



Figure 1 Guidelines for the management of patients on warfarin or clopidogrel undergoing endoscopic procedures (EUS: endoscopic ultrasound, ERCP: endoscopic retrograde cholangiopancreatography, EMR: endoscopic mucosal resection, PEG: percutaneous endoscopic gastroenterostomy, FNA: fine needle aspiration, INR: international normalised ratio, AF: atrial fibrillation, VTE: venous thromboembolism, LMWH: low molecular weight heparin).

with non-anticoagulated patients. (Evidence grade III. Recommendation grade B.)

1.4.2 Clopidogrel

Discontinuation of clopidogrel therapy should only be considered after discussion with the patient's cardiologist. A consultant gastro-intestinal physician or surgeon should be involved to confirm that the endoscopic procedure is essential.

- ▶ If bare metal coronary stents were placed more than 1 month ago then clopidogrel could be temporarily discontinued. (Evidence grade III. Recommendation grade B.)
- ▶ If drug-eluting coronary stents were placed more than 12 months ago then clopidogrel could be temporarily discontinued. (Evidence grade III. Recommendation grade B.)
- ▶ If drug-eluting coronary stents were placed more than 6 months ago, and the procedure is essential, then it may be safe to temporarily discontinue clopidogrel. (Evidence grade IV. Recommendation grade C.)
- ▶ Clopidogrel should be stopped 7 days prior to the procedure.
- ▶ Aspirin therapy should be continued.
- ▶ On the day following the procedure restart clopidogrel.

2.0 ORIGIN AND PURPOSE OF THESE GUIDELINES

These guidelines were commissioned by the British Society of Gastroenterology, and essential expertise was provided by collaboration with the British Committee for Standards in

Haematology and the British Cardiovascular Intervention Society. Prescription of anticoagulants is very common, and in addition there has been increasing prescription of antiplatelet agents for ischaemic heart disease, and in the context of coronary artery stenting. There is a risk of haemorrhage associated with many endoscopic procedures and this may be exacerbated in patients receiving these agents. Excellent guidelines have been produced by the American Society for Gastrointestinal Endoscopy,^{1,2} but these provide limited guidance on the management of cardiac patients on antiplatelet agents. Our guidance does not conflict with the American guidance, but expands upon it. A recent survey of UK endoscopists found a wide variation in practice regarding the management of anticoagulants in patients undergoing endoscopy.³ There is a need for clear up-to-date guidance on the management of patients undergoing endoscopic procedures who are receiving these drugs, and who may be at risk from the procedure itself or from discontinuing their medication.

3.0 PREPARATION OF THE GUIDELINES

These guidelines were drafted by a working party of representative members of the Endoscopy Committee of the British Society of Gastroenterology, the British Committee for Standards in Haematology, and the British Cardiovascular Intervention Society. Authors were nominated as representatives of their respective societies. A literature research was conducted using PubMed, and further sources were obtained from the reference lists of those papers identified. Additional

8.4 Ischaemic heart disease and coronary artery stents

Patients with ischaemic heart disease are generally treated with antiplatelet therapy rather than anticoagulant therapy. Those who have not undergone revascularisation therapy will tend to be taking aspirin alone although if they have had an episode of unstable angina with a troponin release they may require clopidogrel in addition. Clopidogrel in combination with aspirin improves outcomes in acute coronary syndromes without ST elevation, but with an increased risk of haemorrhage.⁵⁸ If patients develop dyspepsia on low-dose aspirin, or in any patient at risk from gastro-intestinal bleeding co-prescription of a proton pump inhibitor (PPI) should be considered initially. Failing that, and after discussion with the cardiologist, the patient taking aspirin alone could be given clopidogrel instead.

Coronary artery stenting has increasingly become the dominant therapy for treating patients with coronary artery disease. Coronary stents may invoke a scar tissue response in 15–20% of patients necessitating a repeat interventional procedure in about 70% of these (~12%). Some patients are at particular risk of within-stent scarring (such as those with long coronary lesions >15 mm, small vessel diameters <3 mm because there is greater impact of the scarring on the lumen of the stented vessel, or in diabetics). In such patients drug-eluting stents may be used. These agents, which are loaded onto the stent, are released locally and may reduce the need for a repeat procedure from 20% to 5% in randomised controlled trials.^{59,60} All stents require a minimum of 1 month combination of dual antiplatelet therapy (aspirin and clopidogrel 75 mg once daily of each). With bare metal stents the risk of stent thrombosis is present until the stent has undergone re-endothelialisation (after 1 month) until that time the risk of interruption of antiplatelet therapy is highly associated with stent thrombosis and a 50% risk of acute myocardial infarction or death. With drug eluting stents re-endothelialisation takes up to 6 months, and following reported cases of late stent thrombosis in patients with drug-eluting stents, the Food and Drug Administration in the United States⁶¹ and the British Cardiovascular Intervention Society now recommend dual antiplatelet therapy for 1 year. Should the patient spontaneously bleed or requires a non-cardiac operative procedure within this time period, the risks associated with stopping antiplatelet therapy are great. In one study which examined factors associated with stent thrombosis, discontinuation of therapy was associated with a hazard ratio of 161.⁶² Of those reported with a stent thrombosis, 27% had discontinued dual antiplatelet therapy. The risk of stent thrombosis increases after 5 days without antiplatelet therapy. If clopidogrel needs to be temporarily stopped in the context of an acute gastro-intestinal haemorrhage then discontinuation of therapy should be limited to this interval.

Patients on clopidogrel requiring coronary artery bypass surgery have an increased risk of haemorrhage if clopidogrel is discontinued for fewer than 5 days.^{58,63} Issues related to the need to consider discontinuation of dual antiplatelet therapy for non-cardiac surgical procedures are discussed in a recent editorial in the *British Medical Journal*.⁶⁴ The key messages are:

- ▶ All patients should carry a warning card.
- ▶ Discuss the case with the interventional cardiologist who performed the procedure so that the risks of stent thrombosis (with its 50% risk of AMI/death) can be weighed against the bleeding risk associated with the non-cardiac surgical procedure.
- ▶ If possible, procedures should be undertaken without complete lack of antiplatelet cover, such that if clopidogrel

does need to be stopped because of excess bleeding risk, then aspirin should be continued if possible.

- ▶ For patients with known high risk of needing a future non-cardiac surgical procedure (eg, planned future surgery for cancer) bare metal stenting will be undertaken since dual antiplatelet therapy will only be required for 1 month.

9.0 HEPARIN AS AN ALTERNATIVE TO ORAL ANTICOAGULANTS

In a meta-analysis short-term LMWH compared favourably to unfractionated heparin (0% thromboembolism) but patients requiring long-term treatment because of intolerance to oral anticoagulants did less well suffering a 20% incidence of thromboembolism.⁶⁵ In a review of outcomes after short-term bridging with LMWH (~10 days) one study reviewed 1082 patients started on enoxaparin 1 mg/kg/12 h or dalteparin 100 anti-factor Xa U/kg, subcutaneously, twice daily.⁸ Minor bleeding was seen in 7.6%, major bleeding in 0.3% but no thromboembolic episodes during the bridging period. While such a practice has been endorsed in this and other publications, there is a need for randomised controlled trials.

10.0 ENDOSCOPY ON ANTICOAGULANTS AND ANTIPLATELET AGENTS: RISK STRATIFICATION

It is apparent that certain endoscopic procedures carry a higher risk of haemorrhage, and certain clinical situations will result in a high risk of thromboembolic complications should anticoagulants or antiplatelet agents be withdrawn. The American Society for Gastrointestinal Endoscopy has produced guidelines on the management of anticoagulants during endoscopy,^{1,2} and we have adapted their risk stratification model for endoscopic procedures in table 1. Procedures have been characterised as high risk or low risk for haemorrhage on anticoagulant or clopidogrel therapy based on data for baseline risks of haemorrhage, and the limited data available regarding endoscopy during therapy with these agents. Tables 2 and 3 stratify risk for discontinuation of anticoagulant or antiplatelet therapy according to clinical scenario and the risks of thromboembolic sequelae on discontinuation of therapy.

Diagnostic endoscopic procedures, with or without biopsy, are classified as low risk. This applies to diagnostic colonoscopy, but polyps are likely to be encountered in 22.5–34.2% in large studies.^{20,24} Endoscopists may therefore choose to manage all colonoscopies as if they were high-risk procedures with respect to anticoagulants and antiplatelet agents. Similar considerations apply to ERCP if there is uncertainty as to the pathology from previous imaging.

11.0 ACKNOWLEDGEMENTS

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12.0 REFERENCES

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