Management of Anticoagulants in patients with Gastrointestinal bleeding and in Elective Endoscopic procedures.

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Gastrointestinal bleeding in patients on Anticoagulants
Bleeding complications in Warfarin users

• Major haemorrhage in Warfarin users (intracranial, gi, gu and respiratory sites): 1–3% per person-year.

• The GI tract is the most common bleeding site (age-standardized incidence rate of 5.8 per 1000 person-year).

• Endoscopic findings are similar between VKA users and patients taking no anticoagulants with peptic ulcer being the main cause of bleeding.

• VKAs-related GI bleeding events are associated with long hospitalization, relevant resource utilization, and a 30-day mortality of up to 15%.

• In contrast to intracranial haemorrhage, warfarin exposure does not seem to significantly increase the GI bleeding mortality, which is mainly affected by patient’s comorbidities.
## Table 1: The relative risk of major GI bleeding in the non-valvular atrial fibrillation population: take home points.

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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>Adjusted-dose warfarin increases the risk of major GI bleeding approximately three-fold compared with placebo.</td>
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<tr>
<td>2.</td>
<td>The addition of aspirin or other anti-platelet agents to warfarin increases the risk of major GI bleeding approximately two-fold (compared with warfarin alone).</td>
</tr>
<tr>
<td>3.</td>
<td>Compared with warfarin, rivaroxaban and dabigatran (at the 150 mg twice daily dose) increase the risk of major GI bleeding approximately 1.5 fold.</td>
</tr>
<tr>
<td>4.</td>
<td>Compared with warfarin, apixaban does not significantly alter the risk of major GI bleeding.</td>
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<tr>
<td>5.</td>
<td>Compared with warfarin, dabigatran 110 mg twice daily does not significantly alter the risk of major GI bleeding.</td>
</tr>
<tr>
<td>6.</td>
<td>Concurrent use of anti-platelet agents increases the risk of major GI bleeding associated with rivaroxaban and of major extra-cranial bleeding (presumably including major GI bleeding) associated with dabigatran. Data related to impact of anti-platelet agents on apixaban-related major GI bleeding are not yet available.</td>
</tr>
</tbody>
</table>
Figure 1: Endoscopic findings for suspected upper (A) and lower (B) GI bleeding in patients receiving systemic anticoagulation with adjusted-dose warfarin (11).
## DOAs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Trade name</th>
<th>Mechanism of action</th>
<th>Excretion</th>
<th>Antidote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td><strong>Pradaxa®</strong></td>
<td>Direct thrombin inhibitors</td>
<td>&gt;2/3 Kidneys</td>
<td>PRAXBIND</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td><strong>Xarelto®</strong></td>
<td>Activated coagulation factor X inhibitors</td>
<td>1/3 Kidneys</td>
<td>None</td>
</tr>
<tr>
<td>Apixaban</td>
<td><strong>Eliquis®</strong></td>
<td>Activated coagulation factor X inhibitors</td>
<td>&lt;1/2 Kidneys</td>
<td>None</td>
</tr>
<tr>
<td>Edoxaban</td>
<td><strong>Lixiana®</strong></td>
<td>Activated coagulation factor X inhibitors</td>
<td>&lt; 1/2 Kidneys</td>
<td>None</td>
</tr>
</tbody>
</table>

New oral anticoagulants (direct oral anticoagulants ,DOACs)

• In general, NOACs reduce the risk of hemorrhagic stroke and have a comparable risk of major bleeding into all organs compared with warfarin.

• NOACs are associated with a modestly increased risk of gastrointestinal (GI) bleeding compared with warfarin.

• Warfarin increases the risk of major GI bleeding approximately 3-fold over placebo in the atrial fibrillation population, and 3 NOACs have been shown to further increase this risk 1.5-fold compared with warfarin.
GI bleeding on DOACs

• When trials were grouped according to the indication for anticoagulant therapy, the risk of GI bleeding in patients with venous thromboembolism was significant lower with DOACs vs. VKAs, whereas no difference was found among AF patients.

• F. Radaelli et al. / Digestive and Liver Disease 47 (2015) 621–627
Table 3: The rates of major GI bleeding in the non-valvular atrial fibrillation population from the three pivotal trials.

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran 150 mg twice daily</th>
<th>Rivaroxaban 20 mg daily</th>
<th>Apixaban 5 mg twice daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard ratio for major GI bleeding (vs. warfarin)</td>
<td>1.49 [CI 1.21–1.84]</td>
<td>1.61 [CI 1.30–1.99]</td>
<td>0.89 [CI 0.70–1.15]</td>
</tr>
</tbody>
</table>
What to do in patients with GI bleeding on anticoagulants?
1. Assess the severity of bleeding, Start hemodynamic resuscitation.
2. Discontinue the Anticoagulant if bleeding is more than minor.
3. Actively reverse the coagulation if bleeding is more than minor.
4. Assess for proper timing for endoscopy.
5. Determine the necessity and proper timing for re-institution of Anticoagulant therapy.
Acute GI bleeding

Urgent clinical assessment and resuscitation, including blood type & cross-match for active and significant bleeding
Complete blood count / Clotting screen (INR, aPTT, fibrinogen)

Active bleeding / Shock
1. Stop VKA
2. Actively reverse anticoagulation:
   - Vitamin K (5-10 mg IV infusion over 30 minutes)
   - PCC 25-50 IU/kg according to baseline INR value
3. Check INR 20-30 minutes after PCC infusion:
   - Adequate correction (INR <1.5): Recheck in 6 hours
   - Inadequate correction: Seek haematologist advice
   - Consider PCC re-infusion
   - Consider emergent endoscopy preferably when INR <2.5

Significant bleeding without haemodynamic compromise
1. Stop VKA
2. Actively reverse anticoagulation:
   - Vitamin K (5-10 mg IV infusion over 30 minutes)

Therapeutic INR
- No further action

Supratherapeutic INR
- Consider PCC infusion if endoscopy is scheduled within 6-12 hours

Minor rectal bleeding

Potential outpatient management

INR < 5
1. Omit one VKA dose
2. Close monitoring

INR ≥ 5 ≤ INR < 9
1. Stop VKA
2. Oral vitamin K (1-2.5 mg)

INR ≥ 9
1. Stop VKA
2. Vitamin K (2.5-5 mg oral or 1 mg IV)

- Recheck clotting screen at 24 hours, or sooner if clinical deterioration
- Consider endoscopy evaluation as appropriate
Treatment options for VKA reversal

Vit K:

- In bleeding patients, IV route is preferred over the oral one.
- Vitamin K1 (phytomenadione), 10 mg (one ampoule) in 100 ml of 0.9% normal saline or 5% glucose solution: 10 ml over 10 minutes (1 mg/10 min) and the remaining over 30 minutes.
- IV vitamin K is associated with an estimated 3/100,000 risk of anaphylaxis; thus, a slow infusion over a minimum of 30 minutes is advised to minimize this risk.
- Following IV infusion of 5–10 mg vitamin K, the INR begins to decrease within 2–4 h and usually reaches a normal range within 24 h.

[References]
Treatment options for VKA reversal

**FFP**

- The recommended dose: IV infusion of 15(10-30) mL/kg corresponding to about 3–4 units of plasma (one unit = 250 mL) in the average adult weighing 70 kg.
- Half the dose can be repeated at 6 hours, as the half-life of the factors is 5 to 8 hours.
- Cons:
  - large infusion volume, risk of fluid overload.
  - prolonged time needed to match blood group and to thaw and transport the units.
  - transfusion-related acute lung injury and a minimal risk of infection transmission
- Time to effect of FFP is 10 min, but it takes a few hours for partial reversal of INR and at least 9 h for complete reversal (i.e., INR < 1.5)

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PCCs

- Lyophilized inactivated concentrates of factors II, IX, and X, with variable amounts of factor VII, derived from the cryoprecipitate supernatant of large plasma pools after at least one viral inactivation step.

- Main advantages of PCCs over FFP:
  - Prompt reconstitution into a small volume (20 mL for about 500 IU), blood group independent, rapid IV infusion over 20–30 min with faster INR correction.

- The PCCs are standardized according to their factor IX content and administered IV, usually at the dose of 25–50 IU of factor IX/Kg, depending on baseline INR.

- Prothrombin complex concentrate combined with factor IX (Prothromplex Immuno TIM 4600 I.U®), Dosage: (required-obtained prothrombin time) x weight in kg x 0.6.

- Activated recombinant factor VII: 80 μg/kg per slow i.v. bolus (2 ml amp = 1.2 mg).
  - Effect takes place within 10 to 30 minutes after administration and lasts up to 12 hours.
  - It should not be combined with prothrombin complexes.
  - It adjusts prothrombin time and corrects platelet function defects.

Patients on DOACs

- Management depends on the severity of bleeding. When bleeding is not severe, temporary drug withdrawal may be the only requirement due to the short half-lives of these drugs.

- In the absence of renal or hepatic failure, the clearance of DOACs and the subsequent loss of anticoagulation is rapid and predictable, occurring gradually over 12–24 h.

- Currently, the only specific reversal agent of DOACs available for clinical use is Praxbind® (idarucizumab), Specific Reversal Agent for Pradaxa® (dabigatran etexilate).
  - PRAXBIND is a humanized monoclonal antibody fragment (Fab) indicated in patients treated with PRADAXA when reversal of the anticoagulant effects of dabigatran is needed.

- Routine laboratory tests are not reliable to measure the anticoagulant effect of DOACs. Although a normal prothrombin time (PT) and a normal activated partial thromboplastin time (aPTT) are advocated as useful tools.

References:
Patients on DOACs...

- **Watch and support**: Given their relatively short half-lives, time is the most important antidote for DOACs.
- **Protamine sulfate, vitamin K and FFP**: no effect.
- **Gastric lavage and oral charcoal**: if DOACs have been ingested within 2–3 h.
- **Hemodialysis**: can be used to reduce the plasma concentration of dabigatran rapidly and efficiently (65% at 2–4 h).
- **Antifibrinolytics**: The effect on bleeding due to DOACs is not known but use of tranexamic acid would be reasonable in some patients.
- **Desmopressin (DDAVP)**: the general haemostatic effect, independent of thrombin or factor Xa might be beneficial although this is unknown.

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Patients on DOACs....

- Prothrombin complex concentrate (PCC) and recombinant factor VIIa (rVIIa):
  - The effects of have not been studied in clinical trials in human patients with bleeding.
  - For patients with life-threatening bleeding, administration of 40–50 IU/kg of PCC has been suggested but there is no clinical evidence as yet that this will reduce clinical bleeding.


Acute GI bleeding

Urgent clinical assessment and resuscitation, including blood type & cross-match for active and significant bleeding
Complete blood count / Clotting screen (INR, aPTT, creatinine clearance)

Active bleeding / Shock

1. Stop DOACs
2. Fluid replacement to maintain diuresis
3. Consider gastric lavage (if overdose < 2-3 hours)
   Consider haemodialysis for clearing dabigatran
   Consider off-label use of PCCs

Consider emergent endoscopy

Significant bleeding without haemodynamic compromise

1. Stop DOACs
2. Fluid replacement to maintain diuresis

Consider endoscopy preferably after 12-24 hours

Minor rectal bleeding

Potential outpatient management

Delay or discontinue next dose

Consider endoscopy evaluation as appropriate
Timing of endoscopy

• Optimal target INR for endoscopic therapy to be safe and effective has yet to be determined.

• Considering the recognized benefits of early endoscopy, various authors have recommended that endoscopy should not be postponed to correct coagulopathy in patients with a INR ≤ 2.5.

• In patients with supra-therapeutic INR values, endoscopy should preferably be postponed until the coagulopathy is partially or completely reversed.
Timing of endoscopy , DOAs

• If bleeding is not rapid, it may be advisable (given the short half-life of the NOACs) to let some time elapse and, in the absence of shock, renal failure, and liver failure, simply support the patient over 12 to 24 hours.

• Endoscopic interventions seem to be as effective and safe as in those off these meds.
Mechanical vs, “non-mechanical” hemostasis

• It makes sense from a pathophysiologic standpoint to mechanically address the bleeding as well as address it with cautery.

• One of the problems with cautery is that an eschar can form that can slough after a week to 10 days. In theory, clips may help to mitigate this problem.
Post-endoscopy management
Should Warfarin be resumed?

• Data from observational studies consistently favor the resumption of VKAs after a major bleeding event; evidence about the timing of VKA resumption is limited.
When to resume Warfarin?

• GI practice guidelines do not specifically address this issue.
• The only available data come from study by Quereshi et al.
  • Lower Mortality when warfarin started \(<7 \text{ days}, 7–15 \text{ days and } 15–21 \text{ days vs. } >30 \text{ days}\) following GI bleeding (p < 0.05 for all comparisons).
  • Patients who resumed warfarin within 7 days had an approximately two-fold higher risk of rebleeding and a non-significant decrease in thromboembolism as compared with patients who resumed anticoagulation after 30 days.
  • The incidence of rebleeding was similar for all groups of patients who resumed warfarin >7 days following bleeding, suggesting that the second week following GI bleeding could be appropriate to resume VKAs in a majority of patients.

DOACs resumption

• Data about DOACs resumption after GI bleeding are lacking.
• The pharmokinetics of DOACs make the role of heparin bridge therapy unnecessary in most cases, but also call for prudence in DOACs resumption, which should probably be deferred after the first week following the bleeding event.
Elective Endoscopic procedures in patients on Anticoagulants
Decision should be based on risk stratification.

1. Risk of bleeding related to the particular procedure.

2. Risk of thrombosis and/or embolism related to the underlying disease.
## PROCEDURE-RELATED BLEEDING RISK

<table>
<thead>
<tr>
<th>High-risk procedures</th>
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</thead>
<tbody>
<tr>
<td>Polypectomy or endoscopic mucosal resection</td>
</tr>
<tr>
<td>Argon plasma coagulation and thermal ablative therapy</td>
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<tr>
<td>Endoscopic sphincterotomy</td>
</tr>
<tr>
<td>Pneumatic or bougie dilation of benign or malignant strictures</td>
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<tr>
<td>Percutaneous endoscopic gastrostomy tube placement</td>
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<tr>
<td>Endoscopic ultrasound (EUS)-guided fine-needle aspiration</td>
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<tr>
<td>Endoscopic hemostasis</td>
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<tr>
<td>Therapeutic balloon assisted enteroscopy</td>
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<tr>
<td>Tissue ablation by any technique</td>
</tr>
<tr>
<td>Cystgastrostomy</td>
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<tr>
<td>Treatment of varices</td>
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</table>

## PROCEDURE-RELATED BLEEDING RISK

**Low-risk procedures**

<table>
<thead>
<tr>
<th>Procedure</th>
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<tbody>
<tr>
<td>Diagnostic upper endoscopy, flexible sigmoidoscopy, and colonoscopy (including biopsies)</td>
</tr>
<tr>
<td>Diagnostic endoscopic retrograde cholangiopancreatography (ERCP)</td>
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<tr>
<td>Biliary stent insertion without endoscopic sphincterotomy</td>
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<tr>
<td>Endosonography</td>
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<tr>
<td>Push enteroscopy and diagnostic balloon assisted enteroscopy</td>
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<tr>
<td>Enteral stent deployment without dilation</td>
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<tr>
<td>Capsule endoscopy</td>
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### RISK OF THROMBOEMBOLIC COMPLICATIONS

<table>
<thead>
<tr>
<th>High-risk conditions</th>
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</thead>
<tbody>
<tr>
<td><strong>Atrial fibrillation associated with</strong> valvular heart disease (including the presence of a mechanical valve)</td>
</tr>
<tr>
<td><strong>Atrial fibrillation associated with</strong> congestive heart failure or a left ventricular ejection fraction of &lt;35 percent</td>
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<tr>
<td><strong>Atrial fibrillation associated with</strong> a history of a thromboembolic event</td>
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<tr>
<td><strong>Atrial fibrillation associated with</strong> hypertension, diabetes, or age &gt;75 years</td>
</tr>
<tr>
<td>Mechanical valves in the mitral position</td>
</tr>
<tr>
<td>Mechanical valves in patients who have had a prior thromboembolic event</td>
</tr>
<tr>
<td>Coronary stents placed within one year</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
</tr>
<tr>
<td>Non-stented percutaneous coronary intervention after myocardial infarction</td>
</tr>
</tbody>
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# RISK OF THROMBOEMBOLIC COMPLICATIONS

<table>
<thead>
<tr>
<th>Low-risk conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis</td>
</tr>
<tr>
<td>Chronic or paroxysmal atrial fibrillation that is not associated with valvular disease</td>
</tr>
<tr>
<td>Bioprosthetic valves</td>
</tr>
<tr>
<td>Mechanical valves in the aortic position</td>
</tr>
</tbody>
</table>

Decision making based on procedure–related risk of bleeding and thrombosis risk
WARFARIN

Low-risk procedures, high or low-risk conditions:

• Warfarin therapy should be continued (low quality evidence, moderate recommendation).

• Check the INR during the week before the endoscopy;
  • INR result within the therapeutic range: continue with the usual daily dose.
  • INR result above the therapeutic range, but less than 5: reduce the daily warfarin dose until the INR returns to within the therapeutic range.
  • INR greater than 5: defer the endoscopy.

Warfarin

High-risk endoscopic procedures in patients at high thrombotic risk

• Stop Warfarin 5 days before the procedure.
• Start Daily therapeutic LMWH two days after stopping warfarin.
• Administer the last dose of LMWH at least 24 h prior to the procedure.
• Check the INR prior to the procedure to ensure its value is <1.5.
• Resume Warfarin on evening of the day of the procedure with the usual dose.
• Restart the daily therapeutic dose of LMWH on the day after the procedure.
• Continue LMWH until a satisfactory INR is achieved.

Warfarin

High-risk procedures, low-risk conditions

• Discontinue five days before the procedure.
• INR should be confirmed to be below 1.4 before the procedure.
• Warfarin can usually be reinstituted on the night of the procedure.

Dabigatran (with normal renal function)

High-risk procedures, low-risk conditions

• Discontinue the drug one to two days prior to the procedure.
• Dabigatran can usually be reinstated following the procedure.

High-risk procedures, high-risk conditions

• The last dose of DOAC be taken ≥48 h before the procedure (very low quality evidence, strong recommendation).

Dabigatran (with normal renal function)


Dabigatran (with normal renal function)

Low-risk endoscopic procedures:

• Omitting the morning dose of DOAC on the day of the procedure (very low quality evidence, weak recommendation)

References:
Dabigatran with abnormal renal function

Dabigatran with CrCl (or estimated glomerular filtration rate, eGFR) of 30–50 mL/min:

- Last dose of DOAC be taken 72 h before the procedure (very low quality evidence, strong recommendation).


Bridge therapy, Warfarin

- **Isolated Atrial fibrillation**: Bridge therapy is not required.

- **Atrial fibrillation + bileaflet aortic valve**: Do not require bridge therapy, but should have their anticoagulant restarted within 24 hours.

- **Atrial fibrillation + (mechanical valve or a history of a CVA or TIA, or a history of systemic embolism)**: Bridge therapy is recommended.

- **Valvular heart disease**: Bridge therapy is recommended for patients with a mechanical mitral valve or a mechanical aortic valve with: AF, previous thromboembolic event, left ventricular dysfunction, hypercoagulable condition, mechanical tricuspid valve, or more than one mechanical valve.
Bridge therapy, Warfarin

Unfractionated Heparin, Inpatient
- Warfarin should be held and unfractionated heparin started once the INR is less than two.
- The heparin should be stopped four to six hours prior to the procedure and resumed following the procedure.
- Warfarin usually can be resumed the evening of the procedure. Once the INR is therapeutic, the heparin can be stopped.

LMW Heparin, outpatient
- If low molecular weight heparin is used, the last dose should be given 24 hours prior to the procedure.
Need for bridging anticoagulation:

- The rapid offset and onset of Dabigatran activity obviates the need for bridging anticoagulation with heparin or LMW heparin

- In general, studies should an increase in bleeding and no decrease in thrombotic events when heparin bridging was used with DOAS.


RESUMPTION OF Anti-coagulation following the procedure
Resumption , Dabigatran

• **Resumption following procedure :**
  - Resume when hemostasis has been achieved.
  - Dabigatran has a rapid onset of action (peak effects two to three hours after intake), caution should be used when resuming dabigatran patients who have had major surgery or other procedures associated with a high bleeding risk.
  - In patients having high bleeding risk surgery or procedures, it is sensible to delay resumption of dabigatran for 2-3 days and, if needed, to administer a lower dabigatran dose for 2-3 postoperative days (eg, 110 mg once daily) or use a low-dose LMW heparin for this period.

• **Resumption following use of Heparin or LMW heparin**
  - It should be given ≤2 hours prior to the time of the next scheduled dose of the LMW heparin or at the time of discontinuation of intravenous heparin.
Risks specific to the procedures

• Diagnostic endoscopy and mucosal biopsy:
  • Diagnostic endoscopies, including mucosal biopsy sampling, harbor a minimal risk of hemorrhage.
  • The safety of taking large numbers of biopsies in patients on warfarin, such as in Barrett’s esophagus surveillance, has not been studied.
  • Due to uncertainty, we suggest omitting the dose of DOAC on the morning of the procedure to allow an adequate safety margin.
Risks specific to the procedures

• Post polypectomy bleeding
  • Polyp size is the most consistent risk factor for colonic PPB, and it has been calculated that every 1-mm increase in polyp diameter increases the risk of PPB by 9%.
  • Prophylactic endoscopic treatments: Submucosal injection of adrenaline, endoclip and detachable snare are all shown to reduce the risk.
  • Care should be taken when clips are placed before snare polypectomy (risk of thermal injury and perforation).

• Resection of sessile polyps: the risk of bleeding may persist for more than two weeks.

Risks specific to the procedures

• Endoscopic mucosal resection:
  • Pooled analysis showed a reduction of delayed PPB if the EMR defect was closed using endoclips (1.8% vs 4.4%) with an OR of 0.40 (95% CI 0.20 to 0.80), especially for large (≥20 mm) polyps.
  • Most relevant for large polyps and duodenal lesions.

Risks specific to the procedures

• Endoscopic retrograde cholangiopancreatography
• Sphincterotomy: the risk of bleeding persists for three to five days.

Thank you
<table>
<thead>
<tr>
<th>Medical Treatment</th>
<th>Low Risk</th>
<th>High Risk</th>
<th>Low Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continue</td>
<td>Biopsy 0%</td>
<td>Standard risk of procedure, except large colonic EMR 6.2–7% with ‘recent’ LDA. Gastric ESD increased risk on LDA to 21.1% vs no increased risk 15.5%</td>
<td>0.51% per year</td>
<td>1.8% at 30 days</td>
</tr>
<tr>
<td>Discontinue 7 days</td>
<td>N/A</td>
<td>Standard risk of procedure</td>
<td>Estimate &lt;1% per year</td>
<td>9% at 30 days</td>
</tr>
<tr>
<td><strong>Warfarin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continue</td>
<td>Biopsy 0%</td>
<td>Polypectomy 0.8–23%</td>
<td>&lt;1% per year</td>
<td>1% per year</td>
</tr>
<tr>
<td>Discontinue 5 days</td>
<td>N/A</td>
<td>Standard risk of procedure; increased PPB risk</td>
<td>AF 0.4% at 30 days</td>
<td>N/A</td>
</tr>
<tr>
<td>Bridge with LMWH</td>
<td>N/A</td>
<td>Standard risk of procedure; increased PPB risk</td>
<td>AF 0.3% at 30 days</td>
<td>Metal heart valves 0%</td>
</tr>
<tr>
<td><strong>Dual APA</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Continue</td>
<td>Biopsy 0%</td>
<td>Polypectomy &lt;1 cm 2.1–6.45%</td>
<td>N/A</td>
<td>1.3% at 9 months</td>
</tr>
<tr>
<td>Discontinue 5 days</td>
<td>N/A</td>
<td>Estimate standard risk of procedure</td>
<td>N/A</td>
<td>Not advised</td>
</tr>
<tr>
<td><strong>DOAC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omit day of procedure</td>
<td>No specific data</td>
<td>N/A</td>
<td>No specific data</td>
<td>DOAC not indicated</td>
</tr>
<tr>
<td>Discontinue 48 h</td>
<td>N/A</td>
<td>No specific data</td>
<td>0.8%</td>
<td>DOAC not indicated</td>
</tr>
</tbody>
</table>

Key references in superscript.
AF, atrial fibrillation; APA, antplatelet agent; DOAC, direct oral anticoagulant; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; LDA, low-dose aspirin; LMWH, low molecular weight heparin; N/A, not applicable; PPB, post-polypectomy bleeding.