Stroke Research Review™

Making Education Easy

Issue 10 - 2014

In this issue:

Abbreviations used in this issue:

BNP = B-type natriuretic peptide
BP = blood pressure
mRS = modified Rankin Scale
NIHSS = National Institutes of Health Stroke Scale
TIA = transient ischaemic attack
tPA = tissue-type plasminogen activator

Welcome to the 10th edition of Stroke Research Review.

Thanks to Dr Robert Henderson for his contribution to this edition. Dr Henderson is a Neurologist at Royal Brisbane and Women's Hospital. One of the papers included in this issue assessed the optimal dose of tPA to treat acute ischaemic stroke. The group reported standard-dose intravenous tPA had a more favourable outcome without increasing the risk of symptomatic intracranial haemorrhage than low-dose tPA. A prospective multicentre study of tPA treatment found it can be safely and efficaciously administered in the Korean population up to the extended time window of 4.5 hours.

Other findings reported in this issue: serum natriuretic peptide levels are strongly associated with cardioembolic stroke; elevated thyroid autoantibodies are independently associated with unfavourable outcome in patients with acute ischaemic stroke; stroke patients with persistent leukocytosis are more likely to present with severe strokes and maintain a high NIHSS score at 24 hours after admission; and more than a third of patients with TIA have impairment of ≥1 cognitive domain within 3 months after their TIA.

A study on post-stroke sleep disturbances in a medical centre in Seoul, South Korea, reported the most powerful factor predicting night-time sleep disturbances in stroke patients was depression. Cortical brain lesion and diabetes mellitus were also associated with night-time sleep disturbances.

I hope this issue provides interesting reading for you and, as always, I invite you to send me your comments, feedback and suggestions.

Kind Regards,

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Persistent cognitive impairment after transient ischemic attack

Authors: van Rooij FG, et al

Summary: One hundred and seven patients with transient ischaemic attack (TIA) underwent comprehensive neuropsychological testing within 3 months and results compared with 81 controls. The authors found TIA patients performed worse on all cognitive domains except episodic memory. Working memory (25%), attention (22%), and information processing speed (16%) were most frequently impaired when compared with the control group. More than 35% of patients with TIA had impairment of ≥1 cognitive domain.

Comment: Vascular patients are more likely to have vascular cognitive impairment. Perhaps 1/3 cognitive involvement is a number to remember but this is a difficult study to control for and longer-term data would be more helpful.

Reference: Stroke 2014 Aug;45(8):2270-4
http://stroke.ahajournals.org/content/45/8/2270.abstract

Blood pressure variability on antihypertensive therapy in acute intracerebral hemorrhage: The stroke acute management with urgent risk-factor assessment and improvement-intracerebral hemorrhage study

Authors: Tanaka E, et al

Summary: This prospective, multicentre, observational study registered 205 patients with hyperacute (<3 hours from onset) intracerebral haemorrhage with initial systolic blood pressure (BP) >180 mm Hg. All patients received antihypertensive therapy to lower and maintain systolic BP between 120 and 160 mm Hg and BPs were measured hourly for the first 24hrs. Of the study cohort, 33 (16%) showed haematoma expansion, 14 (7%) showed neurological deterioration within 72 hours, and 81 (39%) had unfavourable outcomes (modified Rankin Scale [mRS], 4–6) at 3 months. The authors concluded systolic BP variability during the initial 24 hours of acute intracerebral haemorrhage was independently associated with neurological deterioration and unfavourable outcomes.

Comment: Aiming for 120-160 mmHg systolic BP with intravenous nicardipine is strong BP management after intracerebral haemorrhage, but the point of this study is that systolic BP variability in the first 24 hours is associated with neurological deterioration and less favourable outcome at 3 months. They measured the blood pressure hourly but don't provide a practical value for BP variability.

Reference: Stroke 2014 Aug;45(8):2275-9
http://stroke.ahajournals.org/content/45/8/2275.long

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Independent commentary by Dr Robert Henderson, staff neurologist at Royal Brisbane & Women's Hospital where he has been working as a stroke neurologist in a busy Stroke Unit for 13 years, alongside a specific research interest in Motor Neurone Disease. His stroke interest arose from a fellowship with Dr Henry Barnett in Canada, evolved with a neurocritical care focus at the Mayo Clinic with Dr Eelco Widjicks, and has continued with stroke clinical trials, and an interest in the autonomic involvement after stroke.

Standard-dose intravenous tissue-type plasminogen activator for stroke is better than low doses

Authors: Liao X, et al

Summary: This group analysed data from the Thrombolysis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China) to assess whether lower dose intravenous tissue-type plasminogen activator (tPA) for stroke is as effective and safe as the standard dose. A total of 919 patients were divided into 5 groups according to tPA doses given: <0.5, 0.5 to 0.7, 0.7 to 0.85, 0.85 to 0.95, and ≥0.95 mg/kg. Due of sample sizes, only 3 groups were compared, with median tPA doses of 0.64, 0.79, and 0.90 mg. Patients were treated within 4.5 hours after symptom onset and assessed for symptomatic intracranial haemorrhage, mortality, and 90-day outcome (mRS). The group reported standard-dose intravenous tPA had a more favourable outcome without increasing the risk of symptomatic intracranial haemorrhage than low-dose tPA. The optimal dose of tPA to treat acute ischaemic stroke in Asian people should be 0.9 mg/kg.

Comment: We have to assume that the dose of tPA from the original studies was carefully determined so it makes sense not to use a sub-therapeutic dose. Using a smaller dose doesn't necessarily buy you less haemorrhage but it does buy less efficacy. This study also extends evidence to an Asian population. A remaining question is what dose of tPA is appropriate in the morbidly obese patient?

Reference: Stroke 2014 Aug;45(8):2354-8
http://stroke.ahajournals.org/content/45/8/2354.abstract

Cerebrovascular events in 21 105 patients with atrial fibrillation randomized to edoxaban versus warfarin: Effective anticoagulation with factor Xa next generation in atrial fibrillation-thrombolysis in myocardial infarction 48

Authors: Giugliano RP, et al

Summary: These researchers analysed the subtypes of cerebrovascular events in patients participating in the Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48 (ENGAGE AF-TIMI 48) study. The study cohort of 21 105 patients with atrial fibrillation were randomised to warfarin versus once-daily oral factor Xa inhibitor, edoxaban. The researchers reported once-daily edoxaban was as effective as warfarin in preventing all strokes, with significant reductions in various subtypes of intracranial bleeding.

Comment: It looks like it will be getting crowded in the anticoagulation market with the result from this oral factor Xa Inhibitor, edoxaban. The original study was published in the New England Journal of Medicine in 2013, and this paper specifically looks at the cerebrovascular endpoints. We might hear more about high-dose edoxaban.

Reference: Stroke 2014 Aug;45(8):2372-8
http://stroke.ahajournals.org/content/45/8/2372.abstract

Safety and efficacy of intravenous recombinant tissue plasminogen activator administered in the 3- to 4.5-hour window in Korea

Authors: Park TH, et al

Summary: This prospective multicentre study explored the safety and efficacy of intravenous tPA in the Korean population. The team compared outcomes of acute ischaemic stroke patients treated within 3 hours (n=616) versus those treated between 3 and 4.5 hours (n=107). The symptomatic intracranial haemorrhage rate was 4.7% in the 3 to 4.5 hour group compared to 3.1% in the 0 to 3 hour group, but the difference was not significant. There were no significant differences between the groups in the 3-month mortality and the mRS after adjusting for covariates.

Comment: This is an extension of the known tPA results to a specific population using non-randomised data from a prospective multi-centre registry database. A moderate number of patients were treated. In their hands 3 to 4.5 hours appears similar in outcome to 0-3 hours.

Reference: J Stroke Cerebrovasc Dis 2014 Aug;23(7):1805-12
http://www.strokejournal.org/article/S1052-3057%2814%2900217-1/abstract

Predicting cardioembolic stroke with the B-Type natriuretic peptide test: A systematic review and meta-analysis

Authors: Yang HL, et al

Summary: This meta-analysis evaluated the value of B-type natriuretic peptide (BNP) in differentiating cardioembolic stroke from other subtypes of ischaemic stroke. The authors reviewed data from 2 958 patients with ischaemic stroke retrieved from 16 studies. Thirty five per cent of these patients had a final diagnosis of cardioembolic stroke. Overall, the mean diagnostic odds ratio of BNP for cardioembolic stroke was 15.8 (95% confidence interval [CI]: 9.92-25.20). The authors reported serum natriuretic peptide levels showed a strong association with cardioembolic stroke, even after adjustment for multiple clinical predictors.

Comment: We know of the utility of BNP in heart failure. We know that detecting cardioembolic stroke is important in stroke management. NT-proBNP may not be a standard test that we think of for diagnosing cardioembolic stroke but this is a thorough review of the literature. Is a sensitivity and specificity of approximately 80% going to be enough?

Reference: J Stroke Cerebrovasc Dis 2014 Aug;23(7):1882-9
http://www.strokejournal.org/article/S1052-3057%2814%2900101-3/abstract

Impact of thyroid autoantibodies on functional outcome in patients with acute ischemic stroke

Authors: Cho HJ, et al

Summary: These researchers investigated the impact of thyroid autoantibodies on functional outcome in patients with acute ischaemic stroke. Of the 763 acute ischaemic stroke patients who consecutively underwent thyroid autoantibody tests, 121 (15.9%) were positive. The positive thyroid autoantibody group had higher baseline National Institutes of Health Stroke Scale (NIHSS) score, higher prevalence of large-artery atherosclerosis and higher proportion of unfavourable outcome at 3 months (mRS score ≥ 3) compared with the negative thyroid autoantibody group.

Comment: Thyroid autoantibodies aren't the first test to think of after a stroke, but this result is at least hypothesis-building with this finding that elevated thyroid autoantibodies are associated with unfavourable outcome. There is also recent literature on thyroid autoantibodies with Moya-Moya like disease so thyroid autoantibodies might be a topic to keep an eye on?

Reference: J Stroke Cerebrovasc Dis 2014 Aug;23(7):1915-20
http://tinyurl.com/n7r8uz9

Persistent leukocytosis—is this a persistent problem for patients with acute ischemic stroke?

Authors: Boehme AK, et al

Summary: This retrospective study aimed to determine the clinical significance of persistent versus transient leukocytosis during the early phase of acute ischaemic stroke. Four hundred and thirty-eight patients who presented with acute ischaemic stroke within 48 hours of symptom onset were identified by chart review and screened. Forty-nine patients had leukocytosis (defined as white blood cell count >11,000/μL) on admission and of those 24 (49%) had persistent leukocytosis. The researchers found that patients with persistent leukocytosis were more likely to present with severe strokes and maintain a high NIHSS score at 24 hours after admission, unlike patients without leukocytosis or patients with transient leukocytosis. The researchers also reported persistent leukocytosis outside the setting of an infection negatively impacts the short-term functional outcome of acute ischaemic stroke patients.

Comment: We know about C-reactive protein and we know that elevated temperature occurs after a stroke so this probably isn't surprising that a persistently elevated white cell count occurs (in patients without infection), and is associated with poor patient outcome. Are there common mechanisms in stroke and what can we do about it are the next questions.

Reference: J Stroke Cerebrovasc Dis 2014 Aug;23(7):1939-43
http://tinyurl.com/kvnxasa

Sleep disturbances after cerebral infarction: Role of depression and fatigue

Authors: Suh M, et al

Summary: This study evaluated the prevalence, characteristics and factors effecting post-stroke sleep disturbances in 282 patients with acute stroke at a medical centre in Seoul, South Korea. Of the study cohort 21% (n=60) reported sleep duration less than 6 hours/night and 39% (n=110) reported more daytime sleepiness than before the stroke. The study team concluded quality of night-time sleep was independently related to cortical lesion location, diabetes mellitus, and depression, whereas increased daytime sleepiness was independently associated with subcortical lesion location, fatigue, and quality of night-time sleep.

Comment: This is not an easy study to do, particularly when you consider obstructive sleep apnoea isn't even mentioned in the abstract. It's always wise to remember depression in those with sleep disturbance and post-stroke daytime sleepiness appears to be associated with subcortical stroke location.

Reference: J Stroke Cerebrovasc Dis 2014 Aug;23(7):1949-55
http://www.strokejournal.org/article/S1052-3057%2814%2900061-5/abstract

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Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: Difference-in-differences analysis

Authors: Morris S, et al

Summary: These researchers investigated a centralised model of acute stroke care, in which hyperacute care was provided to all patients with stroke across Greater Manchester and London, England. The outcome measures of mortality and length of hospital stay were assessed in the study cohort of 258 915 stroke patients admitted to hospital in January 2008 to March 2012. There was a significant decline in risk adjusted mortality at 3, 30, and 90 days after admission in London. At 90 days the absolute reduction was –1.1%, indicating 168 fewer deaths. There was a significant decline in risk adjusted length of hospital stay in both areas: –2.0 days in Greater Manchester and –1.4 days in London.

Comment: The UK might be a little slow with the "hub and spoke" model of acute stroke care, but at least they have studied it properly, and have shown that a centralised model of hyperacute care provided to all strokes in a large city, can reduce mortality and length of hospital stay. It might be what we already suspected from other countries, but this study did get into the British Medical Journal.

Reference: BMJ 2014 Aug 5;349:g4757
http://www.bmj.com/content/349/bmj.g4757.long

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