

Study: Nitric oxide decreases renal failure after cardiac surgery



Results of a phase IIb prospective randomised controlled trial [Prevention of Renal Failure by Nitric Oxide in Prolonged Cardiopulmonary Bypass](#) showed that nitric oxide (NO) administered during surgery and for 24 hours afterwards was safe, and postoperatively reduced the incidence of acute kidney injury (AKI), transition to stage 3 chronic kidney disease, and major adverse kidney events at 30 days, 90 days, and 1 year.

The study, by Chong Lei, MD, PhD Department of Anesthesiology and Perioperative Medicine, Xijing Hospital, the Fourth Military Medical University, Xi'an, Shaanxi, China and colleagues from China, Italy and the United States, is in press in the *American Journal of Respiratory and Critical Care Medicine*.

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The RCT was performed in the Departments of Anesthesiology and Cardiovascular Surgery of Xijing Hospital, Xian, China, and included 244 adults (mean age 48) undergoing elective, multiple valve replacement surgery (requiring 90 minutes or more cardiopulmonary bypass), mostly due to rheumatic fever, which is responsible for more than half a million deaths in Asia each year. Patients received either NO (treatment - 80 parts-per-million) or nitrogen N₂ (control).

The hypothesis was that administration of 80ppm NO during and for 24h after surgery would convert plasma Oxy-Hb to Met-Hb and prevent intrarenal oxidative reactions and NO scavenging by plasma Oxy-Hb, and thus preserve kidney function.

Results

Primary outcome - Incidence of AKI within 7 days

This was defined as an increase of serum creatinine by 50% within 7 days after surgery, or an increase of serum creatinine by 0.3 mg/dl within 2 days after surgery from preoperative baseline levels of serum creatinine.

NO: 50%
N₂: 64%

Secondary outcomes - Development of stage 3 CKD (eGFR<60 mL/min/1.73m²)²⁶⁻²⁷, loss of 25% of eGFR compared to baseline, and major adverse kidney events (defined as a composite outcome of loss of 25% of eGFR from baseline, end stage renal disease requiring a continuous renal replacement therapy and mortality)²⁵ at 30 days, 90 days, and 1 year following ICU admission.

Stage 3 chronic kidney disease at 90 days

NO: 21%
N₂: 33%

Stage 3 chronic kidney disease at 1 year

NO: 18%
N₂: 31%

Major adverse kidney events were fewer in the NO group at 30d, 90d and 1 year.

There was no difference between the groups in other intra-hospital outcomes or long-term outcome variables, including hospital readmission rate and mortality up to 1 year. Although the study was not powered to test whether NO exposure could reduce mortality, at 1 year, the rate of mortality in the NO treatment group was 3% (3/117) compared to 6% (8/127) in the control group.

The researchers conclude: "Nitric oxide gas is the first pharmacological intervention to show a reduction in the incidence of acute kidney injury and an improvement of long-term kidney function in cardiac-surgical patients after prolonged cardiopulmonary bypass". They recommend that the findings should be assessed in non-Chinese patients without rheumatic fever as the study is also limited by the young mean age of patients

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and the absence of pre-operative severe chronic kidney disease and other cardio-vascular comorbidities in the patient cohort.

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