Dabigatran reversal with idarucizumab before thrombolysis is increasingly accepted as a treatment option for patients presenting with acute ischaemic stroke. Published data to date have included only patients presenting within the conventional thrombolysis window of 4.5 hours. Here we report a successful case of thrombolysis in a patient on dabigatran reversed with idarucizumab, following a wake-up stroke, guided by computed tomography (CT) perfusion imaging.

Case report

A 75-year-old female on dabigatran for atrial fibrillation and with previous bilateral middle cerebral artery infarcts presented to hospital after being found that morning with reduced responsiveness and a right-sided facial droop. She was last seen well the previous evening, 11 hours prior. Although alert, she was agitated and not responding to visual stimuli. She was also noted to have mild dysarthria and dysphasia. At baseline, she was independent with activities of daily living with a Modified Rankin Score of 1 for mild dysphasia, which manifested itself during periods of stress. The National Institutes of Health Stroke Scale (NIHSS), a scoring system used to describe the degree of neurological impairment (range 0–42 with higher scores reflecting greater deficit), was 8.

Investigations included an elevated dilute thrombin clotting time (>80 seconds) consistent with therapeutic dabigatran levels. The stroke protocol CT demonstrated a reduction in cerebral blood volume in the right medial occipital lobe, representing the ischaemic core (Figure 1), with a significantly larger area of increased Tmax in the bilateral posterior cerebral and posterior inferior cerebellar artery territories, representing salvageable penumbra (Figure 2). On angiography, no retrievable thrombus was identified.

Given the favourable imaging and disabling symptoms, we proceeded with idarucizumab reversal followed by thrombolysis 9 hours and 25 minutes post onset (taken from the midpoint of sleep onset and awakening) after obtaining informed assent from the husband.

The following day, there were no new residual neurological findings, and notably her visual fields were normal. Follow-up CT brain scan showed a right medial occipital lobe infarct with mild haemorrhagic staining (Figure 3). Her 24-hour post-thrombolysis NIHSS was 1, for mild dysphasia. On day 7, repeat brain imaging demonstrated favourable appearances. She was restarted on dabigatran and discharged 9 days post-stroke with a NIHSS of 0. Her husband noted post-stroke fatigue but otherwise reported her to be at baseline level of functioning.

Discussion

Atrial fibrillation (AF) increases the risk of intracerebral and systemic thromboembolism fivefold and is responsible for over 15 percent of ischemic strokes. Multiple studies have demonstrated that direct oral anti-coagulants (DOACs) are similar or superior to warfarin in two aspects; stroke prevention and risk of major haemorrhage. However, there remains a 1–2 percent risk of ischaemic stroke per annum in patients on DOACs.

Intravenous thrombolysis with alteplase is the mainstay treatment for acute ischemic stroke. It attempts to restore the blood flow to the ischaemic penumbra. Currently, international guidelines make no recommendation about thrombolysis in patients on DOACs.

There have been attempts to establish the safety and efficacy of dabigatran reversal using idarucizumab before thrombolysis. In a New Zealand-based cohort study of 1,336 patients, similar early post-thrombolysis safety outcomes were seen in idarucizumab reversed dabigatran users and non-anticoagulated patients. Further, a systematic review of 251 patients who received thrombolysis after dabigatran reversal showed similar rates of haemorrhagic transformation, symptomatic intracerebral haemorrhage and mortality compared with previous studies in non-anticoagulated patients.

Following a meta-analysis of perfusion-guided thrombolysis trials, international guidelines now recommend thrombolysis in patients with favourable perfusion imaging presenting up to 9 hours...
**Figure 1:** Cerebral blood volume (core infarct represented by dark blue and purple).

**Figure 2:** Tmax (salvageable ischaemic penumbra represented by green and yellow).

**Figure 3:** Right medial occipital lobe infarct with mild haemorrhagic staining.
from last known well or from the midpoint of sleep. This is given a strong recommendation in the Australasian stroke guidelines, with a number needed to treat for functional independence of 5 and a number needed to harm for death of approximately 40. A recent economic evaluation of alteplase versus placebo in the extended window demonstrated cost-effectiveness. While there is no cost-effectiveness data on prior dabigatran reversal in this cohort, idarucizumab costs $4,250 per treatment. Based on 2015 Aotearoa New Zealand data, in-hospital care costs approximately $1,000 per day and therefore, in our patient, a net cost saving due to a shorter hospital stay is likely despite the higher upfront cost.

To our knowledge, this is the first report of a patient receiving thrombolysis following dabigatran reversal in the extended window using perfusion imaging. This case suggests reversal of dabigatran to facilitate thrombolysis in the extended time window is reasonable, though more data is needed to confirm its safety and efficacy.
COMPETING INTERESTS
Nil

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