REGIONAL CEREBRAL OXYGEN DESATURATIONS IN CORONARY ARTERY BYPASS SURGERY: A MINIMALLY INVASIVE APPROACH

By

____________________________
Benjamin Mills

A Thesis Submitted to the Faculty of the
DEPARTMENT OF MEDICAL PHARMACOLOGY
In Partial Fulfillment of the Requirements
For the Degree of
MASTERS OF SCIENCE
In the Graduate College of The
UNIVERSITY OF ARIZONA
2013
STATEMENT BY AUTHOR

This thesis has been submitted in partial fulfillment of requirements for an advanced degree at The University of Arizona and is deposited in the University Library to be made available to borrowers under rules of the Library.

Brief quotations from this thesis are allowable without special permission, provided that accurate acknowledgment of source is made. Requests for permission for extended quotation from or reproduction of this manuscript in whole or in part may be granted by the head of the major department or the Dean of the Graduate College when in his or her judgment the proposed use of the material is in the interests of scholarship. In all other instances, however, permission must be obtained from the author.

SIGNED: Benjamin Mills

APPROVAL BY THESIS DIRECTOR

This thesis has been approved on the date shown below:

_________________________________________  5/7/13
Robert S. Poston, MD                          Date
Professor & Chief of Cardiothoracic Surgery
ACKNOWLEDGEMENTS

First and foremost, I would like to thank my perfusion program director Douglas F. Larson, PhD CCP for the opportunity to learn so much about perfusion science and earn a Master’s of Science degree in medical pharmacology. He was a motivator in my continued growth throughout the program and encouraged me to attend and present at national meetings that lifted me to even higher levels of academic achievement.

I would also like to thank my primary investigator Robert S. Poston, MD for the opportunity to research in his lab and his assistance in my clinical research that will help in furthering my career. I could not have done my thesis without him and deeply appreciate his knowledge and guidance in facilitating this project to its fruition. I know that my future research endeavors will benefit greatly from this interaction and appreciate his mentorship.

Also, my committee members were invaluable John D. Palmer, MD PhD and Todd Vanderah, PhD. I’d like to express my appreciation for their assistance in furthering my education and guidance in my project. Their entertaining lectures and willingness to give of their time did not go unnoticed and I am grateful to them for their commitment to my education.

Lastly, I would like to thank my wife and family for their continued love and support throughout my life and especially over these last few years. You have always been a great example to me of how to work hard and reach for your dreams. I love you all and thank you for your support as you all have helped me to reach this major milestone in my life.
TABLE OF CONTENTS

LIST OF FIGURES ..............................................................................................................5
LIST OF TABLES................................................................................................................6
ABBREVIATIONS ...............................................................................................................7
ABSTRACT ..........................................................................................................................8
INTRODUCTION ................................................................................................................9
METHODS .......................................................................................................................15
RESULTS ..........................................................................................................................22
DISCUSSION ....................................................................................................................26
REFERENCES ....................................................................................................................37
LIST OF FIGURES

Figure 1: Cerebral Oximeter Sensor .................................................................16
Figure 2: Minimally Invasive r-CABG...............................................................17
Figure 3: Conventional CABG .................................................................18
Figure 4: Mean Natural Log of Total AUC in CABG and r-CABG ...............23
Figure 5: Intraoperative Mean Blood Loss in CABG and r-CABG .............28
Figure 6: Cerebral Oximetry Tracing .........................................................33
Figure 7: Mean AUC in Diabetics and Non-Diabetics Vs. Mode of Surgery...35
LIST OF TABLES

Table 1: Patient Demographics ................................................................. 22
Table 2: Patient Baseline & Intraoperative Data ........................................ 24
Table 3: DM Patients vs. Mean AUC .......................................................... 25
### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD</td>
<td>Coronary Artery Disease</td>
</tr>
<tr>
<td>CABG</td>
<td>Coronary Artery Bypass Graft Surgery</td>
</tr>
<tr>
<td>CPB</td>
<td>Cardiopulmonary Bypass</td>
</tr>
<tr>
<td>OR</td>
<td>Operating Room</td>
</tr>
<tr>
<td>r-CABG</td>
<td>Minimally Invasive Robotic Coronary Artery Bypass Graft Surgery</td>
</tr>
<tr>
<td>BIMA</td>
<td>Bi-Lateral Internal Mammary Artery</td>
</tr>
<tr>
<td>rSO₂</td>
<td>Cerebral Regional Oxygen Saturation</td>
</tr>
<tr>
<td>OPCAB</td>
<td>Off Pump Coronary Artery Bypass Surgery</td>
</tr>
<tr>
<td>LIMA</td>
<td>Left Internal Mammary Artery</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>Partial Pressure of Arterial Carbon Dioxide</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean Arterial Pressure</td>
</tr>
<tr>
<td>AUC</td>
<td>Area Under the Curve</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>BSA</td>
<td>Body Surface Area</td>
</tr>
<tr>
<td>CPP</td>
<td>Cerebral Perfusion Pressure</td>
</tr>
<tr>
<td>CBF</td>
<td>Cerebral Blood Flow</td>
</tr>
</tbody>
</table>
ABSTRACT

Cerebral oximetry has been shown to effectively identify declining regional cerebral oxygen saturations (rSO$_2$) in coronary artery bypass graft (CABG) surgery. Prolonged intraoperative cerebral desaturations have been significantly associated with an increased risk of cognitive decline after CABG surgery. We compared conventional CABG to minimally invasive robotic coronary artery bypass surgery (r-CABG) using cerebral oximetry to determine the beneficial effects of the less invasive procedure. A retrospective study of 32 isolated CABG patients were treated for coronary artery disease (CAD) via conventional CABG (n=20) or r-CABG (n=12) with analysis of cerebral oximetry tracings and intraoperative data. Parameters, such as, blood loss, mean arterial pressure (MAP), partial pressure of carbon dioxide (PaCO$_2$), cardiopulmonary bypass (CPB), and diabetes mellitus (DM) were analyzed against the area under the curve (AUC) from the cerebral oximetry tracing, an indicator of rSO$_2$ desaturations. Many of these parameters showed statistical significance (p<0.05) between conventional CABG and r-CABG including a decreased mean AUC in the latter. In conclusion, minimally invasive r-CABG tends to show beneficial effects for patients by reducing the total mean AUC in comparison to conventional CABG, especially in the DM patient.
INTRODUCTION

For nearly 50 years, myocardial revascularization due to coronary artery disease (CAD) has been treated via coronary artery bypass graft (CABG) surgery via full sternotomy (i.e. the division of the sternum with a bone saw). This surgical method for the treatment of CAD has seen great success but only modest innovation over this time frame. In addition, conventional CABG uses cardiopulmonary bypass (CPB) for circulatory support and induces cardiac arrest for a quiescent, bloodless surgical field. Unabated access to the heart during CABG allows the surgeon to visualize the coronary targets, perform microvascular anastomoses and fully revascularize ischemic myocardium. However, this also comes with complications of sternal bleeding and possible use of allogenic blood products. The use of allogenic blood components is associated with increased morbidity, increased operative costs (Murphy et al., 2007), and a mortality risk that increases 0.5% per unit of blood transfused (Ranucci et al., 2008). Mediastinitis is another post-operative complication (incidence of 1-3%) leading to extended length of hospital stay, increased health care costs, and decreased long-term survival rate (Sjögren, Malmsjö, Gustafsson, & Ingemansson, 2006).

Three decades after the initial introduction of less invasive techniques into surgery, it has become clear that smaller incisions reduce recovery times, in part by
maintaining the perioperative function of organs that drive recovery (i.e. brain, kidneys, cardiac function). However, the exact mechanism of this effect is unclear. Certainly, systemic inflammation is increased when large incisions are made in the chest or abdomen in comparison to smaller, port incisions of laparoscopic or thoracoscopic surgery. Systemic inflammation can serve as an adjuvant to aggravate injury to multiple organs during surgery. There may also be a local inflammatory effect on intrathoracic organs that occurs after opening the sternum. It has been suggested that exposure of internal organs to the dry, cold air of the operating room (OR) environment during open surgery plays a role in transient organ dysfunction that occurs postoperatively in most patients (Hamza et al., 2005). For open chest, cardiac surgery, the air and lights of the OR are conducive of local epicardial dessication on the surface of the heart, which can influence cardiac performance. On the other hand, less invasive surgery is performed via port access, which dramatically reduces exposure of the local surgical field to these environmental OR insults. In addition to reducing systemic inflammation, non-sternotomy approaches for CABG could mitigate local inflammation and its resulting cardiac strain.

Minimally invasive robotic coronary artery bypass graft (r-CABG) surgery has been established as a feasible alternative approach to conventional sternotomy CABG
surgery. Less invasive r-CABG can be performed for multi-vessel revascularization with CPB via femoral cannulation to provide increased access to all regions of the heart via small thoracotomy (Kiani et al., 2012). This procedure is sternal sparing and uses robotic instruments to provide thorascopic access to the mediastinum for bilateral internal mammary artery (BIMA) harvest, pericardiotomy, and identification of the coronary targets, all without the typical risk of poor sternal healing associated with traditional median sternotomy (Jones, Desai, & Poston, 2009). The distal anastomoses are created via an incision that is limited to a small, intercostal thoracotomy performed using port-access stabilization or endoscopic instruments alone (Jones, Desai, &Poston, 2009). Potential benefits of r-CABG procedures include improved cosmetics, less disability, quicker recovery, reduced blood loss, and morbidity associated with sternotomy (Poston et al., 2008). For these reasons, minimally invasive CABG is very attractive to patients whom desire to return to their normal day to day activities as soon as possible. However, as tempting as the benefits associated with minimally invasive CABG procedures seem, it remains controversial among practicing cardiac surgeons at this time because of its technical complexity and the lack of evidence regarding short and long term efficacy and safety of the procedure.
Another complication that is well recognized with CABG surgery is the prevalence of neurocognitive decline in the early postoperative period. Cognitive changes involving memory, executive functions, and motor speed do occur during the first few days to weeks after CABG for many patients. The cause is most likely multifactorial and may involve microemboli, cerebral oxygen desaturations (de Tournay-Jetté et al., 2011), cerebral ischemia from hypoperfusion, and systemic inflammatory response involving the use of CPB. These short-term changes appear to be reversible by 3 months after surgery for most patients (Selnes & McKhann, 2005). However, the incidence of adverse cognitive outcomes, the time course and degree of resolution of the cognitive problems, and the mechanisms underlying the cognitive change is still being debated. Previous attempts to identify specific risk factors for cognitive change after CABG have found certain demographic factors such as age to be predictive, but there is less agreement on perioperative or medical risk factors (Selnes et al., 1999). This issue gives just cause for the use of neuromonitoring devices in the CABG operative suite. A cerebral oximeter is a neuromonitoring device that is being used more frequently in cardiac surgery. It is a non-invasive method to monitor frontal lobe perfusion during cardiac surgery and non-cardiac surgery using near-infrared reflectance spectroscopy to measure oxygenated hemoglobin saturation levels. Intraoperative measurements of low
cerebral oxygen saturation (rSO$_2$) using near-infrared spectroscopy have shown significant relationship to perioperative and long term neurologic complications, prolonged stays in the intensive care unit and hospital after CABG surgery (Goldman, Sutter, Ferdinand, & Trace, 2004; Murkin, 2004; Murkin et al., 2007). Slater et al. (Slater et al., 2009), found that prolonged intraoperative cerebral desaturation is significantly associated with an increased risk of cognitive decline after CABG and that active intraoperative management of cerebral desaturations may mitigate postoperative cognitive decline and the risk of prolonged length of hospital stay after CABG.

Since monitoring rSO$_2$ levels during surgery is a predictor of outcomes in CABG surgery, what technical modifications to this procedure could possibly improve this variable? Off pump coronary artery bypass (OPCAB) surgery is an alternative used by many surgeons to reduce the inflammation and invasiveness of CABG. CPB is not utilized but a full median sternotomy is used to provide surgical access. The heart remains beating and stabilization instruments are placed around the target coronary to aid in anastomosis. Studies on the effects of OPCAB on cerebral blood flow with use of cerebral oximetry are limited. However, Apostolidou et al. (Apostolidou et al., 2012), found that on-pump CABG was associated with lower nadir rSO$_2$ values compared to OPCAB surgery. OPCAB had a lower incidence of desaturations <25% of baseline but
had no effect on absolute rSO$_2$ of $<50\%$ compared to on-pump CABG. Thus, there is minimal pathophysiologic difference in on-pump CABG versus OPCAB according to Apostolidou. In this regard, minimally invasive r-CABG may be more effective in reducing rSO$_2$ desaturations compared to OPCAB or conventional CABG.

In an effort to determine the beneficial effect, if any with the use of minimally invasive r-CABG in reducing cerebral oxygen desaturations, we devised a retrospective study comparing conventional CABG procedures to r-CABG. Our objective was to examine and describe a relationship between intraoperative cerebral oxygen desaturations and blood loss due to the invasive approach of utilizing a full median sternotomy in conventional CABG surgery. Other variables known to effect cerebral blood flow (blood pressure, PaCO$_2$, hematocrit, etc.) will also be analyzed to observe differences between the two procedures.
METHODS

Study Population

Thirty-two patients (23 male and 9 female) presented for isolated CABG procedure spanning April 2012 through March 2013. The institutional review board of the University of Arizona Health Network approved the study. The OR heart team was comprised of seven anesthesiologists and six perfusionists utilizing standard protocols for anesthesia and perfusion techniques. Also, four surgeons performed the surgical procedures utilizing conventional CABG techniques with one surgeon using minimally invasive r-CABG.

Cerebral Oximetry

Prior to induction of anesthesia, all patients in both groups had INVOS cerebral oximeter sensors (INVOS 5100C; Covidien Corp, Boulder, CO) placed bilaterally on their forehead and baseline rSO\textsubscript{2} values were measured before endotracheal intubation. The sensors consist of a light-emitting diode that emits near infrared light of two different wavelengths to measure the ratio of oxyhemoglobin to total hemoglobin in the watershed area of the middle and anterior cerebral artery. Each sensor has one light-emitting diode and two detectors located 3 and 4 cm away from the diode, allowing for the removal of the frontal bone and skin contribution of scattered light (Figure 1). Throughout the
procedure, all patients had rSO$_2$ values continuously displayed and recorded on the somanetics monitor in view of the surgical team.

**Figure 1. Cerebral Oximeter Sensor: Signal from surface tissues (green) are subtracted out**

**Surgical Technique:**

The r-CABG was performed using the da Vinci Surgical System (Intuitive Surgical, Inc, Sunnyvale, CA USA) with instruments telemanipulated via a console. The camera port was inserted in the left fifth intercostal space, 4 cm at the anterior axillary
line, and the right and left robotic ports were inserted through the third and seventh intercostal spaces. Continuous carbon dioxide insufflation was initiated at 8 to 10 mm Hg pressure. The left internal mammary artery (LIMA) and/or right internal mammary artery were dissected using a skeletonized technique. The distal anastomoses of the in situ IMA grafts were accomplished through a small thoracotomy (Figure 2) on the beating heart using suction based stabilization (Octopus 4.3; Medtronic, Inc, Minneapolis, MN). Blood flow and flow waveforms were measured in each graft using transit time ultrasound (Medistim, Inc.) to confirm patency of the anastomosed bypass grafts. Anesthesia management was directed towards extubation in the OR (Poston et al., 2008).

Figure 2. Left: Intraoperative small thoracotomy. Right: Post-op closed thoracotomy with robotic ports.
Conventional CABG was performed with a full median sternotomy, followed by dissection of the LIMA physically by the surgeon (Figure 3). Saphenous vein grafts were also removed via endoscopic vessel harvesting. Distal and proximal anastomoses were performed on the arrested heart through the open chest. After the chest was approximated and the skin closed, the cerebral oximetry pads were disconnected from the monitor. Anesthesia routinely transported the intubated patients to the intensive care unit to be extubated many hours later.

Cardiopulmonary bypass was instituted for every case and the University of Arizona Health Network standards and protocols were adhered to throughout the case. Perfusion flows were delivered with a cardiac index range of 1.6-2.0 L/min/m² in order to
maintain a mean arterial pressure greater than 55 mm Hg, partial pressure of arterial carbon dioxide (PaCO$_2$) greater than 35 mm Hg via alpha-stat management, and hematocrit maintained above 22%. Mild hypothermia (34-37°C), central cannulation, antegrade crystalloid cardioplegia or 4:1 blood cardioplegia were used in conventional CABG with aortic cross clamp. In r-CABG there was no cross clamp on the aorta but a beating heart strategy with pump assist was utilized with normothermic perfusion (36-37°C) and femoral cannulation.

Perfusionists intervened according to desaturations less than 80% of baseline rSO$_2$ displayed by the monitor to assist in correcting rSO$_2$ values to an acceptable range. Patients monitored with cerebral oximetry that had interventions intended to keep the rSO$_2$ >75% of the baseline value had decreased morbidity and mortality (Murkin et al., 2007). Interventions to treat decreasing rSO$_2$ included the following: repositioning of the venous cannulae, increasing the PaO$_2$, increasing systemic MAP, adjusting pump flow rate, volatile anesthetic depth, reducing temperature, or transfusing autologous blood products (Denault, Deschamps, & Murkin, 2007).

**Data Collection:**

Baseline and intraoperative data collected for each patient are listed in Table 2. A reduction of more than 20% from baseline rSO$_2$ values was considered to be an indicator
of hypoperfusion (Slater et al., 2009). From the intraoperative cerebral oximetry data, a cumulative rSO\textsubscript{2} score or area under the curve (AUC) was calculated by the following formula: AUC = 80% baseline rSO\textsubscript{2} - current rSO\textsubscript{2} (%) x time (minutes). The AUC was generated using INVOS analytics tool software (INVOS IAT; Covidien Corp, Boulder, CO) to calculate the total cumulative rSO\textsubscript{2} value (min-%), which accounts for both depth and duration of desaturation below the 80% saturation threshold. Intraoperative hemodynamic data was collected for all patients including cerebral oximetry tracings used in calculating total AUC. Parameters recorded for analysis included: intraoperative blood loss, low temperature on CPB, lactate, hematocrit pre and post-op, lowest hematocrit on CPB, CPB duration, average mean arterial pressure (MAP), average MAP on CPB, average PaCO\textsubscript{2}, and average PaCO\textsubscript{2} on CPB.

Statistics

The primary outcome measure was AUC associated with rSO\textsubscript{2} desaturations that occurred intraoperatively. The AUC data was tested for normality using a one-sample Kolmogorov-Smirnov test. Means with standard deviation were used to summarize continuous data and categorical data was expressed as frequency counts and percentages. A Pearson correlation of AUC, blood loss, MAP, diabetes mellitus (DM), hematocrit, length of stay, PaCO\textsubscript{2}, temperature, creatinine, body mass index (BMI), body surface area
(BSA), and autologous blood transfusions was used to examine simple relationships among the variables. The significance level was set to 0.05 (two-sided) for all statistical tests. However, p-values are more descriptive in nature, as this is more of an exploratory analysis. Statistical analyses were carried out with SPSS version 20.0 (SPSS Sciences, Chicago, Illinois, USA).
RESULTS

A total of 32 patients (23 male, mean age 65.5 ±8.8 years) were treated for CAD via treatment by conventional CABG (n=20) or via r-CABG (n=12). One patient in the CABG group, a 59-year-old male went into cardiac arrest on post-operative day 5 at time of discharge. He was revived and placed on extracorporeal membrane oxygenation then 2 days later expired due to a subsequent stroke. Demographics between the two groups were mostly similar with conventional CABG receiving a larger average number of anastomoses (3.5 ±0.8 vs. 2.0 ±0.6) and containing a larger percentage of patients with a history of DM (Table 1).

<table>
<thead>
<tr>
<th>Table 1: Patient Demographics</th>
<th>Conv. CABG (n=20)</th>
<th>r-CABG (n=12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.9 ±8.1</td>
<td>67.6 ±10.1</td>
<td>0.596</td>
</tr>
<tr>
<td>Male</td>
<td>14 (70%)</td>
<td>9 (75%)</td>
<td>0.770</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>2.01 ±0.18</td>
<td>2.1 ±0.20</td>
<td>0.282</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.7 ±5.5</td>
<td>31.8 ±6.3</td>
<td>0.974</td>
</tr>
<tr>
<td># of Anastomoses</td>
<td>3.5 ±0.8</td>
<td>2.0 ±0.6</td>
<td>0.001</td>
</tr>
<tr>
<td>DM</td>
<td>13 (65%)</td>
<td>4 (33%)</td>
<td>0.087</td>
</tr>
<tr>
<td>Renal Insufficiency&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3 (15%)</td>
<td>2 (17%)</td>
<td>0.229</td>
</tr>
</tbody>
</table>

Data are expressed as numbers (%) or mean ± SD. DM, diabetes mellitus. <sup>a</sup>Serum creatinine concentration ≥1.3 mg/dL for all patients.
The primary parameter, AUC, was tested for normality and had significant positive skew. Due to the skew and exponential nature of AUC data, a natural log transformation of AUC was performed. A one-sample Kolmogorov-Smirnov test was performed on the transformed AUC and it met the normality assumption. This natural log AUC variable was used for analysis of variance (ANOVA) with r-CABG versus conventional CABG (Figure 4).

Figure 4. Mean Natural Log of Total AUC in CABG and r-CABG
Patient baseline rSO\textsubscript{2} values were very similar between conventional CABG and r-CABG, but the natural log AUC was statistically significant (p=0.022; Table 2). The length of stay was reduced in the minimally invasive group by approximately 1.6 days.

An increased number of autologous blood transfusions were given to sternotomy patients even though the intraoperative blood loss was negligible between the groups. Lactate, low hematocrit on CPB, and starting hematocrit all were approximately similar.

Statistically significant differences between procedures appeared in low temperature (p=0.001), end hematocrit (p=0.002), CPB time (p=0.005), and average MAP (p=0.042).

<table>
<thead>
<tr>
<th>Table 2: Patient Baseline &amp; Intraoperative Data</th>
<th>Conv. CABG (n=20)</th>
<th>r-CABG (n=12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rSO\textsubscript{2} Baseline (%)</td>
<td>66.9 ±8.3</td>
<td>66.8 ±9.8</td>
<td>0.977</td>
</tr>
<tr>
<td>Natural log AUC (min-%)</td>
<td>5.5 ±1.8</td>
<td>3.7 ±2.3</td>
<td>0.022</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>6.6 ±3.0</td>
<td>5.0 ±1.3</td>
<td>0.089</td>
</tr>
<tr>
<td>Blood Loss (mL)</td>
<td>368 ±162</td>
<td>321 ±192</td>
<td>0.468</td>
</tr>
<tr>
<td>Blood Transfused (units)</td>
<td>1.2 ±1.5</td>
<td>0.58 ±0.9</td>
<td>0.236</td>
</tr>
<tr>
<td>Low Temperature (°C)</td>
<td>35.1 ±1.1</td>
<td>36.3 ±0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>2.1 ±1.0</td>
<td>1.9 ±0.9</td>
<td>0.612</td>
</tr>
<tr>
<td>Hematocrit Start (%)</td>
<td>35.8 ±5.0</td>
<td>37.2 ±5.5</td>
<td>0.462</td>
</tr>
<tr>
<td>Hematocrit Low (%)</td>
<td>24.8 ±4.4</td>
<td>23.9 ±4.4</td>
<td>0.607</td>
</tr>
<tr>
<td>Hematocrit End (%)</td>
<td>29.0 ±3.7</td>
<td>33.6 ±3.8</td>
<td>0.002</td>
</tr>
<tr>
<td>CPB Time (min)</td>
<td>111.1 ±48.4</td>
<td>65.2 ±23.9</td>
<td>0.005</td>
</tr>
<tr>
<td>CPB PaCO\textsubscript{2} (mmHg)</td>
<td>38.3 ±6.0</td>
<td>35.0 ±5.3</td>
<td>0.126</td>
</tr>
<tr>
<td>PaCO\textsubscript{2} (mmHg)</td>
<td>36.5 ±2.0</td>
<td>34.9 ±3.3</td>
<td>0.098</td>
</tr>
<tr>
<td>CPB MAP (mmHg)</td>
<td>61.6 ±5.7</td>
<td>62.0 ±8.1</td>
<td>0.885</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>73.2 ±6.6</td>
<td>78.8 ±8.2</td>
<td>0.042</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. rSO\textsubscript{2} baseline is pre-intubation baseline. AUC (AUC = 80% baseline rSO\textsubscript{2} - current rSO\textsubscript{2} (%) x time (minutes). Lactate is highest lactate intraoperatively. Hematocrits are intraoperative levels. CPB CO\textsubscript{2} is the average CO\textsubscript{2} on pump. CO\textsubscript{2} is the average CO\textsubscript{2} intraoperatively. MAP has the same association as CO\textsubscript{2}. 
A pairwise comparison was performed on a variable of interest, DM with AUC in both the conventional and robotics group. The analysis revealed an interesting relationship in patients with DM, the type of procedure they received, and their corresponding AUC. The test was statistically significant (p=0.001) for DM patients receiving r-CABG compared to conventional CABG with significantly reduced AUC values (Table 3). There was a smaller reduction in mean AUC for the non-DM patients between the two cohorts with no significant relationship.

<table>
<thead>
<tr>
<th>Table 3: DM Patients vs. Mean AUC</th>
<th>Conv. CABG AUC</th>
<th>r-CABG AUC</th>
<th>p-value</th>
<th>F</th>
<th>Obs. Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-DM Patients</td>
<td>5.01</td>
<td>4.62</td>
<td>0.691</td>
<td>0.162</td>
<td>0.067</td>
</tr>
<tr>
<td>DM Patients</td>
<td>5.70</td>
<td>1.81</td>
<td>0.001</td>
<td>13.277</td>
<td>0.940</td>
</tr>
</tbody>
</table>

Data is mean natural log AUC (AUC = 80% baseline rSO_2 - current rSO_2 (%) x time (minutes)).
DISCUSSION

As the population of CABG patients continues to increase in age, adverse surgical outcomes such as, death, stroke, and acute renal impairment continue to decline (Steinbrook, 2006). Patients have been the beneficiaries of technological advances in OR equipment and resultant surgical skill using new technology. The quick return to a normal quality of life is the foremost concern of most patients. More subtle morbidities still commonly occur in patients’ post-CABG, specifically neurocognitive deficits. Recent evidence has shown that neuromonitoring devices using near infrared spectroscopy to trigger interventional strategies can reduce cerebral oxygen desaturations and potential ischemia to the brain and other tissues, reducing neurologic sequelae, including neurocognitive deficits (Murkin et al., 2007).

This retrospective study was designed to evaluate and compare the impact of cerebral oximetry monitoring in conventional CABG and minimally invasive r-CABG surgeries. The analysis of AUC between the groups was statistically significant (p=0.022, Figure 4), indicating that cerebral desaturations were reduced in r-CABG depth and duration of time they exceeded the 80% of baseline threshold compared to conventional CABG. Given that both procedures utilized CPB, which trigger decreased rSO2 values at
initiation of bypass, our findings suggest alternative variables may be driving the improvement in cerebral oxygenation during r-CABG.

The conventional approach using a full median sternotomy led us to hypothesize that blood loss associated with a morbid wound would lead to intraoperative cerebral oxygen desaturations and an associated increase in AUC with its potential neurologic morbidities. The data for blood loss showed in the conventional CABG group a 368 mL reduction intraoperatively compared to 321 mL for r-CABG, a minimal reduction with no associated statistical significance (Figure 5). The lack of evidence in blood loss association between the two groups led us to investigate further into other parameters of interest.
Figure 5. Intraoperative Mean Blood Loss in CABG and r-CABG

The intraoperative data provides some evidence to the parameters playing the strongest role in potentially aiding in the reduced AUC found in r-CABG. The role of blood loss and autologous blood transfusions is an important factor in the relationship of oxygen carrying capacity and hemoglobin. Losing blood throughout a procedure would theoretically lead to a lower oxygen carrying capacity of hemoglobin with the loss of the hemoglobin rich red blood cells. Conversely, blood transfusions would lead to decreased
AUC as the oxygen carrying capacity of hemoglobin is increased. There was no significance in this regard between the two groups but in association with hematocrit levels intraoperatively there was a statistically significant variable with ending hematocrit (p=0.002). The starting hematocrit and lowest intraoperative hematocrit were not significant with similar averages. However, the ending hematocrit was approximately 4.5% higher in r-CABG compared to conventional. Starting hematocrit to ending hematocrit dropped approximately 7% on average in conventional compared to 4.5% in r-CABG. These two differences may have increased the oxygen carrying capacity of the r-CABG group, thereby playing a role in improved AUC endpoint compared to the sternotomy control.

The effect of temperature on metabolism is well established, for every degree Celsius decrease from 37°C there is a 7% decrease in cellular metabolism. The Pearson analysis for the temperature difference between each procedure shows statistical significance (p=0.001). On average there is a 1.2°C difference between the two cohorts relating to an approximately 7-8% decrease in metabolic demand for conventional CABG. A decrease in temperature is also going to shift the oxygen-hemoglobin dissociation curve to the left increasing the affinity of oxygen to hemoglobin. These factors will
theoretically decrease the AUC values for the conventional CABG group and potentially increase AUC in the r-CABG group.

The use of CPB has consistently shown in cerebral oximetry tracings a profound drop at initiation of bypass. This is mainly due to the hemodilutional effect that decreases the viscosity of the blood and the hematocrit. This initially causes a severe drop in the MAP of the patient but typically resolves within a few minutes with increased pump flows, use of alpha-1 agonists (phenylephrine), and hemoconcentration of the perfusate. This drop in MAP at pump initiation corresponds with significant cerebral desaturations that rebound with the interventions mentioned. The average MAP during CPB was not found to be significant and was approximately equal at 61.6 and 62.0 mmHg. However, the average intraoperative MAP was statistically significant (p=0.042) with a MAP difference of 5.6 mmHg favoring r-CABG (73.2 vs. 78.8 mmHg). Cerebral vascular disease in CAD population occurs at a rate estimated at more than 50%, thereby increasing the potential for hypoperfusion due to impaired autoregulation and requirement for increased cerebral perfusion pressure (CPP) (Denault et al., 2007). Desaturations can occur due to decreased CPP. Thus, an increased MAP in the r-CABG population may lead to reduced AUC compared to the CABG control group.
Cerebral blood flow (CBF) is highly sensitive to changes in the PaCO₂, specifically in the cerebrovasculature (Willie et al., 2012). Hypocapnia tends to decrease CBF and hypercapnia has the opposite effect increasing CBF. The normal PaCO₂ ranges from 35-40 mmHg. The data for PaCO₂ fell into this range and was not statistically significant between the two procedures. Generally, average PaCO₂ for r-CABG was borderline hypocapnic, which could lead to increased AUC values throughout the case. This is most likely due to the use of single lung ventilation for r-CABG and over compensatory hyperventilation. Both procedures could potentially benefit from PaCO₂ around 40 mmHg to induce the vasodilatory effects on cerebral vessels increasing CBF.

In the conventional CABG population, they averaged 1.5 more surgical anastomoses, which related to longer CPB times (111 vs. 65 min). CPB time is statistically significant for the two groups (p=0.005). Initially, this significance seems dramatic, as CPB time is nearly twice as long in the CABG group. Upon further inspection this may bear less significance, as cerebral oximetry tracings between the two groups look very similar at initiation of CPB with a profound desaturation but then tend to trend towards the normal range (<80% of baseline) within the first 60 minutes of bypass (Figure 6). With this observation of a return to a normal range for cerebral oximetry there were certain tracings that seemed to lack this ability to autoregulate.
These anomalous tracings tended to be patients with DM, whom are well known to lack autoregulation. Due to this phenomenon, a pairwise comparison was analyzed between diabetics and non-diabetics with mode of surgery. This analysis revealed statistically significant (p=0.001) evidence that DM patients tend to have much lower mean AUC in r-CABG compared to conventional CABG (Figure 7). Non-DM also tended to have a slightly lower AUC but not on a statistically significant level from an invasive to minimally invasive procedure.
Figure 6. Cerebral Oximetry Tracing. Top: Conventional CABG. Bottom: r-CABG. Compare CPB time and time for rSO2 to return to acceptable range.
Our finding that DM patients were more responsive to the benefits of minimally invasive r-CABG on cerebral oxygenation is consistent with prior evidence suggests that diabetic patients have an insufficient ability to autoregulate vascular responses during major cardiac surgery. Avoiding the systemic and local inflammatory effects of conventional surgery may be a mechanism by which r-CABG is able to improve this protective autoregulation. When combined with a reduced risk of sternal infection after BIMA procurement, any added benefit of r-CABG on maintaining vasoregulation in diabetics compared to an open sternotomy could be a game changer for managing these higher risk diabetic patients. This could be an area of potential research to further investigate the underlying mechanisms that contribute to this reduced AUC value.
In conclusion, minimally invasive r-CABG tends to show beneficial effects for patients by reducing the total mean AUC in comparison to conventional CABG, especially in the DM patient. High AUC or prolonged intraoperative cerebral desaturations have been significantly associated with an increased risk of cognitive decline after CABG (Slater et al., 2009). The data on cerebral oximetry is still debated.
but our findings suggest that further studies may help clarify specific patient populations (e.g. diabetics) likely to benefit the most from minimally invasive r-CABG procedures.
REFERENCES


