LETTERS

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THROMBECTOMY FOR ACUTE STROKE

Cardiology services not ideal for thrombectomy after stroke

Apps and colleagues highlight the need for increased availability of acute thrombectomy services in light of recent stroke trials showing that thrombectomy is more efficacious than thrombolysis.[1] However, involvement of cardiology services is not an effective solution.

A major reason for the success of these trials is careful patient selection based on advanced neuroimaging. In particular, inclusion criteria based on advanced imaging techniques and recruitment of specialist centres that perform high numbers of procedures were related to improved clinical outcomes.[2-6] Expertise in image analysis before thrombectomy is therefore essential. The consequences of an incorrect diagnosis are high, as are the financial implications of futile interventions.[7]

Furthermore, although generic vascular catheter skills may be translatable, navigating the cerebral vasculature is not straightforward. Anyone with the right training can "open a vessel," but the risks of vessel injury or perforation leading to intraparenchymal and subarachnoid haemorrhage are high and the consequences devastating. Neuroradiologists have relevant expertise in dealing with these complications. The applied skills from experience performing multiple routine and acute diagnostic and therapeutic cerebral angiograms should not be undervalued.

SIMON FRASER/FREEMAN HOSPITAL/SPL

We should concentrate on providing the best possible high quality specialist expertise so that our patients have the best outcomes. It is not a question of who can do these procedures but who is best trained and qualified to do so. It is about careful patient selection, risk assessment, and understanding the end organ. Solutions to the current problem of provision are through forming networks of competent and qualified interventional neuroradiologists and further training of neuroradiology subspecialty trainees who have the relevant interests and experience.

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1 Apps A, Firoozan S, Kabir T. Delivering thrombectomy for acute stroke using cardiology services. *BMJ* 2015;351:h3969. (27 July.)

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Location of neurointerventional skills is important

With emerging evidence on the efficacy of thrombectomy for selected patients with acute ischaemic stroke, Apps and colleagues suggested that the coronary primary angioplasty network could be used to cover the demand for this service.[1]

However, the skill in endovascularly opening arteries quickly is not generic, as the authors imply. Despite the similar size of the coronary and cerebral arteries, they differ greatly. Cerebral arteries are more delicate owing to their thinner tunica media and adventitia and there can be great tortuosity proximally, making catheter navigation challenging. There is thus both a systems and practitioner learning curve specific for thrombectomy to ensure that it is performed timely, safely, and effectively.[2] It is not surprising that high volume centres have better outcomes.[3]

The Royal Victoria Hospital in Belfast was the only UK centre to participate in any of the recent randomised trials showing benefit of thrombectomy.[4-8] We agree with the authors that speed is paramount; our local target is less than 60 minutes between computed tomography and final recanalisation. In addition, patient selection based on imaging requires not just the identification of proximal arterial occlusion but also quantification of the extent of infarcted versus ischaemic (salvageable) brain.

For the results of the trials to be replicated elsewhere, practitioners need to be fully competent in neurointerventional techniques. This is too time sensitive and delicate a procedure for a first foray into the intracranial circulation. The brain is much too valuable for that.

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Around 9% of ischaemic strokes are suitable for thrombectomy

As suggested by Apps and colleagues,[1] we have already quantified the group of patients with stroke who are eligible for thrombectomy.

After publication of the thrombectomy trials, we studied all admissions to our hyperacute stroke unit to see how many would be eligible for endovascular therapy if the trial criteria were applied. The criteria were age ≥18 years, pre-morbid Rankin scale 0-1, presentation six hours or less after known symptom onset, National Institute of Health stroke scale score ≥5, normal coagulation, and Alberta stroke programme early computed tomography score ≥7. All trials selected patients with thrombi in the major intracranial vessels, but we could not do this because we do not perform computed tomography angiography and perfusion studies. Data had been routinely collected.

In the first quarter of 2015, 311 stroke patients were admitted; 23 of the 265 with ischaemic stroke fulfilled the above criteria and would have been eligible for thrombectomy. Five of them had radiological evidence of a suitable thrombus on a non-contrast computed tomogram of the head.

Therefore, at our busy stroke unit, 9% of patients with acute ischaemic stroke (about one every five days) might have been eligible for intra-arterial therapy. After the application of computed tomography angiography and perfusion criteria, this number might fall.

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"BREAKTHROUGH" DRUG IN ALZHEIMER'S

Recent trial shows solanezumab has disease modifying effects

McCartney raises important points about the media reporting of solanezumab but does not fully explore the data's real importance.[1]

Current drugs for Alzheimer's disease treat the symptoms only.[2] Disease modifying drugs could reduce the numbers of people living with severe stage Alzheimer's.[3]

The extension study (EXPEDITION-EXT) was designed to assess solanezumab's mechanism of action, not its magnitude of efficacy, by determining whether the difference in cognitive decline in mild Alzheimer's (identified in EXPEDITION and EXPEDITION 2)[4 5] was maintained. The results were consistent with a disease modifying effect.

Some media reports did not explain this or make it clear that the 34% slowing of decline, reported from EXPEDITION and EXPEDITION 2, were old data. Those results represented a modest benefit in real terms, but if solanezumab altered the disease course, the magnitude of effect might possibly increase over time. This remains to be seen, as Alzheimer's Research UK pointed out in interviews and comments about the findings.[6 7] We must also await the completion of EXPEDITION 3, a placebo controlled trial in mild Alzheimer's disease, to confirm the original results.

These latest results could be the first evidence that Alzheimer's disease can be slowed, and that the major hypothesis in Alzheimer's research may be correct. This suggests that in future, we may be able to offer better drugs to people with Alzheimer's disease. While much more work is needed, this first step could be a turning point for research into this devastating disease.

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1 McCartney M. The "breakthrough" drug that's not been shown to help in Alzheimer's disease. *BMJ* 2015;351:h4064. (24 July.)

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Author's reply

Karran says that the EXPEDITION and EXPEDITION 2 trials showed a 34% slowing of cognitive decline—evidence of a disease modifying effect.[1 2]

He did not reference this statement and on PubMed I found only a short presentation ("oral session," apparently from the Alzheimer's Association International Conference 2013).[3] The results read "In the mild population, approximately 34% less cognitive decline (ADAS-Cog 11, ADAS-Cog 14, and MMSE) was observed in the solanezumab versus placebo group (table). In this population, there was no significant difference in overall functional decline between solanezumab versus placebo, but using a subset of instrumental ADLs [activities of daily living] (ADCS-iADL), the difference reached statistical significance (table). In the moderate population, there were no between-treatment group differences in any cognitive or functional measure. In both mild and moderate populations, there were no significant treatment group-differences for Clinical Dementia Rating Scale-Sum of Boxes, Neuropsychiatric Inventory or quality of life measures." The table is available online.

Solazenumab did not slow cognitive decline in the original randomised controlled trial published in the *New England Journal of Medicine*. In the subgroup analysis performed by Lilly (full details not publicly available) of people with mild Alzheimer's disease, Lilly states that a further subset of a scale in an activities of living questionnaire reached significance. No change in functional decline was seen between placebo and active treatment groups. Karran seems to be claiming scientific significance on a subgroup of a subgroup.

It is important to note that the statistical analysis plan for EXPEDITION 2 was amended after the trial started. The analysis Karran seems to cite as proof of disease modification contains pooled data from this and from retrospective analysis of EXPEDITION 1. Readers should look at the cognitive scores from the trials and judge for themselves whether this is a breakthrough and whether the media have been used responsibly in the transmission of evidence based information.

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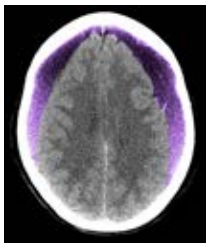
PREDICTION IN SEVERE BRAIN INJURY

Early discussion with family of people with severe brain injury



LIVING ART ENT/SPL

Creutzfeldt and colleagues' balanced discussion on communicating health trajectories after severe acute brain injury omitted an essential component of early communication and decision making processes—that a short window of opportunity (days) often exists, during which withdrawal of active supportive care, usually mechanical ventilation or vasoactive agents, results in a rapid death.[1] Such an approach may be viewed by all concerned as humane and in accordance with the patient's beliefs.

Living with severe neurodisability, with grossly diminished consciousness, awareness, and autonomy, may be considered a fate worse than death by patients (pre-injury) and their friends and family. The decision to opt for heroic procedures or an extended period of maximal intervention can result in a protracted death based solely on the unlikely event of a recovery. The negative consequences of such a death for patients and their friends and family can be considerable.

As clinicians, our ability to provide an accurate prognosis of the extent of long term neurodisability after severe acute brain injury is limited, especially in the first few days. However, we should not avoid early and open discussions about the consequences of postponing decisions merely to reduce our uncertainty.

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1 Creutzfeldt CJ, Longstreth WT, Holloway RG. Predicting decline and survival in severe acute brain injury: the fourth trajectory. *BMJ* 2015;351:h3904. (6 August.)

Cite this as: *BMJ* 2015;351:h4568

UTILITY OF "FIT NOTES"

Occupational therapists and others could issue fit notes

Recent coverage of the "fit note" was based on our research, conducted at the University of Nottingham.[1 2] One key problem, aside from lack of training, was that some GPs did not believe that issuing fit notes was part of their role and would prefer not to be responsible for them.

Given the current workload pressure on GPs and the support we found in the consensus study for other healthcare professions to be involved in issuing such notes, it is surprising that the Allied Health Professions (AHP) advisory fitness for work report seems to be parked on the sidelines.[3] Occupational therapists and physiotherapists are well placed to bridge this gap, so why the delay in progressing this? Or are GPs going to refer all their patients with work problems to the new "fit for work service"?

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1 O'Dowd A. Lack of information on "fit notes" renders them useless, says study. *BMJ* 2015;351:h4214. (4 August.)

Cite this as: *BMJ* 2015;351:h4559