14 ± 1 per min to 15 ± 1 per min, and the HR increased from 82 ± 4 per min to 87 ± 6 per min. In this study, the role of muscle-derived IL-6 should be further clarified in order to accurately document the effect of hypoxia on IL-6.

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REFERENCES


Response

To the Editor:

We thank Drs Su and Chou for their interest in our recent article in CHEST (July 2010), and submit our response to the comments made. We would like to clarify that although our study did demonstrate a rise in markers of coagulation and serum IL-6 in response to hypoxic challenge, such an association does not necessarily imply a causal relationship. We accept that the origin of the rise in serum IL-6 in response to hypoxia is not clear and, moreover, may not necessarily reflect a rise in IL-6 at the tissue level. We agree with the authors that respiratory muscles may be a possible source for increased IL-6 release as a consequence of hypoxia stimulating ventilation. Indeed, our department has demonstrated a rise in serum IL-6 in response to exercise in patients with cystic fibrosis. However, given the modest rise in respiratory rate in the patients undergoing hypoxic challenge, it would seem unlikely that the increased load on respiratory muscles could solely account for the rise in serum IL-6. A number of other studies have similarly demonstrated a rise in serum IL-6 and other inflammatory markers in response to hypoxia, although the exact mechanism for this association is yet to be elucidated.

Of possible greater interest is whether this rise in serum IL-6, regardless of its origin, contributes to the rise in markers of coagulation, as is postulated in other disease states associated with chronic systemic inflammation. Such a question only can be answered by future studies examining the relationship among hypoxia, systemic inflammation, and coagulation in patients with systemic inflammation and healthy control subjects.

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Turning the Dial to Futility

To the Editor:

In a recent editorial in CHEST (April 2010), Hubmayr and Farmer questioned the rationale of “rescuing” patients with 2009 influenza A(H1N1) by using extracorporeal membrane oxygenation (ECMO) when they are failing using conventional treatment. The argument was made that results2 similar to what has been reported in New Zealand4 with the use of ECMO can be achieved without ECMO or other critical-care interventions (eg, nitric oxide [NO], prone positioning). The authors argue that physiologic end
points that have been deemed unsafe may need further study. We agree with the authors that several laboratory investigations call into question the currently considered limits of human physiologic endpoints. Indeed, we have explored some of the same limits in our large animal studies of ARDS, including CO2 removal, pH regulation, and partial respiratory support.8,9

Although we agree that specific entry criteria for ECMO remain a moving target, pushing the physiologic envelope to the point of harm is counterproductive. The lesson learned from the numerous low-tidal-volume and positive end-expiratory pressure trials may be that the ventilator dials can only be “tweaked” to the point of minimizing harm before the point of futility is reached. Patients who cannot be supported by the ventilator are the target ECMO audience. Until we can predict with certainty which patients are at risk for death or long-term morbidity from severe respiratory physiologic extremes, we support ECMO when the “turning of the dials” reaches the point of futility.

We cannot continue to judge the efficacy or risk of ECMO on the basis of 20-year-old (and 30-year-old) trial data. The high morbidity and mortality seen in those trials are no longer relevant to a discussion of critical care in 2010. The real lesson of the CESAR (Conventional Ventilation or ECMO for Severe Adult Respiratory Failure) trial is that patients cared for in a high-volume critical-care hospital with the latest critical-care techniques, including ECMO, NO, and prone positioning, do significantly better than patients in a community hospital.10 The CESAR trial showed that the high morbidity previously reported with cannulation for ECMO is also a thing of the past. Through improved technology, the risk/benefit comparison for ECMO has changed. The best evidence to date remains that outcomes at a hospital with a full armamentarium of critical-care interventions, including ECMO, are better than in a community hospital.

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Response

To the Editor:

We thank Drs Lynch and Zwischenberger for their thoughtful comments regarding the appropriate use of extracorporeal membrane oxygenation (ECMO) in patients with severe or refractory respiratory failure. Dr Lynch and Zwischenberger point out that the real lesson of the CESAR (Conventional Ventilation or ECMO for Severe Adult Respiratory Failure) trial is that patients who are referred to large centers with state-of-the-art critical care facilities do better than those patients cared for in community hospitals.1 We could not agree more! We simply caution that expertise in the delivery of critical-care services should not be confused with the availability of ECMO.

We concur with Drs Lynch and Zwischenberger that continued “turning of the [ventilator] dials,” in spite of a failure to achieve acceptable cardiopulmonary therapeutic end points, can lead to undesired outcomes. But for some patients, further efforts using conventional approaches, with different hands on the dials, can still yield benefit. In the CESAR trial, 22 of the 90 patients who were randomized to the ECMO center actually improved and recovered without ECMO.

Drs Lynch and Zwischenberger also point out that advances in the ease and safety of gaining vascular access have substantially reduced the risk to benefit ratio of ECMO. Once again we agree, only to point out that even in the hands of the CESAR investigators, the risk of serious vascular complications, including hemorrhagic stroke, remains between 3% and 5%. As we previously stated, we believe that this modality remains an experimental rescue therapy to be employed by “ECMO experts,” as opposed to a treatment that should be made generally available to all patients with severe ARDS.2

Considering the spectacular advances of Western medicine’s ability to support failing cardiopulmonary systems, there is no doubt in our minds that in certain centers the use of ECMO in treating patients with severe ARDS has become more than feasible. There

References