Acute Respiratory Distress Syndrome

TO THE EDITOR: In their review of the acute respiratory distress syndrome (ARDS) (Aug. 10 issue), Thompson et al. recommend that patients be placed in the prone position when the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (Pao₂:Fio₂) is less than 120 mm Hg. However, the guidelines for the mechanical ventilation of patients with ARDS recommend this strategy for patients with severe ARDS, which the guidelines define as a Pao₂:Fio₂ of less than 100 mm Hg. Furthermore, one of the inclusion criteria for a trial that showed a decrease in mortality with this maneuver was a Pao₂:Fio₂ of 150 mm Hg or less. In regard to neuromuscular blocking agents, Thompson et al. recommend the use of such drugs when the Pao₂:Fio₂ is less than 150 mm Hg. This statement is in agreement with the guidelines for the use of neuromuscular blocking agents in critically ill patients, but the trial conducted by Papazian et al., which is cited by the authors, showed that these agents had a beneficial effect on survival at 90 days for patients with a baseline Pao₂:Fio₂ of less than 120 mm Hg. This finding has important clinical relevance, since the thresholds defined for the initiation of interventions, if unclear, may lead to inappropriate exposure to these interventions or delays in their withdrawal, either of which may put patients at risk.

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Richard M. Stone, M.D.
Dana–Farber Cancer Institute
Boston, MA
richard_stone@dfci.harvard.edu
Richard A. Larson, M.D.
University of Chicago Medicine
Chicago, IL
Hartmut Döhner, M.D.
University Hospital of Ulm
Ulm, Germany

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THE AUTHORS REPLY: Eskazan speculates that a regimen using daunorubicin at a dose of 90 mg per square meter (with or without midostaurin) would lead to superior outcomes as compared with the regimen of daunorubicin at a dose of 60 mg per square meter plus midostaurin that was used in the CALGB 10603 trial. However, at the time that the trial was designed, neither the results showing the superiority of induction with daunorubicin at a dose of 90 mg per square meter as compared with 45 mg per square meter in FLT3-mutated AML nor those suggesting that the higher dose of this anthracycline might be better than 60 mg per square meter in FLT3-mutated AML were available. These cited data are derived from retrospective analyses that were not powered to show significant differences. With all the caveats involved in comparing one trial with another, the results with the induction of daunorubicin at a dose of 60 mg per square meter plus midostaurin in the CALGB 10603 trial were, if anything, slightly better than the results with a dose of 90 mg per square meter in the Eastern Cooperative Oncology Group 1900 (E1900) trial and the U.K. Medical Research Council AML17 trial.

A detailed analysis of the effect of NPM1 mutations on the outcome in each group of the CALGB 10603 trial is of interest. In the preliminary trial, concurrent administration of midostaurin and chemotherapy had neither a better side-effect profile nor better efficacy than the sequential schedule used in the CALGB 10603 trial. However, we agree that further exploration of midostaurin schedules and effects on target inhibition are warranted.
TO THE EDITOR: Thompson et al. do not include drugs as a possible trigger for ARDS. For example, some of the drugs used to treat cancer, such as cytarabine, gefitinib, gemcitabine, vinblastine, and vincristine, are a well-recognized cause of ARDS. As cytarabine, gefitinib, gemcitabine, vinblastine, and vincristine, are a well-recognized cause of ARDS, and vincristine, are a well-recognized cause of ARDS. For example, some of the drugs used to treat cancer, such as cytarabine, gefitinib, gemcitabine, vinblastine, and vincristine, are a well-recognized cause of ARDS.


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THE AUTHORS REPLY: The official clinical practice guideline of the American Thoracic Society, the European Society of Intensive Care Medicine, and the Society of Critical Care Medicine strongly recommends the use of the prone position in patients with a PaO₂/FIO₂ of 100 mm Hg or less; this approach is supported by data showing a lower risk of death, as compared with the use of mechanical ventilation in the supine position. However, there was a lack of consensus regarding the use of the prone position in patients with a PaO₂/FIO₂ of 101 to 150 mm Hg owing to a “lower confidence in the balance between desirable as compared with undesirable outcomes in this subgroup of patients.”

As we noted in our review, a recent global survey of more than 29,000 patients who received mechanical ventilation showed that ARDS, even in its severest form, is underrecognized. The prone position was used in only 16.3% of patients recognized by clinicians as having severe ARDS (patients with a PaO₂/FIO₂ of less than 100 mm Hg), the subset in which the evidence of benefit is strongest and for which we have consensus. Accordingly, increased recognition of ARDS and increased use of ventilation with patients in the prone position in the subset of patients with severe disease should be high priorities. We agree with Jaramillo-Rocha that thresholds should also guide the decision to change from the prone to the supine position at a PaO₂/FIO₂ of at least 150 mm Hg, measured approximately 4 hours after returning to ventilation in the supine position, with a positive end-expiratory pressure of 10 cm of water or less and an FIO₂ of 0.6 or less, as reported by Guérin et al. We agree that drug-induced lung disease should be considered when assessing a patient with ARDS and note this in Table 3 of our article, available at NEJM.org. We thank Ben Salem for drawing attention to this important clinical caveat.
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