dioxide—has yielded promising preliminary results, enhancing pulmonary function in patients with ARDS, but also has provided no survival benefit. *Lung-replacement therapy with extracorporeal membrane oxygenation* (ECMO), which provides a clear survival benefit in neonatal respiratory distress syndrome, may also have utility in selected adult patients with ARDS.

Data supporting the efficacy of "adjunctive" ventilator therapies (e.g., high PEEP, inverse ratio ventilation, recruitment maneuvers, prone positioning, HFV, ECMO, and PLV) remain incomplete. Accordingly, these modalities are reserved for use as rescue rather than primary therapies.

FLUID MANAGEMENT

(See also Chap. 321) Increased pulmonary vascular permeability leading to interstitial and alveolar edema fluid rich in protein is a central feature of ARDS. In addition, impaired vascular integrity augments the normal increase in extravascular lung water that occurs with increasing left atrial pressure. Maintaining a low left atrial filling pressure minimizes pulmonary edema and prevents further decrements in arterial oxygenation and lung compliance; improves pulmonary mechanics; shortens ICU stay and the duration of mechanical ventilation; and is associated with a lower mortality rate in both medical and surgical ICU patients. Thus, aggressive attempts to reduce left atrial filling pressures with fluid restriction and diuretics should be an important aspect of ARDS management, limited only by hypotension and hypoperfusion of critical organs such as the kidneys.

NEUROMUSCULAR BLOCKADE

In severe ARDS, sedation alone can be inadequate for the patient-ventilator synchrony required for lung-protective ventilation. This clinical problem was recently addressed in a multicenter, randomized, placebo-controlled trial of early neuromuscular blockade (with cisatracurium besylate) for 48 h. In severe ARDS, early neuromuscular blockade increased the rate of survival and ventilator-free days without increasing ICU-acquired paresis. These promising findings support the early administration of neuromuscular blockade if needed to facilitate mechanical ventilation in severe ARDS; however, these results must be replicated prior to their widespread application in clinical practice.

GLUCOCORTICOIDS

Many attempts have been made to treat both early and late ARDS with glucocorticoids, with the goal of reducing potentially deleterious pulmonary inflammation. Few studies have shown any benefit. Current evidence does *not* support the use of high-dose glucocorticoids in the care of ARDS patients.

OTHER THERAPIES

Clinical trials of surfactant replacement and multiple other medical therapies have proved disappointing. Inhaled nitric oxide and inhaled epoprostenol sodium can transiently improve oxygenation but do not improve survival or decrease time on mechanical ventilation.

RECOMMENDATIONS

Many clinical trials have been undertaken to improve the outcome of patients with ARDS; most have been unsuccessful in modifying the natural history. While results of large clinical trials must be judiciously applied to *individual* patients, evidence-based recommendations are summarized in **Table 322-3**, and an algorithm for the initial therapeutic goals and limits in ARDS management is provided in **Fig. 322-5**.

TABLE 322-3 EVIDENCE-BASED RECOMMENDATIONS FOR ARDS THERAPIES

Treatment	Recommendation[a]
Mechanical ventilation	
Low tidal volume	A
Minimized left atrial filling pressures	B
High-PEEP or "open lung"	C
Prone position	C
Recruitment maneuvers	C
High-frequency ventilation	D
ECMO	C
Early neuromuscular blockade	A
Glucocorticoid treatment	D
Surfactant replacement, inhaled NO, inhaled epoprostenol, and other anti-inflammatory therapy (e.g., ketoconazole, PGE1, NSAIDs)	D

[a]Key: A, recommended therapy based on strong clinical evidence from randomized clinical trials; B, recommended therapy based on supportive but limited clinical data; C, recommended only as alternative therapy on the basis of indeterminate evidence; D, not recommended on the basis of clinical evidence against efficacy of therapy.

Abbreviations: ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; NO, nitric oxide; NSAIDs, nonsteroidal anti-inflammatory drugs; PEEP, positive end-expiratory pressure; PGE1, prostaglandin E_1.

PROGNOSIS

Mortality Recent mortality estimates for ARDS range from 26% to 44%. There is substantial variability, but a trend toward improved ARDS outcomes appears evident. Of interest, mortality in ARDS is largely attributable to nonpulmonary causes, with sepsis and nonpulmonary organ failure accounting for >80% of deaths. Thus, improvement in survival is likely secondary to advances in the care of septic/infected patients and those with multiple organ failure **(Chap. 321)**.

The major risk factors for ARDS mortality are nonpulmonary. Advanced age is an important risk factor. Patients >75 years of age have a substantially higher mortality risk (~60%) than those <45 (~20%). Moreover, patients >60 years of age with ARDS and sepsis have a threefold higher mortality risk than those <60. Other risk factors include preexisting organ dysfunction from chronic medical illness—in particular, chronic liver disease, cirrhosis, chronic alcohol abuse, chronic immunosuppression, sepsis, chronic renal disease, failure of any nonpulmonary organ, and increased APACHE III scores **(Chap. 321)**. Patients with ARDS arising from direct lung injury (including pneumonia, pulmonary contusion, and aspiration;

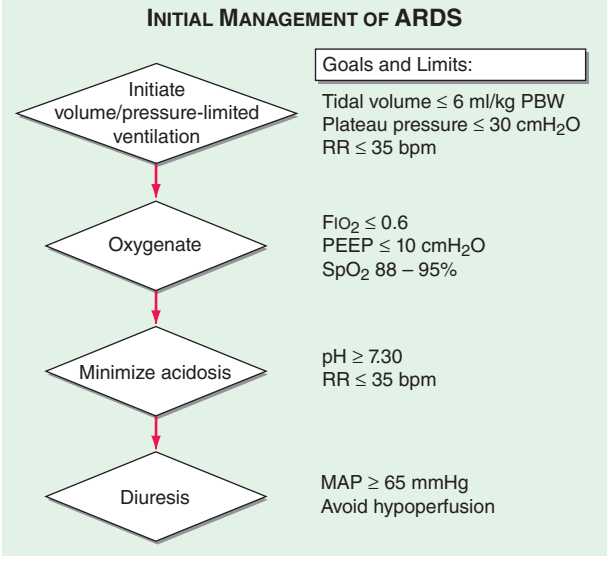

FIGURE 322-5 Algorithm for the initial management of ARDS. Clinical trials have provided evidence-based therapeutic goals for a stepwise approach to the early mechanical ventilation, oxygenation, and correction of acidosis and diuresis of critically ill patients with ARDS. F_{IO_2}, inspired O_2 percentage; MAP, mean arterial pressure; PBW, predicted body weight; PEEP, positive end expiratory pressure; RR, respiratory rate; SpO_2, arterial oxyhemoglobin saturation measured by pulse oximetry.