Claassen *et al*. [8] retrospectively studied 48 patients with ICH (12 patients with PHV). Their clinical data indicate that recurrent OAC-associated ICH is uncommon when anticoagulation is resumed, whereas the risk of thromboembolic events may be comparatively greater in patients who do not reinitiate OAC therapy. However, the clinician deciding whether to restart anticoagulation after an episode of ICH should weigh other factors, including the patient risk factors for systemic haemorrhage like previous episodes of bleeding from extracranial sites (e.g. gastrointestinal tract) and other risk factors including liver and renal disease, hypertension, cancer and stroke. Patients without these risks may benefit from reinstitution of OAC therapy.

De Vleeschouwer *et al*. [9], from a prospective study of 108 patients with ICH (30 had PHV) estimated the overall risk of thromboembolic complications to be 0.66 events/1000 patients at risk. OAC can be stopped safely for a considerable period, with a very low overall thromboembolic event rate. The recurrent bleeding risk after restarting anticoagulation is low. In their study, recurrent bleeding mostly occurred before restarting anticoagulation and was probably caused by insufficient or unsustainable correction of the initial coagulation deficit. Immediate reversal of anticoagulation provides the patient with the best possible treatment options including surgery.

Bertram *et al*. [10] did a retrospective study of 15 patients with ICH (10 with PHV) and concluded that in the acute management of patients with ICH with urgent need for anticoagulation, withdrawal of anticoagulation treatment for >1 week is not safe. However, full-dose intravenous heparin treatment must be discussed in patients with ICH and a high risk of cerebral thromboembolism, provided that early, active and sustained normalization of INR over the first week of the acute illness is necessary.

Kawamata *et al*. [11] retrospectively studied 27 patients with ICH (20 had PHV) and demonstrated that patients with anticoagulant-related haemorrhage may undergo surgery and anticoagulants can be resumed after an interval of 3–30 days. Aggressive surgery should particularly be performed in patients with anticoagulation-related chronic SDH or subcortical haemorrhage, as in the cases of anticoagulant unrelated ICH.

Broderick *et al*. [12] published guidelines for the management of spontaneous intracerebral haemorrhage in adults in their recommendations for the management of ICH related to coagulation and fibrinolysis.

They suggested that the decision to restart antithrombotic therapy after ICH related to antithrombotic therapy depends on the risk of subsequent arterial or venous thromboembolism, the risk of recurrent ICH, and the overall state of the patient. In patients with a very high risk of thromboembolism (like patients with PHV *in situ*) in whom restarting warfarin is considered, warfarin therapy may be restarted at 7 to 10 days after the onset of the original ICH.

CLINICAL BOTTOM LINE

We conclude that anticoagulants, either heparin or OAC, can safely be withheld for a short period of up to 7–14 days in a patient with ICH on OAC with a very low probability of thromboembolic phenomenon and can safely be reinstituted as early as 3 days for heparin and 7 days for OAC without major concerns of rebleeding. At the same time, there is a definite role for the rapid reversal of coagulopathy in acute settings using vitamin K, fresh frozen plasma or prothrombin concentrate.

Conflict of interest: none declared.

REFERENCES

[1] Dunning J, Prendergast B, Mackway-Jones K. Towards evidence-based medicine in cardiothoracic surgery: best BETS. Interact CardioVasc Thorac Surg 2003;2:405–9.
[2] Ananthasubramaniam K, Beattie JN, Rosman HS, Jayam V, Borzac S. How safely and for how long can warfarin therapy be withheld in prosthetic heart valve patients hospitalized with a major hemorrhage? Chest 2001; 119:478–84.
[3] Babikian VL, Kase CS, Pessin MS, Caplan LR, Gorelick PB. Resumption of anticoagulation after intracranial bleeding in patients with heart valves. Stroke 1988;19:407–8.
[4] Butler AC, Tait RC. Restarting anticoagulation in prosthetic heart valve patients after intracranial haemorrhage: a 2-year follow-up. Br J Haematol 1998;103:1064–6.
[5] Leker RR, Abramsky O. Early anticoagulation in patients with prosthetic heart valves and intracerebral hematoma. Neurology 1998;50:1489–91.
[6] Phan TG, Koh M, Wijdicks EFM. Safety of discontinuation of anticoagulation in patients with intracranial hemorrhage at high thromboembolic risk. Arch Neurol 2000;57:1710–3.
[7] Wijdicks EF, Schievink WI, Brown RD, Mullany CJ. The dilemma of discontinuation of anticoagulation therapy for patients with intracranial hemorrhage and mechanical heart valves. Neurosurgery 1998;42: 769–73.
[8] Claassen DO, Kazemi N, Zubkov AY, Wijdicks EF, Rabinstein AA. Restarting anticoagulation therapy after warfarin-associated intracerebral hemorrhage. Arch Neurol 2008;65:1313–8.
[9] De Vleeschouwer S, Van Calenbergh F, van Loon J, Nuttin B, Goffin J, Plets C. Risk analysis of thrombo-embolic and recurrent bleeding events in the management of intracranial haemorrhage due to oral anticoagulation. Acta Chir Belg 2005;105:268–74.
[10] Bertram M, Bonsanto M, Hacke W, Schwab S. Managing the therapeutic dilemma: patients with spontaneous intracerebral hemorrhage and urgent need for anticoagulation. J Neurol 2000;247:209–14.
[11] Kawamata T, Takeshita M, Kubo O, Izawa M, Kagawa M, Takakura K. Management of intracranial hemorrage associated with anticoagulant theraphy. Surg Neurol 1995;44:438–43.
[12] Joseph B, Sander C, Edward F, Daniel H, Carlos K, Derk K. REPRINT: Guidelines for the Management of Spontaneous Intracerebral Hemorrhage in Adults: 2007 Update: A Guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Circulation 2007;116:e391–413.

BEST EVIDENCE TOPIC

eComment. Anticoagulation after intracranial haemorrhage in patients with a high risk of thrombosis

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doi: 10.1093/icvts/ivt080

We have read with great interest the article by Chandra and colleagues [1]. Anticoagulation in patients with warfarin-associated intracranial haemorrhage and a high risk of thrombosis and embolism are difficult questions in modern practice. It applies not only to patients with prosthetic heart valves, but also with venous thrombosis, atrial fibrillation, etc. The frequency of this complication is about 0.25-1.1% per year [2]. According to the study by Yung *et al.*, the predictors of mortality in patients with warfarin-associated intracranial haemorrhage are the degree of initial anticoagulation (INR >3), greater stroke severity and intraventricular haemorrhage [2]. In other words, the amount and duration of bleeding depending on the capacity of the coagulation of blood determines the degree of the brain damage. So we need a rapid and careful recruitment of coagulation, which can be achieved by using the prothrombin complex concentrates. Vitamin K and fresh frozen plasma cannot fully satisfy these requirements. To reduce the

risk of thrombotic events, prothrombin complex concentrates should be used, which comprise the proteins C and S. The frequency of thrombotic complications in that case does not exceed 1% [3]. Anticoagulant therapy may be resumed after the normalization of the INR, but not before carrying out neurosurgical intervention, if necessary. For its performance, we recommend using anticoagulants with a short half-life, such as unfractionated heparin or bivalirudin. It is advisable to administer these drugs with continuous intravenous infusion and close monitoring of partial thromboplastin time (PTT) (or ecarin clotting time for bivalirudin). The normal range of these coagulation parameters should be above 1.5-2. In case of re-bleeding, the infusion of anticoagulation drugs can be stopped easily. It is noted that Bertram *et al.* showed no rebleeding after intracerebral haemorrhage in patients with the normal INR and increased PTT values [4]. Subsequently patients should receive the anticoagulants with prolonged action, prescribed in the hospital. A number of studies have shown a lower risk of intracranial haemorrhage in patients who received non-warfarin anticoagulant therapy, for instance antiplatelet drugs, factor Xa inhibitors [5].

Therefore, for the primary prevention of intracranial haemorrhage in high-risk patients (advanced age, hypertension, prior ischaemic stroke, diabetes mellitus, and alcohol abuse) requiring antithrombotic therapy, alternative drugs should be considered.

Conflict of interest: none declared.

References

[1] Chandra D, Gupta A, Grover V, Gupta VK. When should you restart anticoagulation in patients who suffer an intracranial bleed who also have a prosthetic valve? Interact CardioVasc Thorac Surg 2013;16:520–4.

[2] Yung D, Kapral MK, Asllani E, Fang J, Lee DS. Reinitiation of anticoagulation after warfarin-associated intracranial hemorrhage and mortality risk: the Best Practice for Reinitiating Anticoagulation Therapy After Intracranial Bleeding (BRAIN) study. Can J Cardiol 2012;28:33–9.

[3] Franchini M, Lippi G. Prothrombin complex concentrates: an update. Blood Transfus 2010;8:149–54.

[4] Bertram M, Bonsanto M, Hacke W, Schwab S. Managing the therapeutic dilemma: patients with spontaneous intracerebral hemorrhage and urgent need for anticoagulation. J Neurol 2000;247:209–214.

[5] Hart RG, Diener HC, Yang S, Connolly SJ, Wallentin L, Reilly PA, Ezekowitz MD, Yusuf S. Intracranial hemorrhage in atrial fibrillation patients during anticoagulation with warfarin or dabigatran: the RE-LY trial. Stroke 2012;43:1511–7.