Centre for Clinical Effectiveness
Enhancing patient outcomes through clinical application of the best available evidence

EVIDENCE CENTRE
EVIDENCE REPORT
Series 2002: Intervention

Prone positioning of patients with Acute Respiratory Distress Syndrome (ARDS)

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Southern Health

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SUMMARY STATEMENT:

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REQUEST:

Does prone positioning in ARDS patients in ICU improve patient outcome (lung volume, oxygenation, etc)?

REQUESTED BY:

Catherine Stockton, Physiotherapist, Physiotherapy Department, Monash Medical Centre, Clayton.

SUMMARY OF FINDINGS:

- Five studies were retrieved that met the inclusion and exclusion criteria
- Generally favorable results for oxygenation were seen for prone positioning compared to supine positioning
- Responders to prone positioning are difficult to predict
- Less favourable results for survival after prone positioning
- There were distinct problems with the methodology of the studies cited in the systematic reviews
    - Wide variations in the patient populations, care, method and duration of prone positioning
    - Very small sample sizes which limits generalisation

METHODOLOGY

Search Strategy

The Centre for Clinical Effectiveness defined the 'best available evidence' as that research we can identify that is least susceptible to bias. We determine this according to predefined NHMRC criteria (see Appendix).

First we search for systematic reviews, evidence-based clinical practice guidelines, or health technology assessments, and randomized controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalisable, or have other methodologic difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While we cite observational and case series studies, and narrative reviews and consensus statements, in our reports we do not critically appraise them. Some studies can produce accurate results but they are generally too prone to bias to allow determination of their validity beyond their immediate setting.

Details of Evidence Request:

Patients	Patients with ARDS (or Acute Lung Injury (ALI)) in the ICU
Interventions	Prone positioning
Comparisons	Supine positioning
Outcomes	Oxygenation, mortality, complications

Search terms:

The following search terms were used to scour electronic databases:

Table 1. Search terms used in the retrieval of articles from electronic databases

Field of focus	Search term
Patient-related	Respiratory distress syndrome, adult; respiratory insufficiency; ARDS; lung injury
Diagnostic test-related	Prone position; posture; position$; prone

(see Appendix 2 for exact search strategy)

Resources Searched

We searched the following databases:

The Cochrane Library (CD-ROM) Issue 1, 2002

Medline (OVID) - 1966 to April Week 1 2002

CINAHL (OVID) - 1982 to February Week 4 2002

Current Contents (OVID) - 1993 Week 27 to 2002 Week 16

Premedline (OVID) - April 16, 2002

PubMed – National Library of Medicine – accessed April 17th 2002

Refinements, Searching & Reporting Constraints:

We included items of evidence that were available to us on April 17th 2002. We only included articles published since 1990, in English, and applied the following inclusion and exclusion criteria:

Inclusion Criteria

- Primary studies comparing prone positioning with supine positioning in the treatment of patients with ARDS
- All randomised controlled trials conducted on prone positioning

Exclusion Criteria

- Studies that were case series
- Prone positioning was used in conjunction with nitric oxide i.e. results from prone positioning alone cannot be determined
- Patients with significant co-morbidity (i.e. patients post-coronary bypass)
- Systematic reviews which include data published in more recently published systematic reviews

RESULTS:

The search strategy yielded a total of 72 pertinent articles, the abstracts of which were retrieved and reviewed. Sixty-seven studies were excluded (Table 2) following criteria previously described:

Table 2. Reasons for exclusion of studies identified in search

Reason	Number of studies
Letter / Narrative	24
Combined treatment	2
Guideline	1
<5 Cases	5
Patients post bypass	1
Systematic reviews before 2001	4
Case series included in published systematic review	22
Case series - other	8
Total	**67**

The 5 articles that met the inclusion and exclusion criteria consisted of two systematic reviews of non-randomised trials and three randomised controlled trials (Table 3). We are reasonably confident these studies represent the most important findings published to date.

Table 3. Study designs of included articles

Study Design	Number included
Systematic reviews or meta-analyses	2
Evidence-based clinical practice guidelines	0
Randomised controlled trials	3
Controlled trials, cohort or case-control analytic studies	0

EVIDENCE SUMMARIES

Evidence summaries are in the form of spreadsheets reproduced at the end of this report. Each spreadsheet contains the article citation, the study design with level of evidence available according to NHMRC guidelines (1998), patient description, scientific validity of the article, results, and pertinent remarks from the authors and Centre for Clinical Effectiveness reviewer.

Findings

Overall results

To date, a number of systematic reviews with differing numbers of case series have been conducted to examine the effect of prone positioning on ARDS or ALI patients. Randomised trials have only recently been commenced in this area.
One finding is consistent in all of the systematic reviews. That is, a significant improvement in oxygenation is seen during prone positioning in the ventilated patient with ARDS. The percentage of patients in the case series who responded by an improvement in oxygenation varied from 57% to 100%. However, the definition of response varied between these studies, as did the duration of prone positioning. This finding of an improvement is further supported by two randomised controlled trials that demonstrated an improvement in oxygenation in 73% (>10% PaO_2/FIO_2) and 80% (>20% PaO_2) of their patients. Predictors of response however have been shown to be inconsistent in the case series conducted so far.

Prone positioning has been demonstrated to be relatively safe and rarely worsens a patient's condition. Gattinoni et al (2001) found that there was no significant difference in the complication rate between the prone positioning group and the control group.

The importance of improving oxygenation is to improve the long-term outcome for the ARDS patient. Many of the case series included in the systematic reviews did not address the effect of prone positioning on mortality. In a randomised controlled trial Gattinoni et al (2001) found that the mortality rate did not differ significantly between the prone group and the supine group at the end of the 10-day study period, at discharge or at 6 months follow-up. A post-hoc analysis however showed that the 10-day mortality rate was almost half of the control group for patients with high severity scores, and/or lowed PaO_2/FIO_2 ratios and/or higher tidal volumes. This finding must be interpreted cautiously as the result may be due to the application of multiple tests.

Research Methodology

Systematic reviews of case series are fraught with methodological issues. Analysis of the study populations included in the systematic review is essential to assess the appropriateness of applying the results to a particular clinical setting. As the inclusion criteria differed across all of the studies the likelihood of selection bias is high. This will certainly limit the applicability of the results to other clinical settings. In addition, the small study sample sizes may not truly reflect the characteristics of all patients who have ARDS.

The reviews have included studies that involved patients of varying etiology of ARDS (pulmonary and extrapulmonary), with differing ventilation techniques and duration of ventilation, and prone positioning performed for varying lengths of time (from 15 minutes to 48 hours). The technique for prone positioning has also differed between studies, with some studies supporting the thorax and pelvis or using a mechanical bed to accomplish prone positioning. Patients across the studies have also differed in their stage of ARDS. This is an important factor as in late ARDS (7-10 days), remodeling of the lung architecture and progressive fibrosis may change the response to prone positioning (Johannigman 2000).

Therefore, pooled data from case series is difficult to evaluate due to the heterogeneous study populations, poorly defined inclusion criteria, and the differences in interventions mentioned

above. Generally, studies do not describe the confounding variables to the degree necessary to interpret the results fully.

Results from the randomised controlled trials to date should be used, as they are currently the highest level of evidence. Results from these trials are outlined in the following section of this report.

Focused appraisal

Results from the systematic reviews and randomised controlled trials are shown below:

Study	**Oxygenation, (PaO_2/FIO_2)**	**Responders**	**p**
Systematic Reviews			
Ward (2002) (26 studies)	11 studies showed improved oxygenation among all patients enrolled. The lowest overall increase in mean PaO_2/FIO_2 was 7, and the highest was 161 (average 76).	Response ranged from 57% to 100%. Viewed collectively and using the mixed definitions of response at least 75% had some improvement in oxygenation.	
Meade (2001) (14 studies)		In total, 69% of patients responded with an increase in PaO_2/FIO_2 by 20% or more.	
Randomised Controlled Trials			
Gattinoni (average of after 1 hr of prone positioning and at end of scheduled period)	125.3±48.8 (average change of 63.01±66.8)	In 73.2% of all procedures the ratio increased more than 10, with 69.9% observed during the 1st hour	p=0.02
Rialp (30 minutes prone positioning)	106±58 to 184±67	80% improved PaO_2 by 20%	p≤0.01
Hering (3 hours prone positioning)	194±66 to 269±68	Not reported	p<0.05

Overall, it appears that the majority of patients with ARDS respond favourably to being placed in the prone position with few complications observed. Although one trial has shown no effect on mortality with prone positioning, further randomised controlled trials are required to clarify this.

Future research

Until further randomised controlled trials are conducted the point that prone positioning should be initiated and for how long remain unanswered questions. Concise prone positioning protocols are certainly required. Further trials in more homogenous populations of patients should help elucidate the effect of prone positioning on oxygenation and mortality. Increased collaboration among centres and countries conducting studies of patients with ARDS will certainly be helpful and, indeed, will most likely be necessary to define the real efficacy of this approach.

ARTICLES CRITICALLY APPRAISED FOR THIS REPORT

Systematic Reviews of non-randomised trials

1. Ward, N. S. (2002). "Effects of prone position ventilation in ARDS. An evidence-based review of the literature." Critical Care Clinics 18(1): 35-44.

2. Meade, M. O. and M. S. Herridge (2001). "An evidence-based approach to acute respiratory distress syndrome." Respiratory Care 46(12): 1368-76; discussion 1376-9.

Randomised Controlled Trials

1. Gattinoni, L., G. Tognoni, et al. (2001). "Effect of prone positioning on the survival of patients with acute respiratory failure." New England Journal of Medicine 345(8): 568-73.

2. Hering, R., R. Vorwerk, et al. (2002). "Prone positioning, systemic hemodynamics, hepatic indocyanine green kinetics, and gastric intramucosal energy balance in patients with acute lung injury." Intensive Care Medicine 28(1): 53-58.

3. Rialp, G., A.J. Betbese, et al. (2001). "Short-term Effects of Inhaled Nitric Oxide and Prone Position in Pulmonary and Extrapulmonary Acute Respiratory Distress Syndrome." American Journal of Respiratory and Critical Care Medicine 164:243-249.

OTHER REFERENCES

1. Blanch, L., J. Mancebo, et al. (1997). "Short-term effects of prone position in critically ill patients with acute respiratory distress syndrome." Intensive Care Medicine 23(10): 1033-9.

2. Borelli, M., L. Lampati, et al. (2000). "Hemodynamics and gas exchange response to inhaled nitric oxide and prone positioning in acute respiratory distress syndrome patients." Critical Care Medicine 28(8): 2707-12.

3. Chatte, G., J. M. Sab, et al. (1997). "Prone position in mechanically ventilated patients with severe acute respiratory failure." American Journal of Respiratory & Critical Care Medicine 155(2): 473-8.

4. Dupont, H., H. Mentec, et al. (2000). "Short-term effect of inhaled nitric oxide and prone positioning on gas exchange in patients with severe acute respiratory distress syndrome." Critical Care Medicine 28(2): 304-8.

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6. Fridrich, P., P. Krafft, et al. (1996). "The effects of long-term prone positioning in patients with trauma-induced adult respiratory distress syndrome." Anesthesia & Analgesia 83(6): 1206-11.

7. Gattinoni, L., P. Pelosi, et al. (1991). "Body position changes redistribute lung computed-tomographic density in patients with acute respiratory failure." Anesthesiology 74(1): 15-23.

8. Germann, P., G. Poschl, et al. (1998). "Additive effect of nitric oxide inhalation on the oxygenation benefit of the prone position in the adult respiratory distress syndrome." Anesthesiology 89(6): 1401-6.

9. Gillart, T., J. E. Bazin, et al. (1998). "Combined nitric oxide inhalation, prone positioning and almitrine infusion improve oxygenation in severe ARDS." Canadian Journal of Anaesthesia 45(5 Pt 1): 402-9.

10. Guerin, C., M. Badet, et al. (1999). "Effects of prone position on alveolar recruitment and oxygenation in acute lung injury." Intensive Care Medicine 25(11): 1222-30.

11. Johannigman, J. A., K. Davis, Jr., et al. (2000). "Prone positioning for acute respiratory distress syndrome in the surgical intensive care unit: who, when, and how long?" Surgery 128(4): 708-16.

12. Johannigman, J. A., K. Davis, Jr., et al. (2001). "Prone positioning and inhaled nitric oxide: synergistic therapies for acute respiratory distress syndrome." Journal of Trauma Injury Infection & Critical Care 50(4): 589-96.

13. Jolliet, P., P. Bulpa, et al. (1998). "Effects of the prone position on gas exchange and hemodynamics in severe acute respiratory distress syndrome." Critical Care Medicine 26(12): 1977-85.

14. Jolliet, P., P. Bulpa, et al. (1997). "Additive beneficial effects of the prone position, nitric oxide, and almitrine bismesylate on gas exchange and oxygen transport in acute respiratory distress syndrome." Critical Care Medicine 25(5): 786-94.

15. Lim, C. M., E. K. Kim, et al. (2001). "Comparison of the response to the prone position between pulmonary and extrapulmonary acute respiratory distress syndrome." Intensive Care Medicine 27(3): 477-85.

16. Martinez, M., E. Diaz, et al. (1999). "Improvement in oxygenation by prone position and nitric oxide in patients with acute respiratory distress syndrome." Intensive Care Medicine 25(1): 29-36.

17. Mure, M., C. R. Martling, et al. (1997). "Dramatic effect on oxygenation in patients with severe acute lung insufficiency treated in the prone position." Critical Care Medicine 25(9): 1539-44.

18. Nakos, G., I. Tsangaris, et al. (2000). "Effect of the prone position on patients with hydrostatic pulmonary edema compared with patients with acute respiratory distress syndrome and pulmonary fibrosis." Am J Respir Crit Care Med 161(2 Pt 1): 360-8.

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20. Papazian, L., F. Bregeon, et al. (1998). "Respective and combined effects of prone position and inhaled nitric oxide in patients with acute respiratory distress syndrome." American Journal of Respiratory & Critical Care Medicine 157(2): 580-5.

21. Papazian, L., M. H. Paladini, et al. (2001). "Is a short trial of prone positioning sufficient to predict the improvement in oxygenation in patients with acute respiratory distress syndrome?" Intensive Care Medicine 27(6): 1044-9.

22. Pappert, D., R. Rossaint, et al. (1994). "Influence of positioning on ventilation-perfusion relationships in severe adult respiratory distress syndrome." Chest 106(5): 1511-6.

23. Pelosi, P., P. Caironi, et al. (2001). "Pathophysiology of prone positioning in the healthy lung and in ALI/ARDS." Minerva Anestesiologica 67(4): 238-47.

24. Pelosi, P., D. Tubiolo, et al. (1998). "Effects of the prone position on respiratory mechanics and gas exchange during acute lung injury." Am J Respir Crit Care Med 157(2): 387-93.

25. Servillo, G., E. Roupie, et al. (1997). "Effects of ventilation in ventral decubitus position on respiratory mechanics in adult respiratory distress syndrome." Intensive Care Med 23(12): 1219-24.

26. Stocker, R., T. Neff, et al. (1997). "Prone postioning and low-volume pressure-limited ventilation improve survival in patients with severe ARDS." Chest 111(4): 1008-17.

27. Venet, C., S. Guyomarc'h, et al. (2001). "The oxygenation variations related to prone positioning during mechanical ventilation: a clinical comparison between ARDS and non-ARDS hypoxemic patients." Intensive Care Medicine 27(8): 1352-9.

28. Voggenreiter, G., F. Neudeck, et al. (1999). "Intermittent prone positioning in the treatment of severe and moderate posttraumatic lung injury." Critical Care Medicine 27(11): 2375-82.

29. Vollman, K. M. and J. J. Bander (1996). "Improved oxygenation utilizing a prone positioner in patients with acute respiratory distress syndrome." Intensive Care Medicine 22(10): 1105-11.

30. Wenz, M., B. Hoffmann, et al. (2000). "Angiotensin II formation and endothelin clearance in ARDS patients in supine and prone positions." Intensive Care Med 26(3): 292-8.

Early systematic reviews

1. Balas, M. C. (2000). "Prone positioning of patients with acute respiratory distress syndrome: applying research to practice." Critical Care Nurse 20(1): 24-36.

2. Ball, C. (1999). "Use of the prone position in the management of acute respiratory distress syndrome." Intensive & Critical Care Nursing 15(4): 192-203.

3. Curley, M. A. (1999). "Prone positioning of patients with acute respiratory distress syndrome: a systematic review." American Journal of Critical Care 8(6): 397-405.

4. Wong, W.P. (1999). "Use of body positioning in the mechanically ventilated patient with acute respiratory failure: Application of Sackett's rules of evidence." Physiotherapy Theory and Practice 15(1): 25-41.

ABBREVIATIONS

ARDS	Acute Respiratory Distress Syndrome
ALI	Acute Lung Injury
PaO_2	Partial pressure of arterial oxygen
FIO_2	Inspired Oxygen Fraction

APPENDIX 1

Copyright

Disclaimer

The information in this report is a summary of that available and is primarily designed to give readers a starting point to consider currently available research evidence. Whilst appreciable care has been taken in the preparation of the materials included in this publication, the authors and Southern Health do not warrant the accuracy of this document and deny any representation, implied or expressed, concerning the efficacy, appropriateness or suitability of any treatment or product. In view of the possibility of human error or advances of medical knowledge the authors and Southern Health cannot and do not warrant that the information contained in these pages is in every aspect accurate or complete. Accordingly, they are not and will not be held responsible or liable for any errors of omissions that may be found in this publication. You are therefore encouraged to consult other sources in order to confirm the information contained in this publication and, in the event that medical treatment is required, to take professional expert advice from a legally qualified and appropriately experienced medical practitioner.

Levels of Evidence

As Defined By "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

Level I		Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials.
Level II		Evidence obtained from at least one randomised controlled trial.
Level III	-1	Evidence obtained from pseudo-randomised controlled trials (alternate allocation or some other method).
	-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.
	-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
Level IV		Evidence obtained from case series, either post-test or pretest/post-test.

APPENDIX 2

Search strategy

	Search terms for MEDLINE, CINAHL, EBM- Best Evidence, PREMEDLINE, Current Contents
1	Exp Respiratory Distress Syndrome, Adult/
2	ARDS.tw
3	*Respiratory Insufficiency/
4	Exp Prone Position/
5	Exp Posture/
6	Prone.tw
7	Position$.tw
8	Exp Patient Positioning/
9	or/1-3
10	or/4-8
11	9 and 10
12	Limit 11 to (human and English language and yr=1990-2002)

Evidence Summary Systematic Review Prone positioning of patients with Acute Respiratory Distress Syndrome	Study 1 N.S.Ward (2002). Effects of prone position ventilation in ARDS. Critical Care Clinics 18(1): 35-44.	Study 2 Meade MO and Herridge MS (2001). An Evidence-Based Approach to Acute Respiratory Distress Syndrome. Respiratory Care 46(12): 1368-1379.
STUDY DESIGN & NHMRC LEVELS OF EVIDENCE	III-2 Systematic Review of non-randomised studies and one randomised controlled trial	III-2 Systematic Review of non-randomised studies and one randomised controlled trial
DESCRIPTION: Patient (subjects), Interventions, Comparisons, Outcomes, Inclusion & Exclusion Criteria	**Patient (Subjects):** Adult patients with ARDS **Intervention:** Prone positioning **Comparisons:** Supine positioning **Outcomes:** Oxygenation, lung mechanics, hemodynamics, mortality, complications, predictors of response **Incl criteria:** Patients with respiratory failure receiving mechanical ventilation **Exclusion criteria:** Studies in which patients were placed in prone position for less than 10 minutes.	**Patient (Subjects):** Critically ill adult patients with ARDS or acute lung injury **Intervention:** Prone positioning **Comparisons:** Supine positioning **Outcomes:** Oxygenation, lung mechanics, hemodynamics, complications **Inclusion criteria:** All studies of long-term follow-up of adult survivors of ARDS **Exclusion criteria**: studies evaluating only long-term mortality, studies reporting <5 patients, and studies in languages other than English.
VALIDITY: Methodology, rigour, selection, analysis	**Focussed question:** To assess the effects of prone position ventilation on humans. **Search strategy:** MEDLINE search (no date reported) **Assessed validity:** No **Appropriate analysis of results:** Pooled data for oxygenation from 26 studies (25 were prospective, interventional trials with no controls, 1 was a randomised controlled trial). Other outcomes reported but not pooled.	**Focussed question:** To assess the effects of prone position ventilation on humans. **Search strategy:** MEDLINE search (1966-2000), CINAHL (1982-2000), Cochrane Database of Systematic Reviews. **Assessed validity:** Yes **Appropriate analysis of results:** "Pooled data quantitatively only when it seemed appropriate based on examination of the populations, interventions, and control interventions in the original studies, based on visual inspection of study results, and based on formal tests of heterogeneity among study results."
RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate	All studies showed some beneficial effect on oxygenation with prone position ventilation. Average increase in PO_2 was 41mmHg. Eleven studies showed improved oxygenation as the mean improvement in PaO_2/FIO_2 ratio among all patients enrolled. The lowest increase was 7, and the highest was 161. The average of these values was 76.	Fourteen case series were identified, including 260 ARDS patients, of which 69% responded with an acute improvement in oxygenation. The duration of effect differed across studies. **Complications:** Six studies looked at adverse effects, which were rare but included extubation, central line removal, central line

	Using the most liberal definition of response as any increase in oxygenation, response rates ranged from a low of 58% to a high of 100%. Viewed collectively, at least 460 of 613 (75%) patients had some improvement in oxygenation. **Complications:** No serious clinically relevant complications.	compression, supraventricular tachycardia, acute apical atelectasis, acute deterioration in oxygenation, and hip and shoulder contractures.
AUTHORS COMMENTS: Limitations, implications for practice and research	"Prone positioning is a safe procedure that rarely worsens a patient's respiratory status or causes other complications. There is evidence suggesting that prone positioning may be of most benefit in more severely ill patients."	"It is unreasonable to be dogmatic about the role of prone positioning in ARDS patients. We suggest that … clinicians consider systematically evaluating prone positioning strategies in the context of clinical practice".
OUR COMMENTS: Opportunity for bias, weakness and strength	**Potential for bias:** Systematic review of case series that differed in the method and frequency of turning, duration of prone positioning, number of people required for position changes, patient characteristics. No mention of confounding variables. **Weakness:** Pooling of data not appropriate.	**Potential for bias:** Systematic review of case series that differed in the method and frequency of turning, duration of prone positioning, number of people required for position changes, patient characteristics. No mention of confounding variables.

Evidence Summary **Intervention** Prone positioning of patients with Acute Respiratory Distress Syndrome	Study 3 Hering R, Vorwerk R, Wrigge H *et al* (2000). Prone positioning, systemic hemodynamics, hepatic indocyanine green kinetics, and gastric intramucosal energy balance in patients with acute lung injury. Intensive Care Medicine 28(1): 53-58.	Study 4 Gattinoni L, Tognoni G, Pelosi P *et al* (2001). Effect of Prone Positioning on the Survival of Patients with Acute Respiratory Failure. New England Journal of Medicine 345(8): 568-73.
STUDY DESIGN & NHMRC LEVELS OF EVIDENCE	Level II – Randomised Controlled Trial Factorial design – subjects acted as own controls	Level II – Randomised Controlled Trial
DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria	**Patients (subjects):** 12 mechanically ventilated, hemodynamically stable patients with acute lung injury. **Time from onset of ARDS:** Mean of 5 days after ventilation commenced. **Mean age:** 52±21 years **Intervention:** Positioning prone for 3 hours **Comparisons:** Positioning supine for 3 hours	**Patients (subjects):** 304 patients with acute lung injury or ARDS **Time from onset of ARDS:** Not stated **Mean age:** 59±17 years for prone, 57±16 years for supine **Intervention:** Prone positioning for 6 or more hours daily for ten days **Comparisons:** Supine positioning

	Outcomes: Systemic hemodynamics **Exclusion Criteria:** Unstable cardiovascular function, undergone liver transplantation, cerebral injury, unstable spinal fractures, patients treated for peritonitis with an open-abdomen technique.	**Outcomes:** Hemodynamics, survival **Inclusion Criteria:** Pulmonary artery occlusion pressure <18mmHg, PaO_2/FIO_2 ratio of 200 or less, radiographic evidence of bilateral pulmonary infiltrates. **Exclusion Criteria :** <16 years of age, evidence of cardiogenic pulmonary edema, cerebral edema, intracranial hypertension, clinical conditions that might contraindicate prone position.
VALIDITY: Methodology, rigour, selection	**Randomisation:** Yes, not specified **All patients accounted for:** Yes **Patients treated equally:** Yes **Similar groups:** 60-minute equilibrium between tests, all data collated.	**Randomisation:** Yes, based on a permutated-block algorithm **All patients accounted for:** Yes **Patients treated equally:** Twelve patients in supine group crossed over to the prone group, 91 missed periods of prone positioning in prone group.
RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate	Intra-abdominal pressure (IAP) increased from 10 ± 3 in the supine to 13 ± 4 mmHg in the prone position ($p<0.05$). Cardiac index increased from 3.8 ± 0.9 (supine) to 4.2 ± 0.6 l/m2 per minute (prone) ($p<0.05$). Mean arterial pressure from 75 ±10 (supine) to 81 ±11mmHg (prone) ($p<0.05$). PaO_2/FIO_2 increased from 194±66 (supine) to 269±68 mmHg (prone). No other parameters, including plasma disappearance rate of indocyanine green (ICG) and gastric intramucosal to arterial PCO_2 differed between the 2 positions.	Patients assigned to the prone group remained in the prone position for an average of 7.0±1.8 hrs per day. Mortality rate did not differ significantly between the prone group and the supine group at the end of the 10-day period, at the time of discharge from the ICU, or at 6 months. The PaO_2/FIO_2 increased slightly in the supine group but significantly more ($p=0.02$) in the prone group than the supine group. For all 721 maneuvers, the median change in the PaO_2/FIO_2 ratio was 28 at one hour and 44 at the end of pronation. In 73.2% of the procedures, the ratio increase more than 10, with 69.9% of the total response observed during the first hour. The number of new or worsening pressure sores per patient was significantly higher in the prone group than in the supine group during the 10-day period, whereas the number of days with pressure sores per patient was similar. The percentages of patients with accidental displacement of

		the tracheal or thoracotomy tube or loss of venous access were similar in the two groups. Pos hoc analysis showed that placing patients in the prone position reduced mortality at 10 days in the quartile of patients who were the most ill.
AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research	"Prone positioning in patients with acute lung injury, despite a small increase in IAP, does not negatively affect the hepatic capacity to eliminate ICG and gastric intramucosal energy balance when systemic blood flow and oxygenation are improved".	"Our study confirms that the use of the prone position improves arterial oxygenation and demonstrates that this approach has a limited number of complications."
OUR COMMENTS: Opportunity for bias, weakness and strength	**Potential for bias:** Very small sample size. **Weakness/es:** No mention if equilibrium period returned values to baseline level (the effects of prone positioning may still be present in the group who were placed in the supine position after being placed in the prone position).	**Weakness/es:** Lacked statistical power. Prone position for only 10 days (cannot show any long-term benefit). No mention of consistency of care for patients. Many causes of lung injury – not homogenous. **Strength/s:** Multicentre study. This study generates further questions to be asked about the use of prone positioning in ARDS.

Evidence Summary Therapy/Intervention Prone positioning in patients with ARDS	**Study 5** Rialp G, Betbese AJ, Perez-Marquez *et al* (2001). Short-term Effects of Inhaled Nitric Oxide and Prone Position in Pulmonary and Extrapulmonary Acute Respiratory Distress Syndrome. American Journal of Respiratory and Critical Care Medicine 164: 243-249.
STUDY DESIGN & NHMRC LEVELS OF EVIDENCE	Level II – Randomised Controlled Trial Factorial design – subjects acted as own controls
DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria	**Patients (subjects):** 15 patients with ARDS **Lung Injury Score:** 2.9±0.4 **Time from onset of ARDS:** 3±1 days **Type of ARDS:** Pulmonary and extrapulmonary **Mean age:** 53±17 yrs **Intervention:** Prone position for 30 minutes **Outcomes:** Gas exchange and pulmonary mechanics **Incl & Excl Criteria:** Inclusion: When despite FIO_2 and PEEP greater than 5cm H_2O they had a PaO_2 equal to or less than 200mm Hg for at least 24 hours. No exclusion criteria.
VALIDITY: Methodology, rigour, selection	**Randomisation:** Yes, to order of intervention **All patients accounted for:** Yes **Patients treated equally:** Yes **Similar groups:** One patient group.
RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate	Prone positioning, in comparison with supine positioning, resulted in a significant increase in PaO_2 (<0.001) (106±56 vs 184±67). 80% of patients were PaO_2 responders (increase in PaO_2/FIO_2 of 20% or more with respect of baseline (supine positioning)). No difference in prone positioning was found between pulmonary ARDS and extrapulmonary ARDS in terms of gas exchange. No short-term complications attributable to prone positioning.
AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research	"We should stress that our study may have lacked power to detect small changes".
OUR COMMENTS: Opportunity for bias, weakness and strength	**Potential for bias:** Selection bias – consecutive patients. Only addressed prone positioning for 30 minutes. Very short stabilisation time (effects of one intervention may still be present). **Weakness/es:** High mortality rate (80%). Very small numbers (n=15). Nitric oxide (NO) used only 1 hour prior to prone positioning for some patients (those randomised to NO first).

EXPLANATION OF TERMINOLOGY USED IN SPREADSHEET

Level of evidence: A hierarchy of study evidence that indicates the degree to which bias has been eliminated in the study design.
Focussed question: The review should address a clearly focused issue, in terms of the population studies, the intervention given and the outcomes considered.
Search strategy: A description of methods used to identify relevant studies from various computer databases and other sources.
Systematic review: The process of systematically locating, appraising and synthesising evidence from scientific studies in order to obtain a reliable overview.
Validity: The degree to which reviewers assessed the quality of the studies they included
Of measurement: an expression of the degree to which a measurement measures what it purports to measure; it includes construct and content validity.
Of study: the degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).
Consistent results: The similarity of results from the included studies. Often called heterogeneity which refers to the differences in treatment effect between studies contributing to a meta analysis (systematic review). If there is significant heterogeneity, this suggests that the trials are not estimating a single common treatment effect.
Appropriate analysis of results: When study results are pooled in a meta-analysis it is important that the results are combined in appropriate manner. The studies should be sufficiently similar in study design, the results of included studies should be clearly displayed and reasons for any variation in results should be discussed.
Potential for bias: Bias is a systematic deviation of a measurement from the 'true' value leading to either an over or underestimation of the treatment effect. Bias can originate from many different sources, such as allocation of patients, measurement, interpretation, publication and review of data.