Background

- ASA prevents thrombotic events (venous and arterial) and many patients undergoing surgery are on perioperative ASA (either new or continuing) for prevention of major vascular complications. Many patients are now also receiving DVT prophylaxis with an anticoagulant around the surgery.
- There is no good evidence on the risks/benefits of therapy in this situation though observational studies have suggested a reduction in thrombotic events.
- Current guidelines suggest the following (CHEST 2012)
  1. Low risk patients (i.e., primary prevention of MI/stroke) – can hold ASA
  2. Mod risk patients – not specifically discussed
  3. High risk patients – (i.e., recent stent, recent MI, recent stroke) – consider continuing
  4. When holding ASA/clopidogrel – hold for 7 to 10 days prior to surgery and resume ASA/clopidogrel the day following surgery assuming that there is adequate hemostasis

Trial Summary

General
International, R, C 2x2 trial (ASA, clonidine), funded by CIHR and other organizations with some drugs/funding from drug companies (though likely small bias from this)

Patients
ASA = 4998
PLB = 5012
~69 years, 50% female, 23% hx CAD, 9% PVD, 5% Stroke, 5% vascular surgery, 80% undergoing major surgery, 50% age >70, 37% DM, 86% HTN, 5% hx CABG, 5% hx PCI
40% orthopedic surgery, 27% general surgery, 17% urologic/gynec surgery
65% on DVT prophylaxis, 4.5% on therapeutic anticoagulant, 32% on NSAID
Patients stratified into initiation (not on ASA before) and continuation stratum (starting on ASA)

Inclusion: 1 of (CAD, PVD, stroke, undergoing major vascular surgery) or 3/9 of (age >70, major surgery, CHF, TIA, DM, HTN, preop Cr >175, smoking)

Exclusion: BP <105, HR < 55, DES in last year, BMS last 6 weeks, use of clopidogrel/other, anticoagulation

Interventions
ASA 200 mg x1 then 100 mg daily for 7 days (continuation) or 30 days (initiation) or placebo
Clonidine 0.2 mg po daily or PLB (not discussed here)

Outcomes

Primary
Death/nonfatal MI

Other
Composite of death, nonfatal MI/stroke
Composite of death, nonfatal MI, revascularization, PE, nonfatal DVT

Other tertiary outcomes

Safety
Life threatening bleed, major bleed

Duration
30 days max intervention

Statistics
ITT, censored data for patients on last day available, Cox proportional-hazards models, Power = α = 0.05, β = 0.16, HR 0.75, PLB event rate 6.1% :: n = 10,000

Results

Note: no significant tertiary outcomes (DVT, PE, death etc) apart from AKI with dialysys

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ASA (%)</th>
<th>Placebo (%)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Death/nonfatal MI/stroke</td>
<td>351 (7%)</td>
<td>355 (7.1%)</td>
<td>0.99 (0.86-1.15)</td>
<td>0.92</td>
</tr>
<tr>
<td>Death/nonfatal MI/revasc/PE/DVT</td>
<td>402 (8%)</td>
<td>407 (8.1%)</td>
<td>0.99 (0.86-1.14)</td>
<td>0.9</td>
</tr>
<tr>
<td>AKI with dialysis</td>
<td>33 (0.7%)</td>
<td>19 (0.4%)</td>
<td>1.75 (1.39-2.09)</td>
<td>0.05</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>230 (4.6%)</td>
<td>188 (3.8%)</td>
<td>1.23 (1.01-1.49)</td>
<td>0.04</td>
</tr>
<tr>
<td>Stroke</td>
<td>16 (0.3%)</td>
<td>19 (0.4%)</td>
<td>0.84 (0.43-1.64)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Subgroups
- In general there were no significant interactions (see figure to right). For the tertiary outcome of stroke there was a significant reduction in the subgroup of patients initiated on ASA with HR of 0.25. Authors felt this was likely a chance finding due to multiple testing given the small number of strokes.

Other findings
- Patients experiencing life threatening or major bleeding were more likely to experience an MI
Limitations/Commentary

- Patients in this study were not THAT high risk for cardiovascular events. Only 33% of patients had a history of vascular disease and another 5% of patients were undergoing vascular surgery. Still, there was no trend to benefit even in those higher risk patients so hard to argue that studying a different population would be likely to see a benefit.
- Only 5% of patients had previously undergone stenting and none with BMS in the last 6 weeks or DES in the last year. Means that the results do not apply at all to those patients.
- 65% of patients were on DVT prophylaxis and you wonder whether that confers some reduction in arterial thrombotic events and may have reduced the relative benefit of ASA.
- The authors suggest that part of the reason there was no benefit may have been related to the association between major bleeds and MIs (presumably demand). This could have hidden a reduction in thrombotic MIs.

Bottom Line

Hold ASA prior to surgery and for ~7 days post surgery in most patients. This recommendation does not apply to patients at very high risk of thrombotic events (i.e. recent stenting). This recommendation is based on the lack of apparent benefit with ASA in the perioperative period and increased risk of bleeding and accepts that patients may be more likely to experience thrombotic myocardial infarctions without ASA.