensory Stimulation Assessment Measure
WHIM Wessex Head Injury Matrix
WNSSP Western Neuro Sensory Stimulation Profile

Table 3. The Coma Recovery Scale-Revised
1. Auditory function scale
    4 Consistent movement to command
    3 Reproducible movement to command
    2 Localization to sound
    1 Auditory startle
    0 None

2. Visual function scale
    5 Object recognition
    4 Object localization: reaching
    3 Visual pursuit
    2 Fixation
    1 Visual startle
    0 None

3. Motor function scale
    6 Functional object use
    5 Automatic motor response
    4 Object manipulation
    3 Localization to noxious stimulation
    2 Flexion withdrawal
    1 Abnormal posturing
    0 None/Flaccid

4. Oromotor/Verbal function scale
    3 Intelligible verbalization
    2 Vocalization/Oral movement
    1 Oral reflexive movement
    0 None

5. Communication scale
    2 Functional: accurate
    1 Non-functional: intentional
    0 None

6. Arousal scale
    3 Attention
    2 Eye opening without stimulation
    1 Eye opening with stimulation
    0 Unarousable

4. The examination of patients suffering from HDC

The reliable data on medical history and risk factors are very important.

Information should be collected not just about the previous diseases, such as hypertension, diabetes, cardiovascular or hematological disorders, depression, fever, but the medications too. Life habits are very important (medication? alcohol/drug consumption? problems in the private life or at work?)

It should be questioned if the family members experienced any change in the patient's behavior, difficulty in his/her verbal communication and self-expression, or the signs of lightheadedness. Did the patient complain about numbness, visual problems or double vision? Did he/she experience any trauma? Painful stimuli should be used to assess the severity of the consciousness disorder.

Pain-stimuli

Figure 1. Painful stimuli applied either on the supraorbital area, sternum or on both mastoid processes. The symmetrical or asymmetrical movements of the extremities can be assessed.

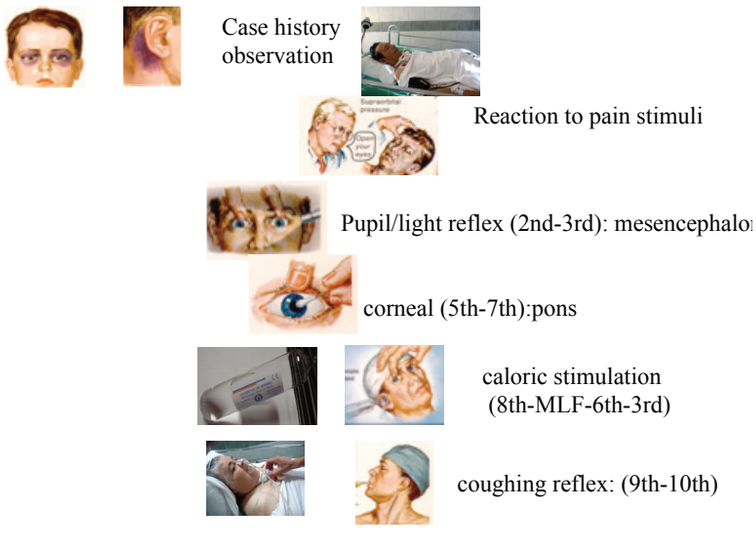

Figure 2. The most important steps of neurological examination in HDC.

5. Bedside differential diagnosis of patients suffering from acute HDC.

The normal conscious state requires the intact function of the reticular formation located in the brainstem and the intact function of the supratentorial region activated by the reticular formation. These facts help us to understand the differential diagnosis of consciousness disorders.
Many agents can harm the supratentorial region directly or indirectly, but
an isolated brainstem lesion can also cause coma (e.g. occlusion of the basilar artery affecting the brainstem reticular formation).

It is essential to understand that whatever damages the supratentorial region, HDC develops only if the pathological process has diffuse/extended effect on the supratentorial area.
(Accepting this postulate it is easy to understand why an acute viral encephalitis or barbiturate intoxication will result in disturbance of consciousness while a large territorial cerebral infarct without mass effect will not alter the consciousness).
With other words: an acute supratentorial focal ischemia or bleeding without mass effect (without midline shift, without increased pressure etc.) will NOT result in HDC, but an acute event with space occupying effect can be accompanied with HCD. Last but not least, all of our statements are valid only for acute events!
A slowly growing tumor or subdural hematoma does not necessarily result in disturbance of consciousness except if the CT reveals space occupying/mass effect with midline shift etc.

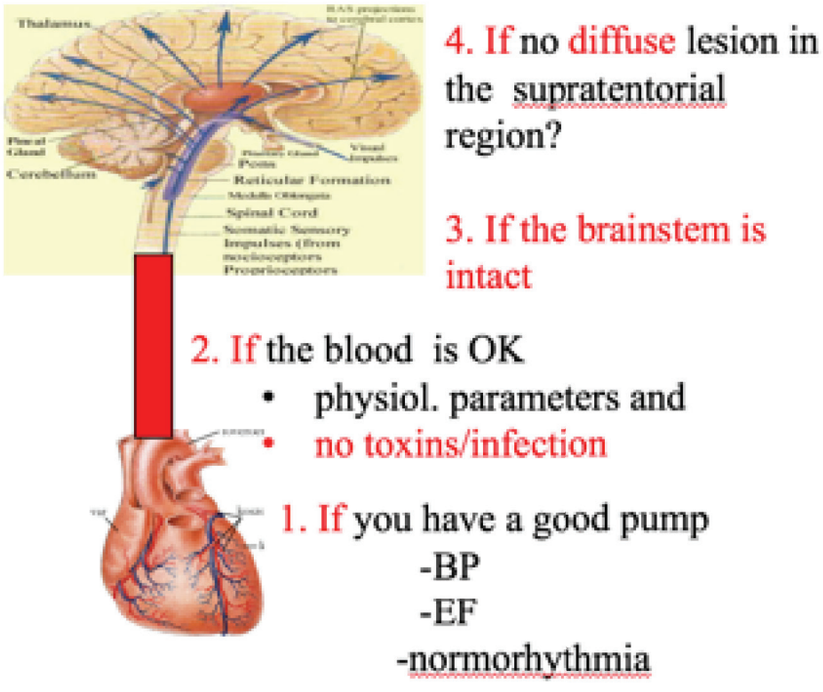

Figure 3. Acute external and internal agents (four groups), that can cause hypnoid disturbance of unconsciousness. You are alert...

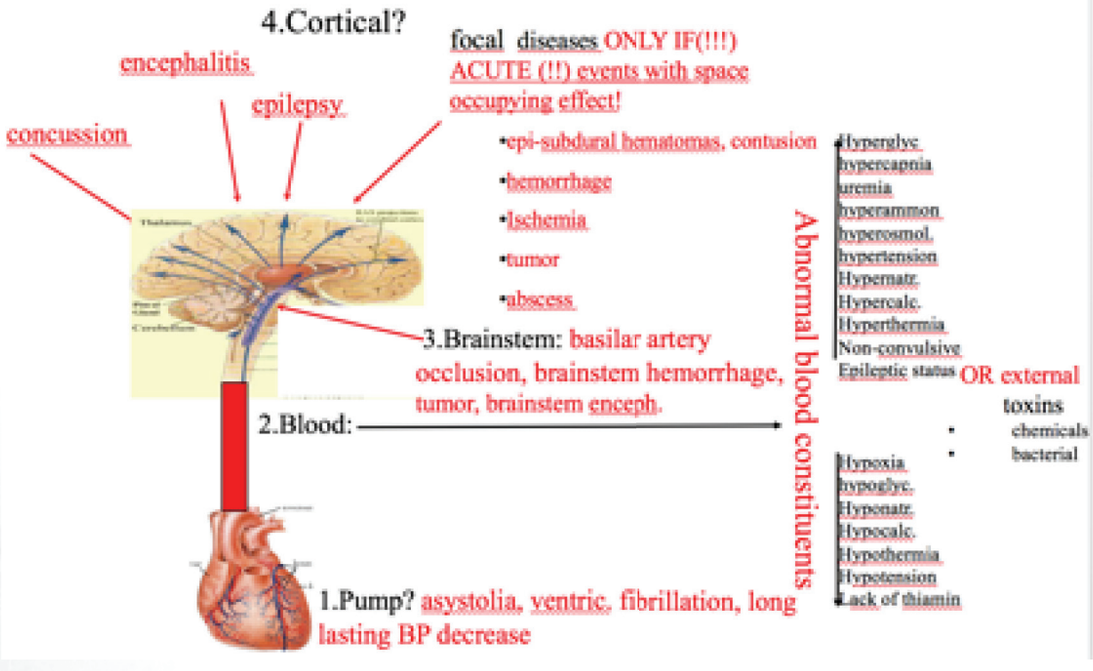

Fig.4 The most common diseases resulting in HDC

The therapy depends on the causative agent, so we do not provide further details about it. In case of basilar occlusion, desobliteration is indicated, if intoxication, detoxification etc.
Important! If CT or MRI reveals ischemia or hemorrhage without any mass effect, and the patient has normal conscious state, but hours later he/she shows the signs of any consciousness disturbances, such as somnolence, the hemorrhage is likely to have increased suddenly, or malignant ischemic cerebral edema could have developed, especially if the patient has normal laboratory result, did not experience fever, and did not get any sedatives. In these cases imaging should be performed again!
6. Prognosis
The prognosis depends on the causative agent, the patient's age and general condition. According to the survey of the American Academy of Neurology, patients suffering from coma caused by cardiac arrest (hypoxia and ischemia) are likely to have poor prognosis after 3 days, if any of the followings is present:
- absent pupillary, corneal, coughing reflexes, absent reaction to caloric reflex test,
absent or extensor motor responses (evidence A), the presence of seizures or myoclonus status epilepticus (evidence B),
- Bilateral absence of the cortical component of the SSEP predicts a poor outcome (evidence B)
- burst-suppression pattern or generalized epileptiform activity are associated with poor outcome (evidence C).
- serum neuron-specific enolase (NSE, only this marker has verified diagnostic value!) levels >33 µg/L at days 1 to 3 predict poor outcome (evidence B),
- There are insufficient data to support or refute whether the measurement of intracranial pressure, the oxygenisation of the brain, and neuroimaging (MRI, CT)are indicative of poor outcome or not.

7. Summary
In case of consciousness disturbances the following examinations are essential:
1. Analysis of the detailed medical history including the information obtained from family members.
2. General physical examination, neurological examination, and the examination of external injuries, including:
- responses to painful stimuli,
- the isocoria of the pupils, eye positions and movements, the presence or absence of pupillary, corneal, and coughing reflexes,

3. The treatment of consciousness disturbances can be operative or conservative depending on the causative agents.

POSSIBILITIES AND OUR EXPECTATIONS FROM THE ULTRASOUND TECHNIQUES IN NEUROLOGY

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Low cost, avoidance of radiation and high temporal resolution are inherent advantages of ultrasound imaging that translate into multiple clinical uses in many domains of neurology.
Modern treatment and prevention of ischemic stroke rely on prompt diagnosis. Ultrasonography has found a place as a noninvasive screening test and bedside technique that provides estimates of the degree of stenosis as well as hemodynamic and structural information about intracranial and extracranial vessels in real time. Other standard applications of neurosonology include detection of vasospasm in patients with subarachnoid hemorrhage, selection of appropriate candidates for blood transfusion among patients with sickle cell anemia (primary stroke prevention), right-to-left shunt testing, emboli detection, vasomotor reactivity assessment, and noninvasive confirmation of cerebral circulatory arrest. Improvement in image quality permits novel uses of ultrasonography in neurodegenerative and peripheral nervous system disorders, providing clinically important information that is complementary to the clinical examination and electrophysiology. Transcranial brain parenchyma sonography may assist in the differential diagnosis of movement disorders, while peripheral nerve

ultrasound using high-frequency probes may provide structural information regarding the underlying etiology of neuropathies. Neurosonology methods also provide noninvasive reliable diagnosis of temporal arteritis and follow-up of its treatment.
The indications for neurosonology are rapidly expanding, increasing its applicability outside the field of cerebrovascular diseases. Ultrasound testing is a noninvasive easily repeatable bedside investigation providing clinically relevant information on a wide spectrum of neurologic disorders.

TRANSCRANIAL BRAIN PARENCHYMA SONOGRAPHY IN NEUROLOGICAL AND PSYCHIATRIC DISEASES

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Transcranial sonography (TCS) has been recently recognized as a reliable and sensitive tool in detecting basal ganglia (BG) abnormalities in several movement disorders, where different patterned hyperechogenic lesions were demonstrated. TCS revealed reduced echogenicity of the brainstem raphe (BR) as a characteristic finding in unipolar depression and in depression associated with Parkinson's (PD) or Wilson's disease (WD), but not in healthy adults, schizophrenia, multiple sclerosis with depression or Parkinson's disease without concomitant depression. TCS showed substantia nigra hyperechogenicity in idiopathic PD and lenticular nuclei hyperechogenicity as a characteristic finding in atypical parkinsonian syndromes.
The postoperative position control of deep brain stimulation electrodes, especially in the subthalamic nucleus, can reliably and safely be performed with TCS.
TCS also revealed BG hyperechogenic changes in several other movement disorders with trace metal accumulation such as WD, several forms of spinocerebelar ataxia as well as some entities of neurodegeneration with brain metal accumulation.
The increasingly broad application of TCS in the early and differential diagnosis of neurodegenerative and psychiatric disorders in many centers all over the world is probably the best evidence for the value of the method.
Main advantages include the easy applicability, the fact that it is quick and repeatedly performable with no limitations as known from other neuroimaging techniques and that it is relatively cheap and side effect free. Principal limitations are still the dependency on the acoustic bone window and operator experience dependence. New automated algorithms may reduce the role of investigator skills in the assessment and interpretation, increasing TCS diagnostic reliability. Recent technological advances including TCS-MRI fusion imaging and upcoming technologies of digitized TCS image analysis are aiming at a more investigator-independent assessment of deep brain structures on TCS.

ULTRASOUND MARKERS IN DEMENTIA

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The vascular contributions to neurodegeneration and neuroinflammation may be assessed by magnetic resonance imaging and ultrasonography (US) that is widely available, safe and relatively low cost tool for differentiating subtypes of cognitive impairment and dementia, tracking disease progression and evaluating response to treatment in various cognitive disorders.
Cerebral hypoperfusion has been linked to cognitive decline either as a risk or an aggravating factor. Hypoperfusion as a consequence of microangiopathy, macroangiopathy or cardiac dysfunction can promote or accelerate neurodegeneration, blood-brain barrier disruption and neuroinflammation. US can evaluate the

cerebrovascular tree for pathological structure and functional changes contributing to cerebral hypoperfusion. Early changes in the blood vessel wall can be detected by early ultrasound screening methods which allow us to detect changes before the disease becomes clinically evident. Intracranial hemodynamics can be assessed by transcranial Doppler sonography (TCD), functional TCD with various functional tests, and TCD detection of cerebral emboli. Extracranial circulation (carotid and vertebral arteries) can be assessed by means of color Doppler flow imaging. Novel ultrasound technology enables non-invasive, portable, bedside detection of early vascular changes such as arterial stiffness, measurement of the intima-media thickness, pulse-wave velocity, flow-mediated dilation, or endothelial dysfunction in order to obtain information necessary to determine more closely the relation between vascular status and disease development, so that the evolution of cardiovascular disease can be prevented or at least postponed.
US is a promising tool with excellent temporal resolution, which have a significant impact on our understanding of the vascular contributions to cognitive impairment and dementia either of vascular and degenerative origin and may also be relevant for assessing future prevention and therapeutic strategies for these conditions.

CERVICAL ARTERY DISSECTION: ACUTE TREATMENT AND SECONDARY PREVENTION

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Cervical artery dissections include both internal carotid and vertebral artery dissections. It should be considered in patients with stroke-like symptoms, a new-onset headache and/or neck pain, and/or other risk factors. Early imaging with computed tomography or magnetic resonance imaging is key to making the diagnosis.
Carotid artery dissection is a cause of stroke, especially in young and middle-aged patients. A dissection occurs when there is an intimal tear or rupture of the vasa vasorum, leading to an intramural hematoma, which is thought to result from trauma or can occur spontaneously, and is likely multifactorial, involving environmental and intrinsic factors. The clinical diagnosis of carotid artery dissection can be challenging, with common presentations including pain, partial Horner syndrome, cranial nerve palsies, or cerebral ischemia. The overall prognosis is good, but does depend on the initial severity of symptoms. However, the diagnosis should not be missed, because treatment may help prevent worsening or persistent ischemia, recurrent dissection, and death. With the use of noninvasive imaging, including ulrasonography, magnetic resonance and computed tomography angiography, the diagnosis of carotid dissection has increased in frequency.
Treatment options include thrombolysis, antiplatelet or anticoagulation therapy, endovascular or surgical interventions. The choice of appropriate therapy remains controversial as most carotid dissections heal spontaneously and there are no randomized trials to compare treatment options.

CAROTID DISEASE: DIAGNOSIS, CLINICAL PRESENTATION AND TREATMENT

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Duplex ultrasonography has a well-established role in the assessment of the degree of stenosis caused by carotid atherosclerosis. This assessment is derived from Doppler velocity changes induced by the narrowing lumen of the artery. New research into the mechanisms for plaque rupture and atheroembolic stroke indicates that the degree of narrowing is an imperfect predictor of stroke risk, and that other factors, such as plaque composition and remodeling and biomechanical forces acting on the plaque, can play a role. New advances in ultrasound imaging technology have made it possible to investigate these measures of plaque vulnerability to

identify pre-embolic unstable carotid plaques. Efforts have been made to quantify the morphologic appearance of the plaque in B-mode images and to correlate them with histology. Additional research has resulted in the first generation of clinically available 3-dimensional ultrasound transducers that reduce operator-dependence and variability. Ultrasonography provides real-time imaging and physiologic information that can be utilized to measure disruptive forces acting on carotid plaques.
In recent years, most studies proved that by evaluating carotid atherosclerosis with ultrasonography, carotid atherosclerosis accounts for the development of cognitive decline in nonstroke patients. Carotid atherosclerosis not only impairs the subtle general cognitive function but also decreases the specific domains of cognitive function, such as memory, motor function, visual perception, attention, and executive function. But, it is still controversial. The possible mechanisms of cognitive impairment in nonstroke patients with carotid atherosclerosis can be classified as systemic global cerebrovascular function, small-vessel diseases, and the mixed lesions. Indicators of vulnerable plaque, such as ulceration, juxtaluminal lucent plaque, intraplaque hemorrhage on magnetic resonance imaging, and plaque inflammation on positron emission tomography/computed tomography are in development for that purpose. The best-validated approach is detection of microemboli on transcranial Doppler. Medical therapy has improved considerably in the past two decades, and this has reduced the stroke rate for both symptomatic and asymptomatic carotid stenoses. Clinicians should consider a variety of clinical and radiologic variables in reaching treatment decisions for patients with carotid stenosis.

CEREBRAL NON-ATHEROSCLEROTIC VASCULOPATHIES

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The common non-atherosclerotic, large-vessel vasculopathies affecting the cerebral vasculature include intracranial aneurysms, cervical artery dissection, fibromuscular dysplasia and moyamoya disease. Together, these entities contribute to a high incidence of devastating cerebrovascular outcomes, including ischemic stroke and subarachnoid hemorrhage, leading to long-term physical and cognitive disability frequently in young otherwise healthy adults.
In addition to well reported clinical overlap, these polygenic phenotypes share epidemiological characteristics, environmental risk and a common pathological weakening of the arterial wall. Identification of the correct etiology is important in establishing treatment strategies and assessing prognosis. Careful history taking and appropriate laboratory testing are essential. Although catheter angiography is the most important diagnostic tool to examine various intracranial arterial diseases, other diagnostic modalities such as computed tomography angiography and magnetic resonance angiography are nowadays widely used. High resolution vessel wall magnetic resonance imaging also can assist in making the correct diagnosis as this can yield information regarding vessel wall pathology.
Refined understanding of shared associations, common biology and gene by environment interactions will hopefully lead to future scientific questions and ultimately better treatment strategies to prevent resultant cerebrovascular events in predisposed individuals going forward.

TREATMENT STRATEGIES FOR INTRACRANIAL STENOSIS

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Intracranial atherosclerotic stenosis (ICAS) is an important etiology subtype of ischemic stroke. Stenosis severity was thought to be the main reference index for clinical treatment and research. However, stenosis could not reflect the ischemia risk completely, instead the hemodynamic state across the lesion, the extent of collateral circulation, and perfusion impairment downstream the stenosis are also very important. For patients with

symptomatic ICAS, antithrombotic agents are the mainstay of therapy. Anticoagulation is not widely used since it is not more effective than aspirin and carries a high risk of bleeding. New oral anticoagulants are showing promise, but their use has not been investigated in appropriate clinical trials. Since the recurrent stroke risk is high with aspirin monotherapy, dual antiplatelets are considered in the early stage of symptomatic ICAS. Based on the Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) and Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) results, aspirin plus clopidogrel has been recommended. However, this combination was not superior to aspirin monotherapy in patients with ICAS in the CHANCE substudy. Progression of ICAS is common, and it is associated with recurrent strokes. In the Trial of Cilostazol in Symptomatic Intracranial Arterial Stenosis (TOSS) study, aspirin plus cilostazol was more effective than aspirin monotherapy in preventing progression. The TOSS II trial showed that the overall change in stenosis was better with aspirin plus cilostazol than with aspirin plus clopidogrel. Aside from antithrombotic therapy, risk factor management is critical for secondary prevention, and high blood pressure is clearly linked to recurrent stroke. However, blood pressure may have to be cautiously managed in the early stage of stroke. Considering that ICAS is the major cause of stroke worldwide, further investigations are needed to establish optimal management strategies for patients with ICAS.

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