Antithrombotics and the Gut

Panelists:
AR Tagahvi MD, N Nozari MD
Moderator:
S Nasser-Moghaddam MD, MPH
IAGH monthly meeting
Shahrivar 1395 (September 2016)
IAGH Conference Hall
Antithrombotic agents

• Anticoagulants
  – warfarin, Dabigatran, Apixban, heparin, and low molecular weight heparin

• Antiplatelet agents
  – aspirin,
  – NSAIDs,
  – Thienopyridines (eg, clopidroglrel & ticlopidine),
  – Glycoprotein IIb/IIIa receptor inhibitors.
• The most common site of significant bleeding in patients receiving oral anticoagulation therapy is the GI tract
General concept

- Low risk procedure for bleeding in high risk pt for thrombosis: Continue anticoagulation
- High risk procedure for bleeding in low risk pt for thrombosis: Discontinue antithrombotic
- ASGE:
  - Low risk procedure for bleeding: <1.5% chance
  - High risk procedure for bleeding: >1.5% chance
• Moderate to high risk thrombosis risk pt undergoing high risk for bleeding procedure

• Communication between
  – Primary provider
  – Proceduralist

• Knowledge of:
  – thrombotic risk,
  – procedure-related bleeding risk,
  – concepts of bridging anticoagulation therapy, and
  – timing of cessation and reinitiation of antithrombotic therapy
Case-1

- A 43 Y/O gentleman w/o any significant past hx presents with substernal pain of 3 hours duration
- Initial evaluation reveals STEMI (extensive anterior wall) without clinical CHF/dysrhythmias
- He receives high dose clopidogrel, ASA, & tissue plasminogen activator
- He undergoes emergency coronary catheterization where a clot is taken out from an occluded LAD and a DES is placed
- He fares well post-up and is ready for discharge on DET the next day when he feels nauseous and brings up abundant fresh blood
Case-1

• What will you do for him?
  – Resuscitation and careful management of hydration/hemodynamics
  – Pantoprazole 80mg IV stat followed by 8mg/h
  – Withhold antiplatelets
  – Check Hb q6h
  – Transfuse 2 units of packed RBC
  – Check PT/PTT and if prolonged correct with FFP
  – EGD
Before the endoscopy

- Consider the urgency of the procedure and the risks of:
  - Bleeding related solely to antithrombotic therapy,
  - Bleeding related to an endoscopic intervention performed in the setting of antithrombotic medication use, and
  - A thromboembolic event related to interruption of antithrombotic therapy
Condition Risk for Thromboembolic Event

High Risk Conditions

• AF with valvular heart disease, prosthetic valves, active congestive heart failure, left ventricular ejection fraction <35%, a history of a thromboembolic event, hypertension, diabetes mellitus, or age >75 y
• Mechanical valve in the mitral position
• Mechanical valve in any position and previous thromboembolic event
• Recently (<1 y) placed coronary stent
• Acute coronary syndrome
• Nonstented percutaneous coronary intervention after myocardial infarction

Low Risk Conditions

• Uncomplicated or paroxysmal nonvalvular atrial fibrillation
• Bioprosthetic valve
• Mechanical valve in the aortic position
• Deep vein thrombosis
Procedure Risk for Bleeding

High Risk Procedures
- Polypectomy
- Biliary or pancreatic sphincterotomy
- Pneumatic or bougie dilation
- PEG placement Therapeutic balloon-assisted enteroscopy
- EUS with FNA
- Enteral stent deployment (without dilation)
- Endoscopic hemostasis
- Tumor ablation by any technique
- Cystogastrostomy
- Treatment of varices

Low Risk Procedures
- Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including biopsy
- ERCP without sphincterotomy
- EUS without FNA
- Enteroscopy and diagnostic balloon-assisted enteroscopy
- Capsule endoscopy
Endoscopic procedures in the acutely bleeding pt on antithrombotics

- Endoscopic evaluation and therapy in patients who have GIB while using antithrombotic agents is both warranted and safe
- The most common causes of GIB in these pts:
  - Upper GI tract:
    - Peptic ulcer disease
    - Erosive gastritis/duodenitis/esophagitis
  - Lower GI tract:
    - Diverticular disease
Urgent endoscopy in the patient with ACS or a recently placed vascular stent

- Incidence of GIB in pts with ACS: 1%-3%
- Mortality in such pts: 4-7 folds
- The rate of procedural complications may be as high as 12% if done on the same day as the ACS
- The overall rate of complications associated with
  - EGD: 1-2%
  - Colonoscopy: 1%
Aspirin/NSAID
- Low Bleeding Risk: Continue
- High Bleeding Risk: Continue
  - Low Thromboembolic Risk: Consider Continuing
  - High Thromboembolic Risk: Consider Discontinuing

Thienopyridines (e.g. Clopidogrel)
- Low Bleeding Risk: Continue
- High Bleeding Risk: Discontinue
  - Low Thromboembolic Risk: Continue
  - High Thromboembolic Risk: Consider Discontinuing

Warfarin
- Low Bleeding Risk: Continue
- High Bleeding Risk: Discontinue
  - In patients with high thromboembolic risk, consider bridge therapy
Management of antithrombotic agents in the urgent endoscopic setting

If unable to delay procedure for 7-10 days, hold as many days as possible up to 7-10 days.

In patients on dual antiplatelet therapy or monotherapy with a thienopyridine, consider continuing aspirin (dual therapy patients) or starting aspirin (thienopyridine monotherapy patients) in the periendoscopic period.
Restarting antithrombotic agents after endoscopic hemostasis

• For aspirin-related PUD with GIB:
  – resumption of aspirin with concurrent proton pump inhibitor therapy is superior to switching to clopidogrel alone
  – Withholding aspirin for 30 days vs resumption at 3-5 days after bleeding associated with:
    • a numerically lower rate of rebleeding (11% vs 19%, P=0.25),
    • 2 months mortality more common (14.5% vs 1.7%, P=0.012)
Case-2

- A 58 Y/O lady has undergone AVR and MVR 20 Y/A (both ball-cage valves)
- She was maintained on warfarin and metformin (for a recently diagnosed Dm) and did well (INR: 3.5, HbA1c: 6%, creatinine: 0.8mg/dl)
- Three weeks prior to referral she noted some fresh blood over her stool for the 1st time
- The blood was mixed with a formed stool
- Her bowel habit had not changed
- She noted another similar episode last week
- No hx of wt loss, anemia, abdominal pain
- No family hx of any significant GI disease
Case-2

- P/E is insignificant except for abdominal obesity and a BMI of 29kg/m²
- The mechanical heart valve sounds appear normal
- Hb: 13.8 g/dl, MCV: 89 fl,
- Platelet/WBC/Dif: WNL, INR: 3.6,
- Creatinine: 0.9mg/dl,
- HbA1c: 6.2, FBS: 145 mg/dl
Case-2

• What will you do for her?
  – Considering that the bleeding was not massive, she is stable with mechanical heart valves, & Hb is WNL, treat as hemorrhoids and follow
  – Wait for another episode of hematochezia and if happened then go for colonoscopy
  – Admit her, D/C warfarin, start UFH, schedule for a colonoscopy ASAP
  – Schedule her for an elective colonoscopy
Case-2

- Hematochezia needs evaluation
- Careful hx, P/E, and early colonoscopy
- This case is not urgent and considering her underlying CVD adequate considerations should be given a priori
Case-2

- She is scheduled for an elective colonoscopy. What will you do now?
  - D/C warfarin 7 days before the procedure, start LMWH and D/C it the day before the procedure
  - Considering the high risk valves for serious thrombotic event, go for the procedure on warfarin and be prepared for management of any bleeding
  - Discuss the case with her cardiologist/cardiac surgeon, D/C warfarin and monitor INR when <2 start LMWH and D/C it the day before the procedure
  - Discuss the case with her cardiologist/cardiac surgeon, D/C warfarin, give 5mg IM vitamin K for 2 successive days and monitor INR when <2 do the procedure
  - Discuss the case with her cardiologist/cardiac surgeon, D/C warfarin and monitor INR when <2 do the procedure
• Risk of major embolism (causing death, residual neurologic deficit, or peripheral ischemia requiring surgery) in patients with mechanical valves
  – Without antithrombotics: 4/100 pt-yr
  – With antiplatelet therapy: 2.2 per 100 pt-yr
  – With warfarin: 1/100 pt-yr
• Absolute risk of an embolic event for patients in whom anticoagulation is interrupted for 4-7 days is approximately 1%.
• Avoid vitamin K to reverse anticoagulation for elective procedures
  – it delays therapeutic anticoagulation once anticoagulants are resumed
• In patients at low risk of thrombosis:
  – Hold warfarin before the procedure
  – Bridge therapy with heparin usually unnecessary
<table>
<thead>
<tr>
<th>Patient History</th>
<th>(&lt;5%/y)</th>
<th>Risk Factors for Thromboembolism*</th>
<th>(&gt;10%/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Annual Risk</td>
<td></td>
<td>Moderate Annual Risk</td>
<td></td>
</tr>
<tr>
<td>Mechanical heart valve</td>
<td>Bileaflet aortic-valve prosthesis without atrial fibrillation, prior stroke or thromboembolic event, or known intracardiac thrombus</td>
<td>Bileaflet aortic-valve prosthesis and atrial fibrillation</td>
<td>Any mitral-valve prosthesis, any caged-ball or tilting-disk aortic-valve prosthesis, multiple mechanical heart valves, or stroke, TIA, or cardioembolic event</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>Venous thromboembolism &gt;12 mo previously and no other risk factor (e.g., provoked and transient)</td>
<td>Venous thromboembolism within previous 3–12 mo, nonsevere thrombophilia†, or recurrent venous thromboembolism</td>
<td>Venous thromboembolism within previous 3 mo, severe thrombophilia,‡ unprovoked venous thromboembolism, or active cancer (cancer diagnosed ≤6 mo or patient undergoing cancer therapy)</td>
</tr>
</tbody>
</table>
Procedure Risk for Bleeding

High Risk Procedures
• Polypectomy
• Biliary or pancreatic sphincterotomy
• Pneumatic or bougie dilation
• PEG placement Therapeutic balloon-assisted enteroscopy
• EUS with FNA
• Enteral stent deployment (without dilation)
• Endoscopic hemostasis
• Tumor ablation by any technique
• Cystogastrostomy
• Treatment of varices

Low Risk Procedures
• Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including biopsy
• ERCP without sphincterotomy
• EUS without FNA
• Enteroscopy and diagnostic balloon-assisted enteroscopy
• Capsule endoscopy
Condition Risk for Thromboembolic Event

**High Risk Conditions**

- AF with valvular heart disease, prosthetic valves, active congestive heart failure, left ventricular ejection fraction <35%, a history of a thromboembolic event, hypertension, diabetes mellitus, or age >75 y
- Mechanical valve in the mitral position
- Mechanical valve in any position and previous thromboembolic event
- Recently (<1 y) placed coronary stent
- Acute coronary syndrome
- Nonstented percutaneous coronary intervention after myocardial infarction

**Low Risk Conditions**

- Uncomplicated or paroxysmal nonvalvular atrial fibrillation
- Bioprosthetic valve
- Mechanical valve in the aortic position
- Deep vein thrombosis
### Periprocedural management of warfarin of pts with AF or VHD undergoing elective endoscopy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Associated diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Hold warfarin 3-5 days before procedure. Restart warfarin within 24 h.*</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Mechanical valve(s) and/or history of cerebrovascular accident, transient ischemic attack, or systemic embolism</td>
<td>Hold warfarin and start UFH when INR ≤ 2.0. Stop UFH 4-6 h before procedure and restart after procedure. Resume warfarin on the evening of the procedure and continue both agents until INR is therapeutic.* Therapeutic doses of SQ UFH or LMWH may be considered in lieu of IV UFH.</td>
</tr>
<tr>
<td></td>
<td>Mechanical bileaflet, aortic valve</td>
<td>Hold warfarin 48-72 h before procedure for a target INR &lt; 1.5. Restart warfarin within 24 h.*</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>Mechanical mitral valve or mechanical aortic valve plus any of the following: atrial fibrillation, previous thromboembolic event, left ventricular dysfunction, hypercoagulable condition, mechanical tricuspid valve or &gt; 1 mechanical valve</td>
<td>Hold warfarin and start UFH when INR ≤ 2.0. Stop UFH 4-6 h before procedure and restart after procedure. Resume warfarin on the evening of the procedure and continue both agents until INR is therapeutic.* Therapeutic doses of SQ UFH or LMWH may be considered in lieu of IV UFH.</td>
</tr>
</tbody>
</table>
The role of bridge therapy in endoscopy

- Unfractionated heparin (UFH) and low molecular weight heparin (LMWH)
- Limited evidence, controversial
• Continue VKA with a Rxc INR in pts with mechanical heart valves undergoing minor procedures (e.g. as dental extractions or cataract removal) where bleeding is easily controlled. *(Level of Evidence: C)*

• Temporarily D/C VKA, w/o bridging agents while the INR is subtherapeutic in pts with a bileaflet mechanical AVR and no other risk factors for thrombosis who are undergoing invasive or surgical procedures. *(Level of Evidence: C)*

• Bridging anticoagulation with either IV UFH or subQ LMWH with subtherapeutic INR preoperatively in patients who are undergoing invasive or surgical procedures with a:
  – mechanical AVR and any thromboembolic risk factor
  – older-generation mechanical AVR,
  – mechanical MVR. *(Level of Evidence: C)*
• D/C anticoagulation (ie, warfarin) in pts with a low risk of thromboembolic events in whom it is safe to do
Aspirin/NSAID

Low Bleeding Risk:
Continue

High Bleeding Risk:

Thienopyridines (e.g. Clopidogrel)

Low Bleeding Risk:
Continue

High Bleeding Risk:

Warfarin

Low Bleeding Risk:
Continue

High Bleeding Risk:
Discontinue
In patients with high thromboembolic risk, consider bridge therapy

Low Thromboembolic Risk:
Consider Continuing

High Thromboembolic Risk:
Continue

Low Thromboembolic Risk:

High Thromboembolic Risk:
Discontinue 7-10 Days Prior

Consider Discontinuing 7-10 Days Prior

In patients with high thromboembolic risk on thienopyridines undergoing elective procedures with high risk for bleeding, consider postponing procedure to time when thromboembolic risk is low
• Continuing therapeutic anticoagulation with warfarin during the periendoscopic period has a low risk of bleeding in diagnostic EGD/Colonoscopy
Bridging anticoagulation: Aims

• Minimize the risk of thromboembolism in high-risk patients when anticoagulation therapy is suspended
• Minimize the risk of bleeding after high-risk procedures
Bridging anticoagulation: Does it help?

### Older Studies

<table>
<thead>
<tr>
<th></th>
<th>Risk of thrombosis</th>
<th>Risk of bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical Heart valves</td>
<td>1.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>0.9%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Venous Thrombembolism</td>
<td>1.8%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

SR and metaanalysis (Siegal D et al, 2012): Increased risk of bleeding w/o significant decrease in thromboembolism
A new Japanese study
Matsumoto et al, BMC gastroenterol 2015

- Heparin Bridge Rx: 171 UGI/74 lower GI
- Controls: 5588 upper GI/6614 lower GI

<table>
<thead>
<tr>
<th></th>
<th>HBT group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>13.5 %</td>
<td>2.7 %</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>(33/245)</td>
<td>(299/11102)</td>
<td></td>
</tr>
<tr>
<td>Upper gastrointestinal tract</td>
<td>14.1 %</td>
<td>4.5 %</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>(25/171)</td>
<td>(204/4488)</td>
<td></td>
</tr>
<tr>
<td>Lower gastrointestinal tract</td>
<td>10.8 %</td>
<td>1.4 %</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>(8/74)</td>
<td>(95/6614)</td>
<td></td>
</tr>
</tbody>
</table>
Case-2

• She undergoes colonoscopy with an INR of 1.5. A 2cm pedunculated polyp is identified in mid-sigmoid and another 15mm sessile one in the distal transverse colon. What will you do?
  – Remove both polyps with snare after injecting beneath them and apply hemoclips
  – Remove both polyps with snare after injecting beneath them
  – Remove the pedunculated one and leave the sessile one for another session when the INR is <1.2
  – Terminate procedure, achieve an INR<1.2 and then do polypectomies
Colonoscopic polypectomy

• Very low risk of post-polypectomy bleeding even on ASA/NSAIDs (exact risk unknown)
• Postpolypectomy bleeding risk:
  – increased for patients taking warfarin or resuming warfarin or heparin within 1 week after polypectomy
Endoscopic procedures in the acutely bleeding pt on antithrombotics

- A retrospective study:
  - 52 pts
  - Correcting INR to 1.5-2.5
  - successful endoscopic Dx & Rx at rates comparable with those achieved in nonanticoagulated pts

- A larger study (246 pts):
  - 95% of INRs 1.3-2.7
  - Endoscopic Rx initial success: 94.7%
  - using a variety of hemostatic techniques including injection therapy, heater probe, and hemoclips
  - rebleeding rate: 23%
  - The preprocedure INR was NOT a predictor of rebleeding

- A retrospective study:
  - INR>4 & INR 2-4: No difference in rates of rebleeding
Case-2

- The polyps are resected successfully w/o any immediate complication. When will you restart the anticoagulation?
  - Immediately after the procedure
  - The next day with heparin and add warfarin on day 3
  - Start warfarin within a few hours after the procedure and UFH the next day
Re-initiation of antithrombotic agents after elective endoscopy

- No consensus
- A study:
  - 94 pts/109 colonoscopies (47% hot biopsy or snare polypectomy)
  - Warfarin restarted the day after the examination.
  - only 1 (0.92%) procedure-related bleeding occurring 7 days after warfarin
  - required hospitalization and transfusion
- Another study:
  - 173 pts
  - Warfarin restarted within 1w
  - Bleeding risk OR: 5.2 (95% CI: 2.2-12.5)
- AHA/ACC recommendation:
  - Patients with valvular heart disease and a low risk of thromboembolism: restart warfarin within 24 hours
  - Patients with high risk of thromboembolism on UFH or LMWH: restart warfarin as soon as “bleeding stability allows” and continued until appropriate INR is reached after a therapeutic procedure,
- UFH may be restarted 2 to 6 hours later.
- The optimal time to restart LMWH after endoscopy has not been determined.
Case-3

- A 62 Y/O gentleman who has underwent PCI with placement of two DES 3 months ago refers for follow-up of colon polyps first diagnosed 4 years ago
- At that time he had 3 polyps 5-25mm in different parts of his colon, all removed and reported to be adenomatous polyps
- He is diabetic, overweight, and hypertensive on metformin, atorvastatin, ASA, clopidogrel, valsartan, and atenolol
- Family hx is negative for CRC
What will you recommend to him?

- Postpone the colonoscopy till after 12 months has elapsed from his PCI
- Progress to the colonoscopy +/-polypectomy on his current medication
- Progress to the colonoscopy +/-polypectomy after D/C Clopidogrel for 5-7 days
- Progress to the colonoscopy +/-polypectomy after D/C ASA for 3 days
- Progress to the colonoscopy +/-polypectomy after D/C ASA & Clopidogrel
Coronary stents

- Dual antiplt Rx
- Premature D/C of Rx $\rightarrow$ increased risk of stent thrombosis and AMI
  - Mortality of $\geq$50%
- Stent type:
  - Bare vs Drug eluting (DES)
- Highest risk of thrombosis:
  - Bare: within 6 weeks
  - DES: in 3-6 months
ENDOSCOPY IN THE PATIENT WITH A VASCULAR STENT OR ACS TAKING ANTITHROMBOTIC DRUGS

• Postpone endoscopic procedure till at least 12 months after a DES on DAT IF POSSIBLE

• Thereafter D/C one
  – Which one?
  – Nobody knows exactly
  – ? Clopidogrel more effective in prevention of thromosis
  – Good data on safety of polypectomies on ASA
Management of antithrombotic agents in the elective endoscopic setting

In patients on dual antiplatelet therapy or monotherapy with a thienopyridine, consider continuing aspirin (dual therapy patients) or starting aspirin (thienopyridine monotherapy patients) in the periendoscopic period.
Case-4

• A 72 Y/O lady undergoes elective CABG
• Three venous grafts are placed successfully and the pt is doing well in ICU while on heparin and ASA
• On the second post-op day, she develops painless massive hematochezia with hemodynamic instability which is corrected rapidly with administration of IV fluids
• Hb 8.5g/dl, PTT: 60s, INR: 1.2, platelet: 254000
Case-4

• What will you do for her after adequate resuscitation and monitoring?
  – D/C ASA/heparin, prepare the pt for urgent clonoscopy
  – D/C ASA/heparin, start IV PPI, schedule the pt for urgent EGD
  – D/C ASA/heparin, observe the pt carefully and if ongoing bleeding happens or hemodynamic instability recurs go for further Dxc procedures
Case-4

- The pt is stabilized, undergoes EGD which does not report any significant lesion
- Is a colonoscopy warranted now?
  - Yes, within the next 7-10 days
  - Yes, can be postponed after 10 days if hemodynamically stable
  - Yes, only if bleeding recurs
  - No, the chances of any significant lower GI pathology is nil considering the massive bleeding & nil EGD
  - No, considering the recent CABG and high risk for any further intervention, finding any pathology in the colon will not affect pt’s management
• Our knowledge is evolving, therefore
• Strong recommendations regarding the management of particular agents in the periendoscopic period cannot be made at this time
• Clinicians are encouraged to seek the input of relevant consultants (eg, cardiology and neurology) before discontinuing any antithrombotic agent
Sphincterotomy and PEG

- Risk of postsphincterotomy bleeding: 0.3% to 2.0%
  - Withholding aspirin or NSAIDs, even as long as 7 days before sphincterotomy, does not seem to reduce the risk of bleeding

- Anticoagulation with oral warfarin or intravenous heparin within 3 days after has been shown to increase the risk of postsphincterotomy bleeding

- PEG placement: 2.5% risk of bleeding complications
  - The risk of bleeding for PEG placement in the patient receiving antithrombotic therapy is unknown
• ENDOSCOPIC PROCEDURES IN THE ACUTELY BLEEDING PATIENT RECEIVING ANTITHROMBOTIC THERAPY
Stopping or reversing antithrombotic agents in the acutely bleeding pt

- Weigh & individualize the risk of thromboembolic consequences against the risk of continued bleeding by maintaining antithrombotic agents
- Hold warfarin
- Give vitamin K (10 mg slow IV)
- Give (for life-threatening bleeding) or consider FFP (for serious bleeding), prothrombin complex concentrate, or recombinant factor VIIa
Procedure Risk for Bleeding

High Risk Procedures

• Polypectomy
• Biliary or pancreatic sphincterotomy
• Pneumatic or bougie dilation
• PEG placement Therapeutic balloon-assisted enteroscopy
• EUS with FNA
• Enteral stent deployment (without dilation)
• Endoscopic hemostasis
• Tumor ablation by any technique
• Cystogastrostomy
• Treatment of varices

Low Risk Procedures

• Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including biopsy
• ERCP without sphincterotomy
• EUS without FNA
• Enteroscopy and diagnostic balloon-assisted enteroscopy
• Capsule endoscopy
Aspirin/NSAID

- Low Bleeding Risk: Continue
- High Bleeding Risk
  - Low Thromboembolic Risk: Consider Continuing
  - High Thromboembolic Risk: Continue

Thienopyridines (e.g. Clopidogrel)

- Low Bleeding Risk: Continue
- High Bleeding Risk
  - Low Thromboembolic Risk: Continue
  - High Thromboembolic Risk
    - In patients with high thromboembolic risk on thienopyridines undergoing elective procedures with high risk for bleeding, consider postponing procedure to time when thromboembolic risk is low

Warfarin

- Low Bleeding Risk: Continue
- High Bleeding Risk: Discontinue
  - In patients with high thromboembolic risk, consider bridge therapy
  - Discontinue 7-10 Days Prior
Condition Risk for Thromboembolic Event

High Risk Conditions

• AF with valvular heart disease, prosthetic valves, active congestive heart failure, left ventricular ejection fraction <35%, a history of a thromboembolic event, hypertension, diabetes mellitus, or age >75 y
• Mechanical valve in the mitral position
• Mechanical valve in any position and previous thromboembolic event
• Recently (<1 y) placed coronary stent
• Acute coronary syndrome
• Nonstented percutaneous coronary intervention after myocardial infarction

Low Risk Conditions

• Uncomplicated or paroxysmal nonvalvular atrial fibrillation
• Bioprosthetic valve
• Mechanical valve in the aortic position
• Deep vein thrombosis
**CHADS\textsubscript{2} Scoring System for Assessing the Risk of Stroke among Patients with Non-valvular Atrial Fibrillation**

<table>
<thead>
<tr>
<th>CHADS\textsubscript{2} Score or Assessment</th>
<th>Risk of Stroke</th>
<th>Stroke Rate per 100 Patient-Yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score of 0, 1, or 2</td>
<td>Low</td>
<td>1.9–4.0 (1.2–5.1)</td>
</tr>
<tr>
<td>Score of 3 or 4</td>
<td>Moderate\textsuperscript{†}</td>
<td>5.9–8.5 (4.6–11.1)</td>
</tr>
<tr>
<td>Score of 5 or 6, stroke or TIA within previous 3 mo, or severe valvular heart disease</td>
<td>High</td>
<td>12.5–18.2 (8.2–27.4)</td>
</tr>
<tr>
<td>Agent</td>
<td>Route of Administration</td>
<td>Mechanism of Action</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-------------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Anticoagulant agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin (Coumadin, Bristol-Myers Squibb)</td>
<td>Oral</td>
<td>Inhibition of vitamin K–dependent factors II, VII, IX, and X for γ-carboxylation; and proteins C and S</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>Intravenous or subcutaneous</td>
<td>Antithrombin activation (inhibition of factors IIa, IXa, Xa, XIa, and XIIa)</td>
</tr>
<tr>
<td>Low-molecular-weight heparins (enoxaparin [Lovenox, Sanofi Aventis] and dalteparin [Fragmin, Eisai])</td>
<td>Subcutaneous</td>
<td>Antithrombin activation (inhibition of factor Xa and, to a lesser extent, factor IIa)</td>
</tr>
<tr>
<td>Fondaparinux (Arixtra, GlaxoSmithKline)</td>
<td>Subcutaneous</td>
<td>Antithrombin activation (factor Xa inhibitor)</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa, Boehringer Ingelheim)</td>
<td>Oral</td>
<td>Direct thrombin inhibitor</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto, Bayer Healthcare)</td>
<td>Oral</td>
<td>Direct factor Xa inhibitor</td>
</tr>
<tr>
<td>Apixaban (Eliquis, Bristol-Myers Squibb)</td>
<td>Oral</td>
<td>Direct factor Xa inhibitor</td>
</tr>
<tr>
<td>Desirudin (Iprivask, Canyon Pharmaceuticals)</td>
<td>Subcutaneous</td>
<td>Direct thrombin inhibitor</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>Route</td>
<td>Action</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Oral</td>
<td>Cyclooxygenase inhibitor (irreversible effect)</td>
</tr>
<tr>
<td>Aspirin and dipyridamole (Aggrenox, Boehringer Ingelheim)</td>
<td>Oral</td>
<td>Phosphodiesterase inhibitor</td>
</tr>
<tr>
<td>Cilostazol (Pletal, Otsuka Pharmaceutical)</td>
<td>Oral</td>
<td>Phosphodiesterase inhibitor</td>
</tr>
<tr>
<td>Thienopyridine agents (clopidogrel [Plavix, Sanofi Aventis], ticlopidine [Ticlid, Roche], prasugrel [Effient, Eli Lilly], and ticagrelor [Brilinta, AstraZeneca])</td>
<td>Oral</td>
<td>ADP receptor antagonist</td>
</tr>
</tbody>
</table>