OPINION

The new oral anticoagulants: new uncertainties for endoscopists

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As endoscopists we frequently encounter patients on anticoagulant and antiplatelet drugs. In these cases we have to balance the risks of discontinuation of these drugs, ie, thrombosis, versus the potentially increased risks of haemorrhage associated with endoscopy if these drugs are continued. There is also the risk of spontaneous gastrointestinal haemorrhage while anticoagulated. Fortunately, we have had useful guidance from national and international organisations.^{1–3} There have, however, been very few high quality studies on the use of anticoagulants and antiplatelet agents in patients undergoing endoscopy, and consequently the evidence base for much of the advice in these guidelines has been limited. The basic recommendations of these guidelines have remained similar since the American guidelines published in 2002,⁴ and there have been no published data to challenge these. Indeed, there have been subsequent studies which support some recommendations which were essentially based on expert opinion.

Previous guidelines for anticoagulants relate to the use of warfarin, either continuing it for low-risk (diagnostic) endoscopic procedures, or discontinuing it for high-risk (therapeutic) endoscopic procedures. In the case of high-risk indications for anticoagulation, bridging with low molecular weight heparin (LMWH) is recommended. Warfarin is effective in preventing thrombotic episodes in patients at risk, but requires dose adjustment and regular monitoring. Newer oral anticoagulants are now available with standardised dosing (depending on renal function) and no need for monitoring of blood for thrombotic indices. Rivaroxaban, dabigatran and apixaban have been demonstrated to be as effective as warfarin in preventing thrombotic episodes in randomised controlled trials, and in the UK are approved by NICE for patients with atrial fibrillation (AF) and

one or more specified additional risk factors for thrombosis.^{5–7} The lack of need for monitoring is a benefit to patients and health providers, but the downside with these agents is the absence of simple effective reversal agents in the event of haemorrhage. In this issue, Woodhouse *et al*⁸ have published a very useful overview of the pharmacology of these drugs, their indication and methods of action. They also make recommendations for the management of patients on these medications who are undergoing endoscopic procedures. These drugs have short half lives and could therefore be discontinued, if necessary for high risk endoscopic procedures, only 24 h prior to the procedure. Bridging with LMWH would not be necessary as this, in any case, is discontinued 24 h prior to a high-risk endoscopic procedure. This policy, as advocated by the authors, makes sense pharmacologically, but has not been tested in the context of endoscopy, or indeed other therapeutic procedures.

Woodhouse *et al* assert that whilst it is safe for patients to remain on warfarin for endoscopic biopsies, this is not the case for rivaroxaban and dabigatran. Their justification for this is that there is no antidote available in the case of haemorrhage. There is however no evidence that biopsies are unsafe in the presence of anticoagulation (in therapeutic doses). There have been no case reports in the literature to contradict this advice since the 2002 American guidelines. In addition, a prospective, though relatively small, Japanese study of endoscopic biopsy in anticoagulated patients found no incidences of significant haemorrhage.⁹ Given the lack of evidence for harm in biopsying anticoagulated patients at endoscopy, and the large administrative burden of discontinuing these agents in patients undergoing endoscopic procedures, it may be argued that the new oral anticoagulants should be continued for

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diagnostic procedures including biopsy. Prospective studies would be valuable, and should be encouraged, but large numbers will be required for statistical significance given the baseline low risk.

In the event of haemorrhage whilst on the new oral anticoagulants, the advice given in the article in this issue seems very reasonable though based on limited data. Haemorrhage is particularly pertinent with regard to these drugs as Rivaroxaban resulted in a gastrointestinal haemorrhage incidence of 3.15% compared to 2.16% with warfarin ($p < 0.001$),¹⁰ and an increased risk with dabigatran ranging from HR1.35 to 1.62 in another comparative study.¹¹ This was most marked for serious and life-threatening GI haemorrhage. Apixaban, in contrast, showed no increased gastrointestinal (GI) bleeding risk in a comparison to warfarin.¹²

Assessment of the risk of thrombosis is also pertinent to management of patients on these drugs, and extrapolation of advice from previous endoscopic anticoagulation guidelines is less helpful. These all characterise non-valvular AF as low-risk for thrombosis if anticoagulation is temporarily discontinued, but do not objectively consider the increased risk of thrombosis associated with AF and other cardiovascular risk factors. This risk can be assessed by the CHADS2 score,¹³ and the NICE guidelines use this as one of the criteria for commencing patients on each of the three new oral anticoagulants. The BSG guidelines mention the thrombotic risks associated with high CHADS2 scores, but do not give specific advice due to lack of data.³

In conclusion, we are faced with new therapeutic dilemmas in endoscopy when faced with patients on the new oral anticoagulants. We can extrapolate recommendations in guidelines based on use of warfarin, and modify them to accommodate the unique characteristics of these drugs, but further studies are required before definitive advice can be given.

Competing interests None.

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REFERENCES

- 1 Boustiere C, Veitch A, Vanbiervliet G, *et al.* Endoscopy and antiplatelet agents. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2011;43:445–61.
- 2 Anderson MA, Ben-Menachem T, *et al.* Management of antithrombotic agents for endoscopic procedures. *Gastrointest Endosc* 2009;70:1060–70.
- 3 Veitch AM, Baglin TP, Gershlick AH, *et al.* Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures. *Gut* 2008;57:1322–9.
- 4 Eisen GM, Baron TH, Dominitz JA, *et al.* Guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures. *Gastrointest Endosc* 2002;55:775–9.
- 5 Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation. NICE technology appraisal guidance 256 2012.
- 6 Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. NICE technology appraisal guidance 249 2012.
- 7 Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation. NICE technology appraisal guidance 275 2013.
- 8 Woodhouse C, Evans G, Muller AE. The new oral anticoagulants: practical management for patients attending for endoscopic procedures. *Frontline Gastroenterology* 2013;4: 213–8.
- 9 Ono S, Fujishiro M, Kodashima S, *et al.* Evaluation of safety of endoscopic biopsy without cessation of antithrombotic agents in Japan. *J Gastroenterol* 2012;47:770–4.
- 10 Patel MR, Mahaffey KW, Garg J, *et al.* Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *New Engl J Med* 2011;365:883–91.
- 11 Connolly SJ, Ezekowitz MD, Yusuf S, *et al.* Dabigatran versus warfarin in patients with atrial fibrillation. *New Engl J Med* 2009;361:1139–51.
- 12 Granger CB, Alexander JH, McMurray JJ, *et al.* Apixaban versus warfarin in patients with atrial fibrillation. *New Engl J Med* 2011;365:981–92.
- 13 Gage BF, Waterman AD, Shannon W, *et al.* Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA* 2001;285:2864–70.