NEUROPSYCHIATRIC CONSEQUENCES OF STROKE

José M Ferro

Department of Neurosciences and Mental Health
Hospital Santa Maria-CHLN, IMM
University of Lisboa, Lisboa, Portugal

NEUROPSYCHIATRIC SEQUELAE OF STROKE

- A substantial proportion of stroke survivors are affected by psychological distress and numerous psychiatric disorders
- These disabling psychiatric outcomes
  - reduce the quality of life
  - are a major source of burden, stress and exhaustion for the caregiver
  - often precipitate institutionalization of the patient

DEPRESSIVE DISTURBANCE due to STROKE

- **With major depressive like episode**
- **Either depressed mood or anhedonia and total of 5 symptoms present during ≥ 2 weeks**
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss or energy
  - Feelings of worthlessness or excessive/inappropriate guilt
  - Diminished ability to think or concentrate
  - Recurrent thoughts of death

DEPRESSIVE DISTURBANCE DUE TO STROKE: CLINICAL COURSE

- Most depressive episodes begin < 1year after stroke
- The depression recovery rate at 1 year after stroke is moderate (15–57%)
- Among patients with stroke-associated depression, the frequency of recurrent episodes of depression increases from 38% at 2 years after stroke to 100% at years 14/15

Ayerbe et al, 2013

SUICIDALITY AFTER STROKE

- Suicide is uncommon after stroke
- Suicidal thoughts can develop shortly after stroke but are more common after a delay
- More common in patients with low education, previous mood disorder, and/or stroke-associated depressive disorder, younger age, functional limitations, insomnia and pain

Santos C et al, 2012; Fuller-Thompson et al, 2012; Yamauchi et al, 2014; Pompili M et al, 2012

DEPRESSIVE DISTURBANCE DUE TO STROKE: OUTCOME

Worse outcome after stroke:

- Higher mortality rate
- More disability
- Higher risk of stroke recurence
- Lower level of social functioning
- Worse quality of life after stroke
- Higher risk of institutionalisation
- Family caregiver depression

Ferro et al. Nature Reviews Neurology. 2016;12: 269-28

GENERALISED ANXIETY DISORDER (GAD) DUE TO STROKE

- Anxious or worried for 6 months
- Difficulty in controlling worries
- 3 or > of
  - Restlessness
  - Easy fatigue
  - Difficulty concentrating
  - Irritability
  - Muscle tension
  - Sleep disturbance
- Significant distress or functional impairment

GAD DUE TO STROKE Risk factors

- **Postroke Depression**
- **Pre-stroke depression**
- **Pre-stroke anxiety**
- History of insomnia
- No individual stroke location
- Impaired on activities of daily living
- Impaired in social functioning
- Social isolation

Ayerbe, 2013; Wright et al, 2017

GAD IN STROKE
Clinical course and outcome

- Only ¼ recover from anxiety at 1 year and 1/3 at 3 years**
- Anxiety with associated depression lasts longer

- Anxiety does not influence functional or cognitive recovery
- Anxiety is associated with worse social functioning and Quality of life

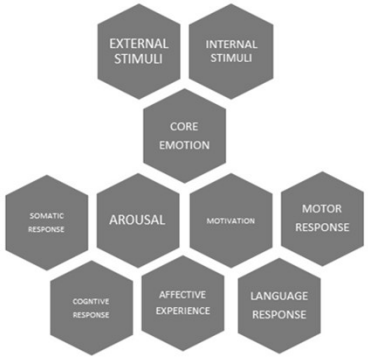
*De Wit L et al 2008; Morrison et al 2005;Schultz et al 97;Burvil et al 96; **Astrom 96; *Castillo et al 95; Sagen et al, 2010*

APATHY AFTER STROKE MANAGEMENT

- No good quality RCTs
- Possible therapeutic interventions:
  - Cognitive-behavioral therapy
  - Dopaminergic agents
  - Nootropic nefiracetam
  - Cholinergic drugs
  - Attention stimulants
  - rTMS
- Modest effect, lack of scientific proof

Ferro JM & Santos AC, 2018

EMOTIONAL DISTURBANCES



- Fear
- Anger
- Emotional indifference (apathy)
- Lack of understanding of other emotions (empathy)
- Lack of emotional expression control (“emotionalism”)

Ferro JM and Santos AC, 2018

NEUROPSYCHIATRIC SEQUELAE OF STROKE

- The psychiatric complications of stroke are under-recognized and undertreated
- Health-care professionals are becoming more aware of the relevance of neuropsychiatric disorders in patients with stroke
- They rarely receive formal training in the screening and management of these disorders

Promotion of post-stroke recovery based on stem and reprogrammed cells

Zaal Kokaia, PhD
Professor, Lund University Stem Cell Center, Lund, Sweden
Zaal.Kokaia@med.lu.se

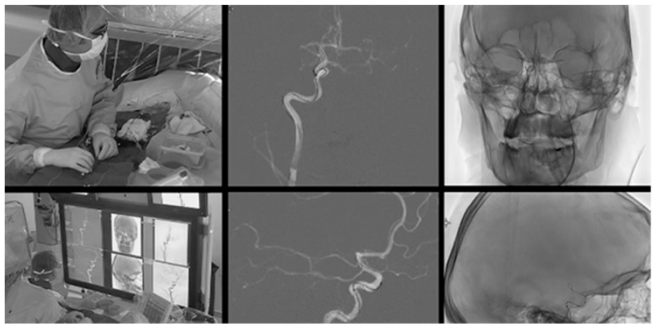
In recent years, the recovery phase of stroke attracted much of the attention of researchers and clinicians, and currently is considered as most suitable target for the stroke therapy. This is justified by the long-term therapeutic window and also intrinsic plasticity-based mechanism of recovery which is operating in the brain and represents suitable target of the therapy. Cells from different sources have been tested for their ability to reconstruct the forebrain and improve function after transplantation in animals subjected to stroke.

We have recently shown improved functional recovery after transplantation of human reprogrammed induced pluripotent stem cells (iPSC)-derived cortical neuronal precursors in a rat model of cortical stroke. In our recent study, we used a rabies virus (RV)-based strategy to explore whether host cells can establish functional synaptic connections with transplanted cells. Two or five months after transplantation of modified lt-NES cells in a rat stroke model, we injected the RV in the location of the graft. Expression of TVA receptor in the mature neurons (synapsin I+) generated from grafted cells makes them suitable for infection with the RV. The presence of Rabies-G glycoprotein in these cells allows the virus to infect the cells that connect to them by functional synapses. Therefore, grafted and infected cells will express nuclear GFP and cytoplasmic RFP while the ones connected to them will only present RFP in the cytoplasm.

Immunohistochemical analysis of injured and transplanted brains one week after the infection with RV revealed the presence of RFP+ neurons in different areas, some of them located far away from the implantation site. Using electrophysiological recordings *in vivo* and optogenetics in brain slices recordings combined with patch-clamp we demonstrated, for the first time, that intracortical grafts of human iPSC-derived cortical neurons establish functional afferent synaptic connections with stroke-injured brain and respond to peripheral sensory stimulation. We currently study how the reconstruction of stroke-lesioned network by grafted stem cell-derived neurons contribute to post-stroke recovery.

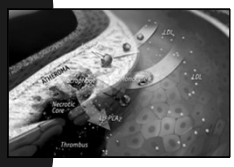
Recent papers demonstrated rapid and efficient conversion of human somatic cell to mature neurons by overexpressing transcription factor combinations. We have attempted to generate projection cortical neurons by direct reprograming of somatic cells. We demonstrated that a combination of three transcription factors convert human fibroblasts to functional excitatory cortical neurons. Single-cell analysis revealed a complex gene expression profile, a subpopulation of neurons displaying a molecular signature similar to human fetal primary cortical neurons.
Our findings indicate that functional excitatory cortical neurons, generated by reprogramming of human somatic cells is feasible and could be further developed for cell therapy strategies.

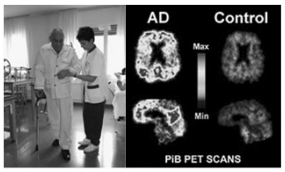
Early neurorepair approaches in acute stroke: what direction should we move to?



JERZY KRUPINSKI M.D.,PhD.,Ds.C. (UK)
DEPARTMENT OF NEUROLOGY, HOSPITAL UNIVERSITARI MÚTUA TERRASSA, BARCELONA, SPAIN

STROKE: TWO PROCESSES ARE LINKED





ACUTE PHASE
Reperfusion
Neuroprotection

RECOVERY
Functional and **Cognitive**
Neuroreparation

NEUROPROTECTION: WHERE ARE WE TODAY?

The heterogeneity of strokes, speed of stroke progression, uncertainty about remaining salvageable brain, enrollment windows, and the low rates of recanalization are formidable challenges to overcome in stand-alone stroke neuroprotection trials.

- numerous pharmacological and non-pharmacological strategies have been evaluated without success to limit the consequences of the ischemic cascade
- rarely the therapies were explored as add on remedies on individuals also receiving reperfusion therapies.
- these putative neuroprotectants never reached the ischemic brain in adequate concentrations

- currently, the concept of neuroprotection incorporates **cerebral perfusion** as an obligatory substrate
- previous neuroprotection trials might have resulted in more favorable results if reperfusion therapies had been co-administered. pharmacological or mechanical thrombectomy are frequently powerless to fully reperfuse the ischemic brain despite achieving a high rate of recanalization.
- the importance of the microcirculation

3

HOW EFFICACIOUS IS ACUTE STROKE TREATMENT IN TERMS OF NEUROPROTECTION?

We agree that (1): stroke neuroprotection is how to maximize the rate of brain reperfusion

- The efficacy and safety of IA vs. IV in patients with AIS has been assessed in a meta-analysis that showed that IA in patients with AIS was significantly more likely to result in a favourable outcome than was IV thrombolysis. However, meta-analyses using different study selection criteria found no significant benefit of IA over IV thrombolysis. Altogether, IA initiated within 6 h of stroke onset might be considered in carefully selected patients who have contraindications to the use of IV alteplase
- Arterial recanalization after IS is associated with a 4- to 5-fold increase in the odds of good long-term functional outcome and a 4- to 5-fold reduction in the odds of death. However, one out of four patients do not reperfuse despite complete recanalization, and one out of two develop full infarctions on regions previously hyperperfused, highlighting the essential role of adequate **brain perfusion** for the final ischemic tissue fate. In recent randomized controlled trials, less than half of patients treated with MT improved stroke outcomes regardless that three out of four had full recanalization.
- Only 38% of the patients obtained full reperfusion after MT, suggesting that the mismatch between complete recanalization and incomplete reperfusion explained the suboptimal efficacy of MT

We agree that (2): penumbra alone does not predict functional outcome unless the reperfusion status is also taken into account

We agree that (3): because only 50% recover after tr, there must other approach although we maybe very much against the neuroprotection

4

HOWEVER,

In the prospective DEFUSE 2 study, target mismatch patients (defined in the prespecifi ed criteria) who had early reperfusion after endovascular thrombectomy had more favourable clinical outcomes , whereas no association between reperfusion and favourable outcomes was noted in patients without target mismatch.

In the EXTEND-IA trial, evidence of salvageable brain tissue and an ischaemic core of less tan 70 mL on CT perfusion imaging was associated with improved reperfusion, early neurological recovery, an improved functional outcome after MT.

Conversely, no differential benefit was reported in patients with a favourable penumbral pattern of substantial salvageable tissue and small infarct core, as compared with those with a non-penumbral pattern, in the MR-RESCUE trial

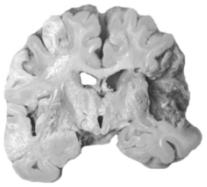
5

2018 GUIDELINES FOR THE EARLY MANAGMENT OF PATIENTS WITH AIS

(*Stroke*. 2018;49:509-510.
DOI: 10.1161/STROKEAHA.118.020176.)

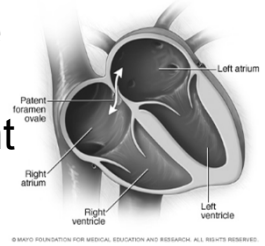
Improvement in selected areas:

- Stroke systems of care
- Imaging
- Thrombectomy elegibility
- Postprocedure managment
- Secondary prevention



Patent Foramen Ovale

Management to Prevent Recurrent Stroke



WSO-ESO Intl. Stroke Meeting, Tiblisi, 28th Sept. 2018

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Heinrich Mattle

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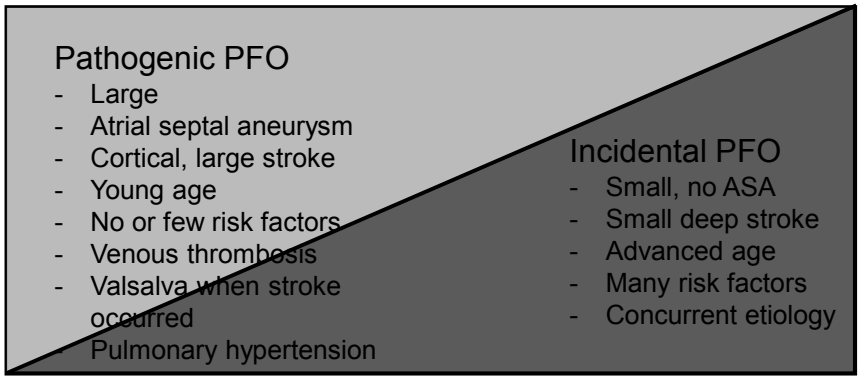
Neurochirugie
Neurologie
Neuropädiatrie
Neuroradiologie
Psychiatrie

Conclusions from randomized trials

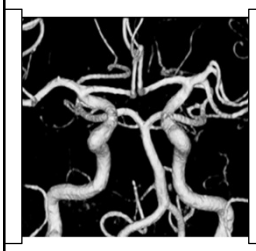
- PFO closure after stroke or TIA in patients < 60 years provides protection from recurrent stroke
- There is no bleeding hazard
- Atrial fibrillation is increased after PFO closure. Clinical significance uncertain.

Pathogenic versus incidental PFO



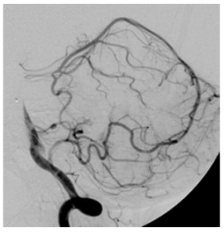
Conclusions on PFO-Closure

PFO as / in	Medical treatment	Device closure
Incidental finding	No	No
Cryptogenic stroke in the young	Yes	Yes
Stroke with concurrent etiology	Yes	Probably not
Stroke and many risk factors / PFO ± ASA	Yes	Balance PFO risk factors for decision



Basilar artery occlusion

Diagnosis and Treatment



WSO / ESO Stroke Intl. Meeting, Tiblisi, 29. Sept. 2018

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Heinrich Mattle

Neuro-Center, University Department of Neurology

BAO: Pathogenesis

- Atherosclerosis and local thrombosis
- Emboli to the VA and BA
- VA dissection
- Other rare causes

BAO: Clinical presentation

- Highly variable, any combination of
- Complete or partial brainstem strokes
  - paramedian artery stroke
  - short and long circumferential artery strokes
- Cerebellar stroke
- Thalamic stroke
- Temporal and occipital lobar strokes

BAO: Clinical presentation

- Prodromal symptoms and signs
  - headache, vertigo, „seizures“
- Main symptoms and signs
  - coma, tetraplegia, brainstem reflexes absent
  - locked-in syndrome
  - top of the basilar syndrome

BAO: Summary

- BAO can be devastating
- Often prodromal symptoms and signs
  – headache, vertigo, „seizures“
- Main symptoms and signs
  – coma, tetraplegia, asymmetric pupils, brainstem reflexes absent
- IVT and MT are effective
- Best treatment unknown
  – mechanical thrombectomy after IVT when indicated ?

Suggested reading

Kubik CS, Adams RD. Occlusion of the basilar artery. Brain 1946; 69: 73-121

Caplan LR. „Top of the basilar“ syndrome. Neurology 1980; 30: 72-9

Mattle HP, Arnold M, Lindsberg P, Schonewille W, Schroth G. Basilar artery occlusion. Lancet Neurology 2011; 10: 1002-14

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Best practice stroke care: a success story
Experience from the Czech Republic

Robert Mikulík, MD, PhD,

Department of Neurology of St. Anne's University Hospital and Medical Faculty of Masaryk University, Brno, Czech Republic

	Czech Republic	Georgia
Population	10 mil	3,7 mil
Area	78 800 sq km	69 700 sq km
Density	134/sq km	53/sq km
GDP per capita	22 000 USD	4000 USD

wikipedia

How did we implemented the evidence-based stroke treatments?

- Rule 1: leadership
- Rule 2: guidelines

At this point, for every stroke patient exist:

- EMS priority
- Arrival time < 20 minutes
- Transportation to the nearest stroke center
- Stroke center equipped (certified)
- Evidence-based treatment supported by national guidelines
- No special motivation for physician to treat or not to treat patients with thrombolysis

How did we implemented the evidence-based stroke treatments

- Rule 1: Leadership
- Rule 2: Guidelines
- Rule 3: Collection of the data + analysis
- Rule 4: Collaboration with stakeholders
- Rule 5: Measurement of all important quality/ performance indicators + feedback – ultimate tool to make sure that patients receive evidence-based treatments

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Thank you for your attention!

Contact:
mikulik@hotmail.com

St. Anne's University Hospital Brno
International Clinical Research Center
Pekařská 53
656 91 Brno, Czech Republic
Phone: + 420 734 415 887

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STROKE PREVENTION IN CAROTID AHEROSCLEROSIS

Zurab Nadareishvili, MD, PhD;

Department of Neurology,
The George Washington University, MFA,
Washington, DC;
Stroke Center, Virginia Hospital Center,
Arlington, VA;

AHA/ASA GUIDELINES

CAS is an alternative to CEA for symptomatic patients with ICA stenosis >70% by noninvasive imaging or >50% by catheter-based imaging or noninvasive imaging with corroboration and the anticipated rate of periprocedural stroke or death is <6% (Class IIa; Level of Evidence B).

Kernan WN, Ovbiagele B, Black HR et al. Stroke. 2014;45:00.

AHA/ASA Guidelines

It is reasonable to consider performing CEA in ACS >70% stenosis of the ICA if the risk of perioperative stroke, MI, and death is low (<3%). However, its effectiveness compared with contemporary best medical management alone is not well established (Class IIa; Level of Evidence A).

Prophylactic CAS might be considered in highly selected patients with ACS (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established (Class IIb; Level of Evidence B).

Meschia JF et al. Stroke. 2014;45:00-00

Conclusions

CEA is the preferred treatment for most patients with symptomatic carotid stenosis > 50%, except women with 50-69% stenosis

The benefit of revascularization in ACS is questionable because of low risk of stroke on medical therapy

In ACS noninvasive diagnostics may identify population at higher risk of stroke who might benefit from carotid revascularization

Embolic Stroke of Undetermined Source (**ESUS**)

George Ntaios

University of Thessaly, Larissa/Greece

Hellenic Stroke Organization

ESO EUROPEAN STROKE ORGANISATION

ESUS: Potential causes

Covert Atrial Fibrillation

Cancer associated

- Covert non-bacterial thrombotic endocarditis
- Tumour emboli from occult cancer

Arteriogenic emboli

- Aortic arch atherosclerotic plaques
- Cerebral artery non-stenotic plaques with ulceration

Paradoxical embolism

- Patent foramen ovale
- Atrial septal defect
- Pulmonary arteriovenous fistula

Minor-risk potential cardioembolic sources

Mitral or Aortic valve

- Myxomatous valvulopathy with prolapse
- Mitral annular calcification
- Aortic valve stenosis or Calcific aortic valve

Non-AF atrial dysrhythmias and stasis

- Atrial asystole and sick-sinus syndrome
- Atrial high-rate episodes
- Atrial appendage stasis with reduced flow velocities or spontaneous echodensities

Atrial structural abnormalities

- Atrial septal aneurysm or Chiari network

Left ventricle

- Moderate systolic or diastolic dysfunction (global or regional)
- Ventricular non-compaction or Endomyocardial fibrosis

Hart, Diener, Conollly, et al. Lancet Neurol. 2014

What if RESPECT-ESUS is positive – do we still need ECG monitoring?

Current recommendations

For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (~30 days) for AF is reasonable within 6 months of the index event *(Class IIa; Level of Evidence C)*

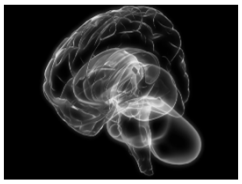
Kernan, *et al. Stroke* 2014

Facts & open questions

ESUS patients are:
- frequent
- younger than AF-stroke patients
- milder strokes than AF-strokes
- high recurrence rate (mostly on antiplatelets)

Antiplatelets or anticoagulants for ESUS patients?

AF is frequently detected after ESUS
Causally related or not?
(How) can we know?
How long should we monitor ECG in ESUS patients?
- now?
- if RESPECT-ESUS is positive?



Prof. Serefnur Ozturk
Selcuk University Faculty of Medicine
Department of Neurology
President of Turkish Neurological Society

STROKE BURDEN AND INCREASING RISK FACTORS

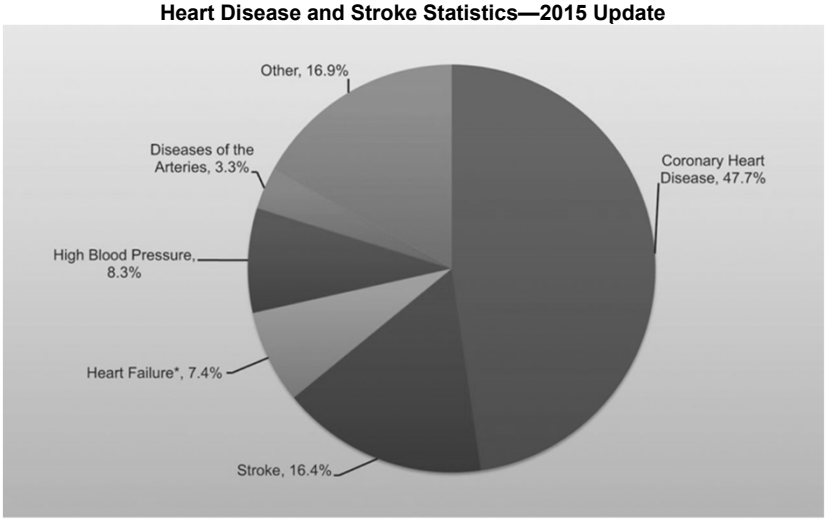
Global Vascular Risk Burden

VASCULAR DISEASE
STROKE, MI, PAD, VASCULAR DEATH

2002: 16.7 MILLION DEATHS
2005: 17.4 MILLION DEATHS
2010: 18.1 MILLION DEATHS
5.9M deaths from Stroke
Second leading cause of death over age 60
Second leading cause of disability
after dementia

Percentage breakdown of deaths attributable to cardiovascular disease (United States: 2011)

Heart Disease and Stroke Statistics—2015 Update



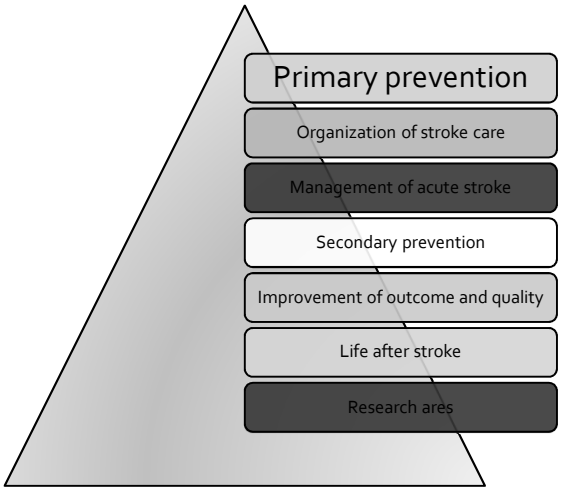
Mozaffarian D et al. Circulation. 2015;131:e29-e322

American Heart Association.

General targets for 2030

- To reduce the absolute number of strokes in Europe by 10%
- To treat 90 % or more of all patients with stroke in Europe in a dedicated stroke unit as the first level of care
- To have national plans for stroke encompassing the entire chain of care from primary prevention to life after stroke.
- To fully implement national strategies for multisector public health interventions to promote and facilitate a healthy lifestyle, and reduce environmental (including air pollution), socioeconomic and educational factors that increase the risk of stroke.

30 targets in 30 areas- 72 research area



MANAGEMENT OF ACUTE STROKE

- Treating 90 % or more of all patients with stroke in Europe in a stroke unit as the first level of care.
- Guaranteeing access to recanalisation therapies to 95% of eligible patients across Europe.
- Decreasing median onset-to-needle times to <120 minutes for intravenous thrombolysis and onset-to-reperfusion times to <200 minutes for endovascular treatment.
- Achieving IVT rates above 15%, and EVT rates above 5%, in all European countries
- Decreasing first-month case-fatality rates to <25% for ICH and SAH, and increasing the rate of good functional outcomes to >50%.

SECONDARY PREVENTION

- Including secondary prevention in national stroke plans with follow-up in primary/community care
- Ensuring that at least 90% of the stroke population is seen by a stroke specialist and have access to secondary prevention management (investigation and treatment)

- Ensure access to key investigational modalities: CT (or MR) scanning, carotid ultrasound, ECG, 24-hour ECG, echocardiography (transthoracic and transoesophageal), blood tests (lipids, glucose, HbA_{1c}, coagulation, erythrocyte sedimentation rate, C-reactive protein, autoantibodies)
- Ensuring access to key preventative strategies: lifestyle advice, antihypertensives, lipid lowering agents, antiplatelets, anticoagulants, oral hypoglycaemic agents and insulin, carotid endarterectomy, and PFO closure.

Clot morphology in acute occlusive stroke

Bartlomiej Piechowski-Jozwiak, M.D.

Staff Neurologist,Cleveland Clinic Abu Dhabi

Clinical Associate Professor of Medicine

Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

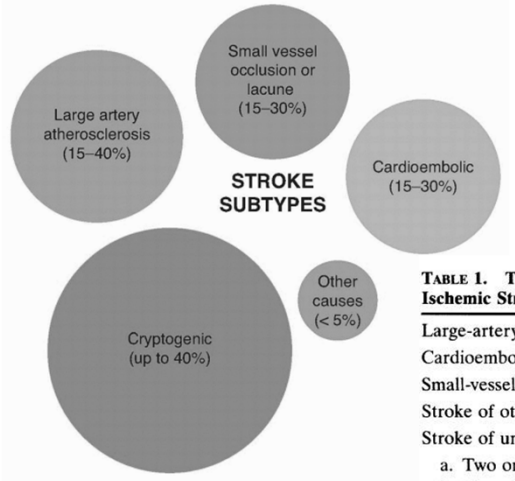


TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke

Large-artery atherosclerosis (embolus/thrombosis)*
Cardioembolism (high-risk/medium-risk)*
Small-vessel occlusion (lacune)*
Stroke of other determined etiology*
Stroke of undetermined etiology
a. Two or more causes identified
b. Negative evaluation
c. Incomplete evaluation

TOAST, Trial of Org 10172 in Acute Stroke Treatment.
*Possible or probable depending on results of ancillary studies.

The ASCOD Phenotyping of Ischemic Stroke (Updated ASCO Phenotyping)

P. Amarenco[a] J. Bogousslavsky[b] L.R. Caplan[c] G.A. Donnan[d] M.E. Wolf[e] M.G. Hennerici[e]

Diagnosis

- Stroke due to embolism of R-MCA
- CTA negative, vasculitis negative
- TTE:
  - Severe mitral valve stenosis
  - Pulmonary hypertension, moderate to severe
  - Moderate aortic regurgitation
  - Rheumatic heart valve stenosis with incompetence
  - Left atrial dilatation
- NIHSS 0

- Clot pathology adding to stroke etiology and classification
- Confounders:
  - Effects of previous preventative treatment
  - Comorbidities, blood rheology
  - Effects of tPA
  - Mechanical changes:
    - Impaction of material in the vessel
    - Manipulation during thrombectomy (number of passes)
  - Absence of material

Neurosonology Role for Patients with CVD and Acute Stroke

Alexander Razumovsky, PhD, FAHA

.

7th WSO REGIONAL MEETING

TBILISI 2018: STROKE PREVENTION, DIAGNOSIS AND TREATMENT

Sept. 28, 2018

What Neurosonology service could achieve for patients with cerebral ischemia

- Immediate bed-side results in ER, OR, Recovery Room, ICU or hospital ward
- Provides accurate CBFV information for determination of disease severity
- Detects even minimal cerebral hemodynamic changes
- Detects emboli
- Ideal tool for following disease progression, therapeutic, radiological, surgical or endovascular revascularization, stages of recovery and long-term therapeutic effects

TCD and Stroke Prevention, Diagnosis and Treatment

- TCD is the only non-invasive examination that provides a reliable evaluation of intracranial blood flow patterns in real-time, adding physiological information to the anatomical information obtained from other neuroimaging modalities
- TCD is relatively cheap, can be performed bedside, and allows monitoring both in acute emergency settings as well as for prolonged periods with a high temporal resolution making it ideal for studying dynamic cerebrovascular responses
- Extended applications of TCD in enhancing i/v thrombolysis in acute stroke, emboli monitoring, right-to-left shunt detection and vasomotor reactivity provide important information about the pathophysiology of cerebrovascular ischemia

TCD and Stroke Prevention, Diagnosis and Treatment

- In acute cerebral ischemia, TCD is capable of providing rapid information about the hemodynamic status of the cerebral circulation, monitoring recanalization in real-time with a potential for enhancing tPA induced thrombolysis
- Advanced applications of TCD make it an important and valuable tool for evaluating stroke mechanisms, plan and monitor treatment and determine prognosis
- *TCD has an established clinical value in the diagnostic workup of stroke patients and must be an essential component of a comprehensive stroke center*

Ischemic stroke in the young

7th World Stroke Organization Regional Meeting
Tbilisi, Georgia – September 28, 2018

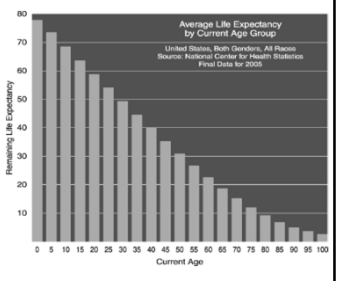
Turgut Tatlisumak, MD, PhD

Dept. of Clinical Neuroscience, Inst. Neuroscience & Physiology, Sahlgrenska Academy at Univ. Gothenburg and

Dept. Neurol. Sahlgrenska Univ. Hospital, Gothenburg, Sweden

Why concept of stroke in young adults?

① Etiology of stroke is extremely diverse in the young as common causes in the elderly, such as large-artery atherosclerosis or atrial fibrillation, are rare.
② Similarly, risk factors differ considerably in young adults compared to those seen in older individuals.
③ Young stroke patients are at their most productive age and usually have under-aged children in their custody—the stroke may thus cause marked long-term socio-economic consequences.
④ Genetic causes may be underlying stroke more frequently in the young than do in the elderly patients, indicating a need for genetic counseling.
⑤ Efficient acute treatment and prevention of stroke in a young adult increases number of quality-weighted life years much more than in elderly patients.
⑥ 5% of all strokes occur in individuals under 45, 10% in those under 50, and ¼ occur in working-age individuals
⑦ Ischemic stroke among young people is increasing while incidence is decreasing in older patients
⑧ Who is actually young ???



Epidemiology of IS in the young

- 3.7% of all stroke patients admitted to hospital in 1981 were 15 to 45 years of age in the USA (Robbins and Baum, Stroke 1981)
- 8% of all stroke cases were 20-44 y in the Northern Manhattan Study over a 4-year period (Jacobs et al, Stroke 2002)
- 2007 Nationwide Inpatient Sample from the USA: 4.9% were 18-44 y with 5% mortality (Ellis C, Disability & Health J 2010)
- ~5% of all strokes occurred in adult subjects under 45 years of age in western countries (Nencini et al, Stroke 1998), higher proportions were reported in developing countries (Radhakristan et al, Acta Neurol Scand 1986; Al Rajeh et al, Cerebrovasc Dis 2002)
- ~10% of all ischemic strokes occur below the age of 50 years (Putaala et al, Stroke 2009)
- Strokes in young adults (<45 y) accounted for 2% of all first-ever strokes in a community-based Italian study (Marini et al, Stroke 2001), 6% of all ischemic strokes admitted to hospitals in Germany (Grau et al, Stroke 2001), and 11% of all consecutive ischemic stroke patients in two centers in Switzerland (Nedeltchev et al, JNNP 2005)
- IS in the young occurs ~13 cases per 100 000 inhabitants per year. Approx. 5% of all IS occur in adults under 45 years, 10% occur in adults under 50 years, and 25% occur in working-age individuals.

Ethnicity and geography

Sickle-cell anemia and thalassemia more common in individuals of African origin or from Mediterranean countries

Chagas and neurocysticercosis are common in Latin America

HIV is a common cause in Sub-Saharan countries

Moyamoya, Takayasu, Kawasaki, and intracranial atherosclerosis are more common among Asians

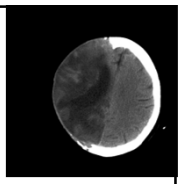
Behcet's disease is more common among Turks, Greeks, and Japanese (and along the Silk Road)

Illicit drug use is prevalent in metropolitan (urban) living areas

Young black and Hispanic Americans + people in developing countries have higher stroke rates

Yesilot N, Putaala J, Bahar SZ, Tatlisumak T. Ethnic and geographical differences in ischaemic stroke among young adults. Current Vascular Pharmacology 2017;15:416-429

Acute Treatment



- Treatment approaches are not specifically investigated in young patients in a randomized fashion and randomized stroke trials included few young patients
- Intravenous thrombolysis is safe and effective (save a minute, save 3 days)
- Intra-arterial treatment (thrombolysis + thrombectomy) is safe and effective (save a minute, save 1 week)
- Rare diseases should be treated according to their own protocols (e.g. enzyme replacements, cortison)
- There is a large gap of knowledge in most esp. rare conditions
- It is worth being more aggressive

Conclusions

- ❑ Ischemic stroke in young adults is not uncommon
- ❑ All young IS patients should be referred to comprehensive stroke centers
- ❑ Proper examinations should aim at mapping risk factors and deciphering the cause
- ❑ Acute and preventive treatments are highly effective and safe
- ❑ Predictors of mortality, recurrence, and poor functional outcome include expected general risk factors and comorbidities. Adequate treatments may improve long-term outcomes.
- ❑ The outcomes are not benign with frequent long-term disability.

Stroke chain of recovery: organizing regional stroke pathways

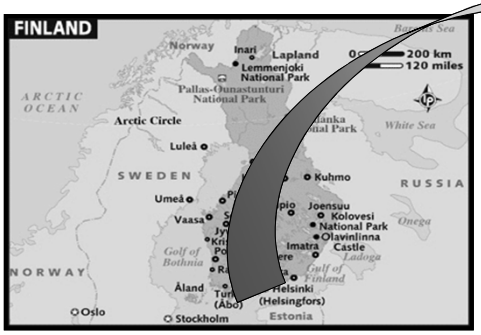
7th World Stroke Organization Regional Meeting
Tbilisi, Georgia – September 29, 2018

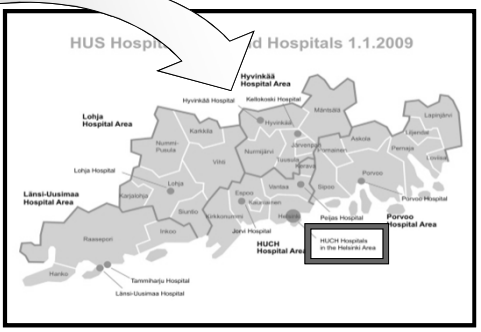
Turgut Tatlisumak, MD, PhD

Dept. of Clinical Neuroscience, Inst. Neuroscience & Physiology,
Sahlgrenska Academy at Univ. Gothenburg and
Dept. Neurol. Sahlgrenska Univ. Hospital
Gothenburg, Sweden

Background

- Department of Neurology, Helsinki University Central Hospital
- The only neurological emergency unit for a population of 1.6 millions (CENTRALIZED)
- Annually 1200 patients with ischemic stroke, 250 with intracerebral hemorrhage, and 500 with transient ischemic attack





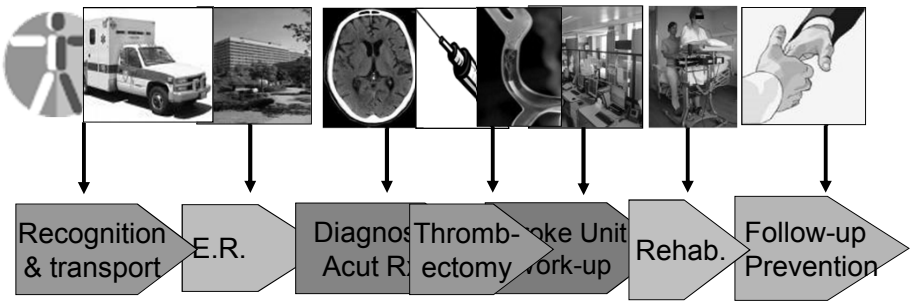
HELSINGIN YLIOPISTO
HELSINGFORS UNIVERSITET
UNIVERSITY OF HELSINKI

HUS

Why do we need to improve stroke care systems?

Because, we finally are having a number of highly efficacious treatments, but they are all time-sensitive…And, this is NOT only about official time frames of 4.5 h for IVT or 6 h of EVT, but every minute counts

Stroke: the new « Chain of survival »



How to organize stroke services within your region with the setting of 1 university hospital (comprehensive stroke center), several satellite hospitals (primary stroke centers), and hospitals not capable of giving acute stroke treatments?

- A) centralize everything
- B) decentralize everything
- C) take a hybrid approach
- D) it is not known which approach is superior
- E) I do not bother giving a thought to that

NIH-recommended Emergency Department Response Times

DNT ≤ 60 min: the "golden hour" for evaluating and treating acute stroke

T=0
Suspected stroke patient arrives at stroke unit

≤10 min
Initial MD evaluation (including patient history, lab work initiation, & NIHSS)

IDEALLY performed prehospital

≤ 15 min
Stroke team notified (including neurological expertise)

≤ 25 min
CT scan initiated

≤ 45 min
CT & labs interpreted

≤ 60 min
rt-PA given if patient is eligible

NINDS NIH website. Stroke proceedings. Latest update 2008.

Intracerebral hemorrhage in patients on oral anticoagulation therapy

Alexander Tsiskaridze, MD, PhD, DSc, FESO
Department of Neurology and Neurosurgery
Tbilisi State University
Tbilisi, Georgia

Oral anticoagulant therapy (OAT)

Vitamin K antagonists (VKAs): coumadin (warfarin), acenocoumarol, phenprocoumon

Direct oral antiacoagulants (DOAC): direct thrombin inhibitor – dabigatran; direct FXa inhibitors – apixaban, rivaroxaban, edoxaban

Main indications:

- Prophylaxis of thromboembolism:
  - cardiac (AF, valve disease, heart failure, cardiomyopathy, prosthetic valves, myocardial infarction)
  - venous
- Critical limb ischemia
- Recurrent thrombosis

Hirsh et al. Chest 2001;119:8S-21S; Wysowsky et al. Arch Intern Med. 2007;167:1414-1419; Ansell et al. Chest 2008;133:160S-198S.

Take home messages…

- Intracerebral hemorrhage is not rare in patients on oral anticoagulants
- Risk of cerebral bleeding is high with VKAs and parallels intensity of anticoagulation; it remains higher also with DOACs
- Advanced age, race, hypertension, prior CVD, intensity of anticoagulation, cerebral microbleeds and comcomitant antiplatelet use are risk factors for OAT-ICH

Take home messages…

- Onset of focal signs (eg, hemiparesis, aphasia, ataxia) with or without headache, nausea and vomiting, obtundation, or confusion in anticoagulated patients warrants urgent evaluation for intracranial bleeding
- OAT-ICH is characterized by larger initial hematoma volume, prolonged expansion (for 24h or more), and more unfavorable outcome
- Potentially modifiable predictors of unfavorable outcome of OAT-ICH are anticoagulation intensity and hematoma expansion

Take home messages…

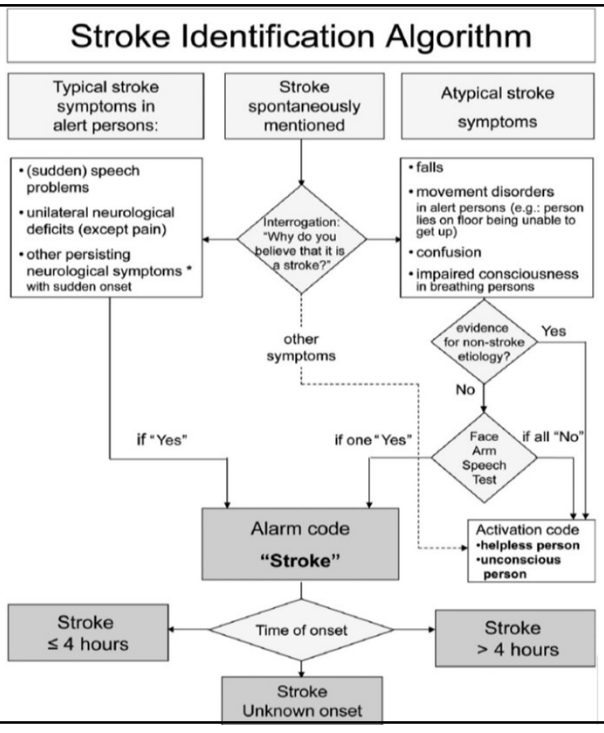
- Immediate (within 4hrs) anticoagulation reversal together with achieving systolic BP<160mm Hg aiming at stopping the hematoma expansion is a mainstream of OAT-ICH management
- Reversal is done by cessation of OAT, intravenous vitamin K (if VKAs used) with 4-factor PCC (preferably); for DOACs – activated charcoal (if last dose <2 hrs), PCC/aPCC; Praxbind® for dabigatran, AndexXa® for others
- Other treatments include: general supportive care (ABC, fluids, electrolytes, ICP, BP management, prevention of complications), surgery (selected cases of ICH)

Take home messages…

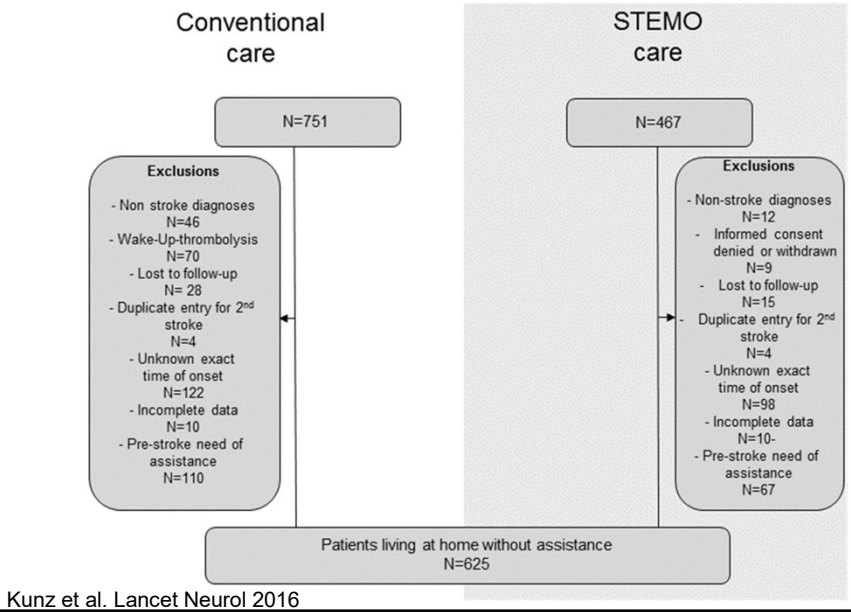
- Before resuming anticoagulation after OAT-associated intracerebral hemorrhage consider the risk of rebleeding vs. the risk of thromboembolism
- The low bleeding risk patients with moderate or high risk of disabling thromboembolism definitely benefit from restarting OAT
- Available evidence shows that OAT can be safely restarted at 1 month in AF patients with low to moderate bleeding risk

Prehospital stroke management in the era of thrombectomy

Heinrich J Audebert
Center for Stroke Research Berlin
Charité Universitätsmedizin Berlin / Germany



Registry comparison



Kunz et al. Lancet Neurol 2016

Prehospital

Summary and conclusions

Prehospital research offers new potentials

- Very short time to treatment
- Variety of target populations and research questions
  - Hemorrhagic stroke
  - Biomarker research
  - Prehospital triage (➔ Wake-Up, intra-arterial treatment)
- Clinical and cost effectiveness of MSUs under investigation in 2 large RCTs

Brain Center
Rudolf Magnus

Space-occupying brain infarction

H. Bart van der Worp

University Medical Center Utrecht

18 – 60 years	≤ 48 hours

Recommendation

We recommend surgical decompression in selected adult patients ≤ 60 years with a diagnosis of space-occupying hemispheric infarction if surgery can be performed within 48 hours of stroke onset, irrespective of the presence of aphasia.

ESO guideline, in preparation

18 – 60 years	> 48 hours

Recommendation

There is insufficient evidence to recommend surgical decompression … if treatment can be started only after 48 hours of stroke onset. However, surgical decompression may be considered in selected cases.

ESO guideline, in preparation

≥ 61 years	≤ 48 hours

Recommendation

In previously independent patients ≥ 61 years who can be treated ≤ 48 hours of stroke onset, surgical decompression may be considered but should only be performed or withheld after a careful discussion with the patient and/or his/her representatives about the high risk of survival with very substantial disability.

Conclusion

Most patients aged 18 – 60 years who have survived severe space-occupying MCA infarction consider their QoL on the long term acceptable.

conclusion

Decompressive surgery might be of benefit in patients with life-threatening space-occupying (haemorrhagic) infarcts caused by cerebral venous sinus thrombosis.

Recommendation

We recommend using decompressive surgery for patients with acute CVST and parenchymal lesion(s) with impending herniation to prevent death.

Ferro 2017 - ESO guideline CVST

Recommendation

Surgical decompression ± CSF drainage may be considered in some patients with space-occupying cerebellar infarction without significant brain stem infarction, but the selection of patients and the timing of treatment remain uncertain. There is insufficient evidence to support its routine use.

Recommendation

CSF drainage alone may be considered in some patients with space-occupying cerebellar infarction and an obstructive hydrocephalus but without significant brain stem compression, but the selection of patients and the timing of treatment remain uncertain.

Recommendation - MRI

MRI with DWI within <6 hours of stroke onset may be used to select patients at high risk of life-threatening oedema formation.

Recommendation

We recommend to consider surgical decompression in patients with:

- DWI lesion volume > 82 mL ≤ 6 h OR
- a combination of:
  - severe focal neurological deficit
  - reduction in consciousness
  - space-occupying infarct ≥ 2/3 MCA
- no signs of irreversible brain stem damage
- treatment possible ≤ 48 hours

Recommendation

Patients in whom the decision to perform surgery is delayed but in whom this is still an option should be monitored closely in an experienced stroke centre with the capacity to perform surgical decompression.

TIA and the risk of subsequent stroke

Daniel Bereczki
Department of Neurology
Semmelweis University
Budapest, HUNGARY

TIA :

practical clinical definitions in everyday clinical practice

- **TIA**: transient ischemic attack.
  - Reversible ischemic injury of the brain.
  - Patient usually has already no signs on examination, we have to rely on history.
  - We have no proof, diagnosis remains an assumption

TIA and ischemic stroke

- A 24-hour limit for transiently symptomatic cerebral ischemic is arbitrary and not reflective of the typical duration of these events.
- Disease definitions in clinical medicine, including those for ischemic injuries, are most useful when tissue based.
- The phrase “typically <1 hour” in the new (i.e. 2002) definition is not helpful because the 1-hour time point, like the 24-hour time point, does not accurately distinguish between patients with or without acute cerebral infarction.
- **Transient ischemic attack (TIA): a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.**
- **Based on the new definitions of TIA, an ischemic stroke is defined as an infarction of central nervous system tissue.**

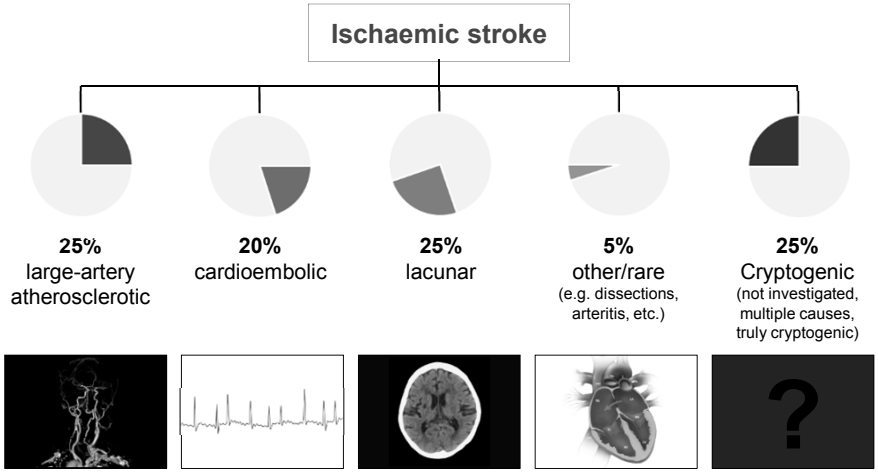
TIA - conclusions

- Definition based on tissue injury rather than duration of clinical signs.
- Stroke follows TIA more frequently than generally thought.
- Stroke risk after TIA can be stratified by traditional stroke risk factors and clinical features.
- TIA needs urgent medical attention!!!!

Secondary stroke prevention - Update

Prof. Natan M. Bornstein M.D.
Director of Brain Division,
Shaare Zedek Medical Center, Jerusalem
Chairman of the Israeli Neurological Association
Vice President of the WSO
natanb@szmc.org.il

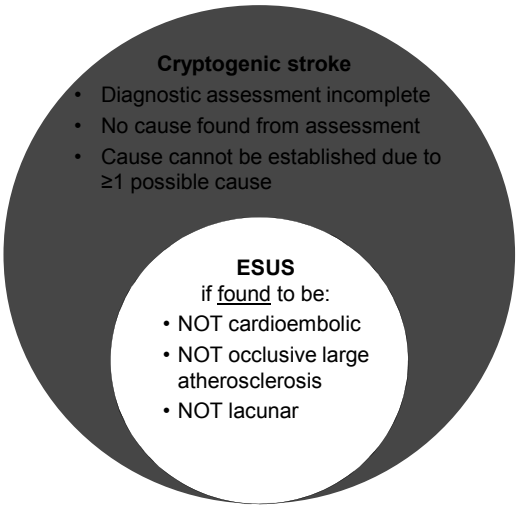
TOAST classification of acute ischaemic stroke subtypes



Adams et al. Stroke 1993; Hart et al. Lancet Neurol 2014
TOAST, Trial of ORG 10172 in Acute Stroke Treatment

2

ESUS is a subset of cryptogenic stroke



The dominant underlying mechanism of cryptogenic stroke is likely an embolism from an unestablished source

ESUS is a non-lacunar brain infarct without large artery stenosis or cardioembolic sources

ESUS, embolic stroke of undetermined source
Hart et al. Lancet Neurol 2014

3

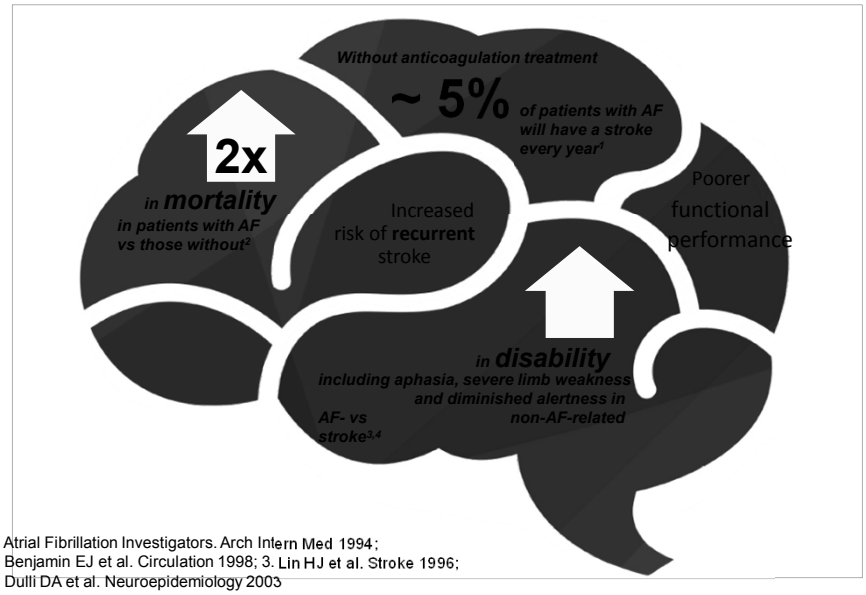
Summary

- Stroke is largely a preventable disease.
- Aggressive risk factor management is important.
- All antiplatelets have almost similar efficacy with marginal benefit of clopidogrel or ASA+DP over aspirin
- “Polypill concept” is yet to be proven for routine use.

Current practice in NVAF patients
Which NOAC to whom?

Prof. Natan M. Bornstein M.D.
Director of Brain Division,
Shaare Zedek Medical Center, Jerusalem
Chairman of the Israeli Neurological Association
Vice President of the WSO
natanb@szmc.org.il

Patients with AF are at increased risk of stroke and related complications if not appropriately anticoagulated



1. Atrial Fibrillation Investigators. Arch Intern Med 1994;
2. Benjamin EJ et al. Circulation 1998; 3. Lin HJ et al. Stroke 1996;
4. Dulli DA et al. Neuroepidemiology 2003

Guidelines support individualized treatment and care for patients with AF

'The guidelines do not…override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient…'

EUROPEAN SOCIETY OF CARDIOLOGY®

'Individuals require a personalized package of care and information'

NICE

'…antithrombotic therapy should be individualized based on shared decision making after discussion of the absolute and RRs of stroke and bleeding, and the patient's values and preferences'

American Heart Association. Learn and Live

AF, atrial fibrillation; NICE, National Institute for Health and Care Excellence; RR, relative risk
Camm et al. Eur Heart J 2012; Atrial fibrillation: the management of atrial fibrillation; available at: http://guidance.nice.org.uk/CG180; January et al. J Am Coll Cardiol 2014

Conclusion 4

- In cases of high risk of ischemic stroke (CHADS2) and moderate risk of cerebral bleeding NOACs are clearly preferred over warfarin
- Re-initiation of oral anticoagulation after 4-8 weeks
- Safety data from prospective registries needed

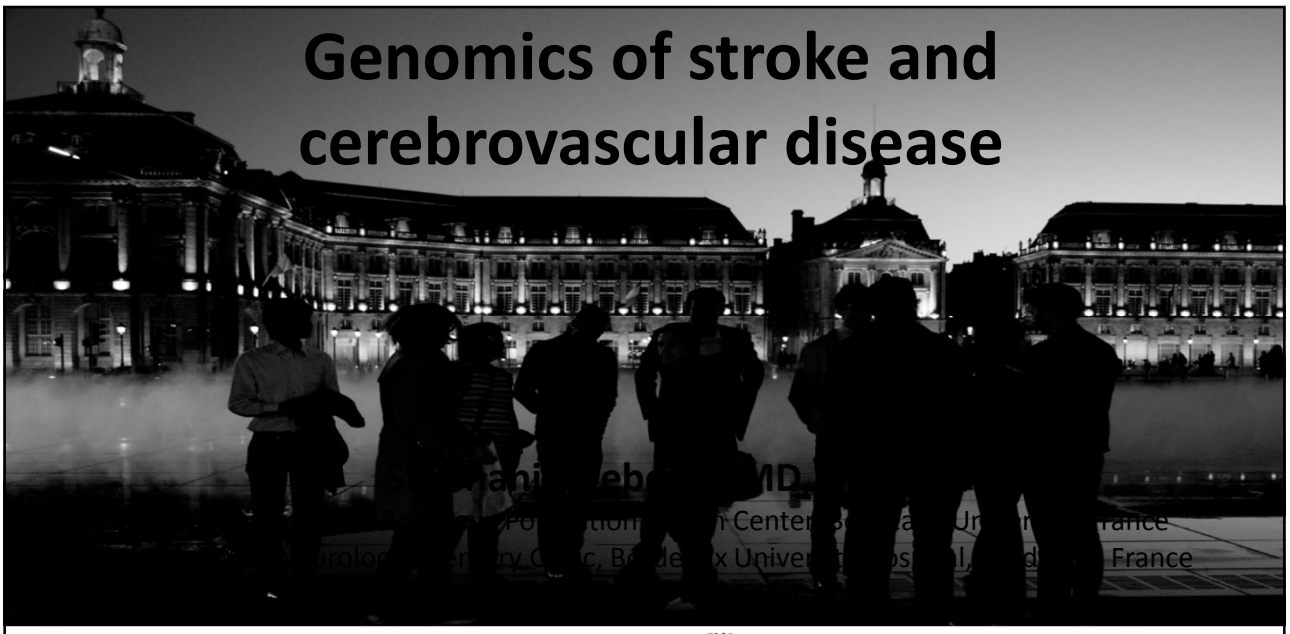
Conclusion

- Prior GI bleed is not a contraindication for anticoagulation with NOACs, especially when the source of bleeding has been identified

Choice of OAC drug to fit the patient profile

- AF patients are a heterogeneous group
- ABCDE:
  - A=abnormally low weight (dose reduction might be needed)
  - B= bleeding risk, especially previous or recent gastrointestinal bleeding
  - C= creatinine clearance (i.e., renal function)
  - D=drug interactions (e.g., P-glycoprotein inhibitors)
  - E= elderly age (dose reduction might be needed).
- Don't add aspirin to NOAC w/o clear indication

6



Genomics of stroke and cerebrovascular disease

[redacted]

Why study the genetics of stroke

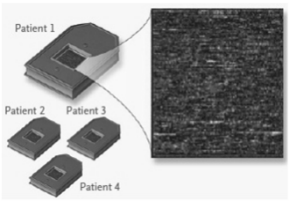
- Conventional risk factors (hypertension, diabetes, smoking, hypercholesterolemia…) explain only a fraction of stroke risk
- Compelling evidence from family studies and more recently from large GWAS that **stroke is heritable**
- Rarely monogenic (<5%)
- Genetic risk factors contribute to stroke mostly as part of **multifactorial predisposition**
  - Heritability estimates based on genome-wide genotypes: **16-40%** depending on subtype: highest for intracerebral hemorrhage

Bevan , Stroke 2012
Devan, Stroke 2013
Falcone, Lancet Neurol 2014

Genome-wide association studies (GWAS)

- Genotype a large number (up to 5,000,000) of single nucleotide polymorphisms (SNPs) distributed across the chromosomes

  →Assume **NO *a priori* hypothesis** on loci of interest



- Made possible thanks to
  - **High-throughput genotyping** technology: automated and rapid genotyping of thousands of samples, for x100,000 to millions of SNPs, using microarrays
  - **HapMap and 1000 Genomes projects** = international projects describing common patterns of genetic variation in various ethnic groups

- Revolutionized the identification of genomic regions associated with complex diseases
  - Thousands of robust associations with hundreds of complex diseases and traits

université de BORDEAUX

Summary

- Recently, the number of loci associated with stroke risk could be tripled, **despite the phenotype heterogeneity**
  - Importance of large samples, added value of the multiethnic approach
- Variants predisposing to stroke may act at **various levels**:
  - On the specific mechanism of stroke subtypes (e.g. atheroma), Upstream (e.g. genes for hypertension…), Downstream (susceptibility to vascular brain injury)
- Genetics can shed **new light on pathophysiology** of stroke and stroke subtypes
  - New avenues for therapeutic targets, « drug repositioning »….
- Genetics of **MRI-defined endophenotypes of stroke** helpful to unravel genomic determinants of cerebral small vessel disease
  - Unexpected predominance of genes involved in glial proliferative pathways

Stroke Prevention – Focus on Lifestyle Modificaation

Vida Demarin, MD, PhD

Fellow of the Croatian Academy of Sciences and Arts,
FAAN, FAHA, FESO, FEAN
International Institute for Brain Health

New AHA/ASA Guideline on Primary Stroke Prevention

- The latest iteration of the guideline, which summarizes the evidence for established and emerging stroke risk factors, is an update of the last AHA statement, published in 2011.
- Targets for stroke prevention in the new document have been "reordered" to align with the AHA's "Life's Simple" public health campaign for cardiovascular health, the authors write.

New AHA/ASA Guideline
Physical Inactivity

1. Physical activity is recommended because it is associated with a reduction in the risk of stroke (*Class I; Level of Evidence B*).

2. Healthy adults should perform at least moderate- to vigorous-intensity aerobic physical activity at least 40 min/d 3 to 4 d/wk (*Class I; Level of Evidence B*).

New AHA/ASA Guideline
Diet and Nutrition: Recommendations

- **Reduced intake of sodium and increased intake of potassium as indicated in the US Dietary Guidelines for Americans are recommended to lower BP (*Class I; Level of Evidence A*).**
- **A DASH-style diet, which emphasizes fruits, vegetables, and low-fat dairy products and reduced saturated fat, is recommended to lower BP (*Class I; Level of Evidence A*).**
- **A diet that is rich in fruits and vegetables and thereby high in potassium is beneficial and may lower the risk of stroke (*Class I; Level of Evidence B*).**
- **A Mediterranean diet supplemented with nuts may be considered in lowering (*Class IIa; Level of Evidence B*)**

EVT update 2018: what have we learned? where do we need more data?

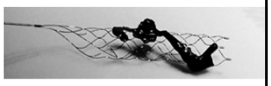
Andrew M. Demchuk MD FRCPC
Director, Calgary Stroke Program
Deputy Department Head, Dept Clinical Neurosciences
HSF Chair in Stroke Research
Professor, Depts of Clinical Neurosciences and Radiology
Cumming School of Medicine
University of Calgary

Financial/Academic Disclosure Slide

- I have not received an honorarium from Hoffman LaRoche (licensure of tPA) but have received honorarium from Medtronic (supplier of SOLITAIRE FR stentriever) for CME events
- No stocks or direct investments with pharmaceutical or device companies involved in stroke
- Shareholder Quikflo Health start-up (acute stroke software)
- Several clinical trial responsibilities:
  - ESCAPE- Neuro-PI
  - REVASCAT- CT core lab co-PI
  - ENCHANTED – International Advisory Committee
  - PRACTICE- DMC chair
  - DEFUSE 3- Safety monitor
  - ESCAPE NA-1- Neuro-PI
  - ENDO-LOW- co-PI

Endovascular Treatment

- Mechanical thrombectomy
  - Stent retriever devices
  - Aspiration devices
  - Combination approaches



- Extracranial carotid intervention
- Intracranial stenosis intervention
- Intra-arterial drug delivery (tPA)

Endovascular treatment around the edges of EBM

	Endo "sweet spot"	Endo modest net benefit	No endo tx
Time from onset	**<150 min**	**150-240 min**	**240-420 min** / **420m-24 h** / **>24 h**
tPA eligibility	**Does not matter, do not wait for tPA decision**		
Gender	**No differences**		
Age	**young**	**elderly (good premorbid status)**	
NIHSS	**≥10**		
Occlusion location/size	**Large** / **ICA cervical T/L proxM1**	**medium** / **distal M1**	
ASPECTS and collaterals	**8-10** / **excellent/good**	**5-7** / **fair**	**3-4** / **poor** / **0-2**

mRS 0-2 benefit 40% 30% 20% 10% 0% HARM

mRS shift ≥1 pt 50% 40% 30% 20% 10% 0% HARM

Mortality reduction 15% 10% 5% 0% HARM

Conclusions

- EVT: Best for proximal/carotid occlusion/long clots
- Technique improving quickly
- Long time window proven but still be quick!
- Lobby hard for resources to do this
- Build a time efficient system of care
- Total gamechanger that saves the system money and patient/family from much suffering!

Intravenous Thrombolysis Decision Making: Who Should and Should Not Be Treated?

Andrew M. Demchuk MD FRCPC
Director, Calgary Stroke Program
Deputy Department Head, Dept Clinical Neurosciences
HSF Chair in Stroke Research
Professor, Depts of Clinical Neurosciences and Radiology
Cumming School of Medicine
University of Calgary

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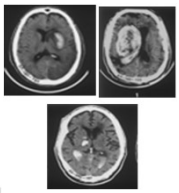
- Co-founder/shareholder Quikflo Health start-up (acute stroke software)
- Several clinical trial responsibilities:
  - IMS-3- Exec committee, CT core lab PI
  - ESCAPE- Neuro-PI
  - REVASCAT- CT core lab co-PI
  - CLOTBUST-ER – CTA substudy PI
  - ARTSS-2 – CTA substudy core lab PI
  - ENCHANTED – International Advisory Committee
  - PRACTICE- DMC chair
  - DEFUSE 3- Safety monitor
  - ANNEXA-4 – Adjudication committee

tPA and ICH risk in SITS-MOST Registry

Lancet 2007;369:275-282

Major intracranial bleeding 3-6%

	Haemorrhages at 22–36 h imaging scans
Local haemorrhages	**n=6283**
None	5369 (85·5%)
Haemorrhagic infarct type 1	338 (5·4%)
Haemorrhagic infarct type 2	250 (4·0%)
Primary intracerebral haemorrhage type 1	166 (2·6%)
Primary intracerebral haemorrhage type 2	160 (2·5%)
Known remote haemorrhages	**n=6282**
No remote haemorrhage	6111 (97·3%)
Remote primary intracerebral haemorrhage type 1	105 (1·7%)
Remote primary intracerebral haemorrhage type 2	66 (1·1%)



What are the tPA contraindications?

Exclusion criteria

- Significant head trauma or prior stroke in the previous 3 mo
- Symptoms suggest SAH
- Arterial puncture at noncompressible site in previous 7 d
- History of previous intracranial hemorrhage
- Intracranial neoplasm, AVM, or aneurysm
- Recent intracranial or intraspinal surgery
- Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
- Active internal bleeding
- Acute bleeding diathesis, including but not limited to
  - Platelet count <100 000/mm^3
  - Heparin received within 48 h resulting in abnormally elevated aPTT above the upper limit of normal
  - Current use of anticoagulant with INR >1.7 or PT >15 s
  - Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as ecarin clotting time, thrombin time, and appropriate factor Xa activity assays)
- Blood glucose concentration <50 mg/dL (2.7 mmol/L)
- CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)

Stroke February 2016

AHA/ASA Scientific Statement

Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

	iv tPA "sweet spot" Bridge to EVT	iv tPA modest net benefit	Conservative tx avoid tPA Don't bridge to EVT
Time from onset	< 90 min	90-180 min 180-270 min wakeup	>270 min
Age	all ages		
BP/glucose	normal	high	very high
NIHSS	6-10 11-21	disabling <5 >21	nondisabling <5
On antithrombotics	DOACs with normal labs	Prior antiplts: single* dual* *consider low dose tPA*	INR>1.7
Leukoaraiosis	**none**	**severe**	
NCCT EIC	**ASPECTS 8-10**	**ASPECTS 5-7** **ASPECTS 3-4**	**ASPECTS 0-2** ***severe hypodensity/vlCBV***
Thrombus characteristics	**Short thrombus**	**Long/large**	
Occlusion location/CTA features	**MCAo - distal M1** **Residual flow** **HU increase in clot on CTA**	**no occlusion ICAo** **no residual flow**	

Are you at risk?

This woman had a stroke at 43

BY PAIGE AKIN
TIMES-DISPATCH STAFF WRITER

Picture a stroke victim.

Odds are it's an older man, retired, past the prime of his life. Because of damage to his brain, his face has fallen, and he can't move one side of his body. He often has trouble speaking and remembering his family.

Then picture Amy Edmunds. She could be that man's daughter.

But at 43, this healthy woman had a stroke.

She's always watched what she eats. She never smoked, never had heart disease, always exercised.

"If you put me in a lineup with 15 people, you would not pick me out as the stroke survivor," said Edmunds, now 47.

But she is. Now, she's trying to educate the under-65 crowd about their risks of stroke. While most stroke sufferers are older — 55 and older — there is a growing risk among younger people, particularly those who

SEE STROKE, PAGE A11 ▶

YoungStroke

1

Research: Young Stroke Patient Questionnaire

YoungStroke 2015 June 27–29 Jacksonville, Florida
Raising Awareness About Management & Treatment of Stroke in Young Adults

Left: Christopher McKevitt, PhD
Kings College, London

Right: Souvik Sen, MD
University of South Carolina

"Development and Validation of a Patient Centered Young Stroke Outcome Measure Tool"
2017 American Academy of Neurology Annual Meeting

Young Stroke Patient Questionnaire

YoungStroke

Development and Validation of a Patient Centered Young Stroke Outcome Measure Tool

Ju
Julian Duda MD1, Viktoriya Duda MPH[1], Erin Suttman[1], Nishanth Kodumuri MBBS[1], Lauren D Giamberardino MHA[1],
Amy L Edmunds[2], Souvik Sen MD, MS, MPH[1].
[1]Department of Neurology, Palmetto Health-University of South Carolina School of Medicine, Columbia, SC, USA. [2]Coastal Carolina University, Conway, SC.

INTRODUCTION

Stroke is a leading cause of adult disability that has long-term impact on outcome of patients. The current outcome measures are felt to be inadequate in measuring the impact of stroke in young patients (≤65) in midst of managing education, career, and family. Because young stoke can be associated with non-conventional risk factors and etiologies, the investigation and treatment of young stroke and the management of young stroke survivors drastically differs from the traditional stroke population.

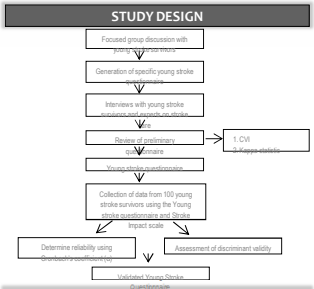
AIMS

-
To determine the reliability of the young stroke questionnaire
- To determine the discriminate validity of the young stroke questionnaire
- To further build upon the knowledge and understanding of young stroke and the specificities of treatment, management, and long-term outcome that are relevant to young stroke survivors.

METHODS

To assess the reliability and discriminate validity of the young stroke questionnaire (YSQ), the development framework involved a two-step process. Initial feedback from stroke survivors and healthcare providers via multiple focus groups helped identify questions used to measure impact of stroke in 4 patient-centered domains: work and leisure, relationships, wellbeing, and healthcare resources. A subsequent focus group prioritized and refined items on the final YSQ. Young ischemic stroke survivors were consented at the Neurology Clinic and clinical assessment information was obtained from 25 patients for analysis. Standardized clinical assessments completed included the modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS), and the Stroke Impact Scale (SIS). Additionally, all patients were asked to complete the patient-centered questionnaire, YSQ.

STUDY DESIGN



DATA ANALYSIS

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.903	.904	25

Domain	Significance (p value)
Work and Leisure	>0.05
Relationships	0.027
Wellbeing	>0.05
Healthcare Resources	0.034

RESULTS

Of 48 ischemic stroke patients screened, 25 (Mean age ± SD = 51 ± 9.2, 36% Males, 40% African-American, 56% White) patients qualified for enrollment into the young stroke questionnaire validation study. Using Levene's test for equality of variance to compare YSQ and standardized clinical assessments, the YSQ was more likely to detect patient-centered disabilities post stroke in the following domains: relationships (p = 0.027) and healthcare resources (p = 0.034). Reliability of the summary measure was assessed using Cronbach's alpha and found to be high (α = 0.903), indicating that the index created by summing the 4 dimensions is internally consistent and reproducible.

DISCUSSION

Standardized clinical assessments are not sensitive to disabilities in young stroke survivors. When compared to standardized clinical assessments, the young stroke questionnaire is significantly capable of differentiating the young survivor perspective of the impact of stroke, specifically in the areas of relationships and healthcare resources. Additional young stroke survivors will be consented to further establish analyses and other associations with the domains in focus.

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Brain imaging strategies in stroke

Prof Andrew Farrall

Programme Director, Edinburgh Imaging Academy
www.ed.ac.uk/edinburgh-imaging/academy

Professor of Neuroimaging & Education, University of Edinburgh
Consultant Neuroradiologist, Division of Clinical Neurosciences

Edinburgh Imaging
www.ed.ac.uk/edinburgh-imaging

NHS Lothian

How does MR compare to CT - imaging?

MR	CT
- Expensive & limited	+ Cheap & available
- Motion sensitive	+ Motion insensitive
- 20%-30% stroke patients have contra-indications	+ Few contraindications
- Not as fast	+ Fast
• Can identify hyperacute / acute haemorrhage intra-axially; extra-axially very difficult	• Can identify hyperacute / acute haemorrhage extra-axially & intra-axially
• Can identify non-ischaemic, non-haemorrhagic lesions	• Can identify non-ischaemic, non-haemorrhagic lesions
+ Posterior fossa evaluation excellent	- Posterior fossa evaluation limited by artefact
+ Excellent identifying haemorrhage after 8-10 days	- Poor identifying haemorrhage after 8-10 days

Brain imaging strategies in stroke

1. Stroke is a clinical syndrome
2. Most important: rule out haemorrhage
   - Routine CT can do this rapidly at low cost
   - ≤20% of stroke patients will be ineligible or never complete MR
3. CT all immediately
   - Best outcome with lowest cost
4. CTA only if considering thrombectomy
5. CTP / MRP & other advanced techniques
   - Require more research before practical, clinical deployment
6. MR for late presenting, young & “odd” strokes
   - Limited availability
   - Up to 20% have contra-indications
   - Stroke patients may be less able to tolerate MR

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- Describe imaging strategies in stroke
- State the role of CT in stroke work-up
- List basic findings in stroke imaging
- Know when CT Angiography is appropriate
- Discuss issues around CT & MR Perfusion
- State the role of MR in stroke work-up
- List limitations of advanced techniques & recognise pitfalls

www.ed.ac.uk/edinburgh-imaging/academy

STROKE IN SYSTEMIC DISEASES

José M Ferro

Department of Neurosciences and Mental Health
Hospital Santa Maria-CHLN, IMM
University of Lisboa, Lisboa, Portugal

STROKE IN SYSTEMIC DISEASES

We included

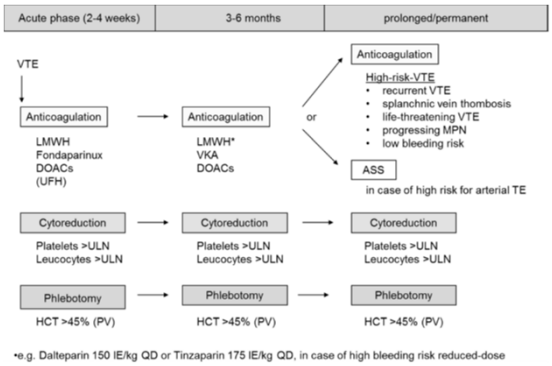
- Hepatic and gastrointestinal diseases
- Cancer
- Haematological diseases

We did not include

- Cardiac diseases
- Infeccious diseases
- Pulmonary diseases
- Renal diseases
- Dermatological diseases
- Genetic causes of stroke
- Rheumathologic diseases
- Primary vasculitis

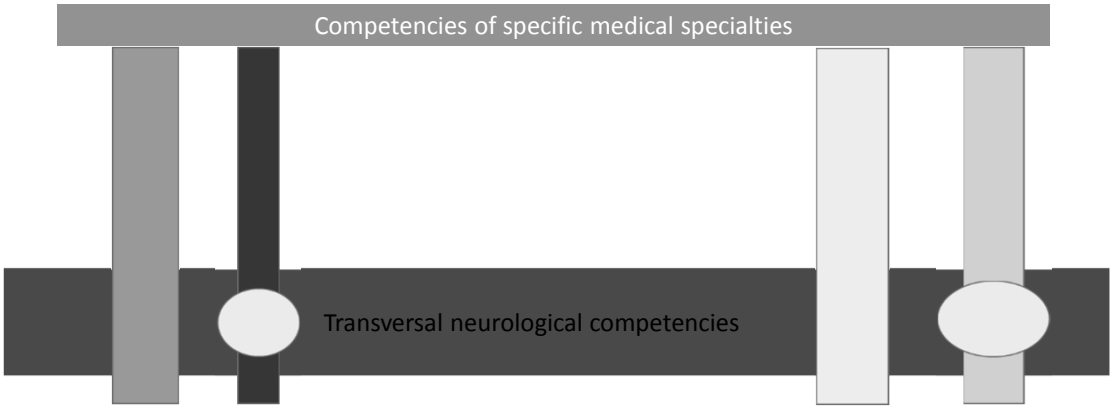
MPN - Treatment of cerebrovascular events

- Follow the general recommendation for the treatment of the different types of stroke
- Therapies to reduce platelet count
- CVT - anticoagulation should be used in the acute phase and for 3-6 months thereafter and in longer periods in high-risk patients only
- Monitor platelet counts during unfractionated heparin treatment, to detect heparin-induced thrombocytopenia



Kreher S et la, Ann Hematol, 2014

Conclusions and Implications



ESO-EAST SUNEP – pilot phase & future directions

Y. Flomin, MD, PhD

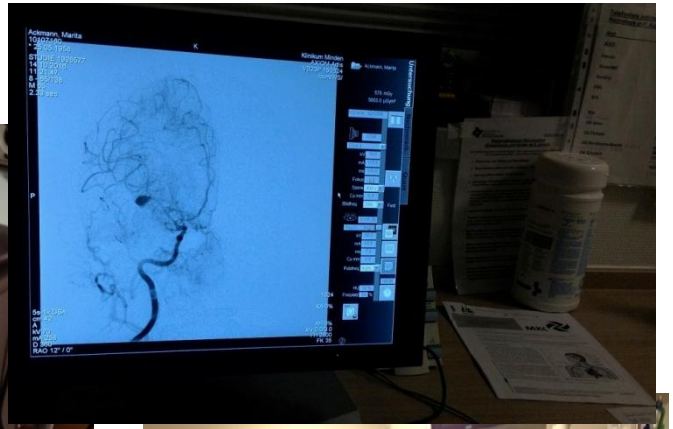
On-site training on a certified Stroke Unit

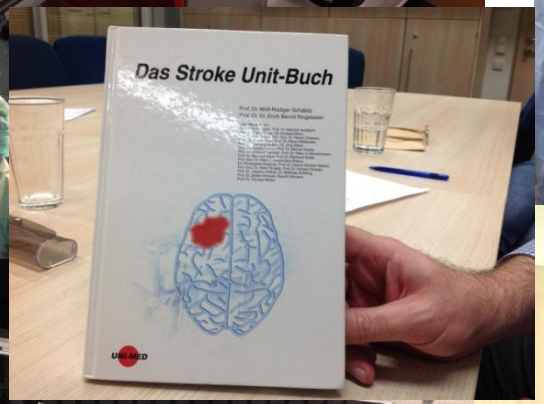
- Arranged by the ESO and Johannes Wesling Klinikum Minden, Germany in collaboration with the Ukrainian Anti-Stroke Association.
- October 3rd through November 9th, 2016.
- Seven small groups, 2.5-day stay (weekdays).
- Stroke Unit certified by the German Stroke Society in 2016 (led by Dr. Joerg Glahn).
- Exposure to high-quality state-of-the-science Stroke Care (structure, processes & outcomes)
- **A picture is worth a thousand words.**


Stroke Unit
JOHANNES WESLING KLINIKUM

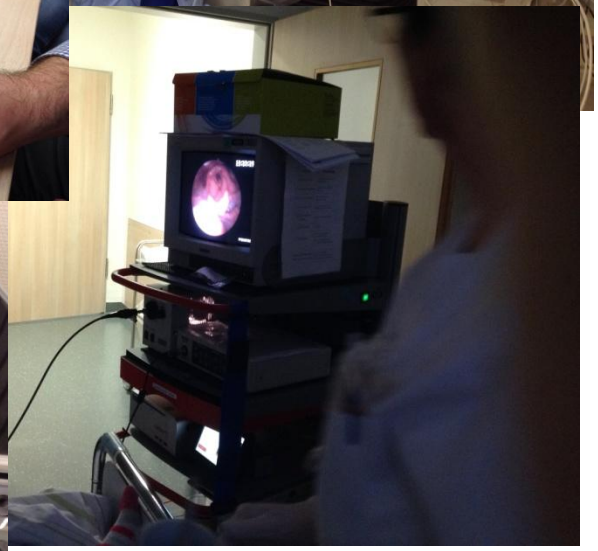

LGA InterCert
Zertifikat
MKK Johannes Wesling Klinikum Minden
Qualitätsmanagement-System
für eine Überregionale Stroke Unit mit 14 Betten
STROKE UNIT


FEUERWEHR




Das Stroke Unit-Buch


Actilyse® 50 mg



EUROPEAN STROKE ORGANISATION

Enhancement and Acceleration of Stroke Treatment (EAST)

In collaboration with German Stroke Society and Ukrainian Anti–Stroke Association

CERTIFICATE

This is to certify that

Mrs.
Karolina Mucha
Poland

participated in

ESO-EAST Stroke Unit Nurse Education project – pilot phase (March – November 2016)

Chair, ESO-EAST
Dr. Robert Mikulik

Project leader
Dr. Yuriy Flomin

Supported by unrestricted grant courtesy of Boehringer Ingelheim International GmbH

Boehringer Ingelheim

Acknowledgement

- Boehringer Ingelheim and personally Mr. Thomas Fischer – for funding.
- Ukrainian Anti-Stroke Association and personally Drs. Maryna and Dmitriy Guliaiev – arrangements for the kick-off meeting and on-site training.
- University Clinic for Neurology and Neurogeriatrics, Johannes Wesling Klinikum Minden and personally Dr. Joerg Glahn – for offering and providing the on-site training.
- ESO and ESO-EAST and personally Prof. Caso and Dr Mikulik – for organisational support and assistance.

ESO-EAST SUNEP recent advances

LITHUANIA

- 2 seminars for Nurses (April 2016) – 280 Nurses
- Section for Nurses at the Lithuanian Stroke Organisation Conference 2017

Lietuvos sveikatos mokslų universitetas
Lietuvos sveikatos mokslų universiteto ligoninė Kauno klinikos
Respublikinė Vilniaus universitetinė ligoninė
Lietuvos slaugytojų vadovų sąjunga

Tarptautinė mokslinė-praktinė konferencija,
skirta Tarptautinei slaugytojų dienai

2016 – SLAUGOS STUDIJŲ, MOKSLO IR PRAKTI INTEGRACIJA:

SLAUGOS KOKYBĖS GERINIMUI

2016 - NURSES: A FORCE FOR CHANGE: IMPROVING HE. SYSTEMS' RESILIENCE

2016 m. balandžio 22 d.

Paralelinė sesija: NEUROLOGIJA — **Session title: NEUROLOGY**
Konferencijų salė: BETA — **Conference hall: BETA**

Moderatoriai: Rima Šimkuvienė; Gražvydė Masiliūnienė — **lietuvių, anglų kalbomis**
Moderators: — **English, Lithuanian translation**

16:30-16:55 **Pagalba pacientams sergantiems išsėtine skleroze**
Nursing of multiple sclerosis patients
Rimutė Šimkuvienė, vyr.
slaugytoja-slaugos
administratorė
Neurologijos skyrius, LSMU ligoninė Kauno klinikos

16:55-17:20 **Clean intermittent self-catheterization as a gold-standard to manage retension-type bladder problems.**
Švarus interminuojantis saves kateterizavimas, kaip auksinis standartas esant retensinio tipo šlapimo pūslės sutrikimui
Inga Zopp, President Baltic MS Nurses Association (BMSNA), Tallinn, Estonia

17:20-17:45 **Naujos išsėtinės sklerozės gydymo galimybės: pegiliuotas interferonas beta – 1a**
A new therapy option for treatment of MS: Pegylated interferon beta-1a
gyd. Vida Šiaudytienė
Neurologijos klinikos, LSMU ligoninė Kauno klinikos

17:45-18:10 **Pacientų, patyrusių ūmų insultą, slauga**
Nursing of acute ischemic stroke patients"
Neringa Skvereckaitė, II Neurologijos skyrius
Respublikinė Vilniaus universitetinė ligoninė

18:10-18:35 **Pacientų, sergančių epilepsija, terapinis mokymas: patirtys ir įžvalgos**
Therapeutic education patients with epilepsy: experience and insights
Daiva Borkienė, Neurologijos klinikos laugos koordinatorė
LSMU ligoninė Kauno klinikos

18:35-19:00 Diskusija ir sertifikatų išdavimas

Lietuvos insulto asociacijos konferencija – 2017
2017m. kovomėn. 31- balandžio mėn. 01 d.,konferencijų centras „Margis"

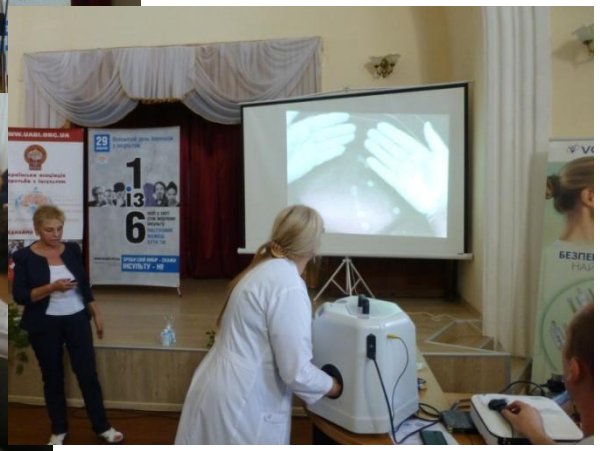
PROGRAMA

MOKSLINĖ-PRAKTINĖ KONFERENCIJA
BENDROSIOS PRAKTIKOS IR BENDRUOMENĖS SLAUGYTOJAMS, GMP DARBUOTOJAMS
2017 m. kovo31 d. („Ežero" salė)

00 – 10.00	Registracija, kava	
.00 – 10.10	Atidarymas	
MINIO INSULTO DIAGNOSTIKA, GYDYMAS IR DARBO ORGANIZAVIMAS		
rmininkauja: prof. D. Jatužis		
.10 – 10.30	Ūminio insulto simptomai: mitai ir realybė	Prof. D. Jatužis (VU)
.30 – 10.50	Galvos svaigimas: ką reikia žinoti slaugytojoms?	Gyd. R. Masiliūnas (VU)
.50 – 11.10	Ko mes tikimės iš GMP?	Gyd. D. Matačiūnienė(VULSK)
.10 – 11.30	Ūminio insulto bazinio gydymo principai	Dr. A. Vilionskis (VU)
.30 – 11.50	Kvėpavimo takų komplikacijos sergant insultu	Gyd. A. Gavrilova (VULSK)
.50 – 12.10	Klausimai-atsakymai, diskusijos	
.10 – 13.00	Pietų pertrauka	
MINĮ INSULTĄ PATYRUSIŲ LIGONIŲ SLAUGA IR REABILITACIJA		
rmininkauja: dr. I. Slautaitė		
.00 – 13.20	Insultą patyrusių ligonių mitybos ypatumai	Dr. I. Slautaitė (VU)
.20 – 13.40	Rijimo sutrikimo vertinimas: kada ir kaip?	b.p.sl. N. Skvereckaitė (VMKL)
.40 – 14.00	Disfagijos ir kalbos sutrikimo korekcijos praktikiniai aspektai	Logop. S. Kudakauskienė (VULSK), R.Almanienė (VULSK)
.00 – 14.20	Reabilitacijos proceso ypatumai sergantiems ūminiu insultu	Gyd. J. Paškevičienė (RVUL)
.20 – 14.40	Socialinė pagalba pacientui patyrusiam insultą	Soc. darbuotoja A. Rynkovičienė (RVUL)
.40 – 15.00	Diskusijos, konferencijos uždarymas	

UKRAINE

- Stroke Nursing School in Kamenets’ (Sep 15, 2016) – about 200 Nurses

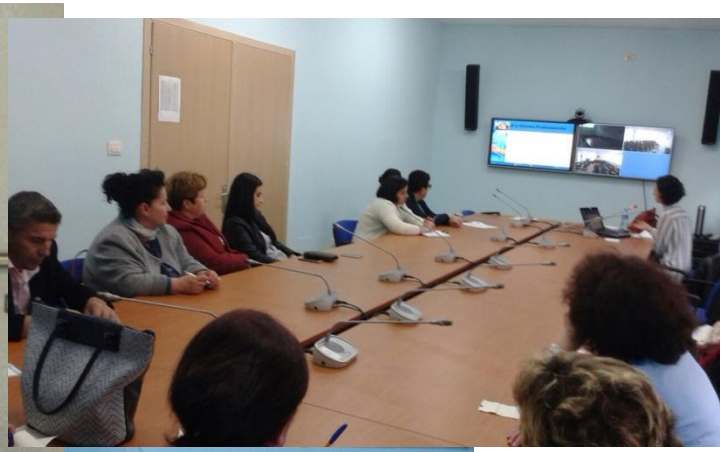


UKRAINE

- Workshop in Ternopil (Feb. 21,2017)–150 Nurses

ALBANIA

- Nursing Care in patient with Dysphagia, 1st Neurosurgery Conference in Tirana (Dec. 2016)



Albania, Macedonia, Kosovo, and Monte Negro

BULGARIA

- A course for Stroke Nurses at the 2nd National Congress of Bulgarian Society of Neurosonology and Cerebral Hemodynamics (Sep. 2016)
- GUSS scale, fall prevention and fever treatment protocols are implemented in UMHAT "Sv. Marina“ hospital (Varna)

ANGELS Academy

- **EDUCATIONAL COURSES**
- PATIENT SIMULATIONS
- SPEAKER RESOURCES
- HOSPITAL TRAINING KIT
- THE STROKE KIT
- TIPS & TRICKS
- ADDITIONAL ASSETS

E-LEARNING: STROKE NURSE CERTIFICATION

COURSE **OVERVIEW**

MODULES FOR STROKE NURSE CERTIFICATION

You must complete all modules to complete the course.

☑ I wish to complete the Stroke Nurse Certification course.

MODULE ONE
MEDICAL BACKGROUND
Module 1 will give you

MODULE TWO
NEUROCRITICAL CARE - RECOGNITION OF EMERGENCIES

MODULE THREE
NEUROCRITICAL CARE - NEUROLOGICAL


Thanks for your attention!
Дякую за увагу!

1. Introduction

Cardiovascular diseases (CVDs) are one of the priority areas of the "Den Sooluk" National Health Reform Programme in the Kyrgyz Republic for 2012–2016, which aims for an expected annual decrease of 1% in the CVD mortality rate. Among noncommunicable diseases (NCDs), **CVDs are responsible for half of the mortalities in Kyrgyzstan:**[1] ischaemic heart disease (IHD) and stroke account for a large share of these, and are the top causes of premature death (Fig. 1).[2]

Fig. 1. Dynamics of the causes of premature mortality in Kyrgyzstan, 2005–2015

2005 ranking		2015 ranking		% change 2005 to 2015
Ischaemic heart disease	1	1	Ischaemic heart disease	Minus 10.1%
Cerebrovascular disease	2	2	Cerebovascular disease	Minus 23.4%
Lower respiratory infections	3	3	Lower respiratory infections	Minus 33.9%
Neonatal encephalopathy	4	4	Neonatal preterm birth	0.6%
Neonatal preterm birth	5	5	Neonatal encephalopathy	Minus 18.4%
Congenital defects	6	6	Congenital defects	7.4%
Road injuries	7	7	Road injuries	Minus 2.9%
COPD	8	8	Self-harm	Minus 15.1%
Self-harm	9	9	COPD	Minus 38.0%
Tuberculosis	10	10	Cirrhosis hepatitis B	Minus 3.9%
Cirrhosis hepatitis B	11	11	Tuberculosis	Minus 33.5%

COPD: chronic obstructive pulmonary disease
Source: Institute of Health Metrics and Evaluation (IHME), Kyrgyzstan [website] (http://www.healthdata.org/kyrgyzstan, accessed 7 February 2017). (http://www.healthdata.org/kyrgyzstan, accessed 7 February 2017).

In support of the implementation of "Den Sooluk" and with the agreement of the Ministry of Health (MoH), a **WHO mission took place during 6–9 October 2016 to review acute and rehabilitative services for heart attack and stroke.** The mission focused on acute and rehabilitation services for heart attack and stroke, given that population-level and individual-level prevention of CVDs had been the subjects of assessments already: for example, an in-depth assessment of tobacco control had taken place in August 2012[3] followed by a review of the tobacco taxation policy in 2015,[4] and an assessment of health systems strengthening for better NCD outcomes in 2013.[5] In the first half of 2016, the United Nations Interagency Task Force (UNIATF) on the Prevention and Control of Noncommunicable Diseases held a joint mission and a mid-term evaluation of the NCD strategy. Together with other reviews of population-level prevention, and the assessment and management of cardiovascular risk factors in primary health care, it helped complete the picture of prevention and control of CVD in Kyrgyzstan.

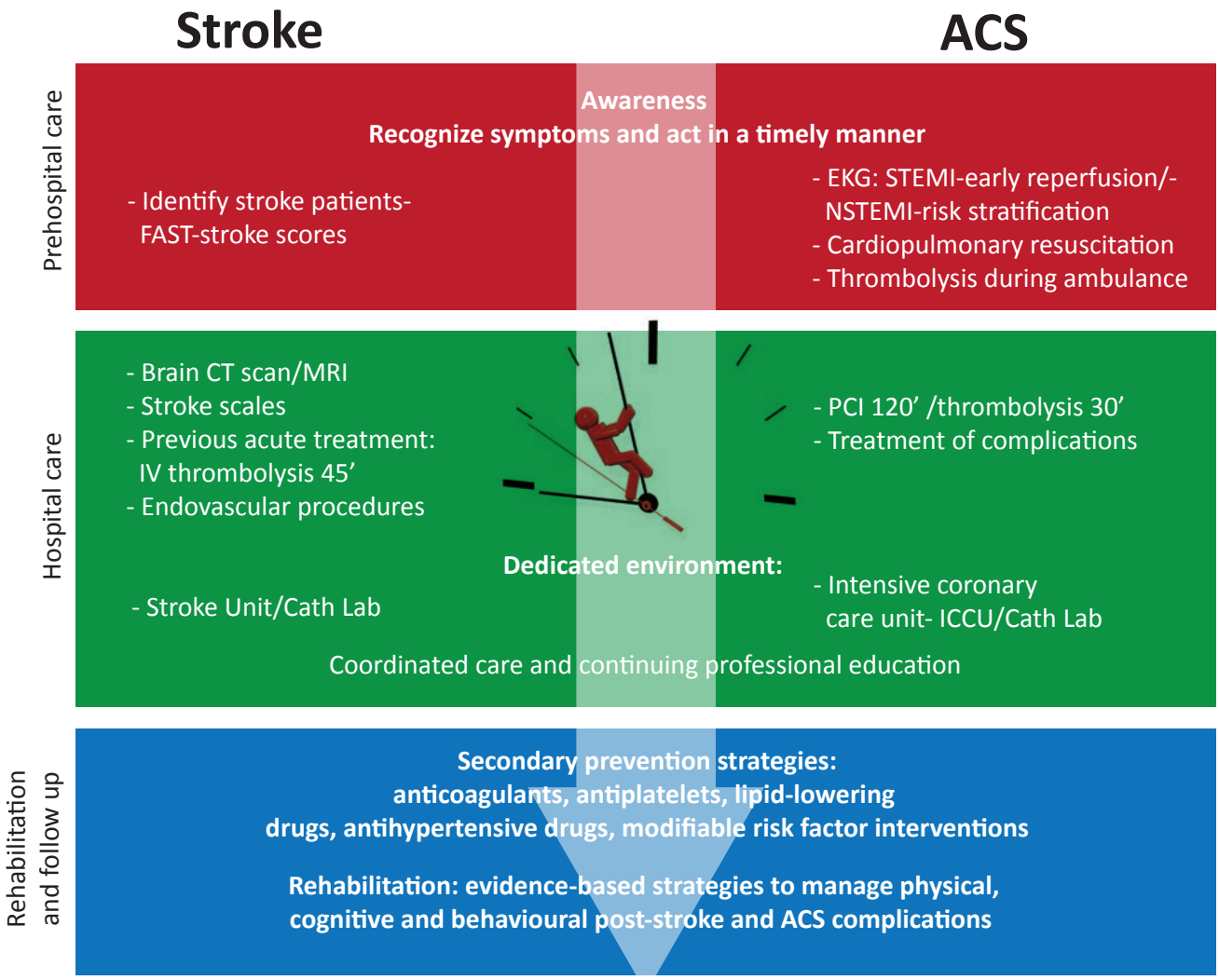
The mission was organized by the WHO Country Office for Kyrgyzstan and the WHO European Office for the Prevention and Control of Noncommunicable Diseases, based in Moscow, Russian Federation. The work forms part of the WHO NCD Project, which is financially supported by a grant from the MoH of the Russian Federation. The European Stroke Organisation (ESO) provided support in identifying a technical expert on stroke care services. The Federal Almazov North-West Medical Research Centre, St Petersburg, Russian Federation, and the Federal State Institution National Research Centre for Preventive Medicine of the MoH of the Russian Federation also supported the work through technical experts.

A second mission took place during 9–10 March 2017 to present the draft report and consult with the Ministry of Health (MoH), CVD Thematic group, PEN Working Group and invited experts within workshops held during this time.

2. Methodology

Observations were based on a desk review of documents and data, interviews with policy-makers, health professionals and patients, and visits to health facilities. A programme of visits is given in Annex 1. Prior to the visit, a broad framework for analysis was developed and checklists were created of performance indicators for the care of acute coronary syndrome (ACS) and stroke, against which data were collected (*see* Annex 2). The joint framework for analysis is shown in Fig. 2.

Fig. 2. Joint framework for analysis



ACS: acute coronary syndrome; EKG: electrocardiograph; FAST: Facial drooping, Arm weakness, Speech difficulties and Time to call emergency services; IV: intravenous; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction
Source: Authors

According to this framework, evidence-based interventions for pre-hospital care, hospital care, rehabilitation and follow up are summarized within this report. The review assessed the strengths and gaps of the situation in Kyrgyzstan against this framework, and highlighted key messages. Preliminary findings were shared with the MoH at the end of the mission period.

3. Epidemiology

Life expectancy at birth in Kyrgyzstan is 75 years for women and 67 years for men.[6] NCDs are estimated to account for 80% of deaths overall, and half of these deaths are due to CVD. The probability of dying between the ages of 30 and 70 years from the four main NCDs is 28%: **among countries of the WHO European Region, Kyrgyzstan has the highest premature mortality rate from CVD, the second-highest death rate from cerebrovascular disease, and the third-highest death rate from IHD (Tables 1 and 2).** Nevertheless, there is a downward trend for premature mortality from NCDs (largely driven by reductions in CVD mortality) and the trajectory to 2025 suggests that Kyrgyzstan will reach the global NCD target of a 25% reduction in mortality by 2025.

According to national data, in recent years, there has been a trend for a stable reduction of the total mortality rate due to CVD (331.3 in 2012 to 300.9 in 2015 per 100 000 population).[7] A relative but stable reduction has also occurred in the mortality rate from stroke and acute myocardial infarction (AMI) in men and women, although the reduction in the AMI mortality rate was higher in women than men. Data on ischaemic stroke are apparently contrary to these trends: according to the National Statistics,[2] mortality for all ages due to ischaemic stroke has increased.

Table 1. Cardiovascular and cerebrovascular morbidity (absolute numbers) in Kyrgyzstan, 2015[8]

Indicator of incidence	Kyrgyzstan	Bishkek
First-ever AMI	886	290
AMI recurrence	78	data not available
First-ever ischaemic stroke	1639	565
First-ever haemorrhagic stroke	603	171
First-ever stroke of unknown origin (CT scan not done)	280	23

Source: Centre for Medical Information, Kyrgyzstan

Table 2. Dynamics of cardiovascular and cerebrovascular mortality from 2011 to 2014 in Kyrgyzstan[2]

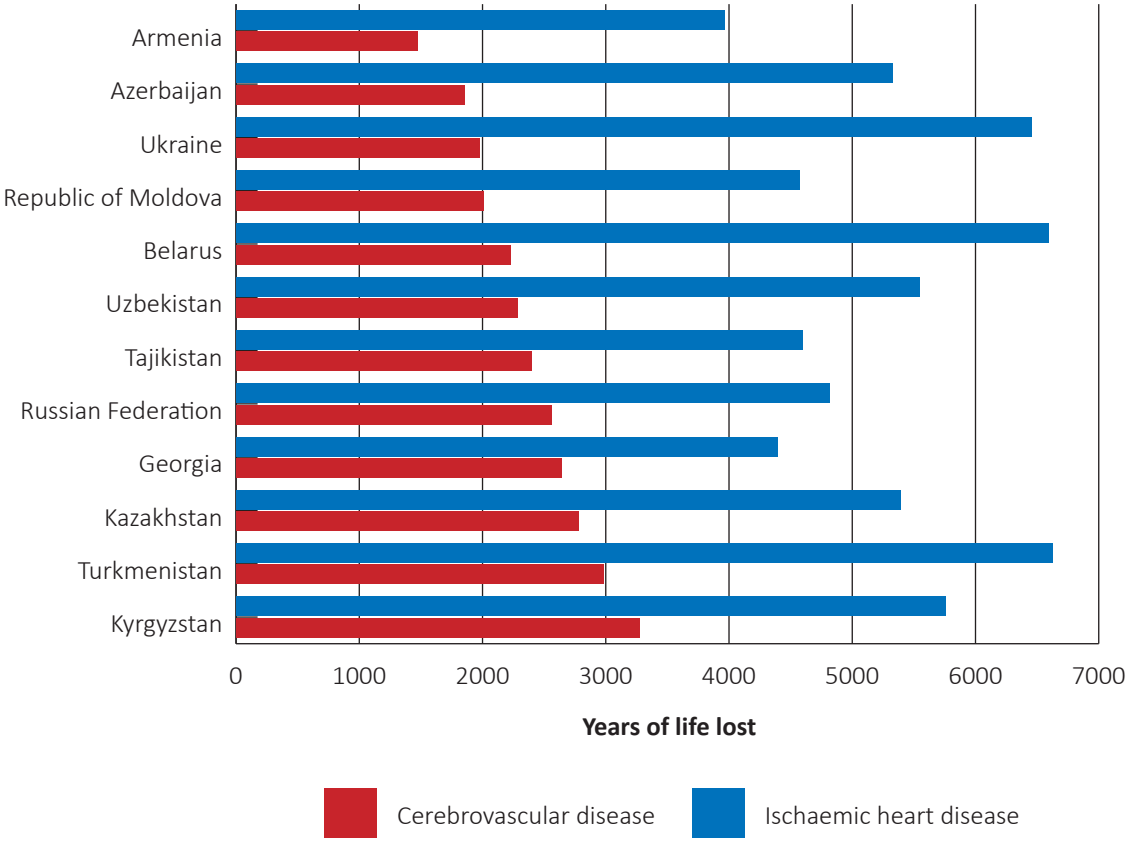
International Classification of Diseases (ICD)-10 code	2011 (per 100 000)	2014 (per 100 000)
ICD-10 61.0 haemorrhagic stroke	7.83	4.8
ICD-10 63.0 ischaemic stroke	2.46	5.1
ICD-10 64.0 stroke not specified	68.7	58.3
ICD-10 21.0 AMI	21.7	19.5
ICD-10 22.0 AMI recurrence	1.0	0.8

Source: Centre for Medical Information, Kyrgyzstan

Significant gender differences exist for CVD mortality. In the 0–64 years age group, mortality from diseases of the circulatory system is higher in men than women by a factor of 2.5, that from IHD by a factor of 3, and that from cerebrovascular disease by a factor of 1.9.[5] Apart from the risk factor prevalence, it has been suggested that other reasons for the higher mortality among men relate to lack of awareness of the signs, symptoms and consequences of raised blood pressure and low utilization of health-care services.[9]

The differences between similar countries should be emphasized: mortality from stroke was much higher in Kyrgyzstan than in other post-Soviet countries and moderately lower in cases of IHD (Fig. 3).

Fig. 3. Comparison of premature mortality (years of life lost) for cerebrovascular disease and ischaemic heart disease among selected post-Soviet countries, 2014



Source: Global Health Observatory, WHO 2017

This does not seem to be related to relative differences in funding for health care. Kyrgyzstan has a relatively low gross domestic product (GDP) compared with other post-Soviet countries and was categorized as a low-income country by the World Bank until 2014. Nevertheless, general government expenditure on health as a percentage of total government expenditure is relatively high compared with equivalent countries, and total expenditure on health as a percentage of GDP is close to the median for this same group of 12 post-Soviet countries.

The issue of timely and accurate diagnosis of stroke and the value of a stroke register is discussed in Section 6. While the quality of coding of cause of death may not be the best (although the proportion of deaths given the ICD-10 code R99 [ill-defined causes] is less than 5%) in general, it may be insufficient to explain on its own the high death rates from stroke. It is more likely to be related to the high cardiovascular risk factor levels, particularly for males. Another factor for consideration is the altitude and steepness of the terrain. Levels and trends of selected causes of death are similar to those in other post-Soviet countries but are slower to change, a matter that may be related to limited health-care capacity for early detection and treatment.

The prevalence of cardiovascular risk factors is high. The three risk factors that account for the greatest disease burden are dietary risk, high blood pressure and tobacco use.[2] A recent WHO study[10] describing the nutritional composition of the foods sold in the marketplaces in Bishkek found that the amounts of trans-fatty acids and salt in common foods are extremely high.

Around half the men smoke. The prevalence of current tobacco smoking among people in Kyrgyzstan 15 years and above in 2013 (latest year) was 3.7% for women, and 50.5% for men.[6] The total annual per capita alcohol consumption among people aged 15 years and above was 3.28 L of pure alcohol per year in 2011.[6] In 2014, the prevalence of overweight in males and females aged 18 years and above was, respectively, 45.2% and 49.1%.[6]

The WHO STEPS NCD survey[11] in 2013 found that 42.9% of adults aged 25–64 years had raised blood pressure (similar in males and females) and 23.6% had a raised total cholesterol level (females more than males). Almost one in five (17.4%) adults were identified as being at high cardiovascular risk, i.e. the probability of their having a cardiovascular event or death in the next ten years was 30% or more. **Over a third of adults (25–64 years) have three or more cardiovascular risk factors**, higher among men (39.5%) and older age groups.

4. Policy framework and NCD context

Policy and legislative frameworks to support the prevention and control of NCDs are in place in Kyrgyzstan. The National Public Health Programme 2020 aims to increase intersectoral actions through a whole-of-society approach. There is a national strategy on NCDs 2013–2020, recently evaluated mid-term, and the National Health Reform Program "Den Sooluk" 2012–2016[12] prioritizes cardiovascular health as one of its main themes. There is no roadmap for ACS and stroke. Regulatory and fiscal frameworks for tobacco and alcohol control are in place to a limited extent, but their scope and enforcement could be improved. **Through the WHO STEPS survey, Kyrgyzstan has developed a baseline on risk factors in the country.**

Among the five objectives of the national NCD strategy, two are particularly relevant for this review:

- improving the quality of health-care delivery in case of NCDs at all levels of the health sector using available interventions consistent with the principles of evidence-based medicine (EBM);
- reducing inequalities in accessibility to medical care by the population, regardless of geographical conditions, transport availability and income.

Funding of the NCD Action Plan includes a component for implementation of a package of essential NCD (PEN) interventions at the primary health-care level (PEN protocols), as well as provision to enable free access to insulin.

"Den Sooluk" was originally planned to end in 2016 but because of a delayed start, the Government of Kyrgyzstan and donor partners agreed to extend it until end-2018. A mid-term review of "Den Sooluk" documented achievements in health outcomes and outputs (25% of the 96 indicators achieved or exceeded) but also presented some mixed results.[13] These are described in Section 9 and Annex 4.

5. Evidence-based practice

Clinical guidelines

An EBM-oriented approach[14] characterized the "Manas National Program on Health Care Reforms 1996–2006" and it is now the backbone of the "Den Sooluk" Program.

Protocols and guidelines for the diagnosis and management of stroke and ACS exist, and appear to be evidence-based. The Evidence-based Medicine (EBM) unit that is responsible for developing guidelines and clinical protocols based on conscientious, explicit and judicious use of current best evidence is within the MoH. In the past five years, the EBM unit has revised clinical protocols on hypertension, stable angina, AMI; in 2015, it published, after approval of the Expert Council, clinical guidelines on atrial fibrillation and diabetes. In 2016, new clinical guidelines on acute stroke care were drafted. We noticed that these do not include some low-cost interventions such as the FeSS (Fever, Sugar, Swallowing) protocol (*see* the Hospital care section).

Guidelines and protocols are available on the MoH website in an EBM-dedicated space. Stroke guidelines and protocols that were obtained and reviewed for this report were found to be evidence-based, comprehensive and detailed, and included references and the strength of evidence for recommendations, even if they were not recently updated (*see* the section on Prehospital setting).

The European Society of Cardiology guidelines have been endorsed by the Kyrgyz Society of Cardiology, although the extent of their implementation, and relationship to national guidelines is unclear.[15] National guidelines are said to be based on the United States and European Society of Cardiology guidelines, and adapted for Kyrgyzstan, although many points cannot be incorporated because of low-cost practice.

As part of the implementation of "Den Sooluk", a "CVD Thematic Group" was established to support effective policies for CVD reduction, and coordinate and empower implementation and dissemination of CVD guidelines, protocols and clinical care best practices.

Professional education

The Kyrgyz Medical Institute of training and retraining organizes courses and workshops for professional development; educational opportunities on CVDs are available but mainly focus on primary care and CVDs, and less on stroke. In 2015, 201 physicians were trained in the provision of care for ACS, 139 in acute cerebrovascular events, 139 in AMI, 727 in CVD; 197 attended educational events on diagnosis and emergency management of stroke and AMI. We were informed at the consultation in March 2017 that some efforts had been made to address the gap in training by the end of 2016 and since our original visit. Courses and seminars were held for the training of workers in the health-care system (doctors, their assistants, paramedics and medical nurses) on the clinical protocols/clinical guidelines; these will be printed and disseminated throughout the country during 2017. Kyrgyz neurologists who have joined the ESO-EAST[16] project of the ESO in 2015 have planned a residential stroke nursing care course that will start in 2017.

Training opportunities on NCDs for family physicians and nurses are available: for example, as part of the implementation of a package of essential NCD (PEN) interventions in primary care, a training course has been developed to teach cardiovascular risk assessment and management, and lifestyle counselling (PEN protocols 1 and 2).[17] Initially aimed at health workers in the PEN project pilot districts, this has been extended to include other districts, community health workers, and teachers of the Kyrgyz Medical Institute of Training and Retraining, and Kyrgyz medical academy of I.K. Akhunbayev. It has also resulted in changes being made to the training programmes of family doctors in the Kyrgyz State Medical Institute of retraining and advanced training.

Over the past five years, there has been an increasing use of e-learning for the training of both medical personnel and nursing staff. Several development partners collaborated in implementing and disseminating this methodology. Since September 2016, webinars are also available, and a complete list of planned lectures is available on the website.[18]

The ambulance service provides for the retraining of ambulance personnel through internal activities (Fig. 4) and offers the possibility of participating in extramural courses (Kyrgyz State Medical Institute of retraining and advanced training).

Fig. 4. Equipment to retrain ambulance personnel

Actions to support evidence-based practice are, nevertheless, limited and fragmented, mainly focused on awareness, management and control of CVD risk factors, and less on stroke. Shortcomings in the implementation of clinical practice guidelines have already been noted.[5]

A list of possible EBM implementation strategies and their actual demonstration for both stroke and ACS in the country is summarized in Table 3.

Table 3. Implementation strategies for ACS and stroke in Kyrgyzstan observed by the mission team

Implementation strategy[19]	ACS	Stroke
Opinion leaders	YES	NO
Multiprofessional collaboration	NO	NO
Multifaceted interventions	NO	NO
Patient associations	NO	NO
National and regional policies		
● mandatory	YES	YES
● non-mandatory	NO	NO
Financial incentives		
● Public	NO	NO
● Private	YES	YES

Implementation strategy[19]	ACS	Stroke
Educational strategies		
● printed/electronic educational material	YES	YES
● educational meetings and workshops	YES	YES
● educational outreach visits	NO	NO
● educational campaigns	NO	NO
● guidelines	YES	YES
Audits and feedback	NO	NO
Reminders		
● electronic reminders	NO	NO
● written reminders	NO	NO
Computerized decision-support systems	NO	NO

Some explanatory notes to the table are as follows:

- The current Minister of Health is a cardiologist and acts as an opinion leader in his field, encouraging the establishment of private cardiological services, for example; there is no such equivalent in the area of stroke.
- There were some occasional observations of multiprofessional collaboration but this did not seem to be consistently present or to be part of an EBM or implementation strategy.
- Private incentives are the backbone of most implementation activities: development partners and drug companies finance different activities, and in some cases, influence them. This is the case with the guidelines on neuroprotective agents for stroke patients, for example. Private incentives may also influence professional education, driving medical attention to certain diseases and/or promoting the implementation of some evidence rather than others.
- Educational campaigns are generally not specific for stroke but instead focus on healthy lifestyles; there are no campaigns on the early signs and symptoms of stroke or AMI.
- Information collected by the ambulance registry is not used to provide feedback to clinicians.

6. Quality control and performance management

There is a substantial evidence base for interventions that are effective in improving outcomes after stroke. Ensuring that patients have timely access to evidence-based interventions is an essential component of good-quality care. **In Kyrgyzstan, measurement of the quality of stroke and ACS care as a part of a process of quality improvement is scarce**.

The ambulance is responsible for managing registries for all cases of stroke and myocardial infarction that the service receives (*see* the section on Prehospital setting for details). Admission cards include information on the ambulance care received, emergency room and discharge diagnoses, and outcome. Data are first collected by the ambulance operator on a hard copy module, while the section on outcome is forwarded to the service centres for updating their registry. Registry data are not used to provide feedback to clinicians, and their use by policy-makers for strategy planning in ACS and stroke care is unclear.

In 1997, a stroke registry was established for the capital city of Bishkek and oblast of Osh. At present, this registry is functioning only in the capital and is managed by the same emergency agency that manages the ambulance system. The neurologist responsible for the Stroke Registry Center is required to adhere to the standards set out for the Physician Stroke Registry by WHO.[20] Moreover, according to the Normative Act Stroke Registry in Bishkek, the registry manager must record every case of acute stroke and death from stroke in Bishkek. The following data are recorded:

- Any type of stroke at the polyclinics and hospitals in Bishkek is recorded.
- Information pertaining to the diagnosis via statistical forms forwarded by family physicians or hospital personnel is recorded.
- Stroke physicians are advised to send patients to a specialized stroke care unit, and in the case of refusal, treatment is administered at the patient's home.
- Physicians are supposed to visit and register stroke patients within 7 days to monitor the patient's condition and to clarify the cause of possible death. Patients who refuse hospitalization should receive a home visit after 7 days.

The stroke registry is responsible for:

- registering all new and recurrent cases of strokes. Strokes occurring repeatedly over the 28 days from the first event are considered a single event;
- noting the stroke type (ischaemic/haemorrhagic or transient ischaemic attack [TIA]) without defining a subtype classification;
- noting the system of the affected artery (for ischaemic stroke) and hemisphere (for haemorrhagic stroke);
- noting the cause of death from stroke, and its type (ischaemic, haemorrhagic).

In 2014, a publication[21] presented the results of the activity and performance of the registry. According to it, the stroke registry physician examines the major proportion of patients with such a diagnosis. In 2011, 86.8% of stroke patients were enrolled in the registry and in 2012, the percentage increased to 94.1%. Reliable sources of information on stroke epidemiology in the rest of the country are lacking. New facilities for stroke patients have been recently added in Narin and Osh (quarter four 2016) but at the moment, there is no expertise or infrastructure to establish a stroke registry. The Bishkek Stroke Registry offers an interesting analysis of stroke trends and epidemiology. It also gives a unique insight into the diagnostic power of the care pathway as it has been in existence for the past 5 years: according to the previously mentioned publication that examined the activities in 2011–12, a correct diagnosis of stroke was made within the first 24 hours from stroke onset only in 58.2% of patients. The rest were diagnosed within 1–3 days (29.63%) and a small percentage after 10 days of onset (2.3%). These figures show that before (or together with) any programme to implement acute therapies, there is a need for a cultural and organizational intervention to empower timely and accurate diagnosis of stroke.

In addition to the previously mentioned Bishkek Stroke Registry, a single stroke centre based in the capital (City Clinical Hospital N°1) is actively recruiting patients for the Safe Implementation of Treatments in Stroke (SITS) General Stroke registry.[22] This international registry records any case of stroke and TIA **not treated** with intravenous (IV) thrombolysis or thrombectomy and, to date, more than 100 patients have been enrolled. These two experiences differ for many reasons. The Bishkek Stroke Registry is mandatory and managed by a local agency; the results are not used to provide feedback to clinicians on a regular basis, whereas the SITS registry relies on the voluntary work of vascular neurologists of the Stroke Centre. It provides information on the performance of the participating centre over time and compares this with other countries. Participation in a second international stroke registry is also on the cards: two stroke centres in Bishkek have recently joined the Registry of Stroke care Quality (RES-Q), which has been developed as an ESO initiative and targeted primarily at supporting countries of Eastern Europe.[23] To date, Kyrgyzstan has not started recruiting patients to this registry.

7. Clinical pathway

An effective system for CVD needs to coordinate and manage patient access to a full range of services and activities for prevention, treatment and rehabilitation of stroke and ACS. The main components of the pre-hospital phase of care within the full stroke and ACS clinical pathway include the pre-hospital system and hospital facilities. The pre-hospital system consists of community-based elements: ambulance service, stroke and ACS awareness campaigns focused on recognition

of stroke symptoms, timely recognition of acute stroke and ACS and ambulance dispatch, screening of potential stroke patients, prehospital diagnosis of ACS (by ambulance ECG and/or tele-ECG), and hospital notification. A timely clinical pathway for stroke and ACS, in order to be most effective, needs to be coordinated by a multidisciplinary team that places the highest priority on minimizing the transfer time of the patient to the most equipped stroke care facility**. In Kyrgyzstan, these components are partially in place; however, even if medical personnel are knowledgeable, the system lacks modern health-care technology, equipment and modern drugs.** There is no well-organized referral and re-referral system for patients with ACS.

Prehospital setting

Evidence-based interventions

Stroke

Stroke is a clinical emergency and its outcome is strongly dependent on both timely assessment and timely treatment. Specifically, narrowing the times to diagnosis and treatment have been proven to significantly lower both mortality and disability in patients with acute stroke. Ambulance services play a leading role in this by identifying acute stroke symptoms and providing transport to qualified stroke treatment centres that are best prepared to administer effective treatment (tissue plasminogen activator [tPA] or endovascular therapy when appropriate and if available). Ambulance personnel who are unable or lack the ability to identify acute stroke symptoms can contribute to delayed and missed diagnoses of stroke.[24]

Prehospital stroke scales screen for stroke in patients with acute neurological deficits and differentiate it from sepsis, hypo- or hyperglycaemia, seizure, tumour, intracranial haemorrhage, migraine and syncope, which may also cause acute neurological disorders. When ambulance providers do not use a stroke scale, they are more likely to miss the diagnosis.[25]

Several scoring systems are currently available for identifying an acute ischaemic stroke in the field. Of these, the most popular are: the FAST test (Facial drooping, Arm weakness, Speech difficulties and Time to call emergency services), the Cincinnati Prehospital Stroke Scale (CPSS) and the Los Angeles Prehospital Stroke Screen (LAPSS). These scores are considered to be more accurate in predicting anterior circulation strokes. To date, no practical prehospital scale is able to accurately predict strokes outside of the middle cerebral artery distribution. FAST and CPSS are easy to use and have shown good reproducibility between physicians and paramedics.[26,27] Regarding their sensitivity and specificity, the FAST score has a reported sensitivity of between 79% and 85%, and specificity of 68%, while CPSS has a reported sensitivity of between 44% and 95% and a specificity of between 23% and 96%.[28] A score of two on the CPSS has been reported to reliably identify patients for thrombolytic therapy with a 96% sensitivity and 65% specificity.[29]

Hypo- or hyperglycaemia can mimic stroke. In fact, hypoglycaemia may cause symptoms such as hemiparesis, hemiplegia, speech or visual disturbances, confusion, and poor coordination; hence, it is critical to measure blood glucose levels when there is concern of a possible stroke.[30] In this regard, the prehospital ROSIER (Recognition of Stroke in the Emergency Room) score assesses facial, arm and leg weakness, speech and visual field deficits, as well as blood glucose levels. The ROSIER score has been reported to have a sensitivity of 80–89% and a specificity of 79–83%.[31] Physicians have confirmed that 64% of strokes and 78% of non-strokes had been previously suspected by ambulance attendants with ROSIER.[32]

Moreover, it is known that cardiac abnormalities can cause or manifest concurrently with stroke. Thus, when stroke is suspected, cardiac monitoring is recommended in the prehospital setting and throughout the first 24 hours of care.[33]

The two most effective therapies to reduce both mortality and disability from ischaemic stroke – IV tPA and endovascular thrombectomy – have restricted windows of delivery;[34] therefore, timely transport of a stroke patient to a stroke centre contributes to limiting cerebral damage.

The American Heart Association (AHA) recommends an ambulance-call-to-dispatch time of less than 90 seconds, an ambulance-response time of less than 8 minutes, and an on-scene ambulance time of no more than 15 minutes.[35] Moreover, AHA guidelines recommend that ambulance personnel document the time “last seen normal” to best define the therapeutic window. It has been demonstrated that greater efficiency in the dispatch and hospital notification of a stroke leads to shorter times for: (1) ambulance call to arrival; (2) assessment by physician; (3) door-to-needle time; (4) door-to-

imaging time. Moreover, when adhering to these parameters, patients were more likely to receive tPA. Finally, authors have reported that patients admitted to stroke units, instead of community hospitals, were more likely to receive tPA and have a lower risk of mortality at 30 days.[36]

Acute coronary syndrome

During the prehospital stage of acute care, the early identification of ACS is very important. The first evaluation should be based on clinical symptoms, which requires at least a basic knowledge of the clinical differential diagnosis of chest pain. An early ECG is essential for the triage and selection of an appropriate treatment strategy. Current international guidelines strongly recommend that an ECG be done within 10 minutes of the first medical contact.[37,38] For patients with a recognized stable ST-segment elevation myocardial infarction (STEMI) on ECG, the time from symptom onset, availability of primary percutaneous coronary intervention (PCI) and suspected time of transport to a PCI centre should be evaluated before making any decision regarding reperfusion strategy. The administration of thrombolysis (within 30 minutes from the first medical contact in the absence of contraindications) is recommended if primary PCI is not available, with a possible delay of up to 90–120 minutes; otherwise, thrombolytics of a second generation are preferable.[38]

Patients without ST-segment elevation on ECG should be transferred to a hospital with a PCI facility for stratification of risk, evaluation of cardiac biomarkers and angiography within the next 24–48 hours.[37]

A patient with ACS complicated by recurrent chest pain, arrhythmia, acute heart failure and/or cardiogenic shock should receive symptomatic treatment for stabilization of the vital functions and thereafter be immediately transferred to a PCI centre.

According to international guidelines, recommended medication during the prehospital stage includes analgesics, antiplatelet drugs, parenteral anticoagulants and, in some cases, vasodilators, diuretics and inotropes.

The most common causes of mortality during the prehospital stage of care in patients with ACS include ventricular tachycardia and ventricular fibrillation. The treatment of these complications requires high-quality cardiopulmonary resuscitation (basic level) and early defibrillation.[39] In order to create a strong and effective link between prehospital and hospital care for ACS patients, a regional ACS network needs to be set up considering local factors.

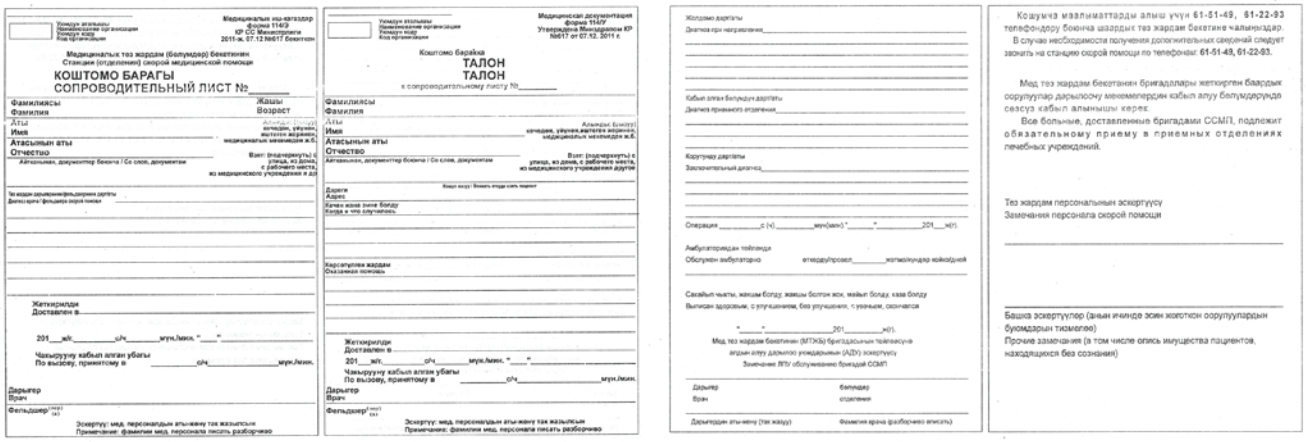
Strengths

In Kyrgyzstan, the ambulance service covers both urban and rural regions, and call centres are open 24/7. Global positioning system (GPS) mapping (Fig. 5) tracks the ambulances and there are 692 emergency service teams, 102 with at least one on-duty physician. Specialized cardiological teams (29 ambulances) have been trained in acute cardiac care, and have both defibrillators and ECG devices at their disposal. There is constant radio communication between the call centres and the ambulances, and the delivery of prehospital care is arranged on a territorial basis, in accordance with hospital schedules. The ambulance service is organized in accordance with the directives of the MoH, which also establishes the general standards of intervention: 4 minutes for ambulance dispatch, whereas the time to reach the patient and take the patient to the nearest hospital facility is up to 110 minutes in Bishkek and Osh, and 130 minutes in the other regions of the Kyrgyz Republic.

Fig. 5. GPS tracking of ambulances

All incoming and outgoing calls, along with their related outcomes, are recorded on both an electronic file and a hard copy (Fig. 6). Ambulance cards, written in both Russian and Kyrgyz, include information on the patient's medical history, diagnosis, time of intervention, and outcome.

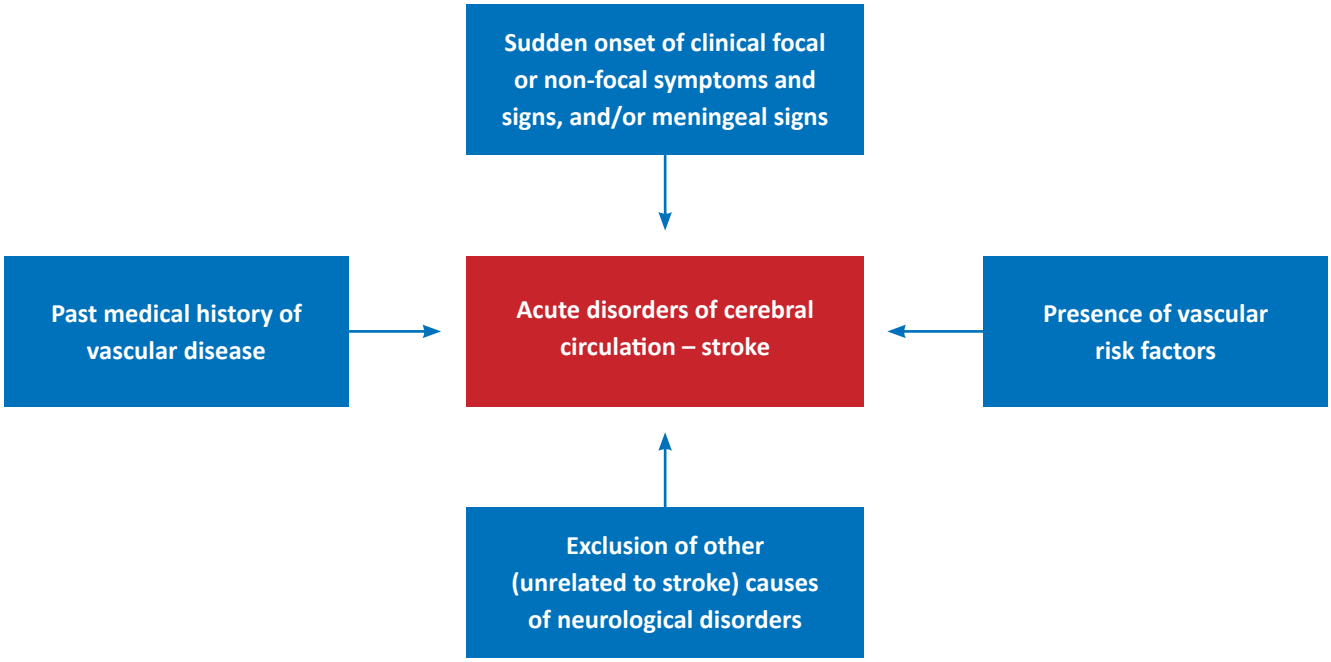
Fig. 6. Admission cards include information on the ambulance care received, emergency room and discharge diagnoses, and outcome



Ground ambulance services operate at a basic life-support level and furnish both emergency and non-emergency transportation. Specialized cardiology teams (17) are trained to resuscitate, defibrillate and gain experience in administering prehospital thrombolysis with streptokinase.

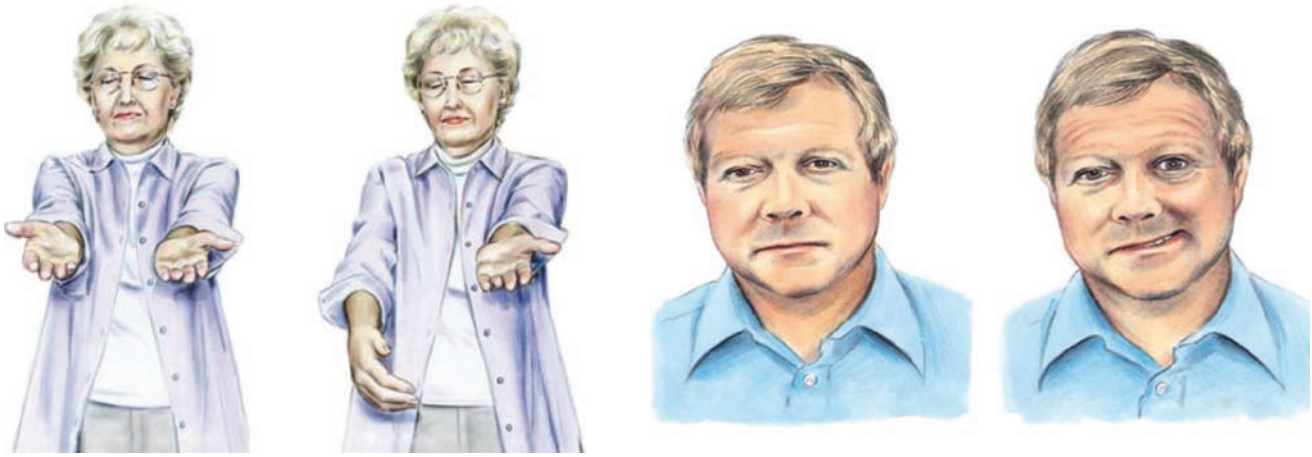
Since 2011, specific evidence-based recommendations have been formulated for prehospital stroke care dealing with the timeliness of interventions and the use of prehospital stroke scales and scores; the actions are summarized in algorithms (Fig. 7).

Fig. 7. Diagnostic stroke algorithm



Guidelines offer evidence-based recommendations for ambulance personnel on how to best identify stroke symptoms in the field. As a diagnosis of stroke is solely clinical, no available tests are able to confirm stroke in a prehospital setting. Thus, the FAST test (Fig. 8) can be utilized only as a screening tool.

Fig. 8. FAST test



Locally developed prehospital stroke care guidelines recommend the following:

- All patients with a diagnosis of stroke/identifiable stroke symptoms should be hospitalized.
- Prior notification to a hospital is recommended for suspected stroke patients.
- Home treatment of patients with suspected stroke is futile and is usually associated with high mortality rates.
- The gold standard regarding time to hospital admission is 1–3 hours from stroke onset.

The guidelines also state absolute contraindications for hospitalization (agonal state) and relative contraindications for hospitalization (end-stage cancer and other chronic somatic diseases, chronic disabling mental disorders [severe dementia] prior to stroke onset).

Guidelines cite telemedicine as an effective strategy for improving the quality of stroke care. In terms of prehospital treatment, critical points such as assessment and management of ABC (airways–breathing–circulation) are addressed, as well as the management of hypertension.

These clinical guidelines have been drafted based on the results of a systematic review and a thorough evaluation of the published literature. A methodological assessment was conducted for each study and the results obtained were used as a reference for the guidelines, indicating the level of evidence according to a standard scale.

Guidelines and algorithms are also available for the diagnosis and treatment of ACS with ST-segment elevation and without ST-segment elevation on ECG, covering diagnostics, triage and treatment (including thrombolysis) at the prehospital stage of care.

Gaps

Currently, services for emergency care and rehabilitation of cases of ACS and stroke are more developed in the capital than in the other regions, i.e. there is inequality in access to medical care of the population, regardless of geographical conditions and accessibility of transport.

In Kyrgyzstan, improvements in prehospital organization specific to the ACS pathway are ongoing, as the existing network does not yet allow each patient with STEMI to receive the best reperfusion treatment. In fact, a part of the patient population with ACS is still referred to private clinics and hospitals where life-saving primary PCI is more readily available.

The implementation of timely interventions recommended by local (such as those cited in the previous paragraph) and international guidelines is gravely hindered by a low ambulance-to-population ratio; at present, the service can cover only 30% of calls effectively due to a shortage of staff and vehicles. In fact, in both Kazakhstan and the Russian Federation, the ambulance services provide, on average, one ambulance for every 10 000 inhabitants: Almaty, with a population of 1.5 million has 156 cars, for example. In contrast, Bishkek, with a registered population of 1.2 million, has 39 working cars. Furthermore, staff have left since the Eurasian Economic Union allowed free movement of workers in 2015: there are 59 vacancies for doctors (out of 168 posts) and 56 vacancies for nurses.

Public ambulance services are free from home to the first hospital. If the patient needs to be transferred to private services or other facilities or back home, the public ambulance (if available) could be hired at a charge (around 260 sum or US$ 3). Prices are listed on the MoH website. Private ambulance services are available in Bishkek.

Likewise, regarding stroke care pathways in the prehospital setting, we found that stroke scores were rarely used. The ability to provide prehospital care to ACS patients is further limited by an insufficient number of ambulance teams. Moreover, most of these ambulance teams are not equipped with ECG devices and defibrillators, and no tele-ECG or prehospital thrombolysis protocol is available. Finally, medications, including second-generation thrombolytics such as tenecteplase and low molecular-weight heparin (LMWH) for the early treatment of ACS, are not available in Kyrgyzstan.

We found anecdotal evidence of ambulance staff offering stroke patients neuroprotective agents for an informal payment (200–300 sum) in the recent past. This practice has been strongly opposed by the competent health authorities,[40] as has the expensive use of non-evidence-based drugs (listed on the MoH website) and non-defined forms of alternative medicine. We learnt at the consultation in March 2017 that during 2017, the national expert group together with leading experts in the MoH, clinical pharmacologists, academic and educational representatives together with WHO experts have reviewed the list of essential medicines in Kyrgyzstan. They found that the list contained medicines that were not on the WHO essential medicines list, do not meet the selection criteria because of lack of evidence of effectiveness, and are obsolete and irrational. This is currently being rectified.

There may also be other issues that prevent patients from seeking early hospitalization, as illustrated by the case of a patient interviewed in one of the stroke units (Box 1). Not seeking early admission to hospital could be due to a range of issues: cultural; lack of awareness or belief that it will improve outcomes; financial considerations. The perceived likelihood of high cost has been identified as a barrier to health-care-seeking behaviour already.[11]

Box 1. Clinical case of patient in a stroke unit in Bishkek

A woman, aged 72 years, had a history of hypertension. She experienced a sudden onset of weakness in the left arm and leg. She waited one day and then called her general practitioner (GP). The GP saw her within one hour and initially tried to reduce her blood pressure at home.

The GP called a neurologist. The patient waited 3 hours for a consultation with the neurologist. The neurologist referred her to a public sector hospital and the patient's daughter took her in her own car. The patient needed to organize and pay for her own MRI to be done in a private diagnostic centre for 3000 sum. The MRI showed left hemisphere ischaemic stroke. Carotid sonography was not done because it was not available.

Note that, although the patient paid a significant amount of money for a diagnostic test, it was unnecessary because the time delays meant that she was already outside the therapeutic window and it did not alter the clinical management.

Hospital care

Evidence-based interventions

Acute coronary syndrome

This section draws on international guidelines.[41,42] Effective organization of care for patients with ACS requires provision of care at different levels. These may be available according to service provider capability. Hospitals with intensive care units (ICUs, monitored beds) and capability for immediate defibrillation and administration of thrombolytics provide basic treatment that reduces mortality from ACS.

Early diagnostic and management protocols guide early risk stratification to determine whether a patient should be managed with either an early invasive strategy or an initial conservative strategy, and can help determine which recommended pharmacological therapies should be used. Patients presenting with chest pain should follow a diagnostic protocol for ACS as soon as possible. The protocol entry point is a 12-lead ECG, and the results should be interpreted within 10 minutes of the first emergency clinical contact. This may involve facilitating referral to a clinician experienced in performing and/or interpreting an ECG. Based on the ECG, the patient should be classified into one of two groups for further management: those with acute chest pain and persistent ST-segment elevation (ST-segment elevation ACS), and those with acute chest pain but no persistent ST-segment elevation.

ST-segment elevation ACS generally reflects an acute total coronary occlusion and most patients will ultimately develop a STEMI. A patient with a STEMI, for whom emergency reperfusion is clinically appropriate, is offered timely PCI or thrombolysis in accordance with the time frames recommended in the current European/national guidelines. In general, according to the European guidelines, primary PCI is recommended if the time from first medical contact to balloon inflation is anticipated to be less than 90 minutes; otherwise, the patient is offered thrombolysis. In patients with AMI, the time from first medical contact to balloon inflation should be 60 minutes if less than 3 hours from symptom onset. For patients presenting in hospitals without a PCI facility, the maximum delay to reperfusion is 120 minutes with a "door-in-door-out" time of less than 30 minutes. The time frame for reperfusion in STEMI is 12 hours, both for thrombolytic therapy and primary PCI, and up to 24 hours for primary PCI in patients with symptoms of ischaemia. Recanalization of a totally occluded artery more than 24 hours from symptom onset in stable patients is not recommended.

Patients with acute chest pain but no persistent ST-segment elevation should be managed according to an assessment of their risk of an adverse event. If patients are identified to be at intermediate or high risk of an adverse cardiac event,

clinicians should discuss with them and/or their carer the risks and benefits of coronary angiography and appropriate revascularization.

Testing serially for biochemical markers of myocardial damage such as troponin during evaluation for ACS adds diagnostic value.

Antithrombotic agents, such as acetylsalicylic acid (aspirin), which reduce the risk of thrombosis by interfering with platelet release and aggregation, are a cornerstone of ACS management and part of WHO "best buys"[43] (acetylsalicylic acid, atenolol and thrombolytic therapy [streptokinase] have also been recommended by WHO for AMI in the current version of Appendix 3,[43] but this is being updated at World Health Assembly 2017). For treatment of AMI, aspirin, a combination of aspirin and anticoagulant therapy, and a combination of aspirin, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors and streptokinase have all been proposed as highly cost-effective measures for Kyrgyzstan.[44]

Stroke

Specialized care in a stroke unit,[45–47] and thrombolytic therapy given within 4.5 hours from the onset of ischaemic stroke[48] and intra-arterial thrombolysis[34] have been demonstrated to improve mortality and disability rates in stroke patients. The primary goal of any stroke care model needs to be that of providing timely access to thrombolysis (systemic or intra-arterial treatment) for eligible stroke patients, and the most rapid transfer to specialized care for all suspected stroke patients.

Coordinated care along the clinical pathway, with effective interaction between the prehospital and the hospital stages of medical and stroke care is critical, reduces delays in diagnosis and treatment and, in turn, improves the long-term clinical outcome of the patient. The prenotification strategy for potential stroke patients has been shown to be effective, though it is still underused even in some Western countries.[49] This strategy initiates a chain of actions: triage priority, and the timely evaluation of patients according to the following recommended time frames for acute stroke algorithm:[40]

- General assessment by a certified stroke team, an emergency physician, or other recognized experts within 10 minutes of arrival at the emergency room (ER), which includes carrying out a computerized tomography (CT) scan;
- ER door-to-stroke team notification ≤15 minutes
- ER door-to-CT scan time ≤25 minutes
- Interpretation of the CT scan within 45 minutes of arrival in the ER;
- ER door-to-fibrinolytic therapy needle time ≤1 hour, or ≤90 minutes from symptom onset;
- ER door-to-monitored bed ≤3 hours for all patients.

To achieve these time frames, an organized protocol must be put into place that prioritizes the emergency evaluation of all potential stroke patients. Any such protocol needs to be tailored to the availability of local resources and the limitations of infrastructure.

Over the past 25 years, the model of organized inpatient care, the so-called "**stroke unit**", for stroke patients has been largely debated. The debate is on whether improving the organization of inpatient stroke care can significantly and cost-effectively improve patient outcome and, if so, whether these benefits are shared across different patient groups. In general, at present, stroke patients are admitted to hospital where they receive care from a range of health-care professionals working in different settings: care of stroke patients is often provided by general/internal medicine and/or neurology geriatric departments where they would be managed alongside a range of other patient groups. In contrast, stroke units are led by multidisciplinary teams, made up of specialized nursing staff and therapists who care and treat only patients with stroke. It has been proven that patients receiving stroke unit care are more likely to survive, regain independence and return home than those receiving a less organized service, irrespective of patient age, sex, stroke severity and subtype.[45–47] Care of acute stroke and rehabilitation in stroke units is one of the effective recommendations by WHO.[43]

Thrombolytic therapy restores cerebral blood flow in patients with acute ischaemic stroke and may lead to an improvement or resolution of neurological deficits. Thrombolytic therapy has been shown to substantially benefit clinical outcomes in selected patients with acute cerebral ischaemia;[48] there is strong evidence to demonstrate that intravenous thrombolytic therapy at the dose used to treat ischaemic stroke within the first 3 hours of onset of ischaemic stroke offers substantial net benefits for virtually all patients with potentially disabling deficits and, within 3–4.5 hours, possible moderate net benefits.[34,48] WHO's "best buy" recommendations on thrombolytic therapy in acute stroke are currently being updated.[43]

Finally, intra-arterial treatment is highly effective for emergency revascularization, and has been demonstrated to be safe and effective in patients with acute ischaemic stroke caused by a proximal intracranial occlusion of the anterior circulation.[34] To perform these treatments, an adequate environment and infrastructure meeting current guideline standards are necessary, as well as a trained and expert dedicated staff. Moreover, it is critical to monitor performance of the care system with adequate indicators and registries (*see* section 6: Quality control and performance management).

The FeSS is a multidisciplinary, supported evidence-based nursing protocol for the management of fever, hyperglycaemia and swallowing dysfunction, and has been demonstrated to significantly improve patient outcomes after discharge from stroke units.[50] A specific educational training programme is available with the protocol; its implementation would not be expensive, would positively impact on the majority of patients admitted to stroke centres, and does not require complex technology.

Strengths

ACS

The model of service delivery in Kyrgyzstan has been rated as a major barrier to the acute management of AMI and stroke.[5]

Basic equipment and basic drugs are available in the public hospital setting for ACS patients. The National Centre of Cardiology in Bishkek is equipped with a CT scanner for CT angiography (12 hours/day) and catheterization laboratory (cath-lab); nevertheless, the cath-lab is not used to its full potential because of the limited availability of catheters and human resources. The cath-lab is used not only for ACS patients but also for other vascular procedures. In the private sector, the medical competence of health professionals and equipment is almost on a par with European Union (EU)-15 countries.

National clinical guidelines, protocols and algorithms for ACS are produced by the MoH, and those reviewed during the mission were found to be evidence-based and updated, although their dissemination (through printed materials) is limited and their implementation in rural areas is still inadequate. Campaigns and actions to empower self-education are conducted, and mainly consist of dissemination of posters and publications focusing on the control and prevention of CVD risk factors.

Stroke

In Kyrgyzstan, dedicated environments with specialized physicians (neurologist) and availability of therapists (physiotherapist and, in some cases, speech therapist) for acute stroke patients are available at four stroke centres: two in Bishkek, the capital city, and one each in the regions of Naryn (Fig. 9–12) and Osh (Fig. 13). The number of stroke patients admitted to hospital wards in Bishkek has been increasing over time; in 2011, it was 70.6% of all stroke patients enrolled in the Bishkek registry, in 2012, it was 79.9%, in 2016 it was above 90%. Data from other regions are not available yet.

Fig. 9–11. Naryn Stroke Unit, dedicated infrastructure and new equipment (opened on 8 September 2016)

Since 2012, a programme to establish stroke units has been led by the MoH within the Den Sooluk National Health Strategy. Nevertheless, some infrastructure and organizational gaps remain that need to be addressed: neuroimaging is not available at all public health facilities with a stroke centre, and stroke patients, once admitted, are for the most part personally responsible for obtaining imaging and other instrumental diagnostic test services through private clinics (and paying for the ambulance to get there).

Fig. 12. Monitored bed in Naryn Stroke Unit

Access to specialists such as a cardiologist or angiologist is possible, and patients may benefit from early neurorehabilitation that includes physiotherapy and, in some cases, a speech therapist. The four stroke centres admitting acute patients are intended to be "intensive" models of care that should have continuous monitoring, high levels of nursing staff and the potential for provision of life support.

The stroke centre at the Naryn Regional Hospital was opened in September 2016 and is equipped with 20 beds, 6 of which are meant to be the ICU; however, neuroimaging is not available and the diagnosis of stroke is done on a clinical basis. To date, one monitor and one ventilator are available (Fig. 9–12). A similar situation can be found at the stroke centre of the Regional Hospital in Osh, where 25 beds are available for stroke patients: no neuroimaging facilities are available and patients who are in a stable condition are referred to a private centre, such as "Yurfaà" (Fig. 13, 14) where, at the price of 3000–4000 sum (US$ 43–58) they can undergo a CT scan or MRI. At both of these stroke centres, multi-professional teams are not employed, though we were told that early rehabilitation strategies in the form of nursing mobilization are available.

Multi-professional teams are in place in the Bishkek Stroke Centres, where 20–30 beds are available. Patients are usually discharged after 12–18 days, either home or to a rehabilitation facility.

As in the case of ACS, private providers are available for stroke care as well (Fig. 14 and 15), offering neuroimaging and diagnostic work-up and in-hospital care comparable to a stroke unit care.

Fig. 13. Osh Stroke Unit

Fig. 14. Yurfaà Centre offers a wide variety of private medical specialist consultations and diagnostics

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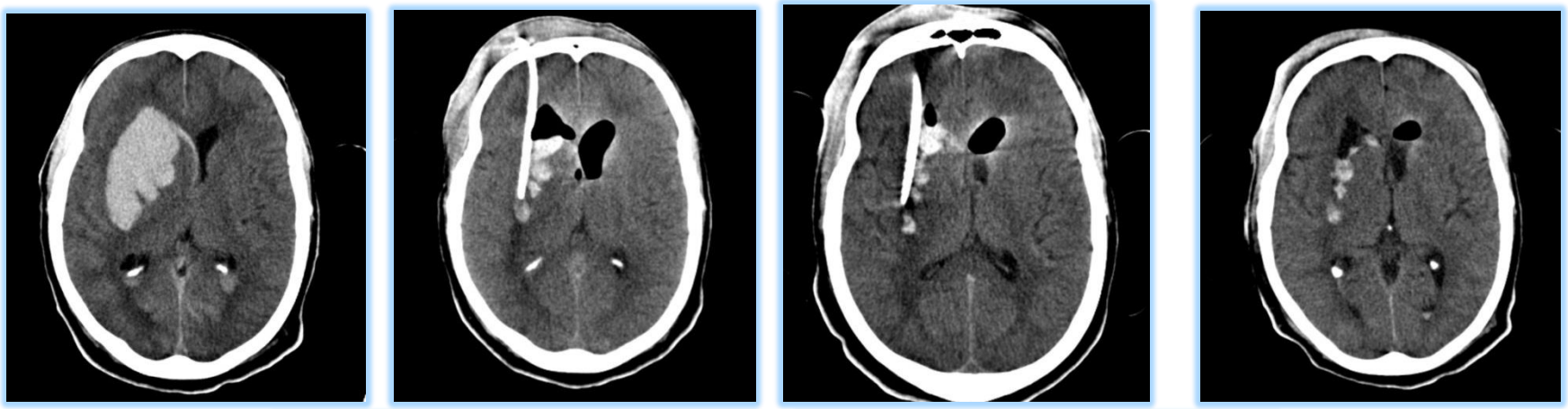
Hanley Daniel
ICH – Whats New?

- MISTIE 3 - Population Demographics and injury Severity
- MISTIE 3 - Trial Execution information, Surgical standardization
- MISTIE 3 - Blinded Results
- MITIE 3 - Tissue injury Hypotheses
- CLEAR 4 - Plan and test patient

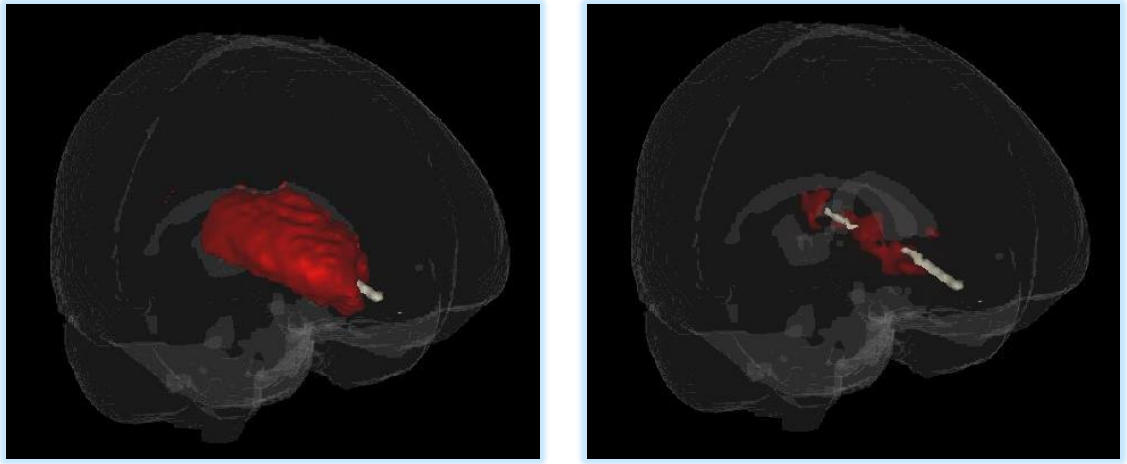
Surgical Intervention & Thrombolysis

Pre-surgery ← Post-Surgery →

+20 Hr. +42 Hr. +52 Hrs.



3D Post-op



3D Post rt-PA

MISTIE III Sites

MISTIE III

Eligibility

Inclusion

- ≥ 18 years old
- Stable, spontaneous, supratentorial ICH ≥ 30mL on CT within 24h of symptom onset
- GCS ≤ 14 **or** a NIHSS ≥ 6; Historical (pre-bleed) Rankin of 0-1
- Stable BP
- Able to randomize within 72 h of diagnostic CT.

Exclusion

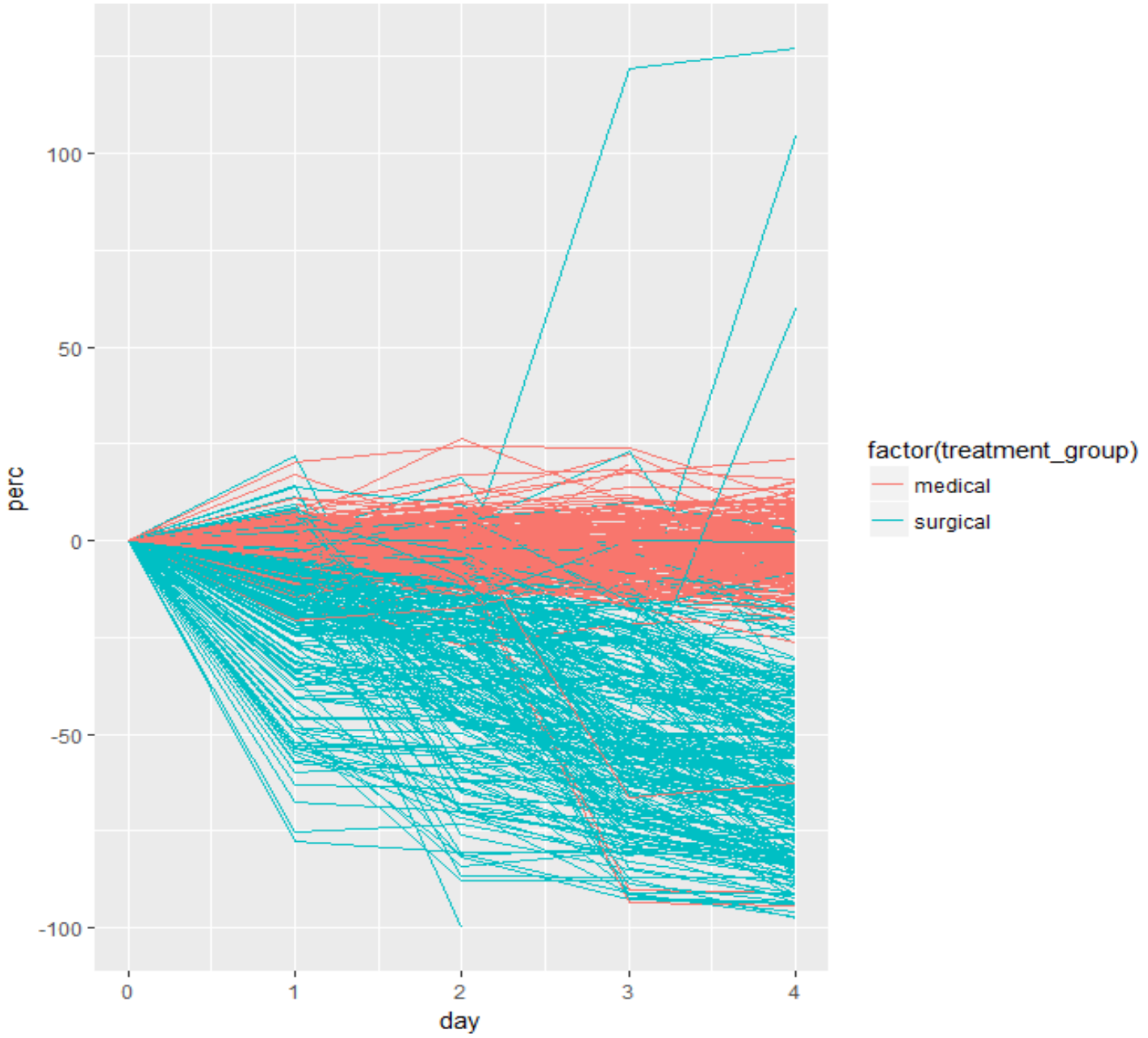
- Underlying vascular etiology
- Midbrain involvement
- IVH-related mass effect requiring EVD
- Coagulopathy
- Other comorbidity(ies) precluding 1-year follow-up
- Risk for embolization
- Unstable and would benefit from emergent, specific intervention

MISTIE III

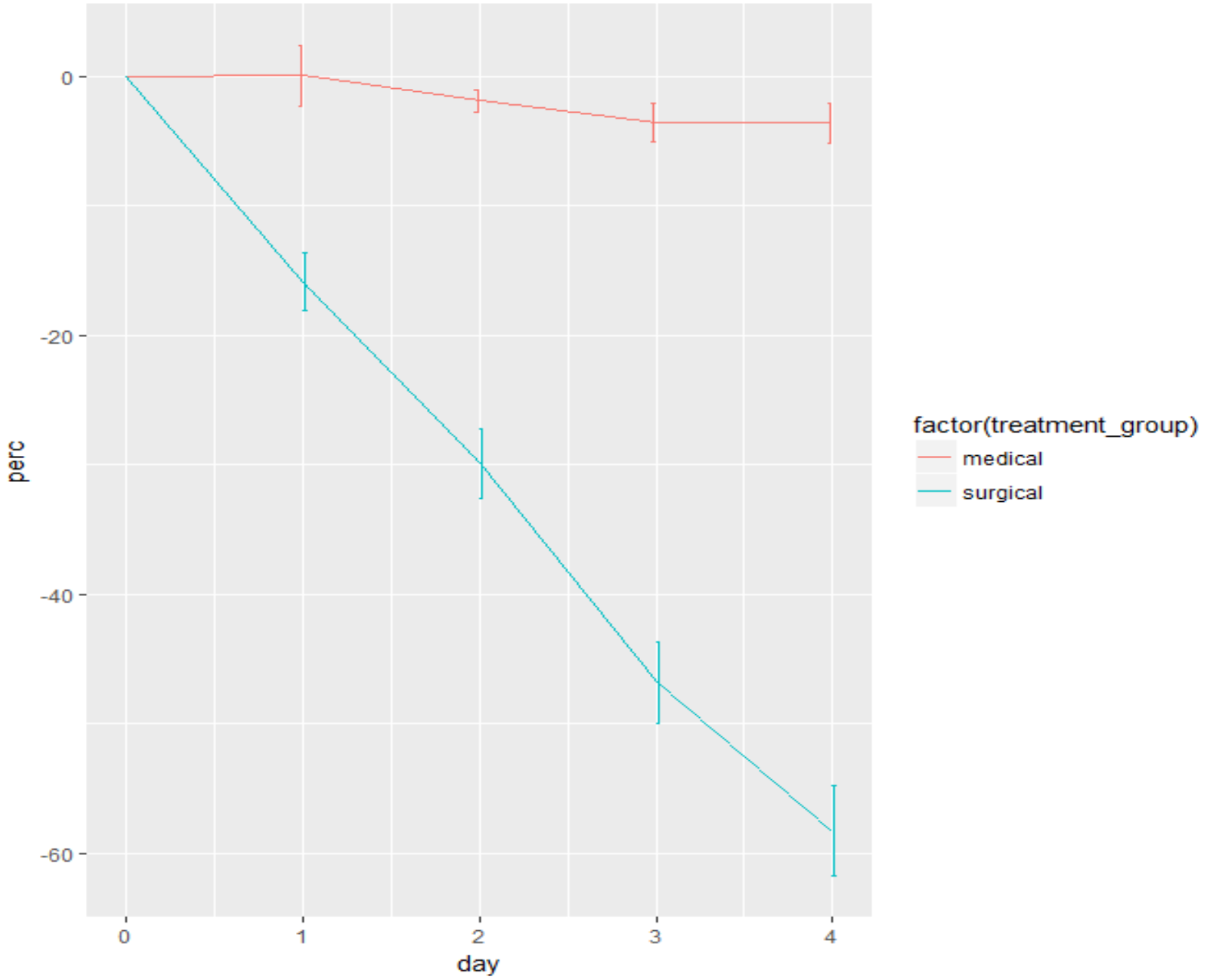
ICH figure

Yi Hao, Dan Hanley

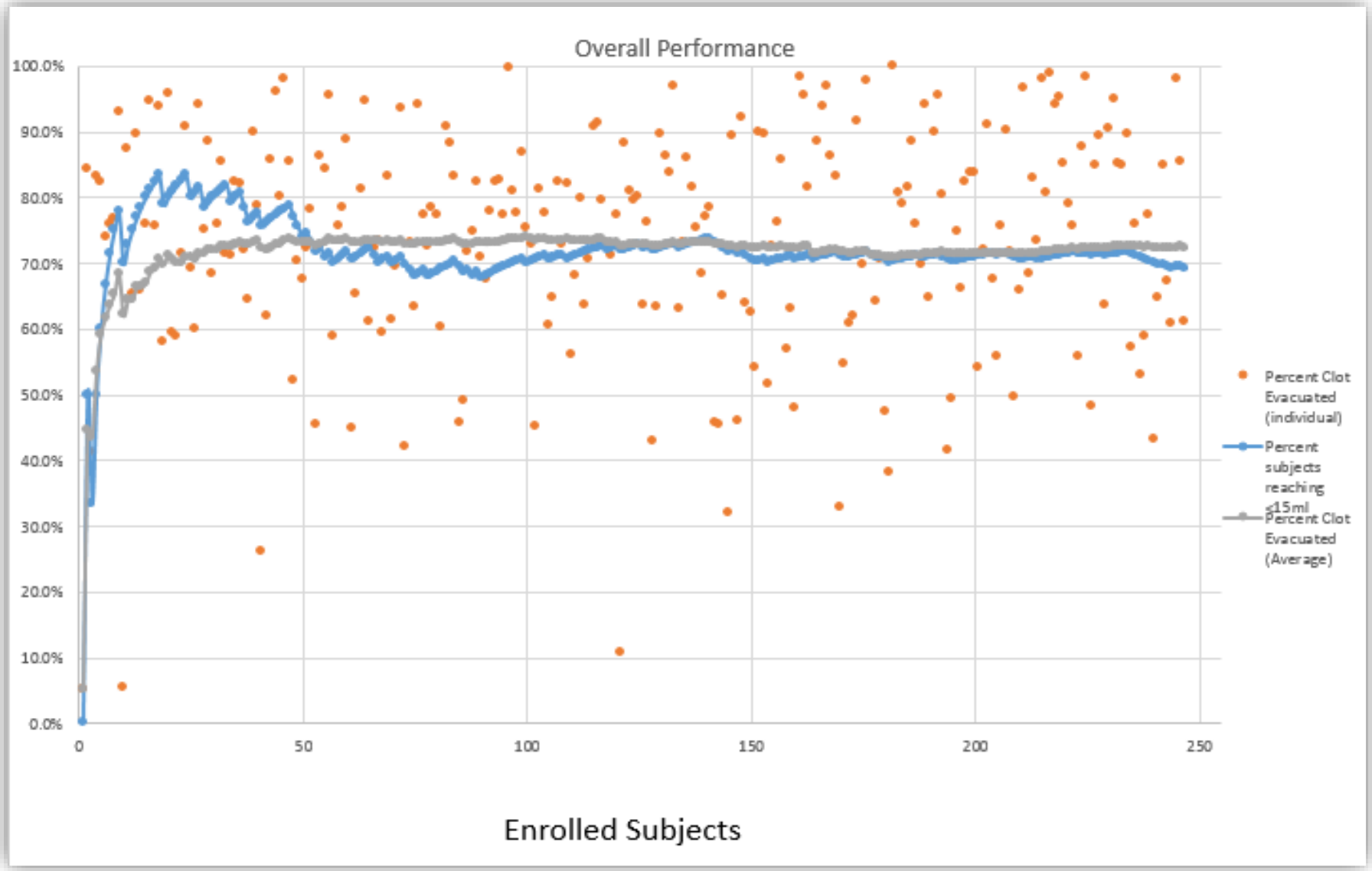
ICH remaining percentage from stability to Day 4 Total 500 patients



Mean of the two groups



Surgical Performance for 250 M3 Surgical Subjects



Surgical Summary: 249 procedures

Patients	Total	Surgeon	% Clot Evacuated
Surgeon Status at time of surgery	Pre-qualified	111	70.5%
	Qualified with probation	79	71.5%
	Fully qualified	60	77%
Catheter Tract/ ICH/IVH Bleeds	Symptomatic	13*	
	Asymptomatic	115*	

* Bleeds in surgical cases, only ICH/IVH expansion or CTH during active phase

Some results – Still Blinded

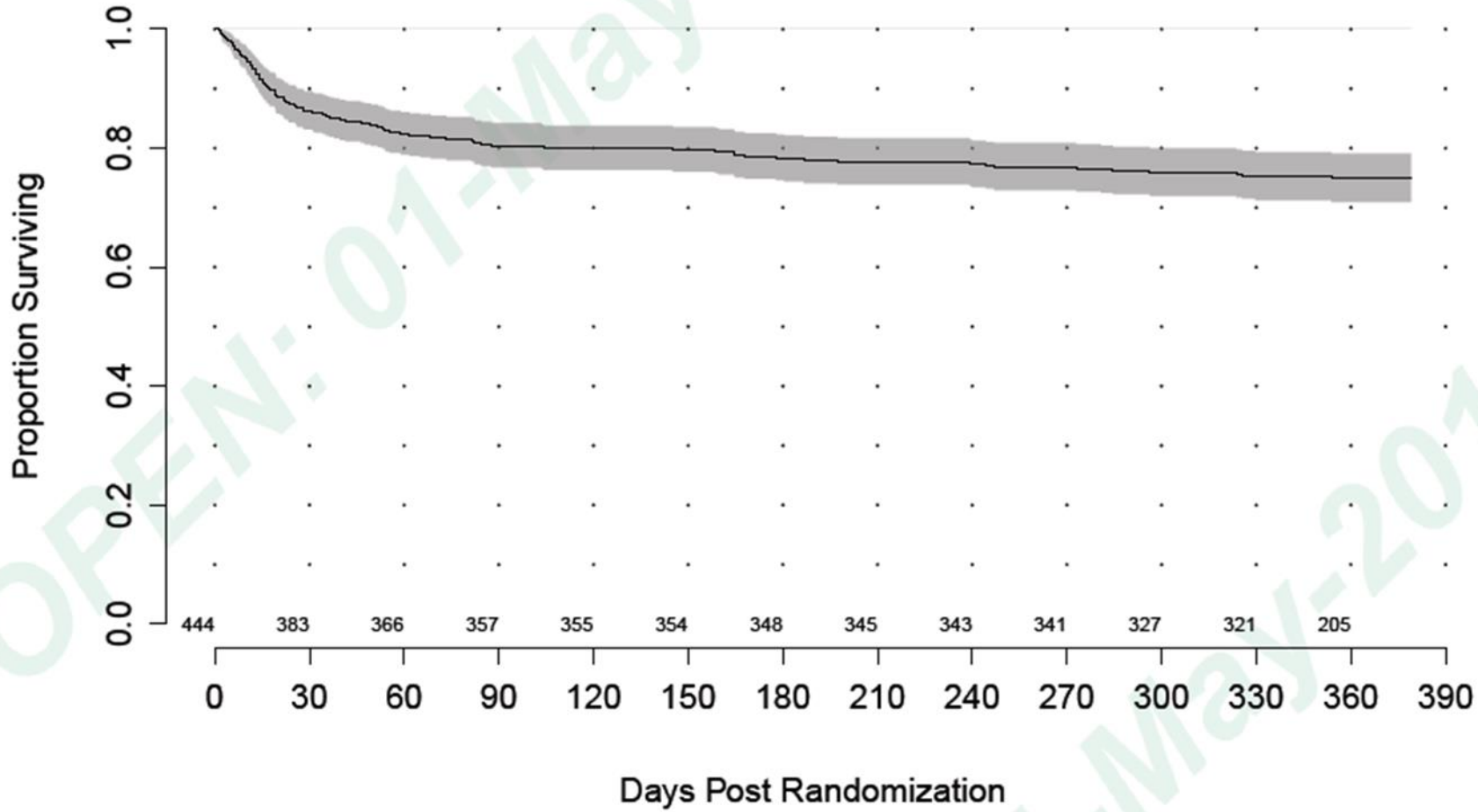


Figure 4.3.1: Kaplan-Meier estimates of survival.

ICH Removal Leads to a Reduction in Perihematomal Edema: Results from the MISTIE III Trial

W. Andrew Mould, Zhiyuan Yu, Hasan Ali, John Muschelli, Radhika Avadhani, Nichol McBee, Karen Lane, Mario Zuccarello, Issam Awad, Daniel Hanley

Introduction

Background

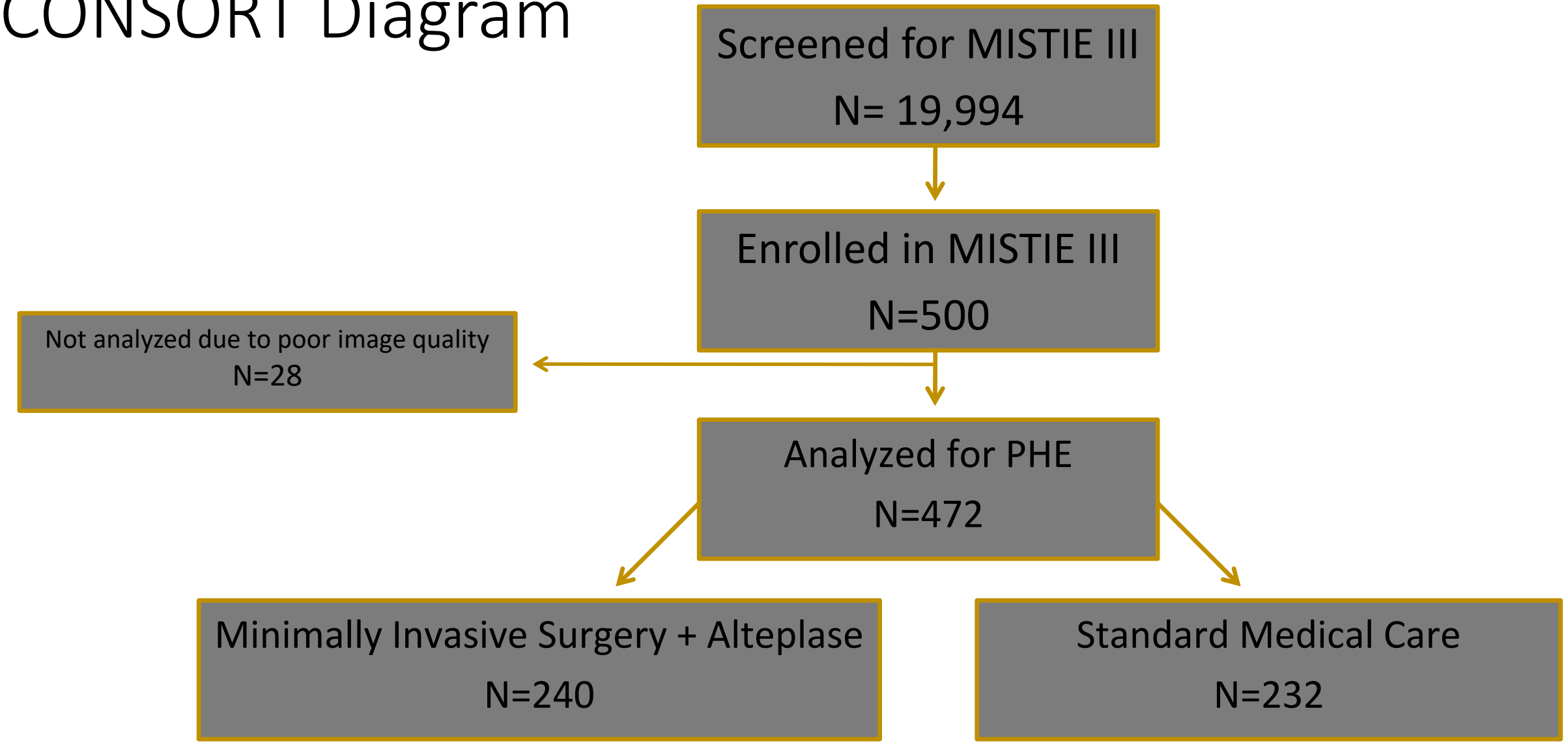
- Intracerebral Hemorrhage (ICH) is a stroke subtype with high mortality and poor functional outcome without a proven treatment
- The secondary tissue injury resulting from perihematomal edema (PHE) appears to contribute to poor patient prognosis
- The MISTIE surgical task is highly standardized and evacuates the clot in the least invasive and most gentle manner compared to all other techniques.

Hypothesis

- We tested the mitigation of the PHE formation in the MISITE III trial where both the surgery and the Imaging were fully standardized.

MISTIE III

CONSORT Diagram



MISTIE III

Results

	Medical (N = 232)	Surgical (N=240)	P-value
Age	61 ± 12.8	61 ± 11.7	0.752
GCS at Randomization	10.5 ± 2.57	10.6 ± 2.65	0.734
Female (%)	97 (41.8)	89 (37.1)	0.293
Lobar Clot location (%)	98 (42.6)	87 (36.3)	0.158
Time from ictus to baseline (Days)	1.66 ± 0.80	1.68 ± 0.89	0.976
Time from ictus to end of treatment (Days)	4.94 ± 0.73	5.63 ± 1.46	<0.0001
Anticoagulated (%)	8 (3.45)	23 (9.58)	0.007
Patients with IVH (%)	94 (40.9)	94 (39.17)	0.636
Baseline ICH volume	48.3 ± 17.8	48.8 ± 17.7	0.690
EOT ICH Volume	46.8 ± 17.4	14.9 ± 12.2	<0.0001

MISTIE III

Conclusions

- These data show the MISTIE II procedure has been successfully reproduced in a large general population of ICHs with a larger group of surgeons in MISTIE III.

- The procedure substantially reduced ICH volumes while also mitigating PHE formation.
- There exists a parallel response between hematoma volume reduction and PHE volume.

MISTIE III