Online only materials

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Sup table I: The structures and functions of the CSPPC stroke prevention and control system

Structure	Functions
National Health Commission of the People's Republic of China	Funding and policy support
The General Office of Stroke Prevention Project Committee, National Health Commission of the People's Republic of China	Stroke treatment technical training, stroke center construction and certification, China Stroke Data Center construction and maintenance, stroke map and stroke treatment green channel construction, supervising the work of Health Commission of Province (City)
The General Office of Stroke Prevention Project Committee, Health Commission of Province (City)	Passing the upper level of Stroke Prevention Project Committee’s work tasks, supervising the hospital's stroke prevention and treatment
Department of medical management and health promotion , disease prevention and control center	Project promotion and specific on-site supervision
Hospital	
Stroke base Hospital / project Hospital	High-risk population screening and intervention, treatment and rehabilitation of stroke patients, primary and secondary prevention

Stroke center hospital	Treatment and rehabilitation of stroke patients, secondary prevention
Regional emergency medical rescue center	Treatment and rehabilitation of stroke patients, secondary prevention
Primary care institutions, community and family doctors	Post-discharge treatment, rehabilitation and follow-up of stroke patients

Sup Table II. China National Stroke Screening Survey Information from 2012 to 2018

Year	Province (city or district)	Screening points	Screening No(million)	Funding (million CNY)
2012	6(40)	80	0.80	40
2013	16(120)	240	1.44	72
2014	31(200)	400	1.20	72
2015	31(200)	400	1.20	72
2016	31(200)	400	1.20	72
2017	31(201)	402	1.256	251.2
2018	31(201)	402	1.256	251.2

Total	31(268)	536	8.352	838.4

Sup Table III. Reporting Information Form from Stroke Center

Contents	Remarks
Basic Information	
Hospital code	
Province	
Name	
Birthdate	
Sex	Male or female
Nation	
Reporting time	
Hospitalization ID	
Stroke onset time	
Arrive time	
Hospitalization time	
Channel to the hospital	Emergency, outpatient, transfer
Way to the hospital	Ambulance, 120, transfer, oneself
Evaluation form at admission	
Aneurysm type	Subarachnoid hemorrhage; subarachnoid hemorrhage and cerebral hemorrhage; not rupture
History of aneurysm	Yes or no
mRS	0-6
NIHSS	0-42
GCS	3-15
Hunt-Hess	0-5
Fisher	1-4
Brain palsy	Yes or no
Physical examination	
Height, cm	100-300
Weight, kg	25-700
BMI	

Systolic blood pressure	40-260
Diastolic blood pressure	40-260
Pulse	40-250
TOAST	
Etiology	LAA; CE; SAA; SOE; SUE
Moyamoya disease	Yes or no
Intravenous thrombolysis	
Treatment status	Yes or no
Reasons of not	Exceed time window; contraindications; Patient rejection; others
Treatment place	Ambulance; 120; CT room; inpatient
Starting time	
ONT	Time from onset to needle
DNT	Time from door to needle
Thrombolytic drugs	rt-PA; Urokinase; Anipase; Reteplase; Tenepase
Dose of r-tPA	20mg≤n≤300mg
Dose of Urokinase	500000IU≤n≤2000000IU
Complications	Intracranial bleeding; Gastrointestinal bleeding; Gingival bleeding; others complications
NIHSS after treatment	0-42
NIHSS at 24hs after treatment	0-42
NIHSS at 7±2days after treatment	0-42
Endovascular treatment	
Treatment status	Yes or no
Reasons of not	Non-macroangiopathy; exceed time window; contraindications; patient rejection; others
Preoperative NIHSS	0-42
Preoperative ASPECT	
Preoperative TICI	0; 1; 2a; 2b; 3
Puncture end time	

OPT	Time from onset to puncture end time
DPT	Time from door to puncture end time
Treatment method	01. Stent retrieval; 02. Throwing; 03. Balloon formation; 04. Stent formation; 05. Arterial thrombolysis; 06. Mechanical thromboembolism
Postoperative NIHSS	0-42
Postoperative TICI	0; 1; 2a; 2b; 3
Revascularization time	
DRT	Time from door to revascularization
Complications	Intracranial bleeding; Arterial dissection; Ischemic; stent falling off; Vascular reocclusion; others
NIHSS at 24hs after treatment	0-42
NIHSS at 7±2days after treatment	0-42
Cerebral hemorrhage	
Site 1	Right or left
Site 2	01. basal ganglia; 02. supratentorial lobe; 03. Cerebellum; 04. Brainstem; 05. ventricle
Bleeding volume	0<N≤200ml
Intracranial examination	CTA; MRA; DSA
Etiology	01. Hypertension; 02. Arteriovenous malformation; 03. Moyamoya disease; 04. Vascular amyloidosis; 05. Intracranial aneurysm; 06. Dural arteriovenous fistula; 07. Cavernous hemangioma; 08. Intracranial venous sinus thrombosis; 09. others
Surgical treatment	Yes or no
Reasons of not	No surgical indication; contraindications; Patient rejection; others
Starting time of surgery	
Time from onset to starting surgery	
Time from door to starting surgery	
Anesthesia type	All anesthesia or local anesthesia
Surgical type	Hematoma removal; Hematoma aspiration; compound surgery;

Complications	01. Cerebral hemorrhage; 02. Cerebral infarction; 03. Secondary epilepsy; 04. Intracranial infection; 05. others
Outcomes	1. cure; 2. improve; 3. Exacerbate; 4. death
Drugs treatment during hospitalization	
Antiplatelet therapy within 48hrs	Yes or no
Drugs	01. Aspirin 02. Clopidogrel 03. Ozaggre 04. Dipyridamole 05. Seclopyridine 06. Cilostazol
Anticoagulant therapy within 48hrs	Yes or no
Drugs	01. Warfarin 02. Rivaroxaban 03. Dabigatran 04. Apixaban 05. Edoxaban 06. Low molecular weight heparin 07. Unfractionated heparin
Antihypertensive	Yes or no
Drugs	01.ACEI 02.ARB 03. Diuretic 04. Beta blocker 05. Calcium antagonist
Lowering blood lipids	Yes or no
Drugs	01. statins 02. niacin and its derivatives 03. fibrates 04. cholesterol absorption inhibitors
Lowering blood sugar	Yes or no
Drugs	01. Insulin 02. Sulfonylurea 03. Biguanide 04. Alpha glycosidase inhibitor 05. Insulin sensitizer 06. Non-sulfonylurea insulin secretagogue
Rehabilitation	
Rehabilitation treatment	Yes or no
Rehabilitation methods	01. Traditional rehabilitation (acupuncture, massage) 02. Exercise therapy (PT) 03. Occupational therapy (OT) 04. Speech training (ST) 99. Others (cognitive training, swallowing therapy, psychotherapy, physiotherapy)
Rehabilitation place	Bedside or rehabilitation department
Health preaching	
Preaching	Yes or no
Methods	01. Collective ward education 02. One-by-one education 99. Others
Discharge assessment	

Discharge time	
Discharge models	1. doctor's advice 2. Transfer to another hospital 3. Transfer to community health service centers 4. disch ama 5. Death
Cause of death	01. Respiratory circulatory failure 02. Cerebrovascular disease 03. Pulmonary infection 04. Upper gastrointestinal bleeding 05. Acute renal failure 06. Injury and poisoning 98. Unknown 99. Others
Death time	
mRS	0-6
NIHSS	0-42
GCS	3-15
Drugs type	

Abbreviation: MRS-Modified Rankin Scale**;** NIHSS-National Institute of Health stroke scale**;** GCS-Glasgow Coma Scale**;** BMI-Body mass index**;** LAA-Large-artery atherosclerosis (embolus / thrombosis)**;** CE-Cardioembolism (high-risk / medium-risk)**;** SAA-Small-vessel occlusion (lacune)**;** SOE- Stroke of other determined etiology; SUE- Stroke of undetermined etiology**;** ONT-Onset-to-needle time**;** DNT-Door-to-needle time**;** r-tPA-recombinant tissue plasminogen activator**;** ASPECTS- Alberta Stroke Program Early CT Score**;** TICI- Thrombolysis in cerebral infarction**;** OPT-Onset-to-puncture time; DPT-Door-to-puncture time**;** DRT-Door-to-revascularization time**;** CTA- computed tomographic angiography **;** MRA- magnetic resonance angiography**;** DSA- digital subtraction angiography**;** ARBs-Angiotensin-receptor blockers**;** ACEI-Angiotensin converting enzyme inhibitors

Sup Table IV. Monitoring information about thrombolytic therapy in 2017 and 2018[#]

	2017	2018
No. of thrombolytic therapy	19349	53504
Age, years, median (IQR)	65(57-74)	65(56-73)
Sex-Male, n (%)	12332(63.7)	33213(62.1)
Thrombolytic drugs, N		
r-tPA	16488	42175
Urokinase	2861	9170
Others	0	2167
DNT, minutes, median (IQR)	50(40-65)	48(35-62)
ONT, minutes, median (IQR)	180(128-235)	175(122-230)
NIHSS at admission, median (IQR)[†]	7(4-12)	6(3-12)
NIHSS at discharge, median (IQR)[†]	3(1-7)	2(0-6)

Complications, n (%) ‡	442(14.8)	1887(12.1)

The discrete variable was expressed in the frequency (percentage), continuous variable was expressed in the medians (IQR).

† N=773 in 2017 and N=367187 in 2018

‡ N=2987 in 2017 and N=15632 in 2018

IQR=interquartile range; r-tPA= recombinant tissue plasminogen activator; ONT=Onset-to-Needle time; DNT-Door-to-Needle time

Supplement V – Stroke Care Systems in US, Europe and Japan

Stroke Care Systems in the United States

Stroke is a leading cause of mortality and disability globally [1]. At the beginning of the 21st century, the American Stroke Association (ASA) convened a multidisciplinary group, the Task Force for developing recommendations on the organization and operation of systems of care for the treatment of stroke patients throughout the United States [2]. According to the recommendations, a stroke system should contain seven key components-the primordial and primary prevention, community education, notification and response of emergency medical services, acute stroke treatment, subacute stroke treatment and secondary prevention, rehabilitation and continuous quality improvement (CQI) activities. Our CSPPC stroke program also follows the above principles.

The primordial and primary prevention focus on modifiable stroke risk factors, either in development or established [3]. Community-based organizations, policymakers, and other stakeholders work together to support and assist in the prevention regimen in the stroke system. With the increasing global stroke burden, it is believed that current primary stroke prevention strategies are not sufficiently effective [4]. More importance should be attached to stroke risk factor modification [5].

Prehospital stroke care delivered by Emergency medical service (EMS) operators and dispatchers play a critical role in determining the patient outcomes by accurate and rapid stroke recognition and transportation of patients to appropriate receiving hospitals. Ongoing stroke-specific training on assessment tools such as stroke scales and feedback greatly helps EMS stroke recognition and triage [6]. Prehospital performances are measured by several EMS target times [7], including the time between the receipt of the call and the dispatch of the response team(<90 seconds), EMS response time(<8 minutes), dispatch time(<1 minute), turnout time(<1 minute), the on-scene time(<15 minutes). The stroke system monitors adherence to these goals and implement process changes. Our stroke map and stroke 'Green Channel' are a good response to pre-hospital care.

Acute stroke treatment begins in the hospital and centered on the stroke team. There are four levels of hospital designation for acute stroke care in the United States: the basic care hospital, acute stroke ready hospital (ASRH), primary stroke center (PSC) and comprehensive stroke center (CSC). We are also building two levels and four layers stroke center system. The ASRH is capable of CT scan of head and intravenous thrombolysis for acute stroke patient 24/7, but there is no stroke unit in ASRH so patient leaves within two

hours of emergency department arrival or once medically stable [8]. ASRH usually transfers patients to PSC or CSC in a so-called drip-and-ship way. National standards for defining stroke center capabilities in the United States began in 2000 by the Brain Attack Coalition first only for PSC [9]. In 2005, further accreditation of CSC was made by the Joint Commission [10]. PSC and CSC are both able to provide acute stroke care and admit stroke patients into stoke unit, but only a CSC is capable to meet concurrent needs of multiple complex stroke patients and to cover full spectrum of hemorrhagic stroke care with 24/7 neurointerventionalist, neurosurgeon, and neurologists.

According to relevant guidelines, subacute care and secondary stroke prevention is critical to optimizing patient outcomes, especially with consistent implementation [11]. The intensity of rehabilitation services often is a critical determinant in the recovery of stroke patients [12]. AHA/ASA guidelines on rehabilitation provide a framework for interdisciplinary rehabilitation care of the stroke patient [13]. The use of coordinated, multidisciplinary stroke rehabilitation teams has been shown to diminish mortality rates for stroke patients [14]. In order to solve this problem, CSPPC implement stroke-doctor training program and stroke community rehabilitation program. As of December 31, 2018, more than 1000 stroke doctors have started to work.

The CQI strategies aim to ensure that the system of stroke care is effective in whole and in part, and finally translates into improved patient outcomes by evaluating performance measures. Important AHA/ASA quality improvement programs include Get with The Guidelines® (GWTG), Target Stroke initiative and Mission: Lifeline® Stroke [15]. GWTG collects data on patient characteristics, hospital adherence to guidelines and patient outcomes [16]. Launched in 2010, Target: Stroke^{SM} was committed to helping health care professionals streamline their processes to achieve shorter DNT times for eligible patients with acute ischemic stroke and achieved great success [17]. The CSPPC also has designed a CQI strategies, which including 30 items. Every year, CSPPC will organize experts to conduct on-site supervision and inspection. In the future work, CSPPC will begin to evaluate the implementation and effective of this CQI strategies. At the 2019 International Stroke Conference, the AHA announced that from phase I to phase II, median DNT time decreased from 66 minutes (interquartile range [IQR] 51–87) to 51 minutes (IQR 38–67) and released Target Stroke: phase III to lead to faster and more complete reperfusion [18]. In 2018, our monitoring data showed that DNT has been reduced to 48 minutes (IQR, 35-62) from 50 minutes in 2017.

Stroke Care Systems in Europe

In Europe, stroke is still one of the leading causes of death and long-term disability, and its overall burden will continue to increase by 35% between 2017 and 2050 largely owing to an aging population [19]. Although the last two decades have seen a tremendous advance in stroke prevention and acute management which has the potential to dramatically reduce the stroke burden [20], one of the biggest problems of the acute stroke care in Europe is the large discrepancy between various geographic regions in the availability and quality of stroke services [21].

The European Stroke Organization (ESO) prepared a European Stroke Action Plan (ESAP) for the years 2018 to 2030, in cooperation with the European patient organization Stroke Alliance for Europe (SAFE) [22]. Similar as the USA, the ESAP also addresses that the stroke care domains include primary prevention, management of acute stroke, secondary prevention, rehabilitation, evaluation of stroke outcome and quality assessment. Differently, organization of stroke services and life after stroke are also covered in the ESAP [34].

There are two levels of institutional stroke care (certificated by the ESO) in Europe: Stroke Unit (SU) and Stroke Center (SC) [23]. The SU provides basic stroke care including IV thrombolysis, neuro-intensive care, secondary prevention, early treatment of complications and start of rehabilitation. In addition to providing the same service as a SU, the SC also offers thrombectomy and other neuroradiological and surgical interventions. The ESO Stroke Unit- Committee performed re-certification every five years, plus random site visits, with the goals of setting standards for stroke treatment in Europe, improving quality and reduce variation [24]. Although to date little attention has been paid to life-long services required after stroke, more and more studies and stroke organizations are underlining the importance of life after stroke [25].

Stroke Care Systems in Japan

Similar as the USA and Europe, stroke also remains a leading cause of death and disability in Japan. However,

there are some differences between Asian (Japan and China) and the western countries. Japan published its own stroke guidelines in an English version in 2011 [26]. There are two kinds of organized stroke unit care in Japan: stroke care units (SCUs) and stroke units (SUs) [26]. SCU in Japan is more like an intensive care unit specializing in stroke, whereas SU, similar as SUs in Europe, refers to a ward in which a stroke team composed of staff with different medical skills providing treatment from acute phase to rehabilitation [27]. It has been demonstrated that compared with the general medical wards, SCUs were associated with a decrease in stroke mortality [28]. The Japanese healthcare payment system allocated special medical fee for SCUs, allowing the cost of treatment in SCUs to be reimbursed at more than twice the cost of treatment in general medical wards. However, SCUs have not been widely established in Japan because of its high organizational requirements, and significant regional variations exist in Japanese stroke care [29].

Stroke Care Systems in China

Stroke is one of the main causes of mortality, long-term physical and cognitive impairment in China [30]. A previous study suggested that in 2016, the global lifetime risk of stroke from the age of 25 years onward was approximately 25%, and China had the highest estimated risk (39.3%; 95% uncertainty interval, 37.5 to 41.1) [31]. The burden is expected to increase further as a result of population ageing, an ongoing high prevalence of risk factors (eg, hypertension), and inadequate management [32]. Furthermore, the unique challenges faced in China included: a vast territory, a huge difference in medical levels between regions, acute stroke treatment is not timely (less than 3% of ischemic stroke received intravenous thrombolysis) and the rate of rehabilitation is low. In order to face the challenge, CSPPC will fully promote the construction of the stroke center, accelerate the promotion of acute stroke treatment techniques, accelerate the construction of a regional stroke treatment system. Furthermore, CSPPC will actively carry out work around the “Reducing Millions of New Disability Projects”, vigorously promote the homogenization of stroke prevention and management and technical capabilities, and comprehensively advance the prevention and treatment of stroke in China. The CSPPC-Stroke program provides a template that can be borrowed for stroke prevention and control in other developing countries around the world.

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