2017

Does Perioperative Angiotensin-Converting Enzyme Inhibitor Therapy Correlate with Increased use of Vasopressors during Posterior Lumbar Interbody Fusion versus those not Receiving Angiotensin-Converting Enzyme Inhibitor Therapy: A Retrospective Study

Joshua Ross
joshuaross1985@gmail.com

Follow this and additional works at: http://mds.marshall.edu/etd

Part of the Anesthesiology Commons, and the Nursing Commons

DOES PERIOPERATIVE ANGIOTENSIN-CONVERTING ENZYME INHIBITOR THERAPY CORRELATE WITH INCREASED USE OF VASOPRESSORS DURING POSTERIOR LUMBAR INTERBODY FUSION VERSUS THOSE NOT RECEIVING ANGIOTENSIN-CONVERTING ENZYME INHIBITOR THERAPY: A RETROSPECTIVE STUDY

A Research Project submitted to
the Graduate College of Business
Marshall University

Final defense submitted in partial fulfillment of requirements for the
Doctorate of Management Practice in Nurse Anesthesia (DMPNA) degree
conferred by Marshall University (MU) in partnership with the
Charleston Area Medical Center (CAMC) based on a collaborative agreement between
the MU College of Business and the CAMC School of Nurse Anesthesia

By

Joshua Ross

Marshall University

November 9, 2017

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Abstract: The purpose of this study was to evaluate if patients who took Angiotensin Converting Enzyme (ACE) inhibitors the morning of surgery for Posterior Lumbar Interbody Fusion (PLIF) required more treatment for intraoperative hypotension.

Introduction: PLIF is a surgical procedure used to correct spinal disorders that include compression, instability, pathological lesions, deformities, and pain. PLIF is completed utilizing the prone position for optimal access to the lumbar spine. Complications associated with prone position have included Post-Operative Vision Loss (POVL), compression of abdominal vessels, and head and neck venous compression resulting in neurologic injury. Currently, there are no set recommendations on ACE Inhibitor continuation before surgery, unlike those on a beta antagonist. There is a lack of research on the effect of the continuation of ACE inhibitors on intraoperative hypotension and vasopressor administration.

Methodology: This study used a retrospective, case-control study design. A chart review was conducted from January 1, 2007, through January 1, 2017 on patients undergoing PLIF. A total of 200 patients were included in this study sepearted into two groups, those who held their ACE inhibitors and those who continued their ACE inhibitors. Patient information collected included: amount of phenylephrine received, amount of ephedrine received, lowest systolic blood pressure, and lowest diastolic blood pressure. The age and BMI was compared using t-tests and chi-square tests for gender and ASA physical status. A total of two linear regressions were completed to examine the lowest systolic blood pressure, lowest diastolic blood pressure, total phenylephrine dose, and total ephedrine dose.

Results: The mean age of the total study sample was $57.25 \pm (12.57)$. There were 47.5% male patients and 52.5% female patients. The mean BMI was $31.01 \pm (6.71)$. The ASA physical status ranged from 2 to 4 with 27% ASA 2, 69% ASA 3, and 4% ASA 4. There was no statistically significant difference found in age, gender, BMI, or ASA physical status between groups. The mean systolic blood pressure was $84.38 \pm (7.45)$, mean diastolic blood pressure was $44.61 \pm (7.38)$, mean ephedrine doses were $4.72 \pm (4.10)$, and mean phenylephrine doses were $3.57 \pm (4.40)$. Data did not support a statistically significant difference in lowest systolic blood pressure, lowest diastolic blood pressure, total phenylephrine dose, or total ephedrine dose between groups.

Discussion: This study did not find an association between patients taking ACE inhibitors and increased requirements of vasopressors, lower systolic blood pressure, or lower diastolic blood pressure. The results of this current study are inconsistent with existing literature and could be explained by the retrospective nature of the study, small sample size, and only one hospital network used for patients. There were several limitations identified and discussed in this study.

Conclusion: In this study, the use of ACE inhibitors the morning of surgery was not associated with more doses of vasopressor medications, lower systolic blood pressure, or lower diastolic blood pressure in patients undergoing PLIF.

Implications/Recommendations: This study provided clinical relevance to anesthesia practitioners, researchers, and physicians about the use of ACE inhibitors for patients undergoing PLIF. Knowledge of ACE inhibitors and their effects help anesthesia providers customize the anesthetic to optimize patient safety.

Key Words: ACE inhibitors, hypotension, posterior lumbar interbody fusion, vasopressors

LIST OF TABLES

INTRODUCTION

Background and Significance

Posterior Lumbar Interbody Fusion (PLIF) is a surgical procedure used to correct spinal disorders that include compression, instability, pathological lesions, deformities, and pain (Takahashi et al, 2016). PLIF is completed utilizing the prone position for optimal access to the lumbar spine. Complications associated with prone position have included Post-Operative Vision Loss (POVL), compression of abdominal vessels, and head and neck venous compression resulting in neurologic injury (Pierce & Kendrick, 2010).

Prone positioning and prolonged procedures pose significant challenges for anesthesia providers to maintain hemodynamic stability and to avoid the resulting decreased venous return from compressed abdominal vessels which reduces cardiac output (Nagelhout & Plaus, 2014). POVL has often been reported in prone spine surgery, and risk factors contributing to vision loss have included hypotension, massive infusions of intravenous fluids, lengthy procedures, and anemia (Pierce & Kendrick, 2010). Nagelhout and Plaus (2014) described the importance of proper positioning during prone spine surgery to prevent eye injuries and prevent abdominal compression. Rapid intervention and assessment must be paramount if sudden hypotension occurs and all members of the surgery team should be informed to efficiently institute appropriate treatment and prevent life-changing complications (Nagelhout & Plaus, 2014).

The Renin-Angiotensin-Aldosterone System (RASS) provides an integral role in the regulation of fluid balance and autonomic nervous system blood pressure control (Chopra, Baby, & Jacob, 2011). Hemodynamic control of blood pressure is controlled by three regulatory systems during anesthesia, the Sympathetic Nervous System, renin-

angiotensin system, and vasopressin (Schulte, Ziefler, Philippi-Hohne, Kaczmarczyk, & Boemke, 2011). Inhibition of the RASS system causes a reduction in fluid volume and decreased blood pressure by preventing the conversion of angiotensin I to angiotensin II which decreases peripheral vascular resistance, reduces aldosterone, norepinephrine, and plasma antidiuretic hormone (Ma, Kam, Yan, & Lam, 2010). ACE inhibitors block angiotensin II, a potent vasoconstrictor, which has shown to be highly useful in the treatment of hypertension and congestive heart failure (Helal & Lane, 2014). Drugs in the ACE inhibitor family include captopril, enalapril, lisinopril, ramipril, quinapril, and fosinopril (Pilote. Abrahamowicz, Eisenberg, Humphries, Behlouli, & Tu, 2008).

RASS antagonists, including ACE inhibitors and their continuation have been linked to intraoperative hypotensive episodes during anesthesia. Studies have found growing evidence that continuing RASS antagonists could be related to adverse outcomes, such as renal failure and death, and temporary withdrawal could attenuate intraoperative hypotension and hypovolemia (Auron, Harte, Kumar, & Michota, 2010). Hypotension has been associated with renal failure and as the severity of hypotension increases the risk for renal injury increases (Lehman, Saeed, Moody, & Mark, 2010).

Perioperative continuation of ACE inhibitors has been linked to refractory intraoperative hypotension, and varying degrees of hypotension can occur depending on the variables of the surgical procedure (Thoma, 2013). Renal excreted ACE inhibitors have a half-life elimination of 10 hours, and this can explain why withdrawing 8 to 24 hours could significantly reduce intraoperative hypotension (Thoma, 2013).

There are a growing number of studies reporting that patients are at increased risk for intraoperative hypotension when patients have been treated with ACE inhibitors

compared to those who were not (Auron et al., 2010). Current research has shown that continuation of ACE inhibitors has been linked to intraoperative hypotension and withholding these drugs could reduce the likelihood (Smith & Jackson, 2010). Treatment of hypotension during anesthesia is achieved with Intravenous (IV) fluid bolus and administration of vasoactive medications, such as phenylephrine and ephedrine Lonjaret, Lairez, Minville, & Geeraerts, 2014). Chronic ACE inhibitor therapy leads to blunting of the RASS system resulting in vasoplegic syndrome causing low systemic vascular resistance and high cardiac output (Hedman, Mann, Spulecki, & Castner, 2016). Vasoplegia leads to poor organ perfusion due to lack of Systemic Vascular Resistance (SVR) and is minimally responsive to agents that increase SVR (Hosseinian, Weiner, Levin, & Fischer, 2016).

Literature Review

Due to the lack of research regarding ACE inhibitors in non-cardiac surgery and the retrospective nature of this study, both non-cardiac and cardiac studies were analyzed. Also, research has been limited to procedures performed in the prone position and ACE inhibitors; therefore, other positions were included. There have been few studies involving ACE inhibitors without the addition of Angiotensin Receptor Blockers (ARB), so they were also included in this review. Some research studies have argued that it is advantageous to stop ACE inhibitors before surgery, while others have supported their continuation. This review described several studies that have argued the continuation or withdraw of ACE inhibitor therapy.

A retrospective study performed by Trentman et al. (2011) reviewed 384 patients undergoing shoulder surgery in the beach chair position containing two groups: those

taking at least one antihypertensive medication and those not taking antihypertensive drugs, including 199 and 185 patients, respectively. The antihypertensive group presented more episodes of hypotension, 62% in those taking antihypertensive medications versus 44% who did not receive antihypertensive therapy with a mean episode per case of 1.7 to 1.2, respectively. Those who took antihypertensive medications received more vasopressor administrations, 75%, versus those who did not take antihypertensive therapy, 54%, with a mean value of 3.0 to 2.1, respectively. The timing of ACE inhibitors and angiotensin receptor antagonist administration did not affect intraoperative hypotension.

Roshanov et al. (2017) conducted an international prospective cohort study on 14, 687 patients of whom 4,802 were receiving ACE inhibitors or angiotensin II receptor blockers before non-cardiac surgery. The authors reported that patients who withheld their ACE inhibitors or angiotensin II receptor blockers in the 24 hours before surgery were less likely to experience death, stroke, myocardial injury (adjusted relative risk 0.82; 95% CI, 0.70 to 0.96; $P = 0.01$), or intraoperative hypotension (adjusted relative risk, 0.80; 95% CI, 0.72 to 0.93; $P < 0.001$).

Comfere et al. (2005) performed a retrospective study of 267 hypertensive patients undergoing elective non-cardiac surgery under general anesthesia who took ACE inhibitors or angiotensin receptor antagonist. In the preoperative screening period, patients were asked to continue or hold their ACE inhibitors or angiotensin receptor antagonist up to 24 hours and the number of hours from the last dose was recorded. Results of the study showed that withdrawing ACE inhibitors or angiotensin receptor antagonist at minimum 10 hours before anesthesia reduced immediate post-induction hypotension, and medications which were taken closer to surgery, less than 10 hours,

were more likely to incur hypotension.

Rajgopal, Rajan, Sapru, and Paul (2014) conducted a randomized prospective double-blinded study to determine the effect of preoperative discontinuation of ACE inhibitors or angiotensin II receptor antagonists on intraoperative blood pressure after induction of anesthesia from 2008 to 2012. A total of 60 patients were included in the study and randomized into two groups, 30 patients that took ACE inhibitors or angiotensin II receptor antagonists and 30 patients who stopped therapy the day before surgery. The results showed that intraoperative hemodynamics could be more safely managed when ACE inhibitors or angiotensin II receptor antagonists were held on the day of surgery. The authors found a significant reduction in systolic blood pressure with a mean difference 37.67 versus 3.47, diastolic blood pressure with a mean difference 3.47 versus 1.93, and mean arterial pressure with a mean difference 24.82 versus 0.13 in the group that continued their ACE inhibitor or angiotensin II receptor antagonist ($p<0.01$, $p<0.05$, $p<0.01$ respectively).

Schulte et al. (2011) examined the effects of long-term treatment with ACE inhibitors and hemodynamic regulation during Total Intravenous Anesthesia (TIVA) in a prospective study. The study included 36 patients undergoing TIVA for minor surgery with 17 patients that continued ACE inhibitors and 19 patients as controls. The researchers showed that long-term ACE inhibitor therapy did not exaggerate hypotension as long as patients' were well hydrated and vasopressors were promptly applied. There was no difference in the amount of fluids or vasopressors used between each group ($p<0.05$).

A retrospective cohort study containing 1,358 adult patients who underwent cardiac surgery was conducted by Arora et al. (2008) to assess the long-term use of ACE inhibitors/ARB and the association of Acute Kidney Injury (AKI) after cardiac surgery. Intraoperative and postoperative dependent variables associated with AKI were hypotension during surgery or postoperative hypotension and the use of vasopressors. It was reported that preoperative use of ACE inhibitors/ARB was associated with a 27.6 % higher risk of postoperative AKI. The ACE inhibitor/ARB group experienced greater intraoperative hypotension than the non- ACE inhibitor/ARB group 47.67% versus 41.41%, respectively (p=0.025).

Vijay, Grover, Coulson, and Myles (2016) performed a prospective observational study of 323 patients with 83 patients stopping ACE inhibitor/ARB therapy and 240 continuing their treatment. It was shown no significant difference in intraoperative vasopressor use, fluid intake, or lowest systolic blood pressure. Despite findings, the researchers recommended withholding ACE inhibitors/ARB before major surgery where large fluid shifts or hypotension could occur, although extra caution should be given to those with heart failure and the risks of exacerbation when ACE inhibitors/ARB were withheld.

A randomized prospective, single-blind study was conducted by Twersky, Goel, Narayan, and Weedon (2014) to observe the effects of ACE inhibitors and ARB on arterial blood pressure recordings during same day ambulatory surgery. The study contained 640 patients randomly assigned to two groups: those who continued and those who discontinued ACE inhibitor/ARB therapy. The researchers assessed the primary outcomes of the presence of Hypertension (HTN) before surgery, cancellations due to

HTN, prolongation and adverse effects, and HTN in the postoperative period. The results of the study showed that discontinuation of ACE inhibitor/ARB therapy did not result in an increased preoperative or postoperative HTN providing evidence for the safety of discontinuation of ACE inhibitors/ARB on the day of surgery.

Statement of the Problem and Research Purpose

The objectives of this study were to evaluate if patients who took ACE inhibitors the morning of surgery versus those who withheld them required more doses of vasopressors, had lower systolic blood pressures, and lower diastolic blood pressures.

Hypotension after the induction of anesthesia is common due to the subsequent reduction in vascular tone and cardiac depression. Hypotension can be further exaggerated when induction of anesthesia is compounded with the use of antihypertensive medications. Prolonged hypotension can cause deleterious outcomes when refractory to traditional treatment measures causing failure to perfuse vital systemic capillary networks (Trotter, 2012). Patients who take ACE inhibitors in the perioperative period could be faced with refractory hypotension producing previously mentioned adverse outcomes.

Currently, there are clear guidelines on continuation for some antihypertensive medications preoperatively for non-cardiac surgery, but clear recommendations are still lacking for ACE inhibitors (Fleisher & Fleishmann, 2014). According to the 2014 American College of Cardiology/American Heart Association Task Force on Practice Guidelines on perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery, the summary found ACE inhibitor continuation to be reasonable during the perioperative period (Fleisher & Fleishmann, 2014). Vijay et al. (2016) found that patients experienced no adverse effects by withholding ACE inhibitor

or angiotensin II receptor blockers and recommending withholding therapy during surgeries that involve significant fluid shifts, hypotension, or large IV fluid requirements.

Further research in the perioperative use of ACE inhibitors could improve clinical outcomes of patients and clinical practice at CAMC and other hospitals performing PLIF. The goal of this research was to determine if patients who took their ACE inhibitors the morning of surgery presented lower systolic blood pressures, lower diastolic blood pressure, and required more doses of vasopressors than those who did not take their ACE inhibitor the morning of surgery.

METHODOLOGY

Research Hypothesis

The first hypothesis for this study was patients who took ACE inhibitors the morning of surgery required more doses of vasopressor medications to treat hypotension versus those who did not take ACE inhibitors the morning before surgery. The second hypothesis was patients who took ACE inhibitors the morning of surgery presented lower systolic blood pressures versus those who did not receive ACE inhibitors the morning of surgery. Lastly, the third hypothesis for this study was patients who took ACE inhibitors the morning of surgery had lower diastolic blood pressures versus those who did not receive ACE inhibitors the morning of surgery.

Research Design and Setting

A review of electronic medical records at CAMC was conducted using patients who took ACE inhibitors at home who required PLIF under general from January 1, 2007, through January 1, 2017 (McKesson Corporation, 2017). This study evaluated if patients who received ACE inhibitors the morning of surgery for PLIF required more doses of

vasopressor medications for hypotension treatment, had lower systolic blood pressures, and lower diastolic blood pressures than those who did not take ACE inhibitors for the same procedure.

The study design was a retrospective, case-control study design. A retrospective design was chosen because data can be collected at CAMC where patient records can be easily accessed. The case-control design allowed for the identification of hypotension and ACE inhibitor therapy during PLIF. A retrospective, case-controlled study design was employed to analyze the data to gain substantial research findings while adhering to limited financial and time constraints when compared with alternative study designs (Schulz & Grimes, 2002).

Sample Population and Description of Sample

The sample population for this study included patients with home medications in the ACE inhibitor family who underwent PLIF at CAMC. Two hundred patients who met the inclusion criteria were included in this study. This sample included 100 patients who took their ACE inhibitor the morning of surgery and 100 patients who did not receive an ACE inhibitor the morning of surgery. The patients in the sample were identified using the International Classification of Diseases 9th revision (ICD-9) and International Classification of diseases 10th revision (ICD-10) codes. Due to the recent nationwide change from ICD-9 to ICD-10 in 2015, both codes were included to fulfill all inclusion and exclusion criteria. ICD- 9 codes 81.08 (Lumbar and lumbosacral fusion of the anterior column, posterior technique) and ICD-10 code OSG10AJ (fusion of two or more lumbar vertebral joints with interbody fusion device, posterior).

Inclusion Criteria:

1. Patient Age 18-80 years old

2. Patient ASA physical status classification I-IV

3. Home medication in the ACE inhibitor family

4. Patients undergoing PLIF

Exclusion Criteria:

1. Patients less than 18 years of age or greater than 80 years of age

2. Patients ASA classification greater IV

Procedure/Protocol

A chart review was conducted from electronic medical records at CAMC on patients

who had PLIF with concurrent ACE inhibitor therapy from January 1, 2007, to January 1,

2017. CAMC is a non-profit, 956-bed regional referral and academic medical center

(CAMC, 2017a). There are three hospitals located in Charleston, West Virginia: General,

Memorial, and Women & Children's. The fourth hospital, Teays Valley Hospital, is

located in Teays Valley, West Virginia (CAMC, 2017a). Preoperative assessments and

intraoperative data were collected from the patients' anesthesia record. Preoperative

collection data included control variables: age, ASA physical status, home medication list,

gender, and Body Mass Index (BMI). BMI was calculated by using the height and weight

obtained from the anesthesia record. BMI is an indicator for amount of body fat and uses

the following formula: Weight (kilograms)/ Height (meters) squared (Centers for Disease

Control and Prevention, 2015). Gender was classified as male or female. Intraoperative

data included total number of ephedrine doses received, number of phenylephrine doses

received, lowest systolic blood pressures recorded in millimeter of mercury (mmHg), and

lowest diastolic blood pressures recorded in millimeter of mercury (mmHg).

Phenylephrine and ephedrine provided two different mechanisms of action to achieve

their vaso-constrictive properties; therefore, there was no formula to convert dose

equivalents between the two drugs. Doses of Ephedrine were quantified as 5 milligrams,

and doses of Phenylephrine were quantified as 100 micrograms. The ASA classification

is a numeric scale developed by the American Society of Anesthesiologists to determine

the general health of the patient (American Society of Anesthesiologists, 2014). The

classifications were:

ASA 1. A normal patient who is healthy.

ASA 2. A patient with mild systemic disease.

ASA 3. A patient with severe systemic disease.

ASA 4. A patient with a severe systemic disease that is a constant threat to life.

ASA 5. A moribund patient who is not expected to survive without the operation.

ASA 6. A brain-dead patient whose organs are being removed for donor purposes.

Data Collection and Instruments

Microsoft Excel was used to organize collected data in a systematic manner. Patients

were individually numbered in the order the data was received. The number did not, in

any way, link the data to the patient it corresponded with. The patients were randomly

assigned by to one of two groups: 1) Received ACE inhibitor the morning of surgery, 2)

Did not receive ACE inhibitor the morning of surgery.

Statistical Design and Analysis

The purpose of this research was to evaluate if perioperative ACE inhibitor therapy

was associated with increased use of vasopressors during posterior lumbar interbody

fusion. First, a T-test was performed to determine if the ACE inhibitor group and the non-

ACE inhibitor group shared similarities in age and BMI. Chi-squared test was used to compare the group's gender and ASA physical status to determine if the groups were similar in these aspects. Two linear regressions were used to determine if there was relationship between ACE inhibitor therapy and a number of doses of the vasopressors phenylephrine and ephedrine received, lowest systolic blood pressure, and lowest diastolic blood pressures. A p-value <0.5 was considered statistically significant. SPSS software version 22 was utilized to determine statistical relevance between collected data (SPSS IBM Company, 2017).

Ethical Considerations

This study was approved by the CAMC and West Virginia University-Charleston Division Institutional Review Board on August 4, 2014 (Appendix C).

RESULTS

Presentation, Analysis, and Interpretation of the Data

The total study sample consisted of 200 patients ages 18-80 years old presenting to CAMC Hospitals for PLIF surgery. The mean age of the total study sample was $57.25 \pm (12.57)$, 47.5% male and 52.5% female, mean BMI $31.01 \pm (6.71)$, and ASA 2 was 27%, ASA 3 was 69%, ASA 4 was 4% (Table 1).

The study sample of 200 patients was then divided into equal groups containing 100 patients by those who took an ACE inhibitor and those who did not take an ACE inhibitor. The mean age in the received ACE inhibitor group (group A) was $58.77 \pm (12.74)$, and the did not receive ACE inhibitor group (group B) $55.74 \pm (12.27)$ with no statistically significant mean difference between groups, $(p > .05)$ (Table 1). Group A consisted of 47% male and 53% female with a mean BMI $30.37 \pm (6.447)$ and group B consisted of

48% male and 52% female with a mean BMI 31.64 ± (6.930) and no statistically

significant mean difference in either category, (p> .05) (Table 1). ASA physical status in

group A contained 24% ASA 2, 73% ASA 3, and 3% ASA 4; Group B contained 30%

ASA 2, 65% ASA 3, and 5% ASA 4 with no statistically significant mean difference

between groups (p> .05) (Table 1).

Table 1: Demographic and Clinical Characteristics of Patients Who Underwent Posterior
Lumbar Interbody Fusion Surgery and comparison of age, gender, BMI, and ASA
between groups

Variable	Total Sample	Study Groups		Statistical Value
	Total N=200 Mean (SD)	Received ACE inhibitor N-100 (50%) Mean (SD)	Did Not receive ACE inhibitor N-100 (50%) Mean (SD)	p-Value
Age (years) N=200	57.25 (12.567)	58.77 (12.739)	55.74 (12.269)	NS
Gender N (%) Male Female N=200	47.5% 52.5%	47% 53%	48% 52%	NS NS
BMI (kg/m2)	31.01 (6.707)	30.37 (6.447)	31.64 (6.930)	NS
ASA N (%) 2 3 4	54 (27%) 138 (69%) 8 (4%)	24 (24%) 73 (73%) 3 (3%)	30 (30%) 65 (65%) 5 (5%)	NS NS NS

NS= Not significant (p> 0.05), SD= Standard Deviation, BMI=Body Mass Index, ASA= American Society
of Anesthesiologist physical status classification

The total sample presented a mean systolic blood pressure of 84.38 ± (7.45), a mean

diastolic blood pressure of 44.61 ± (7.38), mean ephedrine doses 4.72 ± (4.10), and a

mean phenylephrine doses of 3.57 ± (4.40) (Table 2). A t-test was preformed to

determine the mean difference between group A and group B, and there was no

statistically significant difference found between lowest systolic blood pressure, lowest

diastolic blood pressure, total ephedrine doses, and total phenylephrine doses (p > .05).

Group A presented a mean lowest systolic blood pressure of 83.38 ± (6.80), and group B

presented a mean lowest systolic blood pressure of 85.37 ± (7.96) which was not

statistically significant (p> .05). The mean lowest diastolic blood pressure in group A was

42.14 ± (6.80), and the group B mean lowest diastolic blood pressure was 47.07 ± (7.158)

(p> .05). Group A received a mean 5.10 ± (4.08) ephedrine doses, and group B received a

mean 4.34 ± (4.12) ephedrine doses (p> .05). Group A received a mean 3.60 ± (4.90)

phenylephrine doses, and group B received a mean 3.54 ± (3.88) phenylephrine (p> .05)

(Table 2).

Table 2: Comparison of Preoperative ACE Inhibitor Administration on Lowest Systolic
Blood Pressure, Lowest Diastolic Blood Pressure, Total Ephedrine Doses, and Total
Phenylephrine Doses in Those Who Underwent Posterior Lumbar Interbody Fusion

Variable	Total Sample	Study Groups		Statistical Value
	Total N=200 Mean (SD)	Received ACE inhibitor N=100 Mean (SD)	Did Not receive ACE inhibitor N=100 Mean (SD)	p-Value
Lowest Systolic Blood Pressure	84.38 (7.452)	83.38 (6.795)	85.37 (7.965)	NS
Lowest Diastolic Blood Pressure	44.61 (7.378)	42.14 (6.797)	47.07 (7.157)	NS
Ephedrine Doses	4.723 (4.105)	5.100 (4.0788)	4.345 (4.1186)	NS
Phenylephrine Doses	3.570 (4.404)	3.600 (4.8933)	3.540 (3.8780)	NS

NS= Not significant (p> 0.05), SD= Standard Deviation

A linear regression was conducted between lowest systolic blood pressure and age,

gender, BMI, ASA physical status, and ACE inhibitor consumption. Age and gender

were associated with lowest systolic blood pressure which was statistically significant,

(p= .001) and (p= .036), respectively. BMI, ASA physical status, and ACE inhibitor

consumption did not show a statistically significant association (p> .05), (Table 3).

14

Table 3: Linear Regression Analysis between Age, Gender, BMI, and ASA Physical Status and Lowest Systolic Blood Pressure in Patients Who Underwent Posterior Lumbar Interbody Fusion.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	90.303	4.351		20.757	.001
	Age	-.160	.043	-.270	-3.708	*.001
	Gender (Male=1 Female =0)	2.125	1.008	.143	2.109	*.036
	BMI	.036	.080	.032	.449	NS
	ASA (I-IV)	.673	1.028	.046	.654	NS
	Ace Inhibitor (1=took 0=did not take)	-1.465	1.013	-.099	-1.446	NS

Variable: Age, Gender, BMI, and ASA. * Indicates Statistical Significance at (p<. .05), BMI= Body Mass Index, ASA= American Society of Anesthesiologist physical status classification, NS= Not Statistically Significant (p> .05)

A second linear regression was performed between the lowest diastolic blood pressure and age, gender, BMI, and ASA physical status. It was found to show a statistically significant association between lowest diastolic blood pressure and age, gender, and ACE inhibitor consumption (p < .05). BMI and ASA showed no statistically significant difference (p> .05), (Table 4).

Table 4: Linear Regression Analysis between Age, Gender, BMI, and ASA Physical Status and Lowest Diastolic Blood Pressure in Patients Who Underwent Posterior Lumbar Interbody Fusion.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error,	Beta		
1	(Constant)	54.803	4.150		13.204	.001
	Age	-.096	.041	-.163	-2.317	*.022
	Gender (Male=1 Female =0)	2.570	.961	.174	2.673	*.008
	BMI	-.020	.076	-.018	-.266	NS
	ASA (I-IV)	-1.092	.981	-.075	-1.114	NS
	Ace Inhibitor (1=took 0=did not take)	-4.597	.967	-.312	-4.756	*.001

Variable: Age, Gender, BMI, and ASA. * Indicates Statistical Significance at (p<. .05), BMI= Body Mass Index, ASA= American Society of Anesthesiologist physical status classification, NS= Not Statistically Significant (p> .05)

DISCUSSION

Discussion of Study Results

The purpose of this study was to determine if there was an association between taking ACE inhibitors the morning before surgery and increased total doses of vasopressor medications, lower systolic blood pressures, or lower diastolic blood pressures during surgery for PLIF. The hypotheses predicted that those who took ACE inhibitors would require more doses of vasopressor medications, ephedrine or phenylephrine, have lower systolic blood pressures, and have lower diastolic blood pressures. Phenylephrine and ephedrine have two different mechanisms of action, so linear regressions were performed to compare total phenylephrine and ephedrine doses to demographic factors age, gender, BMI, and ASA physical status. The researcher wanted to have equal groups of those who took ACE inhibitors before surgery for PLIF and those who did not, therefore, 100 patients from each group were chosen.

The results of Chi-square and Independent t-tests showed there were not statistically significant mean difference in age, BMI, gender, or ASA physical status between the two groups (Table 1). T-tests demonstrated no statistically significant mean difference in total ephedrine doses, total phenylephrine doses, lowest systolic blood pressure, or lowest diastolic blood pressure (Table 2). These findings do not support the hypotheses.

The results did not show an association between ACE inhibitor consumption before surgery and increased total vasopressors doses, lowest systolic blood pressures, or lowest diastolic blood pressures. These findings are inconsistent with the conclusions of a study done by Comfere et al. (2005). These scholars found during the first 30 minutes after anesthetic induction that 60% of those who continued ACE inhibitors (<10 hours)

compared to 46% who stopped ACE inhibitors experienced hypotension more frequently (p=0.02). The authors found that there was no significant difference (p<0.05) in vasopressor administration between groups, which was consistent with the results of this study.

A retrospective study conducted by Trentman et al. (2011) found that patients taking antihypertensive medications, including ACE inhibitors, had more intraoperative hypotensive episodes and vasopressor administrations (p=0.01). The researchers concluded that preoperative use (<10 hours) of antihypertensive medications was associated with an increased incidence of intraoperative hypotension and require more vasopressor medications to maintain normal blood pressure. These results were inconsistent with the present study. An international prospective cohort study by Roshanov et al. (2017) also found that patients who withheld ACE inhibitors/ARB's 24 hours before surgery were less likely to suffer from intraoperative hypotension. The results of the present study could be explained by the study's relatively small sample size, presence of only one hospital system, and the retrospective design.

Study Limitations

There were many limitations identified in this study. The retrospective, case-control design limits findings to only associations and could result in inaccurate documentation or researcher bias (Schulz & Grimes, 2002). Blood pressure was only documented every 5 minutes on the anesthesia record so that the recorded blood pressures may not have been the lowest blood pressure during the procedure. All patients involved in this study were within the CAMC network and may not represent the overall population.

The retrospective design of this study allowed for the use of various anesthetic techniques that had different impacts on blood pressure. The study did not account for any medications that could negatively impact blood pressure, such as opioid infusions, diuretics, angiotensin II receptor blockers, beta-receptor antagonists, or calcium channel antagonists. Multiple patients were treated for hypotension after receiving sufenta continuous IV drips. The study was limited to patients who only received phenylephrine or ephedrine for hypotensive treatment and did not account for those who received crystalloid fluid bolus or vasopressin administration. The use of crystalloid's and/or vasopressin could decrease the amount of phenylephrine and ephedrine used to treat hypotension. Several patients also received phenylephrine IV continuous infusions for hypotension and total micrograms were not recorded, so those cases could not be converted into 100 microgram doses.

CONCLUSION

In this study, the use of ACE inhibitors the morning of surgery was not associated with more doses of vasopressor medications, lower systolic blood pressure, or lower diastolic blood pressure in patients undergoing PLIF.

IMPLICATIONS AND RECOMMENDATIONS

This study provided clinical relevance to anesthesia practitioners, researchers, and physicians about the use of ACE inhibitors for patients undergoing PLIF. Knowledge of ACE inhibitors and their effects help the anesthesia provider customize the anesthetic to optimize patient safety. This research did not support the association that patients who took ACE inhibitors the morning of surgery for PLIF would require more doses of vasopressor medications, have lower systolic blood pressure, or lower diastolic blood

pressures. Studies have proven an association between preoperative ACE inhibitor use and lower intraoperative blood pressure, greater vasopressor administration, and those who withheld ACE inhibitors were less likely to suffer death, stroke, or myocardial infarction. For this reason, anesthesia providers should consider these findings before continuing an anesthetic for patients undergoing PLIF. Due to the limited studies on preoperative use of ACE inhibitor and PLIF further research should be done to confirm these results and provide clear recommendations on ACE inhibitors and PLIF. New research should be continued on preoperative ACE inhibitor use and perioperative blood pressure for PLIF and other related procedures. Additionally, research using a randomized, prospective study should be implemented that could control factors such as anesthetic technique, other vasopressor medications, timing of ACE inhibitor consumption, and continuous IV vasopressors.

REFERENCES

American Society of Anesthesiologists. (2014). *ASA physical status classification system*.

Retrieved May 25, 2017. from https://www.asahq.org/resources/clinical-

information/asa-physical-status-classification-system

Arora, P., Rajagopalam, S., Ranjan, R., Kolli, H., Singh, M., Venuto, R., & Lohr, J.

(2008). Preoperative Use of Angiotensin-Converting Enzyme

Inhibitors/Angiotensin Receptor Blockers Is Associated with Increased Risk for

Acute Kidney Injury after Cardiovascular Surgery. *Clinical Journal of the*

American Society of Nephrology, 3(5), 1266-1273. doi:10.2215/CJN.05271107

Auron, M., Harte, B., Kumar, A., & Michota, F. (2010). Renineangiotensin system

antagonists in the perioperative setting: clinical consequences and

recommendations for practice. *Postgraduate Medical Journal*, 87(1029) 1-10.

Centers for Disease Control and Prevention [CDC]. (2015). *About BMI for adults*.

Retrieved August 30, 2017, from

https://www.cdc.gov/healthyweight/assessing/bmi/index.html

Charleston Area Medical Center [CAMC], (2017a). *CAMC Hospitals.* Retrieved

September 12, 2017. from http://camc.org/Hospitals

Chopra, S., Baby, C., & Jacob, J. J. (2011). Neuro-endocrine regulation of blood pressure.

Indian Journal of Endocrinology and Metabolism, *15*(Suppl4), 281–288.

http://doi.org/10.4103/2230-8210.86860

Comfere, T., Sprung, J., Kumar, M. M., Draper, M., Wilson, D. P., Williams, B. A., et al.

(2005). Angiotensin System Inhibitors in a General Surgical Population.

Anesthesia & Analgesia, 100 (3), 636-644.

doi:10.1213/01.ANE.0000146521.68059.A1

Fleisher, L. A., & Fleishmann, K. E. (2014). 2014 ACC/AHA Guideline on Perioperative

Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac

Surgery: Executive Summary. 64 (22) 2373-2404. *Journal of the American*

College of Cardiology. doi:10.1016/j.jacc.2014.07.945

Hedman, K., Mann, C. L., Spulecki, C., & Castner, J. (2016). Low-Dose Vasopressin and

Analogues to Treat Intraoperative Refractory Hypotension in Patients Prescribed

Angiotensin-Converting Enzyme Inhibitors Undergoing General Anesthesia: A

Systematic Review. *American Association of Nurse Anesthesits, 84*(6), 413-419.

Helal, F., & Lane, M. E. (2014). Transdermal delivery of angiotensin converting enzyme

inhibitors. *European Journal of Pharmaceutics and Biopharmaceutics,* 88 (1), 1-

7. doi:10.1016/j.ejpb.2014.03.007

Hosseinian, L., Weiner, M., Levin, M. A., & Fischer, G. W. (2016). Methylene Blue:

Magic Bullet for Vasoplegia. *Anesthesia & Analgesia,* 122

(1), 194-201. doi:10.1213/ANE.0000000000001045

Lonjaret, L., Lairez, O., Minville, V., & Geeraerts, T. (2014). Optimal perioperative

management of arterial blood pressure. *Integrated Blood Pressure Control*, *7*, 49–

59. http://doi.org/10.2147/IBPC.S45292

Lehman, L.-w., Saeed, M., Moody, G., & Mark, R. (2010). Hypotension as a Risk Factor

for Acute Kidney Injury in ICU Patients. *Computing in cardiology,* 37 (1), 1095-

1098.

Ma, T. K., Kam, K. K., Yan, B. P., & Lam, Y.-Y. (2010). Renin–angiotensin–aldosterone

system blockade for cardiovascular diseases: current status. *British Journal of Pharmacology*, *160*(6), 1273–1292. http://doi.org/10.1111/j.1476-5381.2010.00750.x

McKesson Corporation. (2017). *Hospital Information Systems.* Retrieved August 20, 2017 from

http://www.mckesson.com/en_us/McKesson.com/For%2BHealthcare%2BProvide rs/Hospitals/Hospital%2BInformation%2BSystems/Hospital%2BInformation%2B Systems.html

Nagelhout, J. J., & Plaus, K. L. (2014). Nurse Anesthesia (5th ed.). St. Louis, MO: Elsevier Saunders.

Pierce, V., & Kendrick, P. (2010). Ischemic Optic Neuropathy After Spine Surgery. *American Association of Nurse Anesthesitis, 78*(2), 141-145. Retrived from www.aana.com/aanajournalonline.aspx

Pilote, L., Abrahamowicz, M., Eisenberg, M., Humphries, K., Behlouli, H., & Tu, J. V. (2008). Effect of different angiotensin-converting-enzyme inhibitors on mortality among elderly patients with congestive heart failure. *CMAJ : Canadian Medical Association Journal*, *178*(10), 1303–1311. http://doi.org/10.1503/cmaj.060068

Rajgopal, R., Rajan, S., Sapru, K., & Paul, J. (2014). Effect of pre-operative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists on intra-operative arterial pressures after induction of general anesthesia. *Anesthesia: Essays and Researches, 8*(1), 32-35. doi:10.4103/0259-1162.128903

Roshanov, P. S., Rochwerg, B., Patel, A., Salehian, O., Duceppe, E., Belley-Cote, E., et al. (2017). Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery. *Anesthesiology,* 126 (1), 16-27.

Schulte, E., Ziefler, D., Philippi-Hohne, C., Kaczmarczyk, G., & Boemke, W. (2011). Angiotensin-converting enzyme inhibition and blood pressure response during total intravenous anaesthesia for minor surgery. *Acta Anaesthesiologica Scandinavica,* 55 (4). doi:10.1111/j.1399-6576.2011.02409.x

Schulz, K., & Grimes, D. (2002). Case-control studies: research in reverse. *Lancet, 359* (9304), 431-434.

Smith, I. & Jackson, I. (2010). Beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers: should they be stopped or not before ambulatory anaesthesia. *Current Opinion in Anaesthesiology,* 23 (6), 687-690. doi:10.1097/ACO.0b013e32833eeb19

SPSS IBM Company. (2017). *SPSS Statistics 22*. Retrieved August 2017 from http://www-01.ibm.com/software/analytics/spss/?source=homepage&hpzone=nav_bar.

Takahashi, T., Hanakita, J., Ohtake, Y., Funakoshi, Y., Oichi, Y., Kawaoka, T., & Watanabe, M. (2016). Current Status of Lumbar Interbody Fusion for Degenerative Spondylolisthesis. *Neurologia Medico-Chirurgica*, *56*(8), 476–484. http://doi.org/10.2176/nmc.ra.2015-0350

Thoma, A. (2013). Pathophysiology and Management of Angiotensin- Converting

    Enzyme Inhibitor–Associated Refrac- tory Hypotension During the Perioperative

    Period. *America Association of Nurse Anesthesia, 81*(2), 133-140.

Trentman, T. L., Fassett, S. L., Thomas, J. K., Noble, B. N., Renfree, K. J., & Hattrup, S.

    J. (2011). More hypotension in patients taking antihypertensives preoperatively

    during shoulder surgery in the beach chair position. *Canadian Anesthesiologists'*

    Society, 58(11), 993-1000. doi:10.1007/s12630-011-9575-6

Trotter, J. (2012). Catecholamine-Resistant Hypotension Following Induction for Spinal

    Exploration *American Association of Nurse Anesthestis, 80*(1), 55-60.

Twersky, R. S., Goel, V., Narayan, P., & Weedon, J. (2014). The risk of hypertension

    after preoperative discontinuation of angiotensin-converting enzyme inhibitors or

    angiotensin receptor antagonists in ambulatory and same-day admission patients.

    Anesthesia & Analgesia, 118(5), 938-944. doi:10.1213/ANE.0000000000000076

Vijay, A., Grover, A., Coulson, T. G., & Myles, P. S. (2016). Perioperative management

    of patients treated with angiotensin-converting enzyme inhibitors and angiotensin

    II receptor blockers: a quality improvement audit. *Anaesthesia & Intensive Care,*

    44(3), 346-352.

APPENDIX A: DATA COLLECTION TOOL 1

Patient Study Number	Patient Identification Number
1	
2	
3	
4	
…	
200	

APPENDIX B: DATA COLLECTION TOOL

Study number	Age (yrs)	Gender Male= 1 Female= 0	ASA Physical Status (I-IV)	Weight (KG)	BMI Kg/m2	Lowest systolic BP (mmHg)	Lowest diastolic BP (mmHg)	Vasopressor administration (mg)
1								
2								
3								
4								
…								
200								

New study by expedited review: Approved

CAMC INSTITUTE

August 01, 2017

School of Nurse Anesthesia
3110 MacCorkle Avenue, SE
Charleston, WV 25304

RE: Initial Review Submission Packet 07/18/2017 10:15:39 AM EDT regarding study number 17-362
DOES PERIOPERATIVE ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITOR THERAPY CORRELATE WITH INCREASED USE OF VASOPRESSORS DURING POSTERIOR LUMBAR INTERBODY FUSION VERSUS THOSE NOT RECIEVING ACE INHIBITOR THERAPY

Dear Priscilla Walkup:

Your request for expedited approval of the new study listed above has been reviewed. This type of study qualifies for expedited review under FDA and DHHS (OHRP) regulations.

This is to confirm that your application is approved. The following items are approved:

1. Protocol Version 1 - 7/17/17

Submission Components			
Form Name	Version		Outcome
Study Document			
Title	Version #	Version Date	Outcome
Walkup COI	Version 1.0	07/18/2017	Approved
Ross COI	Version 1.0	07/17/2017	Approved
Protocol	Version 1.0	07/17/2017	Approved

The accrual goal is 200. You must submit a request to the IRB to increase enrollment beyond the approved accrual goal.

You are granted permission to conduct your study as described effective immediately. The study is subject to continuing review on or before 07/31/2018, unless closed before that date.

3110 MacCorkle Ave. SE, Room 3283   Charleston, WV 25304   (304) 388-9970 Fax (304) 388-9976

Please note that any changes to the study as approved must be promptly reported and approved prior to implementation. Some changes may be approved by expedited review; others require full board review.

Also, serious and/or unanticipated adverse events must also be reported as required by law and in accordance with CAMC/WVU Charleston Division IRB policies. Contact CAMC / WVU Charleston Division IRB at (304) 388-9973 or email michael.whitler@camc.org or april.white@camc.org if you have any questions or require further information.

Sincerely,

Atul Singh, DO
Vice-Chair, CAMC/WVU IRB