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# Complications of Prone Positioning During Extracorporeal Membrane Oxygenation for Respiratory Failure: A Systematic Review

Rachel E Culbreth MPH RRT and Lynda T Goodfellow EdD RRT AE-C FAARC

**BACKGROUND:** Extracorporeal membrane oxygenation (ECMO) is often used in patients with severe respiratory failure to improve oxygenation and survival. ECMO gives the lungs an opportunity to rest and recover. The addition of prone positioning therapy used concurrently with ECMO can further aid in optimizing alveolar recruitment and reducing ventilator-induced lung injury, ultimately resulting in fewer ICU admission days and improved overall survival. The objective of this review is to perform a systematic analysis of the complications reported with prone positioning and ECMO in the adult population and to briefly report on the patient outcomes in the studies. **METHODS:** PubMed, MEDLINE, Cochrane Library, and CINAHL were searched from January 1, 1960 to September 14, 2014. Studies were included if they examined both extracorporeal membrane oxygenation and prone positioning simultaneously for the treatment of respiratory failure in the adult population. **RESULTS:** Seven studies fit the study inclusion criteria (1 prospective cohort study, 3 retrospective cohort studies, and 3 case series). All of the studies in this review reported no occurrence of ECMO cannula dislodgment, and 2 studies reported cannula site bleeding. Chest tube dislodgment and airway dislodgment did not occur in any of the studies included. Bleeding from the chest tube site was reported in 13.5% of prone positioning maneuvers in 1 study, and the rest of the studies reported no evidence of chest tube site bleeding. Of the 2 studies that reported hemodynamic instability during the prone positioning maneuvers, very few adverse hemodynamic episodes were reported. The authors who reported adverse effects stated that the episodes were quickly and successfully reversible. **CONCLUSIONS:** This review highlights the limited complications documented during prone positioning and ECMO. More studies are needed to assess the clinical efficacy of the addition of prone positioning therapy to ECMO for patients in severe respiratory failure. *Key words:* extracorporeal membrane oxygenation; prone position; respiratory insufficiency; acute lung injury; respiratory distress syndrome; adult; anoxia. [Respir Care 2016;61(2):249–254. © 2016 Daedalus Enterprises]

## Introduction

Respiratory failure leading to acute lung injury and ARDS occasionally requires a combination of interventions to improve oxygenation and ultimately survival for the patient.<sup>1</sup> Extracorporeal membrane oxygenation (ECMO) may be offered to provide the lungs an opportunity

to rest and recover.<sup>2</sup> Since the first trial of ECMO in the 1960s, this life support mechanism has transitioned over the years from primarily being used in neonates with cardiac diseases and irregularities to use in adults with a variety of life-threatening conditions, including ARDS. Venovenous ECMO is primarily used in patients with respiratory failure, where a large-bore cannula is typically inserted into the right internal jugular vein, providing a blood infusion pathway, and a large-bore cannula inserted into the femoral vein provides the drainage pathway. The blood is filtered through a membrane oxygenator, providing oxygen-rich blood to be infused into the body. Patients treated with ECMO are typically on the device anywhere between several days to weeks, depending on the disease process and how early the intervention was implemented.

The addition of prone positioning therapy concurrently with ECMO can aid in optimizing alveolar recruitment

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and reducing ventilator-induced lung injury, therefore hopefully reducing ICU admission days and improving overall survival.<sup>1-3</sup> The Guidelines for Adult Respiratory Failure from the Extracorporeal Life Support Organization<sup>4</sup> recommend the consideration of adding prone positioning therapy to patients receiving ECMO if there is posterior consolidation of the lung fields with some lung fields open anteriorly. The guidelines recommend exercising caution to prevent the dislodgment of the ECMO cannulas.<sup>4</sup> Adding prone positioning therapy can also help reduce the risk of memory and other cognitive impairments associated with hypoxemia.<sup>2,5</sup> However, severe complications can potentially result from prone positioning ECMO patients.<sup>2,3,6-11</sup> Prone positioning alone can pose serious risks. Among a study examining prone positioning in subjects without ECMO, a high incidence, 10.7%, of unintended extubations was reported.<sup>12</sup> In addition to unplanned extubations, complications from prone positioning alone include accidental removal of lines, kinks in various tubing, and potential injuries to health-care workers. However, the overwhelming literature supports prone positioning as a treatment option for patients in severe respiratory failure.<sup>13</sup> To reduce the risks of potential complications, trained critical care staff and strict protocol implementation are recommended.<sup>13</sup>

ECMO alone can result in several serious complications. The most common complication of ECMO is bleeding, commonly due to anticoagulation therapy.<sup>4</sup> Other complications can include cannula site infection, thrombocytopenia, and heparin-induced thrombotic thrombocytopenia. Severe neurological injuries can occur as a complication of ECMO, including subarachnoid hemorrhage, encephalopathy, and brain death.<sup>14</sup>

The aim of our review is to perform a systematic analysis of the complications that have been reported with prone positioning and ECMO in the adult population with respiratory failure and to briefly report on the subject outcomes in the studies. The purpose of this review is to provide clinicians with an overview of documented and potential complications from using prone positioning and ECMO to assess the feasibility of adding prone positioning therapy to patients receiving ECMO.

## Methods

### Search Strategy

Databases searched included PubMed, MEDLINE, Cochrane Library, and CINAHL. The terms “prone position” AND “extracorporeal membrane oxygenation” were used as well as “ECMO” AND “respiratory failure.” Alternate word searches were performed for prone positioning, such as “kinetic therapy” and “positioning therapy.” The databases were searched from January 1960 to September 2014.

## QUICK LOOK

### Current knowledge

ARDS is characterized by impaired oxygenation and reduced lung compliance due to dependent atelectasis. The standard of care includes tidal volume normalized to predicted body weight and positive end expiratory pressure to recruit collapsed alveoli. Mortality remains 30–40% despite treatment, and a number of adjunctive therapies are implemented in the face of refractory hypoxemia.

### What this paper contributes to our knowledge

Both prone positioning and extracorporeal membrane oxygenation have been successful in treating refractory hypoxemia in ARDS. Combining these therapies carries the potential risk of cannula dislodgement and bleeding complications. A review of a small number of studies suggests that these therapies can be used in tandem without additional morbidity.

The reference list for each article was scanned for articles that might have been missed.

### Study Inclusion Criteria

Studies were included if they examined both ECMO and prone positioning simultaneously for the treatment of respiratory failure. Subjects included in the systematic analysis were adults and older adolescents within an age range of 15–75 y. Studies performed on neonates and pediatrics were excluded in the systematic review. Case studies (consisting of 1 patient) and editorials were excluded. Studies that were not translated into English were not included due to cost and time restraints. Studies were excluded if the subject was undergoing treatment for another disease process that did not include respiratory failure (eg, cardiac failure). Studies examining multiple interventions and adjuncts for respiratory failure were excluded. The primary interventions were required to be prone positioning and ECMO. Overall survival was calculated, and chi-square tests were performed to analyze the difference between the national survival percentage<sup>4</sup> and the survival percentage in this review.

## Results

Using specified search terms, 71 articles from PubMed, 10 articles from MEDLINE, 4 articles from CINAHL, and 0 articles from Cochrane library were found. A total of 7 articles met the study inclusion criteria (3 retrospective cohort studies, 1 prospective cohort study, and 3 case series) (Table 1). The case series were included due to the

Table 1. Complications With Concurrent Use of Prone Positioning and Extracorporeal Membrane Oxygenation

First Author	Year	Sample Size	Study Type	ECMO Type/Equipment	ECMO Cannulas	Prone Positioning (Manual vs Mechanical)	Complications Reported Related to Prone Positioning, n (%)*
Goettler <sup>7</sup>	2002	Total N = 52, ECMO/prone positioning n = 4	Retrospective Cohort	VV ECMO, equipment unspecified	Multisite large bore cannulas	Manual	No complications reported: cannula dislodgment
Litmathe <sup>6</sup>	2011	N = 2	Case Series	VV ECMO, equipment unspecified	Single sites cannulas	Manual	No complications reported
Oterspoor <sup>3</sup>	2012	N = 2	Case Series	VV ECMO, centrifugal pump system (Maquet Permanent Life Support System) with Rotaflo centrifugal pump	Single sites, 23 French cannula in right femoral vein and 17 French cannula in right internal jugular vein, heparin coated cannulas	Unspecified	Bleeding cannula site = 50% (1 patient experienced due to gradual dislodgment, replaced with no further complications)
Kipping <sup>2</sup>	2013	N = 12	Retrospective Cohort	VV ECMO, occlusive pump system	Multisite, (2 cannulas in femoral veins and 1 in right internal jugular vein), heparin coated cannulas	Manual	Of 74 total prone positions for 12 subjects: bleeding tracheal tube site = 10 (13.5%); bleeding cannula site = 11 (14.9%); bleeding central venous catheter = 8 (10.8%); bleeding chest tube = 10 (13.5%); drop in S <sub>PO2</sub> ≥2% = 10 (13.5%); acute pulmonary embolism (requiring resuscitation) = 1 (1.4%); tracheal tube obstruction (requiring replacement of tracheal tube) = 1 (1.4%); systolic blood pressure <20% from baseline during prone position = 7 (9.5%); short bradycardia (<60 beats/min) or drop in heart rate of more than 20% = 3 (4%)
Masuda <sup>9</sup>	2014	N = 5	Case Series	VV ECMO, centrifugal pump system (Medtronic Bio-Console, Gyro-Pump)	Single sites, 19 French catheter right femoral vein, 15 French catheter in right jugular vein	Manual	No complications reported: bleeding cannula site, cannula dislodgment, cannula obstruction, central venous catheter dislodgment, bleeding/dislodgment tracheal tube, cutaneous pressure sores
Guervilly <sup>10</sup>	2014	N = 15	Prospective Cohort	VV ECMO, centrifugal pump system (Bio-Console 560; Medtronic Perfusion Systems)	Single sites > 20 French catheters	Unspecified	Pneumothorax = 1 (6.7%) No complications reported: bleeding cannula site, no significant hemodynamic variations, cannula dislodgment, central venous catheter dislodgment, bleeding/dislodgment tracheal tube, corneal abrasion
Kredel <sup>11</sup>	2014	N = 9	Retrospective Cohort	VV ECMO using a centrifugal pump-driven ECMO system (Quadrox PLS set, ROTAFLOW console and drive unit)	Single sites, 19–23 French cannulas, heparin coated cannulas	Continuous lateral rotation therapy	Oedemata (edema) = 6 (66.7%); entrance of air into ECMO circuit = 1 (11.1%); centrifugal pump failure = 1 (11.1%) No complications reported: cannula dislodgment, catheter dislodgment, tubing dislocation, cutaneous pressure sores, tracheal tube dislodgment

\* Percentages indicate the percentage of patients who experienced complications out of the total number of patients within each study.  
ECMO = extracorporeal membrane oxygenation  
VV = veno-venous

study sample consisting of >1 patient. Complications resulting from prone positioning during ECMO therapy were assessed in all included studies. A total of 49 subjects from 7 articles were included in this review, and all subjects were receiving veno-venous ECMO. The majority of the subjects experienced no complications from concurrent ECMO and prone positioning therapy.<sup>2,3,6,7,9-11</sup> However, the most common complications included bleeding from the ECMO cannula site. One study reported 11 prone positioning maneuvers, of a total of 74 maneuvers among 12 subjects, resulted in bleeding from the cannula site.<sup>2</sup> In addition, Otterspoor et al<sup>3</sup> reported 1 subject who experienced bleeding from the cannula site; however, the majority of all subjects (94.3%) did not experience this complication. Other documented complications observed while subjects were receiving concurrent ECMO and prone positioning therapy included pneumothorax (2.0%),<sup>10</sup> edema (12.2%),<sup>11</sup> and entrance of air into the ECMO circuit (2.0%).<sup>11</sup>

### ECMO Cannula Complications

Dislodgment of ECMO cannulas has been recognized as potentially the most serious complication resulting from prone positioning during ECMO.<sup>8,9</sup> All of the studies included in this review reported no occurrence of ECMO cannula dislodgment.<sup>2,3,6,7,9-11</sup> Two of 7 studies indicated cannula site bleeding as a complication.<sup>2,3</sup> Bleeding from the ECMO cannula site was also noted in 11 episodes of prone positioning out of a total of 74 prone positions among 12 subjects in 1 study,<sup>2</sup> and bleeding from the cannula site was observed in 1 subject by Otterspoor et al.<sup>3</sup> Although cannula site bleeding was common among these studies, cannula site bleeding is a frequent occurrence of subjects receiving ECMO due to anticoagulation therapy.<sup>8</sup> Although common, this complication is not to be minimized or dismissed, because cannula site bleeding can pose many risks for patients receiving ECMO.<sup>3</sup> It is important to note that this complication cannot be completely attributed to the addition of prone positioning to ECMO.

### Central Venous and Arterial Catheter Complications

Only 1 study<sup>2</sup> reported catheter complications. No central venous or arterial catheters were reported dislodged among all studies.<sup>2,3,6,7,9-11</sup> In the study with one of the largest sample sizes, bleeding from the central catheter was noted in 10.8% of a total of 74 prone position maneuvers among 12 subjects.<sup>2</sup>

### Chest Tube Complications

None of the adult studies reported chest tube dislodgment in this review.<sup>2,3,6,7,9-11</sup> Kipping et al<sup>2</sup> reported bleed-

ing from the chest tube site in 13.5% of prone positioning maneuvers. The rest of the studies reported no chest tube site bleeding.<sup>3,6,7,9-11</sup>

### Airway Dislodgment and Obstruction

Airway dislodgment has been reported as a common complication in prone positioning patients,<sup>12</sup> but among the studies selected, no episodes of tracheal or endotracheal tube dislodgment was found.<sup>2,3,6,7,9-11</sup> Kipping et al<sup>2</sup> reported 1 incident of an endotracheal tube obstruction during the prone positioning maneuver, in which the subject was placed back in a supine position for an emergent bronchoscopy and change of endotracheal tube. Kipping et al<sup>2</sup> was the only study to report obstructions of airways; however, the authors rationalized that patients receiving ECMO were less at risk for severe hypoxemia compared with patients without ECMO. Therefore, airway obstruction or dislodgment would have less severe implications for subjects receiving ECMO compared with subjects not receiving ECMO.<sup>2</sup>

### Hemodynamic Instability During Positioning

Only 2 studies reported episodes of hemodynamic instability.<sup>2,10</sup> Guervilly et al<sup>10</sup> reported no significant hemodynamic variations during the prone positioning maneuvers. Bradycardia (<60 beats/min or drop in heart rate by 50%) was reported by Kipping et al<sup>2</sup> in 3 subjects during the prone positioning maneuver. A 20% decrease in systolic blood pressure was experienced in 7 of the 74 prone positioning maneuvers. The hemodynamic episodes were all quickly treated with success, and the overall rates of the episodes were considered low by the authors.<sup>2</sup>

Kipping et al<sup>2</sup> also reported 1 subject who experienced a pulmonary embolism during the prone positioning maneuver requiring immediate resuscitation; however, the authors did not consider this complication attributable to prone positioning. Patients receiving ECMO are required to be repositioned frequently, and the pulmonary embolism would have probably occurred during routine positioning as well.<sup>2</sup>

Several studies have reported hemodynamic instability during prone positioning without ECMO<sup>12,15</sup>; however, 1 randomized control trial reported no difference in bradycardia and hypotension episodes between subjects receiving prone positioning and subjects not receiving prone positioning.<sup>1</sup>

### Miscellaneous Non-Life-Threatening Complications

Cutaneous pressure sores are considered a potential complication of prone positioning and/or ECMO. None of the studies in this review reported cutaneous pressure sores.<sup>2,3,6,7,9-11</sup>

Facial edema was reported in 66.7% of subjects in 1 study but was reversible.<sup>11</sup> Also, this study reported complications related to ECMO (entrance of air in the circuit and pump failure), but these were deemed unrelated to the prone positioning.<sup>11</sup>

### Prone Positioning Maneuver Type: Mechanical Versus Manual

Only 1 study<sup>11</sup> reported the use of automated, rotating beds to perform prone positioning of subjects. Among the remainder of the studies that reported on the type of prone positioning maneuver used, all studies utilized manual prone positioning techniques.<sup>2,6,7,9</sup>

### ECMO Equipment and Cannula Site

Multiple sites for cannulation were used in several studies. Goettler et al<sup>7</sup> suggest that the location of high-flow catheters does not affect the number of complications or malfunctions. All cannulas were heparin-coated, or, if the cannulas were not specified as heparin-coated, subjects were placed on heparin therapy while receiving ECMO.<sup>2,3,6,7,9-11</sup> Among the studies that reported the type of ECMO equipment used, all studies reported using either a centrifugal pump system<sup>3,9-11</sup> or an occlusive pump system.<sup>2</sup>

Only 1 of the studies<sup>3</sup> reported on the amount of circuit changes required while patients were receiving ECMO. Otterspoor et al<sup>3</sup> reported that 1 subject required a total of 4 circuit changes over a 45-d period receiving ECMO.

### Outcomes: Oxygenation and Survival

Four studies in this review reported oxygenation measures before and after prone positioning maneuvers.<sup>2,9-11</sup> Of these studies, 3 found a significant difference between the  $P_{aO_2}/F_{IO_2}$  ratio before and after prone positioning.<sup>2,9,10</sup> Kipping et al<sup>2</sup> reported that 58% of subjects experienced an improvement in  $P_{aO_2}/F_{IO_2}$  ratio of >20% post-prone positioning compared with pre-prone positioning. A significant increase in  $P_{aO_2}/F_{IO_2}$  ratio was found post-prone positioning compared with pre-prone positioning using the non-parametric Wilcoxon test for pairwise comparisons in the second prone positioning maneuver ( $P = .009$ ).<sup>2</sup> Guervilly et al<sup>10</sup> found significant improvements in  $P_{aO_2}/F_{IO_2}$  ratios after 12 h of prone positioning ( $P = .007$ ). A significant increase in  $P_{aO_2}/F_{IO_2}$  ratio was also found by Masuda et al<sup>9</sup> with a prior median  $P_{aO_2}/F_{IO_2}$  ratio of  $143 \pm 38.1$  to a post-median  $P_{aO_2}/F_{IO_2}$  ratio of  $235.5 \pm 87.1$  ( $P < .05$ ).

Survival was reported in all studies.<sup>2,3,6,7,9-11</sup> Among these studies, 30 of 49 subjects (61.2%) survived. One

subject, 6 y in age, was excluded from the survival analysis due to not meeting the age criterion of 15–75 y.<sup>9</sup> The overall survival proportion for adults receiving ECMO for respiratory failure is 65% ( $n = 7,008$ ).<sup>4</sup> The national survival proportion is not only higher than the survival from our review (65% vs 61.2%, respectively), but there is no statistical significance between survival proportions ( $P = .54$ ). The overall impact of prone positioning and ECMO on long-term oxygenation as well as survival is limited in the literature.<sup>2</sup>

### Discussion

This review highlights the limited number of complications experienced when implementing prone positioning and ECMO concurrently. The survival percentage among the subjects included in this study is lower than the national survival<sup>4</sup> percentage; however, this could be attributed to the severity of the conditions of subjects who are receiving both prone positioning and ECMO compared with ECMO alone.

### Limitations

Several limitations are noted in this review. First, there is a lack of randomized control trials and prospective studies analyzing the concurrent use of ECMO and prone positioning. The small sample size of the total number of studies also limits the statistical power, which could be generated with larger sample sizes to determine the efficacy of adding prone positioning to ECMO in terms of survival. Only 1 study<sup>10</sup> was a prospective, 2-y cohort study. Three of the studies were retrospective cohort studies, whereas the remaining 3 were case series. Due to the nature of retrospective chart reviews, some complications could have been missed, therefore underestimating the complications documented.<sup>7,11</sup> A multi-center, randomized control trial would be beneficial in evaluating the intervention of prone positioning for adult patients receiving ECMO for respiratory failure. Due to the retrospective nature of the studies, adequate  $P_{aO_2}/F_{IO_2}$  ratio comparisons before and after prone positioning are difficult due to other factors that could influence  $P_{aO_2}/F_{IO_2}$  ratios, including pump flow rate and ventilator settings. Keeping these factors constant would allow adequate comparison of adding prone positioning to ECMO patients compared with patients receiving ECMO alone.

Second, some of the studies lacked documentation on the equipment they used for ECMO and prone positioning (manual vs automated). This leads to inadequate conclusions regarding which equipment would best be utilized during prone positioning. Only 1 study<sup>3</sup> reported on the number of ECMO circuit changes that were performed. Documentation of the number of circuit changes would

help in determining the effects of prone positioning on the circuit longevity.

Third, 6 of the 7 studies utilized manual prone positioning techniques.<sup>2,3,6,7,9,10</sup> More studies including prone positioning where automated beds were used would be beneficial in assessing complications.

Last, analyzing overall survival and days spent in the critical care units would be more beneficial to clinicians' decisions than  $P_{aO_2}/F_{IO_2}$  ratios alone. Future studies should include survival analyses as well as the total number of days spent in the critical care unit to determine the overall efficacy of prone positioning and ECMO for respiratory failure.

### Recommendations

All of the studies in this review documented a sufficient number of hospital personnel to assist in the prone positioning maneuver.<sup>2,3,6,7,9-11</sup> The authors recommended highly trained personnel to monitor all catheters and lines as well as vital signs to reduce the risk of appliance dislodgment. One study specifically recommended experienced personnel to be responsible for observing the airway (respiratory therapist) and ECMO cannula position (ECMO specialist) to reduce complications caused by these devices.<sup>8</sup> Automated, rotating beds have emerged in critical care units, and the use of these beds results in a reduced burden on staff.<sup>16</sup> Taccone et al<sup>12</sup> reported fewer tube and catheter dislodgments with the use of automated, rotating beds. More studies are needed to assess the complications among automated, rotating beds versus manual prone positioning maneuvers to adequately inform clinicians. Clinicians should weigh the benefits of prone positioning against the complications noted in this study as well as anticipated complications. The awareness of potential complications and documented complications can lead to safety improvement of the addition of prone positioning therapy to ECMO.

### Conclusions

This review highlights the limited number of complications documented during the addition of prone positioning therapy to ECMO. More studies are needed to assess the clinical efficacy of the addition of prone positioning to adult patients receiving ECMO for respiratory failure.<sup>1</sup> Prospective and randomized control trials are necessary to assess the long-term impact of prone positioning and ECMO on survival as well as the effects on ICU stay and complications. Due to the limited sample size of studies included in this review, the current available literature is unable to fully answer the question of whether concurrent use of ECMO and prone positioning is completely safe. However, the studies included in this review have reported that concurrent use of prone positioning and ECMO is safe.<sup>2,3,7,9-11</sup> Thus, our review has presented the current

literature on the limited complications investigators have found when implementing both interventions simultaneously on adult subjects.<sup>2,3,6,7,9-11</sup>

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