deprivation and hypoxia increased cysteine concentration, whereas homocysteine remained unchanged.

Finally, the biomarkers are very important indicators of abnormal biologic processes. A good biomarker should be precise, be reliable, have great potential in predicting chances for diseases, and be affected by the appropriated treatment. OSA is a multifactorial disease with not only cardiovascular consequences but also cognitive, neurologic, and metabolic consequences. A single biomarker that fulfills all the criteria of a good biomarker is unlikely for a multifactorial disease like OSA. I agree that a large and controlled study is needed, but cysteine could be considered a promising measure that will not replace the need for polysomnography but may help the clinician during follow-up of their patients.

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Financial/nonfinancial disclosures: The author has reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.11-0738

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Active Cytomegalovirus Infection in Nonimmunosuppressed Patients in the ICU

To the Editor:

The overall rate of active cytomegalovirus (CMV) infection in critically ill patients has been reported to be ~20% when using qualitative polymerase chain reaction (PCR) assays or the pp65 antigenemia test for screening1 and is even higher (>30%) when using real-time PCR methods.2,3 I read the article in CHEST (February 2011) by Gilbert et al4 with great interest. The authors found a very low prevalence of CMV viremia (~1%) in a cohort of nonimmunosuppressed patients admitted to a general ICU and concluded that monitoring for CMV DNAemia (although not used in the original text, the term DNAemia [the presence of DNA in plasma] should have been used instead of viremia) in this setting is not justified in the absence of clinical evidence of CMV infection.

In my opinion, the study has some limitations. First, CMV DNA detection in serum was performed by using the Cobas Ampliprep CMV Monitor test (Roche Inc; Basel, Switzerland) (detection threshold, 400 CMV DNA copies/mL). I understand that the ultrasensitive version of the assay (limit of detection, 45 CMV DNA copies/mL) was not used. We previously showed that ICU patients with active CMV infection displayed low levels of plasma CMV DNAemia (median, 67 copies/mL, with CMV DNA loads >400 copies/mL observed in ~15% of samples), as determined by a real-time PCR assay (Abbott CMV PCR kit; Abbott Molecular; Des Plaines, Illinois), with a limit of detection of ~10 copies/mL.3 Thus, the actual incidence of CMV DNAemia in the cohort of Gilbert et al4 might have been underestimated. Second, studies assessing the incidence and clinical relevance of active CMV infection in ICU patients should primarily include patients who are CMV-seropositive at the time of admission, as reactivation of latent infection rather than acquisition of primary infection is the usual mechanism underlying active CMV infection. Only 51% of patients had CMV-specific IgGs in the study by Gilbert et al.4 Third, the mean length of patients’ hospitalization in the ICU was 20.9 days.5 Earlier studies demonstrated that a relevant fraction of episodes of active CMV infection may develop after 3 weeks of ICU stay.6,7 Fourth, in a previous study,5 CMV reactivation was diagnosed in around 25% of ICU patients solely on the basis of the presence of CMV DNA in tracheal aspirates, indicating that monitoring for the presence of CMV in the blood compartment may underestimate the incidence of active CMV infection in this clinical setting.

A causal link between CMV infection and adverse clinical outcomes in ICU patients is far from proven. Only a randomized controlled trial of antiviral prophylaxis with a drug with specific activity against CMV may shed light on this issue.8 Until then, a debate on whether to screen critically ill patients for active CMV infection is pointless.

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DOI: 10.1378/chest.11-0289

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Limitations Inherent to the Simplified Bernoulli Equation

Explain the Inaccuracy of Doppler Echocardiographic Estimates of Pulmonary Artery Pressures in Patients With Pulmonary Hypertension

To the Editor:

I would like to congratulate Rich and colleagues, who, in their recent article in CHEST (May 2011), showed clinically relevant discrepancies between Doppler-estimated and invasively measured pulmonary artery systolic pressure (PASP) in >50% of measurements, discrepancies not resolved by simultaneous measurement of the two entities. Imprecise right atrial pressure estimation, suboptimal alignment between the Doppler beam and the regurgitant jet, and the presence of severe tricuspid valve regurgitation were suggested as the causes of the discrepancy. However, even when beam alignment and right atrial pressure estimation are correct, significant discrepancies between the two measurements should be expected because of limitations inherent to the simplified Bernoulli equation. Indeed, the simplified Bernoulli equation assumes negligible viscous and inertial forces and complete conversion of potential energy (the pressure in the right ventricle) into kinetic energy (that of the regurgitant jet).

However, as highlighted in a recent mock circuit experiment, many conditions commonly encountered in clinical practice can result in an imperfect transformation of potential to kinetic energy. For example, an eccentric regurgitant jet would interact with the nearby atrial wall, causing viscous losses that are evident as the Coanda effect and that are associated with a 24% underestimation by Doppler of invasive pulmonary artery pressure. Increased blood viscosity observed in patients with hypoxemia, and, in particular, in patients with intracardiac defects and Eisenmenger physiology, can also cause discrepancies between Doppler and invasive estimates of PASP. Indeed, increasing hematocrit causes occurrences of viscous losses that are not accounted for by the simplified Bernoulli equation, leading per se to a 49% underestimation of invasive PASP by Doppler.

All factors mentioned so far are associated with underestimation of PASP by Doppler. However, overestimation was as common as underestimation in the article by Rich et al, and some other factors have to intervene to explain this finding. Experimental evidence suggests that when blood viscosity is reduced, such as during anemia, or when absolute right atrial size (in centimeters) is small, such as in children or young women, inertial forces not accounted for by the simplified Bernoulli equation may cause pressure recovery in the receiving chamber, causing overestimation of PASP by Doppler.

As mentioned by Rich et al, transthoracic echocardiography is an invaluable tool in the management of patients with pulmonary hypertension. Because conditions that limit the applicability of the simplified Bernoulli equation are ubiquitous in clinical practice, the education of clinicians in recognizing those conditions is of extreme importance.

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DOI: 10.1378/chest.11-0344

Response

To the Editor:

We thank Dr Giardini for his interest in our study. Dr Giardini suggests that explanations exist beyond those cited in our article to explain the discrepancies in Doppler estimates of pulmonary artery systolic pressure (PASP). He cites limitations inherent to the modified Bernoulli equation, including the assumptions of (1) negligible viscous forces (which may not be the case under hypoxic, anemic, or polycythemic conditions), (2) the complete conversion of potential to kinetic energy (which may not occur in the presence of eccentric regurgitant jets), and (3) inertial forces (which may occur in small receiving chambers, resulting in the pressure recovery phenomenon).

We agree with Dr Giardini that alternative explanations, including some of those he cites, may exist to further explain Doppler-cardiac catheterization PASP discrepancies in patients with pulmonary hypertension. We were particularly interested in the possibility that viscous factors may have accounted for some of the inaccuracies we observed in our study. We, thus, created a multivariate model from our simultaneous Doppler-cardiac catheterization data to evaluate whether oxygen saturation and/or hemoglobin levels were associated with differences in Doppler-cardiac catheterization estimates of PASP. Neither oxygen saturation nor hemoglobin level were associated with differences in Doppler-cardiac catheterization estimates of PASP (β coefficient, –1.72 ± 1.95 and –2.24 ± 3.83, respectively;