Communications to the Editor

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Steady-State End-Tidal Alveolar Dead Space Measure and D-dimer

To the Editor:

We read with interest the article by Dr. Rodger and coworkers in a recent issue of CHEST (July 2001) regarding the use of a bedside combination of plasma d-dimers and alveolar dead space measurement in excluding pulmonary embolism. The authors showed on 246 study patients that the addition of the capnographic measurement of the alveolar dead space to the d-dimer determination allowed the sensitivity to increase from 83 to 97.8% in ruling out pulmonary embolism without additional diagnostic testing.

The d-dimer assays used in the study (latex and whole-blood agglutination tests), even if the most extensively studied rapid d-dimer assays, may be subject to criticism for their suboptimal sensitivity (varying from 63 to 89%), especially since the emergence of new, rapid enzyme-linked immunosorbent d-dimer assays, which have been validated as screening tests for the exclusion of pulmonary embolism with a sensitivity of 99.5%. Consequently, the benefit of associating agglutination d-dimer tests and alveolar dead space fraction measurements in order to better rule out pulmonary embolism (sensitivity 97.8%) is similar to the performance of a rapid enzyme-linked immunosorbent d-dimer assay alone. Therefore, a new question arises to know if alveolar dead space determination with capnography brings some additional information in case of positive d-dimer values (>500 ng/mL) with the rapid enzyme-linked immunosorbent assay.

As explained by Colp and Stein in the editorial of the same issue of CHEST, we are concerned by the diagnostic performance of alveolar dead space measurement in excluding pulmonary embolism. In a recent multicenter study by Kline et al, the alveolar dead space fraction, determined with volumetric capnography, showed a low sensitivity (67%), probably because a proved pulmonary embolism may physiologically be associated with normal alveolar dead space due to a reflex hypocarbic bronchoconstriction or, in case of pulmonary infarction, atelectasis or small peripheral embolisms.

In conclusion, we believe that the interest of capnography as a screening test for pulmonary embolism has still to be evaluated, and that this very interesting article brings more questions than answers.

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References

4 Colp C, Stein M. Re-emergence of an “orphan” test for pulmonary embolism. Chest 2001; 120:5–6

To the Editor:

We agree that enzyme-linked immunosorbent d-dimer assays have been shown to have higher sensitivity than latex and whole-blood agglutination d-dimer assays. However, this higher sensitivity comes at a cost of lower specificity (excluding fewer patients without pulmonary embolism suspected of having pulmonary embolism), less rapid turnaround time, and capital expenditures to set up the enzyme-linked immunosorbent d-dimer assays that are not required for latex and whole-blood agglutination tests. Hence, in smaller hospitals, adoption of latex and whole-blood agglutination d-dimers is more realistic than enzyme-linked immunosorbent assays or rapid enzyme-linked immunosorbent d-dimer assays.

We share the concern of Dr. Verschuren and Dr. Thys that alveolar dead space measurement and these easily adoptable d-dimer assays do not have excellent sensitivity on their own. However, upon further validation, we are optimistic that the combination of low alveolar dead space fraction and negative d-dimers will be able to exclude pulmonary embolism at the bedside in the large proportion of patients with suspected pulmonary embolism.

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Coronary Endothelial Dysfunction in Patients With Hypertrophic Cardiomyopathy

To the Editor:

I read with great interest the letter by Kodama-Takahashi et al. and I disagree with their comments on several points, outlined here.

First, temporal occlusion of the left anterior descending (LAD) coronary artery that developed in some patients was induced by acetylcholine infusion at the highest dose. This occlusive response was also classified as a marker of coronary endothelium dysfunction. Importantly, at a lower dose, acetylcholine constricted the LAD in these patients.

Second, in some patients, even a high dose of acetylcholine (100 μg) induced mild vasodilation (not vasoconstriction) in LAD.

Last, Maseri et al. proposed that it would be reasonable to assume that nonocclusive spasm (defined as segmental constriction reducing local diameter by at least 50% in arteries without significant stenosis) represents the obligatory substrate of occlusive spasm in response to a stronger stimuli. In the article by Kodama et al., the stronger stimulus seems to be the highest dose of acetylcholine. In some patients with endothelial dysfunction, acetylcholine induced vasoconstriction, reducing the diameter > 50%. To evaluate whether patients in the study by Kodama et al. have coronary endothelial dysfunction, I postulated that the authors should present precise data. The dose-dependent effect of acetylcholine (according to the method description, acetylcholine was infused to LAD in increasing doses of 20, 50, and 100 μg) on reduction of LAD diameter should be provided. Also data concerning the occurrence of risk factors of endothelial dysfunction (hypertension, hypercholesterolemia, smoking, and/or diabetes mellitus) are needed to explore whether endothelial dysfunction is a primary defect (due to intrinsic coronary vascular abnormality in hypertrophic cardiomyopathy) or is secondary to the above-mentioned risk factors (as postulated in a previous article of Kodama et al.).

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REFERENCES

To the Editor:

We wish to thank Dr. Dimitrow for his continued interest in our articles. In his letter, he disagreed with our comment that from our two studies alone we are unable to conclude that endothelial dysfunction is an intrinsic abnormality in the coronary artery system of patients with hypertrophic cardiomyopathy (HCM). On the basis of his previous work, he has demonstrated that impaired endothelium-dependent vasodilation of coronary resistance vessels, which is one of the potential mechanisms of myocardial ischemia, is seen in HCM, and that verapamil therapy improves this endothelial dysfunction.

When provocation tests for coronary vasospasm are performed in the catheterization laboratories of our hospitals, an intracoronary bolus injection of acetylcholine of 20 to 100 μg is used because of its effectiveness and safety. In our two previous studies, acetylcholine tests were performed in order to evaluate whether vasospasm at the level of epicardial coronary arteries occurs in patients with and without HCM. The purpose of the acetylcholine injections was not to evaluate whether subjects had coronary endothelial dysfunction. In the first study, coronary vasospasm was induced in 10 of 36 patients (28%) with HCM. At the dose we used, the specificity of the provocation tests using acetylcholine to detect coronary vasospasm is very high in the Japanese patient population. Furthermore, the same dose of acetylcholine does not induce coronary vasospasm in patients without vasospastic angina in Western populations. Thus, the transient total or subtotal occlusion of the epicardial coronary artery that is induced by the highest dose of acetylcholine we used is classified as coronary vasospasm, even in HCM patients.

Acetylcholine has two opposing effects: an endothelium-dependent vasodilator effect and a direct vasoconstrictor effect. The net coronary vasoconstrictor response, either vasodilatation or vasoconstriction, depends on the balance between these two effects. In normal coronary arteries with a functionally intact endothelium, a low concentration of acetylcholine will induce vasodilatation. However, in diseased coronary arteries with dysfunctional endothelium, acetylcholine is expected to induce vasoconstriction even at the same concentration. Thus, a low concentration of acetylcholine, which corresponds to an estimated blood concentration in the coronary bed of 10⁻⁶ to 10⁻⁵ mol/L, has been used as a probe for testing endothelial function. However, even normal coronary arteries with intact endothelial function constrict in response to higher concentrations of acetylcholine by the direct effect of the agent on vascular smooth muscle. The dose of acetylcholine that we used, which corresponds to an estimated blood concentration in the coronary bed of approximately 10⁻⁴ mol/L, is so high that the direct vasoconstrictor effect overrides the endothelium-dependent vasodilator effect. Thus, a relatively high dose of acetylcholine is...