N-Terminal Pro–Brain Natriuretic Peptide or Troponin Testing Followed by Echocardiography for Risk Stratification of Acute Pulmonary Embolism

Lutz Binder, MD; Burkert Pieske, MD; Manfred Olschewski, PhD; Annette Geibel, MD; Beate Klostermann, MD; Christian Reiner, MD; Stavros Konstantinides, MD

Background—Brain natriuretic peptide (BNP) and N-terminal (NT)-proBNP have recently emerged as promising parameters for risk assessment in acute pulmonary embolism (PE). However, their positive predictive value is low, and the prognostic implications of NT-proBNP or troponin elevation alone are questionable.

Methods and Results—To determine whether the combination of NT-proBNP testing with echocardiography may identify both low-risk and high-risk patients with PE, we examined 124 consecutive patients with proved PE. All underwent echocardiography on admission to detect right ventricular dysfunction. NT-proBNP and troponin concentrations were measured in one core laboratory. The primary end point was death or major in-hospital complications. The cutoff level of 1000 pg/mL had a high negative predictive value (95% for a complicated course, 100% for death), but NT-proBNP ≥1000 pg/mL did not independently predict an adverse outcome. Combination of NT-proBNP testing with echocardiography identified 3 major risk groups. A positive echocardiogram was associated with a 12-fold elevation in complication risk compared with patients with low NT-proBNP (P=0.002), whereas NT-proBNP elevation without right ventricular dysfunction on echocardiography only slightly increased the risk of an adverse outcome (P=0.17). The combination of cardiac troponin testing with echocardiography yielded similar complication rates in the lowest-risk group and a similar magnitude of risk elevation for the highest-risk patients, but it also increased the number of intermediate-risk groups.

Conclusions—Our results support a simple risk stratification algorithm for patients with PE, with the use of NT-proBNP or troponin testing as an initial step that should be followed by echocardiography if elevated levels of the biomarker are found. (Circulation. 2005;112:1573-1579.)

Key Words: echocardiography ■ embolism ■ natriuretic peptides ■ prognosis ■ pulmonary heart disease

Contemporary risk assessment strategies in acute pulmonary embolism (PE) concentrate on identification of patients who appear stable at presentation but have impending right ventricular failure and a high death risk. The aim is to better define potential candidates for thrombolytic therapy and help design future therapeutic trials.1,2 To date, bedside echocardiography is the best established method for the detection of right ventricular dysfunction in acute PE,3 and the prognostic relevance of echocardiographic findings has been demonstrated in a number of studies, including 2 large registries.4–6 More recently, reconstructed 4-chamber views of the heart on chest CT also were reported to detect right ventricular enlargement due to PE and predict early death.7 However, it appears impractical to demand imaging studies for risk stratification of every patient with acute PE, particularly when the logistic requirements and the substantial financial burden that such a strategy might impose on many institutions are considered.

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Cardiac biomarkers have recently emerged as promising, relatively simple prognostic indicators in patients with acute PE. For example, we8 and others9–11 showed that cardiac troponins I and T are associated with right ventricular dysfunction on echocardiography and that absence of cardiac troponin elevation at presentation predicts a favorable inhospital outcome. More recently, some reports suggested that brain natriuretic peptide (BNP) and N-terminal (NT)-proBNP levels may have an even higher negative predictive value (approaching 100%) with regard to early death, which makes them particularly useful for ruling out severe, life-threatening PE.12–15 On the other hand, the positive predictive value of
NT-proBNP was low in previous studies, and the prognostic implications of elevated natriuretic peptide levels alone remain uncertain. Therefore, the aim of the present study was to investigate whether the combination of NT-proBNP testing with an imaging modality such as echocardiography may increase the prognostic value of either diagnostic method alone and help define low-, intermediate-, and high-risk groups of patients with acute PE. Furthermore, we compared NT-proBNP with troponin testing to determine which one of the 2 biomarkers could be more appropriate to form (together with echocardiography) the basis of a reliable and simple risk stratification algorithm.

Methods

Patient Population and Study Design
The study was conducted in 2 collaborating university hospitals and prospectively included a total of 124 consecutive patients (74 women, 50 men; mean age, 60±18 years) with proved acute PE over a 45-month period. In accordance with standard diagnostic algorithms followed in both institutions, patients presenting with an intermediate or high clinical probability of venous thromboembolism and a positive D-dimer ELISA test (intermediate or high clinical probability of venous thromboembolism and a positive D-dimer ELISA test) were determined on an ADVIA Centaur Analyzer (Bayer Vital Chemalyzer, Roche Diagnostics). For cardiac troponin T, the manufacturer recommends a quantitative electrochemiluminescence assay (Elecsys 2010 analyzer).

Blood samples were obtained on admission as well as 4, 8, and 24 hours thereafter, and serum was stored at −20°C or colder at the enrolling site before being sent to the Department of Clinical Chemistry of the University of Goettingen, where samples were stored at −80°C. Samples were later analyzed in batches after a single thaw. The investigator responsible for the measurements was unaware of the patients’ baseline parameters or clinical course. The clinicians were unaware of the patients’ biomarker levels throughout the hospital stay.

NT-proBNP and Cardiac Troponin Testing
Blood samples were obtained on admission as well as 4, 8, and 24 hours thereafter, and serum was stored at −20°C or colder at the enrolling site before being sent to the Department of Clinical Chemistry of the University of Goettingen, where samples were stored at −80°C. Samples were later analyzed in batches after a single thaw. The investigator responsible for the measurements was unaware of the patients’ baseline parameters or clinical course. NT-proBNP and cardiac troponin T were determined with the use of a quantitative electrochemiluminescence assay (Elecsys 2010 analyzer, Roche Diagnostics). For cardiac troponin T, the manufacturer reported reference values <0.04 ng/mL. For NT-proBNP, the prognostically relevant cutoff value was determined by receiver operating characteristic (ROC) analysis as described below. Cardiac troponin I was determined on an ADVIA Centaur Analyzer (Bayer Vital GmbH) according to the manufacturer’s instructions. Reported values in normal healthy adults are <0.07 ng/mL.

Table 1. Clinical Symptoms and Relevant Findings at Presentation in 124 Consecutive Patients With Acute PE

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute symptom onset (within 24 h)</td>
<td>64 (52)</td>
</tr>
<tr>
<td>Syncope</td>
<td>33 (27)</td>
</tr>
<tr>
<td>Focal neurological deficit(s)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Peripheral arterial occlusion*</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>Hemodynamic instability†</td>
<td>9 (7.3)</td>
</tr>
<tr>
<td>Recent major surgery (within 14 d)</td>
<td>32 (25)</td>
</tr>
<tr>
<td>Recent major trauma (within 14 d)</td>
<td>7 (5.7)</td>
</tr>
<tr>
<td>History of venous thrombosis</td>
<td>31 (25)</td>
</tr>
<tr>
<td>History of PE</td>
<td>20 (16)</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>19 (15)</td>
</tr>
<tr>
<td>Cancer</td>
<td>25 (20)</td>
</tr>
<tr>
<td>Other predisposing conditions</td>
<td>26 (21)</td>
</tr>
<tr>
<td>RV dysfunction (echocardiogram)</td>
<td>33 (27)</td>
</tr>
<tr>
<td>Cardiac troponin T = 0.04 ng/mL</td>
<td>41 (33)</td>
</tr>
<tr>
<td>Cardiac troponin I ≥ 0.07 ng/mL</td>
<td>46 (37)</td>
</tr>
</tbody>
</table>

RV indicates right ventricular.
*Clinical and laboratory findings signifying renal, intestinal, or limb ischemia.
†Systolic blood pressure persistently <90 mm Hg with or without signs of cardiogenic shock.

Statistical Analysis
The predetermined primary end point of the study was complicated in-hospital course, defined as death or at least 1 of the following: (1) secondary (emergency) thrombolytic treatment; (2) need for catecholamine support of blood pressure (except for dopamine at the rate of ≤5 μg/kg per minute) to maintain adequate tissue perfusion and prevent or treat cardiogenic shock; (3) endotracheal intubation; or (4) cardiopulmonary resuscitation. The secondary end point was overall mortality. The prognostic relevance of the baseline parameters listed in Table 1 as well as gender and NT-proBNP was first analyzed univariately by the χ² test. ROC analysis was performed to determine the optimal NT-proBNP cutoff level with regard to prognosis. Subsequently, a multiple logistic regression model was applied to the primary combined end point, taking into account those variables that reached a probability value of <0.20 in the univariate comparison. In addition, to evaluate the role of a strategy combining cardiac biomarkers with echocardiography for risk stratification of PE, multiple logistic regression analysis compared the complication risk of 3 patient groups defined by the combination of NT-proBNP and echocardiography and of 4 groups defined by troponin T testing plus echocardiography. No adjustments for other baseline parameters were made in this latter model. The results are presented as estimated odds ratios (ORs) with the corresponding 95% CIs. All reported probability values are 2 sided.

Results

Baseline Parameters: Correlation With Clinical Outcome
The patients’ clinical symptoms, predisposing conditions, and relevant findings at presentation are shown in Table 1. Overall, 108 patients (87%) presented with dyspnea, and 64 patients (52%) reported an acute symptom onset. Hemodynamic instability, ie, persistent hypotension (systolic blood pressure <90 mm Hg or a fall in systolic blood pressure of >40 mm Hg for at least 15 minutes), cardiogenic shock, or need for cardiopulmonary resuscitation because of massive PE was present in 9 patients (7%). Importantly, none of our
patients was found to have severe preexisting left ventricular dysfunction as indicated by a left ventricular ejection fraction ≤30% on echocardiography. After clinical and echocardiographic examination, venous thromboembolism was confirmed by leg vein ultrasound imaging in 51 patients (41%), by lung scan in 93 (75%), by spiral CT scan in 27 (22%), and by pulmonary angiography in 3 patients (2.4%), alone or in combination. In 5 patients (4%), none of these procedures could be performed because of extreme hemodynamic instability, and thus PE was diagnosed on the basis of clinical and echocardiographic criteria alone, as described in Methods.

Table 2 shows the incidence of in-hospital clinical events in the study population. Of the clinical baseline parameters listed in Table 1, only hemodynamic instability at presentation was significantly associated with a complicated course by univariate analysis. The frequency of the combined end point was 89% in initially unstable patients compared with 11% in stable patients (P<0.001). In accordance with previous reports, an adverse outcome also was more frequent in patients with echocardiographic evidence of right ventricular dysfunction (37% versus 7%; P<0.001), as it was in patients with elevated cardiac troponin T or I levels (26% versus 10% and 33% versus 7%, respectively; P=0.027 for troponin T and P=0.001 for troponin I).

Table 2. In-Hospital Clinical Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated course</td>
<td>20 (16)</td>
</tr>
<tr>
<td>Death (all causes)</td>
<td>7 (5.6)</td>
</tr>
<tr>
<td>Need for thrombolytic treatment</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Catecholamine administration</td>
<td>14 (11)</td>
</tr>
<tr>
<td>Endotracheal intubation</td>
<td>11 (8.9)</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>Ischemic stroke or peripheral arterial embolism</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>6 (4.8)</td>
</tr>
<tr>
<td>Recurrent PE</td>
<td>8 (6.5)</td>
</tr>
</tbody>
</table>

NT-proBNP for Ruling out an Adverse Outcome in PE

Maximal NT-proBNP levels over the first 24 hours after admission varied widely in the patient population, ranging between 10 and 64 120 pg/mL. In agreement with previous studies, we found higher NT-proBNP levels in women as opposed to men (median, 1797 versus 702 pg/mL; Figure 1). However, no gender-specific differences were observed with regard to the patients’ outcome (incidence of the primary end point, 18% in men versus 15% in women; P=0.65).

The median NT-proBNP concentration was 7176 pg/mL in patients with an adverse clinical outcome as opposed to 864 pg/mL in those with an uncomplicated course (P=0.002). There was a moderate correlation between NT-proBNP and cardiac troponin T levels (r=0.56; P<0.001). ROC analysis (Figure 2) identified a concentration of 1000 pg/mL as a cutoff level for predicting death or major complications in the population of the present study. NT-proBNP levels ≥1000 pg/mL, which were found in 54% of our patients, were significantly associated with the presence of right ventricular dysfunction on echocardiography (P=0.001; Figure 3A) and predicted, by univariate analysis, both a higher overall mortality (10% compared with 0% in patients with NT-proBNP <1000 pg/mL; P=0.012) and a higher incidence of the primary end point (25% versus 5.3%; P=0.002; Figure 3B). Overall, the negative predictive value of NT-proBNP (with the use of the above cutoff point) was 95% for the combined end point and 100% for in-hospital death. On the other hand, the positive predictive value of the biomarker was low (25% for the combined end point; only 10% for death), and multiple logistic regression that included baseline clinical, echocardiographic, and laboratory characteristics (as stated in Methods) demonstrated that hemodynamic instability at presentation (OR, 33.6; 95% CI, 3.05 to 370.2; P=0.004) but not NT-proBNP ≥1000 pg/mL (OR, 1.82; 95% CI, 0.29 to 11.29; P=0.52), cardiac troponin T ≥0.04 ng/mL (OR, 3.23; 95% CI, 0.79 to 13.22; P=0.10), or echocardiographic evidence of right ventricular dysfunction (OR, 1.50; 95% CI, 0.36 to 6.21; P=0.58) independently predicted an adverse outcome in the whole patient population.

Figure 1. Gender-specific differences of NT-proBNP concentrations in patients with PE: distribution of NT-proBNP levels in men (n=50) and women (n=74). The horizontal lines through each group represent medians of the displayed values. Comparison is by Mann-Whitney nonparametric test.

Figure 2. ROC analysis for plasma NT-proBNP with regard to prediction of a complicated clinical course during the hospital stay (prognostic sensitivity and specificity). Arrows indicate some of the tested NT-proBNP concentrations (in pg/mL) as an example.
NT-proBNP or Cardiac Troponin T Combined With Echocardiography for Risk Assessment in PE

The results presented above suggested that NT-proBNP levels alone are capable of ruling out an unfavorable outcome in acute PE, but they are not, by themselves, independent predictors of death or major complications. We therefore tested a strategy combining cardiac biomarker levels with an imaging modality (echocardiography) to define low-, moderate-, and high-risk patient groups. High (>1000 pg/mL) NT-proBNP levels without echocardiographic evidence of right ventricular dysfunction were a rather frequent finding in our study (37 of 124 patients; 30%), whereas, on the other hand, an enlarged (dysfunctional) right ventricle on the echocardiogram was very rarely (3 patients; 2.4% of the study population) encountered in the absence of NT-proBNP elevation. This fact allowed us to define 3 major patient groups: (1) patients with low NT-proBNP levels (reference group; n = 44); (2) patients with high NT-proBNP and a negative echocardiogram (n = 37); and (3) patients with a positive echocardiogram (n = 30). As shown in Figure 4A, complication rates (primary end point) in these 3 groups were 4.6%, 13.5%, and 36.7%, respectively, and mortality rates were 0%, 0%, and 16.7%, respectively. Multiple logistic regression analysis (shown in Table 3) revealed that a positive echo was associated with a 12-fold elevated risk of an adverse outcome in the acute phase of PE (P = 0.002), whereas in the presence of NT-proBNP elevation alone, the risk was slightly but not significantly higher than that in the reference group.

We also investigated whether the combination of cardiac troponin with echocardiography might offer any advantages compared with the aforementioned strategy with regard to risk stratification of acute PE. In this case, 4 patient groups had to be defined: (1) no troponin T elevation and negative echocardiogram (reference group; n = 53); (2) troponin elevation and negative echocardiogram (n = 22); (3) no troponin elevation but positive echocardiogram (n = 12); and (4) troponin elevation combined with a positive echocardiogram (n = 16). As shown in Figure 4B, mortality and complication rates in the first (lowest-risk) group were comparable to those in patients with low NT-proBNP levels (Figure 4A). Moreover, the incidence of the primary end point in the fourth (highest-risk) group was comparable to that of patients with high NT-proBNP and a positive echocardiogram (Figure 4B versus 4A), and the elevation of the complication risk compared with the reference group was also of similar magnitude (10- versus 12-fold; Table 3). Overall, combination of troponin T with echocardiography increased the number of patient groups from 3 to 4 without offering any additional advantages in the intermediate-risk category (Table 3).
Acute pressure overload and failure of the right ventricle is a critical event in the pathophysiology of PE. Patients presenting with overt right heart failure and hemodynamic instability are known to have a high mortality rate in the acute phase of the disease, and there is consensus that emergency thrombolytic, interventional, or surgical therapy is warranted to save their lives. On the other hand, the appropriate management of patients with so-called submassive PE, ie, those with beginning right ventricular dysfunction but apparent hemodynamic stability at presentation, remains controversial to date. Moreover, and importantly, a simple and reliable method (or algorithm) for confirmation or exclusion of right ventricular dysfunction in stable patients with diagnosed PE remains to be defined and confirmed by clinical data. The results of the present study confirm previous reports by showing that low NT-proBNP levels possess a high negative predictive value, thus making NT-proBNP testing particularly useful for ruling out an adverse in-hospital outcome in PE. However, the main finding of our study is that combination of a simple laboratory test, ie, measurement of the levels of the cardiac biomarker NT-proBNP, with a noninvasive imaging method such as echocardiography at the bedside, may permit the identification of both low-risk and high-risk patients with acute PE.

Being released as a result of cardiomyocyte stretch, brain natriuretic peptides are sensitive indicators of neurohumoral activation resulting from ventricular dysfunction. The biologically active C-terminal peptide 77-108 (BNP) and the inactive N-terminal fragment 1-76 (NT-proBNP) are both detectable in human plasma. However, NT-proBNP levels may have, at least theoretically, enhanced ability to assess the severity of heart failure because they exhibit more pronounced increments compared with BNP. Recently, the prognostic value of BNP and NT-proBNP was examined in patients with acute PE in an attempt to detect right ventricular dysfunction. For NT-proBNP, plasma concentrations <500 to 600 pg/mL were reported to predict a benign clinical course. In our population of 124 patients, ROC analysis identified a higher concentration, namely, 1000 pg/mL, as an appropriate cutoff value. Patients with NT-proBNP levels <1000 pg/mL could reliably be identified as a low-risk group, as indicated by the high negative predictive value for in-hospital death and the combined primary end point “complicated clinical course” (100% and 95%, respectively). Possible explanations for the differences between our calculated cutoff value and those proposed by other investigators may include the relatively small sample size of previous studies and differences in the demographic characteristics of the patients included.

In agreement with previous studies, our univariate analysis suggested that elevated NT-proBNP levels, which were found in as many as 54% of the study patients, were associated with an increased complication rate. Importantly, however, concentrations above the cutoff value did not independently predict (rule in) an adverse outcome when adjusted for clinical and echocardiographic baseline parameters. This latter finding appeared consistent with the (proposed but not tested) hypothesis that NT-proBNP testing might need to be combined with echocardiography to also identify the high-risk patients with PE. Further analysis confirmed that patients with a positive echocardiogram (showing a dysfunctional right ventricle) had a >12-fold elevated risk of an adverse outcome compared with those with low NT-proBNP values. These patients had a complication rate of 37% and a death rate of 17% during the acute phase of PE. Therefore, because a positive echocardiogram was rarely encountered (incidence ≤3%) in the absence of NT-proBNP elevation in our patient population and in a previous study, our results support a simple and practical risk stratification algorithm for patients with proved PE. This algorithm could use NT-proBNP testing as an initial step, to

### Discussion

Acute pressure overload and failure of the right ventricle is a critical event in the pathophysiology of PE. Patients presenting with overt right heart failure and hemodynamic instability are known to have a high mortality rate in the acute phase of the disease, and there is consensus that emergency thrombolytic, interventional, or surgical therapy is warranted to save their lives. On the other hand, the appropriate management of patients with so-called submassive PE, ie, those with beginning right ventricular dysfunction but apparent hemodynamic stability at presentation, remains controversial to date. Moreover, and importantly, a simple and reliable method (or algorithm) for confirmation or exclusion of right ventricular dysfunction in stable patients with diagnosed PE remains to be defined and confirmed by clinical data. The results of the present study confirm previous reports by showing that low NT-proBNP levels possess a high negative predictive value, thus making NT-proBNP testing particularly useful for ruling out an adverse in-hospital outcome in PE. However, the main finding of our study is that combination of a simple laboratory test, ie, measurement of the levels of the cardiac biomarker NT-proBNP, with a noninvasive imaging method such as echocardiography at the bedside, may permit the identification of both low-risk and high-risk patients with acute PE.

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### Table 3. Combination of NT-proBNP or Cardiac Troponin T With Echocardiography for Definition of Risk Groups in Patients With Acute PE

<table>
<thead>
<tr>
<th>Event</th>
<th>Complicated In-Hospital Course, OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP combined with echocardiography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1: NT-proBNP &lt;1000 pg/mL</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Group 2: NT-proBNP &gt;1000, echo negative*</td>
<td>3.28 (0.60–18.02)</td>
<td>0.172</td>
</tr>
<tr>
<td>Group 3: Echo positive†</td>
<td>12.16 (2.45–60.29)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cardiac troponin T combined with echocardiography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1: TnT negative,‡ echo negative*</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Group 2: TnT positive,‡ echo negative*</td>
<td>3.70 (0.76–18.18)</td>
<td>0.107</td>
</tr>
<tr>
<td>Group 3: TnT negative,‡ echo positive*</td>
<td>5.56 (0.97–31.99)</td>
<td>0.055</td>
</tr>
<tr>
<td>Group 4: TnT positive,‡ echo positive*</td>
<td>10.00 (2.14–46.80)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

For each of the above combinations of cardiac biomarkers with echocardiography, OR and 95% CI refer to the comparison with group 1. TnT indicates cardiac troponin T.

*Negative and positive echocardiograms denote the absence or presence of right ventricular dysfunction, respectively.
†A positive echo was accompanied by NT-proBNP levels >1000 pg/mL in all but 3 patients of the present study.
‡Negative and positive troponin testing indicates troponin T levels <0.04 and ≥0.04 ng/mL, respectively.
be followed by echocardiography only if elevated levels of the biomarker are found.

Our results indicate that reliable risk stratification of PE is also possible combining troponin T, another cardiac biomarker, with echocardiography. This finding is in accordance with a previous report that demonstrated the incremental prognostic value of troponin I and echocardiography in this setting. In our study, comparison of the 2 strategies (ie, with the use of troponin T versus NT-proBNP as the initial step) revealed similar complication rates in the lowest-risk groups and a similar magnitude of risk elevation for the highest-risk patients. It can be argued that combination of troponin T (instead of NT-proBNP) with echocardiography increases the number of intermediate-risk groups, thus complicating the proposed algorithm without providing additional prognostic information. Moreover, because a positive echocardiogram was frequent even in the absence of troponin elevation, our study suggests that, in contrast to NT-proBNP, troponin testing always needs to be accompanied by echocardiography in patients with proved PE. On the other hand, the predefined reference values for cardiac troponins appear to offer an advantage (better standardization) compared with NT-proBNP cutoff values that, as mentioned above, were defined post hoc and varied in different studies. This fact emphasizes the need for prospective validation of risk stratification algorithms based on predefined reference concentrations of NT-proBNP.

Elevation of natriuretic peptides is often considered a “nonspecific” finding because it may be associated with a multitude of possible risk factors, including preexisting left ventricular dysfunction, patient age, renal impairment, chronic thromboembolic pulmonary hypertension, and chronic lung disease with cor pulmonale. In our study at least, none of the patients was found to have severe preexisting left ventricular dysfunction as indicated by a left ventricular ejection fraction ≤30% on echocardiography. Furthermore, it has been argued that this “nonspecificity” may exactly be what makes natriuretic peptides such powerful prognostic parameters because they may reflect a sum or an integral of various risk markers. Finally, for reasons that remain to be defined, NT-proBNP levels are higher in women than in men. This finding was confirmed in our study population with acute PE, in which the median values in women were more than twice as high as those in men. However, the implications of these differences are unclear, and we found no significant effects of gender on the risk of death or major complications in the acute phase of PE.

In conclusion, the results of the present study demonstrate that NT-proBNP or troponin testing combined with echocardiography may reliably identify both low-risk and high-risk patients with PE. Apart from proposing a simple risk stratification algorithm for use in clinical practice, these findings could provide the background for larger triage studies integrating NT-proBNP or troponins into the management of acute PE and, more specifically, testing the possible benefits of early thrombolysis in the high-risk patient group.

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Disclosure

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