

Aspirin in Patients with Previous Percutaneous Coronary Intervention (PCI) Undergoing Noncardiac Surgery

BACKGROUND: Patients with a history of PCI have an increased risk for major perioperative cardiovascular complications, such as myocardial infarction (MI), while undergoing noncardiac surgery. Uncertainty remains about the effects of aspirin in patients with prior PCI having noncardiac surgery.

OBJECTIVE: To determine whether perioperative low-dose aspirin, compared with placebo, affected 30-day cardiovascular events in patients with previous PCI.

METHODS:

- Study design- Nonprespecified (unplanned) subgroup analysis, based on...
 - POISE-2 (PeriOperative ISchemic Evaluation-2): international, randomized controlled, factorial trial.
- Study duration- July 2010 to December 2013
- Inclusion criteria-
 - Adults aged 45 years or older; Had/were at risk for atherosclerotic disease; Having noncardiac surgery with an expected LOS \geq 1 night.
- Exclusion criteria-
 - Placement of a bare-metal stent within 6 weeks; Placement of a drug-eluting stent within 1 year; Receipt of nonstudy aspirin within 72 hours before surgery.
- Enrollment-
 - POISE-2: 135 centers in 23 countries from July 2010 to December 2013; n=10,010.
 - PCI subgroup: 82 centers in 21 countries; n=470.
 - Initiation stratum if they were *not* receiving long-term aspirin.
 - Continuation stratum if they were receiving long-term aspirin (daily aspirin for at least 1 month within the 6 weeks before surgery).
- Study regimen initiated within 4 hours of surgery and continued at a dosage of 100 mg/day for...
 - 30 days in the initiation stratum or for 7 days in the continuation stratum.
- Primary outcome
 - 30-day primary outcome was a composite of death and nonfatal myocardial infarction.
 - Patients had a troponin measurement (or creatine kinase-MB if troponin was not available) 6 to 12 hours after surgery and on the 1st, 2nd, and 3rd days after surgery.
 - Electrocardiography was done when an elevated troponin or creatine kinase-MB level was detected.
- Secondary outcomes
 - Myocardial infarction. All-cause mortality. Vascular mortality. Stroke. Congestive heart failure. Composite of major and life-threatening bleeding. Major bleeding. Life-threatening bleeding. Clinically important hypotension.
- Power not mentioned in this study, but for POISE-2: 10,000 patients would give the study a power of 84% to detect a hazard ratio of 0.75 in the aspirin group, at a two-sided alpha level of 0.05, on the assumption that the rate of the primary outcome in the placebo group would be 6.1%.
- Research personnel followed patients until 30 days after randomization, collected data, and submitted case report forms and supporting documentation directly to the data management system.
- Patients lost to follow-up before day 30 after randomization with no event reported were censored on the last day their status was known, using intention-to-treat (ITT) analysis.
- Statistical analyses- Cox proportional hazards with 2-sided 95% confidence intervals; Kaplan-Meier estimates.

RESULTS:

Perioperative aspirin may be more likely to benefit rather than harm patients with prior PCI. Low-dose aspirin reduces the primary composite outcome of death and nonfatal myocardial infarction. However, analyses of the component outcomes were significant only for a reduction in myocardial infarction with aspirin versus placebo.

When harms were considered, aspirin increased the risk for the composite of major and life-threatening bleeding events in the overall trial population. However, analyses of the component outcomes were significant only for an increased risk in major bleeding with aspirin versus placebo.

In patients with prior PCI, aspirin...

- Reduced the risk of the primary outcome.
 - 14 aspirin patients [6.0%] vs. 27 placebo patients [11.5%].
 - ARR 5.5% [95% CI, 0.4-10.5%]; HR 0.50 [CI, 0.26-0.95]; P for interaction = 0.036.
- Reduced the risk for myocardial infarction.
 - 12 aspirin patients [5.1%] vs. 26 placebo patients [11.0%].
 - ARR 5.9% [CI, 1-10.8%]; HR 0.44 [CI, 0.22-0.87]; P for interaction = 0.021.
- The effect on the composite of major and life-threatening bleeding was uncertain.
 - ARI 1.3% [CI -2.6-5.2%]. P for interaction = 0.86.

In the overall population, aspirin...

- Increased the risk for major bleeding.
 - 230 aspirin patients [4.6%] vs. 189 placebo patients [3.8%].
 - ARI 0.8% [CI 0.1-1.6%]; HR 1.22 [CI 1.01-1.48]; P for interaction = 0.50.
- For every 1000 patients with prior PCI who have noncardiac surgery, administration of perioperative aspirin would prevent 59 myocardial infarctions (CI 10-108 myocardial infarctions) and cause 8 major bleeding events (CI 1-16 events).

STRENGTHS:

- The factorial design has greater statistical power than a traditional multiple arm trial.
- Based on a very large, international randomized controlled trial.
- Patients were closely followed, monitored post-operatively; 30-day follow-up was incomplete for 1 patient.
- Study drug adherence rates were very high.

LIMITATIONS:

- Nonprespecified subgroup analysis was done with a relatively small sample size.
- The total number of MIs in the PCI subgroup was <50, which may lead to an overestimate of the effect size.
- More than 85% of patients with prior PCI were receiving long-term aspirin. Aspirin daily doses prior to the study were not included in the article.
- This study may be limiting their enrollment and data collection by requiring an expected LOS ≥ 1 night.

CONCLUSIONS:

- Results support the current practice of continuing aspirin therapy in patients with a recent stent who are having noncardiac surgery because of concern over their high risk for myocardial infarction.
- The risk-benefit tradeoff will likely need to be individualized based on the patient's risk for bleeding and myocardial infarction associated with the given type of noncardiac surgery.
- Clinicians should not generalize the results of the study to alternative antiplatelet agents, such as clopidogrel, prasugrel, or ticagrelor.
- Further PCI-specific studies are needed with a larger sample size to determine the true effect size of aspirin.

REFERENCE: Graham MM, Sessler DI, Parlow JL, Biccard BM, Guyatt G, Leslie K et al. Aspirin in Patients With Previous Percutaneous Coronary Intervention Undergoing Noncardiac Surgery. *Ann Intern Med.* 2018 Feb 20;168(4):237-244.

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