非心臓手術周術期のアスピリン使用は重大な出血を増加させる

POISE-2：アスピリンを再開する必要のある患者の術後リスク期間が明らかにされる

POISE-2: Data clarify post-operative risk period for patients who should restart aspirin

非心臓手術後の循環器系の問題を予防するためにアスピリンを投与された患者は、アスピリンを投与されなかった患者と比較し重篤な出血リスクが高い。アスピリンは術後心筋梗塞（MI）発症および死亡を軽減しなかったとの研究結果が第63回American College of Cardiology学会で発表され、*New England Journal of Medicine*オンライン版に掲載された。POISE-2は10,011人の患者を組み入れアスピリン内服の有無によりグループ分けした：術前6週間のうち4週間用量にかかわらずアスピリンを内服していた群（継続層）および内服しなかった群（開始層）。継続層においてはアスピリンの内服を手術の72時間以上前に中止した。全患者がプラセボまたはアスピリン200mgを術直前まで内服した。開始層はアスピリン100mgまたはプラセボを毎日30日間継続した。継続層はアスピリン100mgまたはプラセボを7日間投与され、その後に元のアスピリン療法に戻した。一次エンドポイントである30日間の死亡および非致死性MIは両群間で差がなかった（アスピリン群7%対プラセボ群7.1%）。重大な出血はアスピリン治療群で有意に高かった（4.6%対3.7%）。一次および二次転帰は2つのアスピリン層で同等であった。

Full Text

Patients given aspirin to prevent cardiac problems after non-cardiac-related surgery had a higher risk of serious bleeding than the patients who did not receive aspirin. At the same time, aspirin did not reduce incidence of post-operative myocardial infarction (MI) and death, according to data from POISE-2 presented at the American College of Cardiology's 63rd Annual Scientific Session and published online in the *New England Journal of Medicine*. POISE-2 is the largest clinical trial focused on major cardiovascular complications in non-cardiac surgery.

Although many guidelines address prophylactic aspirin in a surgical setting, the focus is largely on cardiac surgery. Little guidance is available for patients undergoing non-cardiac surgery. This phase III trial followed earlier evidence suggesting that small doses of aspirin and clonidine can ward off heart attacks and heart-related death for such patients. Data for clonidine are to be presented separately at ACC.14.

POISE-2 enrolled 10,011 patients in 23 countries and grouped them by aspirin use: those who had been taking any dose daily for four of the six weeks before surgery, which became the continuation stratum, and those who had not, the initiation stratum. For the continuation stratum, aspirin use was stopped at least 72 hours before surgery. All patients received placebo or 200 mg aspirin just before surgery. The initiation stratum continued 100 mg aspirin or placebo daily for 30 days. The continuation stratum received 100 mg aspirin or placebo for seven days and then resumed their previous aspirin regimen. The primary endpoint of death and non-fatal MI at 30 days was no different between the two groups (7 percent in the aspirin group and 7.1 percent in the placebo group). However, major bleeding was significantly higher in aspirin-treated patients than in the placebo group (4.6 percent vs. 3.7 percent). The primary and secondary outcomes were similar in the two aspirin strata.

"POISE-2 demonstrated that adding aspirin on top of prophylactic anticoagulants in patients who are having non-cardiac surgery is not beneficial," said P.J. Devereaux, M.D., Ph.D., associate professor of clinical epidemiology and biostatistics at McMaster University, and lead investigator for the study. "An important caveat is that 65 percent of our patients were on prophylactic anticoagulants."

There is strong evidence that aspirin prevents perioperative blood clots in veins if an anticoagulant isn't given, he noted. No subgroup effects were seen for vascular versus non-vascular surgery or baseline risk according to the Revised Cardiac Risk Index.

With major bleeding known to increase the likelihood of post-surgical MI and a post-hoc POISE-2 regression analysis demonstrating this relationship, researchers considered why their study found a higher risk for bleeding but not for MI. "One possibility is that aspirin did prevent some MIs, but we were causing enough bleeding to nullify that benefit," Devereaux said. The study used clinical measurements for maximum reliability in identifying MIs, because symptoms are masked by pain-killing drugs in more than 50 percent of patients who have heart attacks after surgery.

According to data analysis, the absolute risk increase for life-threatening and major bleeding with aspirin treatment drops from about 1.2 percent on the day of surgery to 0.9 percent by day four and to 0.3 by day eight. At about the eighth day, the risk returns to normal. This information will help doctors weigh benefits versus potential risks when aspirin might be indicated post-surgically, Devereaux said.

"We're confirming a finding that bleeding itself can cause MIs," he said. "We need to find a better way to prevent bleeding so we can get back to how to prevent some of these thrombotic events." Patients will be followed for a year, and one-year data will be analyzed.

Although POISE-2 is a large trial by perioperative standards, the lower (0.86) and upper (1.15) boundary of the hazard ratio for the primary outcome identifies that the possibility of appreciable benefit or harm has not been excluded, Devereaux said.

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