



Stress-Induced Pulmonary Systolic Hypertension in Patients With Scleroderma

To the Editor:

We read with great interest the study of Alkotob et al (July 2006)¹ on pulmonary hypertension (PHTN) in patients with scleroderma. They demonstrate that stress-induced pulmonary systolic hypertension in patients with scleroderma is highly prevalent, 46%, defined by an abnormal rise in pulmonary artery systolic pressure (PASP) > 40 mm Hg during exercise. The question is: are really all these patients a risk population of PHTN?

Knowledge of the risk for the development PHTN is essential. Chang et al² observed that among 361 patients undergoing serial echocardiography without initial evidence of PHTN, mild-to-moderate PHTN developed in 25.5%, significantly lower than 46% referred.

We have also determined the prevalence of stress-induced pulmonary artery hypertension in 49 patients with scleroderma. We excluded patients receiving treatment with sildenafil, bosentan, or prostacyclin analogues for severe Raynaud phenomenon in 3 months previous.

In our study, the prevalence was 42% (PASP > 40 mm Hg), 31.7% (PASP > 50 mm Hg), 19.5% (PASP > 60 mm Hg), and 9.8% (PASP > 65 mm Hg), respectively. In this last group, all patients had normal resting pulmonary arterial pressure; we observed a significantly higher prevalence of severe Raynaud phenomenon and diffusion capacity < 80% of predicted. Thus far, two patients (50%) with PASP > 65 mm Hg have acquired resting PHTN within the 1-year period, whereas only two patients (10%) with PASP from 50 to 60 mm Hg at exercise acquired PHTN.

The cut-off of PASP at exercise has not been established. We think that for the definition of PHTN, the value at exercise must be > 40 mm Hg, probably 50 mm Hg, and that this group would be intensely observed for the development of resting PHTN.

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Response

To the Editor:

We appreciate the remarks of Callejas et al concerning our recent article in *CHEST* (July 2006).¹ The prevalence of a pulmonary artery systolic pressure of > 40 mm Hg in our patients was similar to that in the population described. In order to qualify as a positive response, we agree that patients should produce a minimum value of 40 mm Hg + right atrial pressure during exercise; a less robust response most often indicates pulmonary venous hypertension. For now, we believe it prudent to study all patients whose resting pulmonary artery pressure is normal and whose exercise pressure exceeds 40 mm Hg + right atrial pressure. Currently, we repeat the exercise echocardiogram every 3 to 6 months in those patients.

As noted,¹ several of our patients ultimately progressed to resting pulmonary hypertension. Both of the markers for such disease progression, and the mechanism for stress-induced pulmonary hypertension remain the subject of intense interest and ongoing investigation.

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Severe Sepsis and Septic Shock

Should Blood Be Transfused To Raise Mixed Venous Oxygen Saturation?

To the Editor:

We share the sentiments expressed by Otero et al¹ (November 2006) regarding the importance of reducing mortality from severe

sepsis, and applaud their efforts to develop early intervention strategies. While agreeing on the salutary effects of early and vigorous fluid resuscitation, we question the focus on mixed venous oxygen saturation (SvO₂) as a centerpiece of the early goal-directed therapy (EGDT) algorithm. Specifically, we add a cautionary note against using blood transfusions to raise SvO₂ > 70%.

In the study by Rivers et al,² basal hematocrit was almost 35% in both groups, which would argue against transfusion. However, 64.1% of the EGDT subjects received transfusions. This we believe was the consequence of two interacting factors related to the study itself. Firstly, the larger volume of IV fluids received in the EGDT group caused greater hemodilution. Secondly, the intervention protocol dictated SvO₂ > 70%. According to the Fick principle, SvO₂ varies directly with arterial oxygen saturation, cardiac output, and hemoglobin concentration and inversely with oxygen consumption. Hemodilution-induced decreases in hemoglobin concentration would have had a depressing effect on SvO₂. Since blood transfusion is the most energy-efficient way to raise SvO₂, more so than the administration of dobutamine, which increases both cardiac output and oxygen consumption, it is not surprising that transfusion became the workhorse with which to achieve SvO₂ > 70%. The unanswered issue is whether a transfusion-induced increase in SvO₂ is tantamount to improved cellular oxygen utilization. We think not.

Otero et al¹ assert that transfusions had a "physiologic effect." Indeed they did, but that effect was the expected increase in SvO₂, not necessarily improved cellular bioenergetics. Transfusion at similar hemoglobin concentrations has been found not to increase tissue oxygen utilization in septic patients³ or in trauma patients.⁴ In addition to these physiologic considerations, the large-scale clinical trials⁵ suggesting harm associated with transfusions remain concerning.

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Response

To the Editor:

We would like to thank Drs. Jha and Gutierrez for emphasizing the importance of evaluating more than a single parameter, such

as central venous oxygen saturation (ScvO₂), as the centerpiece of decisions regarding resuscitation of patients with severe sepsis, especially in the use of transfusion therapy.

Our recent article in *CHEST* (November 2006)¹ was aimed at elucidating the rationale behind the stratified treatment strategy of early goal-directed therapy (EGDT).² EGDT includes optimization of preload, afterload, arterial oxygen content, and subsequently contractility using a serial sequence of end points that incorporates ScvO₂ among other important end points.

Although it is true that ScvO₂ alone cannot be used as the only indicator of oxygen delivery, patients in the control and treatment arms were also monitored with serial assessments of various metabolic parameters including repeated measurements of lactate and base deficit. Although oxygen extraction ratios were not calculated in the original study, one can conceive that the improvement in ScvO₂ in combination with the decrease in lactate level may signify an improvement in the imbalance between systemic oxygen demands and delivery.

As Dr. Jha points out, the baseline hematocrit was not the basis for transfusing a patient 3 h into the resuscitation. It was a uniform observation that the volume provided during the resuscitative course decreased the hematocrit by 30% at 3 h. The hematocrit value in the presence of a decreased ScvO₂ and an increased lactate level signifies supply dependency and inadequate oxygen delivery. This has pathologic consequences in patients with cardiopulmonary comorbidities.³⁻⁵

Dr. Jha also indicated that the Fick equation suggests a direct correlation between oxygen consumption and arterial oxygen content. Previous studies⁶⁻⁸ are inconsistent on whether RBC transfusion increases tissue oxygen utilization. These studies reflect the presence of patients who were in the later stages of ICU admissions and who did not have the same degree of global tissue hypoxia as the patients in the EGDT study.² If one concedes that the resolution of hypoperfusion at a local tissue level is clinically suggested by an increase in lactate clearance, as seen in the EGDT arm, then it logically proceeds that there must be improved perfusion at a cellular level.⁹ While animal and human data indicate deranged rheologic characteristics of RBCs in the setting of sepsis,¹⁰ which may impair microcirculatory flow,¹¹ the outcome implications of these findings remain to be determined in this specific patient population.

One must remember that every component of EGDT has been part of critical care management for > 25 years. The relative contribution of each of these components is difficult to fully quantify, but the absolute consistent benefit of mortality reduction is the most important end point until we come up with something better.

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Dr. Otero has received a research grant from Biosite, Inc., which ran the assays cited in the abstract reference 9. Dr. Rivers has spoken on behalf of Edwards Lifesciences and donates his honorarium to the research fund.

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