

# Prognostic Value of Plasma Heart-Type Fatty Acid-Binding Protein in Patients With Acute Pulmonary Embolism

## A Meta-analysis

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**BACKGROUND:** Several studies have described heart-type fatty acid-binding protein (H-FABP) from early blood samples as a predictor of outcome in acute pulmonary embolism (PE). This systematic review is designed to determine the prognostic value of H-FABP aimed for use in patients with acute PE.

**METHODS:** Studies published prior to January 2013 in PubMed, Ovid, and Embase were reviewed, and the relationship between H-FABP and the risk of acute PE-related death or serious complications was evaluated. A summary estimate was calculated using the bivariate random-effects approach, and covariate analysis was used to examine sources of heterogeneity among studies.

**RESULTS:** A systematic search revealed six studies containing a total of 618 patients. Elevated H-FABP level was significantly associated with short-term death (within 30 days of embolism) (OR, 40.78; 95% CI, 11.87-140.09) and with complicated clinical events (OR, 32.71; 95% CI, 11.98-89.26). The prevalence of serious complications and death in acute PE was 51% (95% CI, 43%-59%) and 31% (95% CI, 24% -39%), respectively. The combined sensitivity and specificity for the prediction of death and serious complications was 98% and 86%, respectively.

**CONCLUSIONS:** H-FABP is associated with an increased risk of mortality or complicated clinical events in patients with acute PE across different studies with a high degree of clinical and methodologic diversity. The result suggests that H-FABP has significant prognostic value for acute PE.

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**ABBREVIATIONS:** CCE = complicated clinical event; H-FABP = heart-type fatty acid-binding protein; PE = pulmonary embolism

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Acute pulmonary embolism (PE) is a serious condition with a poor prognosis that places a significant burden on the health-care system.<sup>1</sup> Timely classification of patients with acute PE may positively impact patient-management decisions: Patients identified as having a low risk of complications may be eligible for outpatient management, whereas high-risk patients may benefit from more aggressive treatment.<sup>2</sup> Several cardiac biomarkers have emerged as indicators of right ventricular dysfunction and predictors of clinical outcome in patients with acute PE.<sup>3-11</sup> A number of studies in unselected patients with acute PE suggest that heart-type fatty acid-binding protein (H-FABP) levels upon hospital admission may more sensitively and specifically predict early adverse clinical outcomes than do cardiac troponins or natriuretic peptides.<sup>4,8-12</sup> H-FABP is an early, highly sensitive marker of myocardial injury and has been evaluated for emergency triage of patients with acute coronary syndromes.<sup>13</sup> Fatty acid-binding proteins

are relatively small cytoplasmic proteins (12-15 kDa) and are abundant in tissues with active fatty acid metabolism, including the heart.<sup>14</sup> After myocardial cell damage, H-FABP diffuses much more rapidly through the interstitial space than do troponins and appears in the circulation as early as 90 min after symptom onset, reaching its peak within 6 h.<sup>13</sup> Moreover, Cox regression analysis revealed a hazard ratio of 1.10 (95% CI, 1.04-1.18) for each 1 ng/mL increase in H-FABP level, and the continuous increase in H-FABP is an independent predictor of adverse outcome by multivariable analysis in chronic thromboembolic pulmonary hypertension.<sup>15</sup> Given the early release of H-FABP, the availability of H-FABP testing,<sup>16</sup> and the current lack of a prognostic marker with good performance in acute PE, we carried out this systematic review and meta-analysis to estimate the prognostic value of increased H-FABP levels as a cardiac biomarker in stratifying the risk of mortality or serious complications in patients with acute PE.

## Materials and Methods

### Literature Search

We performed a systematic electronic search of the PubMed, Ovid, and Embase databases for original articles published before January 1, 2013. In PubMed, the search terms used were “pulmonary embolism” AND “heart-type fatty acid-binding protein,” which yielded 11 results. In Ovid, we used the following strategy: (1) heart type fatty acid binding protein.mp. [mp = ti, ab, tx, ct, mc, st, or, tn, ps, ds, cb, rn, sq, mq, ge, tm, mi, sh, hw, bc, bo, bt, cc, gl, gn, ot, rw, nm, rs, an, ui] (752 results); (2) pulmonary embolism.mp. [mp = ti, ab, tx, ct, mc, st, or, tn, ps, ds, cb, rn, sq, mq, ge, tm, mi, sh, hw, bc, bo, bt, cc, gl, gn, ot, rw, nm, rs, an, ui] (88,551 results); (3) 1 and 2 (54 results). In Embase, we used the following strategy: (1) pulmonary AND “embolism”/exp; (2) “heart”/exp OR heart AND type AND fatty AND (“acid”/exp OR acid) AND binding AND (“protein”/exp OR protein); and (3) 1 and 2 (20 results).

### Selection of Publications

We screened the titles and abstracts of all publications for relevancy. Full-text publications were retrieved for relevant articles without language limitation. Studies were selected on the basis of whether (1) patients had an acute PE confirmed by guidelines, (2) the primary end point of the study was death or serious complications (thrombolysis, cardiopulmonary resuscitation, IV vasopressors) in relation to H-FABP testing; and (3) the completeness of the data (availability of absolute numbers of true-positive, false-positive, true-negative, and false-negative H-FABP results to allow reconstruction of the diagnostic 2 × 2 table).

### Assessment of Study Methods and Data Extraction

Information on the study characteristics (design and quality), the number and type of participants, the types of diagnostic test used, the methods by which the test was executed, and the test results were collected using a standardized data extraction form. Three reviewers (L. B. R., L. H., and P. Z.) reviewed the lists of titles and abstracts independently and used the inclusion criteria to mark potentially relevant articles for full review. Each study that was selected as potentially relevant in the search process was read and abstracted independently by four reviewers (L. B. R., L. H., S. Z., and P. Z.). Besides extracting summary statistics from the published literature for survival end points, the timing of the blood

draw was a factor we considered. The reasons for excluding particular studies are presented in Figure 1.

For each study, information was collected on (1) the use of a valid reference standard in accordance with international PE guidelines; (2) the design of the study (prospective or retrospective, single center or multicenter); (3) the treatment (number of patients who received thrombolytic therapy, underwent cardiopulmonary resuscitation, needed IV vasopressors or pulmonary embolectomy); (4) mortality; and (5) the full description of the H-FABP test and manufacturer, and the method and cutoff value for assays of other biologic markers (Table 1). The reasons for excluding particular studies are presented in Figure 1.

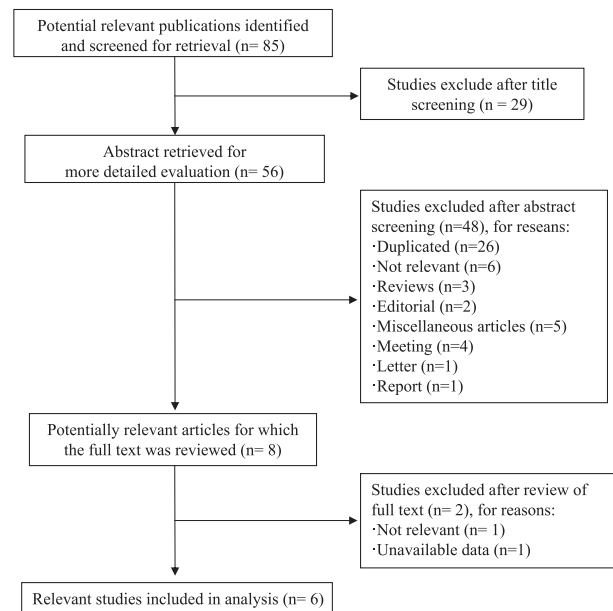


Figure 1 – Selection of studies.

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