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SUPPLEMENT 6

5th Hong Kong Neurological Congress cum 30th Annual Scientific Meeting of The Hong Kong Neurological Society

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List of Speakers

Name	Affiliation
Prof Uccelli Antonio	University of Genoa, Italy
Prof José Biller	Loyola University Chicago, USA
Prof Andrew J Cole	Harvard Medical School, USA
Prof Raffaele De Caterina	G. d'Annunzio University, Italy
Prof Martin Grond	University of Marburg, Germany
Dr David Hargroves	East Kent Hospitals University NHS Foundation Trust, United Kingdom
Dr Jessica Li	Queen Elizabeth Hospital, Hong Kong SAR
Dr Kate Lui	Tseung Kwan O Hospital, Hong Kong SAR
Prof Vincent Mok	The Chinese University of Hong Kong, Hong Kong SAR
Prof Friedemann Paul	Charité Universitätsmedizin Berlin, Germany
Prof Carolyn Sue	University of Sydney, Australia
Prof Eugene Trinka	University Hospital of the Paracelsus Medical University, Austria
Prof Claude M Wischik	University of Aberdeen, United Kingdom
Dr Winnie Wong	Caritas Medical Centre, Hong Kong SAR
Prof Ken KL Yung	Hong Kong Baptist University, Hong Kong SAR

SCIENTIFIC PROGRAMME

Venue: Grand Ballroom, Level 3, JW Marriott Hotel, Admiralty, Hong Kong SAR

11 November 2017, Saturday

08:15 – 08:30	Registration	Function Room
08:30 – 10:00	**EDUCATION SESSION FOR NEUROLOGY TRAINEE** Chairpersons: *Eric Chan, Betty Ng* **Applied Anatomy of the Cranial Nerves** *Jose Biller* **Applied Anatomy of the Brainstem** *Jose Biller* **Applied Anatomy of the Spinal Cord Vascular Supply** *Jose Biller*	**POSTER PRESENTATION**
10:00 – 10:30	Coffee Break	
10:30 – 11:30	**DISSERTATION HIGHLIGHTS** Chairpersons: *Carlin Chang, WK Cheng* Judges: *Paul Chang, WC Fong*	
11:30 – 12:15	**BAYER STROKE SYMPOSIUM** Chairpersons: *WC Fong, PW Ng* **Evidence-based Strategy for Patients with Atrial Fibrillation and High Risk of Stroke with an Update of UK Use of Telemedicine and Intravenous and Intra-arterial Recanalisation Therapy** *David Hargroves*	
12:30 – 12:45	**OPENING CEREMONY** Guest of Honour: *Prof Philip Li, President of Hong Kong College of Physician*	
12:45 – 13:45	**DAIICHI SANKYO LUNCH SYMPOSIUM** Chairpersons: *Richard Li, Joshua Fok* **Stroke Prevention in Vulnerable Patients with Atrial Fibrillation: Latest Evidence and Practical Consideration** *Raffaele De Caterina*	
14:00 – 14:45	**BOEHRINGER STROKE SYMPOSIUM** Chairpersons: *Yannie Soo, SH Li* **Challenges in Acute Stroke Management for Patients on Novel Oral Anticoagulant: Clinical Applications of Reversal Agents** *Martin Grond*	
14:45 – 15:30	**FREE PAPER PRESENTATIONS** Chairpersons: *Carlin Chang, SH Ng* Judges: *WC Fong, WK Cheng*	
15:30 – 15:45	Coffee Break	
15:45 – 16:30	**STROKE SYMPOSIUM** Chairpersons: *CY Huang, Mona Tse* **Special Cases in Acute Stroke: Challenging the Norm** *Jose Biller*	
18:00	Faculty Dinner (by invitation only)	

12 November 2017, Sunday

		Function Room
08:15 – 08:30	Registration	
08:30 – 10:00	**MOVEMENT DISORDERS SYMPOSIUM** Chairpersons: *KL Tsang, Germaine Chan*	**POSTER PRESENTATION**
	Phenotype Meets Genotypes in Movement Disorders *Carolyn Sue*	
	Nomenclature of Genetic Movement Disorders *Carolyn Sue*	
	Neural Stem Cell Harvesting Technology Using Magnetic Nanoparticles *Ken KL Yung*	
10:00 – 10:15	Coffee Break / Poster Viewing Session Judges: *Bell Tse, KL Shiu*	
10:15 – 11:45	**EISAI EPILEPSY SYMPOSIUM** (CO-ORGANISED WITH HKES) Chairpersons: *Colin Lui, Gardian Fong*	
	Absence of Tau Pathology in Surgically Resected Brain Tissue from Adults with Medication-refractory Epilepsy *Kate Lui*	
	Epilepsy and Dementia *Andrew J Cole*	
	Epilepsy in Elderly: Special Consideration and Challenges *Eugene Trinka*	
12:00 – 13:00	**MERCK LUNCH SYMPOSIUM** Chairperson: *WK Cheng*	
	Introduction of the Novel Drug Targets in Multiple Sclerosis *Uccelli Antonio*	
13:10 – 14:40	**NOVARTIS MULTIPLE SCLEROSIS SYMPOSIUM** (CO-ORGANISED WITH HKMSS) Chairpersons: *KL Shiu, TH Tsoi*	
	Updates on Neuromyelitis Optica *Friedemann Paul*	
	Neuromyelitis Optica: East Meets West *Jessica Li*	
	The Hong Kong Neuromyelitis Optica Spectrum Disorder Registry *Winnie Wong*	
14:40 – 14:50	Coffee Break	
14:50 – 16:20	**DEMENTIA SYMPOSIUM** Chairpersons: *B Sheng, Richard Kay*	
	Tau Pathology and the Potential of Anti-tau-aggregation Therapy in Alzheimer Disease *Claude M Wischik*	
	Targeting Cerebral Small Vessel Disease for Dementia Prevention *Vincent Mok*	
16:20 – 16:30	Closing Ceremony and Award Presentations	

Appied Anatomy of the Cranial Nerves

ES 1

José Biller
Loyola University Chicago Stritch School of Medicine, Chicago, USA

The objective of this session is to review the applied anatomy of the cranial nerves using the clinical-anatomic-pathologic correlation methods.

Applied Anatomy of the Brainstem

ES 2

José Biller
Loyola University Chicago Stritch School of Medicine, Chicago, USA

The objective of this session is to review the applied anatomy of the brainstem using the clinical-anatomic-pathologic correlation methods.

Applied Anatomy of the Spinal Cord Vascular Supply

ES 3

José Biller
Loyola University Chicago Stritch School of Medicine, Chicago, USA

The spinal cord contains lower motor neurons, first-order sensory neurons, second-order spinothalamic neurons, interneurons, as well as ascending and descending tracts connecting these cells with the brain. The objective of this session is to review the applied anatomy of the spinal cord vascular supply using the clinical-anatomic-pathologic correlation methods.

DH 1

Outcomes of Carotid Artery Stenting for Radiation-induced Carotid Stenosis with or without Temporal Lobe Necrosis

Simon CH Chan
Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Background: This study aimed to evaluate the short-term and long-term outcomes of carotid artery stenting (CAS) for radiation-induced carotid stenosis by comparing the outcomes of CAS for radiation-induced versus atherosclerotic carotid stenosis, with a particular interest in the concomitant presence of temporal lobe necrosis, which is associated with radiation-induced carotid stenosis as both are mediated by radiation-induced vascular injury.

Methods: A retrospective cohort analysis was conducted for 32 patients with radiation-induced carotid stenosis after radiotherapy for nasopharyngeal carcinoma and 69 patients with atherosclerotic carotid stenosis who underwent CAS between January 2011 and December 2014 in Queen Elizabeth Hospital. Primary outcomes included perioperative complication composite endpoint (including cerebrovascular events, myocardial infarction, and all-cause mortality), ipsilateral ischaemic stroke or transient ischaemic attack (TIA) beyond 30 days after CAS, and a primary composite endpoint of perioperative complication composite endpoint and ipsilateral ischaemic stroke or TIA beyond 30 days after CAS. Secondary outcomes included mortality beyond 30 days after CAS and development of in-stent restenosis of ≥50% on follow-up imaging. Survival analyses of the primary and secondary outcomes in radiation-induced and atherosclerotic carotid stenosis and in radiation-induced carotid stenosis with or without temporal lobe necrosis were performed.

Results: In patients with radiation-induced carotid stenosis, there was a non-significant trend of lower perioperative complication risk (absolute risk difference= -4.5%, odds ratio=0.521, 95% confidence interval [CI]=0.102-2.649, P=0.715), particularly in terms of cerebrovascular events. In addition, there was a non-significant trend of higher risk of ipsilateral ischaemic stroke or TIA beyond 30 days after CAS (absolute risk difference=3.9%, hazard ratio [HR]=1.432, 95% CI=0.383-5.354, P=0.594). In patients with radiation-induced versus atherosclerotic carotid stenosis, there were no significant differences in the primary composite endpoint (absolute risk difference=0.8%, HR=0.980, 95% CI=0.361-2.657, P=0.980), mortality beyond 30 days after CAS (absolute risk difference=2.6%, HR=1.176, 95% CI=0.394-3.511, P=0.772), and development of in-stent restenosis of ≥50% on follow-up imaging (absolute risk difference=2.6%, HR=1.236, 95% CI=0.348-4.385, P=0.743). In patients with radiation-induced carotid stenosis, the concomitant presence of temporal lobe necrosis did not have a significant impact on the incidence of primary and secondary outcomes.

Conclusion: In patients who underwent CAS for radiation-induced carotid stenosis, there was a non-significant trend of lower perioperative complication risk but higher long-term risk of ipsilateral cerebrovascular ischaemic events. In patients who underwent CAS for radiation-induced versus atherosclerotic carotid stenosis, there were no significant differences in terms of mortality and in-stent restenosis. In patients who underwent CAS for radiation-induced carotid stenosis, the concomitant presence of temporal lobe necrosis did not have a significant impact on the incidence of primary and secondary outcomes. Further large-scale trials are required to determine factors associated with perioperative complication risk and long-term risk of ipsilateral cerebrovascular ischaemic events.

DH 2

A Review of Myotonic Dystrophy in Hong Kong

CF Cheung
Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong SAR

Background: Myotonic dystrophy (DM) is the most common adult-onset muscular dystrophy, with multi-systemic involvement and significant morbidity.
Objective: To describe the clinical characteristics of local DM population and explore the association between cytosine-thymine-guanine (CTG) repeat size and clinical presentation. It is hoped that better understanding of the disease nature may improve the quality of care.
Methods: Clinical records of patients diagnosed with MD in seven major hospitals in Hong Kong from June 2006 to September 2016 were retrospectively reviewed. Only patients with genetic confirmation or the typical clinical and electrophysiological evidence of DM were included.
Results: A total of 91 patients was included; the male-to-female ratio was 1:1.2. Of whom 62 (68.1%) patients had genetically confirmed DM and all were DM type 1. Full genetic reports were available in 45 patients whose CTG repeats were 50 to 149 (n=1, 2.2%), 150 to 999 (n=26, 57.8%), or ≥1000 (n=18, 40%). The mean age of symptom onset was 33.5±14.5 years. Baldness was more common in male than female patients (70.4% vs 28.0%, P=0.001), whereas psychiatric disorders were more frequent in female than male patients (18.4% vs 2.0%, P=0.020). CTG repeat size negatively correlated with age of symptom onset (r= -0.337, P=0.024). Compared with those with <1000 CTG repeats, patient with ≥1000 CTG repeats tended to develop more systemic complications, especially cataracts (44.4% vs 14.8%, P=0.041), dysphagia (72.2% vs 25.9%, P=0.002), falls (94.4% vs 55.6 %, P=0.006), thyroid disorders (44.4% vs 14.8%, P=0.041), and mental retardation (27.8% vs 3.7%, P=0.031). Over the 10-year period, 25 (27.4%) patients had died at the mean age of 55.8±6.9 years, with chest infection (40%) and sudden death (24%) being the most common causes. Predictors for all-cause mortality were severe proximal weakness (odds ratio [OR]=25.50, 95% confidence interval [CI]=4.03-161.01), severe electrocardiography abnormalities (OR=13.83, 95% CI=2.43-78.71), and thyroid disorder (OR=11.50, 95% CI=1.81-73.21).
Conclusion: MD is a multi-systemic illness with significant morbidity and mortality. Patients with more CTG repeats tended to have earlier disease onset and develop more systemic complications. Chest infection and sudden death were the major causes of death. Predictors for all-cause mortality were severe proximal weakness, severe electrocardiography abnormalities, and thyroid disorders. This study provides important background information to facilitate the development of a structured care model for MD in Hong Kong.

DH 3

Incidence of Subtypes, Clinical Features, and Outcome of Guillain-Barre Syndrome and Miller Fisher Syndrome in Hong Kong

ML Li
Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong SAR

Objective: Acute inflammatory demyelinating polyneuropathy (AIDP) was the predominant form of Guillain-Barre syndrome (GBS), whereas Miller Fisher syndrome (MFS) was uncommonly found. In recent years, MFS appeared more frequent. This study aimed to investigate the incidence of subtypes, clinical features, and outcome of GBS and MFS in Hong Kong.

Methods: Medical records of GBS and MFS patients in Tuen Mun Hospital from 2006 to 2016 were retrospectively analysed. GBS and MFS were classified into various subtypes according to the clinical and electrophysiological criteria. The corresponding clinical features and investigation findings were used for prognostic analysis according to the GBS disability score at 6 months.

Results: A total of 75 patients was included for analysis; the male-to-female ratio was 1.88:1. The disease incidence increased with age until 70 years and then declined. Seasonal preponderance was significant in spring and winter (P=0.017). Overall, the disease subtypes were AIDP (n=30, 40%), paraparetic GBS (n=3, 4%), bifacial weakness with paraesthesia (n=1, 1.3%), acute motor axonal neuropathy (n=1, 1.3%), acute motor and sensory axonal neuropathy (n=1, 1.3%), classic MFS (n=12, 16%), acute ophthalmoparesis (n=12, 16%), acute ataxic neuropathy (n=4, 5.3%), and GBS/MFS overlap (n=2, 2.7%). MFS subtypes accounted for 28 patients (37.3%). From 2010 to 2015, the number of patients diagnosed with MFS (n=27, 42.9%) exceeded that with AIDP (n=22, 34.9%). MFS has become a predominant subtype since 2010. Functional outcome at 6 months was significantly associated with GBS disability score at nadir (P<0.001), dysautonomia, reduced distal compound muscle action potential amplitude (odds ratio=6.03, P=0.012), and hyponatremia upon admission (odds ratio=4.43, P=0.021). High GBS disability score at nadir was an independent predictor for poor functional outcome at 6 months.

Conclusions: The incidence of MFS has increased considerably since 2010 and has become the major subtype of all GBS spectrum disorders. Functional outcome at 6 months was significantly associated with GBS disability score at nadir, dysautonomia, reduced distal compound muscle action potential amplitude, and hyponatremia upon admission. GBS disability score at nadir was independently predictive for functional outcome at 6 months.

DH 4

Clinical Features and Neurological Outcomes in a Cohort of Chinese Patients with Anti-GQ1b Antibody Syndrome: a Retrospective Study

TY Wai
Department of Medicine, Northern District Hospital, Hong Kong SAR

Background: Anti-GQ1b antibody has been found in patients with Miller Fisher syndrome, Guillain-Barre syndrome, Bickerstaff brainstem encephalitis, acute ophthalmoplegia without ataxia, acute ataxia without ophthalmoplegia, and ataxic Guillain-Barre syndrome. This study aimed to investigate the clinical features, investigation findings, and outcomes of the spectrum of diseases.

Methods: Data were collected in patients with anti-GQ1b antibody syndrome in terms of presenting symptoms, clinical features, cerebrospinal fluid results, nerve conduction studies, electroencephalography findings, imaging findings, treatment choices, and outcome in terms of functional disability. Comparison was made between patients with positive anti-GQ1b antibody and those with negative anti-GQ1b antibody, and between those with good outcome and those with poor outcome at 3 months from disease onset.

Results: A total of 108 patients who were clinically diagnosed with anti-GQ1b antibody syndrome was identified from three regional hospitals. Of whom, 50 were serologically tested for their anti-ganglioside antibodies; 32 (64%) of them were positive for anti-GQ1b antibody and more likely to develop Miller Fisher syndrome, acute ophthalmoplegia without ataxia, Bickerstaff brainstem encephalitis, and ataxic Guillain-Barre syndrome, whereas Guillain-Barre syndrome was more common in GQ1b-seronegative patients. Patients with preceding respiratory infections had a higher chance of developing anti-GQ1b antibodies. Seropositive patients presented more commonly with ataxia (72% vs 33%) and ophthalmoplegia (72% vs 17%). Prognosis was generally good in GQ1b-seropositive patients, with 86% and 89% of them having a modified Rankin Scale score of 0 to 2 by 3 and 6 months after disease onset, respectively. Prognostic factors of poor outcome included presence of limb weakness, respiratory failure, need for ventilatory support, axonal neuropathy, and abnormal F-wave latencies in nerve conduction studies. A higher modified Rankin Scale score and a more severe degree of limb weakness at initial presentation predicted a poorer outcome.

Conclusions: Patients with anti-GQ1b antibody in general have good prognosis with recovery by 3 to 6 months. Limb weakness, respiratory failure, and need for ventilatory support predict poorer outcome along the disease course.

Evidence-based Strategy for Patients with Atrial Fibrillation and High Risk of Stroke with an Update of UK Use of Telemedicine and Intravenous and Intra-arterial Recanalisation Therapy

David Hargroves

Randomised phase III clinical trials are the gold standard in establishing the core efficacy and safety profile of a new drug. Stringent protocols and extensive inclusion/exclusion criteria are necessary to ensure data as robust and 'pure' as possible. However, these also limit the applicability of results to actual patient populations. Physicians may ask whether a treatment is suitable for their patients with multiple comorbidities or unusual characteristics if few or no such patients are included or analysed in randomised trials. Therefore, it is also important to investigate the benefit-risk profile of new drugs in patients representative of those in routine clinical practice.

There are several retrospective post-marketing surveillance studies and prospective observational studies of the non-vitamin K antagonist oral anticoagulant (NOAC) for stroke prevention in patients with non-valvular atrial fibrillation. Nonetheless, real-world data are limited in comparison of each NOAC to warfarin in patients with non-valvular atrial fibrillation who have had a previous ischaemic stroke or transient ischaemic attack (TIA).

The latest real-world evidence of NOAC, the RE-AFFIRM study provides supporting evidence on how to manage such high-risk patients in routine clinical practice. Results from our study of the three NOACs versus warfarin in non-valvular atrial fibrillation patients with a history of stroke/transient ischaemic attack are relatively consistent with the respective phase III trials and previous stroke/transient ischaemic attack subgroup analyses. All NOACs seemed no worse than warfarin in respect to ischaemic stroke, intracranial haemorrhage, or major bleeding risk. Yet, rivaroxaban is the only NOAC associated with a significant reduction in the composite endpoints (ischaemic stroke/intracranial haemorrhage).

XANTUS (Xarelto for Prevention of Stroke in Patients with Atrial Fibrillation) is an international, prospective, single-arm, observational study to observe the rates of major bleeding and stroke over 1 year in people with non-valvular atrial fibrillation taking rivaroxaban for stroke prevention in Europe, Canada and Israel. XANTUS found the rates and patterns of major bleeding in routine clinical practice to be generally consistent with phase III studies. Of the 6784 patients taking Xarelto, the incidence of major bleeding was 2.1 per 100 person-years. Fatal bleeding, critical organ bleeding, and intracranial haemorrhage were uncommon, and observed in 0.2, 0.7, and 0.4 per 100 person-years, respectively. The incidence of stroke was 0.7 per 100 person-years. The low major bleeding and stroke incidences support findings of the landmark ROCKET AF trial.

The UK has seen a significant uptake of novel telemedicine solutions to facilitate early recanalisation therapy in acute ischaemic stroke. By 2016, 105 of 156 stroke units used some form of telemedicine to aid access to intravenous thrombolysis, 62% of which were networked with other hospitals.

S 2

Stroke Prevention in Vulnerable Patients with Atrial Fibrillation: Latest Evidence and Practical Consideration

Raffaele De Caterina
University Cardiology Division, G. d'Annunzio University, Italy

Atrial fibrillation (AF) is the most common abnormal cardiac arrhythmia in clinical practice, associated with increased morbidity and mortality secondary to stroke and systemic thromboembolism. People with AF are at a much higher risk of stroke. The risk can vary, depending on the presence of other medical conditions such as hypertension, diabetes mellitus, heart failure, and whether the patient has already had a prior stroke, as well as the age of the patient. Therapeutic decision making for patients with AF at risk for stroke is a process that varies from one physician to the next. Guidelines that provide an evidence-based approach to the diagnosis, staging, and tracking of AF-associated stroke are desired. The objective of this lecture is to present a concise overview of the management of AF, with reference to the latest evidence-based approach from various international AF management guidelines. This lecture would also discuss the practical consideration that physicians may come across in their daily practice.

S 4

Special Cases in Acute Stroke: Challenging the Norm

José Biller
Loyola University Chicago, Stritch School of Medicine, Chicago, USA

Learning objectives:

* Provide a roadmap in patients who have known intracranial (or intraspinal) vascular lesions requiring anticoagulant therapy for non-valvular atrial fibrillation, mechanical heart valve prosthesis, left ventricular assist devices, and pulmonary embolism
* Management of novel oral anticoagulant (NOAC) complications in acute settings
* Management of acute ischaemic stroke in patients taking NOACs
* Thrombolysis, endovascular interventions, and NOACs: decision-making guide in acute stroke
* Management of NOAC intracranial haemorrhage
* Risk assessment and management strategies in re-starting anticoagulation after stroke and haemorrhage
* Recommendation for surgical interventions and post-surgical course for those on antithrombotics
* A case in point: real-life use of thrombolytics and antithrombotics

Phenotype Meets Genotypes in Movement Disorders

S 5

Carolyn Sue
Department of Neurogenetics, University of Sydney, Australia

Advances in genomics have led to the realisation that specific clinical phenotypes may have multiple genetic causes. This is illustrated by the phenotypic spectrum of dystonia. For example, patients with craniocervical dystonia may have mutations in *TOR1A*, *GNAL* or *THAP1*; patients with myoclonus and dystonia may have mutations in *SGCE*, *ADCY5* or mtDNA; and patients with dystonia and parkinsonism may have mutations in Parkin, *PLA2G6*, *POLG* or *SPR*. Identification of a causative genetic mutation can inform family planning and thus genetic diagnosis is warranted in affected families. Causative genes may be transmitted by Mendelian traits (ie autosomal dominant and autosomal recessive) or follow an X-linked or maternal pattern (for mtDNA-related dystonia) on inheritance. The diagnosis of dystonia is thus reliant on careful clinical examination, family history, and selective genetic testing. Next-generation sequencing protocols may assist in identifying causative genetic mutations, despite the overlap between clinical phenotypes.

Nomenclature of Genetic Movement Disorders

S 6

Carolyn Sue
Department of Neurogenetics, University of Sydney, Australia

There is a wide spectrum of movement disorders that are genetically determined. The Genetic Task force of the International Movement Disorder Society reviewed the nomenclature of genetic movement disorders and proposed a revised system to correct erroneously assigned loci, duplicated loci, and to provide information of the genetic causes associated with each movement disorder phenotype. Recommendations to assign appropriate phenotype-prefix relationships and link them to causative gene names were made. Due to variable phenotype-genotype correlations, less common movement disorder phenotypes associated with mutations in causative genes were also noted. Loci that conferred increased risk were not included, providing greater clarity to the clinician when reviewing the list of genes that may be associated with each specific phenotype. Nomenclature for Parkinsonism, dystonia, paroxysmal movement disorders, dominant spinocerebellar ataxias, hereditary choreas, hereditary spastic paraplegias, and primary brain familial calcification were proposed.

Neural Stem Cell Harvesting Technology Using Magnetic Nanoparticles

S 7

Ken KL Yung
Department of Biology, Hong Kong Baptist University, Hong Kong SAR

Target-specific cell-harvesting technology has multiple usages and applications in clinical and biomedical research. In order to harvest neural stem cells from the brain for treatment of neurodegenerative diseases including Alzheimer's and Parkinson's diseases, we have developed and patented a novel cell-harvesting technology. We have successfully performed neural stem cells isolation in live subjects by applying specific designed magnetic iron oxide nanoparticles. The magnetically isolated but active stems cells can be developed into neurons for repair of the damage brains. This autologous approach enables the development of a new personalised autologous cell replacement therapy for patients with neurodegeneration. Target-specific cell-harvesting technology has great potential in clinical applications for treatments of various incurable diseases.

Absence of Tau Pathology in Surgically Resected Brain Tissue from Adults with Medication-refractory Epilepsy

Kate Lui
Medical Department, Tseung Kwan O Hospital, Hong Kong SAR

Introduction: Temporal lobe epilepsy is associated with higher prevalence of cognitive impairment. The prevalence and incidence rates of seizures were found to be increased two to six-fold in patients with Alzheimer's disease, compared with age-adjusted controls. The neuropathological hallmarks of Alzheimer's disease include amyloid plaques (extracellular aggregates of the amyloid-β peptide) and neurofibrillary tangles (intracellular aggregates composed of abnormally hyperphosphorylated tau protein). Several studies utilising surgically resected or post-mortem tissue from the brain of people with medication-refractory epilepsy have demonstrated the presence of pathological tau aggregates. Tau aggregation in patients with epilepsy has been reported in the setting of hippocampal sclerosis, focal cortical dysplasia, cortical tubers, glioneuronal tumours, and vascular malformations. The more extensive the tau pathology, the greater the decline in verbal learning and recall. Reduction of endogenous tau levels in various animal models of epilepsy has been shown to be protective against seizures, raising the question of whether certain types of epilepsy should be considered 'tauopathies'. This study aimed to investigate the prevalence and type of tau pathology in adults with medication-refractory epilepsy by evaluating a series of surgical specimens of cortical and/or hippocampal tissue from adults who underwent resective surgery for medication-refractory epilepsy.

Methods: Epilepsy surgical specimens from 44 patients were examined for total tau protein by immunohistochemistry. At the time of surgery, the mean patient age was 44.5 (range, 30-59) years and the mean duration of epilepsy was 23.6 (range, 1-51) years. Histopathological diagnoses included hippocampal sclerosis (n=21), non-specific gliosis (n=5), cortical dysplasia (n=4), dysembryoplastic neuroepithelial tumour (n=4), vascular neoplasms/malformations (n=3), World Health Organization grade II gliomas (n=3), and others (n=4). Tissue from both the hippocampus and cortex was available in 32 patients, hippocampus only in one patient, and cortex only in 11 patients. For immunohistochemistry, anti-human pan-Tau antibody (1:150; A0024, Dako) was used to stain five micron sections obtained from formalin-fixed, paraffin-embedded tissue. Documented cases of Alzheimer's disease were used as positive controls.

Results: Only one out of 44 patients demonstrated tau-related tangles by immunohistochemistry. This patient was a 54-year-old woman with a history of epilepsy for 25 years. Tissue obtained from an anterior temporal lobectomy revealed hippocampal sclerosis with extensive loss of neurons and gliosis in the dentate fascia, CA1, CA2, CA4, and part of CA3. On immunohistochemical staining, tau-related tangles were present in the entorhinal cortex (Braak & Braak stage I of VI). The remaining 43 patients were negative for definitive immunohistochemical staining of tau, with absent subpial band staining, neuropil threads, and neurofibrillary tangles.

Conclusions: In our series of 44 surgical specimens from adults with medication-refractory epilepsy, little evidence of tau pathology was found. This is in contrast to prior studies. Our cohort was significantly younger than those in prior studies; this may have contributed to the absence of tau pathology. Further studies are needed to better understand whether tau pathology plays a role in epilepsy.

Epilepsy and Dementia

S 9

Andrew J Cole
Department of Neurology, Harvard Medical School, Boston, Massachusetts, USA

Both Alzheimer's disease (AD) and temporal lobe epilepsy lead to dysfunction of hippocampal networks associated with circuit remodelling and cell loss that impairs memory. Epilepsy may masquerade as dementia in some individuals with complaints of memory dysfunction, an entity termed 'epileptic pseudodementia'. Treatment with anticonvulsant drugs reversed cognitive symptoms in these patients. Episodic confusion is commonly seen in incipient AD patients and is also a cardinal sign of mesial temporal epilepsy. Recent evidence suggests that the relationship between AD and hippocampal epilepsy may be a vicious cycle that accelerates hippocampal remodelling, cell death, and cognitive decline. The three known genes for early-onset familial AD are highly correlated with clinical seizures, but the occurrence in sporadic AD is less clear. Little is known about network excitability in human AD hippocampal circuitry, as it is seldom detected by standard analysis of routine scalp electroencephalographic recordings. The brief (30 minute) routine scalp electroencephalographic recording in awake AD patients is clinically uninformative and has not been recommended for diagnosis. New evidence from minimally invasive foramen ovale electrode recordings reveals *clinically silent* seizures and abnormal spike discharges in these regions during sleep in patients with early AD-type dementia. Animal studies indicate that the hyperexcitability precedes measurable cognitive deficits. These data suggest that early hippocampal epilepsy in AD patients may be a possible contributor to cognitive dysfunction and disease progression, and thus it may be important to recognise and treat the epileptic phenotype in AD. It is critical to ascertain the incidence of an epileptic phenotype in AD, to develop less invasive tools for detecting the phenotype, and to develop targeted therapeutic agents to attenuate epileptic hippocampal activity without causing drug-mediated cognitive dysfunction.

Epilepsy in Elderly: Special Consideration and Challenges

S 10

Eugene Trinka
University Hospital of the Paracelsus Medical University, Austria

Elderly people are generally defined as those over 60 or 65 years old, but they are a heterogeneous group and may be subdivided based on age and health status. The incidence of epilepsy is highest in elderly people. With a progressive increase in life expectancy, this is the fastest growing segment of patients with epilepsy.

Epilepsies in elderly patients, compared with the younger adults, differ in aetiology, clinical presentation, and prognosis. Challenges in the pharmacologic treatment of elderly patients include physiologic changes associated with ageing, adverse events to which the elderly patients are especially vulnerable, the increased risk in patients taking multiple medications, and toxicity from drug-drug interactions.

Older patients most often have focal seizures, with less prominent auras and automatisms and longer duration of postictal confusion, compared with younger patients. Status epilepticus is more frequent and has a higher mortality, compared with younger patients. The most common specific aetiology is cerebrovascular disease, but the cause remains unknown in many patients.

Diagnosis can be challenging because of several patient-related, physician-related, and investigation-related factors. Over-diagnosis and under-diagnosis are common. We discuss the implications of using newer-generation anti-epileptic drugs in order to educate physicians in choosing appropriate anti-epileptic drugs for older patients. In elderly patients, an optimal treatment outcome of seizure control with minimal or no adverse events depends on the well-informed choice of an anti-epileptic drug by a physician.

Updates on Neuromyelitis Optica

S 12

Friedemann Paul
Charité Universitätsmedizin Berlin, Germany

Neuromyelitis optica (NMO) is a rare autoimmune inflammatory disorder of the central nervous system that predominantly affects the optic nerve, the brainstem, and the spinal cord. NMO had been considered a rare variant of multiple sclerosis, but in 2004 the seminal detection of a highly specific serum biomarker, an autoantibody targeting the astrocyte water channel aquaporin-4, that is present in up to 80% of NMO patients made clear that NMO is a neuroimmunological disease entity distinct from multiple sclerosis. Research activities and publications on various aspects of the disease such as immune mechanisms, animal models, epidemiology, imaging findings, clinical course, and effects of immune therapies have since exploded. In 2015, an international panel of experts proposed new diagnostic criteria for NMO spectrum disorders. Since 2014 several randomised controlled trials have investigated the effect of modern immunomodulatory drugs on relapse rates and disease course in NMO. An increasing number of reports on patients with an NMO phenotype harbouring serum autoantibodies to myelin oligodendrocyte glycoprotein has further dynamicised the NMO research. This presentation provides a comprehensive and clinically useful overview on the new diagnostic criteria for NMO spectrum disorder, as well as on recent insights from basic, clinical, and imaging research, and may guide the audience through new therapeutic approaches and state-of-the-art treatment algorithms for NMO spectrum disorder.

Neuromyelitis Optica: East Meets West

S 13

Jessica Li
Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Neuromyelitis optica (NMO) is a demyelinating disease most commonly affecting the optic nerves and spinal cords. Focusing on anti-aquaporin 4 antibody positive NMO patients, ethnicity may affect the clinical presentation, disease phenotype, and disability outcomes, while recent studies have reviewed similarities in incidence and prevalence of the disease. A global understanding of this disease may facilitate its early recognition, timely and tailor-made treatment for patients in specific regions.

The Hong Kong Neuromyelitis Optica Spectrum Disorder Registry

S 14

Winnie Wong
Department of Medicine and Geriatrics, Caritas Medical Centre, Hong Kong SAR

With the expansion in the knowledge on demyelinating diseases and the advancement in magnetic resonance imaging techniques, the prevalence neuromyelitis optica spectrum disorder (NMOSD) has increased in recent years. Although public awareness and availability of treatment options for multiple sclerosis are increasing, patients with NMOSD are in great deficit of such attention and resources.

Recognising the lack of local epidemiological status of NMOSD, the Hong Kong Multiple Sclerosis Society initiates the Hong Kong NMOSD Registry in 2017. Invitations have been sent to collaborators from both public and private hospitals. Clinical data of patients diagnosed with NMOSD based on the Wingerchuk's criteria were collected. The Registry aims to promote local research collaboration and to benefit patient care by providing data to government bodies for new treatment options. It also serves as a platform for observational studies.

In this presentation, we share the preliminary data of the Registry from most hospitals in Hong Kong. The territory-wide NMOSD Registry is an important resource to facilitate future clinical studies. Moreover, the epidemiological data may assist the application of future resources for NMOSD patients.

Tau Pathology and the Potential of Anti-tau-aggregation Therapy in Alzheimer Disease

S 15

Claude M Wischik
University of Aberdeen, Scotland, UK

In patients with Alzheimer disease (AD), clinical deterioration, functional imaging deficits, and progression of brain atrophy progress in parallel with the accumulation of aggregated tau, beginning 20 years before dementia symptoms appear. Toxic tau oligomers seed further tau aggregation in an autocatalytic manner and propagate the pathology into previously healthy brain regions. Targeting this prion-like processing of tau protein offers an attractive approach for disease modifying and preventative treatment for AD.

Diaminophenothizines reverse the proteolytic stability of tau aggregates isolated from AD brain, reverse pathology and behavioural deficits in transgenic tau mice, and as methylthioninium showed prolonged clinical benefit over 2 years in a phase 2 trial. A stable reduced form known as leuco-methylthioninium-bis(hydromethanesulfonate) [LMTM], taken forward in two phase 3 clinical trials over 15 to 18 months in mild to moderate AD, compared doses of 8 mg/day (as intended control) with 150-250 mg/day. The 8 mg/day dose was found to be effective as monotherapy on cognitive and activities of daily living measures in both trials and higher doses offered no additional benefit. After 9 months, LMTM monotherapy reduced progression of whole brain atrophy from the mild AD rate to the normal elderly control rate, and prevented deterioration in glucose uptake. Efficacy in combination with symptomatic AD treatments is inversely proportional to relative basal forebrain atrophy.

A further trial comparing LMTM 8 mg/day monotherapy with true placebo is required to confirm the findings. LMTM offers the potential to be a first-line disease-modifying treatment from the earliest detectable stages of AD at an oral dose, which is safe and well-tolerated.

Targeting Cerebral Small Vessel Disease for Dementia Prevention

Vincent Mok
The Chinese University of Hong Kong, Hong Kong SAR

Lacunar stroke and deep intracerebral haemorrhage are manifestations of cerebral small vessel disease (SVD). With the advancement in magnetic resonance imaging technology, cerebral SVD has been increasingly recognised to be a highly prevalent condition in the elderly population, associated with other clinical manifestations including cognitive impairment, dementia, Parkinsonism, behavioural disorders, urinary incontinence, and glaucoma. As a whole, cerebral SVD can be considered as one of the commonest brain diseases among the elderly population. In the CU-STRIDE study, the presence of severe SVD has been reported to increase the odds of incident dementia by more than 3 times over a period of 3 years after stroke. Note that most of the subjects with SVD experienced progressive clinical deterioration despite receiving optimal current stroke preventive measures. Given the prevalence and relevance of cerebral SVD, further studies are needed to untangle the pathophysiological mechanisms of sporadic SVD, so as to develop novel and targeted treatments to prevent progression of SVD and its clinical consequences.

Early Atrial Fibrillation Detection by Mobile Phone–based Electrocardiography Programme in Acute Stroke Unit

FP 1

SH Ma, K Ma, B Ip, V Ip, YY Chan, H Leung, Y Soo, T Leung, V Mok
Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR

Background: Atrial fibrillation (AF) is a common cause of ischaemic stroke and results in high morbidity and recurrence rates. Early AF detection is crucial for secondary prevention. Nonetheless, the detection rate of AF with routine electrocardiography (ECG) is low. Prolonged rhythm monitoring by a Holter or implantable loop recorder for every stroke patient is not feasible due to its cost and limited availability. Commercially available ECG interpretation programmes are now available for AF detection using a mobile phone with an additional sensor. We investigate the feasibility and accuracy of implementing the mobile phone–based cardiac rhythm interpretation programme in the acute stroke unit.

Methods: A prospective study was conducted for consecutive patients admitted to the acute stroke unit of Prince of Wales Hospital from April 2016 to August 2017 with the diagnosis of acute ischaemic stroke without a known history of AF. In addition to routine 12-lead ECG, each subject underwent intermittent mobile phone–based cardiac rhythm monitoring at least three times per day until discharge. The programme showed three possible outcomes: possible AF, non-AF, and non-interpretable. Possible AF was required to be confirmed by 12-lead ECG; otherwise, it would be considered as false positive. A 24-hour Holter recording would be arranged after discharge. The primary outcome was the rate of new AF detection by mobile phone–based rhythm monitoring.

Results: A total of 127 subjects was recruited while 15 subjects were excluded. All subjects underwent at least one mobile phone–based rhythm monitoring. The overall incidence of newly onset AF was 4.7% (5 out of 112). Mobile phone–based ECG showed possible AF in 14 subjects, while 12-lead ECG confirmed AF in four of them. The sensitivity and specificity for mobile phone–based ECG monitoring was 80% (95% confidence interval [CI]=28%-99%) and 90% (95% CI=83%-95%), respectively.

Conclusion: Mobile phone–based cardiac rhythm monitoring in the acute stroke unit is feasible. It is a cost effective and accurate means to detect early AF.

Functional Motor Disorders Rehabilitation Programme in Hong Kong

FP 2

KK Ma, Mandy Mak, Eric Chan, SH Ng, MS Chi
Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong SAR

Functional motor disorder (FMD) is one of the disorders seen in neurology or psychiatry clinics. The term 'functional' refers to the condition that no organic cause is identified to explain the clinical presentation. Yet, the diagnosis of FMD is based not only on the absence of evidence of organic disorder but also on positive criteria. This is a conversion disorder under the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Patients unconsciously produce these symptoms secondary to a psychological disorder for primary and secondary gains. The diagnosis should be made by an experienced neurologist.

There has been increasing evidence for physiotherapy to improve such disorder although the exact underlying mechanism is still under exploration. A multidisciplinary team (headed by Jon Stone and Glenn Nielsen) at the Sobell Centre, Queen Square, London has succeeded in treating these patients with physiotherapy and cognitive behavioural therapy. In 2016, Tuen Mun Hospital has adopted a similar approach with the 'Functional Motor Disorders Rehabilitation Programme'. Patients recruited must fulfil the following two criteria: (1) diagnosis was endorsed by both the neurology and rehabilitation teams without major psychosis nor legal, insurance, or workman compensation-related affairs; (2) patients and caregivers were well informed of their illness and cooperative and positive of our programme in helping them. The initial results are promising. This is a preliminary report to be shared with our local colleagues.

FP 3

Transient Ischaemic Attack Clinic is Efficient and Safe for Secondary Stroke Prevention: a Retrospective Cohort of a Tertiary Hospital in Hong Kong

M Ismail, WC Fong, YF Cheung, KW Fong, LT Chan, HF Chan, WT Lo, TC Li, FCC Chan, CH Chan, CO Luk, WY Kwok, MK Yuen, ST Chan, CS Fong, HF Or
Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Background: Transient ischaemic attack (TIA) is an important treatment target as it implies an increased risk of stroke. Prompt treatment can reduce the risk of recurrent stroke in TIA patients. This retrospective cohort study aimed to determine the efficiency and safety of the TIA clinic service.
Methods: In 2012, a fast-track TIA clinic with prompt neurological assessment accessible to the accident and emergency department (AED) referral was established in Queen Elizabeth Hospital. All case records from the TIA clinic attendance from September 2012 to December 2015 were reviewed.
Results: 225 cases from AED, 409 from in-patient, and 125 from private practitioner or government out-patient clinics were referred to the TIA clinic during the specified period. The median waiting time for neurologist consultation for AED cases was 12 days. 163 (72.4%) of cases were diagnosed to have TIA. Stroke recurrence rate of these patients were 0.6% at 2 days, 0.6% at 7 days, 1.8% at 30 days, 1.9% at 90 days, and 3.1% at 1 year.
Conclusion: The TIA clinic service in Queen Elizabeth Hospital is efficient and safe. The risk of stroke recurrence in this cohort is lower than that in international published data.

FP 4

Public Education on Stroke Recognition and Use of 999-ambulance to Promulgate Acute Stroke Treatment

CS Leung, MF Lee, SH Ho, PM Ng, Ellen Yu, KK Lau
Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong SAR

Introduction: We studied the percentage of stroke patients who could arrive at hospital within therapeutic time window between ambulance users and non-ambulance users.
Method: This was a prospective cohort study in a tertiary hospital in Hong Kong from 1 January 2017 to 30 June 2017. All stroke patients admitted to the acute stroke unit were recruited. Patients with stroke occurred in hospital or patients transferred from other hospital were excluded. Patients were divided into ambulance users or non-ambulance users. Therapeutic time window was divided into three phases: phase I was from onset to calling 999; phase II was from calling 999 to the arrival of accident and emergency department; and phase III was from arrival to medical doctor assessment.
Results: 102 consecutive patients were recruited. 48 (47%) patients arrived by ambulance, and 54 (53%) patients did not use ambulance. The median time was significantly shorter for ambulance users than non-ambulance users in terms of phase I (77.5 vs 720 minutes, (P<0.001), phase II (32 vs 44.5 minutes, P<0.001), and phase III (8 vs 15 minutes, P<0.001). 31 (64.6%) out of 48 ambulance users arrived within therapeutic window, compare with 16 (29.6%) out of 54 non-ambulance users (P<0.001).
Conclusions: Public education especially on proper use of ambulance after stroke should be provided.

A Man with Rapidly Progressive Cognitive Decline

P 1

MF Ip, SH Li, TY Wi
Division of Neurology, Department of Medicine, North District Hospital, Hong Kong SAR

Limbic encephalitis is an autoimmune disorder characterised by subacute progressive memory impairment, cognitive decline, psychiatric features, and seizure. The discovery of autoantibodies against different intracellular or cell surface synaptic antigen has led to increasing recognition of the disorder, as well as increasing interest and vigorous research in this field. We present a patient with anti-α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antibody positive limbic encephalitis. We review the literature on the demographics, clinical features, treatment, and prognosis regarding anti-AMPA receptor encephalitis.

A Pale-looking Man with Generalised Weakness

P 2

MF Ip, SH Li, TY Wi
Division of Neurology, Department of Medicine, North District Hospital, Hong Kong SAR

Lead is a naturally occurring heavy metal and is considered by World Health Organization as one of 10 chemicals that is of major public health concern. In Hong Kong, lead poisoning is not common. In the past, lead poisoning was mainly related to occupational exposure (such as welding, battery manufacturing, repairing lead weights–contaminated fishnets in fishermen) and use of proprietary Chinese Medicine. The manifestations of lead poisoning involve multiple organ systems and hence involve various specialties. We present a patient with severe anaemia and severe generalised polyneuropathies who subsequently found to have lead poisoning.

Review on the Performance of Stroke Patients in Geriatric Day Hospital of Caritas Medical Centre

P 3

ML Lee
Department of Occupational Therapy, Caritas Medical Centre, Hong Kong SAR

Background: To evaluate the effectiveness of geriatric day hospital (GDH) training for stroke patients.
Methods: Data of 152 stroke patients who underwent GDH training and assessment by occupational therapists during April 2016 to March 2017 were reviewed.
Results: Of the 152 stroke patients, 40.1% were over 80 years old and 26.3% were between 41 to 65 years old, whereas 70.7% had ischaemic stroke and 23.3% had haemorrhagic stroke. For those who could complete the Cantonese version of Mini-Mental State Examination, 65.8% were classified as cognitively impaired. Overall, GDH training resulted in significant improvement in the Barthel Index, Lawton Instrumental Activity of Daily Living, Hong Kong version of the Functional Test for the Hemiplegic Upper Extremity, and Nine Hole Peg Test (P<0.001). Those aged <65 years achieved greater improvement (not significantly) in the Barthel Index compared with those aged >80 years. The mean pre-discharge Barthel Index was similar between younger and older patients. The initial Barthel Index in haemorrhagic stroke patients was lower than that in ischaemic stroke patients (53.2 vs 63.8), but the improvement in the Barthel Index was significantly greater in haemorrhagic stroke patients than in ischaemic stroke patients (15.3 vs 10.2, P=0.024).
Conclusion: GDH training could improve stroke patients' self-care performance and upper limb function. A quarter of our patients were aged 41 to 65 years; although they had greater improvement (not significantly) in the Barthel Index, they were still moderately dependent upon discharge. Extended rehabilitation service was indicated for younger stroke patients to further improve their self-care independency and decrease the burden to the health care system in the long run. Haemorrhagic stroke patients who had lower post-morbid functional level would need longer rehabilitation to maximise their function.

Review of Factors Associated with Rehabilitation Outcome in Stroke Patients

P 4

Florence Leung
Department of Occupational Therapy, Caritas Medical Centre, Hong Kong SAR

Background: To understand rehabilitation needs and facilitate discharge planning of stroke patients by determining factors associated with rehabilitation outcome.
Methods: Data of stroke patients who received occupational therapy service between April 2016 and March 2017 were reviewed.
Results: Of 522 stroke patients, 28.3% were aged <65 years. Compared with age groups of 65-79 years and ≥80 years, those aged <65 years had significantly higher pre-discharge Barthel Index (BI) [75.25 vs 63.53 vs 39.02] and greater improvement in BI (18.8 vs 6.15 vs 6.38) [P<0.001]. Their cognition (measured by Mini-Mental State Examination score) was higher than that of patients aged ≥80 years (20.37 vs 13.31, P<0.001). Over 80% of patients aged <65 years were discharged home, compared with 60% and 45% in age groups of 65-79 years and ≥80 years, respectively. Compared with ischaemic/infarct stroke patients, haemorrhagic stroke patients had lower initial/pre-discharge BI (P<0.001) and cognition (P<0.007) but greater improvement (P<0.034). Those with initial BI of 21-60 achieved greatest improvement, compared with those with initial BI of 0-20 or 61-90. In multivariable analysis, age, cognition, and initial BI were significantly associated with pre-discharge BI and BI improvement. Pre-discharge BI, premorbid living status, age, and initial BI were also significantly associated with placement decision upon discharge.
Conclusion: Rehabilitation outcome and discharge planning were associated with multiple factors. Younger patients had greater rehabilitation potential and most of them were discharged home. Nonetheless, their pre-discharge functional performance remained moderately dependent and with cognitive impairment. Intensive, continuous, and extended rehabilitation is recommended to optimise functioning and to ensure community re-integration, safety in daily living, and relief of caregiver burden. For geriatrics, basic activities of daily living and cognitive training with caregiver education are main concerns. Patients with haemorrhagic stroke can also be benefited from extended rehabilitation to optimise functional improvement.

P 5

Cortical Microinfarcts Detected with 3T Magnetic Resonance Imaging in Patients with Atrial Fibrillation

Y Soo[1], J Abrigo[2], KT Leung[1], V Liu[1], SF Tsang[1], B Lam[1], WC Fong[3], SH Li[4], R Li[5], PW Ng[6], J Fok[7], KK Wong[7], F Chen[1], W Chu[2], L Wong[1], V Mok[1], T Leung[1]

[1] Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR
[2] Department of Imaging and Interventional Radiology, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR
[3] Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR
[4] Department of Medicine, Northern District Hospital, Hong Kong SAR
[5] Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR
[6] Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong SAR
[7] Department of Medicine, Yan Chai Hospital, Hong Kong SAR

Background: Cortical microinfarcts (CMI) detected by 3T magnetic resonance imaging are a newly emerged radiological marker, representing microscopic regions of ischaemic-related cell death at the brain cortex. CMI is associated with small vessel disease and commonly identified in patients with Alzheimer's disease and vascular dementia, which have demonstrated to be associated with subclinical cardiac disease, suggesting a possible role of microembolism contributing to CMI. This study aimed to determine if CMI is associated with clinical ischaemic stroke in patients with atrial fibrillation.

Methods: We recruited patients with atrial fibrillation on oral anticoagulants for 3T magnetic resonance imaging of the brain. Presence of CMI was correlated with white matter score and clinical history of ischaemic stroke.

Results: A total of 517 patients was included. CMIs were observed in 58 (11.2%) of patients. Compared with patients without CMI, patients with CMIs were more likely to have a history of ischaemic stroke or transient ischaemic attack and higher CHA2DS-VASc score. In multiple logistic regression, both CMI and CHA2DS2-VASc score were independent predictors for ischaemic stroke and transient ischaemic attack. Combining CMI with CHA2DS2-VASc score improved risk prediction for ischaemic stroke and transient ischaemic attack.

Conclusions: Detection of CMI may help improve stroke risk prediction in patients with atrial fibrillation. CMI may serve as an adjunctive risk-stratification tool for patients with low CHA2DS2-VASc score when decision for anticoagulation is difficult based on clinical risk factors alone.

AUTHOR INDEX

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