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## Nitrous oxide shows promise in patients at risk for cardiovascular disease

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Nitrous oxide, an effective and inexpensive anesthetic, is safe for surgical patients who have or are at risk for cardiovascular disease, according to results of a large randomized controlled trial being presented at the ANESTHESIOLOGY® 2015 annual meeting.

The ENIGMA-II Trial (Evaluation of Nitrous Oxide in the Gas Mixture for Anesthesia) compared outcomes of nearly 6,000 patients who had non-cardiac surgery, half of whom received general anesthesia with nitrous oxide, while the other half had general anesthesia with nitrogen. One year post surgery, there was no difference in death rate, heart attack, stroke or disability between the groups, according to the study, also published today in the Online First edition of *Anesthesiology*, the official medical journal of the American Society of Anesthesiologists (ASA).

"This helps alleviate concerns raised in recent years about the effect of nitrous oxide on the heart and vascular system," said Kate Leslie, M.D., lead author of the study and professor in the Department of Anaesthesia and Pain Management at Royal Melbourne Hospital, Australia. "It's welcome news because nitrous oxide is widely used around the world as part of the mixture of agents for general anesthesia. This is because nitrous oxide is inexpensive, simple to administer and helps with pain as well as anesthesia."

Nitrous oxide is typically used in combination with another powerful anesthetic, such as sevoflurane or propofol, to provide general anesthesia.

The ENIGMA-II international, multi-center study included patients, age 45 years or older, who were at risk for cardiovascular complications during surgery. Fifty percent of patients received anesthesia that contained 70 percent nitrous oxide, 30 percent oxygen, while the other 50 percent received anesthesia that contained 70 percent nitrogen, 30 percent oxygen. The level of anesthesia provided was the same in both groups through the addition of other anesthetic medications, such as sevoflurane or propofol.

One-year outcomes were similar between the two groups: death (8 percent nitrous oxide, 7 percent nitrogen), heart attack (8.9 percent nitrous oxide, 9.3 percent nitrogen), stroke (2.1 percent nitrous oxide, 2 percent nitrogen) and disability or death (11.3 percent nitrous oxide, 10.7 percent nitrogen).

ENIGMA I, a previous study about half the size of ENIGMA II, hinted that nitrous oxide may increase the incidence of heart attack in patients, Dr. Leslie said. But that study did not include high-risk patients. Wanting to explore this finding further, researchers undertook a much larger study and focused on patients who had or were at risk for cardiovascular disease. This time, they found the use of nitrous oxide did not increase the risk of heart attack or other negative outcomes.

Authors of an accompanying editorial published in *Anesthesiology* note: "The assessment of long-term follow-up of the ENIGMA-II trial was critical in ensuring that the question of nitrous oxide's safety was fully addressed. Based upon the results, we can conclude that nitrous oxide is safe for the general population and in patients with cardiovascular disease undergoing non-cardiac surgery when the concentration of oxygen is held constant."

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Source:

American Society of Anesthesiologists (ASA)

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