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An Educational Module Highlighting the Efficacy of Intravenous Ascorbic Acid in Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery: A Quality Improvement Project

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Abstract

Background: Tourniquets are often used in orthopedic surgery because empirical data suggests that they significantly reduce blood loss and transfusion requirements, facilitate the identification of critical anatomical structures, and provide an optimum operating field. In ischemic limbs, tourniquet inflation increases arterial pressures and results in hypoxia, acidosis, and hyperkalemia.[1-3] When a tourniquet is removed, metabolites produced from ischemic areas enter the systemic circulation, resulting in hypotension and hypoxia. Excessive oxygen-free radicals are produced during reperfusion and oxygenation, contributing to leucocytic activation and endothelial damage in blood vessels.[2,4] The excess oxygen-free radicals peroxide polyunsaturated fatty acids in membrane and plasma lipoproteins and directly inhibit mitochondrial respiratory chain enzymes, affecting major organ functions. As a result, oxygen-free radicals play a crucial role in developing significant cardiovascular complications following reperfusion injury.[1-4] These complications are especially problematic in patients with pre-existing cardiovascular disease undergoing orthopedic procedures such as total knee replacement (TKR) with tourniquet application. [5,6]

Methods: An extensive search of CINAHL and MEDLINE (ProQuest) databases was undertaken to acquire research articles evaluating the efficacy of perioperative intravenous vitamin C in minimizing hemodynamic fluctuations caused by tourniquet-induced ischemic-reperfusion damage.

Results*:* Four studies were identified as potentially relevant for analysis. The research covered in this review addresses the mechanisms behind tourniquet-induced ischemic-reperfusion damage and the efficacy of perioperative intravenous vitamin C in reducing hemodynamic fluctuations and improving patient outcomes.

Keywords: tourniquet-induced ischemic reperfusion injury, orthopedic surgery, intravenous administration of ascorbic acid, hemodynamic fluctuations.

Purpose/PICO Clinical Questions/Objectives

PICO Question or Purpose

Population (P): In anesthesia providers

Intervention (I): Will an education module on perioperative administration of intravenous ascorbic acid

Compare (C): In comparison to no education.

Outcomes (O): Increase knowledge and implementation of intravenous ascorbic acid perioperative administration to attenuate tourniquet-induced hemodynamic fluctuations.

Introduction

Problem Identification

Pneumatic tourniquets are an essential part of several orthopedic surgical procedures involving the lower limbs.[1-3] The use of the tourniquet drastically decreases blood loss and transfusion needs, enhances visualization of critical anatomical structures, and creates an adequate surgical field.[4] While appearing to be beneficial, the use of pneumatic tourniquets in adults undergoing orthopedic surgery has been associated with an increased risk of wound hematoma, Deep Vein Thrombosis (DVT), Myocardial Infarction (MI), Pulmonary Embolism (PE), and excessive oxidative stress caused by ischemic reperfusion injury to the vascular endothelium.[2-4] The processes underlying tourniquet-induced Ischemic-Reperfusion Injury (IRI) have been related to oxidative endothelial cell toxicity caused by the immense release of Reactive Oxygen Species (ROS) following tourniquet usage.[1-5] When ischemic tissues are re-perfused, significant quantities of ROS results in impairment of membrane lipids, proteins, and DNA, ensuing in necrosis and apoptotic cell death leading to organ malfunction.[1-3] The dysfunction of endothelium causes hypotension by impairing the response to endothelial-dependent vasodilators and vasoconstrictors. Additionally, the failure of the endothelium barrier leads to consequent leakage of plasma fluid from the vasculature, resulting in edema, hypovolemia, and hypotension.[4-7] Edema to the organs exacerbates the difficulty of gas exchange and oxygenation in the lungs, leading to numerous organ failures.

Recent research has indicated that ischemia/reperfusion damage caused by oxygen exposure is related to an increased risk of arrhythmias, heart failure, cardiogenic shock, and long-term mortality.[1-3,7-9] Regardless of the advancements in the knowledge of the processes underlying ischemia-reperfusion injury, evidence-based attenuation of ischemic injury has been uneven and varied, particularly in terms of patient outcomes. Due to the lack of empirical information addressing the prevention of tourniquet-induced ischemia-reperfusion damage, anesthesia providers must study and create objective, evidence-based clinical implications that may serve as a starting point for subsequent practice change implementation.[1-2,5,9-11] The purpose of this research is to increase clinicians' understanding of perioperative intravenous ascorbic acid as an additional therapy to reduce blood pressure fluctuations, myocardial damage, and arrhythmias and enhance microcirculation and neurological patient outcomes.[8]

Background

Tourniquets are often used in orthopedic surgery because empirical evidence indicates that they considerably minimize blood loss and transfusion needs, enhance identification of vital anatomical structures, and allow for an optimal operative field.[4] Tourniquet inflation elevates arterial pressures and induces hypoxia, acidosis, and hyperkalemia in ischemic limbs. When a tourniquet is deflated, metabolites released from ischemic regions reach the systemic circulation cause hypotension and hypoxia. As a result of reperfusion and oxygenation, an excessive amount of oxygen free radicals is generated, resulting in leucocytic activation and endothelial damage in blood vessels.[4] Excessive oxygen-free radicals peroxidize polyunsaturated fatty acids in membrane and plasma lipoproteins and directly block mitochondrial respiratory chain enzymes, impairing major organ function. Consequently, oxygen-free radicals are critical in developing severe cardiovascular problems following reperfusion damage.[4] These consequences are particularly concerning in patients with pre-existing cardiovascular comorbidities and orthopedic operations such as total knee replacement (TKR) with tourniquet application.[5,6,11-16]

Although the pneumatic tourniquet is a crucial component of many orthopedic surgical procedures involving the lower limbs to control intraoperative bleeding and clear the surgical area, prolonged use of tourniquets may increase the likelihood of adverse events.[2] Even though the use of pneumatic tourniquets for orthopedic surgery may seem beneficial, it has been linked with increased incidences of Myocardial Infarction (MI), Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), Cerebral Vascular Accident (CVA), multisystem organ dysfunction, and increased post-operative rates of morbidity and mortality.[2-5,11-14]

Scope of the Problem

A patient may require lower extremity orthopedic surgery for various reasons, including a pre-existing musculoskeletal disease, an acute traumatic incident, or most commonly, osteoarthritis. In the United States, osteoarthritis (OA) of the knee is the primary cause of hospitalization for individuals aged 45–84 years, accounting for 60% of adults over 65. Total Knee Arthroplasty (TKA) successfully treats persistent knee discomfort caused by osteoarthritis. A recent survey of Medicare beneficiaries concluded that OA is the primary diagnosis for 94 percent of all patients undergoing TKA in the United States. In 2008, the United States conducted over 650,000 TKAs at the cost of $9 billion. This financial load will only rise in relevance as the geriatric population grows. Furthermore, the number of TKAs conducted yearly in the United States will reach 3.5 million by 2030. Thus, optimizing TKA performance is critical for both qualities of treatment and cost reduction. [3,6]

According to a 2009 survey, 95% of orthopedic surgeons use a tourniquet on patients who have been cleared of vascular disease. Despite TKA's remarkable effectiveness in relieving knee pain caused by OA, post-operative recovery is sometimes hampered by complications related to tourniquet usage. Studies indicate that ischemia followed by reperfusion caused by tourniquet usage may have clinically significant consequences.[1-3,7-9] Tourniquet-induced IRI can manifest itself in regional skeletal muscle, systemic circulation, and even remote organs, all of which can be potentially detrimental to patients.[3,6]

Consequences of the Problem

The processes underlying tourniquet-induced ischemic-reperfusion damage have been related to the enormous oxidative endothelial cell toxicity that occurs due to the tourniquet's massive release of reactive oxygen species.[1-3,7-9] When large concentrations of ROS are introduced during reperfusion, they can cause reversible or permanent injury to proteins, lipids, and nucleic acids, resulting in endothelial dysfunction, cellular injury, and various organ failure.[1-3,7-9] Endothelial dysfunction is a common ROS-mediated complication of ischemia/reperfusion injury and sepsis. Additionally, ROS-induced damage to the glycocalyx, cellular membranes, and junctions results in increased permeability, leukocyte and platelet adhesion, local promotion of inflammation and coagulation, loss of endothelial vasodilation, and attenuation of the vascular response to vasoconstrictors.[1-4,7-9] Subsequent hypotension, vascular leakage, and microcirculatory flow degradation after reperfusion exacerbate tissue hypoxia due to the increased oxygen diffusion distance, therefore accelerating cellular damage and organ failure.[11-17]

Knowledge Gaps

Despite significant advances in scientific understanding of the processes behind the ischemia-reperfusion injury, the translation of research for attenuating tourniquet-induced ischemic injury into clinical practice has been uneven and varied, particularly concerning patient outcomes. Current research indicates that intravenous ascorbic acid treatment during surgery as an additional therapy reduces the occurrence of fluctuations in blood pressure, arrhythmias caused by damage to the myocardium and improve microcirculation and neurological outcomes.[8,10,16] According to the literature, administration of vitamin C intraoperatively could help avoid and restore microcirculatory flow impairment by preventing the activation of nicotinamide adenine dinucleotide phosphate-oxidase and inducible nitric oxide synthase, modulation of tetrahydrobiopterin, inhibiting oxidative phosphorylation uncoupling, and reducing superoxide and peroxynitrite development.[10,11] Additionally, by maintaining cyclic guanylate phosphatase, IV ascorbic acid can restore vascular reactivity to vasoconstrictors and retain the endothelium barrier.[10-12] Vitamin C's possible function in IRI caused by tourniquet usage is also strengthened by data from burns, sepsis, and cardiac studies, which demonstrate quicker healing from organ dysfunction and improved survival rates.[11-15,17]

Proposal Solution

Despite literature demonstrating positive outcomes, there is a lack of consensus in published guidelines regarding the perioperative administration of intravenous ascorbic acid as a systematic strategy for mitigating hemodynamic changes related to IRI induced by tourniquet use.[1-3,6] Owing to the lack of empirical information addressing the prevention of tourniquet-induced ischemia-reperfusion damage, anesthesia providers must study and create objective, evidence-based clinical implications that may serve as a framework for future practice change implementation.[1-3,6] By educating anesthesia providers about the value and efficacy of perioperative intravenous ascorbic acid administration, the project proposed may assist as a step towards instituting objective, evidence-based clinical suggestions for lowering the adverse outcomes associated with tourniquet-induced ischemic-reperfusion injury.

Rationale

Despite considerable advancements in the scientific evidence of the mechanisms behind the ischemia-reperfusion injury, translation of research into clinical practice for attenuating tourniquet-induced ischemic injury has been uneven and inconsistent, particularly concerning patient outcomes. Available literature suggests that administering intravenous ascorbic acid during surgery as an adjunctive therapy lowers the occurrence of blood pressure variations and arrhythmias caused by myocardial injury while also enhancing microcirculation and neurological outcomes.[8,10-12]

According to the literature, intraoperative vitamin C administration may help prevent and restore microcirculatory flow impairment by inhibiting nicotinamide adenine dinucleotide phosphate-oxidase and inducible nitric oxide synthase activation, modulating tetrahydrobiopterin, inhibiting oxidative phosphorylation uncoupling, and reducing superoxide and peroxynitrite formation.[10,11] Additionally, IV ascorbic acid can restore vascular responsiveness to vasoconstrictors and preserve the endothelial barrier by sustaining cyclic guanylate phosphatase.[10-12]

Intravenous Vitamin C's potential role in IRI induced by tourniquet use is further supported by data from burns, sepsis, and cardiac research, which indicate faster organ dysfunction repair and higher survival rates.[11-15] Despite favorable outcomes, there is a scarcity of published consensus guidelines addressing intravenous ascorbic acid as a standard strategy for mitigating hemodynamic shifts associated with IRI produced by tourniquet usage.[1-7] By educating anesthesia providers about the value and efficacy of perioperative intravenous ascorbic acid administration, the proposed project may pave the way for implementing objective, evidence-based clinical recommendations to reduce the adverse outcomes associated with tourniquet-induced ischemic-reperfusion injury.[11-17]

Objective

This literature review first aims to investigate available evidence and evaluate each study's findings on the efficacy of ascorbic acid administration in preventing tourniquet-induced oxidative injury in patients undergoing lower limb orthopedic surgery. Secondly, this review intends to enhance the knowledge of anesthesia providers regarding the antioxidant effects of ascorbic acid to prevent adverse hemodynamic effects associated with tourniquet-induced ischemic reperfusion injury of vascular endothelium. Such adverse effects include hypotension, metabolic acidosis, arrhythmias, progression of atherosclerotic lesions, plaque instability, and subsequent myocardial infarction or stroke. Finally, the third objective is to increase the implementation of perioperative administration of intravenous ascorbic acid to attenuate tourniquet-induced hemodynamic fluctuations and improve patient outcomes.

Methodology

Eligibility Criteria

The studies evaluated for this literature review were chosen based on the inclusion and exclusion criteria set to discern the objectives best. Inclusion criteria included research studies involving human participants published in peer-reviewed journals. The studies were excluded if they were retrospective studies, descriptive articles, editorials, or case reports. Database sources used for the research were accessed via Florida International University (FIU) library services.

Based on the clinical question, the following search keywords were identified using the appropriate Boolean operators and search symbols: tourniquet-induced ischemic reperfusion injury, ischemia-reperfusion damage, coronary artery disease, orthopedic surgery, intravenous administration of ascorbic acid, vitamin C, hemodynamic fluctuations.

Information Sources

The databases utilized for the search included Excerpta Medica Database (EMBASE), The Cumulative Index to Nursing and Allied Health Literature (CINAHL), and MEDLINE (ProQuest). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) further guided the literature review.

Search Strategy

With the assistance of the FIU Health Science Librarian, the key search terms were further expanded to include: (Tourniquet-induced ischemic reperfusion injury * OR Ischemia-reperfusion damage * OR Endothelium Injury*) AND (Ascorbic Acid* OR Vitamin C*) AND (Perioperative* OR Intraoperative* OR Preoperative*) AND (Intravenous* OR "IV") AND (Orthopedic Surgery*) AND (Lower Extremity* OR Extremity *) AND (Hemodynamic fluctuations OR "Hypotension").

Study Selection

The initial search through database searching (CINHAL, EMBASE, and MEDLINE) yielded 112 articles. There were 21 duplicate articles that were removed, leaving 91 total articles for further review. Titles were further excluded if they did not meet inclusion criteria. For example, articles that included studies not based on human participants, retrospective studies, descriptive articles, editorials, case reports, questionnaires. An additional 75 articles were removed. The remaining 16 articles were retrieved and sent to the citation database Covidence for review. Sixteen articles were reviewed and approved for a full review of the abstract. Of the sixteen articles, ten articles met the criteria and were further analyzed by reading the full text. Articles that were removed included those that did not meet intervention or outcome requirements. Only the articles that met the highest level of research were chosen, leaving four articles for summarization.

Study Characteristics

The four articles chosen for this literature review analyzed the effects of perioperative administration of ascorbic acid on hemodynamics in patients having orthopedic surgeries. The study by authors Mohamed et al. (2016) investigated the comparative effectiveness of ascorbic acid to other pharmacologic interventions.[7] The purpose of this comparison was to evaluate which pharmacologic intervention proved to be most effective in reducing the effects of tourniquet-induced ischemic reperfusion injury during lower limb surgery. The study by Lee et al. (2010) examined the effects of high doses of vitamin C on myocardial enzymes and oxygen-free radical production after tourniquet ischemic reperfusion injury during bilateral total knee replacement.[4] Another study by Kim et al. (2008) investigates vitamin C's effect on hemodynamics and arterial blood gas during unilateral total knee replacement. The focus of their study was to evaluate the cytoprotective effects of vitamin C by reducing free radicals.[8] The remaining study by Behrend et al. (2019) examined the relationship between vitamin C levels and total knee arthroplasty. The authors examined the association between perioperative vitamin C supplementation and overall functional outcomes after total knee arthroplasty.[5] All of the studies were primarily focused on the perioperative implantation of vitamin C in patients undergoing orthopedic surgeries that required the use of tourniquets on the lower extremities.

Additionally, all four of the studies selected for this literature review were randomized controlled trials that ensure the most substantial evidence level.[4-5,7-8]

Summary of the Literature

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Author(s)	Purpose	Methodology/ Research Design	Intervention(s)/ Measures	Sampling/Setting	Primary Results	Relevant Conclusions
Kim et al., (2008).[8]	To investigate the effect of vitamin C on hemodynamics and arterial blood gas during unilateral total knee replacement.[8]	Randomized Controlled Trial (RCT) Level I Quality B.[8]	In the vitamin C group, patients were administrated with vitamin C: a priming bolus of vitamin C 0.06 g/kg mixed with 100 ml saline infused for 20 min at 10 min before deflation of tourniquet, followed by vitamin C 0.02 g/kg mixed with 30 ml saline at 0.5 ml/min. In the control group, patients were infused with 100 ml saline.[8]	Mean arterial blood pressure, heart rate, and arterial blood gas were measured at 20 min after anesthesia induction, just before deflation, 5 min after deflation, and 20 min after deflation of tourniquet.[8] Sample sizes for the VC group: N = 19, and control group: N = 15.[8]	Mean arterial blood pressure in the VC group was maintained higher than the control group at 1 min after deflation of the tourniquet. Arterial O2 tension and saturation in the VC group were higher than the control group at 5 min and 20 min after deflation of the tourniquet.[8]	The study concluded that the administration of vitamin C during total knee replacement could significantly inhibit the decline of mean arterial blood pressure and arterial oxygenation induced by ischemia-reperfusion.[8]
Lee et al., (2018).[4]	To investigate the effects of high-dose vitamin C on oxygen free radical production and cardiac enzymes after tourniquet application and ischemia-reperfusion injury during bilateral total knee replacement	Randomized, double-blinded, placebo-controlled clinical trial. Level I Quality A.[4]	In the vitamin C (VC) group during surgery, patients received a priming bolus of 0.06 g/kg vitamin C with 100 ml saline followed by 0.02 g/kg vitamin C mixed with 30 ml saline intravenously. The control group received no intra-operative vitamin C.[4] Blood samples for arterial blood gas and	Patients aged 65 – 75 years who underwent bilateral TKR in hospital settings between June 2008 and July 2009 were randomly enrolled in this study. Patients included in the study had to have American Society of Anesthesiologists physical status I or II and were randomly assigned either to receive intraoperative high-dose	In the VC group, malondialdehyde levels were lower, and arterial oxygen tension and mean blood pressure were higher than in controls after post-operative deflation of both knee tourniquets. Troponin I levels were lower in the VC group than in controls eighth hours postoperatively.[4]	Administering high-dose vitamin C during bilateral TKR prevents oxygen-free radical production and a decline in arterial oxygen tension and mean blood pressure induced by ischemia-reperfusion injury, thereby protecting the myocardium.[4]

	(TKR) in elderly patients.[4]		MDA analysis were obtained at the following time points: 20 min after the induction of anesthesia; prior to deflation of the first and second tourniquets; at 5 min after deflation of the first and second tourniquets; and at 20 min after deflation of the first and second tourniquets. Mean arterial pressure and heart rate, as well as arterial oxygen tension (PaO2), arterial carbon dioxide tension (PaCO2), and oxygen saturation levels of the cardiac enzymes creatine phosphokinase-myocardial band (CPK-MB) and troponin I was measured at 20 min following anesthetic induction.[4]	vitamin C (VC group) or not to receive vitamin C (control group). In total, 32 patients were enrolled in the study: 16 in the VC group and 16 in the control group.[4]		
Mohamed et al. (2016).[7]	To investigate and compare the effects of perioperative	Randomized, double-blinded, placebo-controlled	A total of 60 patients scheduled for unilateral lower extremity surgery with a	Sixty patients ASA physical status I or II, aged 25–45 years, scheduled for unilateral	Levels of MDA, IL-6, and IL-8 were significantly increased in group C after	Findings concluded that both N-acetyl cysteine and ascorbic acid reduce post-

	intravenous infusion of N-acetyl cysteine and ascorbic acid on malondialdehyde (MDA) production as a marker of oxidative stress and IL-6 and IL-8 as markers of systemic inflammation after ischemic-reperfusion as primary ` outcomes. Both agents were compared regarding post-deflation hemodynamic effects and post-deflation changes in arterial pH and lactic acid as secondary outcomes.[7]	clinical trial. Level I Quality B.[7]	pneumatic tourniquet were included. Baseline collection of blood samples was done, and then patients were randomly classified into three groups: Group A; received 1 g Ascorbic acid, group N; received 10 mg/kg NAC and group C (control group): received 100 ml saline infusion. Two blood samples were drawn at each assessment time. One sample for arterial blood pH and lactic acid measurement and the other blood sample was centrifuged and stored at −20 °C for subsequent analysis of MDA, IL-6, and IL-8.[7]	lower extremity surgery with a pneumatic tourniquet for 60–90 min, were included in this study. With each group: N = 20.[7]	tourniquet release compared with the baseline. In groups A and N, MDA did not increase over baseline values, but IL-6 and IL-8 levels were increased, and their levels were significantly less than in the control group. Changes in hemodynamics, pH, and serum lactate were more evident in group C than groups A and N.[7]	deflation increase in blood levels of oxidative stress markers and markers of systemic inflammation. Thus, both are beneficial in preventing post-tourniquet deflation ischemic reperfusion injury in lower limb surgery.[7]
Behrend et al., (2019).[5]	To determine whether perioperative supplementation of vitamin C (VC) improves range of	Single-center, double-blind, randomized, placebo-controlled	Ninety-five patients undergoing TKA were randomized to either Vitamin C (VC) administration or placebo (48 VC group,	Ninety-five patients aged ≥ 18 years undergoing TKA for advanced knee osteoarthritis (grade 3 or 4 osteoarthritides according to Kellgren–	ROM at one year was not different between study groups. The prevalence of AF was 5 of 48 (10.4%) in the VC group compared to	The study concluded that TKA results in VC depletion. Perioperative VC supplementation prevents VC

	motion (ROM) and reduces the risk of arthrofibrosis (AF) following total knee arthroplasty (TKA).[5]	study. Level I Quality B.[5]	47 placebo group). The effect of VC supplementation was tested on ROM, AF, WOMAC, FJS-12, and VC plasma concentrations. VC concentrations were analyzed in both patient groups before surgery, 4 and 7 days after surgery.[5]	Lawrence) were recruited. 48= VC group, 47 =placebo group.[5]	11 of 47 (23.4%) in the placebo group ($p = 0.09$). VC concentrations decreased post-operatively in the placebo group (49–12 µmol/l on day 7, $p < 0.001$) but not in the VC group (53–57 µmol/l). Patients with a perioperative drop of VC concentrations ≥ 30 µmol/l developed significantly more AF at one year than patients with VC concentrations drop of < 30 µmol/l ($p = 0.007$).[5]	concentrations drop in most patients undergoing TKA and may lower the incidence of AF. The clinical relevance of this study is that VC supplementation seems to be a cheap and safe adjunct to improve functional outcomes after TKA.[5]

Systematic Review

In the study by Kim et al. (2008), the authors wanted to investigate the effect of vitamin C on hemodynamics and arterial blood gas during unilateral total knee replacement.[8] The authors designed the study to evaluate several parameters: blood pressure, mean arterial pressure, arterial oxygen partial pressure, and oxygen saturation.[8] The patients were randomly divided into the vitamin C group and a controlled group. In the vitamin C group (VC group: N = 19), patients were administrated a priming bolus of vitamin C 0.06 g/kg mixed with 100 ml saline infused for 20 min at 10 min before deflation of tourniquet, followed by vitamin C 0.02 g/kg mixed with 30 ml saline at 0.5 ml/min. In the control group (control group: N = 15), patients were infused with 100 ml saline.[8] The authors excluded patients who were pharmacotherapies such as beta-blockers and vasodilators. Patients with a history of previous myocardial infarction and kidney or ureter stones were also excluded from this study. To ensure the most consistent analysis of parameters, the mean arterial blood pressure, heart rate, and arterial blood gas were measured at 20 min after anesthesia induction, just before deflation, 5 min after deflation, and 20 min after deflation of tourniquet.[8]

All statistical analyses were performed using the SPSS® statistical package, version 14.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Data are shown as mean ± SD. Differences in demographics and baseline clinical characteristics between the two groups, including age, weight, hypertension, and hemoglobin level, were analyzed using the Student's t-test.[8] Between-group differences in arterial blood gas and hemodynamic profiles were analyzed using a repeated measure analysis of variance (ANOVA) with adjustments for age, diabetes mellitus, and hemoglobin status. A P-value < 0.05 was considered to be statistically significant.[8] Upon analysis, there was no significant difference in the tourniquet time between the two groups. The data analysis revealed that the mean arterial pressure was significantly higher in the VC group than in the control group at 5 minutes after decompression of the tourniquet. Mean arterial pressure in the controlled group was significantly reduced 5 minutes after tourniquet decompression compared from the values just before deflation to low ($P < 0.05$).[8] There was no difference in the pulse rate between the VC group and the controlled group. In both groups, the analysis of arterial blood gas showed the pH measured after anesthesia was significantly reduced at 5 and 20 minutes after tourniquet decompression. After tourniquet decompression in the control group at 5 min, arterial oxygen partial pressure and saturation significantly decreased ($P < 0.05$). In comparison, at 5 and 20 minutes after tourniquet decompression, the arterial oxygen partial pressure and oxygen saturation were higher in the VC group with a significant increase ($P < 0.05$).[8]

The authors concluded that the mean arterial blood pressure in the VC group was maintained higher than the control group at 1 min after deflation of the tourniquet. Furthermore, the study results demonstrated that the arterial oxygen partial pressure and saturation in the VC group were higher than the control group at 5 min and 20 min after deflation of the tourniquet. The authors determined that during unilateral total knee replacement among the elderly, the administration of intravenous vitamin C could significantly prevent the decline of mean arterial blood pressure and arterial oxygenation induced by ischemia-reperfusion injury.[8]

While in the study conducted by Kim et al. (2008), the authors wanted to investigate the effect of vitamin C on hemodynamics and arterial blood gas, Lee et al. (2018) explored the effect of high-dose vitamin c on oxygen free radical production and myocardial enzyme after tourniquet ischemia-reperfusion injury during bilateral total knee replacement.[4] The authors designed a randomized, double-blinded, placebo-controlled clinical trial to examine if high dose vitamin C during the perioperative period could reduce the effects of ischemic-reperfusion injury associated with pneumatic tourniquets.[4] To examine these effects of vitamin C, the authors measured the levels of Malondialdehyde (MDA), a biomarker for oxidative stress, and levels of cardiac enzymes creatine phosphokinase-myocardial band (CPK-MB) and troponin I. Patients aged 65 – 75 years who underwent bilateral TKR in hospital settings between June 2008 and July 2009 were randomly enrolled in this study. Patients included in the study had to have American Society of Anesthesiologists physical status I or II and were randomly assigned either to receive intraoperative high-dose vitamin C (VC group) or not to receive vitamin C (control group).[4] The exclusion criteria were myocardial ischemia or a history of uncontrolled hypertension, or the presence of diarrhea or renal calculus. In total, 32 patients were enrolled in the study: 16 in the VC group and 16 in the control group. In the vitamin C (VC) group (VC group, n = 16), during surgery, patients received a priming bolus of 0.06 g/kg vitamin C with 100 ml saline followed by 0.02 g/kg vitamin C mixed with 30 ml saline, intravenously. The control group (n = 16) received no intra-operative vitamin C.[4]

Blood samples for arterial blood gas and MDA analysis were obtained at the following time points: 20 min after the induction of anesthesia; before deflation of the first and second tourniquets; at 5 min after deflation of the first and second tourniquets; and at 20 min after deflation of the first and second tourniquets.[4] Mean arterial pressure and heart rate, as well as arterial oxygen tension (PaO2), arterial carbon dioxide tension (PaCO2), and oxygen saturation levels of the cardiac enzymes creatine phosphokinase-myocardial band (CPK-MB) and troponin I were measured at 20 min following anesthetic induction. This study assumed a mean difference and standard deviation of MDA of 0.7 and 0.7, respectively. As a result, assuming a withdrawal rate of 10%, it was estimated that 16 patients in each group would be needed to provide the study with a statistical power of 80% and a significance level of 0.05 to detect clinically meaningful differences between the control the VC group.[4]

All statistical analyses were performed using the SPSS® statistical package, version 14.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Data are shown as mean ± SD. Differences in demographics and baseline clinical characteristics between the two groups, including age, weight, hypertension, and hemoglobin level, were analyzed using the Student's t-test.[4] Between-group differences in arterial blood gas, hemodynamic profile, and MDA level were analyzed using a repeated measure analysis of variance (ANOVA) with adjustments for age, diabetes mellitus, and hemoglobin status. Within-group time-dependent differences in these parameters were also compared using ANOVA. Analyses of CPK-MB and troponin I levels were performed using analysis of covariance. A P value < 0.05 was considered to be statistically significant.[4]

The authors did not find any significant between-group differences in demographics and baseline clinical characteristics upon analyzing the data. Comparing both groups, at 5 min after deflation of both the first and second tourniquets, the serum levels of MDA were significantly lower in the VC group compared with the control group ($P < 0.05$). Within the VC group, there were no significant differences in MDA levels at any time point. In the control group, serum MDA levels increased significantly at 5 and 20 min after deflation of the first tourniquet compared with at 20 min after the induction of anesthesia, i.e., before deflation of the tourniquet ($P < 0.05$).[4] In addition, compared with serum MDA levels observed prior to deflation of the second tourniquet, serum MDA levels were significantly increased 5 min after deflation of the second tourniquet (P < 0.05). A significant decrease in serum MDA levels was also observed at 20 min compared with 5 min after the deflation of the second tourniquet (P < 0.05).[4]

While evaluating hemodynamic, the authors found that mean arterial pressure was significantly lower at 5 min after the first tourniquet deflation in the control group as compared with the VC group (P < 0.05), but following deflation of the second tourniquet, no significant differences were observed between the two groups.[4] In the VC group, CPK-MB levels were decreased at eight hours post-operation compared with levels observed in the control group, but the difference was not statistically significant. Troponin I levels were significantly lower at eight hours post-operation in the VC group than in the control group (P < 0.05).[4]

The study concluded that administering high-dose vitamin C to elderly patients undergoing bilateral TKR surgery could lower MDA levels and prevent the unstable hemodynamics and hypoxia caused by ischemia-reperfusion injury in both knees.[4] As a result, the myocardium could be protected more effectively. Particularly in elderly patients with concurrent severe pulmonary or cardiac disease, administering high-dose vitamin C intra-operatively might, therefore, decrease both cardiopulmonary complication and mortality rates.[4]

Both studies were done by Kim et al. (2008), and Lee et al. (2010) investigated the effects of vitamin C as the sole intervention. The authors of Mohamed et al. (2016) designed a double-blind, randomized, placebo-controlled clinical trial to compare two different pharmacologic interventions.[7] The study investigated and compared the effects of perioperative intravenous infusion of N-acetyl cysteine and ascorbic acid on malondialdehyde (MDA) production as a marker of oxidative stress and IL-6 and IL-8 as markers of systemic inflammation after ischemic-reperfusion as primary outcomes.[7] Additionally, the authors compared both agents concerning post-deflation hemodynamic effects and post-deflation changes in arterial pH and lactic acid as secondary outcomes.[7] In this study, 60 patients were included with an ASA physical status I or II, aged 25–45 years, scheduled for unilateral lower extremity surgery with a pneumatic tourniquet for 60–90 minutes. Exclusion criteria included the presence of vascular disease, cardiorespiratory disease, renal insufficiency, liver dysfunction, diabetes, or the administration of any antioxidant or anti-inflammatory drug.[7]

Baseline collection of blood samples was done, and then patients were randomly classified into three groups: Group A; received 1 g Ascorbic acid, group N; received 10 mg/kg NAC and group C (control group): received 100 ml saline infusion. Each group had 20 participants within their perspective group.[7] Two blood samples were drawn at each assessment time at baseline (T0), 1 min after tourniquet placement (T1), 1 min before tourniquet release (T2), 5 min after tourniquet release (T3), 20 min ATR (T4), and one-hour ATR (after tourniquet release) (T5). One sample was for arterial blood pH and lactic acid measurement, and the other blood sample was centrifuged and stored at −20 °C for subsequent analysis of MDA, IL-6, and IL-8.[7]

Statistical analysis was done using GraphPad© Prism© for Windows© version 6 and GraphPad© Instat© version 3.05 (GraphPad Software, Inc., San Diego California, USA).[7] It was estimated that a sample of 20 patients per group would have a power of 86% to detect a large effect size of (f = 0.45) as regards the primary outcome (production of malondialdehyde, IL-6, and IL-8) measures using the F-test and assuming a two-sided type I error of 0.05. Continuous numerical variables were presented as mean (SD), and intergroup comparisons were made using one-way analysis of variance (ANOVA) with the use of the Tukey–Kramer test for post hoc comparisons. Discrete variables were presented as median (interquartile range), and the Kruskal–

Wallis test was used to compare the groups. Categorical data were presented as a ratio or as number (%), and the Pearson chi-square test was used to test between-group differences.[7]

The data revealed that Levels of MDA, IL-6, and IL-8 were significantly increased in group C after tourniquet release compared with the baseline. [7] MDA levels did not increase over baseline values in groups A and N, but IL-6 and IL-8 levels were increased, and their levels were significantly less than in the control group.[7] Changes in hemodynamics, pH, and serum lactate were more evident in group C than groups A and N. The study results allowed the authors to conclude that both N-acetyl cysteine and ascorbic acid reduce post-deflation increase in blood levels of oxidative stress markers and systemic inflammation markers. Thus, both are beneficial in preventing post-tourniquet deflation ischemic reperfusion injury in lower limb surgery.[7]

The study by Behrend et al. (2019) examined the relationship between vitamin C levels and total knee arthroplasty.[5] The authors designed this study to determine whether perioperative supplementation of vitamin C (VC) improves range of motion (ROM) and reduces the risk of arthrofibrosis (AF) following total knee arthroplasty (TKA).[5] The trial was designed as a single-center, double-blind, randomized, placebo-controlled study. Ninety-five patients undergoing TKA were randomized to either Vitamin C administration or placebo (48 VC group, 47 placebo group). The effect of VC supplementation was tested on ROM, AF, WOMAC, FJS-12, and VC plasma concentrations analyzed in both patient groups before surgery, 4 and 7 days after surgery.[5]

Fasting vitamin C plasma concentration was analyzed preoperatively and on post-operative days 4 and 7. Complete Vitamin C plasma levels were available for a total of 75 patients. [5] Patients were stratified into groups with and without VC drop, depending on whether the perioperative VC plasma concentration dropped ≥ 30 or < 30 μmol/l from pre-operative to post-operative day 7. The rationale for this threshold was the rounded difference from average (> 50 µmol/l) to hypovitaminosis C (< 23 µmol/l).[5] The primary outcome parameter was knee joint ROM over the first post-operative year as measured with a goniometer by a trained study nurse blinded to the research history. In all cases, knee joint ROM was assessed preoperatively, at eight weeks and 12 months post-operatively. Secondary endpoints included the incidence of AF, patient-reported outcome measures, and the VC plasma concentration. [5]

All TKAs (cemented LCS® complete™ low contact stress complete knee system, Leeds, UK, DePuy Synthes) were performed with a computer-assisted ligament balancing technique (Vector Vision, CT-free, optoelectronic, passive marker navigation system, Brain-Lab, Munich, Germany) using a medial parapatellar approach with a tourniquet. [5] A uniform pain relief protocol was used in all patients postoperatively.[5] Rehabilitation consisted of continuous passive motion in the hospital, ROM exercises instructed by physiotherapists, and two crutches for six weeks with full weight-bearing as tolerated. Patient-reported outcome (PRO) was evaluated using the WOMAC score and the Forgotten Joint Score-12 (FJS-12). Descriptive statistics included medians, standard deviations, ranges, and proportions. Comparative statistics included unpaired t-tests and Chi-square test (where appropriate, Fisher's exact test was alternatively applied). The confidence level for rejecting null hypotheses was set at 95% (p-value < 0.05).[5]

The data from the study proposed that ROM at one year was not different between study groups. The prevalence of AF was 5 of 48 (10.4%) in the VC group compared to 11 of 47 (23.4%) in the placebo group ($p = 0.09$).[5] Interestingly, this study found that VC plasma concentrations decreased post-operatively in the placebo group (49–12 µmol/l on day 7, $p < 0.001$), but not in the VC group (53–57 µmol/l).[5] Furthermore, patients with a perioperative drop of VC plasma concentration of ≥ 30 µmol/l developed significantly more AF at one year than patients with a VC plasma concentration drop of < 30 μmol/l ($p = 0.007$).[5] The authors concluded that total knee arthroplasty does result in depletion of vitamin C plasma concentrations.[5] Moreover, the data determined that perioperative VC supplementation prevents VC plasma concentration drop in most patients undergoing TKA and may lower the incidence of AF. The clinical relevance of this study is that VC supplementation seems to be a cheap and safe adjunct to improve functional outcomes after TKA.[5]

Discussion

Tourniquets are often used in orthopedic surgery because empirical evidence indicates that they considerably minimize blood loss and transfusion needs, enhance identification of vital anatomical structures, and allow for an optimal operative field.[1-5] Tourniquet inflation elevates arterial pressures and induces hypoxia, acidosis, and hyperkalemia in ischemic limbs. When a tourniquet is deflated, metabolites released from ischemic regions reach the systemic circulation cause hypotension and hypoxia.[1-5] As a result of reperfusion and oxygenation, excessive oxygen free radicals are generated, resulting in leucocytic activation and endothelial damage in blood vessels.[4-7] Consequently, oxygen-free radicals are critical in developing severe cardiovascular problems following reperfusion damage.[4] These consequences are particularly concerning in patients with pre-existing cardiovascular comorbidities and orthopedic operations such as total knee replacement (TKR) with tourniquet application.[1-5]

Current research indicates that intravenous ascorbic acid treatment during surgery as an additional therapy reduces the occurrence of fluctuations in blood pressure, arrhythmias caused by damage to the myocardium and improve microcirculation and neurological outcomes.[8,10,16] For instance, the study conducted by Kim et al. (2008) investigated the effect of vitamin C on hemodynamics and arterial blood gas during unilateral total knee replacement.[8] The study determined that the mean arterial blood pressure for patients who were administered intravenous vitamin C during the intraoperative period was maintained higher than the control group at 1 min after deflation of the tourniquet.[8] Additionally, the results also demonstrated that patients given intravenous vitamin C had higher arterial oxygen partial pressure and saturation than the control group at 5 min and 20 min after deflation of the tourniquet.[8]

The excessive oxidative stress caused by the deflation of the pneumatic tourniquet can potentially damage many organs throughout the body, including the heart.[4] In the study by Lee et al. (2018), the authors examined the effect of high-dose vitamin c on oxygen-free radical production and myocardial enzyme after tourniquet ischemia-reperfusion injury during bilateral total knee replacement. The authors designed a double-blinded study to evaluate how intraoperative treatment of high dose vitamin C would influence Malondialdehyde (MDA), a biomarker for oxidative stress, and levels of cardiac enzymes creatine phosphokinase-myocardial band (CPK-MB) and troponin I.[4] The results from the study concluded that administering high-dose vitamin C to elderly patients undergoing bilateral TKR surgery could lower MDA levels and prevent the unstable hemodynamics and hypoxia caused by ischemia-reperfusion injury in both knees.[4] Hence, showcasing that high dose vitamin C during the intraoperative period could have myocardium protective effects, particularly in elderly patients with concurrent severe pulmonary or cardiac disease.[1-4]

With the possible positive outcomes of perioperative ascorbic acid in mind, the authors of Mohamed et al. (2016) pursued to compare the different pharmacologic interventions to manage oxidative stress caused by the tourniquet released during orthopedic surgeries.[7] Their study investigated and compared the effects of perioperative intravenous infusion of N-acetyl cysteine and ascorbic acid on malondialdehyde (MDA) production as a marker of oxidative stress and IL-

6 and IL-8 as markers of systemic inflammation after ischemic-reperfusion.[7-10] Additionally, the authors evaluated the serum lactate and pH levels in all of the groups in the study. The data analysis showed that patients who did not receive any intervention had significantly higher levels of MDA, IL-6, and IL-8 after tourniquet release compared with the baseline.[7] In comparison, patients given a perioperative intravenous infusion of N-acetyl cysteine and ascorbic acid had no increase in the MDA levels compared to baseline values. Furthermore, the changes in hemodynamics, pH, and serum lactate were more evident in the control group compared to the intervention groups.[7]

Lastly, in their study, Behrend et al. (2019) analyzed the relationship between vitamin C levels and total knee arthroplasty.[5] The authors investigated whether perioperative supplementation of vitamin C (VC) improves range of motion (ROM) and reduces the risk of arthrofibrosis (AF) following total knee arthroplasty (TKA).[5] Interestingly, the researchers determined that total knee arthroplasty results in depletion of vitamin C plasma concentrations.[5] In addition, the data established that perioperative VC supplementation prevents VC plasma concentration drop in most patients undergoing TKA and may lower the incidence of AF.[5] The findings of these studies help support that perioperative intravenous vitamin C should be utilized routinely for patients undergoing orthopedic surgeries in which a pneumatic tourniquet may be employed to minimize IRI injuries and achieve optimal outcomes.[4-6,7-8]

Conclusion

Despite considerable improvements in scientific understanding of the mechanisms behind the ischemia-reperfusion injury, translation of research into clinical practice for attenuating tourniquet-induced ischemic injury has been uneven and inconsistent, particularly concerning patient outcomes. This research indicates that administering intravenous ascorbic acid during surgery as an adjunctive therapy minimizes the occurrence of blood pressure variations and arrhythmias caused by myocardial injury while also enhancing microcirculation and neurological outcomes.[8,10,16] According to the literature, intraoperative vitamin C administration may help prevent and restore microcirculatory flow impairment by inhibiting nicotinamide adenine dinucleotide phosphate-oxidase and inducible nitric oxide synthase activation, modulating tetrahydrobiopterin, inhibiting oxidative phosphorylation uncoupling, and reducing superoxide and peroxynitrite formation.[10,11] Additionally, IV ascorbic acid can restore vascular responsiveness to vasoconstrictors and preserve the endothelial barrier by sustaining cyclic guanylate phosphatase.[10-12] Vitamin C's potential role in IRI produced by tourniquet use is supported by data from burns, sepsis, and cardiac investigations, demonstrating faster healing and increased survival rates following organ failure.[10-11 13-17]

There is a lack of consensus published guidelines regarding the perioperative administration of intravenous ascorbic acid as a systematic strategy for mitigating hemodynamic changes related to IRI induced by tourniquet use despite literature demonstrating positive outcomes. Owing to the lack of guidelines for preventing tourniquet-induced ischemia-reperfusion damage, anesthesia providers must utilize evidence-based research to drive their clinical interventions to minimize IRI injuries and achieve optimal outcomes.[1-3,15-17] By educating anesthesia providers about the value and efficacy of perioperative intravenous ascorbic acid administration, the project proposed may assist as a step towards instituting objective, evidence-based clinical suggestions for lowering the adverse outcomes associated with tourniquet-induced ischemic-reperfusion injury.

Organizational Assessment

Implementing the evidence-based guideline for perioperative intravenous ascorbic acid will be conducted within a collaborative team approach. We will first determine the steps needed to develop the evidence-based guideline for perioperative intravenous ascorbic acid. A flowchart will be formed to represent the visualization of the process steps. Data can be analyzed and compared with the goals and expectations devised during the planning phase through chart reviews of hemodynamic fluctuations pre-and post- perioperative intravenous ascorbic acid implementation. In the evaluation phase, the anesthesia providers will be interviewed to input the program’s overall effectiveness. Additionally, the interdisciplinary team will be expected to present a summary of the program's significant findings. The report must be concise and include a description of the program, the interventions used, a purpose statement, the methods used for data collection and analysis, which should include the background and history of the clinical issues, the tools used to collect information, and how data was analyzed, significant findings and conclusions, unexpected and unanticipated outcomes, design flaws, and recommendations to improve the program.

Primary DNP Project Goal

A pneumatic tourniquet is an integral component of many orthopedic surgical procedures of the lower extremities.[1-3] While beneficial at first sight, the use of pneumatic tourniquet in patients undergoing orthopedic surgery has also been associated with increased long-term mortality, systolic and diastolic heart failure, cardiogenic shock, myocardial stunning, and arrhythmias.[1-6] Despite the growing understanding of the mechanisms of ischemia-reperfusion injury, the translation of evidence into clinical practice for attenuation of tourniquet-induced ischemic injury has been inconsistent and variable, particularly concerning patient outcomes.

According to current studies, perioperative intravenous administration of ascorbic acid as an adjunct treatment has shown to attenuate incidences of blood pressure fluctuations, myocardial injury, arrhythmias and improves microcirculation and neurological patient outcomes.[7-9]

Literature suggests that intraoperative infusion of vitamin C can prevent "microcirculatory flow impairment by inhibiting activation of nicotinamide adenine dinucleotide phosphate-oxidase and inducible nitric oxide synthase, augmenting tetrahydrobiopterin, preventing uncoupling of oxidative phosphorylation, and decreasing the formation of superoxide and peroxynitrite, and by directly scavenging superoxide".[7-9] Additionally, IV administration of ascorbic acid can also restore vascular responsiveness to vasoconstrictors and preserve endothelial barrier by maintaining cyclic guanylate phosphatase.[1-6,9-11] Based on the common pathophysiological pathways, the potential role of vitamin C for tourniquet-induced ischemia-reperfusion injury is further supported by the results of sepsis, burns, and cardiac studies, showing earlier recovery from organ failure and higher survival rates.[1-5,7-12]

Despite literature demonstrating the positive outcomes of intravenous administration of ascorbic acid, published consensus guidelines have not yet included its implementation as a standard intervention for preventing the hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury.[1-5,7-12] Anesthesia providers possess the ability to intervene and reduce hemodynamic fluctuations caused by tourniquet-induced ischemic reperfusion injury by incorporating perioperative intravenous administration of ascorbic acid.[1-5,7-9] Hence, there is a need for educational evidence-based recommendations on dealing with this common phenomenon to reduce variations in practice. The primary goal of developing an evidence-based recommendation regarding the use of perioperative ascorbic acid is to provide all anesthesia providers a guideline for managing hemodynamic fluctuations when taking care of patients undergoing orthopedic surgery using a pneumatic tourniquet. The recommendation's objective is to re-examine traditional practices and replace them with evidence-based guidelines to reduce the effects caused by tourniquet-induced ischemic reperfusion injury.

Goals and Outcomes

To guide the development of the goal objectives, the acronym SMART was utilized. SMART details that the objectives should be specific, measurable, achievable, realistic, and timely.[18]

Specific

Anesthesia providers will have a standardized, evidence-based recommendation of perioperative intravenous administration of ascorbic acid protocol for hemodynamic management of patients undergoing orthopedic surgery using a pneumatic tourniquet.

Measurable

The effectiveness of the educational program of utilizing perioperative administration of ascorbic acid will be calculated by analyzing a questionnaire that will be provided to participants before and after an educational intervention. Outcomes will be measured by evaluating the variations in providers' knowledge of tourniquet induced ischemic reperfusion injury, the consequences of reperfusion injury on organ systems, pharmacodynamic properties of ascorbic acid, the available recommendation for managing oxidative stress, and the effectiveness of ascorbic acid to manage oxidative stress caused by tourniquet release pre-and post-intervention. In order to generate reports, Qualtrics® software will be used to create the surveys and analyze data.

Achievable

Anesthesiologists, Certified Registered Nurse Anesthetists, Anesthesiologist Assistants, Pharmacists, Orthopedic and trauma surgeons would collaborate to develop an evidence-based guideline for perioperative intravenous ascorbic acid use.

Realistic

Anesthesia providers and surgeons who perform orthopedic surgeries requiring a pneumatic tourniquet will be educated on the benefits of utilizing perioperative infusion of ascorbic acid. Facility informatics will collaborate with pharmacies and providers to develop an electronic order set for easy access.

Timely

All anesthesia providers are educated through an online education module presented through a Voiceover PowerPoint presentation on implementing an evidence-based algorithm and pamphlets given to those who cannot attend. All staff will be aware of the background of the problem, evidence-based supporting practice change, and the practice change suggestion within a 6-month time frame. The outcome of this initiative will be as follows: within six months, all anesthesia providers will be able to discuss hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury and when to initiate IV administration of Vitamin C in orthopedic procedures.

Program Structure

Developing an evidence-based guideline for perioperative intravenous ascorbic acid use will require a collaborative, multidisciplinary team effort. A comprehensive assessment will be performed to identify opportunities and the importance, value, and significance of the project to all stakeholders.[13] The strength, weakness, opportunities, and threats (SWOT) analysis assessment tool will be utilized to evaluate the internal and external characteristics and threats to the program's development.

The project aims to determine the anesthesia providers' knowledge of using perioperative ascorbic acid to manage hemodynamic fluctuations when taking care of patients undergoing orthopedic surgery using a pneumatic tourniquet. The expert stakeholders of this project are the anesthesia providers and orthopedic surgeons who will guide the development of an evidence-based guideline for perioperative intravenous ascorbic acid and the providers' educational intervention. The participants will first be provided with a questionnaire to measure their knowledge of tourniquet induced ischemic reperfusion injury, the consequences of reperfusion injury on organ systems, pharmacodynamic properties of ascorbic acid, the available recommendation for managing oxidative stress, and the effectiveness of ascorbic acid to manage oxidative stress caused by tourniquet release. Participants will then be provided with an educational course addressing the use of perioperative ascorbic acid for managing hemodynamic fluctuations when taking care of patients undergoing orthopedic surgery using a pneumatic tourniquet. This course will be provided to all anesthesia providers and surgeons through a Clinical Site Presentation on implementing an evidence-based algorithm, and pamphlets will be given to those who cannot attend. After the intervention, participants will be asked to take a survey to analyze the variations in their knowledge before and after the educational course.

Strengths

In the United States, osteoarthritis (OA) of the knee is the primary cause of hospitalization for individuals aged 45–84 years, accounting for 60% of adults over 65.[6] Total Knee Arthroplasty (TKA) successfully treats persistent knee discomfort caused by osteoarthritis. A recent survey of Medicare beneficiaries concluded that OA is the primary diagnosis for 94 percent of all patients undergoing TKA in the United States.[6] In 2008, the United States conducted over 650,000 TKAs at the cost of $9 billion. This financial load will only rise in relevance as the geriatric population grows.[6]

Furthermore, the number of TKAs conducted yearly in the United States will reach 3.5 million by 2030. Thus, optimizing TKA performance is critical for both qualities of treatment and cost reduction.[3,6] Developing an evidence-based guideline for perioperative intravenous ascorbic acid can improve patient outcomes and increase patient satisfaction and overall experience. Additionally, another major strength of this project is that there are minimal side effects and contraindications. Furthermore, the low cost of intravenous ascorbic acid administration is also appealing for facilities when incorporating a new practice change.[6]

Weakness

As Moran et al. (2020) defined, the plan's weaknesses are any internal issues that may be damaging to the program.[13] An internal problem identified is the lack of pre-existing suggestions to use as a guidance tool while developing new recommendations for implementation at the facility. Furthermore, the lack of sufficient knowledge regarding the tourniquet induced ischemic reperfusion injury, the consequences of reperfusion injury on organ systems, pharmacodynamic properties of ascorbic acid, the available recommendation for managing oxidative stress, and the effectiveness of ascorbic acid to manage oxidative stress caused by tourniquet release can also present as a weakness. Another weakness of the proposed project can come from the surgeon's preference regarding their preferred method of patient care. Orthopedic surgeons may have other preferences for their patients and may be resistant to incorporating new practices. These preferences can make implementing the proposed recommendation of intravenous ascorbic acid difficult for anesthesia providers.

Opportunities

Implementing an evidence-based guideline for perioperative intravenous ascorbic acid can collaborate with other disciplines such as orthopedic surgeons and trauma teams. There is a high prevalence of geriatric patients undergoing orthopedic procedures in lower extremities, which further serves as an opportunity for implementing the recommended use of perioperative intravenous ascorbic acid. Additionally, the recommendation of intravenous ascorbic acid serves as an inexpensive intervention change for the facility with the possibility of improved patients' outcomes, increased patient satisfaction, and overall experience

Threats

Factors that may potentially harm the process or interfere with the program's ability to achieve its objectives must be evaluated.[13] Risks to the program may include the anesthesia providers' negative feelings towards the perioperative intravenous ascorbic acid use because of the deviation from the current standard of care. These negative feelings can present as a lack of participation and cooperation from anesthesia providers. The orthopedic surgical team may also be unwilling to participate in the practice change due to similar feelings. Because the successful implementation of an evidence-based guideline for the perioperative intravenous ascorbic acid program is heavily dependent on provider compliance, surgeons and anesthesia providers must feel a vested interest in the process and indicate their agreement to engage in a new protocol different from current perioperative management.

Conceptual Underpinning and Theoretical Framework of the Project

The theoretical framework serves as a guide or can be thought of as a road map for the DNP project. The conceptual framework establishes the actions and foundations for the technique used in the DNP project.[13] Lewin's Change Theory will be the basis for this DNP project. Unfreezing, change, and refreezing are the three stages in Lewin's approach.[19] The unfreezing stage provides an awareness of the need for change, which is subsequently evaluated.[19] Recognizing the repercussions of tourniquet-induced ischemia-reperfusion damage would necessitate a change. The second stage is to ascertain where change is required and where it is already occurring.[19] The second stage would be for changes to the protocol or processes, such as intravenous ascorbic acid. The third and final stage, refreezing, occurs once equilibrium has been achieved and lasting alteration has transpired.[19] Refreezing or integrating the project would require establishing standards to minimize hemodynamic changes in patients undergoing orthopedic surgery using a pneumatic tourniquet. Lewin's Change Theory provides a framework for companies to identify and acknowledge the possibility of change, examine feasible modifications, and finally execute the policy or behavior changes.[19] Additionally, Lewin's Change Theory aids change agents in overcoming resistance and promoting the adoption of best practices in healthcare.[19]

Methodology

Setting and Participants

Proper implementation of this quality improvement project requires a group of study participants to receive an educational presentation on the anesthetic implications of tourniquet-induced ischemic reperfusion injury. The primary setting of this quality improvement project will take place at a significant, level 1 trauma center in southwest Florida. Primary participants include all anesthesia providers employed at this facility. The participants will be recruited voluntarily, and the anticipated sample size will be between 5-15 participants.

The principal methodology of the proposed project is to administer an online educational presentation to anesthesia providers encompassing the anesthetic implications of tourniquet-induced ischemic reperfusion injury. Participants will first complete an online pre-intervention test, evaluating current knowledge of tourniquet-induced ischemic reperfusion injury. Participants will then be given a 10-minute online educational presentation on tourniquet-induced ischemic reperfusion injury, the use of intra-operative use of intravenous ascorbic acid, and related anesthetic implications. Participants will then be evaluated on knowledge gained as evidenced by a post-intervention test.

Results obtained in the post-intervention test will provide feedback regarding the impact of the educational presentation. The pre/post-testing provides relevant information regarding the efficacy of the educational presentation and seeks to improve anesthetic care of patients undergoing orthopedic surgeries of the lower extremities. Outcomes will also demonstrate if additional anesthesia provider education is needed.

Protection of Human Subjects

The recruitment population will include anesthesia providers at a level 1 trauma center in southwest Florida for this quality improvement project. This population is significant because they deliver anesthesia care to patients undergoing orthopedic surgeries of the lower extremities. Participant recruitment will be conducted via email invitation to all anesthesia providers at this location. Participation will be voluntary with no penalty for withdrawing withdraw from the project. There are no perceived risks to the study as it only requires the time spent by each participant in the education intervention.

Data Collection

Data collection will include a pre-and post-test to determine the effects of the educational intervention. Both assessments will be conducted using surveys consisting of approximately ten questions focusing on knowledge and practice using Qualtrics. The pre-test will assess knowledge of tourniquet-induced ischemic reperfusion injury and associated anesthetic implications, while the post-test survey will determine if the participants gained knowledge from the intervention. The instrument reliability and validity will be measured in accordance with the intervention provided and its effectiveness for the participants. The data collected will be confidential, and no subject identifiers will be recorded during any study component.

Data Management and Analysis Plan

The DNP student will be responsible for administering the pre-test, educational intervention, and post-test. Results will be kept using Microsoft Excel software and only accessible to the DNP student and FIU faculty members. This data will be stored on a password-protected computer, ensuring confidentiality. Pre- and post-test results will be recorded to identify knowledge bases before and after the educational intervention. Statistical analysis will be performed to determine the effectiveness of the educational presentation and its impact on the anesthesia provider.

Results

Pre/Post-Test Demographics

The pre-test demographics are represented below in Table 2.

Table 2. Pre/Post-Test Demographics

Consent – I consent to participate.

#	Answer	%	Count
1	Yes	100.00%	7
2	No	0.00%	0
	Total	100%	7

Q1 – Please indicate the gender you identify as.

#	Answer	%	Count
1	Male	57.14%	4
2	Female	42.86%	3
3	Non-binary	0.00%	0
4	Prefer not to answer	0.00%	0
	Total	100%	7

Q2 – Please indicate your age.

#	Answer	%	Count
1	25-35	42.86%	3
2	36-45	14.29%	1
3	46-55	28.57%	2
4	56-65	0.00%	0
5	>65	14.29%	1
	Total	100%	7

Q3 – Please indicate your ethnicity.

#	Answer	%	Count
1	Hispanic	42.86%	3
2	Caucasian (non-Hispanic)	28.57%	2
3	African American	14.29%	1
4	Asian	0.00%	0
5	Other	14.29%	1
	Total	100%	7

Q4 – Please indicate your highest education level.

#	Answer	%	Count
1	Associates	0.00%	0
2	Bachelors	0.00%	0
3	Masters	28.57%	2
4	Doctorate	71.43%	5
5	Others	0.00%	0
	Total	100%	7

Q5 – Please indicate the numbers of years that you have been an anesthesia provider.

#	Answer	%	Count
1	Less than 5 years	57.14%	4
2	5-10	14.29%	1
3	10-15	0.00%	0
4	Greater than 15	28.57%	2
	Total	100%	7

There was a total of seven participants completed the study in its entirety. The pre-test demographics represented the following participant gender identities, female (n = 3; 42.8%), and male (n= 4, 57.1%). Various ethnicities were also represented among the participants, with the majority being Hispanic (n = 3, 42.8%), followed by Caucasian (n = 2; 28.5%), African American (n = 1; 14.2%), and Other (n = 1; 14.2%). There was a vast age range of participants with ages 25 to 35 years old (n = 3; 42.8%), 36 to 45 years old (n = 1; 14.2%), 46 to 55 years old (n = 2; 28.5%), and greater than 65 years old (n = 1; 14.2%). A vast majority of participants held a Doctorate degree (n = 5; 71.4%), followed by a Master's degree (n = 2; 28.5%). Lastly, all participants were asked how many years they have been an anesthesia provider; 0 to 5 years (n = 4; 57.1%), 6 to 10 years (n = 1; 14.2%), and greater than 15 years (n = 2; 28.5%).

Pre-Test Identification of Knowledge on Pneumatic Tourniquet and Use of Intravenous Ascorbic Acid to Attenuate Hemodynamic Fluctuations

The pre-test consisted of ten questions that assessed current knowledge on pneumatic tourniquets and the use of intravenous ascorbic acid to attenuate hemodynamic fluctuations. 100% (n = 7) of the participants correctly identified the benefits of utilizing pneumatic tourniquets for orthopedic surgeries. 87.5 (n = 6) of the participants correctly identified the physiologic effects of inflating the pneumatic tourniquet. Similarly, 87.5 (n = 6) of the participants correctly identified the effects caused by metabolites produced from the ischemic area entering systemic circulation upon deflating the pneumatic tourniquet. 71.4% (n = 5) of the participants correctly identified that excessive oxygen-free radicals are produced during reperfusion and oxygenation, which contributes to leucocytic activation and endothelial damage in blood vessels. A total of 71.4% (n = 5) of the participants correctly identified the increased incidence of events associated with the use of a pneumatic tourniquet. The participants selected 57.1% (n = 4) always, 28.6% (n = 2) most of the time, 14.3% (n = 1) sometimes, to altering their anesthetic plan for orthopedic surgery when their patient has cardiopulmonary comorbidities. None of the participants identified utilizing intravenous ascorbic acid infusion during their anesthetic management for orthopedic surgeries involving a pneumatic tourniquet. Most participants, 71.4% (n = 5), could identify that intravenous ascorbic can be utilized intraoperatively for its antioxidant properties to attenuate hemodynamic fluctuation caused by oxygen-free radicals. Only four participants (n = 4, 57.1%) correctly identified the antioxidant effects of ascorbic acid had been shown to reduce intraoperative variations in hemodynamics and incidences of arrhythmias. Correspondingly, four participants (n = 4, 57.1%) correctly identified that incorporating high-dose ascorbic acid administration intraoperatively has myocardium protective effects for patients with concurrent severe pulmonary or cardiac disease.

Post-Test Identification of Knowledge on Pneumatic Tourniquet and Use of Intravenous Ascorbic Acid to Attenuate Hemodynamic Fluctuations

After the voiceover PowerPoint presentation, all the areas except two illustrated an increase in knowledge compared to baseline knowledge on the topics. There was a significant increase of 100% in participant response to utilizing intravenous ascorbic acid infusion during your anesthetic management for orthopedic surgeries involving a pneumatic tourniquet in the future. Two other content areas showed a 42.9% increase in the knowledge rates on identifying the correct antioxidant and myocardium protective effects of ascorbic acid for patients with concurrent severe pulmonary or cardiac disease.

Three content areas illustrated a 28.6% increase in knowledge compared to baseline. These areas include correctly identifying that excessive oxygen-free radicals are produced during reperfusion and oxygenation, recognizing which events have increased incidences with the use of a pneumatic tourniquet and that intravenous ascorbic can be utilized intraoperatively for its antioxidant properties to attenuate hemodynamic fluctuation caused by oxygen-free radicals. Two content areas demonstrated a 14.3% increase in knowledge on identifying physiologic effects of inflating the pneumatic tourniquet and the effects caused by metabolites produced from the ischemic area entering systemic circulation upon deflating the pneumatic tourniquet. The two content areas that did not show any increase in knowledge were correctly identifying the benefits of utilizing pneumatic tourniquets for orthopedic surgeries and the frequency of providers altering their anesthetic management for orthopedic surgery when your patient has cardiopulmonary comorbidities. Table 3 below highlights the pre-test and post-test differences in responses.

Table 3. Difference in Pre-test and Post-test Knowledge

Question	**Pre-test**	**Post-test**	**Difference**
What are the benefits of utilizing pneumatic tourniquets for orthopedic surgeries?	100% (n = 7)	100% (n = 7)	0%
Inflation of pneumatic tourniquet results in what physiologic effects?	85.7% (n = 6)	100% (n = 7)	14.3%

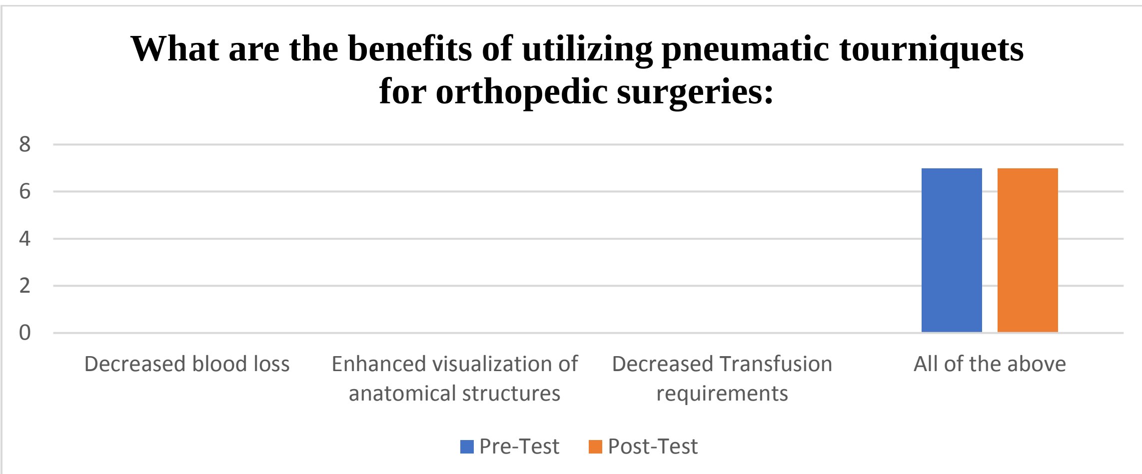
Upon deflation of the pneumatic tourniquet, the metabolites produced from ischemic area enter systemic circulation and produce what effects?	85.7% (n = 6)	100% (n = 7)	14.3%
During reperfusion and oxygenation, what is produced which contributes to leucocytic activation and endothelial damage in blood vessels?	71.4% (n = 5)	100% (n = 7)	28.6%
Pneumatic tourniquet use is associated with increased incidences of which of the following?	71.4% (n = 5)	100% (n = 7)	28.6%
Intravenous ascorbic can be utilized intraoperatively for its antioxidant properties to attenuate hemodynamic fluctuation caused by oxygen-free radicals.	71.4% (n = 5)	100% (n = 7)	28.6%
The antioxidant effects of ascorbic acid have shown to reduce intraoperative variations in hemodynamics and incidences of arrhythmias	57.1% (n = 4)	100% (n = 7)	42.9%
Incorporating high-dose ascorbic acid administration intraoperatively has myocardium protective effects for patients with concurrent severe pulmonary or cardiac disease.	57.1% (n = 4)	100% (n = 7)	42.9%
Have you/would you ever utilized intravenous ascorbic acid infusion during your anesthetic management for orthopedic surgeries involving a pneumatic tourniquet?	0% (n = 7)	100% (n = 7)	100%
How frequent do you change your anesthetic plan for orthopedic surgery when your patient has cardiopulmonary comorbidities?	57.1% (n = 4)	57.1% (n = 4)	0%

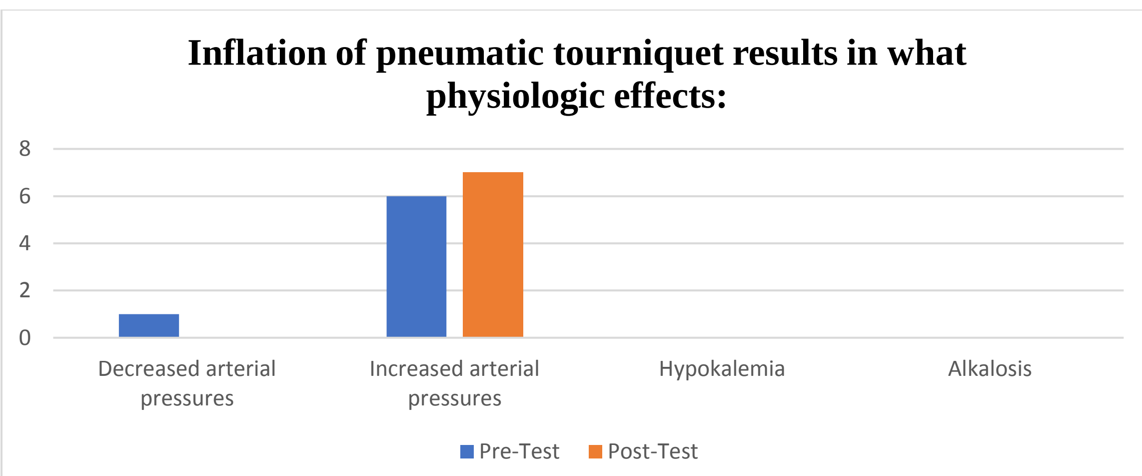
Summary of Data

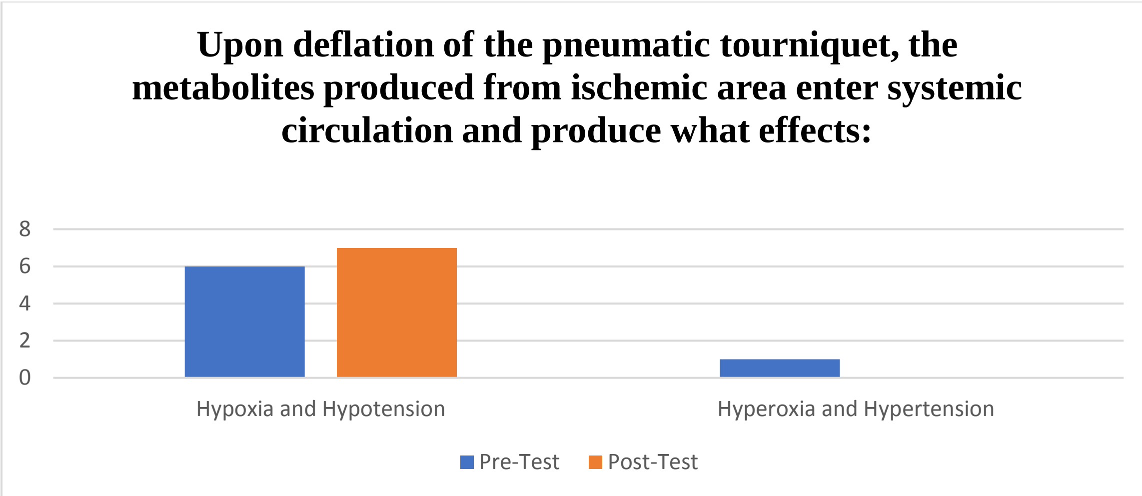
Overall, the results demonstrated an increase in knowledge rates between the pre-test and post-tests, except for correctly identifying the benefits of utilizing pneumatic tourniquets for orthopedic surgeries and the frequency of providers altering their anesthetic management for orthopedic surgery when your patient has cardiopulmonary comorbidities, which yielded a 0%

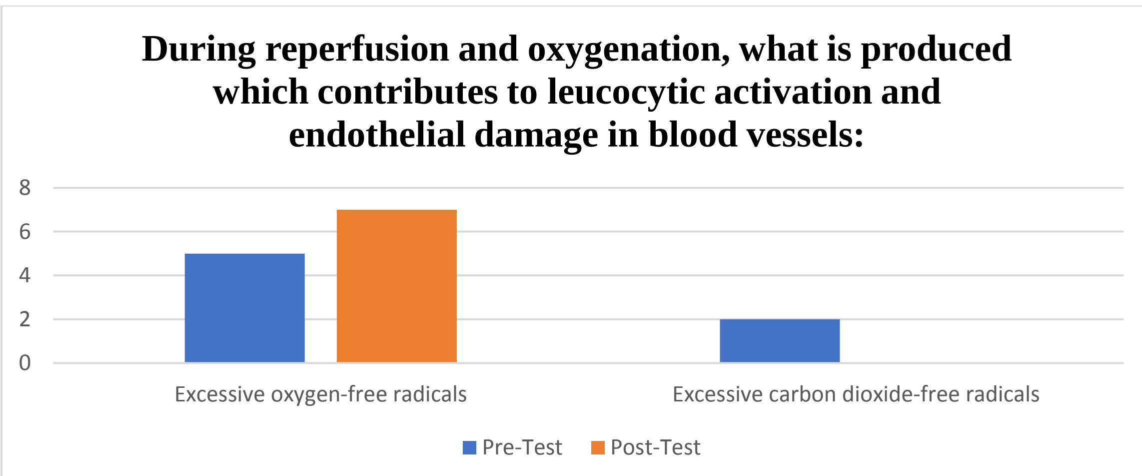
difference. There was a substantial increase of 100% in participant response to utilizing intravenous ascorbic acid infusion during your anesthetic management for orthopedic surgeries involving a pneumatic tourniquet in the future. Furthermore, other content areas showed a noteworthy increase of 42.9 % in the knowledge rates on identifying the correct on identifying the correct antioxidant and myocardium protective effects of ascorbic acid for patients with concurrent severe pulmonary or cardiac disease. Graph 1 below illustrates the individual pre-test and post-test results of each question.

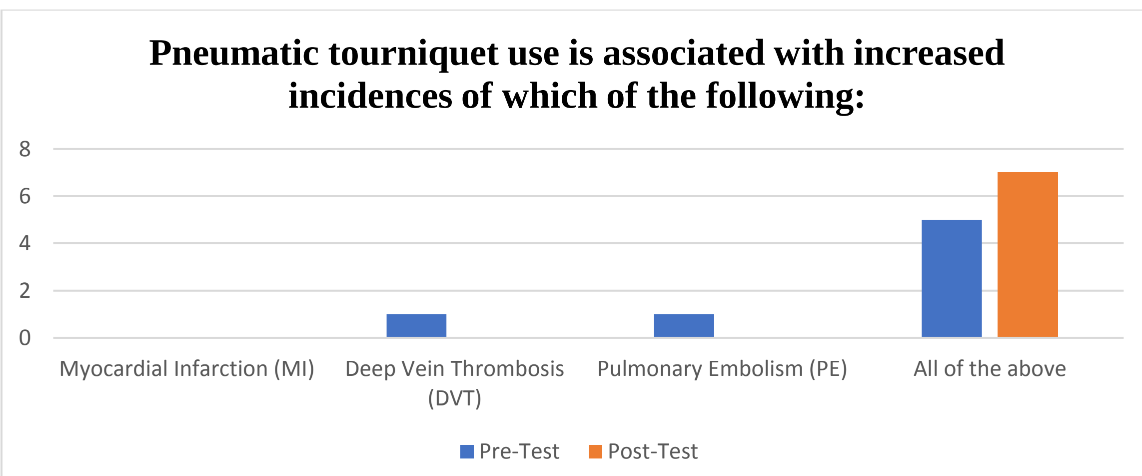
Graph 1. Individual Pre-test and Post-test Results

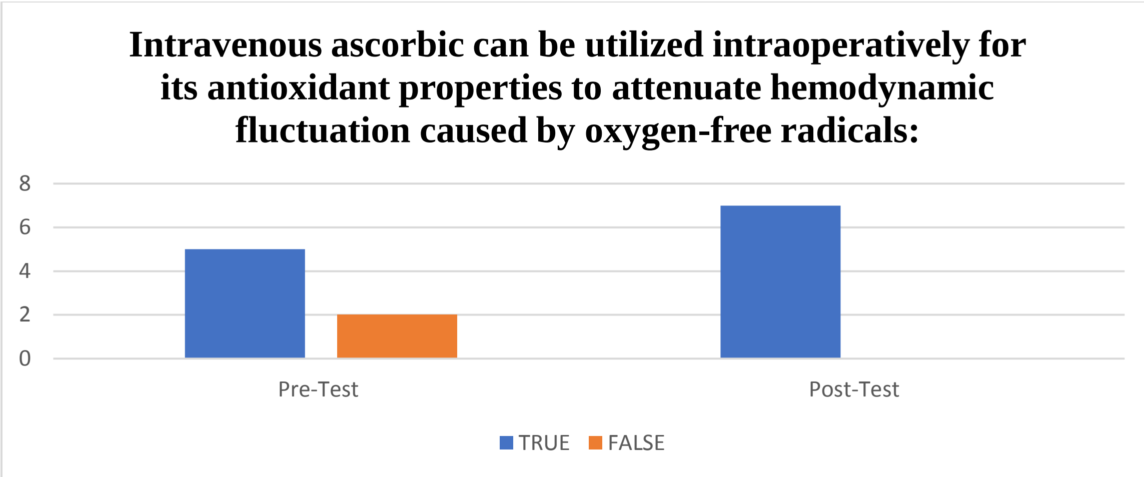


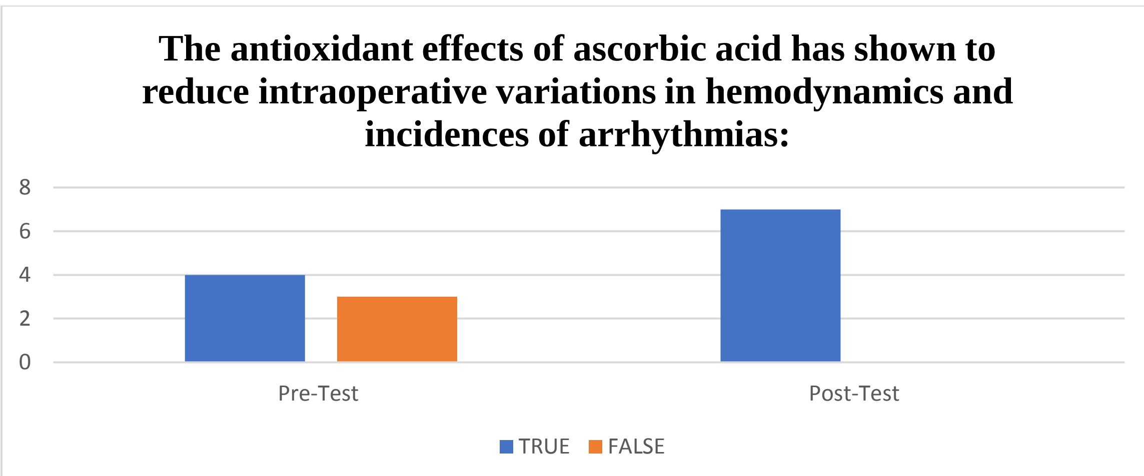


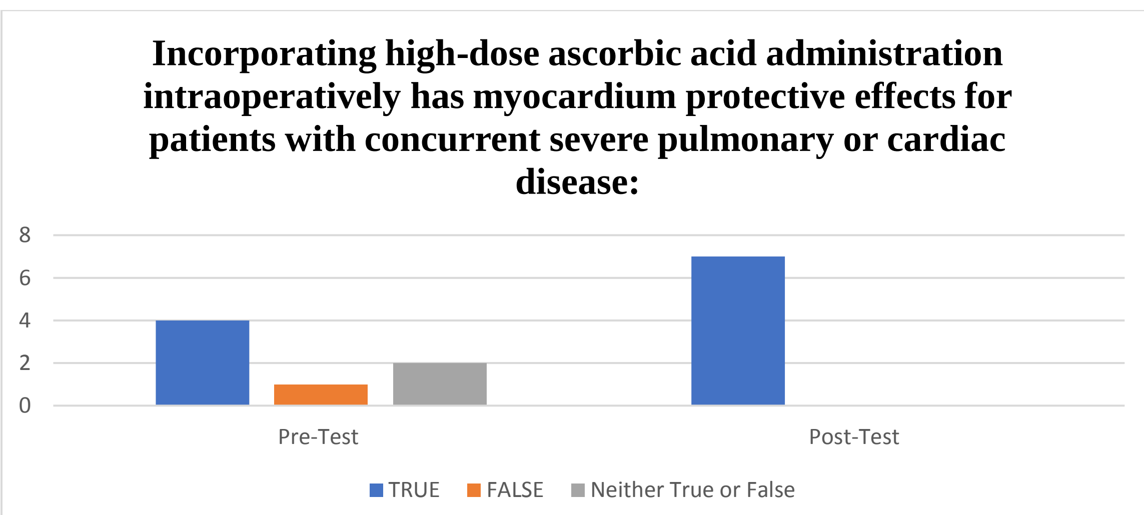

Upon deflation of the pneumatic tourniquet, the metabolites produced from ischemic area enter systemic circulation and produce what effects:
8
6
4
2
0
Hypoxia and Hypotension
Hyperoxia and Hypertension
Pre-Test
Post-Test

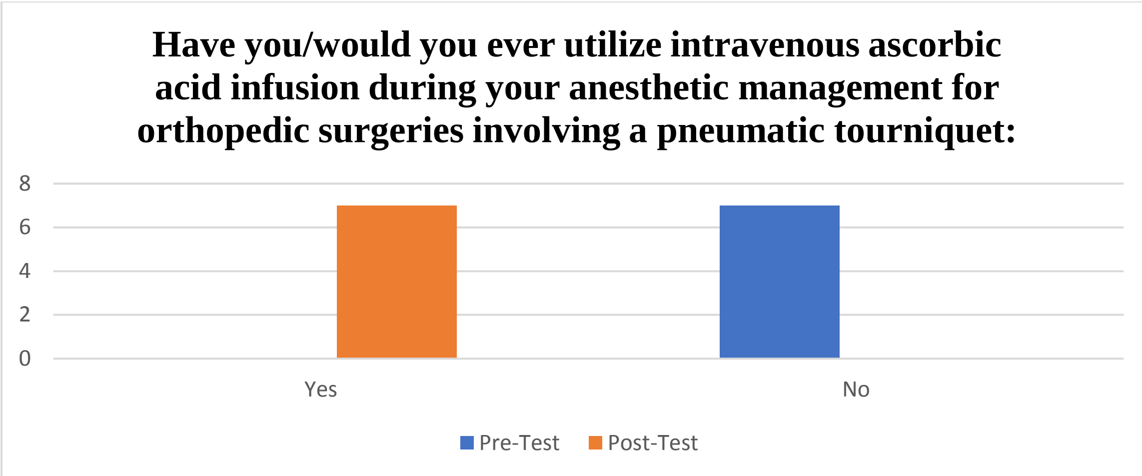

During reperfusion and oxygenation, what is produced which contributes to leucocytic activation and endothelial damage in blood vessels:
8
6
4
2
0
Excessive oxygen-free radicals
Excessive carbon dioxide-free radicals
Pre-Test
Post-Test

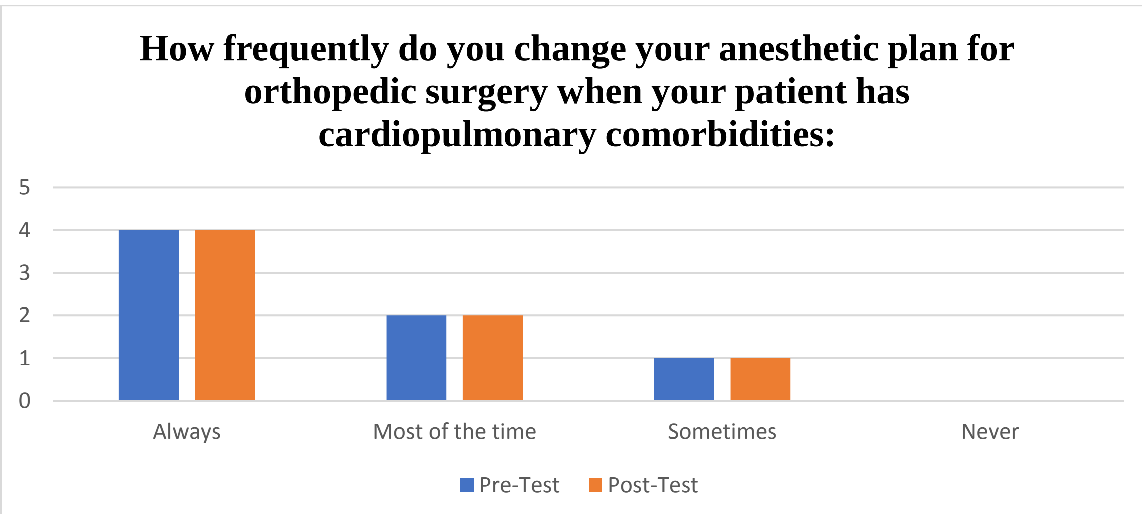

Pneumatic tourniquet use is associated with increased incidences of which of the following:
8
6
4
2
0
Myocardial Infarction (MI)
Deep Vein Thrombosis (DVT)
Pulmonary Embolism (PE)
All of the above
Pre-Test
Post-Test


Intravenous ascorbic can be utilized intraoperatively for its antioxidant properties to attenuate hemodynamic fluctuation caused by oxygen-free radicals:
8
6
4
2
0
Pre-Test
Post-Test
TRUE
FALSE


The antioxidant effects of ascorbic acid has shown to reduce intraoperative variations in hemodynamics and incidences of arrhythmias:
8
6
4
2
0
Pre-Test
Post-Test
TRUE
FALSE


Incorporating high-dose ascorbic acid administration intraoperatively has myocardium protective effects for patients with concurrent severe pulmonary or cardiac disease:
8
6
4
2
0
Pre-Test
Post-Test
TRUE
FALSE
Neither True or False





Discussion

Limitations

This study had several limitations, including a small sample size and the length of time required for participants to complete the study. Out of the 34 emails sent to anesthesia providers from the ANESCO anesthesia group at Broward Health Medical Center, only seven participants completed the pre-test and post-test survey. A larger and more diverse sample size would have reflected a more accurate representation of the knowledge base on the care of the transgender patient population and the need for education. Furthermore, participants were given a limited time of two weeks to complete the education module, and an extended time frame may have increased the response rate.

Future Implications for Advanced Nursing Practice

The increasing use of pneumatic tourniquets for orthopedic surgeries has also increased the possibility of tourniquet-induced ischemic reperfusion injury. Despite new research, insufficient knowledge exists regarding the pharmacodynamic benefits of ascorbic acid for managing oxidative stress caused by tourniquet-induced ischemic reperfusion injury. The developed and implemented educational module for this study demonstrated an increase in knowledge rate compared to baseline knowledge rates in all areas except for two. There were no increases in knowledge of correctly identifying the benefits of utilizing pneumatic tourniquets for orthopedic surgeries and the frequency of providers altering their anesthetic management for orthopedic surgery when your patient has cardiopulmonary comorbidities. The data showed that the educational module effectively increased healthcare providers' knowledge and confidence in using intravenous ascorbic acid as an available recommendation for managing oxidative stress. Anesthesia providers need to understand the possible implications of poorly managed oxidative stress relating to anesthetic management. Furthermore, it is imperative to stay informed with current research on this topic, and more research will need to be conducted to provide safe, quality patient care.

Conclusion

There is a lack of consensus published guidelines regarding the perioperative administration of intravenous ascorbic acid as a systematic strategy for mitigating hemodynamic changes related to IRI induced by tourniquet use despite literature demonstrating positive outcomes. Owing to the lack of guidelines for preventing tourniquet-induced ischemia-reperfusion damage, anesthesia providers must utilize evidence-based research to drive their clinical interventions to minimize IRI injuries and achieve optimal outcomes. Educational interventions such as this quality improvement project can effectively increase provider knowledge and the likelihood of utilizing current evidence-based research to provide safe, quality care and improve overall patient outcomes.

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Appendix A: IRB Exemption

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Office of Research Integrity
Research Compliance, MARC 414

MEMORANDUM

To:	Dr. Fernando Alfonso
CC:	Bilal Mohammad
From:	Elizabeth Juhasz, Ph.D., IRB Coordinator EJ
Date:	March 28, 2022
Protocol Title:	**"An Educational Module Highlighting the Efficacy of Intravenous Ascorbic Acid in Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery: A Quality Improvement Project"**

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #:	IRB-22-0119	**IRB Exemption Date:**	03/28/22
TOPAZ Reference #:	111573		

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
3) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

EJ

Appendix B: QI Project Consent

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CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT

"Efficacy Of Intravenous Ascorbic Acid for Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery"

SUMMARY INFORMATION

Things you should know about this study:

- **Purpose:** Educational module regarding the efficacy of intravenous ascorbic acid for attenuating hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury in patients undergoing lower extremity orthopedic surgery.
- **Procedures**: Participate in a pre-test, view an Educational Module via voice over PowerPoint, then participate in a post test
- **Duration:** This will take about a total of 20 minutes.
- **Risks**: The main risk or discomfort from this research is minimal
- **Benefits:** The main benefit to you from this research is increase the participant's knowledge of intravenous ascorbic acid for attenuating hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury in patients undergoing lower extremity orthopedic surgery.
- **Alternatives:** There are no known alternatives available to you other than not taking part in this study.
- **Participation:** Taking part in this research project is voluntary.

Please carefully read the entire document before agreeing to participate.

PURPOSE OF THE PROJECT

The goal of this project is to improve health care provider knowledge regarding the efficacy of intravenous ascorbic acid for attenuating hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury in patients undergoing lower extremity orthopedic surgery. You are being asked to participate in this quality improvement project

DURATION OF THE PROJECT

Your participation will require about 20 minutes of your time, you will be one of 10 people in this study

PROCEDURES

If you agree to be in the project, we will ask you to do the following things: Participate in a pretest view, an Educational Module via voice over PowerPoint, then participate in a post test.

RISKS AND/OR DISCOMFORTS
Minimal risk, risk not greater than if participant was conducting similar activity. Physical, psychological, social, legal, and economic risks minimal and no greater than if a participant was participating in a similar activity. Similar activity such as filling out an online survey and watching voice over PowerPoint.

BENEFITS
The following benefits with your participation in this project: An increase in your knowledge of intravenous ascorbic acid for attenuating hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury in patients undergoing lower extremity orthopedic surgery.

ALTERNATIVES
There are no known alternatives available to you other than not taking part in this project. However, if you would like to receive the educational material given to the participants in this project, it will be provided to you at no cost.

CONFIDENTIALITY
The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, we might publish, we will not include any information that will make it possible to identify you as a participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this research project is voluntary.

COMPENSATION & COSTS
There is no cost or payment to you for receiving the health education and/or for participating in this project.

RIGHT TO DECLINE OR WITHDRAW
Your participation in this project is voluntary. You are free to participate in the project or withdraw your consent at any time during the project. Your withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove you without your consent at such time that they feel it is in the best interest.

RESEARCHER CONTACT INFORMATION
If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Bilal Mohammad at 954-512-0276, bmoha008@fiu.eduj or Dr. Jorge Valdes at 305-348-7729/jvalde@fiu.edu.

IRB CONTACT INFORMATION
If you would like to talk with someone about your rights pertaining to being a subject in this project or about ethical issues with this project, you may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT

I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions I have about this study, and they have been answered for me. By clicking on the "consent to participate" button below I am providing my informed consent.

(Insert Consent to Participate Button Here on the Website)

Appendix C: Recruitment Letter

Efficacy of Intravenous Ascorbic Acid in Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery: A Quality Improvement Project

Dear Broward Health ANESCO anesthesia provider,

My name is Bilal Mohammad, and I am a student from the Anesthesiology Nursing Program Department of Nurse Anesthetist Practice at Florida International University. I am writing to invite you to participate in my quality improvement project. The goal of this project is to improve health care provider knowledge on efficacy of intravenous ascorbic acid in attenuating hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury in patients undergoing lower extremity orthopedic surgery. You are eligible to take part in this project because you are an anesthesia provider at Broward Health.

If you decide to participate in this project, you will be asked to complete and sign a consent form for participation. Next, you will complete a pre-test questionnaire, which is expected to take approximately 5 minutes. You will then be asked to view an approximately 15-minute-long educational presentation online. After watching the video, you will be asked to complete the post-test questionnaire, which is expected to take approximately 5 minutes. *No compensation will be provided.*

Remember, this is completely voluntary. You can choose to be in the study or not. If you'd like to participate or have any questions about the study, please email or contact me at bmoha008@fiu.edu or 954-512-0276.

Thank you very much.

Sincerely,

Bilal Mohammad

Appendix D: Letter of Support

February 1, 2022

Fernando Alfonso, DNP, CRNA, APRN
Clinical Assistant Professor,
Department of Nurse Anesthesiology
Florida International University

Dr. Alfonso,

Thank you for inviting Broward Health to participate in Doctor of Nursing Practice (DNP) project conducted by Bilal Mohammad entitled "The Efficacy of Intravenous Ascorbic Acid in Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery: An Educational Module." in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthetist Practice at Florida International University. I have warranted his permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best outcomes for patients by selecting interventions supported by the evidence. This project intends to evaluate if a structured education targeting providers will increase knowledge on the use of Intravenous Ascorbic Acid in Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery.

We understand that participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password encrypted digital cloud, and only be accessible to the investigators of this study: Bilal Mohammad and Dr. Alfonso. We expect that Bilal Mohammad will not interfere with normal hospital performance, behaving in a professional manner and following standards of care.

Prior to the implementation of this Educational project the Florida International University Institutional Review Board will evaluate and approve the procedures to conduct this project. Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

February 1, 2022

Edward Punzalan, DNP, CRNA, APRN — Date
Administrative Director of Nurse Anesthesia
Healthcare Performance Anesco

Appendix E: Pretest and Posttest Questionnaire

Pretest and Posttest Questionnaire:

An Educational Module Highlighting the Efficacy of Intravenous Ascorbic Acid in Attenuating Hemodynamic Fluctuations Associated with Tourniquet-Induced Ischemic Reperfusion Injury in Patients Undergoing Lower Extremity Orthopedic Surgery: A Quality Improvement Project

INTRODUCTION

The primary aim of this QI project is to improve the knowledge of anesthesia providers regarding the management of tourniquet induced ischemic reperfusion injury and the efficacy of intravenous ascorbic acid.

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format. These questions are meant to measure knowledge, perception, and understanding of tourniquet induced ischemic reperfusion injury, the associated effects and the efficacy of intravenous ascorbic acid.

PERSONAL INFORMATION

1. Gender
   a. Male
   b. Female
   c. Non-binary
   d. Prefer not to answer

2. Age in years
   a. 25-35
   b. 36-45
   c. 46-55
   d. 56-65
   e. > 65

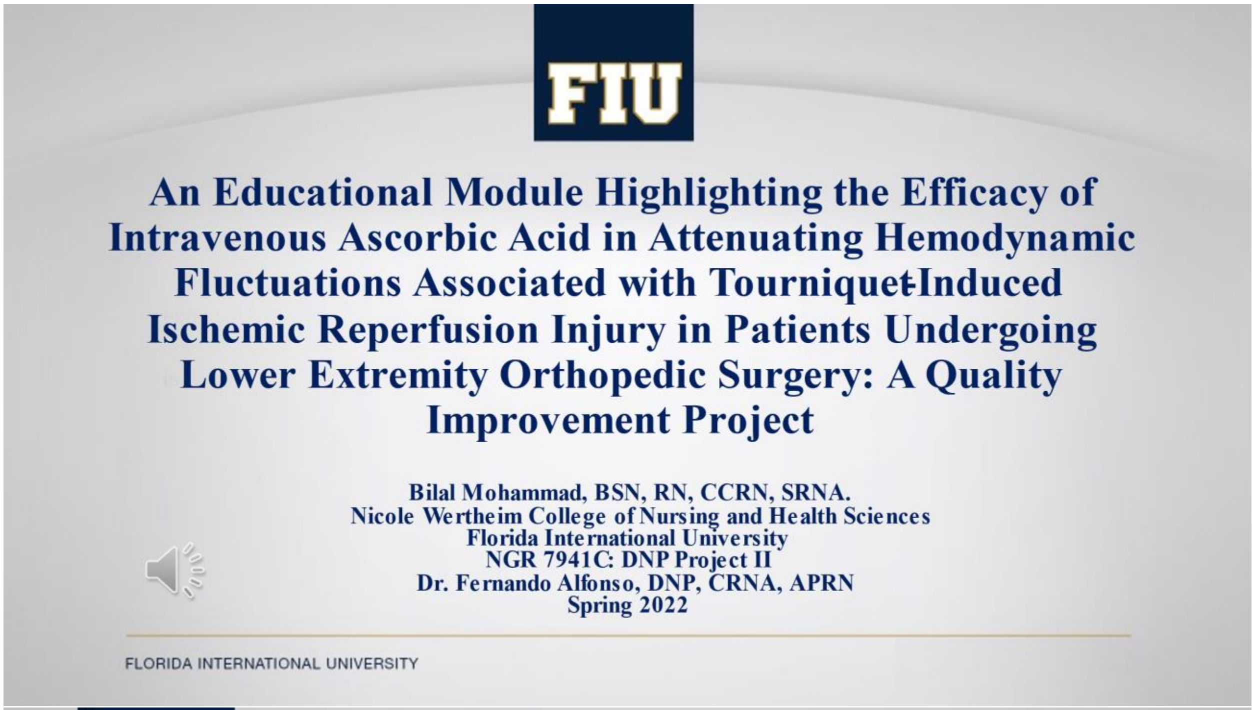
3. Ethnicity:
   a. Hispanic
   b. Caucasian (non-Hispanic)
   c. African American
   d. Asian
   e. Other
4. Position/Title
   a. Certified Registered Nurse Anesthetist
   b. MD anesthesia
5. Highest level of education
   a. Associates
   b. Bachelors
   c. Masters
   d. Doctorate
   e. Other
6. Years of practice as an anesthesia provider
   a. Less than 5
   b. 5-10
   c. 10-15
   d. Greater than 15

QUESTIONNAIRE

1. What are the benefits of utilizing pneumatic tourniquets for orthopedic surgeries?
    a. Decreased blood loss
    b. Enhanced visualization of anatomical structures
    c. Decreased Transfusion requirements
    d. All of the above
2. Inflation of pneumatic tourniquet results in what physiologic effects?
    a. Decreased arterial pressures
    b. Increased arterial pressures
    c. Hypokalemia
    d. Alkalosis
3. Upon deflation of the pneumatic tourniquet, the metabolites produced from ischemic area enter systemic circulation and produce what effects?
    a. Hypoxia and Hypotension
    b. Hypertension and Hyperoxia
4. During reperfusion and oxygenation, what is produced which contributes to leucocytic activation and endothelial damage in blood vessels?
    a. Excessive oxygen-free radicals
    b. Excessive carbon dioxide-free radicals
5. Pneumatic tourniquet use is associated with increased incidences of which of the following?
    a. Myocardial Infarction (MI),
    b. Deep Vein Thrombosis (DVT)
    c. Pulmonary Embolism (PE)
    d. All of the above
6. Intravenous ascorbic can be utilized intraoperatively for its antioxidant properties to attenuate hemodynamic fluctuation caused by oxygen-free radicals.
    a. True
    b. False
7. The antioxidant effects of ascorbic acid has shown to reduce intraoperative variations in hemodynamics and incidences of arrhythmias.
    a. True
    b. False
8. Incorporating high-dose ascorbic acid administration intraoperatively has myocardium protective effects for patients with concurrent severe pulmonary or cardiac disease.
    a. True
    b. False
9. Have you ever utilized intravenous ascorbic acid infusion during your anesthetic management for orthopedic surgeries involving a pneumatic tourniquet?
    a. Yes
    b. No
10. How frequent do you change your anesthetic plan for orthopedic surgery when your patient has cardiopulmonary comorbidities?
    a. Always
    b. Often

c. Sometimes
d. Never

Appendix F: QI Educational Module



Background

- Pneumatic tourniquets are an essential part of several orthopedic surgical procedures involving the lower limbs. [1-6]
- Their use drastically decreases blood loss and transfusion needs, enhances visualization of critical anatomical structures, and creates an adequate surgical field. [1-6]
- Tourniquet inflation increases arterial pressures and results in hypoxia, acidosis, and hyperkalemia. [1-5]
- When removed, metabolites produced from ischemic areas enter the systemic circulation, resulting in hypotension and hypoxia. [1-6]
- Excessive oxygen-free radicals are produced during reperfusion and oxygenation, contributing to leucocytic activation and endothelial damage in blood vessels. [1-6]

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Background (cont.)

- The excess oxygen-free radicals peroxide polyunsaturated fatty acids in membrane and plasma lipoproteins and directly inhibit mitochondrial respiratory chain enzymes, affecting major organ functions. [1-6]
- This sequela of is known as tourniquet -induced Ischemic Reperfusion Injury (IRI). [1-6]
- Oxygen-free radicals play a crucial role in developing significant cardiovascular complications following reperfusion injury. [1-6]
- These complications are especially problematic in patients with pre -existing cardiovascular disease undergoing orthopedic procedures such as total knee replacement (TKR) with tourniquet application. [1-6]

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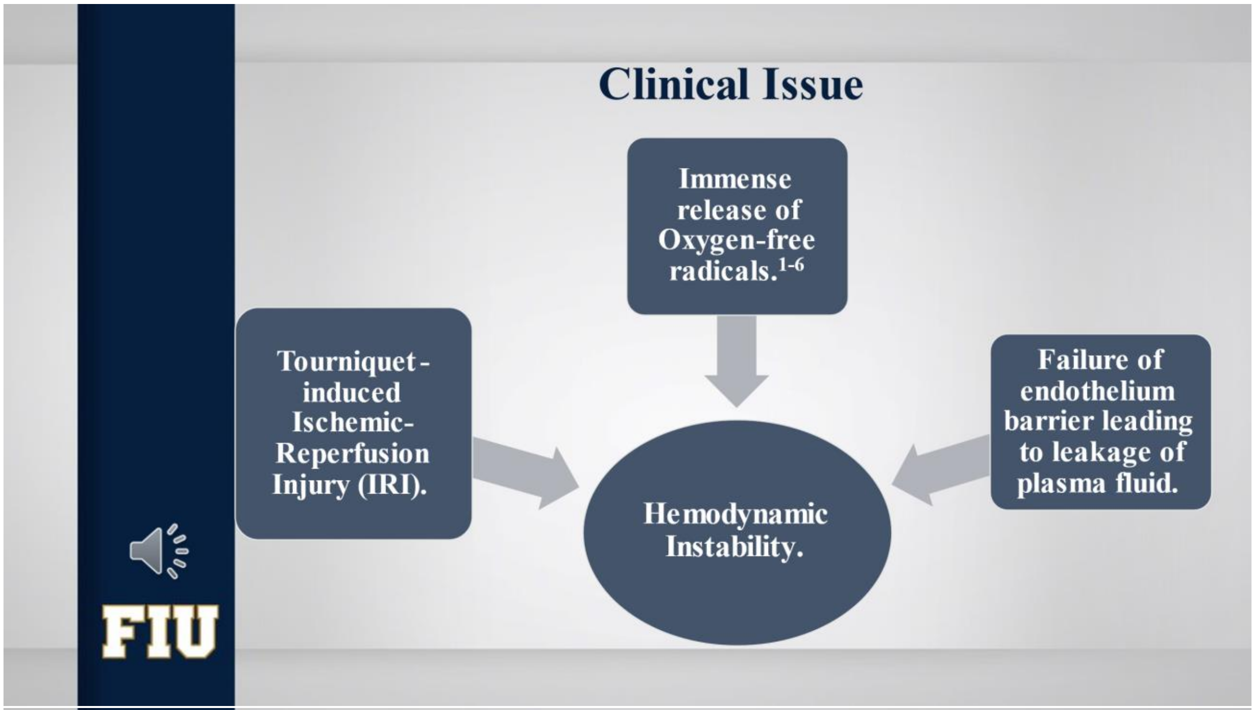
Clinical Issue
Immense release of Oxygen-free radicals.1-6
Tourniquet-induced Ischemic-Reperfusion Injury (IRI).
Failure of endothelium barrier leading to leakage of plasma fluid.
Hemodynamic Instability.
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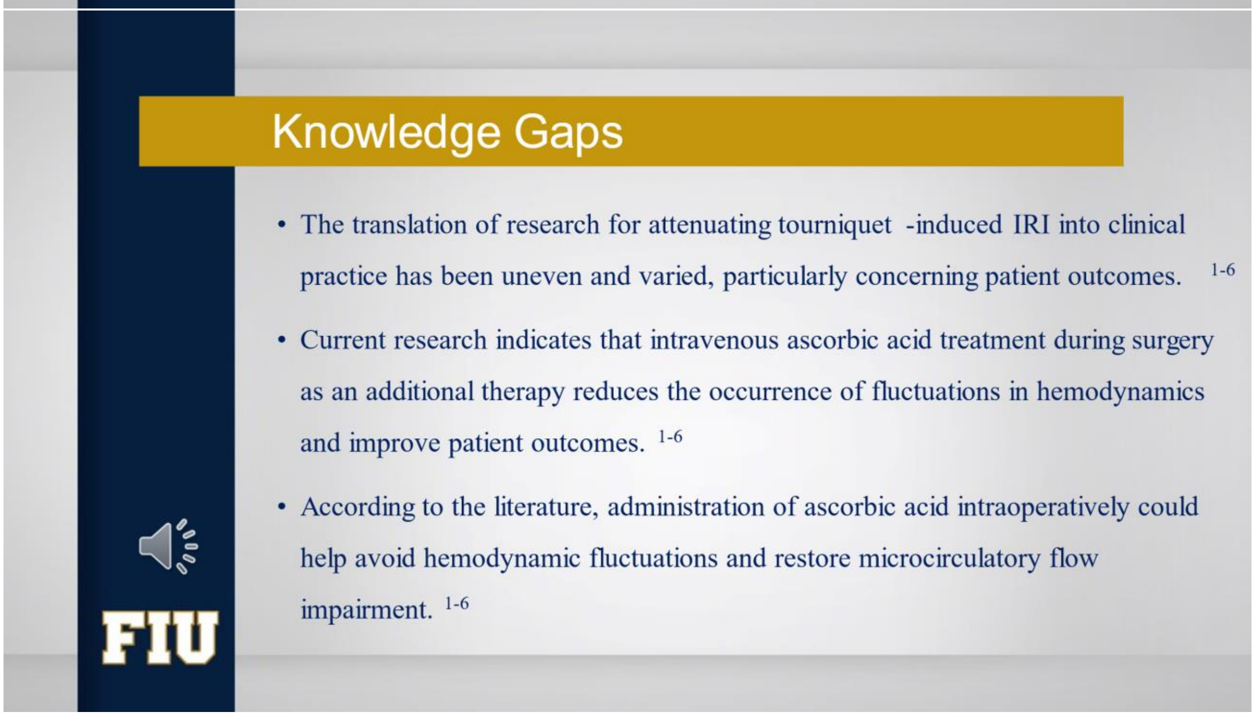
Knowledge Gaps
• The translation of research for attenuating tourniquet -induced IRI into clinical practice has been uneven and varied, particularly concerning patient outcomes. 1-6
• Current research indicates that intravenous ascorbic acid treatment during surgery as an additional therapy reduces the occurrence of fluctuations in hemodynamics and improve patient outcomes. 1-6
• According to the literature, administration of ascorbic acid intraoperatively could help avoid hemodynamic fluctuations and restore microcirculatory flow impairment. 1-6
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Proposed Solution

- According to the literature, intraoperative ascorbic acid administration can help attenuate hemodynamic fluctuation caused by IRI. [1-6]
- When used as an adjunctive therapy, the antioxidant effects of ascorbic acid helps prevents adverse hemodynamic effects associated with tourniquet -induced IRI of vascular endothelium. [1-6]
- These antioxidant effects help reduce intraoperative variations in hemodynamics and incidences of arrhythmias. [1-6]

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Anesthesia Implications

- Pneumatic tourniquet use is associated with increased incidences of Myocardial Infarction (MI), Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), Cerebral Vascular Accident (CVA), multisystem organ dysfunction, and increased post -operative rates of morbidity and mortality.[1-6]
- Oxygen free radicals are critical in developing severe cardiovascular problems following reperfusion damage. [1-6]
- Current research indicates that high dose ascorbic acid administration during the intraoperative period could have myocardium protective effects, particularly in elderly patients with concurrent severe pulmonary or cardiac disease. [1-6]

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Take Home Points

- Pneumatic tourniquet use is associated with increased incidences of MI, DVT, PE, MOD, and increased post-operative rates of morbidity and mortality.[1-6]
- Current research indicates that high dose ascorbic acid administration during the intraoperative periodhas proven to reduce intraoperative fluctuations and improve postoperative patient outcomes.[1-6]
- The use of intravenous ascorbic acid is efficacious in attenuating hemodynamic fluctuations associated with tourniquet-induced ischemic reperfusion injury in patients undergoing lower extremity orthopedic surgery.[1-6]

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