



## The bleeding edge

**To the Editor:** We read with great interest the study by Ebrahim *et al.*<sup>[1]</sup> in the June SAMJ, titled 'Poor anticoagulation control in patients taking warfarin at a tertiary and district-level prothrombin clinic in Cape Town, South Africa'. This was a retrospective review of anticoagulation control in patients taking warfarin at two international normalised ratio (INR) monitoring centres in Cape Town. The authors found that time in the therapeutic range (TTR), which reflects the time in which the patient's INR was within the desired range, was remarkably low, at a mean of 47%. For anticoagulation to be effective, the accepted TTR is >65%. A *post hoc* analysis of the multicentre ACTIVE-W trial that looked at patients with atrial fibrillation (AF) treated with either warfarin or dual antiplatelet therapy identified a threshold TTR range for therapeutic efficacy of oral anticoagulants (OACs) of 58 - 65%, below which OACs were no better than platelet blockade.<sup>[2]</sup> Furthermore, an earlier subgroup analysis of combined data from the SPORTIF III and V trials looked at patients with AF randomised to warfarin. White *et al.*<sup>[3]</sup> found that poor INR control, defined as TTR of <60%, with a median of 48% (similar to the local data), was associated with a significant risk of complications including myocardial infarction and ischaemic and haemorrhagic stroke,<sup>[3]</sup> since time outside the therapeutic range includes both sub- and supratherapeutic levels.

Levels above the desired range are known to increase the risk of major bleeding, one of the complications of which is intracranial haemorrhage, a potentially devastating condition. At our neurosurgical centre, we see a steady number of patients every month with this complication. The most common presentations are intracerebral haematoma (ICH) and acute or chronic subdural haematomas. It is known that ICHs associated with warfarin anticoagulation are larger than spontaneous ICHs in non-warfarin users, tend to expand within 72 hours, and are associated with poorer prognosis in the form of either death or disability, with in-hospital mortality of up to 42%.<sup>[4-6]</sup> Treatment of these haematomas is compounded by the fact that numerous studies have shown that surgery fails to change this prognostic outcome.<sup>[7,8]</sup> Chronic subdural haematomas, which generally carry mortality between 1% and 3%, can be recurrent and when occurring in the elderly can have a mortality rate of up to 20 - 32%.<sup>[9]</sup> It is reassuring then that Ebrahim and his colleagues<sup>[1]</sup> found a higher rate of TTR among older patients. Surgical treatment for these lesions is further hindered by the need to reverse what are sometimes remarkably high INRs, and there remains controversy over the best way to do this.

We have begun to look systematically at this patient population to better quantify this problem, and therefore wish to congratulate the authors on a very timely and appropriate study of relevance to

multiple disciplines across a broad patient population. With the limited availability of alternative anticoagulants, a discussion on how to improve our anticoagulation monitoring to better protect our patients against life-threatening complications is overdue. And if we cannot improve our mean TTR, should we consider platelet inhibition instead for conditions such as AF, or should healthcare funders make alternatives like direct thrombin inhibitors more available to the state?

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