ダビガトランは非心臓手術後の心筋障害を軽減する (Abstract 18-LB-18909-ACC)

MANAGE：非心臓手術後にダビガトランを投与された患者において死亡率および心血管イベント発現率は低下する

MANAGE: Reduced mortality and cardiovascular events in patients receiving dabigatran after noncardiac surgery

死亡、心筋梗塞（MI）、脳卒中およびその他の心臓または血管合併症の高リスク患者において、抗凝固薬ダビガトランによる治療は非心臓大手術後に発現する心損傷によるこれらのリスクを有意に軽減させた、とAmerican College of Cardiology's 67th Annual Scientific Session で発表された。平均追跡期間16か月後、1つ以上の主要評価項目を発現した患者は、ダビガトラン投与患者の11.1% に対し、プラセボ投与患者では15.2% であった。この結果は、ダビガトラン投与患者においてリスクが28% 低下したと解釈される。

Full Text

Treatment with the anticoagulant dabigatran significantly reduced the risk of death, myocardial infarction (MI), stroke and other heart or blood-vessel complications among patients who were at elevated risk for these events because of heart damage that occurred after major noncardiac surgery, according to research presented at the American College of Cardiology's 67th Annual Scientific Session.

In the first randomized controlled trial to evaluate a treatment for a condition dubbed myocardial injury after noncardiac surgery (MINS), researchers found that patients treated with dabigatran twice daily were 28 percent less likely to die, have a myocardial infarction or stroke, develop blood clots or need an amputation due to cardiovascular disease, compared with patients who received a placebo.

"We have shown for the first time that dabigatran reduces the risk of major cardiovascular complications and offers an option for improving outcomes in a large at-risk population who have MINS," said P.J. Devereaux, MD, PhD, director of cardiology at McMaster University in Hamilton, Canada, and lead author of the study.

Approximately 8 million people every year develop MINS after undergoing surgery such as a hip or knee replacement, bowel resection or abdominal aortic aneurysm repair. This study builds on research that Devereaux and his colleagues presented at the American College of Cardiology's 66th Annual Scientific Session in 2017 showing that MINS may account for about 1 in 4 deaths during the first 30 days after surgery. That research also showed a blood test for high-sensitivity troponin T, which is released into the bloodstream when injury to the heart occurs, can identify patients with MINS whose lives could potentially be saved with timely treatment.

MANAGE was a large international, double-blind study, in which 1,754 patients with MINS were randomized to receive dabigatran 110 mg twice daily or matching placebo. The patients received dabigatran for a maximum of two years and a minimum of four months. The primary efficacy endpoint was a major vascular complication – a composite of vascular mortality and MI, nonhemorrhagic stroke, peripheral arterial thrombosis, amputation and symptomatic venous thromboembolism. The primary safety endpoint was a composite of life-threatening bleeding, major bleeding and critical organ bleeding.

Most cases of MINS currently go undetected, Devereaux said, because at present it is not standard practice in most centers to monitor blood levels of troponin in patients who had major noncardiac surgery. Devereaux said he is hopeful this will change now that this study has shown treatment with dabigatran can improve outcomes for patients with MINS. "Our findings reaffirm that patients who develop MINS are at high risk for bad outcomes," he said. "We owe it to our patients to identify this risk and do what we can to reduce it."

The study enrolled 1,754 patients in 19 countries, 51percent of whom were men, with an average age of 70 years. The primary efficacy outcome was the combined rate of death from a cardiovascular cause, myocardial infarction (MI), stroke due to inadequate blood supply, blood clots or amputation due to cardiovascular disease. The primary safety outcome was the combined rate of life-threatening, major and critical organ bleeding.

During the study, patients, health care providers and research staff were blinded to which group received dabigatran and which received a placebo. After an average follow-up of 16 months, 11.1 percent of patients treated with dabigatran experienced one or more of the primary efficacy outcome events, compared with 15.2 percent of patients who received a placebo. This translates to a 28 percent reduction in risk for patients receiving dabigatran.

When researchers analyzed occurrence rates for the events comprising the primary efficacy outcome, they found trends of benefit for each component. For example, patients treated with dabigatran were 20 percent less likely to die of a cardiovascular cause, 20 percent less likely to have an MI, 30 percent less likely to have an amputation and 53percent less likely to have a venous blood clot than patients who received a placebo.

The result for nonhemorrhagic stroke also demonstrated a benefit with an 80 percent reduction in risk, a difference that was statistically significant compared with patients who were randomized to placebo. There were no statistically significant differences between the two groups in life-threatening, major or critical organ bleeding.

Compared with the placebo group, however, more patients in the dabigatran group experienced bleeding in the lower gastrointestinal tract and minor bleeding.

"It's encouraging that we did not see an increase in major or life-threatening bleeding in patients on dabigatran," Devereaux said.

Researchers noted that while nearly all patients (98.9 percent) completed follow-up, 45.3 percent of those on dabigatran had discontinued the study drug. The most common reason for drug discontinuation was patient request; however, 14percent of these patients had a major complication (e.g., MI, stroke, bleeding).

According to Devereaux, analyses that counted patients up to seven days after they discontinued the study drug showed even larger treatment effects, with 46 percent reductions in major cardiovascular complications with dabigatran and no excess of life-threatening, major or critical organ bleeding.

Devereaux said that future research is needed to evaluate other treatment options for this high-risk group of patients.

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