How do Patient Risk Factors and Antiplatelet Medications Influence Myocardial Ischemia and Infarction in Patients Undergoing Open Arterial Operations: What Can Be Done to Decrease These Adverse Events?

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PAD has an Aggressive Platelet Phenotype

Data from NYU: platelet activation in the perioperative period

Background
- Platelets are a major contributor to atherothrombosis and likely contribute to an increased risk of perioperative cardiovascular events
- Myocardial ischemia (symptomatic or asymptomatic) in the perioperative period is an independent predictor of short- and long-term mortality following vascular surgery
- Can we prevent these events in our patients using perioperative medical management?

Background
- Platelet activity plays a major role in the pathogenesis of myocardial ischemia and subsequent troponin release
- Antiplatelet agents are routinely used in the non-operative setting to decrease the risk of thrombotic complications
- However, there is no clear consensus regarding the optimal use of antiplatelet therapy in surgical patients in part due to the perceived increased risk of bleeding
- Our goal was to determine both the incidence and the factors associated with cardiovascular and bleeding complications following open vascular surgery
Methods

- We retrospectively analyzed data from 220 consecutive patients from 9/2009-9/2010 that underwent open vascular surgery and had troponin levels checked in the perioperative period.
- Included operations consisted of carotid endarterectomy, above/below knee amputation, open aneurysm repair, extremity bypass, and thromboembolectomy.
- Perioperative antiplatelet use was recorded for each patient and defined as use within 72 hours prior to surgery.

Primary End Points:
- Perioperative myocardial infarction (ESC/ACC definition)
- Perioperative myocardial ischemia (cTnT ≥ 0.10 ng/ml)*
- Used by majority of papers; The cutoff level of 0.10 ng/ml is associated with increased 30 day mortality compared to lower cutoff levels (11.8% vs. 3.9%, P < 0.001)

Secondary End Points:
- Perioperative bleeding rates (ISTH definition, 2010)
- Univariate and multivariate Cox regression models were used to compare groups for each of the primary endpoints.

Results

- 220 patients were evaluated for this study
- Mean age was 74.3 ± 10.8 years
- 73 (33.2%) women and 147 (66.8%) men
- 13 (5.9%) patients were diagnosed with myocardial infarction
- 54 (24.5%) patients developed myocardial ischemia
- Significant demographic predictors of myocardial ischemia were diabetes, chronic kidney disease, and congestive heart failure.

Among specific high-risk groups, the prevalence of myocardial ischemia was:
- 36.5% in diabetics (vs. 15.3% in non-diabetics, p < 0.001)
- 25.2% in patients with hypertension (vs. 12.0% in patients without hypertension, p = 0.14)
- 34.6% in patients with a history of coronary artery disease (vs. 15.0% in patients without known coronary artery disease, p = 0.001)
- 58.3% in patients with congestive heart failure (vs. 17.3% in patients without congestive heart failure, p < 0.001).
- Perioperative use of aspirin or clopidogrel was associated with a lower risk of myocardial ischemia
- Odds ratio 0.41 (95% CI 0.18-0.94)
- The combined use of aspirin and clopidogrel perioperatively was infrequent (10%) and not significantly associated with a reduced risk of myocardial ischemia.
Division of Vascular and Endovascular Surgery

What else can we do to modify this risk?

Beta-blocker: Recommendations

- ACC/AHA and ESC: Pts already on chronic B blocker tx should be maintained on meds during the periop period
- ESC: B blockers should be started on all pts with known ischemic HD or evidence of MI on preop testing
- ACC/AHA considers this recommendation to be weak
- ESC strongly recommends B blockers for patients undergoing high risk NCVS
- ACA/AHA does not support starting this group of pts on B blockers
- Both groups agree that if they are going to be used, they should be started at least 7 days prior to surgery
- Target heart rate 60-80 as per AHA and 60 as per ESC
- Choice of B blocker meds is unclear, but longer acting agents are likely safer than shorter acting drugs

Beta blockers - Conclusions

- Overall, B - blockers appear to have more benefit than harm in the highest risk patients and in the highest risk surgeries.
- Longer acting B-blockers that achieve a resting heart rate of 70 or less may decrease the incidence of all cause and cardiac related mortality in these patients undergoing non-cardiac vascular surgery

Statins – existing recommendations

- ACA/AHA recommends continuing statins during the perioperative period in pts already on statins, AND starting statin therapy on all pts undergoing NCVS
- ESC recommends starting statins on high risk surgery pts at least 1 week, but optimally 30 days before NCVS
- Discontinuation of statins may cause a “rebound” type effect that may increase cardiac risk

Anti-platelet medications

- No randomized trials have examined the specific issue of antiplatelet use in the perioperative period for NCVS
- However, antiplatelet therapy has been shown to reduce the risk of nonfatal MI, ischemic stroke and vascular death.
Anti-platelet medications

- Antithrombotic Trialists’ Collaboration – meta analysis
  - 33% lower risk of nonfatal MI, 23% lower risk of stroke, 16.6% lower risk of vascular death
- CAPRIE trial:
  - Clopidogrel treated patients had an 8.7% reduction in combined endpoints of stroke, MI and death as compared with the aspirin group.
  - Subgroup analysis revealed a 24% risk reduction of cardiac events was noted in the clopidogrel group

CAPRIE trial:

- ACC/AHA does not make specific recommendations unless it relates to coronary stents
- With peripheral angioplasty and stenting procedures, patients are generally treated with at least four weeks of aspirin and/or clopidogrel therapy
- Clopidogrel has not been shown to increase bleeding in VS patients
- Recommendations: Antiplatelet agents should be used for patients for the prevention of cardiovascular events and should be continued during the perioperative period unless some specific contraindication exists.

EUCLID Study Design

Inclusion Criteria:

- Symptomatic PAD AND
- One of the following:
  - A. ABI ≤0.80 at Visit 1
  - ≤0.85 at Visit 2
  - OR
  - B. Prior lower extremity revascularization > 30 days

Key Exclusion Criteria:

- Poor metabolizer for CYP2C19
- Patients requiring dual anti-platelet therapy

Patients with Symptomatic PAD

- Ticagrelor 90 mg bid
- Clopidogrel 75 mg od
- N ~ 13,500

Follow-Up Visits 2, 6, 12 Months, Every 6 months after 1st year
- Telephone visits @ a 3 month interval between regular visits

Primary Endpoint: cardiovascular death, myocardial infarction, or ischemic stroke

Duration: approximately 18 month recruitment and 18 month follow up

Conclusions –

- Myocardial ischemia and infarction are frequent events following open peripheral vascular surgery
- A history of diabetes, chronic kidney disease, or congestive heart failure is associated with an increased risk of myocardial ischemia
- Perioperative use of aspirin or clopidogrel appears to be associated with a lower risk of myocardial ischemia
- The use of one antiplatelet agent was not associated with an increased rate of bleeding complications
- Appropriate use of statins and β-blockers should be strongly considered in vascular surgery patients as well.

References / Acknowledgements