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Primary Registry and Trial Identifying Number	**ClinicalTrials: NCT02836899**
Date of Registration	July 19 2016
Secondary Identifying Numbers	IRB ID#: 2016 P001629
Source(s) of Monetary Support	National Heart, Lung, and Blood Institute (NHLBI) (Award Reference Number K23 HL128882-01A1)
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Public Title	Effect of Nitric Oxide in Cardiac Surgery Patients With Endothelial Dysfunction
Scientific Title	Prevention of Acute Kidney Injury by Nitric Oxide in Prolonged Cardiopulmonary Bypass: A Double-Blind Controlled Randomized Trial in Cardiac Surgical Subjects with Endothelial Dysfunction
Countries of Recruitment	United States
Health Condition(s) or Problem(s) Studied	Cardiopulmonary bypass associated-Acute Kidney Injury

Intervention(s)

Trial arm 1: Nitric oxide (NO) Group (intervention arm).

NO gas 80 parts-per-million is administered via the oxygenator during CPB, then by inhalation when mechanical ventilation is resumed. Once the subject is extubated, NO gas is delivered by high flow nasal cannula.The treatment begins at the onset of the cardiopulmonary bypass and lasts 24h.

Trial arm 2: Nitrogen (N_2) Group (Control arm).

N_2 gas is administered via the oxygenator during CPB, then by inhalation when mechanical ventilation is resumed. Once the subject is extubated, N_2 gas is delivered by high flow nasal cannula. The N_2 administration begins at the onset of the cardiopulmonary bypass and lasts 24h.

Trial Type

Interventional

Allocation: Randomized

Intervention model: Parallel assignment

Blinding: Clinicians blinded to intervention, participants blinded to intervention, study

	investigators blinded to intervention, primary outcome assessor blinded to intervention. For safety and gas monitoring, only the clinician administering the test gas remains unblind to the treatment. This clinician is not part of the anesthesia, ICU, or surgical physician team delivering care. Assignment: Parallel Primary purpose: Prevention
Date of First Enrollment	June, 2017
Target Sample Size	250 patients
Recruitment Status	Recruiting
Key Enrollment Criteria	Inclusion criteria: Age ≥ 18 years of age; Elective cardiac or aortic surgery with expected CPB > 90 minutes; Clinical evidence of endothelial dysfunction assessed by a specifically designed questionnaire; Stable preoperative renal function without evidence of a plasma creatinine increase of ≥ 0.3 mg/dL within 3 months of study entry and without receiving RRT. Key exclusion criteria:

	estimated glomerular filtration rate (eGFR) <30 ml/min/1.73m^2, mPAP ≥40 mmHg and intravenous (I.V.) contrast infusion within 48 hours before surgery.
Primary Outcome(s)	Outcome name: Incidence of Acute Kidney Injury (AKI) Method of measurement: KDIGO criteria Time points of interest: 7 days after surgery
Key Secondary Outcomes	Outcome name: AKI severity Method of measurement: KDIGO stages Time points of interest: 7 days after cardiac surgery Outcome name: Renal Replacement Therapy Method of measurement: Medical record review Time points of interest: Up to 1 year. Outcome name: Major Adverse Kidney Events (MAKE) Method of measurement: Medical record

review

Time points of interest: 6 weeks after cardiac surgery.

Outcome name: Organ dysfunction (SOFA score)

Method of measurement: Medical record review

Time points of interest: ICU stay (up to seven days)

Outcome name: Prolonged cardiovascular support

Method of measurement: Medical record review

Time points of interest: 48 hours after cardiac surgery

Outcome name: duration of mechanical ventilation

Method of measurement: Medical record review

Time points of interest: up to 6 weeks

Outcome name: Intensive care unit length of stay (ICU-LOS)

Method of measurement: Medical record review

Time points of interest: up to 6 weeks

Outcome name: Hospital length of stay (LOS)

Method of measurement: Medical record review

Time points of interest: up to 1 year

Data and Safety Monitoring Board:

DSMB Chair:

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Responsibilities include: reviewing and evaluating the trial data to ensure participant safety, trial conduct, progress, and efficacy, and making recommendations regarding the continuation, or termination of the trial.