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IV beta blockers before angioplasty are safe, but offer no clinical benefit

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Giving intravenous beta blockers before performing a coronary angioplasty in patients who had experienced the deadliest form of heart attack—ST-segment elevation myocardial infarction (STEMI)—was safe but did not reduce heart attack severity or improve blood flow from the heart's main pumping chamber, according to research presented at the American College of Cardiology's 65th Annual Scientific Session.

"In patients with STEMI, beta blockers have been shown to improve survival, reduce the risk of another heart attack, reduce life-threatening arrhythmias and prevent enlargement of the heart," said Vincent Roolvink, M.D., of Isala Klinieken in Zwolle, Netherlands, and lead author of the study. "This was the first large, double-blind, randomized, placebo-controlled trial to assess whether giving intravenous beta blockers before these patients undergo angioplasty would further improve their outcomes. Unfortunately, we showed that it did not."

STEMI is a severe form of heart attack caused by prolonged blockage of blood supply in the heart. It requires immediate angioplasty, a non-surgical procedure in which a balloon is fed into the blood vessels through a catheter and inflated to open narrowed or blocked arteries, allowing blood to flow. A stent is often placed at the blockage site to keep the artery open. In the United States, about 250,000 people experience a STEMI every year.

Results from two previous trials had suggested that giving intravenous beta blockers to STEMI patients before they underwent angioplasty

could reduce heart attack severity or improve blood flow from the left ventricle, the heart's main pumping chamber, but these trials had shortcomings, Roolvink said. One had a small enrollment and the other, while larger, was not blinded or placebo-controlled and enrolled only patients whose STEMIs involved the front wall of the left ventricle.

In the EARLY-BAMI (Effect of Early Beta-blocker Administration before primary PCI in patients with ST-elevation Myocardial Infarction) trial, which was conducted in the Netherlands and Spain, 683 patients (average age 62, 75 percent male) with acute STEMI symptoms of less than 12 hours duration were randomly assigned to receive the beta blocker metoprolol or a placebo before undergoing angioplasty. The primary endpoint was the severity of the heart attack as measured by magnetic resonance imaging (MRI) at 30 days. Secondary endpoints were levels of cardiac enzymes and number of occurrences of ventricular arrhythmia. Safety endpoints were symptoms of an abnormally slow heart rate, symptoms of abnormally low blood pressure and cardiogenic shock (sudden inability of the heart to pump enough blood to meet the body's needs).

At 30 days of follow up, the primary endpoint of average heart attack severity measured by MRI was 15.3 percent of left ventricular volume on average in the beta blockers group, compared with 14.9 percent in the placebo group, a difference that was not statistically significant, Roolvink said. Nor were there significant differences between the two groups on blood flow from the left ventricle or levels of cardiac enzymes (secondary endpoints). Ventricular arrhythmias occurred in 3.6 percent of patients who received beta blockers and in 6.9 percent of those who received a placebo, a difference that met the threshold for statistical significance but did not result in a clinically significant difference, Roolvink said. Sixteen patients in the beta blockers group experienced symptoms of an abnormally slow heart rate, symptoms of abnormally low blood pressure, or cardiogenic shock, compared with 21 patients in

the placebo group, a difference that again was not statistically significant.

A limitation of the study is that overall heart attack severity among enrolled patients was lower than expected, which could explain why beta blocker treatment appeared to offer no benefit, Roolvink said. Also, although MRI analyses for the primary endpoint were blinded for both heart rate and study medication, it was not possible to blind physicians and nurses to patients' heart rate and blood pressure.

Going forward, researchers said additional large randomized trials are needed to clarify whether intravenous beta blocker treatment before angioplasty offers any benefit for STEMI patients.

The Early-BAMI trial was funded by the Dutch Heart Foundation and by an unrestricted grant from Medtronic, Inc.

The study was published in the *Journal of the American College of Cardiology* simultaneously with its presentation at the scientific session.

More information: Vincent Roolvink et al. Early Administration of intravenous Beta blockers in patients with ST-elevation myocardial infarction before primary PCI, *Journal of the American College of Cardiology* (2016). DOI: 10.1016/j.jacc.2016.03.522

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