Acute lung failure in adults is characterized by a persisting impairment of pulmonary gas exchange which – depending on the severity of lung damage – reflects varying degrees of impairment of pulmonary distribution of ventilation and perfusion (1). Under physiological conditions, the ratio of ventilation (VA) to perfusion (Q) in the large gas exchange area of the lung (about 300 million alveoli with accompanying capillaries in adults) is finely tuned to ensure an optimal ratio of alveolar ventilation to pulmonary perfusion, and hence an effective exchange of the respiratory gases oxygen and carbon dioxide. Severe disturbances of the VA/Q ratio develop in acute pulmonary diseases, such as pneumonia, edema, lung contusion or aspiration. Extrapulmonary diseases such as massive transfusion, trauma, sepsis, “neurogenic” lung edema secondary to cerebral lesion, acute peritonitis or pancreatitis can also cause these disturbances. The main mechanisms implicated in the impairment of pulmonary function are shown in diagram 1. Following an American-European Consensus Conference (2), the severity of pulmonary failure is classified according to the degree of oxygenation impairment into two categories (box 1) on which specific therapeutic strategies are based. The acute onset, extent of hypoxemia and the absence of acute cardiac insufficiency are common to both forms of respiratory insufficiency. Acute respiratory distress syndrome (ARDS) is the more severe form of acute lung failure, which is characterized pathophysiologically by endothelial and epithelial damage to the alveolocapillary structures with consecutive influx of fluid, loss of surfactant and destruction of the alveolar architecture (3).

Acute respiratory failure is one of the main admission diagnoses to intensive care units (ICUs). The most important therapeutic principles currently implemented for acute lung failure include differentiated ventilation strategies, fluid and dietary management, adequate antibiotic therapy, pharmacological interventions and special positioning techniques.
Particular importance is attached to mechanical ventilation, firstly because it is the most important symptomatic therapeutic principle in lung failure, but secondly because it can itself be the source of severe undesirable effects, particularly because of the reversal of intrathoracic pressure conditions. Especially the lung, but also non-pulmonary organs, can sustain further damage on exposure to pressure, volume and shear forces. In the area of acute lung failure, major research efforts are therefore being channeled into developing supportive therapeutic principles which – without damaging the lung – contribute to improving pulmonary function.

Ventilation in prone position has been the subject of numerous clinical scientific studies in recent years and is used to treat acute lung failure in many ICUs. The (patho)physiological principles, clinical experiences and current status of scientific knowledge relating to the concept of prone position ventilation are reported below. The authors conducted an extensive literature search in the PubMed/Medline, Embase and Cochrane databases. 384 published articles dealing with positioning therapy in acute respiratory failure (prospective randomized studies, cohort studies, case reports, reviews, editorials) were analyzed and those satisfying the quality criteria of the Oxford Centre for Evidence Based medicine were selected.

**Classification of acute lung failure**

- **Acute lung injury (ALI)**
  - Acute onset
  - \(\text{PaO}_2/\text{FIO}_2 \leq 300\ \text{mmHg}\) (irrespective of PEEP level)
  - Bilateral infiltrates in anteroposterior chest radiography
  - No clinical signs of left atrial hypertension

- **Acute respiratory distress syndrome (ARDS)**
  - Acute onset
  - \(\text{PaO}_2/\text{FIO}_2 \leq 200\ \text{mmHg}\) (irrespective of PEEP level)
  - Bilateral infiltrates in anteroposterior chest radiography
  - No clinical signs of left atrial hypertension

*according to the American-European Consensus Conference (2); \(\text{PaO}_2\), arterial oxygen partial pressure; \(\text{FIO}_2\), inspiratory oxygen concentration; PEEP, positive end-expiratory pressure*

**Effect of prone position in acute lung failure**

Not only the mechanisms illustrated in diagram 1, which induce a restriction of gas exchange during the development of pulmonary failure, but also artificial airways and mechanical ventilation lead to additional, typical changes in the respiratory system. Analgesic-based sedation, intubation and mechanical ventilation themselves induce a decrease in thoracic diameter and a change in the diaphragm configuration: besides causing cranial displacement...
and flattening of the diaphragm, they adversely influence the geometry and elasticity of all components of the thoracic wall and abdominal muscles (6). In the ventilated intensive care patient, this produced a tendency of the middle and small airways to collapse followed by formation of atelectases. In the diseased lung parenchyma, this effect is exacerbated by bronchoalveolar secretion, edema formation and reduced production and dysfunction of the pulmonary surfactant system (7).

Atelectases are therefore formed mainly in the dorsal segments close to the diaphragm. They considerably reduce the proportion of ventilated lung parenchyma, but continue to be perfused with blood because they are located in the gravitation-dependent lung regions. This mismatch between ventilation and perfusion is termed intrapulmonary shunt and largely determines the extent of the impairment of pulmonary gas exchange. In these regions, no ventilation takes place although blood perfusion is undiminished or even increased (figure 1), but without contact between blood and gas. Interventions designed to open up these atelectases and thereby improve gas exchange are thus of particular therapeutic interest.

As long as 30 years ago, reports were published describing the use of prone positioning in acute lung failure (8). This approach was shown to significantly improve oxygenation, but the exact mechanism remained unknown for a long time. Not until the introduction of computed tomography (CT) and the development of more advanced techniques for the physiological evaluation of lung function, such as the multiple inert gas elimination technique (MIGET), was it possible to accurately quantify the effect of prone positioning on the damaged lung (box 3). The prone position brings about a homogenization of respiratory gas distribution and pulmonary perfusion (9) and thereby a reduction in the V̇ₚ/Q mismatch (diagram 2). Furthermore, the CT studies showed that prone positioning improves respiratory mechanics, increases diaphragm dynamics and, because of the reversal of gravitational conditions, contributes to re-opening of dorsobasal "dependent" regions of the lung. This reduced the intrapulmonary shunt fraction (10).

Figure 1: Computed tomographic image of the lung of a patient with acute lung failure. Section below the carina. Clearly recognizable are typical dorsobasal atelectases with regions of hypoventilation.

BOX 2

Concepts for treatment of acute lung failure
- Lung protective ventilation
- Positive end-expiratory pressure (PEEP)
- Recruitment maneuver (open lung)
- Early integration of spontaneous breathing
- Balanced volume therapy
- Positioning therapy (prone position)
- Pharmacological intervention
- Extracorporeal pulmonary support
Evidence situation for ventilation in prone position

Numerous studies have shown that prone positioning provides an increase in oxygenation in patients with acute lung failure (10–15). A beneficial effect was observed especially in patients with post-traumatic respiratory insufficiency (16). The improvement in gas exchange was often observed to occur after a short time and could be increased over a period of hours. In most studies, the duration of prone positioning was 6 hours, and daily repetition of the maneuver in the interval led to a continuous and persisting improvement in pulmonary gas exchange. As a result, prone positioning came to be used as an “emergency intervention” especially for severe forms of ARDS which are acutely life threatening because of the hypoxemia. In comparative studies, prolonged prone positioning for 12 or more hours was superior to the shorter duration of 6 hours as regards the effect on oxygenation (17, 18). However, further studies that would make it possible to establish a clear algorithm are still lacking. For example, neither the optimal time for intervention, prophylactic or therapeutic, the specific indication, acute lung injury (ALI) or ARDS, nor duration and repetition have been clearly defined. The indication for the use of further
emergency measures to enhance gas exchange in life-threatening impairment of oxygenation, such as the inhalation of nitrogen monoxide or prostacycline and extracorporeal lung assist, has not been conclusively established because of the lack of informative prospective studies.

In the last few years, the clinical outcome of ventilation in prone position has been the subject of 3 large multicenter studies (19–21) performed to establish whether systematic prone positioning can reduce the mortality associated with acute lung failure. The main results are presented in the table. The studies of Gattinoni et al. (19) as well as Guerin et al. (20) chose moderate pulmonary failure (ALI) as inclusion criterion and performed prone positioning for 8 hours daily. In these studies with large sample sizes and similar ventilation regimens, no difference in mortality was found between the prone positioning group and the control group. However, Guerin et al. showed a reduction in the incidence of ventilation-associated pneumonias in the patients who were regularly placed in the prone position for several days.

The rate of complications, such as position-related pressure damage, was higher in the prone positioning group. In the study of Mancebo et al. (21) with clearly defined inclusion criteria – only patients with clinically apparent ARDS were enrolled – and longer prone positioning periods of 20 hours, there was a trend towards lower mortality in the intervention group, although the results failed to reach significance. The study had to be discontinued for logistic reasons after enrolling 136 patients.

| Table: Comparison of study design and results of 3 large, prospective multicenter studies on prone positioning in acute lung failure |
|-----------------|-----------------|-----------------|
|                  | Gattinoni (19)  | Guerin (20)     | Mancebo (21)   |
| Patients        | 152 SP, 152 PP | 387 SP, 413 PP  | 60 SP, 76 PP  |
| Criterion       | (PaO₂/FIO₂ < 300 mmHg) | (PaO₂/FIO₂ < 300 mmHg) | (PaO₂/FIO₂ < 200 mmHg) |
| Hours PP/day    | 7 h             | 8 h             | 20 h           |
| Tidal volume    | 10 ml/kg        | 8–10 ml/kg      | 8 ml/kg        |
| PEEP            | 10 cm H₂O       | 8 cm H₂O        | 8 cm H₂O       |
| Mortality       | no difference   | no difference   | no difference  |
| Pneumonia       | not recorded    | reduced in PP   | no difference  |
| Oxygenation     | ↑↑              | ↑↑              | ↑              |
| Ventilation     | no difference   | no difference   | difference doubtful |
| Complication    | more pressure damage | more pressure damage | not recorded |
In the final analysis, therefore, there is a lack of large multicenter studies conclusively demonstrating a positive effect of prone positioning on duration of ventilation, intensive care management period and mortality. In particular, there is a lack of clear inclusion criteria and a strict study protocol in which uniform intensive care therapy is compulsory and ventilation settings are defined. All these studies were the subject of vigorous methodological debate. Main points of criticism are that there were different positioning protocols which were not consistently applied, that there was little previous experience with positioning and the patients were not unambiguously characterized. All studies included subgroups which evidently benefited from the intervention, and it will therefore be essential in future studies to focus on the precise definition of the clinical entities and conditions investigated. It should also be taken into account that the ventilation settings used in these 3 large studies only partly correspond to the currently recommended concept of “lung protective” ventilation. For example, the Acute Respiratory Distress Syndrome Network (22) now recommends a high positive end-expiratory pressure (PEEP) and a low tidal volume. Inconsistency in complying with this recommendation could have contributed to the fact that there was no difference in mortality between the intervention and the control group.
Prone positioning in intensive medical care

Even without conclusive proof of effectiveness, ventilation in prone position is practiced in many ICUs (figure 2). It requires careful preparation and good coordination between nursing and medical staff to avoid complications (box 4). These include not only accidental loss of the tube or catheters, but also and especially hemodynamic and pulmonary compromise resulting from autonomic stress or dyscoordination between the ventilator machine and the patient when insufficiently sedated. Moreover, with particularly slim or overweight patients and when using vasopressor substances (catecholamines), exposed areas of skin such as the knee, pelvis, chest, nose and face suffer considerable pressure damage. Turning of the well prepared patient (circulatory stabilization, adequate analgesic-based sedation, securing and/or lengthening of catheters, drains, tube) should be carried out by several members of nursing staff with a physician present, who should devote particular attention to securing the artificial airway and the intravascular access lines (23). As a risk management concept, an emergency algorithm including an emergency vehicle and a planned procedure in the event of tube or catheter loss must be in place before turning the patient. When the patient is in the prone position, care must be taken to ensure soft, compression free positioning of the head, pelvis and knee. These contact points should also be checked repeatedly during the intervention. If pulmonary gas exchange and respiratory mechanics improve as a result of prone positioning, it is advisable to correct the ventilation parameters. To protect the lung, the inspiratory oxygen concentration, ventilatory pressure, and tidal volume can be reduced.

If there is hemodynamic and respiratory tolerance, a duration of 8 to 12 hours is recommended for the intervention. Returning the patient to the original position should be carried out observing the same criteria of care as for prone positioning. If there is a positive effect on gas exchange, it may be valuable to return to prone position ventilation after 8 to 12 hours. Depending on the severity of lung failure, this concept can be retained for several days to one week. To avoid the aspiration of tube feeding diet in the prone position, enteral nutrition should be discontinued during the positioning maneuver and then re-instituted in a suitable dosage (≤ 40 ml/h). Acute shock syndrome and spinal instability are regarded as absolute contraindications for prone positioning; in the presence of relative contraindications, the procedure should be decided on a casewise basis. Relative contraindications include acute traumatic or non-traumatic cerebral lesion, severe midfacial injuries and acute abdomen, especially with unclosed laparotomy and mesh inlay. To reduce position-associated complications, a method widely practiced in many intensive care units is “incomplete” prone positioning (135° positioning), in which one side of the patient is raised by means of a positioning aid. Above all, this 135° positioning offers several advantages for nursing care (oral and tracheal aspiration, regular pupillary monitoring, lead-out of abdominal or thoracic drains). In severe ARDS with the risk of hypoxemia, however, the effect of the incomplete prone position on gas exchange is less pronounced compared to complete 180° prone positioning (24). In patients with severely impaired gas exchange, therefore, complete 180° prone positioning is recommended, whereas for moderate impairment of lung function the 135° positioning option is to be preferred as a prophylactic approach – to mobilize exudates, avoid nosocomial pneumonia and prevent atelectases.

Guidelines for the positioning therapy of intensive care patients in the form of systematically elaborated descriptions and recommendations aimed at providing support for intensive care physicians in deciding on appropriate positioning interventions are currently being developed under the coordination of the first author of this article and with the support of the Association of the Scientific Medical Societies. Following adoption by the Executive Committee of the German Society for Anesthesiology and Intensive Medicine, a publication is expected to appear in spring 2008. In the already published S2 Guidelines ”Diagnosis and Treatment of Sepsis”, the prone position is recommended with a weak recommendation grade C for critically impaired oxygenation (PaO2/FIO2 = 88 mmHg) (PaO2 = arterial oxygen partial pressure; FIO2 = inspiratory oxygen concentration). A Cochrane analysis or a systematic meta-analysis of medical aspects has not yet been performed.
Summary
In artificially ventilated intensive care patients with acute lung failure, intermittent prone positioning for about 12 hours alternating with supine positioning is suitable for improving pulmonary gas exchange because turning onto the abdomen reduces the ventilation-perfusion mismatch (box 5). Although this effect has been demonstrated in numerous studies and prone positioning is widely used in clinical practice, generally conclusive proof that the mortality rate is reduced by this intervention is lacking. Further, carefully planned randomized prospective studies will be necessary in this area to produce valid statements in well defined patient populations. Changing to the prone position can potentially be associated with sometimes serious complications (25) and requires a structured approach by intensive care medical personnel. This includes thorough preparation of the patient, careful organization of the intervention, well-considered risk management and close monitoring of the positioned patient.

Conflict of Interest Statement
Prof. Bein has received lecture fees from the medical device manufacturer KCI, Wiesbaden. Prof. Quintel has advised the medical device manufacturer KCI, Wiesbaden. Prof. Kuhlen declares that there is no conflict of interest as defined in the guidelines of the International Committee of Medical Journal Editors.

Manuscript submitted on 19 December 2006, final version accepted on 30 April 2007.

Translated from the original German by mt-g.

REFERENCES


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