PRONE POSITIONING IN ACUTE RESPIRATORY DISTRESS SYNDROME:

A RETROSPECTIVE REVIEW

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Abstract

PRONE POSITIONING IN ACUTE RESPIRATORY DISTRESS SYNDROME:
A RETROSPECTIVE REVIEW

Kimberly Hawkins

Statement of Problem
Acute respiratory distress syndrome (ARDS) is a condition that causes irreversible damage to the lungs. High-quality supportive care is the only option for ARDS treatment. Although supportive care for ARDS patients has improved over the last few decades, prognosis is still poor with mortality estimates ranging from 40 to 60 percent (Villar et al., 2011; Zambon & Vincent, 2008). Recent evidence indicates that prone positioning not only improves oxygenation but significantly reduces mortality (Abroug et al., 2011; Guerin et al., 2013; Sud et al., 2010). This suggests that ARDS patients may have a better chance of survival if placed in a prone position. The associated patient risks and cost with prone positioning make this therapy debatable in the absence of unwavering prognostic improvement. Replication and further investigation of the relationship between prone positioning and the outcome of survival is essential for determining the best treatment regime for ARDS patients.

Sources of Data
Convenience sampling was the method used to select the patient population from a large metropolitan hospital system in San Diego County. Clinical information was extracted from medical records of individuals that were treated for ARDS within the time-period of January 2012 to August 2014.

Conclusions Reached
The independent variables of position placement (p=0.028) and stage of ARDS (p=0.006) were both significant predictors for the dependent variable of mortality in ARDS patients within the sample population (α= 0.05). The odds of mortality occurring in severe ARDS patients were 2.6 times greater than the odds of mortality occurring in moderate ARDS patients [OR 2.598 (95% CI 1.321 to 5.111)]. The odds of mortality occurring in supine patients was approximately 60 percent less than the odds of mortality occurring in prone positioned patients [OR 0.401 (95% CI 0.177 to 0.907)].

JoAnn Daugherty, Ph.D, RN, CNE, Committee Chair — 4/13/2015 Date

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Prone Positioning in Acute Respiratory Distress Syndrome: A Retrospective Review

CHAPTER ONE: INTRODUCTION

The use of prone positioning as an intervention for acute respiratory distress syndrome (ARDS) has been used for decades. Although evidence repeatedly shows oxygenation improvement when ARDS patients are placed in a prone position, establishing a relationship between prone positioning and survival has proven to be difficult. Recent research indicates that prone positioning may significantly reduce mortality. Replication and further exploration of prognostic outcomes is imperative for developing evidence-based recommendations for optimal clinical management of ARDS patients. This retrospective, quantitative study will explore the relationship between mortality and the two variables of prone positioning and severity of ARDS within a major hospital system in Southern California.

Background and Significance

ARDS is a life-threatening inflammatory condition of the lungs that has the potential to result in refractory hypoxemic respiratory failure (Hodgson et al., 2013). Approximately 190,000 individuals are affected by ARDS annually in the United States (National Institute of Health, 2007). Although research has broadened the pathophysiological understanding of ARDS over recent decades, the mortality rates for this condition remain exceptionally high at 40 to 60 percent (Villar et al., 2011; Zambon & Vincent, 2008). In addition, ARDS is associated with a longer hospital stay which increases the risk for complications and leads to inflated medical expenses (Rubenfeld et al., 2005). Incurred hospital costs from ARDS patients in the United States average

$57,400 per admission (Angus et al., 2006). Over the course of the last decade, the United States healthcare system has evolved into one that focuses on careful allocation of resources in an effort to minimize cost while improving outcomes (Chassin & Loeb, 2011). In fact, research shows that outcome improvement reduces overall healthcare costs (James & Savitz, 2011). As a result, evidence-based research demonstrating outcome improvement is used to guide clinical practice in the U.S. healthcare system today (Chassin & Loeb, 2011).

ARDS treatment priorities involve the expeditious identification and management of the underlying clinical disorder coupled with high quality supportive care that aims to prevent infection, multi-organ failure, and other associated complications (Sharma, 2009). Several specialized therapies, commonly referred to as "rescue therapies," have been used for the supportive care of ARDS patients (Collins & Blank, 2011). These interventions include the use of inhaled vasodilators (nitric oxide, prostacyclin), almitrine bismethylate infusion, extracorporeal membrane oxygenation (ECMO), and prone positioning (Collins & Blank, 2011). These therapies have evolved over the years and are used indiscriminately for ARDS patients throughout hospitals in the United States (Hodgson et al., 2013). Although evidence supports these therapies as effective interventions for the improvement of oxygenation, evidence linking each of them to survival in ARDS populations is largely unavailable (Sharma, 2009).

The use of prone positioning to improve oxygenation of mechanically ventilated patients has been well documented since the 1970s (Piehl & Brown, 1976). Studies over the years have built a robust case to support the relationship between prone positioning

and oxygenation improvement in patients specifically diagnosed with respiratory failure and ARDS (Abroug, Ouanes-Besbes, Elatrous, & Brochard, 2008; Gattinoni et al., 2001; Guerin et al., 2004; Mancebo et al., 2006; Voggenreiter et al., 2005). This evidence has brought about an increased use of prone positioning to treat ARDS patients in recent years. Current research expands on this evidence and suggests that prone positioning has the potential to improve outcomes such as survival in severe ARDS cases (Abroug, Ouanes-Besbes, Dachraoui, Ouanes, & Brochard, 2011; Guerin et al., 2013; Sud et al., 2010). As a result, many healthcare systems have taken steps to evaluate their therapeutic protocols and consider pronation as a standard of care in severe ARDS patients (Guerin et al., 2013).

In the past few decades, the United States healthcare system has widely adopted evidence-based approaches to guide the clinical management of all patients (McClellan, McGinnis, Nabel, & Olsen, 2007). Now an important component in practicing medicine, evidence-based research is crucial in determining the best practice for disease management. Many evidence-based practices observed in hospitals are utilized because they improve outcomes such as survival (Deutschman & Neligan, 2010). Research to support the argument that prone positioning may improve outcomes in ARDS patients exists but is not abundant. Thus, there is a need for replication and further research to support the most recent findings of Abroug et al. (2011), Guerin et al. (2013), and Sud et al. (2010). Additional research in this area will add to the growing body of knowledge regarding ARDS management.

The Problem

ARDS is a condition that causes irreversible damage to the lungs. High-quality supportive care is the only option for ARDS treatment. Although supportive care for ARDS patients has improved over the last few decades, prognosis is still poor with mortality estimates ranging from 40 to 60 percent (Villar et al., 2011; Zambon & Vincent, 2008). Several rescue therapies are used in the setting of ARDS for the purpose of improving oxygenation. Recent evidence, however, indicates that prone positioning not only improves oxygenation but significantly reduces mortality (Abroug et al., 2011; Guerin et al., 2013; Sud et al., 2010). This suggests that ARDS patients may have a better chance of survival if placed in a prone position. The associated patient risks and cost with prone positioning make this therapy debatable in the absence of unwavering prognostic improvement. Replication and further investigation of the relationship between prone positioning and the outcome of survival is essential for determining the best practice management of ARDS patients.

Purpose of the Research

The purpose of this research was to explore the outcome of mortality in ARDS patients treated in a major hospital system in Southern California. This study investigated the ability to predict mortality in ARDS patients based on position placement (supine or prone). This study also investigated the predictability of mortality in ARDS patients based on the severity of ARDS (moderate or severe).

Research Question

Does position placement (supine or prone) and stage of ARDS (moderate or severe) predict mortality in ARDS patients?

Research Hypothesis

Position placement (supine or prone) and stage of ARDS (moderate or severe) will predict mortality.

Research Variables

The dependent variable was mortality, defined as death by any cause that occurred during the patient's hospital stay during which they were diagnosed with ARDS. The two independent variable groups were position placement (supine or prone) and stage of ARDS (moderate or severe). Supine patients remained in the supine position for the duration of their hospital stay. Prone positioned patients were placed in a prone position for a minimum amount of time based on current literature. The stage of ARDS was determined differently for patients depending on their position placement. The details of these variables will be further discussed in the literature review.

The demographic variables included age, gender, body mass index (BMI), Sequential Organ Failure Assessment (SOFA) score, presence of sepsis, use of inhaled nitric oxide, and a history of comorbid conditions which included coronary artery disease (CAD), diabetes (DM), renal failure (RF), and hepatic disease (HD). All demographic variables were used exclusively for the purpose of describing the population.

CHAPTER TWO: LITERATURE REVIEW

The United States healthcare system has evolved into one that hinges clinical decision-making on evidence-based research. The process of determining the most appropriate clinical management of any disease requires a complete understanding of the disease pathophysiology. It also necessitates a review and critique of the existing research on the subject. Recent research suggests that position placement affects survivability in ARDS patients. Furthering the development of ARDS research begins with an extensive review of all literature concerning ARDS treatment and outcomes.

The literature search began with the use of Google Scholar. Initially, the term "prone position in ARDS" generated greater than twenty thousand articles. Other search terms used included, "prone position physiology," "ARDS prone position," "prone position nursing," and "ARDS treatment." The search was narrowed to peer-reviewed articles published no earlier than 2010. Some articles with earlier publication dates were used due to the limited research available involving ARDS and the outcome of mortality. Research extracted and reviewed from this database included articles from peer-reviewed journals such as randomized controlled trials (RCTs), meta-analyses, systematic reviews and consensus reports. Databases such as CINAHL, PubMed, and Cochrane Database of Systematic Reviews were utilized as well. Literature used for this review originated from peer-reviewed sources and was chosen based on high-quality design, appropriateness of research outcome variables, and clear articulation of findings. Studies that involved prone positioning for acute respiratory failure, acute lung injury (ALI), and ARDS were

all used. Studies published in a foreign language were excluded and studies that involved pediatric participants in any part of the study were also excluded.

Conceptual Framework

The conceptual framework used for this study is embedded in physiology. To appreciate the approach to ARDS management, it is crucial to understand the underlying pathophysiology of this condition. It is also imperative to explore the physiological underpinnings of oxygenation in both supine and prone positions and how this difference in position is known to affect ARDS patients. Together these subjects provide the structure for the conceptual framework that guides this study. The pathophysiology of ARDS, the physiological understanding of oxygenation in both supine and prone positions, and the physiological effects of position change in the setting of ARDS are discussed in depth as part of the review of literature.

Certain physiological assumptions must exist in the application of this conceptual framework. ARDS can result from a number of different diseases and conditions. Regardless of the cause, the clinical picture of ARDS remains the same in all adults. Therefore, for the purpose of this study, it was assumed that all ARDS patients in the moderate and severe groups had comparable presentations of the ARDS process within each stage regardless of the primary disease or condition that caused ARDS. In addition, all patients who met the inclusion criteria were assumed to have comparable pre-existing pulmonary function and a comparable physiological potential to recover from ARDS.

Pathophysiology of ARDS

ARDS can result from direct lung injury caused by pneumonia, aspiration, inhalation injury, pulmonary contusion, fat or air emboli, near drowning, or reperfusion injury (Ware, 2006). Direct lung injury is commonly referred to as acute lung injury (ALI), a term often used to describe a subgroup of ARDS patients that originally presented with the aforementioned etiologies (Sud, Sud, Friedrich, & Adhikari, 2008). ARDS can also result from indirect injury to the lung such as sepsis, severe trauma, burns, multiple transfusions, cardiopulmonary bypass, drug overdose, toxic ingestion, or acute pancreatitis (Ware, 2006). The ARDS pathology is best described by diffuse alveolar damage that causes an increase in pulmonary alveolar-capillary membrane permeability (Barbas, Matos, Amato, & Carvalho, 2012). This damage can result from injury to alveolar epithelium (as in inhalation exposures) or injury to the capillary epithelium (as in sepsis) (Choi, 2010).

Despite the nature of the initial lung injury, ARDS follows a predictable course that involves three phases: exudative, proliferative, and fibrotic (Choi, 2010). The exudative phase occurs 1 to 7 days after initial injury and involves interstitial edema, intra-alveolar hemorrhage, and a presence of hyaline membranes in alveolar ducts and walls (Choi, 2010). The proliferative phase, 1 to 3 weeks following the initial insult, consists of type II pneumocyte hyperplasia, mononuclear cell predominance, and organization of alveolar exudates (Choi, 2010). The fibrotic phase occurs weeks to months after initial injury and is characterized by chronic inflammation, interstitial fibrosis, and continued type II pneumocyte hyperplasia (Choi, 2010). With early

recognition and treatment of the cause, some ARDS patients have successful resolution of diffuse alveolar damage during the proliferative phase (Choi, 2010). Patients who progress to fibrotic stages and remodeling of the lung tissue are associated with poor clinical outcome (Barbas et al., 2012). Thus, the importance of identifying and treating ARDS in its early stages of the disease process cannot be overemphasized.

The physiological process behind oxygenation improvement in ARDS patients when placed in a prone position lacks a clear and concise explanation. However, the physiological understanding of lung function in both supine and prone positions lends to several logical reasons for this phenomenon. As a general rule, regional alveolar inflation is greater in the nondependent areas of the lung than the dependent areas of the lung (Gattinoni et al., 2010). Therefore, in the supine position, the size of alveolar units decreases exponentially from ventral (nondependent) to dorsal (dependent) lung regions (Gattinoni, Pelosi, Valenza, & Mascheroni, 2004). This indicates the inflating forces of the lung decrease along the ventral-to-dorsal axis in the supine position due to an increase in pleural pressure in the dependent lung regions (Gattinoni & Caironi, 2010). In healthy individuals, this increase in pressure in the dependent areas is thought to be a result of the abdominal organs and the heart pushing towards the lungs (Gattinoni & Caironi, 2010). In ARDS, the edema in the lungs may triple the normal lung mass (Gattinoni et al., 2006). Therefore, the dependent lung regions are not only compressed by organs but also by the abnormal weight of the edematous lung tissue (Gattinoni et al., 2006). This leads to a ventilation/perfusion (V/Q) mismatch due to a greater area of lung compression and

the subsequent inability to recruit a sufficient amount of alveoli (Gattinoni & Caironi, 2010).

When an ARDS patient is placed in the prone position, the same physiological events occur, but the asymmetrical shape of the lungs produces a different result in the presence of edema (Gattinoni et al., 2010). In a prone position, the dorsal region of the lung becomes the nondependent area and the ventral the dependent. Anatomically, the lung tissue mass is significantly greater in the dorsal regions (Gattinoni & Caironi, 2010). Thus, when the weight of the lung is shifted to the ventral region, the greater dorsal portion of the lung is able to re-inflate (Gattinoni et al., 2010). This shift results in a relative increase in alveolar recruitment compared to that in the supine position (Gattinoni et al., 2010). The prone position also leads to more homogeneous lung inflation and more homogenous alveolar ventilation, decreasing the risk of ventilator-induced lung injury (Galiatsou et al., 2006; Valenza et al., 2005). This greater homogeneity in the prone position is thought to also improve V/Q mismatch and promote better gas exchange (Gattinoni et al., 2010; Pelosi, Brazzi, & Gattinoni, 2002). Theoretically, this may prevent advancement of the lung tissue to fibrotic stages. Even further, treatment of hypoxemia with this therapy may maintain global perfusion, ultimately preventing the multi-organ failure that commonly causes death in ARDS patients (Sharma, 2009).

Oxygenation Improvement in ARDS

Oxygenation is determined through the arterial partial pressure of oxygen (PaO2), a value obtained with an arterial blood gas sample (Brochard et al., 2012). When the

arterial partial pressure of oxygen (PaO2) is divided by the inspired fraction of oxygen (FiO2), the PaO2/FiO2 (P/F) ratio is obtained (Brochard et al., 2012). This ratio is the value most frequently used to determine severity of lung failure and is currently used to differentiate between mild, moderate, and severe stages of ARDS (The ARDS Definition Task Force, 2012). In ARDS patients, the P/F ratio is largely dependent on the physiologic factors of hemodynamic status (mixed venous oxygen tension) and intracardiac shunt potential (Brochard et al., 2012). The P/F ratio may also be affected by clinical interventions such as low tidal volume ventilation, the use of positive end expiratory pressure (PEEP), the use of inhaled vasodilators, and positional changes (Brochard et al., 2012).

Low tidal volume ventilation. Additional variability in oxygenation between patients may result from differences in the tidal volume ventilation of a patient. Normal tidal volume selection is based on 10 milliliters per kilogram of predicted body weight (Kopterides, Siempos, & Armaganidis, 2009). Low tidal volume ventilation (6 milliliter per kilogram of predicted body weight) is a lung protective maneuver frequently (but not always) used in the prone position to minimize lung over-distention (Kopterides, Siempos, & Armaganidis, 2009). Ultimately, clinicians seek a balance between maintenance of alveolar recruitment and avoidance of pulmonary over-distention, V/Q mismatch, and hemodynamic compromise (Hess & Thompson, 2005). This balance may require different ventilation volumes depending on the unique physiological makeup and condition of each patient.

PEEP. PEEP is a ventilating mechanism used in the management of respiratory failure to recruit alveoli for optimal gas exchange. High PEEP levels (greater than 10 cm H2O) in mechanically ventilated and supine ARDS patients can improve oxygenation and P/F ratio in the presence of functional alveolar recruitment (Di Marco et al., 2010). Conversely, 0 cm H2O of PEEP is likely harmful to patients with ALI/ARDS in the supine position (Ferguson et al., 2005). In the prone position, however, evidence indicates that lower PEEP (less than 10 cm H20) is necessary for optimal gas exchange (Cakar, Der Kloot, Youngblood, Adams, & Nahum, 2000; Gainnier et al., 2003; Petersson et al., 2010). Currently, no standard recommendation exists for PEEP requirements in either supine or prone position for an ARDS patient. Literature indicates that PEEP undoubtedly has an effect on oxygenation and P/F ratio in ARDS (Di Marco et al., 2010). Thus, a minimum PEEP of 5 cm H2O is required for a patient to meet the definition for ARDS. This definition will be discussed in the Major Variables Defined section of this paper.

Inhaled vasodilators. Inhaled nitric oxide (iNO) is a potent vasodilator that has been shown to improve P/F ratio and V/Q mismatch in ARDS patients (Hodgson et al., 2013; McCartney, Saha, Rees, Lawy, & Mosaheb, 2013). When inhaled, nitric oxide causes smooth muscle relaxation and dilatation in the pulmonary vasculature (McCartney et al., 2013). While literature demonstrates improvement in P/F ratio and V/Q mismatch with the use of iNO, it also continues to rebut the hypothesis that these interventions have any effect on mortality (Adhikari et al., 2007; Afshari, Brok, Moller, & Wetterslev, 2011; Taylor et al., 2004).

Prone Positioning. Oxygenation improvement in hypoxemic patients placed in a prone position was first documented over 30 years ago (Piehl & Brown, 1976). Throughout the years, research has demonstrated this same correlation repeatedly with many different ARDS etiologies (Guerin et al., 2004). Gattinoni et al. (2001) and Guerin et al. (2004) found that placing patients in acute respiratory failure in a prone position improves oxygenation greater than 60 percent of the time. Voggenreiter et al. (2005) found that oxygenation improved in post-traumatic lung injury patients in the first 4 days of pronation, reducing the prevalence of ARDS and pneumonia. Another study showed improved oxygenation with prone positioning in patients with ARDS that resulted from community-acquired pneumonia (Chan et al., 2007). Sud et al. (2010) found a 27 to 39 percent improvement of oxygenation in the first 3 days of prone positioning in a variety of different ARDS/ALI etiologies. The evidence that supports physiological improvement with pronation in the diverse hypoxemic population has resulted in the formulation of the next logical hypothesis that prone positioning improves the outcome of survival. Thus, a rigorous effort has ensued in the scientific community to link this intervention with better prognostic outcomes in the setting of ARDS.

Prone Positioning and Mortality Correlations

Despite the consistent documentation of sustained oxygenation improvement that occurs with prone positioning, research has found challenges in proving that this intervention has any impact on mortality. The inability to significantly identify an association between prone positioning and mortality may be attributed to the lack of subgroup data in most trials (Sud et al., 2010). This means the lack of significant

findings may be related to the wide spectrum of hypoxemic severity observed within patient samples in the past. For example, many studies included ARDS patients with P/F ratios as high as 300 mmHg (Gattinoni et al., 2001; Tiruvoipati, Bangash, Manktelow, & Peek, 2008). When subgroup analysis is performed to include only severe ARDS patients (P/F ratio less than 100 mmHg), a significant mortality reduction is observed across many studies (Abroug et al., 2011; Alsaghir & Martin, 2008; Kopterides, Siempos, & Armaganidis, 2009; Taccone et al., 2009).

Experts also believe that limited sample sizing in past RCTs contributed to the inability to significantly link prone positioning with mortality (Abroug et al., 2011). Meta-analysis has since been used to overcome sample size limitations, revealing significant mortality reduction in severe ARDS cases within the intensive care unit (ICU) (Sud et al., 2010). Sud et al. (2010) conducted a meta-analysis and found a significant difference in mortality rate in prone positioned patients with a P/F ratio less than 100 mmHg compared to prone positioned patients that had a P/F ratio greater than 100 mmHg (risk ratio= 0.84, 95% CI [0.74, 0.96], P= 0.01). This is a trend also observed in other studies, indicating that the use of a prone position may be more appropriate for severely hypoxemic patients (Gattinoni et al., 2010; Sud et al., 2010).

Abroug et al. (2011) conducted a meta-analysis on seven high-quality RCTs. Prone positioning RCT studies published before 2006, typically used a shorter duration of prone positioning (less than 17 hours per day) and applied this intervention to both ALI and ARDS patients (Gattinoni et al., 2001; Guerin et al., 2004; Voggenreiter et al., 2005). More recent RCT studies (studies after 2006) applied the longest prone positioning

durations ranging from 17 to 24 hours per day and focused exclusively on ARDS patients (Chan et al., 2007; Fernandez et al., 2008; Mancebo et al., 2006; Taccone et al., 2009). Prone positioning did not reduce ICU mortality when all seven RCTs were considered (odds ratio= 0.91, 95% CI [0.75, 1.2], P= 0.39) (Abroug et al., 2011). However, ICU mortality was significantly reduced in the more recent studies that used greater than 17 hours per day of prone positioning on ARDS patients only (odds ratio= 0.71, 95% CI [0.5, 0.99], P= 0.048) (Abroug et al., 2011). This raises the question of how the pathologies of ALI and ARDS caused by indirect lung injury might contribute differently to prone positioning outcomes, but also demonstrates a greater potential effect on mortality with longer prone duration.

The most recent and significant article, otherwise known as the Proning Severe ARDS Patients (PROSEVA) study, involved a prospective, RCT that investigated mortality outcomes in 466 severe ARDS patients (P/F ratio < 100 mmHg) (Guerin et al., 2013). The experimental protocol required strict adherence to a number of inclusion parameters. Each patient selected for the experimental prone group remained in a prone position for a minimum of 16 hours per day, allowing 4 hours within a 24 hour period to properly bathe and assess the patient in a supine position. The results from this study reported a significant decrease in both 28-day and 90-day mortality with the early application of prolonged prone positioning (Guerin et al., 2013). 28-day mortality for the prone group was 16 percent and 32.8 percent for the supine group (P < 0.001) (Guerin et al., 2013). The hazard ratio reported for death in the prone group at 28 days was 0.39 with a 95% CI [0.25, 0.63] (Guerin et al., 2013). 90-day mortality for the prone group

was 23.6 percent and 41 percent for the supine group (P<0.001) (Guerin et al., 2013). The hazard ratio reported for death in the prone group at 90 days was 0.44 with a 95% CI [0.29, 0.67] (Guerin et al., 2013).

Limitations of this particular study include a possible lack of generalizability to other countries since participants were strictly European. Adverse outcomes may vary between facilities due to the experience difference amongst staff in implementing pronation therapy. Additionally, the average body mass index of the participants in this study was 29 kilograms per meter squared, indicating that the ideal population for prone ventilation may be obese individuals. If this is the case, it is important to consider the risk this intervention poses to staff members, especially when using a conventional bed. Despite limitations, research community interest in this data has sparked much inquiry on the ideal practice for ARDS treatment procedures. Studies like this require replication and further investigation regarding the optimal stage to initiate pronation, the optimal duration of therapy, and the ideal population for this intervention.

Prone Positioning Costs and Risks

Prone positioning can be a costly intervention. The process of placing a patient in the prone position requires a coordinated team effort with skilled staff to prevent adverse events (Guerin et al., 2013). This includes allocation of nursing staff so that prone positioned patients are given a nursing ratio of one-to-one. This results in an increase in staffing requirements for the intensive care unit and a subsequent increase in cost. A patient can be placed in a prone position with a conventional bed or with a specialized rotational bed (Goldhill, Imhoff, McLean, & Waldmann, 2007). Both techniques pose

many risks for both patient and nurse. Bajwa, Arasi, Canabal, & Kramer (2010) suggest that the use of an automated prone positioning bed reduces the incidence of adverse events. The increase in daily hospital cost for the specialty bed rental charges is noteworthy if the hospital does not own one already.

Adverse occurrences from pronation are uncommon but potentially serious (Sharma, 2009). Guerin et al. (2013) suggests that the application of this intervention by experienced and properly trained personnel may reduce the rate of complications. Placing a patient in a prone position requires moving the patient in a way that risks injury to both patient and staff. Prone positioning increases the risk of pressure ulcers and potentiates the dislodgement of endotracheal tubes, intravenous lines, and chest tubes (Sud et al., 2010; Tiruvoipati et al., 2008). Moving patients from one bed to another risks spinal injury to staff, but the use of an automated bed may decrease this risk overall (Bajwa et al., 2010). Contraindications for prone positioning include spinal instability, uncontrolled intracranial pressure, and, in some cases, hemodynamic and cardiac instability (Sharma, 2009). When assessing patients for prone positioning appropriateness, the approach must be individualized and collaborative. While it is important to identify which patients are not suitable for prone positioning, many times the benefits may outweigh the risks and costs of this intervention.

Major Variables Defined

Stage of ARDS. Originally described in 1967 by Ashbaugh, Bigelow, Petty, & Levine (1967), the definition of ARDS for the purpose of diagnosis continues to be refined. The organization of the clinical and pathophysiological information of ARDS

into a process that yields proper diagnosis has always been controversial (Ranieri, Rubenfeld, & Thompson, 2013). According to the American-European Consensus Conference (AECC) criteria, ARDS was previously defined in the clinical setting with the following diagnostic criteria:

1. Acute onset of symptoms
2. P/F ratio less than or equal to 200 mmHg
3. Airway pressure (Paw) less than or equal to 18 mmHg
4. Bilateral infiltrates seen on frontal chest radiograph (Bernard et al., 1994)

This definition has since been revised to better prognosticate ARDS outcomes. The newly adopted and currently used Berlin definition of ARDS consists of the following clearly-defined parameters:

1. Onset less than or equal to 7 days from predisposing clinical insult
2. Bilateral opacities consistent with pulmonary edema detected on either chest computed tomography (CT) or chest X-ray (CXR)
3. Respiratory failure not fully explained by cardiogenic pulmonary edema or volume overload
4. When the patient meets the previous three criteria and is receiving a PEEP equal to or greater than 5 cm H2O, the patient is then placed into one of the following categories:
    a. Mild ARDS: P/F ratio 200-300 mmHg
    b. Moderate ARDS: P/F ratio 100-200 mmHg

c. Severe ARDS: P/F ratio less than 100 mmHg (The ARDS Definition Task Force, 2012)

This definition currently aids all clinical practitioners in the early identification of ARDS with the ultimate goal of reducing mortality and improving prognosis. For the purpose of this study, the stage of ARDS for each patient was confirmed using the Berlin Definition. All of the above criteria were confirmed in each ARDS patient through the chart review process using data collected from physician notes, nursing notes, radiology reports, and laboratory results. The PaO2/FiO2 ratio determined the staging of ARDS (moderate or severe) for each patient, but the process in determining the PaO2/FiO2 ratio differed based on their position placement. The stage of ARDS for *supine* patients was determined by their worst PaO2/FiO2 ratio during their course of ARDS treatment. The stage of ARDS for *prone* positioned patients was determined by the worst PaO2/FiO2 ratio prior to prone position placement.

Respiratory Failure and Acute Lung Injury (ALI). According to the National Institute of Health, respiratory failure is defined as an impairment of oxygen and/or carbon dioxide exchange (National Institute of Health, 2011). It can be acute or chronic and occurs concurrently with ALI and ARDS (Gattinoni et al., 2004). ALI is a term often used interchangeably with ARDS in literature, with ARDS typically representing a more advanced stage of ALI (Sud, Sud, Friedrich, & Adhikari, 2008). In the setting of respiratory failure, ALI and ARDS complicate the gas exchange impairment with severe hypoxemia and bilateral lung injury (Gao & Barnes, 2009). The distinction between ALI and ARDS is arbitrary (Sharma, 2009). The severity of hypoxia does not correlate

reliably between the two pathologies and does not influence prognosis (Sharma, 2009). Thus, for the purpose of this study, patients selected for participation may have been referred to as having acute respiratory failure or ALI in the chart but met the specific criteria for the Berlin Definition of ARDS.

Position Placement. Supine patients remained in the supine position the entire duration of their hospital stay. They may have been on specialized beds that provided automated rotation from side to side at various degrees. However, they remained in a supine position for the full course of their hospital visit. A standard therapeutic time for prone positioning does not exist. Any amount of time in the prone position could be considered a confounding factor. Therefore, supine patients were not placed in a prone position for any amount of time. This ensured that supine patients received absolutely no therapeutic benefit from being placed in a prone position.

In the absence of therapeutic standards for the prone intervention, the minimum duration of prone placement for each patient in this study was determined by the existing research on the subject. As previously discussed, some studies suggest that a longer duration of prone positioning throughout each 24 hour period may increase its effect on mortality (Chan et al., 2007; Fernandez et al., 2008; Mancebo et al., 2006; Taccone et al., 2009). Taccone et al. (2009) also found that ARDS patients did not reach statistically significant oxygenation improvement until the beginning of the third day of pronation therapy. The minimum number of days needed to achieve therapeutic improvement from prone positioning was not reported as a variable in any other study. Rather, oxygenation improvement was generally reported to occur within the first few days of prone

positioning therapy (Sud et al., 2010; Voggenreiter et al., 2005). Total number of days that pronation was applied varied in all studies because weaning was dependent on the clinical improvement of the patient which ranged from a few hours to many days (Sud et al., 2010). Thus, for the purposes of this study, the minimum time required to achieve a therapeutic level of prone positioning was 16 hours per day for two consecutive days (48 hours) based on data presented by Taccone et al. (2009).

Mortality. The single dependent variable of mortality was determined for each patient. Mortality was recorded if death occurred during the hospital admission in which the diagnosis of ARDS was given. Mortality from any cause was reported during the hospital admission for which ARDS occurred. The hospital system from which this data originated does not provide long-term medical follow-up on every patient after discharge from the hospital. Therefore, hospital mortality was the only mortality information that could be extracted from the chart review.

Sequential Organ Failure Assessment (SOFA) score. The SOFA score is a method of scoring patients based on their organ dysfunction to determine their mortality risk at a certain point in time (Ferriera, Bota, Bross, Melot, & Vincent, 2001). The SOFA score reflects a cumulative scoring of six different organ systems (Vincent et al., 1996). These organ systems include respiratory (PaO2/FiO2 ratio), coagulation (platelet count), liver function (total bilirubin), cardiovascular (hypotension severity), central nervous system (Glascow Coma Scale), and renal system (creatinine) (Vincent et al., 1996). In the SOFA calculation, each organ system is assigned a point value ranging from 0 to 4. All organ system points are added up to total the SOFA score which corresponds to a

specific category of mortality risk (Vincent et al., 1996). The mortality risk categories consist of the following (Vincent et al., 1996):

1. A score of 0 to 6 has less than 10 percent mortality risk
2. A score of 7 to 9 has 15 to 20 percent mortality risk.
3. A score of 10 to 12 has 40 to 50 percent mortality risk.
4. A score of 13 to 14 has 50 to 60 percent mortality risk.
5. A score of 15 has greater than 80 percent mortality risk.
6. A score of 15 to 24 has greater than 90 percent mortality risk.

The SOFA score was calculated for each ARDS patient within 24 hours after they were admitted to the ICU. Some patients were in and out of the ICU more than once during the course of their hospital stay and some were treated for ARDS in more than one ICU stay. In such cases, the SOFA score was calculated at the 24 hour mark for the first ICU stay that diagnosed and treated them for ARDS. The SOFA score in this study provided a baseline acuity assessment for the ARDS population in this study.

Sepsis. Approximately 71 percent of all ARDS patients have sepsis (Barbas et al., 2012), making this an important subject to address in the context of this study. Septic patients have a higher mortality rate, a greater length of hospital stay, and increased risk of complications than patients without sepsis (Hall, Williams, DeFrances, & Golosinskiy, 2011). These rates, however, have improved over the years with the use of evidence-based practice guidelines to assist with earlier diagnosis and effective treatment of sepsis (Dellinger et al., 2013). It is important to consider that ARDS patients with sepsis may have a more complicated course of illness. Even though sepsis may be a confounding

variable for mortality, it was imperative to include such patients so that an adequate sample size could be obtained for this study. Furthermore, eliminating septic patients from this study would have reduced the generalizability of the findings to the ARDS population which happens to be more septic than not. Thus, the presence of sepsis was recorded for each ARDS patient within this study.

Inhaled Nitric Oxide. Inhaled nitric oxide (iNO) was recorded for any patient that received any amount of nitric oxide for any amount of time during their treatment for ARDS. Although it is not an evidence-based intervention for improving outcomes in ARDS patients, many ARDS patients in this chart review were found to be treated with iNO for severe hypoxemia. Many of the patients that received iNO were also placed in a prone position, making it difficult to obtain an adequate sample size of prone positioned patients without iNO therapy. The use of iNO would be a logical confounding variable in this study due to its ability to increase oxygenation (Adhikari et al., 2007). However, the existing iNO research repeatedly demonstrates that iNO does not affect hospital mortality (Adhikari et al., 2007; Afshari et al., 2011; Taylor et al., 2004). Therefore, ARDS patients that received iNO during the course of their treatment for ARDS were included in this study, allowing for the inclusion of a greater number of prone positioned ARDS patients. Frequency of iNO use in the sample population was recorded for descriptive purposes only.

Comorbid Conditions. The comorbid conditions recorded in this study reflect a patient history of major chronic illnesses that have the potential to affect the ability to maintain adequate organ function during an acute illness. The comorbid conditions

considered for this study included coronary artery disease, diabetes, renal disease, and hepatic disease. Each condition was scored only if it was a pre-existing condition prior to hospital admission.

Inclusion and Exclusion Criteria

Attempts to limit the confounding variables within this study involved the use of specific inclusion and exclusion criteria. To ensure appropriate sampling of the population and avoid selection bias, patients were systematically included into the study using the following criteria. ARDS patients used for this study were included only if they met the specific Berlin Definition criteria for moderate and severe ARDS as previously discussed (The ARDS Definition Task Force, 2012). Prone positioning in adult patients is based on homogenous pleural pressure distribution gradient and changes in chest wall compliance (Abroug et al., 2011). The same physiological responses to prone positioning in ARDS are not proven to take place in children (Abroug et al., 2011). Therefore, patients were included only if they were 18 years of age and older. Specific positioning criteria were established as well. Patients coded for the supine group were never placed in a prone position for any amount of time. In addition, patients coded for the prone group received the predetermined therapeutic duration of prone positioning (Taccone et al., 2009). For the purpose of this study, that therapeutic amount was 16 hours per day for 48 hours as previously discussed.

The pathophysiological complexity of ARDS requires the application of specific exclusion criteria as well. Patients were excluded from the study entirely if they were placed in a prone position but did not remain in prone position for the minimum

therapeutic time. This ensured that each patient placed in the prone group received a therapeutic level of prone time according to Taccone et al. (2009). This also eliminated the potential for a sub-therapeutic prone time to affect outcomes of patients that remained supine. Patients less than 18 years of age were excluded from this study as discussed earlier. Patients that were transferred from or to another hospital during the course of their ARDS treatment were eliminated from the study as well because lack of clinical data and outcome information.

This study also excluded patients with particular pulmonary histories such as COPD, pulmonary fibrosis, interstitial lung disease, lung cancer, and lung resection. Patients with underlying pulmonary fibrosis and interstitial lung disease are known to have a very poor prognosis in the setting of ARDS due to the fibrotic lung state that already exists within the tissue of the lungs (Ley, Collard, & King, 2011). The existence of COPD in patients that have ARDS significantly reduces their survival rate due to the reduced lung compliance (Fadi, Mohamed, Komara, & Guzman, 2011). Furthermore, a lack of viable lung tissue due to cancer growth or previous lung resection has the potential to severely limit pulmonary function and recovery from ARDS (Dulu et al., 2006). Thus, patients with these underlying pulmonary conditions were entirely excluded.

Extracorporeal membrane oxygenation (ECMO) is an additional therapy used to treat severe hypoxemia (Hodgson et al., 2013). A therapy sometimes used for the treatment of ARDS, this therapy can be used alone or in conjunction with other therapies to treat severe hypoxemia (Hodgson et al., 2013). Although recent research suggests that

ECMO may have an effect on survival in ARDS patients, this subject is still a topic of debate (Robak et al., 2014). Since ECMO has the potential to affect mortality rates in ARDS treatment and directly affects oxygenation in any condition, patients that received this therapy were excluded from the study.

Summary

The use of prone positioning in ARDS patients continues to be a topic of debate despite its frequent use in hypoxemic patients over the years. The firmly established link between this intervention and improved oxygenation in ARDS implies that it may also improve survival. Research has found challenges in providing evidence to support this hypothesis due to inadequate sample sizing and lack of subgroup analysis. Literature review of current research yielded two meta-analyses and one RCT that were able to overcome these limitations and demonstrate significant reduction in mortality with prone positioning in ARDS patients. These results have spurred much inquiry in the medical community regarding current ARDS treatment and whether this evidence supports the formulation of a new standardized practice in ARDS management. Regardless, replication and further investigation of outcomes related to prone positioning is necessary. This scholarly thesis expands on the existing literature by retrospectively assessing if position placement and severity of ARDS significantly affects the outcomes of mortality in one particular hospital system.

CHAPTER THREE: METHODOLOGY

The outcome of mortality is of specific concern in the ARDS population. This study focused on the two variables of stage of ARDS and position placement and their ability to predict mortality. Although recent research has demonstrated a possible relationship between prone positioning and increase in survival in severe ARDS, this evidence lacks replication. A conceptual model to predict the outcome of mortality with these variables does not yet exist. Assessing the outcome of mortality in ARDS patients through a retrospective chart review can provide the groundwork to build and test predictive models that could be used to guide the clinical management of ARDS prospectively. The formulation of a predictive model could potentiate the standardization of effective therapies in ARDS management system-wide and improve overall outcome.

For the purpose of this study, a binary logistic regression was chosen to determine how well the independent dichotomous variables of stage of ARDS (moderate and severe) and position placement (supine and prone) might predict the dependent dichotomous variable of mortality. This type of model also determined whether each independent variable significantly contributed to the variance between the other independent variable and mortality. Ultimately, strength and directionality of each independent variable in relation to mortality was determined after adjusting for the influence of the other independent variable (Plichta & Kelvin, 2013).

Research Question

Does position placement (supine or prone) and stage of ARDS (moderate or severe) predict mortality in ARDS patients?

Research Hypothesis

Position placement (supine or prone) and stage of ARDS (moderate or severe) will predict mortality.

Identification of Setting

Retrospective data for this study came from five major hospitals within a particular healthcare system in San Diego, California. The hospital sites used for this study regularly provide care for ARDS patients in both supine and prone positions. Data came from medical records of ARDS patients that were admitted to these five hospitals between January 2011 and August 2014. The hospitals chosen for this study serve a diverse population with a variety of different diagnoses in San Diego County. ARDS patients typically receive care in the intensive care unit during the most critical phase of their illness and are subsequently transferred to lower acuity units. Therefore, ARDS patients included in this study may have received care in various inpatient areas within the hospital setting including the intensive care unit, the step-down unit, and the medical-surgical unit.

Research Design

Reduction in mortality with prone positioning in ARDS has been demonstrated through meta-analysis and large randomized controlled trials (RCTs) (Abroug, Ouanes-Besbes, Dachraoui, Ouanes, & Brochard, 2011; Guerin et al., 2013). These two research methods were used to overcome limitations of inadequate sample size and lack of subgroup analysis in the ARDS population. A retrospective quantitative study was chosen for this research for similar reasons. Medical record review provided patient-

specific data that was used to determine stage of ARDS and position placement for analysis. It also provided the demographic and clinical data required to perform descriptive statistics and the final regression analysis.

Although this design had the potential to overcome limitations identified in previous studies, the internal validity of this research design was compromised by the lack of protocol to guide prone positioning practice. Lack of a standard protocol meant that clinical decision making had the potential to vary greatly from case to case. In addition, ARDS patients are often complicated with confounding factors that involve acute, non-pulmonary-related events such as myocardial infarction, stroke, sepsis, hospital-acquired infections. In addition, there was a large variation in the use of particular therapies such as vasopressors, paralytics, and mechanical ventilation techniques. All of these factors contribute to the complex nature of each ARDS patient.

Population and Sample

Patient records for this study were obtained through convenience sampling. An a priori power analysis was calculated for logistic regression with the G*Power 3.1.7 software system (Faul, Buchner, Erdfelder, & Lang, 1992-2012) using an odds ratio of 0.3 (Abroug et al., 2011), an H0 of 0.9, an alpha of 0.05, and a power of 0.80. The population sample (n=171) exceeded the minimum sample size of 64 required to carry out a multiple logistic regression analysis. This exceedance of sample population was a result of oversampling to achieve a minimum representative sample of prone patients (n=32). Ideally, the sample would be balanced in a logistic regression. However, position placement of ARDS patients within the data set was so disproportionate that

sampling was continued until at least half of the minimum sample size was obtained (n=32). Incidentally, the number of prone positioned patients that were identified within the designated sampling period happened to be 32. See Appendix A for the G Power analysis.

A query request was run through the informatics division of the participating healthcare system. The query required specific ICD 9 codes to generate the patient population. Within the ICD 9 classification system, no specific code for ARDS exists. Therefore, 80 pulmonary-related ICD 9 codes were used for the query in an attempt to include all possible patients that may have been diagnosed with ARDS during their hospital admission. See Appendix B for the list of ICD 9 codes that were used to generate a population of potential ARDS patients through the hospital informatics system. The query produced a list of 8990 patient medical records. The size of this output limited how far back in time the query could search. Therefore, the period of time that ARDS patients were pulled from was limited to January 2011 through August 2014. Patient information ended in August of 2014 because this was the time at which the query was generated.

Each medical record number was entered into the GE Centricity search engine. Discharge summaries were reviewed for every patient admitted to the hospital within the time period of January 2011 to August 2014 (n=8990). If ARDS was discussed as part of patient's medical course, they were placed on a secondary list that was later reviewed in depth for inclusion to the study. A few patients had multiple admissions for ARDS. In such cases, the first admission that involved ARDS treatment was used due to the

propensity to develop pulmonary fibrosis after ARDS (Ley et al., 2011). An additional list of patients was also obtained from the Arjo Huntleigh bed rental agency. This list included all patients that used a rotational bed during their hospital stay. These patients were also placed on the secondary list for in-depth review. Then, medical records from the secondary list were extensively reviewed using GE Centricity and McKesson applications. The diagnosis of ARDS was confirmed and inclusion to the study was determined for each patient using the previously discussed inclusion and exclusion criteria.

Measurement Methods

Measurements for the variables in this study came from the meticulous review of physician notes, physician dictations, physician orders, nursing notes, radiology reports, discharge paperwork, and death reports. In the participating hospital system, physician notes, physician orders, and nursing notes were handwritten and scanned into the electronic medical records. Thus, information was extracted from electronically generated and handwritten paper generated medical records. All variables were measured by systematically combing through each medical record for the desired data and recording it in a spreadsheet. Independent and dependent variables were measured as dichotomous variables. All dichotomous variables were entered into the spreadsheet using the predetermined coding system. See Appendix C for the coding system that was used.

Data Collection Process

Institutional Review Board (IRB) approval from the University of California San Marcos was requested and received prior to data collection initiation in June 2014. Approval through the healthcare institution was completed through the Quality Improvement division. Collected data from this project was ultimately used for a quality improvement project within the healthcare system. Thus, IRB approval within the healthcare institution was not required. The chart review and data collection process took place in the hospital at all times and took a total of four months to complete.

All medical records were accessed through a secure, password protected computer in the office of the intensive care unit manager. Data was organized in electronic spreadsheets using Microsoft Excel (2010). All data collection files were saved and stored on a password protected USB device called an iron key. Once included into the study, each medical record number was assigned a unique research identification number. An electronic list containing each research identification number and corresponding medical record number was maintained on the iron key. Thus, personal identification information was not included in the master spreadsheet used for the data collection and subsequent analysis. After each data collection session, the iron key was disconnected from the computer and locked in the manager's cabinet while not in use.

Coding and Scoring

The data collected for this study involved the coding of several dichotomous variables. All independent and dependent variables in this study were dichotomous and required coding for statistical analysis. Demographic variables for this study included

age, gender, BMI, SOFA score, comorbid conditions, use of iNO, and presence of sepsis. The ratio variables of age, BMI, and SOFA score were recorded as their true values. All other demographic variables were coded due to their dichotomous nature. See Appendix C for the list of variables collected and the corresponding numerical codes that were used for both descriptive and statistical purposes.

Data Analysis

Data collected and recorded in the Microsoft Excel 2010 spreadsheet was imported to IBM SPSS Statistic 20 software (2011) for analysis. Demographic information was used for reporting the characteristics of the sample population and was not used in the analysis as a predictor to determine statistical significance. Frequencies and descriptive statistics were used to summarize the demographic information extracted from the chart review to provide a general impression of the sample population.

As mentioned previously, a binary logistic regression was chosen to determine the predictability of the dichotomous variable of mortality based upon the two independent variables of stage of ARDS and position placement. Because the dependent variable of mortality was dichotomous, logistic regression was the most appropriate test to determine predictability. Prior to performing this analysis, regression diagnostics were performed to confirm that the data met all assumptions for regression analysis. This involved performing bivariate correlations and running collinearity diagnostics. Residual statistics and scatterplots were not performed to determine outliers due to the binary nature of the predictor variables.

Upon determining that the data met all assumptions for regression, correlations using Spearman's rho were computed for an initial look at how the independent variables correlated with the dependent variable. The binary logistic regression was then performed using the standard or simultaneous method in which all independent variables were included in the analysis at the same time. Dummy variables were not required. This logit model determined whether each independent variable significantly contributed to the variance in the relationship between the other independent variable and mortality. Strength and directionality of each independent variable in relation to mortality was determined after adjusting for the influence of the other independent variable. This will be discussed further in the results and discussion section.

Bias

Bias is a common problem in retrospective studies. The two types of bias that may have affected this study are selection bias and information bias. Selection bias is caused by error in choosing the appropriate individuals for the study (Polit & Beck, 2012). Although the sample population was initially generated through a computerized query, each participant's record was manually screened to determine if he or she met the criteria. Strict inclusion and exclusion criteria were created to avoid any bias in the selection process. In addition, every identified ARDS patient that met inclusion criteria for this study was used. No ARDS patients identified within the time period of January 2012 to August 2014 were rejected from the sample.

Information bias arises from measurement error and can involve situational contaminants, administration variants, instrument clarity, and instrument format (Polit &

Beck, 2012). These factors were particularly difficult to control in a retrospective study involving. Missing or incorrect data within the medical chart was not rectifiable and, in many cases, undetectable. For example, the process of scanning documents into the medical record could have easily omitted a key piece of information that may have been used to determine the stage of ARDS. However, much of the data collected for this study was dichotomous in nature and recorded as either present or not present. Therefore, information bias was minimized despite the uncontrollable nature of a retrospective review.

Ethical Considerations

The nature of retrospective research limits the issues of ethical dilemma. However, the principle of justice and the right to privacy in relation to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) is of primary concern (United States Government, 2011). To limit the risk of inappropriate health information transmission, the medical record number was the only patient identifying information used in the data collection process. This was the only considerable patient risk within this study. Therefore, patient consent was not necessary. As discussed earlier, medical record numbers were used to access medical records. However, patient medical record numbers were assigned corresponding research identification numbers and stored on a password protected USB device in a secure place. The research identification number was then used to record all variable information on the master data collection spreadsheet that was ultimately used for statistical use. This prevented any identifiable information from being inappropriately accessed.

Summary

This study aimed to determine the predictability of mortality with the independent variables of stage of ARDS and position placement. Data collection was performed exclusively at the healthcare institution that provided medical record access for this retrospective chart review. Patient information was handled in accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) (United States Government, 2011). All variables used for the statistical analysis were dichotomous and coded appropriately for use in IBM SPSS Statistic 20 software (2011). Characteristics of the population were summarized using descriptive statistic and frequencies. Patient data met all assumptions for logistic regression. A binary logistic regression analysis was then used to determine the predictability of mortality with the two independent variables of stage of ARDS and position placement.

CHAPTER FOUR: RESULTS

This retrospective quantitative chart review aimed to investigate how well stage of ARDS and position placement was able to predict mortality in the setting of a regional healthcare system in San Diego. The retrospective chart review resulted in a total of 171 patients that were admitted and treated in one of the five hospitals within a major healthcare system in San Diego County for ARDS between January 2011 and August 2014. A post hoc power analysis was conducted using an odds ratio of 0.3 (Abroug et al., 2011, an H0 of 0.9, an alpha of 0.05, and the obtained sample number of 171. The post hoc analysis generated by the G*Power 3.1.7 software system (Faul et al., 1992-2012) yielded a power of 0.998.

Sample

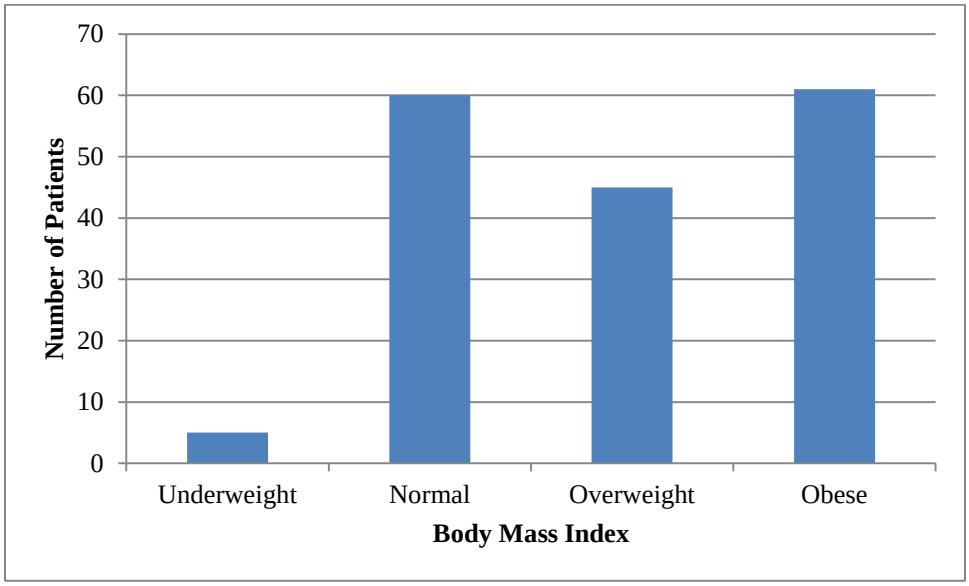
Descriptive information from the ARDS patient medical records was extracted during the chart review for the purpose of quantitatively describing the population. Out of the 171 patients, 58 percent (n=99) were male and 42 percent were female (n=72). Mean age of the population was 60 years old with the youngest patient at 22 years of age and the oldest at 98 years of age (Table 1). Over half of the individuals in the sample population were either overweight or obese. Figure 1 categorizes the patients into the standard BMI ranges as recommended by the Centers for Disease Control and Prevention [CDC] (2014).

Table 1

Age of the Sample Population in years (n= 171)

Variable	Statistical Value
Mean	60
Median	59
Mode	57
Standard Deviation	17.06
Minimum	22
Maximum	98

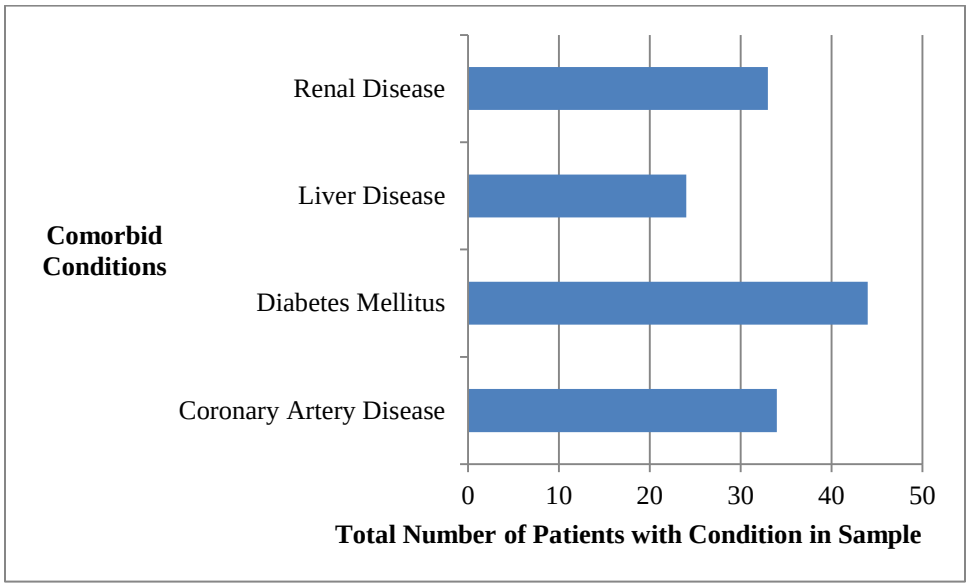
Figure 1. Frequency of Body Mass Index (kg/m2) (n=171)



Note: Underweight range: less than 18.5 kg/m2, normal weight range: 18.5 to 24.9 kg/m2; overweight range: 25.0 to 29.9 kg/m2; obese weight range: 30 kg/m2 and above (CDC, 2014).

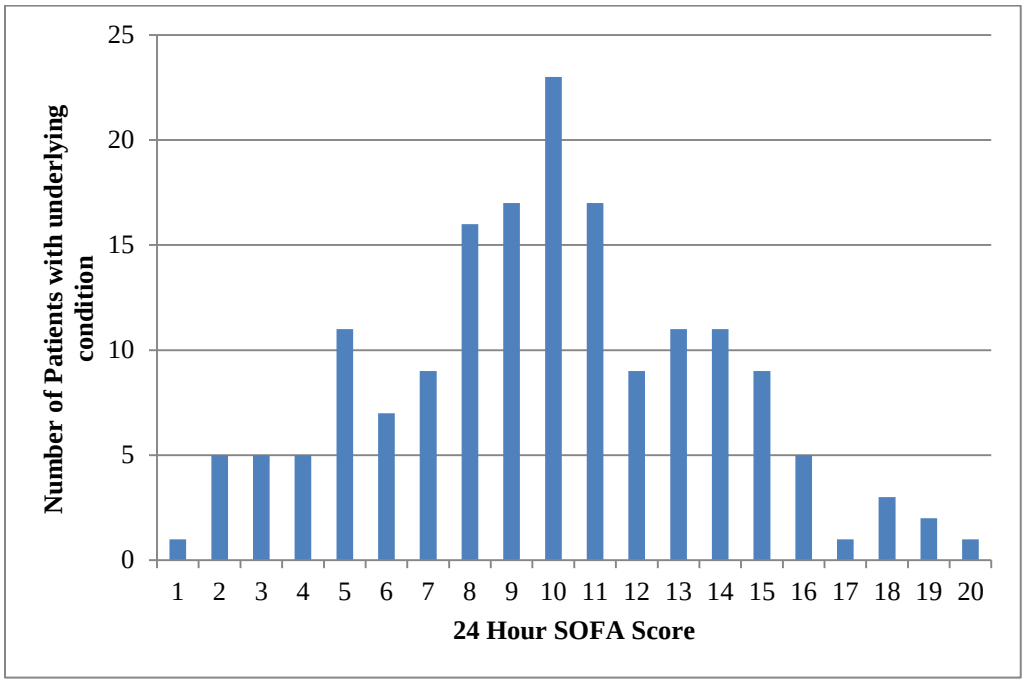
Clinical data were collected to describe the medical complexity of the ARDS patients. Of the comorbidities that were considered, 19.9 percent had a history of coronary artery disease, 25.7 percent had underlying diabetes mellitus, 14 percent had a history of liver disease, and 19.3 percent had underlying renal disease. Figure 2 shows the frequencies of the comorbid conditions for the sample population.

Figure 2. Frequency of Comorbid Conditions (n=171)



Additional clinical data collected included the SOFA score, the frequency of iNO use, and the frequency of sepsis during the treatment of ARDS. Figure 3 summarizes the 24 hour SOFA scores for the sample population. The mean 24 hour SOFA score for the sample population was 8.8 which. This value is associated with a 15 to 20 percent risk of hospital mortality. The 24 hour SOFA score mode, however, was 10. This value is associated with a 40 to 50 percent risk of hospital mortality. Inhaled nitric oxide was used in 22.8 percent of the patients during the course of their ARDS treatment. Sepsis occurred in 73.7 percent of patients during the course of their treatment for ARDS.

Figure 3. Frequency of 24 hour SOFA Score (n=171)



Of the 171 ARDS patients, 32.2 percent (n=55) were classified as moderate ARDS and 67.8 percent (n=116) were classified as severe ARDS (Table 2). Approximately 81 percent (n=139) of the ARDS patients remained in a supine position, while approximately 19 percent (n=32) were placed in a prone position (Table 3). The descriptive information presented will be discussed further in the discussion chapter of this paper.

Table 2

Stage of ARDS (n=171)

Stage of ARDS	Number of Patients
Moderate	55
Severe	116

Table 3

Position Placement (n=171)

Position Placement	Number of Patients
Supine	139
Prone	32

Data Collection and Preparation

All assumptions were met for the binary logistic regression. This was confirmed by performing a specific set of diagnostics with SPSS prior to completing the analysis. These tests included bivariate correlations using the predictor variables and collinearity diagnostics. Bivariate correlations were performed to ensure a low degree of inter-correlation between predictor variables. The correlation coefficient (r = -0.138) represented a weak correlation between the predictor variables of position placement and stage of ARDS (Table 4). Collinearity diagnostics were also performed to confirm that the predictor variables were not significantly inter-correlated (Table 5). The tolerance statistic was greater than 0.10 and the variance inflation factor (VIF) statistic was less than 10. Both of these values indicate that there was minimal collinearity among the predictor variables.

Table 4

Coefficient Correlations

Predictor Variable	Position	Stage of ARDS
Position	1	-0.138
Stage of ARDS	-0.138	1

Table 5

Collinearity Statistics

Predictor Variable	Tolerance	VIF
Stage of ARDS	0.981	1.019
Position	0.981	1.019

Statistical Results

Initial analysis involved a Spearman's rho correlation that was calculated using a two-tailed approach and an alpha of 0.05. The Spearman's rho results indicated there is a small to moderate and significant correlation in mortality becoming more likely as the stage of ARDS increases from moderate to severe (ρ=0.191; p-value=0.012). There was a small to moderate but non-significant negative correlation in the relationship between position and mortality (ρ= -0.140; p-value= 0.068). Thus, as the position changed from supine to prone, the likelihood of the patient dying increased. This relationship, however, did not reach the 0.05 level of significance for the Spearman's rho correlation.

Table 6

Spearman's rho Correlation

Variable	Stage of ARDS	Position	Mortality
Stage of ARDS			
Correlation Coefficient	1.000	0.138	0.191
Sig. (2-tailed)	.	0.072	0.012
N	171	171	171
Position			
Correlation Coefficient	0.138	1.000	-0.140
Sig. (2-tailed)	0.072	.	0.068
N	171	171	171
Mortality			
Correlation Coefficient	0.191	-0.140	1.000
Sig. (2-tailed)	0.012	0.068	.
N	171	171	171

The binary logistic regression generated a series of results that aimed to answer the proposed research question regarding the outcome of mortality. The classification table in Block 0 indicated that the overall predictive capacity of the null model (mortality in ARDS patients) without the independent variables was 52 percent. This suggests that without the consideration of the independent variables, this model predicts the outcome of mortality correctly approximately fifty percent of the time. This value was then compared to the model's predictive capacity when considering the independent variables.

The classification table in Block 1 indicated that the capacity of this model to predict mortality increased from 52 percent to 64.3 percent when stage of ARDS and position placement were considered. This indicated that there was a 12.3 percent increase in classification accuracy when the independent variables were added to the equation. In other words, nearly 65 percent of the mortality outcome was predicted by this regression model. The proportional by chance accuracy criteria was 62.5 percent. This value was less than the overall accuracy rate of 64.3 percent, indicating the criteria for classification accuracy was satisfied.

The Omnibus Tests of Model Coefficients table produced a Chi-square value (X^2= 11.2) with a significance level of 0.004, indicating that the regression model has the potential to be a good prediction tool. Other measures obtained in the regression model included the Cox and Snell R square value and the Nagelkerke R Square value. These pseudo R square values were used to measure the usefulness of the model. The Cox and Snell R Square (R^2= 0.064) and the Nagelkerke R square (R^2= 0.085) both indicated that stage of ARDS and position placement have a small effect size on mortality. The

Nagelkerke R square value is the most commonly reported pseudo R square value in logistic regression. Its value of 0.085 indicated that approximately 8.5 percent of the variance in mortality was explained by ARDS severity and positioning. In addition, the Hosmer and Lemeshow Test compared the predicted outcomes with the observed outcomes within the sample population and determined that the model is a small to moderately good fit for the proposed research question with a *p*-value of 0.148.

Table 7 summarizes the pertinent values from the Variables in the Equation Table generated by the logistic regression analysis in SPSS. This table provides information used to determine how the independent variables were able to predict the outcome of mortality using this model. In this particular study, stage of ARDS (p value= 0.006) and position (p value= 0.028) were statistically significant predictors in the regression equation model. The null hypothesis that the β coefficient for stage of ARDS was equal to zero was rejected. The null hypothesis that the β coefficient for position placement was equal to zero was rejected as well. The significance was estimated using a Wald statistic with one degree of freedom. The standard error for the two variables and the constant was less than 2.0, indicating that multicollinearity among the independent variables was not a concern for this model.

Table 7

Simultaneous Logistic Regression: Variables in the Equation

Variable	B	S.E.	Significance	Exp(B)	95% Confidence Interval for Exp(B)	
					Upper	Lower
Stage of ARDS	0.955	0.345	0.006	2.598	1.321	5.111
Positon	-0.914	0.417	0.028	0.401	0.177	0.907
Constant	-0.395	0.282	0.161	0.674		

The exponentiation of the β coefficient [Exp(B)] is the adjusted odds ratio (OR) for this logistic regression study. The OR for stage of ARDS was 2.598 (95% confidence interval [CI] 1.321 to 5.111). In other words, the odds of mortality occurring in severe ARDS patients were 2.6 times greater than the odds of mortality occurring in moderate ARDS patients. The OR for position placement was 0.401 (95% CI 0.177 to 0.907). OR values less than 1.00 indicate a decreased odds ratio for increase in one unit of the independent variable. Thus, the odds of mortality occurring in supine patients were approximately 60 percent less than the odds of mortality occurring in prone positioned patients.

Summary

The binary logistic regression found stage of ARDS and position placement to be significant predictor variables in the outcome of mortality in ARDS patients within the sample population. All assumptions were met for the use of a binary logistic regression model. The model was determined to be a good prediction tool and a small to moderately good fit for the study. There was no evidence of numerical problems in the solution and the classification accuracy surpassed the proportional by chance accuracy criteria, supporting the utility of the model. An increase in severity of ARDS was associated with an increased likelihood of mortality in the sample population used for this study. This supports the existing literature regarding the clinical course and associated outcomes of ARDS. An increase in value of position placement (prone positioning) was significantly associated with a decreased probability of mortality. This inverse association contradicts

the recent evidence that supports the benefits of prone positioning in ARDS treatment. These results will be discussed further in the following chapter.

CHAPTER FIVE: DISCUSSION

Recent research suggests that placing severe ARDS patients in a prone position can decrease the risk or mortality. These findings have become evident through meta-analysis of several previous studies where patient data was grouped together to create a large sample population (Abroug et al., 2011). The most significant study that demonstrated a reduced risk of mortality with prone positioning involved a randomized controlled trial that included strict inclusion criteria, a protocol that guided clinical management, and a patient sample population of over 400 individuals (Guerin et al., 2013). The study described in this scholarly paper found a statistically significant relationship between both independent variables (stage of ARDS and position placement) and the dependent variable (mortality). However, the directionality of the relationship between position placement and mortality opposes the findings of recent research concerning this subject.

Major Findings

The hypothesis for this research study states the following: Position placement (supine or prone) and stage of ARDS at the time of prone positioning initiation (moderate or severe) will predict mortality. The results of this study support the hypothesis that position placement and stage of ARDS are able to predict mortality. Severe ARDS patients were had significantly higher risk of mortality than moderate ARDS patients which was an expected relationship based on evidence within the research community (Abroug et al., 2011). Contrary to what was described in Guerin et al. (2013), however, prone positioning significantly increased the probability of mortality in this study.

Spearman's rho correlations found a significant relationship between stage of ARDS and mortality, but the correlation between position placement and mortality was not significant. The lack of significant correlation makes the predictability of mortality with position placement questionable. Although predictability with position placement was significant in the analysis, there are many limitations and potential confounding variables to consider in this study. In light of the limitations and confounding variables involved in this study, the results of this study cannot be used to formulate a prediction equation for the outcome of mortality using the independent variables of stage of ARDS and position placement.

Although the limitations are great enough to question the utility of the analysis, the process of collecting data has brought into focus many aspects about the management of ARDS within the particular hospital system used for this study. For one, the number of ARDS cases managed with prone positioning was far less than expected. Only 19 percent of the ARDS patients were placed in a prone position. This may be related to the lack of evidence to support prone positioning during the period of time the sample was collected. In addition, several prone positioned ARDS cases were excluded from this study due to the inability of the prone duration to meet the inclusion criteria. Several others were excluded because of their medical history of COPD or previous pulmonary disease. This suggests that a greater number of patients may have been included if the therapeutic time for prone duration was shorter. It also suggests that patients are being placed in a prone position indiscriminate of any underlying pulmonary disease process.

Although evidence repeatedly demonstrates that iNO does not affect mortality in ARDS, the frequency of iNO use in the treatment of ARDS was surprisingly high. Approximately 23 percent of the ARDS patients in this study received this costly intervention during the course of their treatment. Although iNO may improve oxygenation, evidence does not support this practice as an intervention to improve the outcome or mortality (Adhikari et al., 2007; Afshari et al., 2011; Taylor et al., 2004). This may be a practice worth investigating for cost-effectiveness within the hospital system used for this study.

Limitations

The sample population in this study was selected through convenience sampling. Randomization of subjects was not possible due to the nature of the retrospective review. Lack of a specific ICD-9-CM code for ARDS made it difficult to systematically identify ARDS patients within the electronic medical record system. This sampling method limitation made it difficult to say that all ARDS patients were accurately represented in the sample population. The possibility of ARDS patients being unaccounted for was high due to the potential human error involved in reading and interpreting discharge summaries to identify the diagnosis of ARDS.

The *a priori* G*Power sample number (n=64) was exceeded in the sample population. However, the number of prone positioned ARDS patients was far less than supine positioned ARDS patients. Of the 171 ARDS patients included in the study, only 32 of them were placed in a prone position and met inclusion criteria. This equaled exactly half of the required 64 patients calculated in the *a priori* G*Power analysis, a

number that should be sufficient for the binary logistic regression. Nevertheless, the large difference in numbers of supine versus prone patients may have affected the results in both the Spearman's rho correlations and the logistic regression.

The small frequency of prone positioned ARDS patients in this hospital system leads to the logical consideration of additional limitations such as inexperience of staff and variance in clinical decision-making amongst medical practitioners. The infrequency of ARDS cases treated with prone position placement over the predetermined sampling period may have contributed to lack of experience and variation in clinical practice, factors that could considerably affect patient outcome. This small volume of prone positioned cases does not allow for nurses or physicians to become familiar and remain oriented with the process of managing a prone positioned patient. As discussed earlier, no standardized protocol for prone position placement existed in this hospital system during the sampling period. This factor may have also contributed to variation in clinical practice. In addition, the sample comes from only one hospital system which may have different philosophies and clinical approaches to treating ARDS when compared to other hospital systems. Generalizability may be reduced as well because the sample population represents ARDS patients from the one specific geographical location of San Diego County.

Other important considerations regarding the sample population were the various therapies that the patients may have received during their admission. Such therapies to consider include the use of vasopressors, paralytics, specialized ventilation techniques, or the use of specialty rotational beds. Some of the ARDS patients that remained supine

were placed on specialty beds that vigorously rotated them frequently from 60 degrees on the left to 60 degrees on the right in a supine position. This type of rotational positioning could have greatly impacted the outcome of the supine ARDS patients. This therapy was not accounted for in this study but was often observed through the process of collecting patient data.

Inhaled nitric oxide was another therapy that may have affected the outcome of mortality. 22.8 percent of the ARDS patients received iNO during the course of their treatment for ARDS. ARDS patients that received iNO were included in the study to allow for a greater number of prone positioned patients. If these patients were eliminated from the sample population, the sample would not have been large enough to perform the logistic regression analysis. The inclusion of ARDS patients that received iNO was rationalized with the literature that shows iNO does not affect mortality in ARDS patients (Adhikari et al., 2007; Afshari et al., 2011; Taylor et al., 2004).

Sepsis is another condition that must be considered as a potential confounding variable in this study. Evidence shows that sepsis increases mortality, lengthens hospital stay, and increases risk of complications (Hall et al., 2011). 73.7 percent of the ARDS patients in this study were also diagnosed with sepsis. This rate was comparable to the rate of occurrence of sepsis in ARDS found in literature (Barbas et al., 2012). Eliminating patients with sepsis to avoid this potential confounding variable was not an option due to the high rate of occurrence. In addition, eliminating ARDS patients with sepsis would not accurately represent the general ARDS population because the prevalence of sepsis in ARDS is so great. Thus, septic ARDS patients were included in

the sample population to maintain generalizability of the study. The ability for sepsis to exclusively affect the outcome of mortality in ARDS patients must be considered.

Implications for Nursing Practice and Research

The complex nature and high mortality rate of acute respiratory distress syndrome (ARDS) fuels the ongoing effort for nursing and medical practitioners to explore the outcomes of various ARDS treatments. Research continues to demonstrate the improvement of oxygenation in ARDS patients with prone positioning (Chan et al., 2011; Sud et al., 2010; Voggenreiter et al., 2005). The increase survivability with prone positioning in ARDS presented by Guerin et al. (2013) warrant a need for replication and further exploration of this subject. Prognostic outcomes are very important aspects of clinical healthcare management. A treatment that has the potential to improve prognostic outcomes should be investigated thoroughly.

In the intensive care environment, advanced nurse practitioners (APNs) and registered nurses serve as part of a multidisciplinary team that manages the clinical care of ARDS patients. As a part of this team, nursing staff has the unique opportunity to participate in and contribute to the body of critical care research with the ultimate goal of promoting evidence-based practices for clinical management of patients. Within this role, advanced practice nurses can grow the body of knowledge regarding ARDS treatment through their own research by participating on panels that organize randomized clinical trials and by creating their own research opportunities through retrospective review, meta-analysis, or through systematic review. Modern day healthcare systems base clinical management on research. Advanced practice nurses have the ability to

greatly impact clinical practice by contributing to research and participating in the process of implementing evidence-based interventions at the bedside.

Recommendations for Future Research

Randomized controlled trials, meta-analyses, and systematic reviews have the greatest epistemological strength when it comes to formulating evidence-based recommendations for clinical practice (Polit & Beck, 2012). The reduction in mortality with prone positioning demonstrated by Guerin et al. (2013) came from a randomized controlled trial with a large sample size, strict inclusion criteria, and a clinical management protocol. Reproducing this type of study would be ideal for future research on this particular subject. Although this type of prospective randomized controlled trial requires a tremendous amount of resources, time, and cooperation within an entire hospital system, this type of study allows for a higher level of control within the patient population with the use of a protocol. It also has the potential to yield a larger experimental group which allows for subgroup analysis. With a larger sample population other predictor variables such as sepsis, iNO, and advance rotational therapy could be explored. In addition, research focusing on the optimal duration of prone position placement would help guide practice and protocol standardization.

Many aspects of this retrospective review could be improved upon if it were to be replicated. Most significantly, it would be ideal to generate a query for ARDS patients after the ICD 10 diagnoses codes have been implemented within the hospital system. This would ensure that the queried patients actually have the ARDS diagnosis, simplifying the search for ARDS patients. Stratified sampling may be more effective at

achieving proportionate numbers across homogenous populations. With stratification, each ARDS subgroup would need to contain at least 33 percent of the entire ARDS population. For example, each of the supine and prone subgroups would need to have numbers that reflect at least 33 percent of the overall sample population. Optimally, this would prevent underrepresentation of particular subgroup which might skew results. Nonetheless, the population needs to exist in order to meet these requirements. In addition, performing the review within a hospital system that uses a standardized protocol for the management of ARDS would provide a setting with more congruent clinical practices. This would eliminate factors that may have influenced outcome due to variation in medical practice.

Summary

The ability for prone positioning to improve oxygenation in the setting of ARDS is well-documented. The next logical hypothesis leads to the prediction that it might reduce mortality. Only recently has research been able to support the relationship between prone positioning and mortality reduction. Replication and additional exploration of this association is required to support this hypothesis. This scholarly research project explored the ability for stage of ARDS and position placement to predict the outcome of mortality in ARDS patients. Although both independent variables were found to be adequate predictors of mortality in the analysis, the integrity of the study is questionable due to the sampling limitations and the use of therapies such as iNO and specialty rotation beds. In light of such limitations, the results of this study cannot be used to formulate a prediction equation for the outcome of mortality in ARDS patients.

Through the process of this study, many aspects of ARDS management within the specific hospital system used for this study have been observed. The use of rotational beds and iNO in the treatment of ARDS are both factors that warrant further outcome exploration. Continuing to evaluate ARDS outcomes as ICD 10 codes are implemented and as the use of prone positioning becomes more frequent will be imperative in determining optimal ARDS management within the hospital system used in this study. Replication and additional research with the use of randomized controlled trials will help all evidence-based practitioners better understand how we can optimize ARDS treatment. As the research for ARDS management expands, the therapeutic interventions available for this complex condition will be better understood and utilized appropriately with the ultimate goal of improving outcomes.

Appendix A

G*Power Analysis Output

z tests - Logistic regression

Options:	Large sample z-Test, Demidenko (2007) with var corr	
Analysis:	A priori: Compute required sample size	
Input:	Tail(s)	= Two
	Odds ratio	= 0.3
	Pr(Y=1|X=1) H0	= 0.9
	α err prob	= 0.05
	Power (1-β err prob)	= 0.80
	R^2 other X	= 0
	X distribution	= Normal
	X parm μ	= 0
	X parm σ	= 1
Output:	Critical z	= -1.9599640
	Total sample size	= 64
	Actual power	= 0.8040087

Appendix B

List of ICD 9 CM Codes

ICD 9 CM Code	Diagnosis
480.00	Pneumonia due to adenovirus
480.10	Pneumonia due to RSV
480.20	Pneumonia due to parainfluenza virus
480.30	Pneumonia due to SARS-associated coronavirus
480.80	Pneumonis due to other virus not elsewhere classified
480.90	Unspecified
481.00	Pneumococcal pneumonia
482.00	Pneumonia due to Klebsiella pneumoniae
482.10	Pneumonia due to Pseudomonas
482.20	Pneumonia due Hemophilus influenzae
482.30	Pneumonia due to Streptococcus, unspecified
482.31	Pneumonia due to Streptococcus, group A
482.32	Pneumonia due to Streptococcus, group B
482.39	Pneumonia due to other Streptococcus
482.40	Pneumonia due to Staphylococcus, unspecified
482.41	Methicillin susceptible pneumonia due to Staphylococcus aureus
482.42	Methicillin resistant pneumonia due to Staphylococcus aureus
482.49	Other Staphylococcus pneumonia
482.81	Pneumonia due to anaerobes
482.82	Pneumonia due to escherichia coli
482.83	Pneumonia due to other gram-negative bacteria
482.84	Pneumonia due to Legionnaires' disease
482.89	Pneumonia due to other specified bacteria
482.90	Bacterial pneumonia, unspecified
483.00	Pneumonia due to mycoplasma organism
483.10	Pneumonia due to chlamydia
483.80	Pneumonia due to other specified organism
484.10	Pneumonia in cytomegalic inclusion disease
484.30	Pneumonia in whooping cough
484.50	Pneumonia in anthrax
484.60	Pneumonia in aspergillosis
484.70	Pneumonia in other sytemic mycoses
484.80	Pneumonia in other infectious diseases classified elsewhere

485.00	Bronchpneumonia, organism unspecified
486.00	Pneumonia, organism unspecified
487.00	Influenza with pneumonia
487.10	Influenza with other respiratory manifestations
487.80	Influenza with other manifestations
488.01	Influenza due to identified avian influenza virus with pneumonia
488.02	Influenza due to identified avian influenza virus with other respiratory manifestations
488.09	Influenza due to identified avian influenza virus with other manifestations
488.11	Influenza due to identified 2009 H1N1 influenza virus with pneumonia
488.12	Influenza due to identified 2009 H1N1 influenza virus with other respiratory manifestations
488.19	Influenza due to identified 2009 H1N1 influenza virus with other manifestations
488.81	Influenza due to identified novel influenza A virus with pneumonia
488.82	Influenza due to identified novel influenza A virus with other respiratory manifestations
488.89	Influenza due to identified novel influenza A virus with other manifestations
506.00	Bronchitis and pneumonitis due to fumes and vapors
506.10	Acute pulmonary edema due to fumes and vapors
506.30	Other acute and subacute respiratory conditions due to fumes and vapors
506.90	Unspecified respiratory conditions due to fumes and vapors
507.00	Pneumonitis due to inhalation of food or vomitus
507.10	Pneumonitis due to inhalation of oils and essences
507.80	Pneumonitis due to other solids and liquids
508.20	Respiratory conditions due to smoke inhalation
508.80	Respiratory conditions due to other specified external agents
508.90	Respiratory conditions due to unspecified external agent
514.00	Pulmonary congestion and hypostasis
516.30	Idiopathic interstitial pneumonia not otherwise specified
516.32	Idiopathic non-specific interstitial pneumonitis
516.33	Acute interstitial pneumonitis
516.34	Respiratory bronchiolitis interstitial lung disease
516.35	Idiopathic lymphoid interstitial pneumonia
516.36	Cryptogenic organizing pneumonia
516.37	Desquamative interstitial pneumonia
516.80	Other specified alveolar and parietoalveolar pneumonopathies
516.90	Unspecified alveolar and parietoalveolar pneumonopathy

518.40	Acute edema of lung, unspecified
518.51	Acute respiratory failure following trauma and surgery
518.52	Other pulmonary insufficiency, not elsewhere classified, following trauma and surgery
518.53	Acute and chronic respiratory failure following trauma and surgery
518.60	Allergic bronchopulmonary aspergillosis
518.70	Transfusion related acute lung injury (TRALI)
518.81	Acute respiratory failure following trauma and surgery
518.82	Other pulmonary insufficiency, not elsewhere classified, following trauma and surgery
518.83	Chronic respiratory failure
518.84	Acute and chronic respiratory failure following trauma and surgery
518.89	Other diseases of the lung not elsewhere classified
519.90	Unspecified disease of respiratory system

Appendix C

Coding of Variables

Variable	Description	Coding
Age	Years	None, ratio
Gender	Male	0
	Female	1
Body Mass Index (BMI)	kg/m2	None, ratio
SOFA24	Score within 24 hours in ICU	None, ratio
Comorbid Conditions	Coronary Artery Disease (CM0)	no= 0; yes= 1
	Diabetes Mellitus (CM1)	no= 0; yes= 1
	Hepatic Disease (CM2)	no= 0; yes= 1
	Renal Disease (CM3)	no= 0; yes= 1
Sepsis	Presence of Sepsis	no= 0; yes= 1
iNO	Use of Inhaled Nitric Oxide (iNO)	no= 0; yes= 1
Stage ARDS	Severity of ARDS	Moderate= 0; Severe= 1
Position	Position Placement	Supine= 0; Prone= 1
Mortality	Occurred or did not occur	no= 0; yes= 1

References

Abroug, F., Ouanes-Besbes, L., Dachraoui, F., Ouanes, I., & Brochard, L. (2011). An updated study-level meta-analysis of randomised controlled trials on proning in ARDS and acute lung injury. *Critical Care*, *15*, 1-9. http://dx.doi.org/10.1186/cc9403

Abroug, F., Ouanes-Besbes, L., Elatrous, S., & Brochard, L. (2008). The effect of prone positioning in acute respiratory distress syndrome or acute lung injury: A meta-analysis. Areas of uncertainty and recommendations for research. *Intensive Care Medicine*, *34*, 1002-1011. http://dx.doi.org/10.1007/s00134-008-1062-3

Adhikari, N. K., Burns, K. E., Friedrich, J. O., Granton, J. T., Cook, D. J., & Meade, M. O. (2007, April 14). Effect of nitric oxide on oxygenation and mortality in acute lung injury: Systematic review and meta-analysis. *British Medical Journal*, *334*(7597), 1-8. http://dx.doi.org/10.1136/bmj.39139.716794.55

Afshari, A., Brok, J., Moller, A. M., & Wetterslev, J. (2011, June). Inhaled nitric oxide for acute respiratory distress syndrome and acute lung injury in adults and children: A systematic review with meta-analysis and trial sequential analysis. *Anesthesia and Analgesia*, *112*, 1411-1421. http://dx.doi.org/10.1213/ANE.0b013e31820bd185

Alsaghir, A. H., & Martin, C. M. (2008, February). Effect of prone positioning in patients with acute respiratory distress syndrome: A meta-analysis. *Critical Care Medicine*, *36*, 603-609. http://dx.doi.org/10.1097/01.CCM.0000299739.98236.05

Angus, D. C., Clermont, G., Linde-Zwirble, W. T., Musthafa, A. A., Dremsizov, T. T., Lidicker, J., & Lave, J. R. (2006, December). Healthcare costs and long-term outcomes after acute respiratory distress syndrome: A phase III trial of inhaled nitric oxide. *Critical Care Medicine, 34,* 2883-2890. http://dx.doi.org/10.1097/01.CCM.0000248727.29055.25

Ashbaugh, D. G., Bigelow, D. B., Petty, T. L., & Levine, B. E. (1967, August 1*2*). Acute respiratory distress in adults. *Lancet,* 2, 319-323.

Bajwa, A. A., Arasi, L., Canabal, J. M., & Kramer, D. J. (2010). Automated prone positioning and axial rotation in critically ill, nontrauma patients with acute respiratory distress syndrome (ARDS). *Journal of Intensive Care Medicine, 25,* 121-125. http://dx.doi.org/10.1177/0885066609356050

Barbas, C. S., Matos, G. F., Amato, M. B., & Carvalho, C. R. (*2012*). Goal-oriented respiratory management for critically ill patients with acute respiratory distress syndrome. *Critical Care Research and Practice,* 2012, 1-13. http://dx.doi.org/10.1155/2012/952168

Bernard, G. R., Artigas, A., Brigham, K. L., Carlet, J., Falke, K., Hudson, L., ... Spragg, R. (1994). Report of the American-European consensus conference on ARDS: Definitions, mechanisms, relevant outcomes and clinical trial coordination. *Intensive Care Medicine, 20,* 225-232. http://dx.doi.org/10.1007/BF01704707

Brochard, L., Martin, G. S., Blanch, L., Pelosi, P., Belda, F. J., Jubran, A., ... Vincent, J. (2012). Clinical review: Respiratory monitoring in the ICU- a consensus of *16. Critical Care,* 16, 1-14. http://dx.doi.org/10.1186/cc11146

Cakar, N., Der Kloot, T. V., Youngblood, M., Adams, A., & Nahum, A. (2000, June). Oxygenation response to a recruitment maneuver during supine and prone positions in an oleic acid-induced lung injury model. *American Journal of Respiratory and Critical Care Medicine*, *161*, 1949-1956. http://dx.doi.org/10.1164/ajrccm.161.6.9907113

Centers for Disease Control and Prevention. (2014). About BMI for adults. Retrieved from http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html

Chan, M. C., Hsu, J. Y., Lee, H. H., Pong, S. C., Chang, L. Y., Kuo, B. I., & Wu, C. L. (2007, September). Effects of prone position on inflammatory markers in patients with ARDS due to community-acquired pneumonia. *Journal of the Formosan Medical Association*, *106*, 708-716. http://dx.doi.org/10.1016/S0929-6646(08)60032-7

Chassin, M. R., & Loeb, J. M. (2011). The ongoing quality improvement journey: Next stop, high reliability. *Health Affairs*, *30*, 559-568. http://dx.doi.org/10.1377/hlthaff.2011.0076

Cheung, A. M., Tansey, C. M., Tomlinson, G., Diaz-Granados, N., Matte, A., Barr, A., ... Herridge, M. S. (2006, September). Two-year outcomes, health care use, and costs of survivors of acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*, *174*, 538-544. http://dx.doi.org/10.1164/rccm.200505-693OC

Choi, A. M. (Ed.). (2010). *Acute respiratory distress syndrome* (2nd ed.). New York, NY: Informa Healthcare USA, Inc.

Collins, S. R., & Blank, R. S. (2011). Approaches to refractory hypoxemia in acute respiratory distress syndrome: Current understanding, evidence, and debate. *Respiratory Care*, *56*, 1573-1582. http://dx.doi.org/10.4187/respcare.01366

Collins, S. R., & Blank, R. S. (2011, October). Approaches to refractory hypoxemia in acute respiratory distress syndrome: Current understanding, evidence, and debate. *Respiratory Care*, *56*, 1573-1582. http://dx.doi.org/10.4187/respcare.01366

Davies, H. T., Crombie, I. K., & Tavakoli, M. (1998). When can odds ratios mislead? *British Medical Journal*, *316*, 989. http://dx.doi.org/10.1136/bmj.316.7136.989

Dellinger, R. P., Levy, M. M., Rhodes, A., Annane, D., Gerlach, H., Opal, S. M., ... Moreno, R. (2013). Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Medicine*, *39*, 165-228. http://dx.doi.org/10.1007/s00134-012-2769-8

Deutschman, C. S., & Neligan, P. J. (2010). *Evidence-based practice of critical care*. Philadelphia, PA: Sauders Elsevier.

Di Marco, F., Devaquet, J., Lyazidi, A., Galia, F., Da Costa, N. P., Fumagalli, R., & Brochard, L. (2010, January). Positive end-expiratory pressure-induced functional recruitment in patients with acute respiratory distress syndrome. *Critical Care Medicine*, *38*, 127-132. http://dx.doi.org/10.1097/CCM.0b013e3181b4a7e7

Dulu, A., Pastores, S. M., Park, B., Reidel, E., Rusch, V., & Halpern, N. A. (2006). Prevalence and mortality of acute lung injury and ARDS after lung resection. *Chest*, *130*, 73-78. http://dx.doi.org/10.1378/chest.130.1.73

Fadi, A. E., Mohamed, H., Komara, J., & Guzman, J. A. (2011, December). Survival of ALI/ARDS is adversely affected by an underlying diagnosis of advanced COPD. *Critical Care Medicine, 39,* 91. http://dx.doi.org/10.1097/01.ccm.0000408627.24229.88

Faul, F., Buchner, A., Erdfelder, E., & Lang, A. (1992-2012). G*Power Version 3.1.7 [Apparatus and software]. Published instrument. Retrieved from https://cougarapps.csusm.edu/vpn/index.html

Ferguson, N. D., Fan, E., Camporota, L., Antonelli, M., Anzueto, A., Beale, R., ... Ranieri, V. M. (2012, October). The Berlin definition of ARDS: An expanded rationale, justification, and supplementary material. *Intensive Care Medicine, 38,* 1573-1582. http://dx.doi.org/10.1007/s00134-012-2682-1

Ferguson, N. D., Frutos-Vivar, F., Esteban, A., Anzueto, A., Alia, I., Brower, R. G., ... Brochard, L. (2005, January). Airway pressures, tidal volumes, and mortality in patients with acute respiratory distress syndrome. *Critical Care Medicine, 33,* 21-30. http://dx.doi.org/ 10.1097/01.ccm.0000150652.91411.66

Fernandez, R., Trenchs, X., Klamburg, J., Castedo, J., Serrano, J. M., Besso, G., ... Lopez, M. J. (2008, August). Prone positioning in acute respiratory distress syndrome: A multicenter randomized clinical trial. *Intensive Care Medicine, 34,* 1487-1491. http://dx.doi.org/10.1007/s00134-008-1119-3

Ferriera, F. L., Bota, D. P., Bross, A., Melot, C., & Vincent, J. (2001, October 10). Serial evaluation of the SOFA score to predict outcome in critically ill patients. *Journal of American Medical Association, 286,* 1754-1758.

Froese, A. B., & Bryan, A. C. (1974). Effects of anesthesia and paralysis on diaphragmatic mechanics in man. *Anesthesiology, 41*, 242-255. http://dx.doi.org/10.1097/00000542-197409000-00006

Fry, M. (2011, March-April). Literature review of the impact of nurse practitioners in critical care services. *Nursing Critical Care, 16*, 58-66. http://dx.doi.org/10.1111/j.1478-5153.2010.00437.x

Gainnier, M., Michelet, P., Thirion, X., Arnal, J. M., Sainty, J. M., & Papazian, L. (2003, December). Prone position and positive end-expiratory pressure in acute respiratory distress syndrome. *Critical Care Medicine*, *12*, 2719-2726. http://dx.doi.org/10.1097/01.CCM.0000094216.49129.4B

Galiatsou, E., Kostanti, E., Svarna, E., Kitsakos, A., Koulouras, V., Efremidis, S. C., & Nakos, G. (2006). Prone position augments recruitment and prevents alveolar overinflation in acute lung injury. *American Journal of Respiratory and Critical Care Medicine*, *174*, 187-197. http://dx.doi.org/ 10.1164/rccm.200506-899OC

Gao, L., & Barnes, K. C. (2009, February). Recent advances in genetic predisposition to clinical acute lung injury. *American Journal of Physiology*, *296*, L713-L725. http://dx.doi.org/10.1152/ajplung.90269.2008

Gattinoni, L., & Caironi, P. (2010, December). Prone positioning: Beyond physiology. *Anesthesiology*, *113*, 1262-1264. http://dx.doi.org/10.1097/ALN.0b013e3181fcd97e

Gattinoni, L., Caironi, P., Cressoni, M., Chiumello, D., Ranieri, V. M., Quintel, M., ... Bugedo, G. (2006, April). Lung recruitment in patients with the acute respiratory

distress syndrome. *The New England Journal of Medicine, 354*, 1775-1786. http://dx.doi.org/10.1056/NEJMoa052052

Gattinoni, L., Carlesso, E., Taccone, P., Polli, F., Guerin, C., & Mancebo, J. (2010). Prone positioning improves survival in severe ARDS: A pathophysiologic review and individual patiet meta-analysis. *Minerva Anestesiologica, 76*, 448-454. Retrieved from http://www.minervamedica.it/en/getfreepdf/lggQe%252F%252BGMe82skSHePvj09YG7gxtk9LfsjUUB246DSltp3U5WbIDEq9r06j%252FNervfQdj4l%252BbNlHIfatcK58a3w%253D%253D/R02Y2010N06A0448.pdf

Gattinoni, L., Pelosi, P., Valenza, F., & Mascheroni, D. (2004). *Patient positioning in acute respiratory failure, principles and practice of mechanical ventilation.* M. Tobin (Ed.). New York, NY: McGraw Hill.

Gattinoni, L., Toqnoni, G., Pesenti, A., Taccone, P., Mascheroni, D., Labarta, V., ... Latini, R. (2001, August). Effect of prone positioning of the survival of patients with acute respiratory failure. *New England Journal of Medicine, 345*, 568-573. http://dx.doi.org/10.1056/NEJMoa010043

Goldhill, D. R., Imhoff, M., McLean, B., & Waldmann, C. (2007). Rotational bed therapy to prevent and treat respiratory complications: A review and meta-analysis. *American Journal of Critical Care, 16*, 50-61. Retrieved from http://ajcc.aacnjournals.org/content/16/1/50.full.pdf+html

Guerin, C., Gaillard, S., Lemasson, S., Ayzac, L., Girard, R., Beuret, P., ... Kaidomar, M. (2004, November). Effects of systematic prone positioning in hypoxemic acute

respiratory failure: A randomized controlled trial. *The Journal of the American Medical Association, 292*, 2379-2387. http://dx.doi.org/10.1001/jama.292.19.2379

Guerin, C., Reignier, J., Richard, J., Beuret, P., Gacouin, A., Boulain, T., ... Ayzac, L. (2013, June 6). Prone positioning in severe acute respiratory distress syndrome. *The New England Journal of Medicine, 368,* 2159-2168. http://dx.doi.org/10.1056/NEJMoa1214103

Guyatt, G. H., Oxman, A. D., Vist, G. E., Kunz, R., Falck-Ytter, Y., Alonso-Ceollo, P., & Schunemann, H. J. (2008, April). Rating quality of evidence and strength of recommendations: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *British Medical Journal, 336*, 924-926. http://dx.doi.org/10.1136/bmj.39489.470347.AD

Guyatt, G., Oxman, A. D., Akl, E. A., Kunz, R., Vist, G., Brozek, J., ... Schunemann, H. J. (2011). GRADE guidelines: 1. Introduction- GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology, 64,* 383-394. http://dx.doi.org/10.1016/j.jclinepi.2010.04.026

Hall, M. J., Williams, S. N., DeFrances, C. J., & Golosinskiy, A. (2011). *Inpatient care for septicemia or sepsis: A challenge for patients and hospitals* [NCHS Data Brief]. Retrieved from Centers for Disease Control and Prevention: http://www.cdc.gov/nchs/data/databriefs/db62.pdf

Hauck, K., & Zhao, X. (2011, December). How dangerous is a day in the hospital? A model of adverse events and length of stay for medical inpatients. *Medical Care*, *49*, 1068-1075. http://dx.doi.org/10.1097/MLR.0b013e31822efb09

Herridge, M. S., Cheung, A. M., Tansey, C. M., Matte-Martyn, A., Diaz-Granados, N., Al-Saidi, F., ... Slutsky, A. S. (2003). One-year outcomes in survivors of the acute respiratory distress syndrome. *New England Journal of Medicine*, *348*, 683-893. http://dx.doi.org/10.1056/NEJMoa022450

Hess, D. R., & Thompson, B. T. (2005). Ventilatory strategies in patients with sepsis and respiratory failure. *Current Infectious Disease Reports*, *7*, 342-348. Retrieved from http://download.springer.com/static/pdf/468/art%253A10.1007%252Fs11908-005-0007-z.pdf?auth66=1385592566_a05614a2593de943df0917d1e01bd653&ext=.pdf

Hodgson, C., Carteaux, G., Tuxen, D. V., Davies, A. R., Pellegrino, V., Capellier, G., ... Nichol, A. (2013). Hypoxaemic rescue therapies in acute respiratory distress syndrome: Why, when, what and which one? *Injury: International Journal of the Care of the Injured*, *44*, 1700-1709. http://dx.doi.org/10.1016/j.injury.2012.11.017

James, B. C., & Savitz, L. A. (2011, June). How Intermountain trimmed health care costs through robust quality improvement efforts. *Health Affairs*, *30*, 1185-1191. http://dx.doi.org/10.1377/hlthaff.2011.0358

Kopterides, P., Siempos, I. I., & Armaganidis, A. (2009). Prone positioning in hypoxemic respiratory failure: Meta-analysis of randomized controlled trials. *Journal of Critical Care, 24*, 89-100. http://dx.doi.org/10.1016/j.jcrc.2007.12.014

LeBlanc, P. M., Schaufeli, W. B., Salanova, M., Llorens, S., & Nap, R. E. (2010, February). Efficacy beliefs predict collaborative practice among intensive care unit nurses. *Journal of Advanced Nursing*, *66*, 583-594. http://dx.doi.org/10.1111/j.1365-2648.2009.05229.x

Ley, B., Collard, H. R., & King, T. E. (2011). Clinical course and prediction of survival in idiopathic pulmonary fibrosis. *American Journal of Respiratory and Critical Care Medicine*, *183*, 431-440. http://dx.doi.org/ 10.1164/rccm.201006-0894CI

Mancebo, J., Fernandez, R., Blanch, L., Rialp, G., Gordo, F., Ferrer, M., ... Albert, R. K. (2006, June). A multicenter trial of prolonged prone ventilation in sever acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*, *173*, 1233-1239. http://dx.doi.org/ 10.1164/rccm.200503-353OC

McCartney, R., Saha, S., Rees, J., Lawy, T., & Mosaheb, R. (2013). Inhaled nitric oxide: A review of the action, current literature, and an analysis of its use in the NHS today. *Journal of the Intesive Care Society*, *14*, 231-234. Retrieved from http://journal.ics.ac.uk/pdf/1403231.pdf

McClellan, M. B., McGinnis, J. M., Nabel, E. G., & Olsen, L. M. (2007). *Evidence-based medicine and the changing nature of health care: Meeting summary*. Washington D.C.: The National Academies Press.

Morrell, N. (2010). Prone positioning in patients with acute respiratory distress syndrome. *Nursing Standard*, *24*, 42-45. Retrieved from http://rcnpublishing.com/doi/pdfplus/10.7748/ns2010.01.24.21.42.c7488

National Institute of Health. (2007). Acute respiratory distress syndrome (ARDS): What is ARDS? Retrieved from http://www.nhlbi.nih.gov/health/health-topics/topics/ards/

National Institute of Health. (2011). What is respiratory failure? Retrieved from http://www.nhlbi.nih.gov/health/health-topics/topics/rf/

Pelosi, P., Brazzi, L., & Gattinoni, L. (*20*02, October). Prone position in acute respiratory distress syndrome. *European Respiratory Journal*, 20, 1017-1028. http://dx.doi.org/10.1183/09031936.02.00401702

Petersson, J., Ax, M., Frey, J., Sanchez-Crespo, A., Lindahl, S. G., & Mure, M. (2010). Positive end-expiratory pressure redistributes regional blood flow and ventilation differently in supine and prone humans. *Anesthesiology, 113*, 1361-1369. http://dx.doi.org/10.1097/ALN.0b013e3181fcec4f

Phua, J., Badia, J. R., Adhikari, N. K., Friedrich, J. O., Fowler, R. A., Singh, J. M., ... Ferguson, N. D. (2009). Has mortality from acute respiratory distress syndrome decreased over time? A systematic review. *American Journal of Respiratory and Critical Care Medicine, 179,* 220-227. http://dx.doi.org/10.1164/rccm.200805-722OC

Piehl, M. A., & Brown, R. S. (1976). Use of extreme position changes in acute respiratory failure. *Critical Care Medicine, 4*, 13-14.

Plichta, S. B., & Kelvin, E. (2013). *Statistical methods for health care research* (6th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Polit, D. F., & Beck, C. T. (2012). *Nursing research: Generating and assessing evidence for nursing practice* (9th ed.). Philadelphia, PA: Lippincott Williams and Wilkins.

Ranieri, V. M., Rubenfeld, G. D., & Thompson, B. T. (2013). Defining ARDS: Do we need a mandatory waiting period? *Intensive Care Medicine, 39,* 775-778. http://dx.doi.org/10.1007/s00134-013-2834-y

Robak, O., Lakatos, P. K., Bojic, A., Hermann, A., Laczika, K. F., Chiari, A.,...Locker, G. J. (2014). Influence of different oxygenator types on changing frequency, infection incidence, and mortality in ARDS patients on veno-venous ECMO. *Journal of Artificial Organs, 37,* 748-752. http://dx.doi.org/10.5301/ijao.5000360

Rubenfeld, G. D., Caldwell, E., Peabody, E., Weaver, J., Martin, D. P., Neff, M., ... Hudson, L. D. (2005, October). Incidence and outcomes of acute lung injury. *The New England Journal of Medicine, 353,* 1685-1693. http://dx.doi.org/10.1056/NEJMoa050333

Sharma, S. (2009, December). Acute respiratory distress syndrome. *Clincal Evidence, 11*(1511), 1-18. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217743/

Sigma Theta Tau International. (2005). Evidence-based nursing position statement. Retrieved from http://www.nursingsociety.org/aboutus/PositionPapers/Pages/EBN_positionpaper.aspx

Stapleton, R., Wang, B., Hudson, L., Rubenfeld, G., Caldwell, E., & Steinberg, K. (2005). Causes and timing of death in patients with ARDS. *Chest, 128*, 525-532.

Straus, S. E., Glasziou, P., Richardson, W. S., & Haynes, R. B. (2011). *Evidence-based medicine: How to practice and teach it* (4th ed.). Philadelphia, PA: Elsevier.

Sud, S., Friedrich, J. O., Taccone, P., Polli, F., Adhikari, N. K., Latini, R., ... Gattinoni, L. (2010, April). Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: Systematic review and meta-analysis. *Intensive Care Medicine*, *36*, 585-599. http://dx.doi.org/10.1007/s00134-009-1748-1

Sud, S., Sud, M., Friedrich, J. O., & Adhikari, N. K. (2008, April). Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxemic respiratory failure: A systemic review and meta-analysis. *Canadian Medical Association Journal*, *178*, 1158-1161. http://dx.doi.org/10.1503/cmaj.071802

Taccone, P., Pesenti, A., Latini, R., Polli, F., Vagginelli, F., Mieto, C., ... Gattinoni, L. (2009, November). . *Prone positioning in patients with moderate and severe acute respiratory distress syndrome: A randomized controlled trial*, *302*, 1977-1984. http://dx.doi.org/10.1001/jama.2009.1614

Taylor, R. W., Zimmerman, J. L., Dellinger, R. P., Straube, R. C., Criner, G. J., Davis, K.,...Small, R. J. (2004, April 7). Low-dose inhaled nitric oxide in patients with acute lung injury. *Journal of American Medical Association, 291*, 1603-1609. http://dx.doi.org/10.1001/jama.291.13.1603

The ARDS Definition Task Force. (2012, June 20). Acute respiratory distress syndrome: The berlin definition. *The Journal of the American Medical Association, 307,* 2526-2533. http://dx.doi.org/10.1001/jama.2012.5669

Tiruvoipati, R., Bangash, M., Manktelow, B., & Peek, G. J. (2008). Efficacy of prone ventilation in adult patients with acute respiratory failure: A meta-analysis. *Journal of Critical Care, 23,* 101-110. http://dx.doi.org/10.1016/j.jcrc.2007.09.003

Titler, M. G., Kleiber, C., Steelman, V. J., Rakel, B. A., Budreau, G., Buckwalter, K. C., ... Goode, C. J. (2001). The Iowa model of evidence based practice to promote quality care. *Critical care nursing clinics of North America, 13,* 497-509.

United States Government. (1996). *Health insurance portability and accountability act of 1996* (Report No. 104-736). Washington, DC: Government Printing Office.

Valenza, F., Guglielmi, M., Maffioletti, M., Tedesco, C., Maccagni, P., Fossali, T., ... Gattinoni, L. (2005, February). Prone position delays the progression of ventilator-induced lung injury in rats: Does lung strain distribution play a role? *Critical Care Medicine, 33,* 361-367. http://dx.doi.org/10.1097/01.CCM.0000150660.45376.7C

Villar, J., Blanco, J., Anon, J. M., Santos-Bouza, A., Blanch, L., Ambros, A., ... Kacmarek, R. M. (2011, December). The ALIEN study: Incidence and outcome of acute respiratory distress syndrome in the era of lung protective ventilation. *Intensive Care Medicine, 37,* 1932-1941. http://dx.doi.org/10.1007/s00134-011-2380-4

Vincent, J. L., Moreno, R., Takala, J., Willatts, S., De Mendonca, A., Bruining, H.,...Thijs, L. G. (1996, July). The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European Society of Intensive Care Medicine. *Intensive Care Medicine*, *22*, 707-710.

Voggenreiter, G., Aufmkolk, M., Stilletto, R. J., Baacke, M. G., Waydhas, C., Ose, C., ... Nast-Kolb, D. (2005). Prone positioning improves oxygenation in post-traumatic lung injury- A prospective randomized trial. *The Journal of Trauma*, *59*, 333-341. http://dx.doi.org/10.1097/01.ta.0000179952.95921.49

Ward, N. S., Afessa, B., Kleinpell, R., Tisherman, S., Ries, M., Howell, M., ... Kahn, J. (2013, February). Intensivist/patient ratios in closed ICUs: A statement from the Society of *Critical Care Medicine* Taskforce on ICU staffing. Critical Care Medicine, *41*, 638-645. http://dx.doi.org/10.1097/CCM.0b013e3182741478

Ware, L. B. (2006). Pathophysiology of acute lung injury and the acute respiratory distress syndrome. *Seminars in Respiratory and Critical Care Medicine*, *27*, 337-349. http://dx.doi.org/10.1055/s-2006-948288

Zambon, M., & Vincent, J. L. (2008, May). Mortality rates for patients with acute lung injury/ARDS have decreased over time. *Chest*, *133*, 1120-1127. http://dx.doi.org/10.1378/chest.07-2134