Anaesth Intensive Care 1999; **27:** 194-201

Review

Prone Ventilation—it's Time

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SUMMARY

Prone positioning to improve oxygenation in acute lung injury was first reported over 20 years ago. Although this and several subsequent studies have shown that prone positioning improved oxygenation in the majority of patients, it has failed to become common practice in intensive care units. This paper reviews the mechanism by which prone positioning improves oxygenation and the clinical studies of its use to date.

Key Words: VENTILATION: mechanical, prone, acute respiratory distress syndrome

Acute respiratory distress syndrome (ARDS) is characterized by non-cardiogenic pulmonary oedema and hypoxaemia due to atelectasis and shunt. Over recent years a number of new modes of ventilation and non-ventilatory gas exchange methods have been used in this condition to contend with the refractory hypoxia and the complications of mechanical ventilation seen in this condition. Although the overall mortality from ARDS is decreasing, no single advance in respiratory support appears to be responsible[1].

Prone ventilation was shown to improve oxygenation in diffuse lung injury as long ago as 1976[2]. Over the years these findings have been confirmed by several other groups and a number of editorials supporting the use of prone ventilation have appeared[3-8]. Despite this, prone ventilation for acute lung injury has failed to become common practice in intensive care units. Information from both animal and human studies have elucidated the mechanism by which prone ventilation improves oxygenation and it has recently been suggested that prone ventilation may lessen the complications of mechanical ventilation in diffuse lung injury[9]. There is now sufficient evidence to support the use of prone positioning in individuals with acute lung injury and refractory hypoxia requiring mechanical ventilation.

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Accepted for publication on November 30, 1998.

PATHOPHYSIOLOGY

Normals

Prone positioning was first advocated for paralysed and ventilated patients in 1974[10]. The rationale was that in the supine position, ventilation shifts from the usual dorsal predominance to ventral predominance and that turning the patient prone may be a mechanism by which this could be corrected. In awake normal humans in the supine position, there is a vertical gradient in both ventilation and perfusion, both being greatest in the dorsal aspect of the lung[11,12]. Pleural pressure increases down the chest from ventral to dorsal resulting in a vertical gradient in regional lung volumes[13]. Because of this there is a gradient in regional compliance such that compliance is greatest dorsally. During spontaneous ventilation, diaphragmatic excursion is greatest dorsally[14] and this in addition to the compliance gradient results in preferential ventilation of dependent lung[13].

In the paralysed supine human there is a cephalad shift in the diaphragm and this is most marked at the dorsal aspect of the diaphragm due to the cephalad pressure exerted by the abdominal contents[14]. Positive pressure ventilation results in predominant movement of the ventral diaphragm with a reduction in motion of the dorsal aspect[14] and a relative shift in ventilation to the ventral lung[13]. This would result in $\dot{V}/\dot{Q}$ mismatching if perfusion continued to be distributed preferentially to the dorsal lung.

CT scans of the chest of normal humans after anaesthesia and paralysis show the rapid development of dependent crest-shaped opacities most marked in the caudal lung[15]. The application of PEEP results in partial or complete resolution of these

densities and on ceasing PEEP they recur. Contrast injection shows that the densities are perfused. These findings are consistent with the densities representing areas of atelectasis that act as areas of low $\dot{V}/\dot{Q}$ or shunt. Furthermore it has been demonstrated that the degree of hypoxia and shunt correlates with the amount of density seen on CT scan[16]. The appearance of the densities is probably due to a local increase in the pleural pressure due to cephalad movement of the diaphragm with resultant small airway closure and atelectasis. The higher closing volume in supine patients with low diaphragmatic tone supports this theory[17]. The application of PEEP partially corrects this but it does not restore diaphragmatic movement to its pre-anaesthetic pattern, with dorsal movement remaining retarded[14].

ARDS patients

Patients with ARDS demonstrate a similar but exaggerated pattern of pulmonary opacities to those seen in anaesthetized and paralysed normals[18.] CT scans of patients with ARDS demonstrate predominantly dorsal areas of consolidation/opacity[19]. In ARDS there is increased lung density due to inflammation and oedema with the result that the vertical gradient in pleural pressure is considerably increased[20]. As a consequence, pleural pressure will exceed opening pressure for a greater proportion of the lung, contributing to the greater dorsal opacity seen in this disease. Paralysis and sedation, as is frequently used in ARDS patients, will further increase the pleural pressure and atelectasis in the dorsal lung regions as discussed previously. PEEP decreases these densities and this is associated with improved oxygenation[19,20]. The improvement in oxygenation is due to a reduction in shunt and is proportional to the decrease in the opacities[18]. The amount of PEEP required is proportional to the weight of the overlying lung[21] and as lung density may be two to three times greater than normal in ARDS, pressures of 10 to 15 cm H_2O may be required in adults[21]. Thus, part of the hypoxaemia in ARDS is due to areas of atelectasis which are the result of pleural pressure exceeding the opening pressure of airways in the dorsal lung. These areas of atelectasis are potentially recruitable for gas exchange.

Even with PEEP adjusted to individuals' pressure volume curves, studies of prone ventilation have demonstrated significant improvements in oxygenation in some patients when turned prone[22]. This improvement is rapid and sustained[22,23]. CT scans of patients with ARDS show that when a patient is turned prone there is a rapid redistribution of the pulmonary opacities from the dorsal to the ventral aspect of the chest[24]. This is consistent with the lung behaving as an elastic body with compression of airways in the most dependent part of the chest where the pleural pressure exceeds opening pressure. If this is the case, why is it that oxygenation improves in the prone position?

Ventilation/perfusion relationships in diffuse lung injury have been studied in both animal models and in humans using the multiple inert gas elimination technique (MIGET). Beck[27] studied $\dot{V}/\dot{Q}$ matching with MIGET and perfusion using labeled microspheres in anaesthetized normal dogs in prone and supine positions. It was shown that $\dot{V}/\dot{Q}$ mismatching was greater in the supine position with a resultant lower PO_2. Also, perfusion was more heterogeneous due to a vertical gradient in perfusion that was not present in the prone position. Pappert[22] used MIGET to investigate the changes in $\dot{V}/\dot{Q}$ when ARDS patients were turned from supine to prone. The cause for improved oxygenation was a reduction in the shunt fraction with an increase in the number of $\dot{V}/\dot{Q}$ units with near normal ratios. This can be explained by the recruitment of previously unventilated but perfused lung units in the dorsum of the lung. These dorsal lung units remain well perfused on turning prone due to the absence of a vertical perfusion gradient in the prone position. The absence of a vertical perfusion gradient probably reflects the balance of lung architecture favouring dorsal blood flow[28] and gravity favouring ventral flow. This compares favourably to the supine position where both lung structure and gravity favour dorsal blood flow.

The distribution of ventilation in the normal human lung is not the same in the supine and prone positions. It is known that there is a vertical gradient in both ventilation and perfusion in the supine human with both increasing as one goes dorsally[11,12]. Amis[29] however found that ventilation in the prone position was more uniform. He also demonstrated that ventilation was reduced in the caudal aspect of the lung in the supine position but this was less marked in the prone position. Reheder[30] found that during anaesthesia in normal patients, dorsal ventilation was reduced compared with wakefulness but found no change in ventilation distribution in the prone position. Similar findings have been shown in dogs[31]. The flatter slope of phase three of nitrogen washout in the prone position also suggests more even ventilation with the trace being similar to that seen in upright humans[32].

The reason for the more even distribution of ventilation, less atelectatic lung and less shunt in the prone

position is that the pleural pressure gradient is not the same in supine and prone positions. In animals it has been demonstrated that the pleural pressure gradient is considerably less in the prone position[33,34] and markedly less when the animal is volume loaded, increasing lung weight and/or abdominal pressure[33]. Thus, in the prone position, the pleural pressure is less likely to exceed airway opening pressure and cause airway closure. This difference would be exaggerated in conditions such as ARDS where the lung weight is increased or conditions such as anaesthesia/paralysis where there is a cephalad shift in the diaphragm. As perfusion is more evenly distributed in the prone position, the recruitment of dorsal airways results in an increase in lung units with near normal $\dot{V}/\dot{Q}$ ratios and a reduction in shunt[22,24]. The difference in pleural pressure gradient is due to the action of gravity on the mediastinal and abdominal contents and the shape of the chest wall[35,36]. In the prone position the mediastinal and abdominal contents are supported by the sternum and ribs rather than the dorsal lung[35]. An example of this is the reduction in ventilation to the left lower lobe seen in humans with cardiomegaly whilst in the supine position but not in the prone postion[38] (Figure 1).

In summary, ARDS is characterized by increased lung weight and diaphragmatic dysfunction due to sedation/muscle paralysis, which results in an increase in pleural pressure and dependent airway closure and atelectasis. This, in part, is responsible for the shunt and hypoxia that occurs in ARDS. By turning patients prone, the pleural pressure gradient is reduced and this leads to less atelectatic lung and a more even distribution of ventilation. This, in addi-

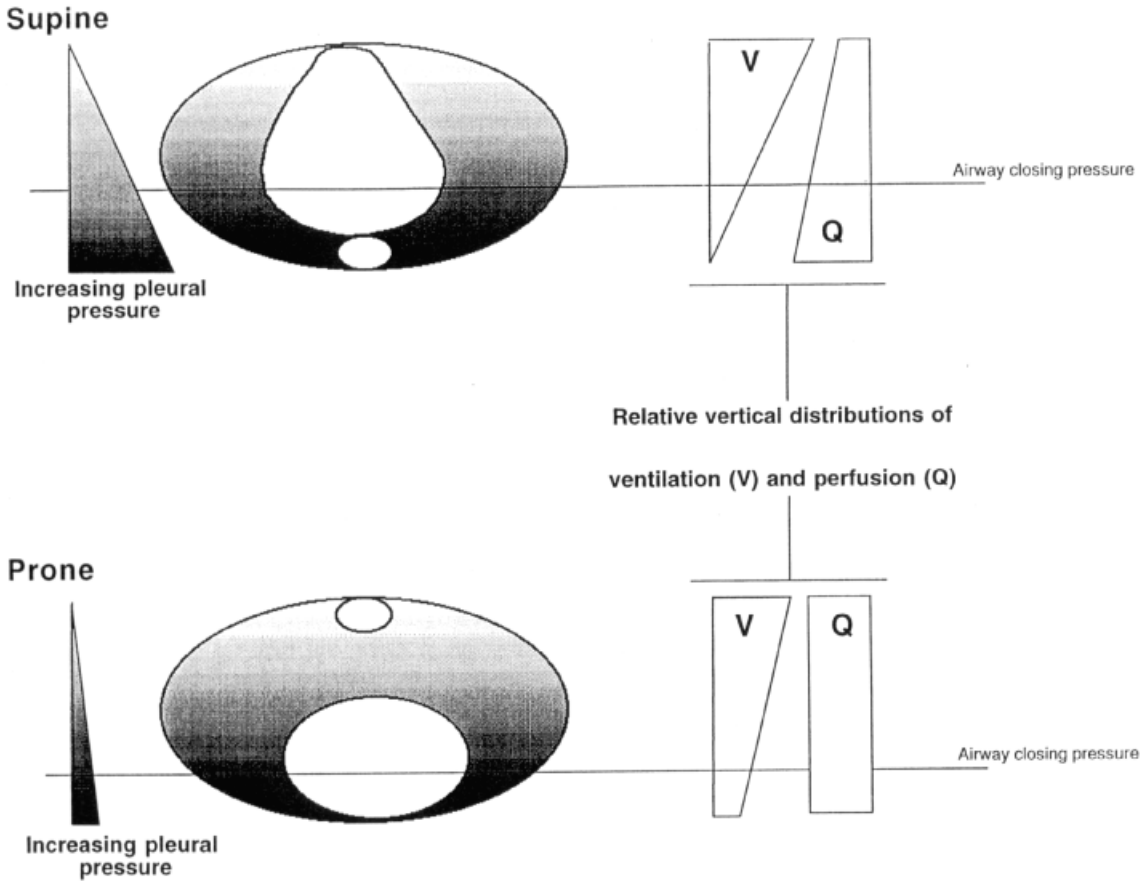

FIGURE 1: In the supine position, the greater vertical pleural pressure and the shape of the chest results in more lung tissue being exposed to pressure above airway closing pressure. More atelectasis therefore occurs compared to the prone position. The vertical distribution of ventilation (V) and perfusion (Q) in the supine position are in opposite directions resulting in mismatch. However, in the prone position, the absence of a vertical gradient in perfusion and more even ventilation distribution allows better V/Q matching.

tion to the more homogeneous distribution of perfusion seen in the prone position, results in better $\dot{V}/\dot{Q}$ matching and reduced shunt with improved oxygenation.

CLINICAL STUDIES

Since the first study of prone ventilation reported in 1976, there have been a number of case reports and non-randomized, uncontrolled trials reported in the medical literature. Overall, these have demonstrated that in the short-term the majority of patients with ARDS will have improvement in oxygenation on turning prone with little change in P_aCO_2 or haemodynamic variables.

Piehl[2] reported the effect of turning five patients with ARDS prone using a CircOlectric Bed. It was found that oxygenation improved in all patients (mean P_aO_2 increased from 82±3 by 47±16 Torr) and that removal of secretions was improved. Oxygen levels decreased after four to eight hours in the prone position although over this time ventilator settings and FiO_2 had been altered. Douglas[39] studied six patients with acute respiratory failure due to pneumonia or pulmonary oedema, one of whom was not intubated. Five of the six patients responded to initial prone positioning with an increase in P_aO_2 that enabled FiO_2 to be reduced. There was little change in P_aCO_2. It was found that the oxygenation worsened on returning the patient to supine in 12 of 14 instances and that on turning back to the prone position oxygenation improved again. There was no relationship between obesity and response and no significant change in effective compliance of the respiratory system. One third of the patients died whilst requiring ventilation.

Brussel[40] reported the use of prone ventilation in 10 patients with acute respiratory failure after cardiac surgery that was not due to cardiac failure. Thoracic CT scans were performed as part of the protocol and if these showed crest shaped densities in the dependent lung correlating with shunt, prone ventilation was considered. Ventilatory settings used a modest level of PEEP (5 to 7.5 cm H_2O), an I:E ratio of 0.5 and VT of 10 to 15 ml/kg. Patients were ventilated prone for between 10 and 42 hours (mean 26.7). There was a significant increase in P_aO_2/FiO_2 (114± 47.4 to 241±91.7mmHg) allowing a reduction in FiO_2. A-a gradient and shunt decreased significantly. There was no significant change in haemodynamic variables or in oxygen delivery. One of the 10 patients died as a result of multi-organ failure.

Langer[26] in 1988 studied gas exchange and haemodynamics before and after a two hour period of prone ventilation in 13 patients with ARDS who were sedated and paralysed. Eight of the 13 were responders with an increase in the P_aO_2 (70±8 to 90±8 mmHg) in the prone position. There was an insignificant decrease in P_aO_2 in non-responders but prone ventilation did not have to be stopped because of clinical deterioration in any individual. In responders P_aO_2 was better at two hours than at 30 minutes and remained higher than baseline even when returned to the supine position. Those who had a CT scan showed a change in the distribution of opacities from the dorsal to the ventral lung. There was no significant change in P_aCO_2, shunt, cardiac index or pulmonary artery pressure. There was no discernible difference at baseline between responders and non-responders.

Pappert in 1994[22] reported eight responders from a group of 12 patients with ARDS who were ventilated (pressure control) in the prone position for two hours. The responders had a significant increase in P_aO_2 (95.9±55.3 to 163.3±112.1 mmHg) that was rapid and sustained whilst in the prone position. $\dot{V}/\dot{Q}$ ratio assessed by MIGET showed a reduction in blood flow to unventilated areas and a corresponding increase in perfusion to areas with normal $\dot{V}/\dot{Q}$ ratios. Return to the supine position resulted in a significant decline in P_aO_2 and in normal $\dot{V}/\dot{Q}$ units. There was a significant decrease in minute ventilation (14.3±3.7 to 13.0±3.2 l/min) and rise in P_aCO_2 (52.1±11.9 to 57.3±13.5 mmHg) in the prone position which returned to previous levels on returning to the supine position. There was no significant difference or change in haemodynamic variables between or within groups. Outcome was not reported.

Three cases of patients with ARDS who were difficult to ventilate were reported by Turner[41] in 1994, stating that it was the first time its use had been reported in South Africa. All cases showed a rapid improvement in oxygenation with FiO_2 being reduced from 1.0 or 0.9 to 0.5 or less within 24 hours of being turned prone. Two of the three patients maintained the improvement in oxygenation up to 24 hours after returning to the supine position. An explanation for the persistence of improvement in the supine position may be related to the different pressures required to open an airway and then to subsequently maintain its patency.

In 1996 Vollman[42] performed prone ventilation in 15 patients with ARDS using a custom-made turning frame to turn and support them. They sought to determine whether prone ventilation improved oxygenation and whether they could find differences between responders and non-responders. Nine of the

15 responded with an increase in P_aO_2 (89.1±14.1 to 122±27.4 mmHg) and a decrease in shunt and in cardiac output. Non-responders had a significant decrease in P_aO_2 that did not require intervention. Non-responders as a group had been ventilated longer, had higher inspiratory and pulmonary artery pressures, and had higher P_aCO_2 for a similar minute ventilation. One possible explanation for this difference is that with more prolonged ARDS there is fibrosis that prevents recruitment of lung units.

Hormann[43] turned seven patients with ARDS from supine to prone at twelve-hourly intervals and confirmed the redistribution of atelectasis with CT scans. Patients were intermittently turned for 6.5±1.1 days. Oxygenation and shunt improved with no significant changes seen in cardiovascular parameters. FiO_2 could be reduced by the second day and constant ventilator settings were associated with reductions in airway pressure. Fridrich[23] performed a "long term" study of prone ventilation in ARDS patients. Twenty patients with ARDS following multi-trauma were ventilated prone for 20 hours a day with the procedure repeated on a daily basis (mean 7.7±4.1 days). All patients responded with an increase in P_aO_2 and a decrease in shunt. The increase in P_aO_2 was sustained over the 20 hours with a partial return to baseline on turning supine. These changes were repeated for subsequent turns over 96 hours (four turns). After recovery from severe ARDS a period of conventional ventilation was required. Mortality was 10%.

The largest study of prone ventilation was by Chatte[44] in 1997. A group of 32 patients with acute respiratory failure (predominantly ARDS) were turned prone for a period of four hours. Seven of the patients were non-responders two of whom did not tolerate the period of prone ventilation. Responders had a significant improvement in P_aO_2/FiO_2 from 108±26 before prone to 144±51 and 174±51 mmHg at one and four hours respectively. In responders, 13 of 23 evaluable patients had a persisting improvement in P_aO_2/FiO_2 after turning back to supine. Non-responders were on higher PEEP and had been ventilated for a shorter period when compared with responders. For patients ventilated in control mode (22/32) no changes in peak pressure occurred. For those on pressure controlled inverse ratio ventilation (10/32) there was an insignificant decrease in tidal volume (V_T). There was no difference in oxygenation or P_aCO_2 between the ventilatory modes. Haemodynamic variables were stable throughout .

Blanch et al[45] studied 23 patients without pre-existing COPD, CCF or chest wall disease who had ARDS. All patients tolerated turning. Sixteen of 23 were responders with an increase of 15% or more in P_aO_2/FiO_2 on turning prone. It is not clear in the article what period of time each patient spent in the prone position prior to data collection. P_aO_2/FiO_2 for the group as a whole increased from 78±37 mmHg to 115±51 mmHg. There was no significant change in haemodynamic parameters and no complications. Responders were more hypoxic (70±23 vs 99±53 mmHg), more hypercapnic (70±27 vs 64±9 mmHg) and had been ventilated for a shorter period (11.8±16 vs 32.8 (42 days) compared with non-responders. There was a small but significant increase in respiratory system compliance (Crs) in responders but not in non-responders. Similar changes in compliance were seen in a study of 12 ARDS patients ventilated in the prone position by Sevillo et al[46]. Ten of the 12 patients were classed as responders with an increase in P_aO_2/FiO_2 on turning prone. Compliance increased significantly for the group and remained significantly increased on returning supine. P_aO_2/FiO_2 was significantly correlated with Crs.

Pelosi et al[47] studied gas exchange and lung mechanics in 16 patients with acute lung injury before, during and after a two-hour period of ventilation in the prone position. Eleven of the 16 met the criteria for ARDS and none had asthma, COPD or cardiogenic pulmonary oedema. Twelve patients had an increase in PO_2 (range 9 to 73 mmHg) and in four the PO_2 decreased (range 7 to 16 mmHg). There was no significant change in Crs or lung compliance (Cl) but chest wall compliance (Ccw) decreased significantly. Improved oxygenation was correlated with a higher Ccw in the supine position. There was a modest correlation between change in chest wall compliance on turning prone and increase in PO_2. The authors stated that the reduction in chest wall compliance may be integral to the improvement seen in oxygenation. They proposed that the reduction in Ccw could act to shift ventilation to the ventral lung improving gas exchange in the dependent poorly ventilated areas and that the greater the reduction in chest wall compliance the greater this shift in ventilation would be.

From these studies it is clear that prone positioning safely improves oxygenation in the majority of patients with ARDS. Patients that have been ventilated for a shorter time[42,45], who have more hypoxia[45] and who are more hypercapnic[45] may be more likely to respond to prone positioning. The changes in lung mechanics demonstrated are interesting but more studies are needed before the interaction of lung mechanics and response to prone positioning in ARDS is fully understood and of use in predicting or

monitoring an individual's response to turning. A recent study in pigs has shown that abdominal distention is a predictor of greater improvement in oxygenation in response to prone positioning in anaesthetized normal animals[48]. This presumably reflects the greater pressure applied to the dorsal diaphragm by abdominal distention in the supine position and hence greater dorsal atelectasis. If these findings are confirmed in humans, this may have treatment implications for patients with ARDS due to abdominal pathology associated with abdominal distention.

Positioning

Methods of turning and positioning have varied between the studies. Piehl[2] used a rotating bed, the CircOlectic Bed, as did Douglas[39] for four of six patients but did not describe in detail its design or action. Douglas[39] also supported the chest and pelvis to allow free abdominal movement and the head to prevent pressure to the orbit. Pappert[22] used pillows beneath the chest and pelvis to avoid abdominal pressure and diaphragmatic restriction whilst Langer[26] used only a pillow beneath the pelvis to attain a position similar to that used for postero-basal drainage. Vollman[42] used a metal frame with supports for the forehead, chin, chest and pelvis that was strapped to the patient prior to being turned prone by three persons. This frame also allowed free movement of the abdomen. A study of lung volumes in various different prone postures in ten awake normal volunteers demonstrated no difference in lung volumes between unsupported prone positioning and positioning with shoulder and pelvic supports[49]. Chatte[44] used four attendants to turn patients. Patients were first turned to the lateral position and then laid prone. Arms were laid by the side and the head turned to one side. The shoulders and face were supported with folded sheets. Both supported[46] and unsupported[45] positioning of prone patients has been associated with improved oxygenation and increased respiratory system compliance. At present there is no clear evidence to support the use of particular body supports. Instead attention should be given to a well rehearsed turning procedure to limit disturbance to lines and tubes and to the prevention of pressure areas.

Complications

Side-effects related to prone ventilation are few. The most frequent side-effects are skin and mucosal injuries to the chest, forehead, tongue and lips[43,47]. Dislodgment of vascular catheters or endotracheal tubes and their compression is also a risk[47]. Other potential risks include blindness due to orbital compression, peripheral nerve injury associated with turning or compression, hypotension due to IVC compression and cervical cord injury from hyperextension[50]. Absolute contraindications to the prone position are unstable spinal injuries and unstable cardiac rhythm that may require defibrillation or cardiac compression. Relative contraindications are facial trauma, open chest or abdominal wounds and unstable circulation.

Lung Injury

Prone ventilation in addition to improving oxygenation may have a role in reducing lung injury during mechanical ventilation. By increasing P_aO_2/FiO_2, prone ventilation may allow the use of lower inspired oxygen tensions and thus reduce the risk of oxygen toxicity. In addition the use of lower FiO_2 reduces the risk of absorption atelectasis. Studies of ventilation in animals have shown that PEEP protects against lung injury from ventilation with high pressures[51] presumably in part by preventing trauma due to the shearing forces associated with repeated opening and closing of the airways and the depletion of surfactant. By turning the patient prone and recruiting airways in the dorsal lung, prone positioning is achieving similar beneficial effects as PEEP but without the risks of barotrauma or interference with cardiac function. That this may be the case is supported by Broccard's study of prone ventilation in dogs with oleic acid lung injury[9]. In this study histologic tissue damage was less in the prone group primarily due to a reduction in the extent and severity of injury in the dependent portions of the lung. This difference occurred even with the application of PEEP set at the lower inflection point.

CONCLUSION

Maximizing lung recruitment, limiting airway pressure and alveolar over-distention and keeping FiO_2 <0.6 are important strategies to limit lung damage during mechanical ventilation in ARDS[1,52,53,54]. Various ventilatory techniques including PEEP, permissive hypercapnia, and extended or inverse ratio ventilation are often used to achieve this. There is now evidence to suggest that prone ventilation may also be of assistance in achieving these goals. Prone positioning by reducing pleural pressure reduces atelectasis and results in a more even distribution of ventilation. This, in conjunction with the more homogeneous distribution of perfusion seen in the prone position, reduces shunt, improves $\dot{V}/\dot{Q}$ matching and thus

improves oxygenation. Clinical studies, although small and uncontrolled, demonstrate an acute improvement in oxygenation without significant side-effects in the majority of patients that may allow a reduction in FiO_2 and possibly PEEP. A controlled multicentre prospective trial[55] is now underway to determine whether the acute benefits translate to mortality and morbidity benefits. Whilst this more definitive information is awaited however, prone ventilation should be considered one of the repertoire of ventilation techniques useful in ARDS and its application considered in all patients with moderate to severe ARDS.

REFERENCES

1. Hudson LD. New therapies for ARDS. Chest 1995; 108:79S-91S.
2. Piehl MA, Brown RS. Use of extreme position changes in acute respiratory failure. Crit Care Med 1976; 4:13-14.
3. Webster NR. Ventilation in the prone position. Lancet 1997; 349:1638-1639.
4. Ryan DW, Pelosi P. The prone position in acute respiratory distress syndrome. BMJ 1996; 312:860-861.
5. Albert RK. One good turn. Intensive Care Med 1994; 20:247-248.
6. Marini JJ. Down side up—a prone and partial liquid asset. Intensive Care Med 1995; 21:963-965.
7. Pappert D, Falke KJ. When is a patient prone for prone? Anesth Analg 1996; 83:1139-1140.
8. Albert RK. For every thing (turn ... turn ... turn ...). Am J Respir Crit Care Med 1997; 155:393-394.
9. Broccard AF, Shapiro RS, Schmitz LL, Ravenscraft SA, Marini JJ. Influence of prone position on the extent and distribution of lung injury in a high tidal volume oleic acid model of acute respiratory distress syndrome. Crit Care Med 1997; 25:16-27.
10. Bryan AC. Comments of a devils advocate. Am Rev Respir Dis 1974; 110(suppl):143-144.
11. Kaneko K, Milic-Emili J, Dolovich MB, Dawson A, Bates DV. Regional distribution of ventilation and perfusion as a function of body position. J Appl Physiol 1966; 21:767-777.
12. Orphanidou D, Hughes JMB, Myers MJ, Al-Suhali A-R, Henderson B. Tomography of regional ventilation and perfusion using krypton 81 in normal subjects and asthmatic patients. Thorax 1986; 41:542-551.
13. Rehder K, Sessler AD, Rodarte JR. Regional intrapulmonary gas distribution in awake and anesthetized-paralysed man. J Appl Physiol 1977; 42: 391-402.
14. Froese AB, Bryan AC. Effects of anaesthesia and paralysis on diaphragmatic mechanics in man. Anesthesiology 1974; 41:242-255.
15. Brismar B, Hedenstierna G, Lundquist H, Strandberg A, Svensson L, Tokics L. Pulmonary densities during anesthesia with muscular relaxation—A proposal of atelectasis. Anesthesiology 1985; 62:422-428.
16. Hedenstierna G, Tokics L, Strandberg A, Lundquist H, Brismar B. Correlation of gas exchange impairment to the development of atelectasis during anaesthesia and muscle paralysis. Acta Anaesthsiol Scand 1986; 30:183-191.
17. Roussos C, Fukuchi Y, Macklem PT, Engel LA. Influence of diaphragmatic contraction on ventilation distribution in horizontal man. J Appl Physiol 1976; 40:417-424.
18. Gattinoni L, Mascheroni D, Torresin A, et al. Morphological response to positive end expiratory pressure in acute respiratory failure. Computerized tomography study. Intensive Care Med 1986; 12:137-142.
19. Gattinoni L, Pesenti A, Bombino M, et al. Relationships between lung computed tomographic density, gas exchange, and PEEP in acute respiratory failure. Anesthesiology 1988; 69:824-832.
20. Pelosi P, D'Andrea L, Vitale G, Pesenti A, Gattinoni L. Vertical gradient of regional lung inflation in adult respiratory distress syndrome. Am J Respir Crit Care Med 1994; 149:8-13.
21. Gattinoni L, D'Andrea L, Pelosi P, et al. Regional effects and mechanism of end-expiratory pressure in early adult respiratory distress syndrome. JAMA 1993; 269:2122-2127.
22. Pappert D, Rossaint R, Slama K, Gruning T, Falke K. Influence of positioning on ventilation-perfusion relationships in severe adult respiratory distress syndrome. Chest 1994; 106:1511-1516.
23. Fridrich P, Krafft P, Hochleuthner H, Mauritz W. The effects of long-term prone positioning in patients with trauma-induced adult respiratory distress syndrome. Anesth Analg 1996; 83:1206-1211.
24. Gattinoni L, Pelosi P, Vitale G, Pesent A, D'Andrea L, Mascheroni D. Body position changes redistribute lung computed-tomographic density in patients with acute respiratory failure. Anesthesiology 1991; 74:15-23.
25. Wiener C, Kirk W, Albert R. Prone position reverses gravitational distribution of perfusion in dog lungs with oleic acid-induced injury. J Appl Physiol 1990; 68:1386-1392.
26. Langer M, Mascheroni D, Marcolin R, Gattinoni L. The prone position in ARDS patients. A clinical study. Chest 1988; 94:103-107.
27. Beck K, Vettermann J, Rehder K. Gas exchange in dogs in the prone and supine positions. J Appl Physiol 1992; 72:2292-2297.
28. Beck K, Rehder K. Differences in regional vascular conductances in isolated dog lungs. J Appl Physiol 1986; 61:530-538.
29. Amis TC, Jones HA, Hughes JMB. Effect of posture on interregional distribution of pulmonary ventilation in man. Respir Physiol 1984; 56:145-167.
30. Rehder K, Knopp TJ, Sessler AD. Regional intrapulmonary gas distribution in awake and anesthetised-paralysed prone man. J Appl Physiol 1978; 45:528-535.
31. Hubmayr RD, Walters BJ, Chevalier PA, Rodarte JR, Olson LE. Topographical distribution of regional lung volume in anesthetized dogs. J Appl Physiol 1983; 54:1048-1055.
32. Cortese D, Rodarte J, Rehder K, Hyatt R. Effect of posture on the single-breath oxygen test in normal subjects. J Appl Physiol 1976; 41:474-479.
33. Mutoh T, Guest RJ, Lamm WJE, Albert RK. Prone position alters the effect of volume overload on regional pleural pressures and improves hypoxaemia in pigs in vivo. Am Rev Respir Dis 1992; 146:300-306.
34. Yang Q, Kaplowitz MR, Lai-Fook SJ. Regional variations in lung expansion in rabbits: prone vs supine positions J Appl Physiol 1989; 67:1371-1376.
35. Lamm WJE, Graham MM, Albert RK. Mechanism by which prone position improves oxygenation in acute lung injury. Am J Respir Crit Care Med 1994; 150:184-193.
36. Liu S, Marguiles SS, Wilson TA. Deformation of the dog lung in the chest wall. J Appl Physiol 1990; 68:1979-1987.
37. Lai-Fook SJ, Rodarte JR. Pleural pressure distribution and its relationship to lung volume and interstitial pressure. J Appl Physiol 1991; 70:967-978.
38. Weiner CM, Mckenna WJ, Myers MJ, Lavender JP, Hughes

JMB. Left lower lobe ventilation is reduced in patients with cardiomegaly in the supine but not the prone position. Am Rev Resp Dis 1990; 141:150-155.
39. Douglas WW, Rehder K, Beynen FM, Sessler AD, Marsh HM. Improved oxygenation in patients with acute respiratory failure: The prone position. Am Rev Respir Dis 1977; 115:559-566.
40. Brussel T, Hachenburg T, Roos N, et al. Mechanical ventilation in the prone position for acute respiratory failure after cardiac surgery. J Cardiothorac Vasc Anesth 1993; 7:541-546.
41. Turner JS, Smith G, Theunissen D. Prone position for ventilation in patients with severe adult respiratory distress syndrome. SAMJ 1994; 84:803-806.
42. Vollman KM, Bander JJ. Improved oxygenation utilizing a prone positioner in patients with acute respiratory distress syndrome. Intensive Care Med 1996; 22:1105-1111.
43. Hormann C, Benzer H, Baum M, Wicke K, Putensen C Putz G, Hartlieb S. The prone position in ARDS. A successful therapeutic strategy. [German] Anaesthetist 1994;43:454-462.
44. Chatte G, Sab J-M, Dubois J-M, Sirodot M, Gaussorgues P, Robert D. Prone position in mechanically ventilated patients with severe acute respiratory failure. Am J Respir Crit Care Med 1997; 155:473-478.
45. Blanch L, Mancebo J, Perez M, et al Short term effects of prone position in critically ill patients with acute respiratory distress syndrome. Intensive Care Med 1997; 23:1033-1039.
46. Servillo G, Roupie R, De Robertis E, et al. Effects of ventilation in ventral decubitus position on respiratory mechanics in adult respiratory distress syndrome. Intensive Care Med 1997; 23:1219-1224.
47. Pelosi P, Tubiolo D, Mascheroni D, et al. Effects of the prone position on respiratory mechanics and gas exchange during acute lung injury. Am J Respir Crit Care Med 1998; 157:387-393.
48. Mure M, Glenny R, Domino K, Hilastala M. Pulmonary gas exchange improves in the prone position with abdominal distention. Am J Respir Crit Care Med 1988; 157:1785-1790.
49. Mahajan RP, Hennessy N, Aitkenhead AR, Jellinek D. Effect of three different surgical prone positions on lung volumes in healthy volunteers. Anaesthesia 1994; 49:583-586.
50. Anderson J. The prone position for the surgical patient; a historical review of the principles and hazards. Br J Anaesth 1991; 67:452-463.
51. Webb HH, Tierney DF. Experimental pulmonary edema due to intermittent positive pressure ventilation with high inflation pressures. Protection by positive end-expiratory pressure. Rev Respir Dis 1974; 110:556-565.
52. Hickling KG. Acute lung injury: new concepts in ventilatory support. In Evans TW, Hinds CJ, eds. Recent advances in Critical Care Medicine 4. Churchill Livingstone 1996; 21-43.
53. Slutsky AS. Mechanical Ventilation. Chest 1993; 104:1833-1859.
54. Burchardi H. New strategies in mechanical ventilation for acute lung injury. Eur Respir J 1996; 9;1063-1072.
55. Gattinoni L, Tognoni G, Brazzi L, et al. Ventilation in the prone position. Letter. Lancet 1997; 350:815.