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Is Current Evidence that Avoidance of Inhalation Agents and Opioids May Decrease Metastasis Strong Enough for CRNAs to Show a Willingness to Change Practice?

Michael Wesley Tillman
University of Southern Mississippi

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IS CURRENT EVIDENCE THAT AVOIDANCE OF INHALATION AGENTS AND OPIOIDS MAY DECREASE METASTASIS STRONG ENOUGH FOR CRNAS TO SHOW A WILLINGNESS TO CHANGE PRACTICE?

by

Michael Wesley Tillman

A Capstone Project
Submitted to the Graduate School and the Department of Advanced Practice at The University of Southern Mississippi in Partial Fulfillment of the Requirements for the Degree of Doctor of Nursing Practice

Approved:

________________________________________
Dr. Marjorie Geisz-Everson, Committee Chair
Assistant Professor, Advanced Practice

________________________________________
Dr. Sat Ananda Hayden, Committee Member
Assistant Professor, Systems Leadership and Health Outcomes

________________________________________
Dr. Bonnie L. Harbaugh, Committee Member
Professor, Systems Leadership and Health Outcomes

________________________________________
Dr. Karen S. Coats
Dean of the Graduate School

December 2016
ABSTRACT

IS CURRENT EVIDENCE THAT AVOIDANCE OF INHALATION AGENTS AND OPIOIDS MAY DECREASE METASTASIS STRONG ENOUGH FOR CRNAS TO SHOW A WILLINGNESS TO CHANGE PRACTICE?

by Michael Wesley Tillman

December 2016

Metastasis following the surgical resection of primary site breast cancer is a medical issue, which plagues mastectomy patients. The intention of this project was to synthesize current literature in order to make a presentation and disseminate it to Certified Registered Nurse Anesthetists (CRNAs) in southern Mississippi and assess the providers' willingness to change practice. CRNAs took part in a Qualtrics survey after viewing a PowerPoint presentation of evidence regarding anesthesia and metastasis. The presentation illustrated the anesthetic techniques and pharmacological agents utilized, which either mitigate or potentiate a patient's risk for metastasis. The survey assessed for a willingness to change practice. Results from the survey indicate a willingness to change current practice by 18 of the 32 participants based on the evidence presented.
ACKNOWLEDGMENTS

I would like to thank my committee chair Dr. Marjorie Geisz-Everson, and two committee members Dr. Sat Ananda Hayden and Dr. Bonnie L. Harbaugh for their tireless guidance and support throughout this project.
DEDICATION

I would like to thank my loving wife Kristin and two sons Cillian and Cade for the sacrifices which they endured throughout this process. Without them and my family's support, this would not have been possible.
# TABLE OF CONTENTS

ABSTRACT ........................................................................................................... ii

ACKNOWLEDGMENTS .......................................................................................... iii

DEDICATION ......................................................................................................... iv

LIST OF ABBREVIATIONS .................................................................................... viii

CHAPTER I - INTRODUCTION ............................................................................... 1

Clinical Question ................................................................................................. 1

Purpose of the Project .......................................................................................... 2

Problem Statement ............................................................................................... 2

Needs Assessment ................................................................................................ 3

Significance and Implications ............................................................................... 3

Theoretical Framework ......................................................................................... 4

Doctor of Nursing Practice Essentials ............................................................... 5

CHAPTER II - REVIEW OF THE LITERATURE ..................................................... 6

Metastasis and Factors of Metastasis ................................................................... 6

Surgical Stress, Immune Status, and Metastasis ................................................... 7

Effects of Pharmacological Agents Regarding Metastasis ................................. 8

Inhalation Agents ................................................................................................ 9

Opioids and Pain Management .......................................................................... 10

Local Anesthetics ............................................................................................... 11
APPENDIX A – DNP Essentials ................................................................. 24
APPENDIX B – Logic Model ..................................................................... 25
APPENDIX C – SWOT .............................................................................. 26
APPENDIX D – Survey ............................................................................ 27
APPENDIX E – Consent ........................................................................... 28
APPENDIX F – Support Letter ................................................................. 29
APPENDIX G – Question Four and Five ................................................... 30
APPENDIX H – Question Six and Seven .................................................. 31
APPENDIX I – Question Eight ................................................................. 32
REFERENCES .......................................................................................... 33
### LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>COX</td>
<td>Cyclooxygenase</td>
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<tr>
<td>CRNA</td>
<td>Certified Registered Nurse Anesthetist</td>
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<td>DNP</td>
<td>Doctoral of Nursing Practice</td>
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<td>EGF</td>
<td>Endothelial Growth Factor</td>
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<td>HSC</td>
<td>Hemopoietic Stem Cell</td>
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<td>IRB</td>
<td>Institutional Review Board</td>
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<tr>
<td>LAs</td>
<td>Local Anesthetics</td>
</tr>
<tr>
<td>MAC</td>
<td>Minimum Alveolar Concentration</td>
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<tr>
<td>MANA</td>
<td>Mississippi Association of Nurse Anesthetists</td>
</tr>
<tr>
<td>NK</td>
<td>Natural killer cell</td>
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<tr>
<td>NSAIDS</td>
<td>Nonsteroidal Antiinflammatory Drugs</td>
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<tr>
<td>SWOT</td>
<td>Strengths, Weaknesses, Opportunities, and Threats</td>
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<tr>
<td>TIVA</td>
<td>Total Intravenous Anesthesia</td>
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CHAPTER I - INTRODUCTION

The choices CRNAs make regarding anesthesia for their patients directly impact the patient's immediate well-being and their long-term prognosis (Snyder & Greenberg, 2010). One widely utilized strategy for the treatment of primary site solid breast carcinomas is surgery (Heaney & Buggy, 2012). General anesthesia and surgery are known to play roles in the suppression and inhibition of the immune system (Barash, Cullen, Stoelting, Cahalan, & Stock, 2009). Therefore, surgical removal of the tumor with the use of general anesthesia may place the patient at risk for future metastasis. Risks associated with the surgical removal of cancer may be alleviated or exacerbated by the anesthetics and analgesics the patient receives before, during, and after the operative procedure (Heaney & Buggy, 2012). Evidence is accumulating suggesting that a multimodal approach to the anesthetic management of this patient population may decrease cancer recurrence following mastectomy surgery.

Clinical Question

Is there a willingness to change practice when CRNAs are provided with current evidence related to which anesthetic techniques influence the surgical mastectomy patient's risk of metastasis? Numerous techniques exist to provide anesthesia and analgesia to this patient population. Opioids and inhalation agents have been found to increase a patient's risk for metastasis while other techniques, such as the use of neuraxial blockade, regional anesthesia, and a multimodal approach, decrease the risk (Exadaktylos, Buggy, Moriarty, Mascha, & Sessler, 2006; Heaney & Buggy, 2012; Snyder & Greenberg, 2010).
Purpose of the Project

The purpose of this doctoral project was to assess the willingness of CRNAs to change practice when presented with a synthesis of current evidence from the literature related to anesthesia and metastasis. The synthesis illustrates which anesthetic techniques and pharmacological agents may either mitigate or potentiate a patient's risk for metastasis. The project explores ways to improve not only the mastectomy patient's experience throughout the operative period but also recognize the contributions of anesthesia and analgesia and how those factors can improve the patient's health long-term (Heaney & Buggy, 2012). Multimodal anesthesia approaches the pain experienced by a patient during surgery using a variety of routes instead of the single approach of opioids (Peters, Brayton, & Erickson, 2006). The patient who receives a multimodal approach to care, such as a regional or neuraxial blockade coupled with cyclooxygenase (COX) inhibitors and sedatives, requires less inhalation agent and fewer opioids throughout the perioperative period (Hodgson & Liu, 2001; Sinatra, De Leon-Casasola, Ginsberg, & Viscusi, 2009). The utilization of multimodal approach with either a neuraxial block or regional block would allow for a decrease in the use of inhalation agents during general anesthesia which may reduce the incidence of metastasis (Exadaktylos et al., 2006; Heaney & Buggy, 2012; Snyder & Greenberg, 2010). After viewing a presentation with the current data, the CRNAs' willingness to change practice was assessed.

Problem Statement

Within healthcare and the implementation of research, a gap exists and is referred to as the evidence-practice gap (Kristensen, Nymann, & Konradsen, 2016). Kristensen
and colleagues (2016) define the evidence-practice gap as the prolonged time in which it takes for emerging research methods to be translated into practice changes. The existence of the gap allows for the prolonged use of outdated practices. Integration of emerging research into practice change remains a problem in today's healthcare system (Kristensen et al., 2016).

Needs Assessment

Snyder and Greenberg (2010), found the anesthesia provided perioperatively influences the long-term prognosis post-operatively. Their findings revolve around the current knowledge concerning tumor biology and the patient's defense mechanisms. Currently, general anesthesia combined with opioids is the approach suggested for the anesthesia for mastectomy surgery (Fitzgerald-Macksey, Sowka, Cipcic, Kaufman, & Callaway, 2012). The direct effects of each anesthetic and pharmacologic medication on the patient's immune system vary from agent to agent (Nagelhout & Plaus, 2014). How anesthesia and analgesia influences inflammation and the alteration of the immune system induced by surgery influencing metastasis is an area of interest within research. Some anesthetics and pharmacologic agents such as nitrous oxide and opioids may decrease the patient's immune responses while others, such as local anesthetics (LAs) and COX inhibitors, may offer benefits for the immune system (Heaney & Buggy, 2012).

Significance and Implications

The purpose of this doctoral project was to assess the willingness of CRNAs to change practice when presented with a synthesis of current evidence from the literature related to anesthesia and metastasis. CRNAs are positioned to implement change within today's healthcare system. Implementation of anesthetic techniques which decrease the
risk of metastasis for patients will require utilization of pharmacologic agents that are beneficial to the patient's immune system. The implication exists that a CRNA may be able to decrease metastasis based on their anesthetic technique (Heaney & Buggy, 2012; Snyder & Greenberg 2012). Nurse anesthetists are educated on the implementation of research data, and as new methods become available they should be put into practice.

Theoretical Framework

Lewin's change theory (1947) proposes a planned change approach to asserting a change within a given system. A cultural change must permeate all levels of a system. This theory affords the ability to implement research into a change in practice. The change must be a change in the cultural atmosphere, not just a change of a single item (Burnes, 2004). Initially, Lewin's change theory was utilized successfully by industries in the 1940's to introduce a change in a system or process (Butts & Rich, 2015).

Industry utilized this theory as a way to implement positive movement increasing production. Lewin portrayed the change as a dynamic force inside an organization that pulls in conflicting directions (Lewin, 1947). Two opposing forces are at work within a system change, one that pushes for change, and one resisting the change. Butts and Rich (2015) affirm Lewin viewed change as a balance of these forces, not a single event.

Lewin's change theory has three distinct phases. The phases include, unfreezing, moving, and refreezing (Lewin, 1947). In phase one, the new research must be identified to spark the change. The old practice must be discarded and deemed no longer the gold standard to allow for further progression. General anesthesia and opioids must be viewed as increasing the risk of metastasis. Moving into phase two, a change of thought must be accomplished within the system. The change in thought will allow for the proposed idea
to replace the old norm. The new idea must be founded on data that supports the change. Multimodal anesthesia and the use of local anesthesia may decrease the risk of metastasis (Fodale, D'Arrigo, Triolo, Mondello, & La Torre, 2014). Lastly, in phase three, the new method must become the norm within the culture (Lewin, 1947).

Doctor of Nursing Practice Essentials

As a doctoral level nursing capstone project, the doctor of nursing practice (DNP) essentials must be met in some way within the project. The adherence of this doctoral level nursing capstone project to the DNP essentials is found in Appendix A. Each essential is listed in the appendix with a brief statement of how the project met the essential.
CHAPTER II - REVIEW OF THE LITERATURE

Since the turn of the century, advances have been made in the medical understanding of cancer. Specifically, one area of research examines techniques to mitigate the risks associated with the surgical removal of cancer. Surgical removal of primary tumors is a viable option for the treatment of most cancer patients (Cooper, 2009). In this literature review, the articles focus on decreasing the risk of metastasis associated with anesthetic techniques and pharmacological agents. Included in the review are factors related to the implications of surgical stress, alterations of immune status during anesthesia, inhalation agents, opioids and pain management, LAs, and multimodal approaches and the impact on the cancer patient. From this review, a conclusion on the modalities which are beneficial or harmful to the mastectomy patient population were made.

Metastasis and Factors of Metastasis

An understanding of the times at which a tumor cell may metastasize requires a description of the process of metastasis. Briefly, to summarize the metastatic processes of a cancerous cell, the cell must detach, migrate, implant, and begin angiogenesis or the development of a blood supply for metastasis to occur (Talmadge & Fidler, 2010). The progression of a cancer cell to metastasize is complex and multifactorial with many external factors influencing the tumor cell during the process.

Specific factors noted as possible influences of cancer recurrence are: stimulation of cytokine and neuroendocrine stress response; restraint of cell-mediated immunity, dispersal of tumor emboli, and the promotion of tumor growth and metastasis (Heaney & Buggy, 2012). Throughout the literature, science supports the idea that over stimulation
or suppression of the stress response increases the likelihood of cancer recurrence postoperatively (Gottschalk, Sharma, Ford, Durieux, & Tiouririne, 2010). Heaney and Buggy (2012), echo an earlier postulation by Gottschalk et al. (2010) which draw a correlation between the anesthetic events that occur during surgery and metastasis. Fodale and colleagues (2014) show in vitro and in vivo studies provide information that the patient's physiological response to surgical stress plays a role in the metastatic spread of cancer. A relationship between the patient's response to surgery, anesthetics, and possible metastasis becomes evident within the literature.

Surgical Stress, Immune Status, and Metastasis

While surgical removal of solid tumors is the core of cancer treatment (Snyder & Greenberg, 2010), the need to ameliorate the stresses of the surgical experience exists. Surgery imparts stressors on the patient (Exadaktylos et al., 2006; Reiche, Vargas Nunes, & Morimoto, 2004). According to Barash et al. (2009), surgical stress induces the release of cytokines and adversely influences the neuroendocrine and sympathoadrenal responses. The actions of surgical stress are detrimental to the physiological responses of the patient under anesthesia (Barash et al., 2009). CRNAs play a role in stress relief of the cancer patient (Gottschalk, Sharma, Ford, Durieux, & Tiouririne, 2010). The stress response is vital in healing postoperatively, for over stimulation or suppression of the stress response may lead to metastasis (Gottschalk et al., 2010). Fodale et al. (2014) state surgery causes alterations in the stress response, which determine upregulation of malignant pathways involved in cancer recurrence. Inadvertent dispersal of tumor cells during surgical manipulation, with a coexisting suppression of cell-mediated immunity, and the effects of proangiogenic (factors associated with vascular supply formation)
anesthetics are noted as being keys to the dispersion and development of cancer recurrence (Heaney & Buggy, 2012). Through the use of different anesthetics and analgesics, the risk of metastasis may be mitigated.

Surgical stress may cause a decrease in homeostasis of the immune system and allow metastasis to occur. An inference resonating throughout the literature is that surgery and the events occurring during the perioperative period decrease immune system function (Exadaktylos et al., 2006; Fodale et al., 2014; Heaney & Buggy, 2012; Reiche et al., 2004; Snyder & Greenberg, 2010). The cancer patient's immune system is recognized as the primary defense against metastasis (Bar-Yosef et al., 2001). Recent findings by Fodale et al. (2014), suggest that surgery, anesthesia, and analgesia cause immunosuppression by secreting proinflammatory and anti-inflammatory cytokines promoting the evasion of tumor cells from immune control. Dewan et al. (2007) and Exadaktylos et al. (2006) illustrated the vital role of natural killer (NK) cells, within the immune system and their defense against tumor cells. Prior studies have shown a low level of circulating NK cells during the perioperative period is associated with a rise in morbidity and mortality in cancer patients (Britenden, Heys, Ross, & Eremin, 1996; Vujanovic, Basse, Beberman, & Whiteside, 1996). With immunological status playing a role in metastasis, methods to mitigate the deleterious effects during this time must be identified. A multimodal approach may offer benefits to the surgical mastectomy patient, related to a decrease in the amount of perioperative inhalation agent and opioids required.

Effects of Pharmacological Agents Regarding Metastasis

Anesthetics and analgesics used during surgery likely have effects beyond the perioperative period (Fodale et al., 2014). Heaney and Buggy (2012), and Gottschalk et
al. (2014) both provide specific traits of anesthetic pharmacologic agents and their potential effects on the surgical cancer patient. A synthesis of the information presented within the literature reviewed, in regards to pharmacological agents and their effects on the host’s immune system and homeostasis is presented in this section.

Inhalation Agents

Inhalation anesthetic agents are often used to accomplish general anesthesia during surgery. Sevoflurane and isoflurane are shown to bring on apoptosis (programmed cell death) in T-lymphocytes in a manner which has a direct relationship with the amount of agent used (Heaney & Buggy, 2012; Loop et al., 2005). Tedore (2015) deduced that inhalation agents were noted to increase pro-angiogenic factors, promote hypoxia-inducible factors, and increase cancer cell migration-promoting the recurrence of cancer. Snyder and Greenberg (2010) noted a decrease in NK cells, neutrophils, macrophages, dendritic, and impaired T-cell function with inhalation agents. Heaney and Buggy noted the implications of nitrous oxide with immune-altering effects in the laboratory and clinical studies (Heaney & Buggy, 2012), yet in a study by Fleischmann et al. (2009), no significant recurrence in cancer was found while using nitrous oxide. Snyder and Greenberg (2010) correlate nitrous oxide with the inhibition of the formation of hematopoietic stem cells (HSCs), which are a factor relevant in tumor surveillance. HSCs promote cell production which may deliver an uninterrupted supply of targeted anti-cancer cells (Gschweng, De Oliveire, & Kohn, 2014). While the literature is inconclusive regarding the use of nitrous oxide and the incidence of the recurrence of cancer, the literature at this time indicates sevoflurane and isoflurane depress the immune system and promote metastasis through their actions.
**Opioids and Pain Management**

During the perioperative period, opioids are frequently used for the management of pain (Heaney & Buggy, 2012). Opioids can cause inhibition of cellular and humoral immunity (Fodale et al., 2014; Gottschalk et al., 2010). As described earlier, any depression in a patient's immune system throughout the operative experience increases the risk of cancer recurrence.

Opioids inhibit cell-mediated immunity and the host's anti-tumor defenses including the necessary action of NK cells (Fodale et al., 2014; Snyder & Greenberg, 2010). In lab rat studies, Fentanyl has been shown to provide a sharp rise in NK cell action during the initial 24 hours perioperatively, yet followed by the increase is a prolonged and significant eight-day depression (Forget, Collet, Land’homme, & De Kock, 2010). Morphine, a commonly used opioid postoperatively, may activate vascular endothelial growth factors (EGF) (Heaney & Buggy, 2012). With the activation of EGF, a tumor cell can develop a vascular supply which could promote cancer recurrence (Talmadge & Fidler, 2010). The findings of Heaney and Buggy (2012) corroborate the studies on fentanyl and morphine, suggesting opioids have additive deleterious effects in the breast cancer patient as they promote cancer cell migration and angiogenesis.

Decreasing pain throughout the operative experience, without the utilization of opioids, affords a patient's immune system optimal effectiveness (Heaney & Buggy, 2012). Opioids stimulate tumor growth, promote cell migration, and promote angiogenesis, while opioid antagonists exhibit therapeutic effects on cancer progression (Fodale et al., 2014). Taking these actions into account, the use of alternatives to opiates in this population could be beneficial.
Local Anesthetics

The use of LAs to decrease perioperative pain and thus reduce the use of opioids and inhalation agents requirements during the surgery has been studied. Le-Wendling, Nin, and Capdevila (2016) have found the benefits of LAs in decreasing the recurrence of cancer have theoretical basis while also having the support of existing literature. LAs are currently utilized for cancer patients through modalities such as neuraxial anesthesia, regional anesthesia and surgical site infiltration (Le-Wendling et al., 2016; Sessler, Ben-Eliyahu, Mascha, Parat, & Buggy, 2008; Weng et al., 2016). A neuraxial block is the use of LAs injected into an area which targets a nerve root to block the transmission of pain, and is accomplished through the use of a spinal or epidural blockade (Nagelhout & Plaus, 2014). Regional anesthesia is the injection of LAs around a nerve to block the transmission of pain targeting a more localized area of the body (Nagelhout & Plaus, 2014). Surgical site injection of LAs can also be used to alleviate the pain experienced by a patient postoperatively (Nagelhout & Plaus, 2014). LA agents also decrease the pain a patient experiences (Albi-Feldzer et al., 2013).

LAs provide a decrease in cancer recurrence based on their anti-proliferative effects on neoplastic cells coupled with the decreased need for immune-suppressive treatments like opioids (Heaney & Buggy, 2012; Sessler et al., 2008; Snyder & Greenberg, 2010). The finding that LA agents decrease immunosuppression is supported by Lucchinetti et al. (2012). Amide LAs were implicated by Lucchinetti et al. (2012) for their impedance on mesenchymal stem cells, which are key players in tumor growth and metastasis formation. Lidocaine was implicated by Snyder and Greenberg, (2010), in having a direct inhibitory influence on the endothelial growth factor receptor, which
directly inhibits the proliferation of the tumor cell. The benefits of LAs may be appreciated through the use of neuraxial anesthesia, regional or peripheral blocks, and surgical site injection.

The logical deduction can be made that, with a reduction in the pain experienced there is a subsequent decline in the need for opioids. Increased use of LAs, through the use of the continuous intercostal block for mastectomy patients, may provide a sharp decline in postoperative pain and narcotics needed (M. Herren, personal communication, June 3, 2016). The intercostal block utilized by Dr. Herren provides a continuous infusion of ropivacaine, decreasing the patient's pain for three days. Anecdotally, the lack of pain experienced by Dr. Herren's patients is accompanied by a reduction in opioid use during the postoperative period. This anecdotal evidence is supported by the findings of Albi-Feldzer et al. (2013). Furthermore, if the pain is not alleviated, the treatment of the pain with opioids can cause a deficit of NK cells and stimulate tumor development (Fodale et al., 2014).

In a meta-analysis of 21 studies conducted by Weng et al. (2016), a significant association between neuraxial anesthesia and a decrease in cancer recurrence was identified. The use of LAs attenuated the neuroendocrine stress response, which decreased the need for opioids and inhalation agents (Sessler et al., 2008). The reduction in recurrence of metastasis after mastectomy surgery was verified, in a study by Sessler and colleagues (2008). In this study, neuraxial blockade and light sedation were found to reduce recurrence when compared to inhalation agents and opioids alone. When utilized with multimodal anesthesia/analgesia, both the techniques of neuraxial and regional anesthesia, are reported to increase immune system function.
Multimodal Approach

Sedation during surgery does not have to be accomplished through the use of inhalation agents during the perioperative period (Fodale et al., 2014). Sedation can be accomplished through the utilization of other pharmacological agents such as ketamine, propofol, thiopental, or alpha-agonists. Ketamine and thiopental are implicated in increasing the number of viable cancer cells while suppressing NK cell activity (Snyder and Greenberg, 2010). Beilin et al. (2007) found ketamine suppressed NK cells while attenuating pro-inflammatory cytokines, IL-6, and TNF-α. Propofol, a commonly used anesthetic agent, has not been implicated as a negative influence on the immune system (Snyder & Greenberg, 2010). Das, Kumar, Khanna, and Mehta (2014) promote the use of propofol over inhalation agents, for the antitumor effects via inhibition of COX and prostaglandins.

The non-steroidal anti-inflammatory drugs (NSAIDs) restrain prostaglandin synthesis through the inhibition of the COX enzyme (Nagelhout & Plaus, 2014). The COX-2 inhibitors are of increasing interest in providing care for the surgical cancer patient due to their pharmacodynamics (Snyder & Greenber, 2010). Inhibition of COX-2 by celecoxib has been shown to induce apoptosis in tumor cells, delay tumor growth, inhibit metastasis, and suppress angiogenesis of metastatic cells (Leahy et al., 2002). COX-2 inhibitors are beneficial considering the over-expression of COX-2 and increase in prostaglandins found in a variety of cancers such as colorectal, breast, bladder, cervical, and ovarian (Heaney & Buggy, 2012). White (2016) promotes the use of aggressive multimodal techniques during the perioperative period, even without the support of prospective clinical data.
Conclusion

The variables which influence the risk of metastasis are numerous, but alternatives to inhalation agents with the use of opioids, which may promote metastasis, exist. After synthesizing the current data regarding metastasis in the cancer patient, care plans for the surgical cancer patient may be derived. Optimally, the surgical patient would receive no opioids or inhalation agents. Total intravenous agents provide safer anesthesia than inhalation agents. Pain controlled through the use of LAs, neuraxial or regional blockade, and pharmacologic agents such as COX-2 inhibitors and NSAIDs provide a decreased risk of metastasis. The authors of the studies agree on the need for further studies surrounding this topic. The evidence is not supported by prospective randomized control trials at this time. Without the support of strong evidence, such as a completed randomized control trial, it is still logical to conclude a multimodal approach with refrain from inhalation agents and opioids may help decrease the risk of metastasis. The utilization of multimodal analgesic techniques during the perioperative period for the surgical cancer patient may offer the most optimal outcome. The literature reveals, a connection for cancer recurrence and the use of opioid analgesics and inhalation agents. A multimodal approach if utilized could sever the connection. A multimodal approach decreases the need for inhalation agents and opioids for pain control thus possibly reducing the risk of metastasis.
CHAPTER III - METHODOLOGY

The purpose of this doctoral project was to assess the willingness of CRNAs to change practice when presented with a synthesis of current evidence from the literature related to anesthesia and metastasis. Evidence gained from the literature review inferred a correlation between metastasis and the possible role of anesthetics and analgesics. With the given evidence, a clinical update was formulated. The evidence-based update was then disseminated to CRNAs, practicing in Mississippi, who were members of the Mississippi Association of Nurse Anesthetists (MANA) via a mass email from MANA. Evaluation of the information presented and the impact of the information was analyzed using a posthoc survey which was included in the email. The methodology section of this project is in the following order: 1) Sample, 2) Synthesis of Evidence, 3) Dissemination of Evidence, 4) Evaluation of Impact on Providers, 5) Methods, 6) Analysis.

Sample

A convenience sample consisting of CRNAs who were members of the MANA were used for this project. MANA membership is comprised of nearly 600 nurse anesthetists. MANA was contacted for support of the project and their letter of support is attached as Appendix G. MANA agreed to disseminate an email of the project to all CRNAs within the association. Identified providers were sent an e-mail invitation to participate in the project. Inclusion criteria were limited to members of MANA. All other anesthesia providers were excluded from the project.

Synthesis of Evidence

A review of the literature was performed to formulate an evidence-based recommendation for anesthesia practice regarding the surgical mastectomy patient
population. The review of the literature was guided by clinical anesthetics and analgesics, which influence the surgical mastectomy patient's risk of metastasis. Numerous databases were used to identify relevant articles; databases searched include CINAHL with full text, MEDLINE, Pubmed, OVID, and Google Scholar. Keywords used included anesthetic influence and cancer long-term survival, anesthesia and breast cancer surgery, analgesia and breast cancer surgery, anesthesia and influence and metastasis, anesthetic agents and metastasis risk, analgesics and cancer recurrence, analgesics and metastatic risk, and the role of anesthesia in cancer prognosis. Any research that discussed anesthetic agents and analgesic techniques concerning metastasis probability were included. Only articles that were peer-reviewed or appeared in professional journals and were written in English were included. Fifty-four articles were reviewed for inclusion, and out of those, 15 were found to be viable for inclusion in the project. Only articles produced from 2009-2016 and seminal articles on the topic were integrated into this review of literature.

Dissemination of Evidence

All CRNAs who were members of MANA received an email inviting them to participate in the project. The email contained a presentation and a link to the survey. The results of the synthesis of evidence were shared with the participants, via a succinct powerpoint presentation. The email also contained a link to a Qualtrics survey. Participants were made aware that their participation in the survey implied informed consent. The aim of this doctoral project was to identify if a willingness to change practice was present in CRNAs when presented with information regarding a possible connection between metastasis and anesthesia and analgesia in breast cancer patients.
Impact on CRNAs

The CRNAs viewed a powerpoint presentation and completed a survey about the evidence presented. The presentation and the survey required approximately five to ten minutes to complete. Demographic data along with a self-assessment of the individual CRNA's willingness to change practice and identification of barriers that might impede a change in practice were collected. A logic model was constructed to assist in maintaining focus on the impact of the project and can be found in Appendix C.

Strategies

Within the anesthetic care of this patient population, there are modifiable risk factors that may be accomplished by the anesthesia provider to mitigate further risk to the patient. Using Lewin's change theory (1947), unfreezing of outdated practices will occur and re-freezing of new evidence-based practice changes will become the norm. The key to implementation of change is identification and recognition of strengths, weaknesses, opportunities, and threats (SWOT) to a proposed change (Appendix D).

Methods

After obtaining Institutional Review Board (IRB) approval (Appendix E) from the University of Southern Mississippi, all CRNAs within the sample were invited to participate in the project via e-mail. The e-mail contained directions for informed consent, participation, the abstract of the project, a PowerPoint presentation, and a link to the Qualtrics survey. The presentation highlighted evidence synthesized about anesthetic techniques and agents utilized, and their implications on the surgical mastectomy patient population. No specific recommendations to implement change were presented.
After viewing the presentation, the CRNAs completed the Qualtrics survey. A single reusable link to the survey was located directly under the link to the presented evidence within the email. The survey was formatted utilizing Qualtrics, a sample of the survey questions are found in Appendix F. The providers were instructed to read the questions and answer using a Likert-type scale. With the scale measurement being: 1) strongly disagree, 2) disagree, 3) neutral, 4) agree, and 5) strongly agree. The survey contained forced response questions. The CRNA participants were required to answer the previous question to move on to the next question. The goal of the survey was to identify a willingness to change practice in the care of the mastectomy patient by participants.

Data collected was anonymized. There were no anticipated risks to participants by completing the survey. The informed consent statement is located in Appendix G. Completion implied informed consent. The survey was available for two calendar weeks (14 days) from the date the emails were disseminated to the participants. The timeline was clearly indicated in the email. Data collected was saved in a password encrypted file, and on a dual-password protected laptop. All data collected will be destroyed after or on July 1, 2017.
CHAPTER IV – ANALYSIS

The purpose of this doctoral project was to assess the willingness of CRNAs to change practice when presented with a synthesis of current evidence from the literature related to anesthesia and metastasis. The participants had access to the synthesis and the survey for two weeks. Data acquired from the Qualtrics surveys was assessed for any indication of willingness to change by CRNAs and possible barriers to a practice change.

After the close of the survey data was analyzed. The data from the surveys was cleaned. Incomplete surveys were removed from the analysis. During the survey period, 34 CRNAs participated in the project by viewing the presentation, and of those 34 CRNAs, 32 completed the survey.

Descriptive statistics were used to summarize the sample of 32 using gender, age, and years of practice. The sample of CRNAs who participated in the project consisted of 19 males (59.4%) and 13 females (40.6%). Participants in the survey ranged from 27 to 64 years of age with an average respondent age of 41 years old. The CRNAs who took part in the project had between zero and 39 years of experience in the profession. Four of the CRNAs had zero years of experience. Ten years of experience was the average years of experience was of the CRNAs.

Results

The survey questions used a Likert-type scale to assess the participants’ responses to the survey. A sample of the survey is found in Appendix F. Four different questions were utilized to assess for a willingness to change practice. Question four was utilized to assess the participant's opinion of the quality of the information. Question five assessed the participants' opinion as to the best method of anesthesia and analgesia for the surgical
mastectomy patient. Questions six and seven assessed for a willingness to change their current practice. Question eight was utilized to assess the CRNAs' current practice when caring for the surgical mastectomy patient.

**Question 4**

The effectiveness of the presentation was assessed using question four from the survey. The CRNAs were asked if the evidence regarding anesthesia and different anesthetic techniques and their relationship to metastasis was presented in an understandable way. Out of the total 32 survey participants, 18 (56.25%) strongly agreed while 10 (31.25%) somewhat agreed the information was presented in an understandable way. One participant (3.1%) surveyed did not agree or disagree. A total of three participants (9.4%) did not feel the information was presented in an understandable way.

**Question 5**

The opinion of the participants regarding a multimodal approach with a lower minimum alveolar concentration (MAC) of inhalation agent or total intravenous anesthesia (TIVA) as the best method of anesthesia and analgesia for the mastectomy population was assessed using question five. Overall, 23 CRNAs agreed either strongly (34.4%) or somewhat (37.5%), that a multimodal approach may be the best method. The nine other participants (28.1%) neither agreed nor disagreed.

**Question 6**

Questions six assessed the participant's willingness to change their practice based on the information presented. The participants were asked, how likely they were to change their practice when caring for the mastectomy patient population based of the evidence given. A total of 21 participants agreed they would change their practice; six
strongly agreed (18.8%) and 15 somewhat agreed (46.9%). Seven participants (21.9%) neither agreed nor disagreed. While four total participants, three (9.4%) somewhat disagreed and one or (3.1%) strongly disagreed that the information given was strong enough to change practice.

Question 7

The CRNA's opinion regarding the sufficiency of evidence to change practice was assessed using question seven. Of the participants surveyed 18 respondents (56.2%) agreed the evidence was sufficient to change practice. Five strongly agreed (15.6%) and 13 (40.6%) somewhat agreed in the evidence. Nine CRNAs (28.1%) did not agree or disagree. While five (15.6%) participants disagreed with the sufficiency of the evidence. Of those that disagreed with the sufficiency of the evidence four (12.5%) somewhat disagreed and one (3.1%) strongly disagreed.

Question 8

The CRNA's current practice, when providing care to the surgical mastectomy patient, was assessed with question eight. CRNAs were asked to select all methods that closely resembled their current practice. The majority of participants (27 at 84.4%) indicated inhalation agents were utilized. Opioids were utilized by 25 (78.1%) of participants. Local anesthetics were used by 13 (40.6%) of participants. A multimodal approach was indicated as being used by 15 (46.9%) of participants. Total intravenous anesthesia was not used by any of the participants surveyed.

Discussion

The purpose of this doctoral project was to assess the willingness of CRNAs to change practice when presented with a synthesis of current evidence from the literature
related to anesthesia and metastasis. An overwhelming majority of participants (87.5%) believed the material was presented in an understandable way. Participants indicated their current use of anesthesia and analgesia for this patient population included all techniques except TIVA. With the majority of participants (84.4%) currently using inhalation agents and opioids (78.1%). After data analysis it became apparent that the majority participants (65.6%) were willing to change their practice when caring for the surgical mastectomy patient.

**Limitations**

All CRNAs who are members of MANA were invited to participate in the project. There are approximately 600 CRNAs who are members of MANA. With the total sample size being 32, a low response rate (5.3%) is noticed. Given the low response rate it is difficult to determine whether the sample correlates with the larger population.

**Future Implications**

CRNAs who participated in the project displayed a willingness to change practice when presented with evidence that may improve patient outcomes. With the majority of respondents currently indicating the use of inhalation agents and opioids for this patient population, an area for a change is identified. Further information regarding the role of anesthesia and analgesia in metastasis need to be made readily available to CRNAs.

**Conclusion**

The purpose of this project was to identify if a willingness to change practice was present in CRNAs after being presented with a synthesis of current evidence from the literature related to anesthesia and metastasis. The overall goal was to incite a change in practice within CRNAs when providing care for the surgical mastectomy population.
The change must be based on the most current evidence-based research. Results from the survey indicate a willingness to change current practice by 18 of the 32 participants based on the evidence presented.
## APPENDIX A – DNP Essentials

<table>
<thead>
<tr>
<th>Doctor of Nursing Essentials</th>
<th>How the Essential is Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Scientific Underpinnings for Practice</td>
<td>The utilization of current scientific data including the use of lab animal studies coupled with a logical approach to attempt to solve an issue that hinders patient outcomes.</td>
</tr>
<tr>
<td>II. Organizational and Systems Leadership for Quality Improvement and Systems Thinking</td>
<td>The purpose of this doctoral project is to identify the willingness of CRNAs to make a change in practice. To change their current practice and improve patient outcomes.</td>
</tr>
<tr>
<td>III. Clinical Scholarship and Analytical Methods for Evidence-Based Practice</td>
<td>Essential III, was met through the literature reviewed to synthesize best practice. Analytical methods were used when deriving the most appropriate methods to care for the population.</td>
</tr>
<tr>
<td>IV. Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care</td>
<td>This doctoral project aims to exhibit if a willingness exists in changing practice, and the generation of the evidence is derived from strides in technology.</td>
</tr>
<tr>
<td>V. Health Care Policy for Advocacy in Health Care</td>
<td>Understanding if a provider is willing to change current practice regarding the mastectomy patient will assist in future studies and research on the impact of the change and a possible policy change.</td>
</tr>
<tr>
<td>VI. Interprofessional Collaboration for Improving Patient and Population Health Outcomes</td>
<td>This doctoral project is dependent on the effective exchange of information and communication regarding the anesthetics and analgesics that either increases the risk of metastasis or decreases the risk of metastasis.</td>
</tr>
<tr>
<td>VII. Clinical Prevention and Population Health for Improving the Nation’s Health</td>
<td>Metastasis is a possibility after mastectomy surgery. This project revolves around the willingness of CRNAs to change their practice regarding the interventions that may decrease the mastectomy patients risk of metastasis.</td>
</tr>
<tr>
<td>VIII. Advanced Nursing Practice</td>
<td>The analysis of the latest evidence, the synthesis of data, the presentation of the synthesized data, and the assessment of the impact of the information once provided to CRNAs.</td>
</tr>
</tbody>
</table>
## APPENDIX B – Logic Model

<table>
<thead>
<tr>
<th>Input</th>
<th>Output</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Activities</td>
<td>Participation</td>
</tr>
<tr>
<td>Time</td>
<td>Literature Review</td>
<td>CRNAs who are members of MANA</td>
</tr>
<tr>
<td>Computer Equipment and Software</td>
<td>Personal Interviews</td>
<td></td>
</tr>
<tr>
<td>University Library Resources</td>
<td>Disseminate Evidence</td>
<td></td>
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<tr>
<td></td>
<td>Survey</td>
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</tr>
<tr>
<td></td>
<td>Development of Presentation</td>
<td></td>
</tr>
</tbody>
</table>

Risks Factors: Provider “buy in”, participants willingness to change, fiscal benefit.
Assumption: The use of regional anesthesia will be shown to reduce metastasis rates in current on-going randomized control trials.
APPENDIX C – SWOT

Strengths

A strength of the project is the drive that resides within all healthcare providers to provide the best care possible to their population. Once a provider is presented with evidence, that if utilized, may positively impact outcomes in the mastectomy patient population, they may consider the change of practice.

Weaknesses

A foreseen weakness within the proposed change to practice is there are no completed prospective randomized control trials (RCT) despite sound assumptions based on stress responses, metastasis, and effects of anesthetic and analgesic methods.

Opportunities

Opportunities to implement change evolve as science progresses. With the groundwork being laid by numerous studies, systematic reviews, and integrated literature reviews, the foundation for change is forming. The science and data from the reviews already accomplished must be presented in a way to maximize the desire to change practice. The completion of an RCT would provide concrete evidence whether general anesthesia, with the utilization of opioids for pain relief during the perioperative period, is inferior and leads to higher metastasis rates than the use of regional anesthesia and lower minimum alveolar concentrations of inhalation agents.

Threats

The biggest threat to change related to this project is the "buy-in" of the providers. Without the “buy-in” of providers, no willingness to change will be observed.
APPENDIX D – Survey

Age: _____  Gender:_____  Years of Experience: ____

The Likert scale utilized for this survey is as follows:

1= Strongly Disagree  2= Disagree  3= Neutral  4= Agree  5= Strongly Agree

This posthoc survey provides the researcher with data that will assess an anesthesia provider’s willingness to change practice based on data presented. Please circle your response to each question.

Was the evidence regarding anesthesia and different anesthetic techniques and their relationship to metastasis presented in an understandable way?

1 Strongly Disagree  2 Disagree  3 Neutral  4 Agree  5 Strongly Agree

A multimodal approach with a lower MAC or TIVA may be the best method of anesthesia and analgesia for the mastectomy population.

1 Strongly Disagree  2 Disagree  3 Neutral  4 Agree  5 Strongly Agree

I am likely to change my practice when caring for the mastectomy patient population based on the evidence given.

1 Strongly Disagree  2 Disagree  3 Neutral  4 Agree  5 Strongly Agree

I feel there is sufficient evidence to change practice.

1 Strongly Disagree  2 Disagree  3 Neutral  4 Agree  5 Strongly Agree

Below please circle all answer that most closely resemble your current practice when providing care to the surgical mastectomy patient?

1 Inhalation Agent  2 Opioids  3 LAs  4 Multimodal Approach  5 TIVA
APPENDIX E – Consent

Dear Participant,

On behalf of the University of Southern Mississippi (USM) Nurse Anesthesia Program, you are invited to take part in a research study to determine if CRNAs who are shown evidence of regional or neuraxial, and multimodal anesthesia decreasing metastasis rates are willing to change their practice.

Your participation should be no more than approximately 10 minutes. There are no known risks or discomforts associated with this study, and your participation is completely voluntary. The results from this project could indicate the need for further studies into the role of anesthesia and decreasing metastasis rates.

To participate in the study, you are invited to view a PowerPoint presentation with regards to current evidence regarding the possible role of anesthesia and analgesia in metastasis. After viewing the presentation, you are invited to take part in an anonymous survey. Each question within the survey must be answered to progress within the survey. Your responses will be kept strictly confidential, and digital data will be stored in secure computer file after it is entered. All data collected will be destroyed July 1, 2017. Any report of this research that is made available to the public will not include your name or any other identifying information by which you could be identified. You may withdraw from the survey at any time without any negative consequences. Completing this survey indicates that you are a CRNA. Your consent to participate in the research is expressed by your participation in the survey.

Michael Tillman, a current DNP candidate in the nurse anesthesia program at USM, is conducting this project. Please email any questions or comments to xxx.xxx@usm.edu.

This project has been reviewed and approved by the Institutional Review Board of USM. If you have questions, concerns, or want a summary of this project, feel free to contact Dr. Marjorie Geisz-Everson, Capstone Chair, at 601-xxx-xxxx, or via email at xxx.xxx@usm.edu.

To complete your participation in the project:

1) Please download and view the PowerPoint below.

2) After viewing the PowerPoint please complete this short survey by accessing the link below. The survey will be open from 12:01 AM on 9/14/2016 until 11:59 on 9/28/2016.

Thank you for your participation in this project.
Sincerely yours, Michael Tillman BSN, RN, SRNA
APPENDIX F – Support Letter

MISSISSIPPI ASSOCIATION OF NURSE ANESTHETISTS, INC.

July 11, 2016

Re: Project of Doctoral Candidate Michael Tillman

I am the President of the Mississippi Association of Nurse Anesthetists (MANA). I am pleased to offer this letter of support for SRNA doctoral candidate, Michael Tillman, in his doctoral project titled: “When presented with evidence-based data that avoidance of opioids and inhalation agents decrease metastasis is a willingness to change practice made by providers?”

I understand that Mr. Tillman is a doctoral candidate in the nurse anesthesia program at the University of Southern Mississippi who is planning to graduate in December of 2016. This letter of support will be included in the University of Southern Mississippi IRB application. I understand that open participation will be presented to anesthesia providers who are members of MANA. There is no compensation for their participation.

I understand the planned dates for his research are from August 1, 2016 to October 1, 2016, after USM IRB approval is received. Mr. Tillman’s chair contact information is Dr. Marjorie Geisz-Everson at xxx.xxx@usm.edu and (601) xxx-xxxx.

I understand that participation is completely anonymous and voluntary. Anesthesia providers within this association may choose not to participate or withdraw from the study at any time there will be no penalty.

I am looking forward to hearing the results of research and its effect on clinical practice.

Sincerely,

Paul Carpenter
President
Mississippi Association Nurse Anesthetists

1022 Highland Colony Parkway, Suite 101, Ridgeland, Mississippi 39157
Telephone: (601) xxx-xxxx   Fax: (601) xxx-xxxx
APPENDIX G – Question Four and Five

Q4 - Was the evidence regarding anesthesia and different anesthetic techniques and their relationship to metastasis presented in an understandable way?

- Strongly agree: 56.25%
- Somewhat agree: 31.26%
- Neither agree nor disagree: 3.13%
- Somewhat disagree: 3.13%
- Strongly disagree: 6.25%

Q5 - A multimodal approach with a lower MAC or TIVA may be the best method of anesthesia and analgesia for the mastectomy population.

- Somewhat agree: 37.50%
- Strongly agree: 34.38%
- Neither agree nor disagree: 28.13%
- Somewhat disagree: 28.13%
- Strongly disagree: 28.13%
APPENDIX H – Question Six and Seven

Q6 - I am likely to change my practice when caring for the mastectomy patient population based on the evidence given.

Q7 - I feel there is sufficient evidence to change practice.
APPENDIX I – Question Eight

Q8 - Below please mark all answers that most closely resemble your current practice when providing care to the surgical mastectomy patient.

- Inhalation Agents
- Opioids
- Local Anesthetics
- Multimodal Approach
- Total Intravenous Anesthesia
REFERENCES


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