Fluid-Management Strategies in Acute Lung Injury

TO THE EDITOR: The results of the Fluid and Catheter Treatment Trial (FACTT) conducted by the National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network (June 15 issue)[1] support a conservative strategy of fluid management in patients with acute lung injury. This strategy should be recognized as only a step in the right direction. The furosemide dosing algorithm in the conservative-strategy group (range, 128 to 167 mg per 24 hours) simply resulted in an even — not negative — net fluid balance, which may have mitigated the potential magnitude of the benefit. Protocol-guided diuretic management, with individualized titration of the dose to achieve a net diuresis, can be readily and safely implemented in the intensive care unit (ICU) and is typically associated with higher doses of furosemide (range, 400 to 440 mg per 24 hours) than those used in FACTT, with the potential for even faster resolution of pulmonary edema.[2] The FACTT algorithm should not yet be viewed as "optimal" therapy, but only as an improvement on what heretofore has been considered "conventional" therapy.

Dan Schuller, M.D.

Creighton University
Omaha, NE 68131
schuller@creighton.edu

Daniel P. Schuster, M.D.

Washington University School of Medicine
St. Louis, MO 63110

1. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006;354:2564-75.
2. Schuller D, Lynch JP, Fine D. Protocol-guided diuretic management: comparison of furosemide by continuous infusion and intermittent bolus. Crit Care Med 1997;25:1969-75.

TO THE EDITOR: The investigators from the ARDS Clinical Trials Network recommend a conservative strategy of fluid management because it "shortened the duration of mechanical ventilation and intensive care." As compared with the liberal-strategy group, from day 1 to day 28 there were 2.5 more ventilator-free days and 2.2 more ICU-free days in the conservative-strategy group. Yet, the investigators do not recommend the use of methylprednisolone for ARDS despite reporting previously that patients who received methylprednisolone, as compared with placebo, had 4.2 more ventilator-free days and 2.7 more ICU-free days at day 28.[1] The investigators' conclusions regarding the management of ARDS with restrictive fluids and methylprednisolone seem contradictory. If less time on ventilators and shorter ICU stays are important end points, then methylprednisolone seems a more potent means to achieve those goals than fluid-restrictive therapy. However, if we are to focus only on survival, then neither therapy should be advocated.

Alex Morizio, M.D.
Yizhak Kupfer, M.D.
Sidney Tessler, M.D.

Maimonides Medical Center
Brooklyn, NY 11219
stessler@maimonidesmed.org

1. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl J Med 2006;354:1671-84.

TO THE EDITOR: Investigators in the ARDS Clinical Trials Network report the results of a randomized study of two strategies for volume resuscitation. They conclude that "the conservative strategy of fluid management improved lung function and shortened the duration of mechanical ventilation and intensive care" without affecting mortality adversely. Unfortunately, the number of days without mechanical ventilation is presented in Figure 3 of the report but is not analyzed. The "free-day" analysis presented in the article is a combined end point including mortality; therefore, it is inappropriate to draw conclusions about the duration of mechanical ventilation as compared with free days.

The authors should provide the duration of mechanical ventilation and ICU stay (mean, median, and a measure of dispersion) in the two groups for all patients, and these data should be separated according to survivors and nonsurvivors.[1]

Andre C.K.B. Amaral, M.D.

Hospital São Lucas
70390 155 Brasilia, Brazil
decopastorius@yahoo.com.br

Veronica M. Amado, M.D., Ph.D.

University of Brasilia
70840 901 Brasilia, Brazil

Dr. Amaral reports having received funding from Eli Lilly.

1. McMahon RP, Harrell FE Jr. Joint testing of mortality and a non-fatal outcome in clinical trials. Stat Med 2001;20:1165-72.

Downloaded from www.nejm.org by JOHN VOGEL MD on July 31, 2009 .
Copyright © 2006 Massachusetts Medical Society. All rights reserved.

THE AUTHORS REPLY: In response to Schuller and Schuster, we emphasize that patients in the conservative-strategy group in FACTT received individualized protocol-guided diuretic management in which the use of furosemide was titrated to an end point (e.g., central venous pressure <4 mm Hg) or to a physiological event usually considered to be limiting (e.g., hypotension). We believe that diuretic therapy was essentially maximized in these patients. Although the mean fluid balance over a period of 7 days in this group was 0 ml, some subgroups had a negative fluid balance. For example, in the conservative-strategy group, for patients who were not in shock at baseline, the mean fluid balance was –1576 ml. Comparisons between our study and that of Schuller and colleagues[1] are confounded by major differences in patient characteristics. Whereas the 1000 patients enrolled in FACTT all had a clinical diagnosis of acute lung injury and ARDS, all 33 patients in the study by Schuller and colleagues had a condition for which "aggressive intravenous diuresis was intended." Twenty-six (79%) of these patients had congestive heart failure, and some others had renal failure with fluid overload. It is not surprising that these patients received a higher average daily dose of furosemide and had a more negative fluid balance than patients in FACTT.

Morizio and colleagues correctly point out that the use of corticosteroids increased ventilator-free days at day 28 in patients with persistent ARDS.[2] However, the difference in the proportion of patients who were breathing without assistance narrowed substantially after day 28.[2] Twenty patients in the methylprednisolone group required resumption of ventilatory assistance after attainment of unassisted breathing as compared with only six patients in the placebo group. Furthermore, serious adverse events of neuromyopathy were reported in nine patients, all of whom were in the methylprednisolone group. In view of these considerations, the ARDS Clinical Trials Network investigators do not think that the routine use of methylprednisolone for ARDS can be supported, unless the risk–benefit profile can be modified. In contrast, the conservative fluid-management strategy in FACTT was safe, and the benefit in the proportion of patients breathing without assistance was sustained beyond day 28.

Amaral and Amado are correct in pointing out that ventilator-free days and the duration of mechanical ventilation are not equivalent. In stating that the conservative fluid-management strategy shortened the duration of mechanical ventilation, we were referring only to survivors. The data to support this statement (Table 1) were not included in our report for the sake of brevity.

Table 1. Duration of Mechanical Ventilation.*

Fluid Strategy	No. of Patients	No. of Days of Mechanical Ventilation		
		Mean	Median	Standard Error
Liberal	356	13.59	9.00	0.77
Conservative	375	10.37	6.00	0.66

* P<0.001 by the Wilcoxon test.

Herbert P. Wiedemann, M.D.
Cleveland Clinic
Cleveland, OH 44195
wiedemh@ccf.org

Arthur P. Wheeler, M.D.
Vanderbilt University
Nashville, TN 37235

Douglas Hayden, M.A.
Massachusetts General Hospital
Boston, MA 02114

1. Schuller D, Lynch JP, Fine D. Protocol-guided diuretic management: comparison of furosemide by continuous infusion and intermittent bolus. Crit Care Med 1997;25:1969-75.
2. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl J Med 2006;354:1671-84.

Downloaded from www.nejm.org by JOHN VOGEL MD on July 31, 2009 .
Copyright © 2006 Massachusetts Medical Society. All rights reserved.