Significant changes in the management of adult patients with severe acute respiratory distress syndrome and hypoxemia by means of systems using extracorporeal oxygenation has been questioned. A National Institutes of Health multicentre study, published in 1979, reported survival rates of 9.5% and 8.3% in extracorporeally and ventilator managed patients, respectively. Another recent study reports survival rates of 33% and 42% in ventilator and extracorporeally managed patients, respectively. None of these differences was statistically significant. Indications for extracorporeal oxygenation may need to be re-evaluated to clarify those cases that would not be manageable with current ventilation strategies and, hence, would merit extracorporeal support.

Key Words: Acute respiratory distress syndrome, Extracorporeal membrane oxygenation, Hypoxemia

The usefulness of managing adult patients with severe acute respiratory distress syndrome and hypoxemia by means of systems using extracorporeal oxygenation has been questioned. A National Institutes of Health multicentre study, published in 1979, reported survival rates of 9.5% and 8.3% in extracorporeally and ventilator managed patients, respectively. Another recent study reports survival rates of 33% and 42% in ventilator and extracorporeally managed patients, respectively. None of these differences was statistically significant. Indications for extracorporeal oxygenation may need to be re-evaluated to clarify those cases that would not be manageable with current ventilation strategies and, hence, would merit extracorporeal support.

Key Words: Acute respiratory distress syndrome, Extracorporeal membrane oxygenation, Hypoxemia
DEMAGO

TABLE 1
Extracorporeal membrane oxygenation entry criteria: \( \text{PaO}_{2} < 50 \, \text{mmHg} \) (repeated three times)

| Criteria         | Rapid  | Slow   |
|------------------|--------|--------|
| Testing time (h) | 2      | 12     |
| FiO2             | 1.0    | >0.6   |
| PEEP (cm H2O)    | >5     | >5     |
| Qs/Qt            | –      | >0.3   |
| \( \text{PaCO}_{2} \) (mmHg) | 30-45 | 30-45  |
| ICU (h)          | –      | >48    |

FiO2: Fraction of inspired oxygen; ICU: Intensive care unit; PEEP: Positive end-expiratory pressure; Qs/Qt: Right-to-left shunt fraction

The membrane lungs were connected in series and ventilated with a humidified mixture of room air and oxygen at a flow rate of usually 15 L/min, achieving 100% saturation of the blood perfused through the two membranes. The membrane lungs were connected in series and ventilated with a humidified mixture of room air and oxygen at a flow rate of usually 15 L/min, achieving 100% saturation of the blood perfused through the two membranes.

In 1984 Gattinoni et al (8) reported a survival rate of 48.8% in 43 patients selected by the same criteria as those listed in Table 1. Although this was not a randomized controlled study it certainly constituted a dramatic improvement over the previous reports, in a population of patients that carried a projected mortality of 90%. The Toronto Group reported a survival rate of 22% in a 10-year review (1976 to 1986) of patients managed with ECMO and conventional ventilation (9). We have since 1989 had an improvement to 47% in patients managed with a modified ECMO technique and ‘lung rest’. A number of other groups in Europe, adopting the Gattinoni technique, likewise reported a survival rate of approximately 50%. The ECMO technique used by the Toronto group consists of percutaneous insertion of cannulas, 19 and 22 French gauges, respectively, into the internal jugular and the femoral vein. The circulation of blood through the membranes is accomplished by means of a centrifugal pump. We also minimize ventilation during ECMO, although we do not insufflate oxygen via the endotracheal tube. Patients are ventilated at a frequency of four to six breaths/min and the appropriate PEEP level to minimize right-to-left shunting; peak airway pressures are controlled at less than 40 cm H2O. As the lungs improve, ventilation is increased and the percentage of the bloodflow through the membranes is reduced.

Gattinoni et al (8) had earlier reported a 77% survival in severe ARDS after support with pressure-controlled inverse ratio ventilation (PCIRV), followed, if necessary, by LFPPV-ECCO2R. Of the survivors, 57% recovered after PCIRV alone, without ever requiring LFPPV-ECCO2R, while 43% of those managed with ECMO recovered. The work of various authors in the intervening years increased appreciation of the potential adverse impact of ventilation, specifically high pressures and large tidal volumes, and changes in the ventilation management had been introduced. Hickling (10) in 1992 reported increased survival in patients with severe ARDS managed with PCIRV and permissive hypercapnia. These considerations indicated the need for a controlled randomized comparison of PCIRV with LFPPV-ECCO2R to determine the true mortality in severe ARDS and the relative advantages of the two modes of management.

Morris et al (11) in 1994 performed a randomized study comparing PCIRV with LFPPV-ECCO2R in patients fulfilling the ECMO entry criteria. PCIRV was delivered according to a computerized program in order to standardize management. The characteristics of the patients were similar in demographics, illness severity and duration, and Apache II scores. They were also comparable in physiological characteristics (Table 2). Similar numbers in both groups were enrolled via the fast and slow entry criteria.

Morris et al reported a survival rate of 42% in the PCIRV
group and 33% in the ECCO2R; these were not statistically different. This study confirmed the improved outcome reported for both PCIRV and ECCO2R but failed to show any significant advantage in the ECCO2R group. The complication rates were different in the two groups (Table 3), and seven patients had to be disconnected from the ECMO circuit, five of whom nonetheless survived. Four patients had significant intrapulmonary hemorrhage and their outcome is unclear. Four patients also had clotting of the circuit, usually a disastrous complication and, again, the outcome of these patients is not indicated.

Some centres, in an attempt to reduce bleeding, which is the most common and significant complication, use heparin-coated membranes and treat the patients, before and during ECMO, with antifibrinolytic drugs (12). Maintaining high concentrations of antithrombin III through the administration of fresh frozen plasma is recommended by some authors (13). The Toronto Group uses antifibrinolytic therapy and fresh frozen plasma administration in our patients and have not had bleeding complications in the six so managed.

The study of Morris et al has raised significant doubts as to the additional benefit that can be derived from extracorporeal support and suggests that survival with PCIRV is markedly better than previously reported in severe ARDS patients fulfilling ECMO criteria. It also confirmed the previously reported survival rates in patients treated with extracorporeal support. We believe that some patients presenting with severe ARDS, who cannot be supported with PCIRV on FiO2 of 1 after a PEEP trial, should be treated with extracorporeal support. We define a PCIRV failure as arterial oxygen saturation less than 0.85 and/or venous oxygen saturation less than 0.6, with elevated serum lactate acid. We exclude patients who have any or all of significant chronic system disease, contraindications to the use of anticoagulants, malignancies or immunosuppression. We believe that the criteria for instituting ECMO should be changed so that only patients with evidence of tissue ischemia, as reflected in venous oxygen saturation, serum lactate and hypoxic organ dysfunction, would be treated with this modality.

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### TABLE 2

| All patients | PCIRV | ECMO | P |
|-------------|-------|------|---|
| pho2 | 57±2 | 58±3 | 56±3 | 0.99 |
| PO2 | 9.0±0.2 | 9.0±0.2 | 0.9±0.2 | 0.88 |
| PEEP | 16±0.8 | 16±1.0 | 17±1.0 | 0.97 |
| CTH | 20±2.0 | 22±3.0 | 18±2.0 | 0.63 |
| Qs/Qt | 0.47±0.01 | 0.44±0.02 | 0.5±0.02 | 0.10 |
| SaO2 | 83±1.0 | 84±1.0 | 81±2.0 | 0.35 |
| P peak | 56±2.0 | 56±2.0 | 55±3.0 | 0.29 |
| Pco2 | 49±2.0 | 48±4.0 | 50±3.0 | 0.19 |

*CTH: Total thoracic compliance (mL/cmH2O); ECMO: Extracorporeal membrane oxygenation; FiO2: Fraction of inspired oxygen; P peak: Peak airway pressure (cm H2O); PCIRV: Pressure-controlled inverse ratio ventilation; Qs/Qt: Right-to-left shunt fraction; SaO2: Arterial oxy- 

### TABLE 3

| Category | PCIRV | ECCO2R |
|----------|-------|--------|
| Cardiac dysrhythmia arrest | 2 | 2 |
| Cardiac tamponade | 1 | 1 |
| Central nervous system | 1 | 1 |
| Intracranial hemorrhage | 1 | 1 |
| Cerebral arterial gas embolism | 1 | 1 |
| Cerebral hypoxia depression | 1 | 1 |
| Peripheral vascular | 2 | 1 |
| Extremity ischemia | 2 | 1 |
| Arterial embolism | 3 | 2 |
| Venous thrombosis | 4 | 7 |
| Vasculitis | 2 | 7 |
| Dermatitis | 1 | 4 |
| Hypertension | 1 | 2 |
| Neuromuscular (weakness) | 3 | 2 |
| Hemorrhage (noncentral nervous system) | 4 | 2 |
| Intrapulmonic | 4 | 2 |
| Packed red blood cells transfusion | 10 | 1 |
| >0.8 L/day | 7 | 4 |
| ECCO2R discontinuation | 7 | 4 |
| Circum clotting | 4 | 4 |

ECCO2R Extracorporeal carbon dioxide removal; PCIRV Pressure-controlled inverse ratio ventilation