Platelet Inhibition and Anticoagulation in Visceral Interventions

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Keywords

Platelet inhibition · Anticoagulation · Visceral intervention · Procedure risk · Thromboembolic risk

Abstract

Background: Platelet inhibition and anticoagulation are widely used therapeutic approaches in many patients. Despite their undoubted cardiovascular benefits, they may cause gastrointestinal harm either spontaneously or as part of endoscopic procedures. Strategies which harmonize both aspects are, therefore, of clinical interest. **Method:** The websites of the German (DGVS), European (ESGE), and American (ASGE) Societies of Gastroenterology and Endoscopy were searched for guidelines on antithrombotic agents and endoscopic procedures. Over and beyond this, PubMed was analyzed for originals and reviews by using the keywords “hemostasis affecting drugs,” “antithrombotic drugs,” “platelet inhibition,” “anticoagulation,” AND endoscopy. **Conclusion:** If elective endoscopy is planned, we should consider postponing the procedure in cases of temporally restricted platelet inhibition therapy or anticoagulation. Urgent endoscopy must balance the procedural risk against the risk of continuing or stopping the medication, with respect to thromboembolic events on the one hand and gastrointestinal bleeding on the other. There are decision criteria which facilitate individual risk stratification as a basis for diagnostic and therapeutic algorithms. **Key Message:** If endoscopic interventions under platelet inhibition and/or anticoagulation cannot be postponed for a limited period of time, diagnostic and therapeutic strategies have to be performed against the background of well-defined decision criteria. These include the

procedural risk (low vs. high) and the risk of thromboembolic events occurring (low vs. high) if the medication is stopped. In cases where both risks are considered to be high, an interdisciplinary approach should be favored.

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Introduction

Gastrointestinal bleeding is a common and sometimes life-threatening event that occurs particularly, but not exclusively, in older people. There is often a drug-induced cause (Table 1) [1]. Some drugs like acetylsalicylic acid (ASA) or nonsteroidal anti-inflammatory drugs (NSAIDs) may induce structural lesions like ulcers or colitis with a consequent bleeding risk. Others increase the tendency for gastrointestinal bleeding without causing an underlying lesion. Finally, bleeding may be triggered by an overdose of the drug(s) used.

Besides NSAIDs, platelet inhibitors and anticoagulants are nowadays in widespread use for the prevention and treatment of cardiovascular diseases. Despite their undoubted therapeutic benefits, their potential to cause gastrointestinal bleeding must be taken into consideration. When planning an endoscopic intervention, a careful balance of the thromboembolic risk on the one hand and gastrointestinal harm on the other has to be considered as basis for any individual decision. This article focuses on the use of platelet inhibitors and anticoagulants and the need for elective and urgent endoscopic procedures.

Three possible scenarios must be distinguished in this context:

Table 1. Drugs that can induce gastrointestinal bleeding

Analgesics/antiphlogistics
Traditional nonsteroidal anti-inflammatory drugs (tNSAIDs): diclofenac, ibuprofen
Selective COX-2 inhibitors (COXIBs): celecoxib, etoricoxib
Platelet inhibitors
Acetylsalicylic acid (ASA)
Clopidogrel
Dipyridamol
Prasugrel
Ticagrelor
Ticlopidine
Abciximab
Eptifibatide
Tirofiban
Anticoagulants
Vitamin K-antagonists: phenprocoumon, warfarin
Unfractionated heparin
Low-molecular heparin (NMH)
Direct oral anticoagulants (DOACs): apixaban, dabigatran, edoxaban, rivaroxaban, argatroban
Direct thrombin inhibitors: bivalirudine, desirudine, lepirudine
Indirect Factor Xa inhibitors: fondaparinux
Corticosteroids
Selective serotonin reuptake inhibitors (SSRIs): fluoxetine, paroxetine, citalopram, escitalopram, sertraline.

Table 2. Procedural risk

Low-risk procedures	High-risk procedures
Diagnostic endoscopy + biopsies (esophagogastroduodenoscopy; colonoscopy; enteroscopy; video capsule endoscopy)	Polypectomy >10 mm, EMR, ESD
Polypectomy in the colon (<10 mm)	EST
ERCP (without sphincterotomy) + stent	Balloon dilatation of strictures
EUS without FNA	EUS with FNA
Enteral stent without dilatation	Cystic drainage
APC of gastrointestinal bleedings	Variceal ligation/sclerotherapy
Thermal coagulation	Tumor ablation (laser, RFA) PEG; PTC/PTCD

APC, argon plasma coagulation; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; EST, endoscopic sphincterotomy; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; PEG, percutaneous endoscopic gastrostomy; RFA, radiofrequency ablation.

Table 3. Risk of thromboembolic events (when stopping medication)

Low thromboembolic risk	High thromboembolic risk
Uncomplicated or paroxysmal atrial fibrillation (without risk factors)	Atrial fibrillation with valvular disease or risk factors
Bioprosthetic heart valve	Artificial mitral valve
Artificial aortic valve	Artificial valve of any location and prior embolism
Venous thromboembolism >3 months	Venous thromboembolism <3 months or pulmonary embolism <6–12 months
Cerebral ischemia >6 months without structural heart disease	Cerebral ischemia <6 months
	Acute coronary syndrome
Coronary stent (drug-eluting stent) >12 months or bare-metal stent >6 weeks without risk factors	Coronary stent (drug-eluting stent) <12 months or bare-metal stent <6 weeks and >6 weeks plus risk factors, respectively

- Elective endoscopy under platelet inhibition and/or anticoagulation (i.e., screening colonoscopy in individuals with a normal carcinoma risk)
- Urgent endoscopy under platelet inhibition and/or anticoagulation (i.e., colonoscopy after a positive fecal occult blood test in cases of anemia or perianal bleeding)

- Gastrointestinal bleeding under platelet inhibition and/or anticoagulation

What are the main decision criteria? In each case, the risk associated with the endoscopic intervention (procedural risk; Table 2) and the risk of thromboembolic events occurring if the medication is interrupted (Table 3) must be taken into account. In the case of atrial fibrillation, the

Fig. 1. Recommended approach in case of urgent endoscopy under platelet inhibition therapy and/or anticoagulation.

CHA₂DS₂-VASc score represents an additional tool for estimating the thromboembolic risk. Both procedural risk and the risk of thromboembolic events facilitate individual risk stratification as a basis for the algorithms, as pointed out below.

Elective Endoscopy under Platelet Inhibition and/or Anticoagulation

In the case of elective endoscopy, there is the opportunity to decide if it is possible to postpone the procedure. In many cases, dual platelet inhibition or anticoagulation is temporally restricted, thus presenting this opportunity. A screening colonoscopy in individuals at a normal risk can certainly be delayed for a restricted period. If such a delay does not seem suitable or is undesired, an approach as for urgent endoscopy is recommended (Fig. 1).

Urgent Endoscopy under Platelet Inhibition and/or Anticoagulation

In cases where urgent endoscopy is required, a structured approach that takes into consideration the outlined decision criteria (Tables 2, 3) is appropriate. Apart from this, the type of platelet inhibition (ASA mono, non-ASA, dual platelet inhibition therapy, etc.) and anticoagulation used are predictors of future management because the intensity of the antithromboembolic therapy clearly influences the strategy deployed, i.e., single inhibition with

Table 4. Platelet inhibitors and duration of action [2, 3]

Antithrombotic agent	Duration of action
Acetylsalicylic acid (ASA)	10 days
Clopidogrel	3–7 days
Ticlopidine	3–7 days
Prasugrel	at least 7 days
Ticagrelor	up to 72 h
Abciximab	up to 48 h

ASA mono can be handled quite easily as opposed to combination therapy. Figure 1 summarizes the clinical conditions of urgent endoscopy under platelet inhibition therapy and/or anticoagulation.

Patients on ASA mono and with a low procedural risk can continue their medication. In the case of a high procedural risk and a low risk of thromboembolic events occurring, ASA can be continued or may briefly be suspended. If both risks are considered as high, an individual interdisciplinary approach is necessary.

Patients on non-ASA platelet inhibition can continue therapy if there is a low procedural risk. A switch to ASA could be an alternative in this situation. Assuming there is a high procedural risk and a low thromboembolic risk, non-ASA platelet inhibition therapy should be stopped some days ahead of the endoscopy (Table 4). This is not an option in cases of high thromboembolic risk, where a decision about a temporary switch to ASA or an individual approach is necessary.

Fig. 2. Diagnostic and therapeutic strategy in case of gastrointestinal bleeding under platelet inhibition therapy and/or anticoagulation.

Table 5. Anticoagulants: half-life, stop ahead of endoscopy, and reuptake [3, 4]

Direct oral anticoagulants (DOACs)	Half-life	Stop ahead of endoscopy	Earliest reuptake after endoscopy
Apixaban	9–14 h	24–48 h	12–24 h
Dabigatran	12–17 h	24–48 h	12–24 h
Edoxaban	9–11 h	24–48 h	12–24 h
Rivaroxaban	5–13 h	24 h	12–24 h
Phenprocoumon	160 h (6–7 days)	7 days	12–24 h
Low-molecular heparin (prophylactic – therapeutic dose)		12–24 h	6–12 h
Unfractionated heparin		4 h	2–6 h

In patients on dual platelet inhibition therapy, a temporary switch to ASA mono can be recommended in cases of low thromboembolic risk irrespective of the procedural risk. There is a need for an individual approach if the risk of thromboembolic events is considered high.

If there is an indication for urgent low-risk endoscopy, patients can proceed with their anticoagulation therapy. In cases where there is a both a high procedural risk and a high thromboembolic risk, an individual decision about the different anticoagulants (Table 5) is mandatory. Direct oral anticoagulants (DOACs) are usually discontinued 1–2 days before a planned endoscopy. In the case of renal insufficiency, stopping earlier (72–96 h) is advisable. Vitamin K antagonists must be stopped 6–7 days ahead of endoscopy. Bridging with unfractionated or low-molecular heparin in cases with a high thromboembolic risk is not necessarily more suitable. Two prospec-

tive studies on perioperative and periendoscopic heparin bridging therapy revealed no benefits with respect to thromboembolic events [5, 6]. However, the risk of bleeding risk was significantly higher than in the control group. Analysis of a large Japanese database found an elevated risk of bleeding as well as thromboembolic events if patients on warfarin or DOACs received heparin as a periendoscopic bridging therapy [7].

An Interdisciplinary Approach in Cases with a High Procedural Risk and a High Risk of Thromboembolic Events Occurring

If both procedural risk and the risk of thromboembolic events occurring are considered to be high according to the abovementioned criteria (Tables 2, 3), an indi-

Table 6. Options of primary and secondary prevention of gastrointestinal bleedings under platelet inhibition and anticoagulation [9]

Medication	Clinical situation	PPI comedication
ASA/DOAC/VKA	Monotherapy plus >1 risk factor ^a	Can
ASA/DOAC/VKA	Ulcer bleeding under monotherapy	Should
A combination of 2 coagulation-modifying drugs	Primary prevention	Must
Platelet inhibition and anticoagulation	In combination with traditional NSAIDs	Must
All	Consider testing for <i>Helicobacter pylori</i> and eradication therapy if positive	

ASA, acetylsalicylic acid; DOAC, direct oral anticoagulants; VKA, vitamin K antagonists; PPI, proton pump inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs.

^a Older age; a history of ulcers; severe general illness; comedication with glucocorticoids, coagulation-modifying drugs, or selective serotonin reuptake inhibitors

vidual approach is necessary to successfully meet this challenge. In such a situation, an interdisciplinary discussion that involves the gastroenterologist and the surgeon on the one hand and the cardiologist or neurologist on the other is highly recommended.

Gastrointestinal Bleeding under Platelet Inhibition and/or Anticoagulation

In cases of minor gastrointestinal bleeding, platelet inhibition therapy and/or anticoagulation should be stopped and early endoscopy should be planned (Fig. 2) [8]. If major bleeding and circulatory instability are evident stabilization of the patient, intensive care and emergency endoscopy are required. It should be emphasized that this topic is also raised in the article by Götz et al. [8] in this issue of *Visceral Medicine*. When the bleeding is successfully controlled, possible secondary preventative measures should be considered. These are summarized in Table 6 and follow the recommendations of the current German S2k guideline [9]. In this context, it must be noted that these strategies are also effective for the primary prevention of gastrointestinal bleeding before starting platelet inhibition therapy and anticoagulation.

Over and beyond comedication with proton-pump inhibitors, testing for *Helicobacter pylori* infection should

be considered and eradication therapy should be started in patients with a previous history of ulcers (primary prevention) or in the case of a gastroduodenal bleed (secondary prevention) [9].

Conclusion

If endoscopy has to be performed in patients under platelet inhibition therapy and/or anticoagulation, thorough diagnostic and therapeutic algorithms based on individual risk stratification are mandatory. Decision criteria include the procedural risk as well the risk of thromboembolic events occurring when the medication is stopped. An individual approach based on an interdisciplinary discussion seems appropriate when both risks are considered as high.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

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