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#### Original Article

## Regional Cerebral Oxygen Saturation Level Predicts 30-Day Mortality Rate After Left Ventricular Assist Device Surgery

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Objective: Left ventricular assist device (LVAD) surgery is complex, high risk, and expensive. The authors' hypothesis is baseline regional cerebral oxygen saturation (rSO<sub>2</sub>) might be a predictor of postoperative clinical outcomes.

Design: Retrospective review of 210 consecutive continuous flow LVAD patients between 2008 and 2014. The primary measure is 30-day mortality rate and secondary measures include modified major adverse cardiocerebral events (MACE), length of stay (LOS), and intensive care unit (ICU) stay. Multiple logistic regression models were applied to examine if a binary outcome variable, such as 30-day mortality and MACE, is associated with rSO<sub>2</sub> at baseline. Log-linear model was used to examine whether LOS or ICU stay hours is associated with rSO<sub>2</sub> at baseline. Setting: Single institution, academic hospital.

Participants: Patients who received LVAD surgery at Jewish Hospital, Louisville, KY.

Interventions: All patients received LVAD surgery. Cerebral oximetry monitoring was used in both the preoperative and intraoperative periods. *Measurements and Main Results:* The authors found that higher rSO<sub>2</sub> at baseline is associated with lower 30-day mortality with an odds ratio of 0.94 and 95% confidence interval (0.888, 0.995) for every 1% increase of rSO<sub>2</sub>. For secondary outcomes, baseline rSO<sub>2</sub> was not significantly associated with MACE, requirement for postoperative renal failure/dialysis, reoperation for bleeding, and LOS or ICU hours.

Conclusions: Regional cerebral oxygen saturation levels at baseline are significantly associated with 30-day mortality after LVAD surgeries. © 2017 Elsevier Inc. All rights reserved.

Key Words: left ventricular assist device; cerebral oxygen saturation; clinical outcome

S.G. and J.T. contributed equally to this work and are co-first authors.

Previous Presentation: This study was presented at the American Society for Artificial Internal Organs annual conference; June 25, 2015; Chicago, Illinois; and at the Society of Cardiovascular Anesthesiologist annual meeting; April 25, 2017; Orlando, Florida.

Conflict of Interest: Jiapeng Huang is on the Advisory Board for Medtronic, Minneapolis. MN.

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LEFT VENTRICULAR ASSIST DEVICES (LVAD) have become the mainstay treatment for end-stage heart failure as destination therapy, bridge to transplantation, or bridge to recovery. LVAD implantation is a high-risk, costly, and complex operation. Current cost estimates for LVAD implantation are over \$100,000 per quality year gained. Determining whether these sick patients are optimized preoperatively and intraoperatively remains difficult and challenging. Cerebral oxygen saturation measurements utilize 2 to 5 near-

infrared light wavelengths (depending on different manufacturers) for oxyhemoglobin and deoxyhemoglobin to calculate the percentage of oxyhemoglobin in the superficial layers of the frontal cortex by paired optodes on either side of the forehead.<sup>4</sup> The commonly cited 25/75 arterial to venous blood ratio in the brain originates from Mchedlishvili's calculations based on cerebrovascular resistance measured by another investigator, not through direct measurements in vivo.<sup>5</sup> A recent study in anesthetized children demonstrated that cerebral blood is an admixture of 16% arterial and 84% venous blood using cerebral oximetry technology.<sup>6,7</sup> Intraoperative regional cerebral oxygen (rSO<sub>2</sub>) desaturation was found to be significantly associated with an increased risk of cognitive decline and prolonged hospital stay after coronary artery bypass surgery.8 However, several other studies result in different conclusions and most have recognized limitations.8-10

Studies on whether preoperative or intraoperative rSO<sub>2</sub> absolute values are related to postoperative complications and mortalities might provide more guiding information. A prospective study showed that preoperative rSO2 levels are closely related to relevant measures of cardiopulmonary function, postoperative morbidity, and short- and long-term mortality. 11 In a large retrospective, single institution study, Sun et al also found that patients with preoperative rSO<sub>2</sub> (measured after receiving 2 minutes of 100% oxygen with a flow of 3-5 L/min by face mask) below 60% experienced higher operative mortality and emerged as an independent predictor of increased mortality. 12 A recent prospective pilot study found that low preoperative cerebral tissue oxygen saturation is associated with unfavorable outcomes after major elective non-cardiac surgery. 13 rSO<sub>2</sub> could be merely a marker for severity of diseases or reflect preoperative medical optimization. If rSO<sub>2</sub> could be further improved preoperatively or intraoperatively and rSO2 was associated with serious postoperative morbidity or mortality, an intervention that improves rSO<sub>2</sub> might affect surgical outcomes. One extreme example is during cardiac arrest resuscitation, higher cerebral oxygenation during cardiopulmonary resuscitation is associated with return of spontaneous circulation and neurologically favorable survival to hospital discharge. Achieving higher regional cerebral oxygenation during resuscitation may optimize the chances of cardiac arrest favorable outcomes.14

The authors' primary hypothesis was that increased preoperative or intraoperative skin closure rSO<sub>2</sub> in LVAD candidates could be associated with decreased 30-day mortality through either less severe coexisting comorbidities or better optimization of cardiopulmonary functions, and brain and other vital organ perfusion. The secondary hypothesis was that imbalances of oxygen supply and demand could be linked to neurologic, non-neurologic morbidities and associated mortalities. Our secondary measures included modified major adverse cardiocerebral events (MACE, which includes permanent or transient stroke, coma, perioperative myocardial infarction, heart block, death and cardiac arrest according to the Society of Thoracic Surgeons [STS] national criteria), hospital length of stay (LOS), and intensive care unit (ICU) stay.

#### Methods

Data Collection

Institutional review board approval by the Human Subjects Protection Program Office, University of Louisville, Louisville, KY was obtained before conducting the study, and individual consent was waived by the institutional review board because this is a retrospective chart review study. A retrospective cohort analysis of 210 consecutive patients who were implanted with a continuous flow LVAD at Jewish Hospital, Louisville, KY from January 2008 to December 2014 was performed. The authors' current database (2008-2014) was used to reflect contemporary LVAD care. Patient data was collected and organized to follow the template of the STS national database, including demographics, patient history, medical record information, preoperative risk factors, preoperative medications, intraoperative data, postoperative cardiocerebral events, renal failure, 30-day all-cause mortality, and left and right rSO2 at baseline and at skin closure in the operating room. Individual investigators collected these data independently during hospitalization for cardiac surgery.

#### Cerebral Oxygen Saturation

For LVAD surgery, all patients were brought to the operating room and standard American Society of Anesthesiologists monitors placed. The rSO<sub>2</sub> was measured by means of the INVOS 5100C cerebral oximeter (Medtronic, Minneapolis, MN). After cleaning with alcohol, the paired sensors were positioned bilaterally on the patient's forehead. Baseline rSO<sub>2</sub> was obtained and recorded while the patient was breathing room air or at his/her baseline preoperative oxygen requirement level for 5 minutes. Arterial line, central venous pressure monitoring, and pulmonary artery catheters were then inserted and anesthesia was induced. The right and left rSO<sub>2</sub> were continuously monitored, recorded, and managed during the whole surgery.

The attending anesthesiologist adjusted his/her management based on hemodynamics, Bispectral Index (BIS), cerebral oximetry data, and other information. Recommendations for rSO<sub>2</sub> management include head repositioning, control and optimization of carbon dioxide, optimization of mean arterial pressure, and reevaluation and optimization of cardiac performance (or pump flow on cardiopulmonary bypass) and transfusion triggers. Once LVAD support was initiated, surgeon/ anesthesiologist modified their clinical management and LVAD speed according to continuous bi-hemispherical rSO<sub>2</sub> monitoring in addition to the standard monitors including electrocardiogram, SaO<sub>2</sub>, invasive blood pressure, central venous pressure, pulmonary artery pressures, continuous cardiac output, and mixed venous oxygen saturations. After surgical dressings were applied, hemodynamic stability achieved and end- tidal CO<sub>2</sub> normalized, bilateral rSO<sub>2</sub> levels were measured again and recorded. All patients were ventilated with F<sub>1</sub>O<sub>2</sub> of 1.0 at skin closure. The patients were transferred to the cardiovascular ICU and cared for by intensivists after surgery.

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