Rapid and accurate risk stratification of acute pulmonary embolism (PE) has focused on the anatomic size of the thrombus as well as the PE’s physiological effects on systemic arterial pressure, heart rate, and chest computed tomographic or echocardiographic evidence of right ventricular enlargement or dysfunction. Pulmonary embolism can also unleash a myriad of detrimental biochemical consequences. For example, release of neurohumoral factors such as serotonin can explain, at least in part, the pulmonary arterial hypertensive response to PE. The same cardiac biomarkers used to assess heart damage due to acute myocardial infarction can be used to help prognosticate after the diagnosis of acute PE is established. To quantify micronecrosis and microinfarction of the right ventricle, assay of troponin levels is part of the standard workup (1). We can also quantify right ventricular myocardial stretch due to right ventricular overload by relying on 2 additional cardiac biomarkers—brain natriuretic peptide (BNP) (2) and pro-BNP (3)—even though their utility in clinical decision-making for PE management remains uncertain.

Fatty acid binding proteins are small cytoplasmic proteins that reversibly bind hydrophobic ligands such as saturated and unsaturated long chain fatty acids, eicosanoids, and other lipids (4). Fatty acid binding proteins help maintain membrane integrity by protecting the cell from the detergent effects of excess nonprotein-bound fatty acids. They also facilitate transport of fatty acids and other lipid mediators throughout the cytoplasm of the cell.

Heart-type fatty acid binding proteins (hFABPs) are a sensitive biomarker of myocardial necrosis. After myocardial ischemic damage, hFABPs are released from damaged myocytes within 1 to 3 h and return to normal within 12 to 24 h (5). The hFABP levels can be measured by several different enzyme-linked immunoassorbent assay kits, but none have been approved for clinical diagnostic use. However, a commercially available point-of-care test kits (6) for whole blood samples (Rennesens, Berlin, Germany) (7) has been approved for diagnosis of myocardial infarction in Europe and in approximately 20 non-European countries but not in the U.S. In a registry of 2,287 acute coronary syndrome patients, hFABP elevation was independently associated with an increased risk of death, heart failure, and recurrent ischemic events (8). In a subsequent registry of 1,448 patients with acute coronary syndrome, elevated hFABP levels predicted long-term mortality and identified high-risk patients in a manner additive to clinical risk factors, troponin, and C-reactive protein. The purported mechanism to explain the advantage of hFABP is that detectable hFABP is released faster than troponin. In addition, hFABP might be released after myocardial ischemia with or without necrosis (9), whereas troponin is released only after necrosis.

Puls et al. (10) studied hFABP in 107 consecutive patients with acute PE. Abnormally elevated (i.e., >6 ng/ml) plasma levels of hFABP on admission were very reliable predictors of adverse outcome. Their prognostic value seemed superior to that of troponin and proBNP. There was almost no overlap between patients who subsequently suffered major complications and those with an uncomplicated course with regard to baseline hFABP concentrations. No patients with initially normal hFABP levels had a complicated 30-day outcome or died of PE-related causes. With respect to death or major PE-related complications, the positive predictive value (41%) of hFABP was superior to that of troponin (29%) and proBNP (19%). The hFABP but not troponin or proBNP remained a highly significant predictor of adverse outcome when the 3 biomarkers were compared with multivariable analysis. Moreover, analysis of hFABP in combination with echocardiography revealed that cardiac ultrasound offered no incremental prognostic information in the presence of a normal hFABP test. By contrast, in patients with hFABP >6 ng/ml on admission (27% of the entire study population), complication rates doubled, and the relative risk of an adverse
outcome was 4 times higher in the presence of right ventricular dysfunction on echocardiography.

In this issue of the Journal, the Konstantinides Laboratory has made an important contribution to our knowledge about cardiac biomarker use in normotensive patients with newly diagnosed acute PE (11). They studied 126 consecutive normotensive acute PE patients, of whom 7% suffered death, resuscitation, intubation, or use of catecholamines within 30 days. An elevated hFABP level was associated with an independent 16-fold increased likelihood of death or major complication within 30 days. The hFABP was also a strong predictor of long-term mortality. Most striking are the 2 figures in this report. The first figure provides receiver operating characteristic curves for hFABP, troponin, and proBNP levels. The hFABP was far more sensitive and specific for predicting 30-day complications than the other cardiac biomarkers. Qualitatively, this is depicted with a much higher “left shoulder” on the receiver operating characteristic curve than troponin or proBNP. The second figure shows that an elevated hFABP level is a much more powerful predictor of reduced long-term survival than elevation in troponin or pro-BNP.

These findings about the clinical utility of hFABP for acute PE risk stratification are welcome news. Too often, elevated troponin levels have served as “false alarms,” with patients subjected to prolonged hospital stay and triage to Intensive Care Unit beds on the basis of a “troponin leak.” Of course, no biomarker should be used outside of the clinical context for which it is developed. In the case of acute PE, no biomarker testing at all is required if the patient presents with massive PE, especially accompanied by systemic arterial hypotension requiring pressor support. At the other end of the spectrum, a PE patient who seems clinically stable, with a normal heart rate, blood pressure, and respiratory rate, as well as normal oxygen saturation and normal right ventricular size on chest computed tomography scan, will have an excellent prognosis. Cardiac biomarker testing in this context might be “icing on the cake.” However, even though the cost of biomarker testing is modest, we might not be able to afford this luxury routinely if we wish to maximize the impact of each health care dollar that we spend.

For now, I think that hFABP testing should be paired with troponin so that we can create a larger database to determine the day-to-day clinical utility of the hFABP biomarker in acute PE management. Reports on only several hundred PE patients have been published. We can assume that the enzyme-linked immunosorbent assay, which was used in the current study and which provides precise quantitative results, will be a more useful test than the qualitative point-of-care device that is widely available in Europe. Another unresolved issue is how the time course of PE will affect the hFABP result. In acute myocardial infarction, hFABP returns to normal within 24 h. Will a larger sample of acute PE patients, who are often not diagnosed until 5 days or longer after the onset of symptoms, reveal that high-risk patients with late presentation have normal hFABP levels? Finally, we must ask whether hFABP will compare favorably to the new generation of high-sensitivity troponin assays (12).

The present study opens the door to possibly more precise prognostication in patients with acute PE. The authors showed that the combination of elevated hFABP and tachycardia was especially ominous. As clinical research intensifies for PE risk stratification, hFABP seems to be a welcome addition to our armamentarium of clinical assessment, imaging, and biomarker evaluation.

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