

A conservative fluid management strategy did not affect risk for death but shortened duration of ventilation in acute lung injury

Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564-75.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Endocrinology ★★★★★☆

QUESTION

In patients with acute lung injury (ALI), what are the risks and benefits of a conservative compared with a liberal fluid-management strategy?

METHODS

Design: Randomized controlled trial.

Allocation: Concealed.*

Blinding: Unblinded.*

Follow-up period: 60 days.

Setting: 20 centers in North America.

Patients: 1001 patients (mean age 50 y, 54% men) who were intubated and receiving positive-pressure ventilation, had a ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen < 300, and had bilateral infiltrates on chest radiography consistent with pulmonary edema, without evidence of left atrial hypertension. Exclusion criteria included pulmonary artery catheter after onset of ALI; ALI > 48 hours; and coexisting chronic conditions that could influence short- and long-term survival, impair weaning, or compromise compliance with the protocol.

Intervention: Conservative ($n = 503$) or liberal ($n = 498$) fluid-management strategy. Every 4 hours for 7 days, patients were assigned to 1 of 20 options in the fluid-management protocol on the basis of central venous pressure or pulmonary-artery occlusion pressure (depending on type of catheter available), presence or absence of shock (mean arterial blood pressure < 60 mm Hg

or need for inotropes), presence or absence of oliguria (urinary output < 0.5 mL/kg per h), and presence or absence of ineffective circulation (cardiac index < 2.5 L/min per m² or cold, mottled skin with capillary refilling time > 2 sec).

Outcomes: Death at 60 days. Secondary outcomes were ventilator-free days from day 1 to 28, and intensive care unit (ICU)-free days and organ failure-free days at days 1 to 7 and 1 to 28. The study had 90% power to detect a 10% difference between groups in death at 60 days.

Patient follow-up: 99.9% (intention-to-treat analysis).

MAIN RESULTS

During the study, the 7-day cumulative fluid balance was lower in the conservative-strategy group than in the liberal-strategy group (-136 vs 6992 mL, $P < 0.001$). The conservative- and liberal-strategy groups did not differ for mortality at 60 days (Table). The

conservative strategy led to more ventilator-free days, ICU-free days (Table), and days free of central nervous system failure (from d 1 to 7 and d 1 to 28), although it led to a small excess in cardiovascular dysfunction during the first 7 (but not 28) days. Groups did not differ for days free of cardiovascular, renal, or hepatic failure or for coagulation abnormalities in the first 28 days.

CONCLUSION

In patients with acute lung injury, a conservative fluid-management strategy improved lung function and shortened the duration of mechanical ventilation and intensive care without increasing nonpulmonary organ failure and without affecting overall mortality.

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*See Glossary.

Conservative vs liberal fluid management strategy for acute lung injury†

Outcomes	Follow-up	Conservative	Liberal	RRR (95% CI)	NNT
Death	60 d	25.5%	28.4%	10% (-10 to 27)	Not significant
Difference (CI)					
Ventilator-free d	28 d	14.6	12.1	2.5 (1.1 to 3.9)	
ICU-free d	28 d	13.4	11.2	2.2 (1.1 to 3.3)	

†ICU = intensive care unit. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The trial by Wiedemann and colleagues compared a conservative with a liberal fluid strategy, both using an explicit hemodynamic protocol. Of the 11 512 patients screened, 10 511 were excluded. Exclusion criteria included renal failure requiring dialysis, chronic lung disease (e.g., FEV₁ < 20 mL/kg), recent myocardial infarction, and severe liver dysfunction. The enrolled and randomized patients were relatively young (mean age 50 y), with disease of mild severity and oxygen index of moderate severity. It is therefore likely that the excluded patients represent those who intensivists treat frequently, thus limiting the generalizability of the study.

A previous practice-changing study by Rivers and colleagues (1) showed that vigorous resuscitation of patients in septic shock with an early, goal-directed therapy protocol (meaning copious fluids in the first 6 h) was associated with a large mortality benefit (> 30% relative and > 15% absolute risk reductions). Direct comparison of the 2 studies is problematic because of differences in stage of patients' critical illness:

early shock within hours of presentation compared with a postresuscitation phase > 40 hours after ICU admission. Thus, we could and probably should differentiate between the 2 situations: patients in early septic shock who require goal-directed fluid resuscitation and those at a later stage who are adequately resuscitated but showing signs of ALI.

The study by Wiedemann and colleagues supports the hypothesis that a conservative fluid strategy helps to wean patients from mechanical ventilation and in the context of other knowledge reminds us that patient selection is key. Caution should be exercised to avoid applying this strategy to high-risk, inadequately resuscitated patients in early shock.

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Reference

- Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345:1368-77.