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Correspondence

Association of Levels of N-Terminal-Pro-BNP-Type Natriuretic Peptide with Localisation of Thrombus in Acute Pulmonary Embolism

To The Editor: I read the article published in your journal with great interest.[1] However, I would like to offer some comments and seek some clarifications on this study. First, whether the study was prospective or retrospective in nature and what was the study duration. Secondly, N-terminal-pro-brain natriuretic peptide (NT-pro-BNP) assay was done before or after confirmation of thrombi by helical computed tomography (CT) scan. Moreover, the cut-off used for NT-pro-BNP in this study[2] is actually validated for congestive heart failure and the same may not be applicable for pulmonary embolism. Most other studies have used a higher cut-off ranging from 500 to 1000 pg/mL.[3] Thirdly, it is well established that cardiac biomarkers like BNP and NT-pro-BNP are indirect surrogate for right ventricular dysfunction (RVD) and central embolus is a strongest predictor of RVD both by echocardiography and radiologic evaluation.[3-5] The degree of right ventricular dysfunction is directly proportional to the amount of pulmonary vascular bed that is compromised by an embolus. More central the obstruction is more the pulmonary vascular resistance and stress on the right heart. In this study NT-pro-BNP was significantly high in patients who had central emboli (9/49) or features of RVD like pulmonary hypertension, interventricular septal hypokinesia and chamber dilatation. The authors have not mentioned what was the total number of patients having RVD and amongst them how many had central or peripheral emboli. It will be ideal to know this data to interpret whether elevated NT-pro-BNP is a better predictor for RVD than the central embolus. Fourthly, NT-pro-BNP is a non-specific biomarker and can be elevated in left ventricular dysfunction, chronic lung diseases and chronic renal failure and pulmonary embolism can be a cause for the acute exacerbation of these conditions. It may not always be possible to differentiate patients with pulmonary embolism alone from those with pulmonary embolism and co-existing diseases that can lead to elevated serum NT-pro-BNP level, especially in emergency department before initiation of treatment. I would like to know how many patients were excluded from this study due to co-existing illness that can elevate NT-pro-BNP level and at what stage of presentation, i.e. in the emergency department, within 24 hour or later in their hospital stay. Even if I exclude these conditions, an elevated NT-pro-BNP level alone may suggest but cannot diagnose pulmonary embolism, and hence, do not avoid the need for a CT angiography which anyway will reveal the embolus either central or peripheral, if present. Moreover, high BNP or NT-pro-BNP level alone does not justify aggressive treatment like thrombolysis in the absence of RVD or shock.[3,6] Then what is the practical usefulness of this biomarker. Do I really need a biomarker as predictor of central embolus. Is it justified to spend crucial 18 to 20 minutes for biomarker testing in an emergency for a patient who is critically ill. In my view, more apt way to conclude is that higher NT-pro-BNP levels predict more severe RVD which is mostly an after-effect of central embolus.

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The Author's Reply: I read the letter about our article published in the *Indian Journal of Chest Diseases and Allied Sciences*. I want to thank Dr Panigrahi for his interest to our article. I hope the points that he is curious about will be more clear after my reply.

The study was a prospective study and its duration was 10 months. The patients initially evaluated in emergency department. The level of N-terminal-Pro-BNP (NT-pro-BNP) was evaluated just before computed tomography angiography, concurrent with echocardiogram.

Cut-off value of NT-pro-BNP in acute pulmonary embolism varies in different studies.[1-3] We use the cut-off that is suggested by the manufacturer.[3] The value of NT-pro-BNP increased with the same mechanism, myocardial strain, both in congestive heart failure and acute pulmonary embolism. Although when the risk strafication of acute pulmonary embolism was determined, NT-pro-BNP levels higher than 500 pg/mL shows higher risk for short-term adverse outcome, in some studies lower cut-off levels were used according to manufacturer's advise of commercial kit.[1,2]

Ten patients were excluded from the study due to co-existing diseases (congestive heart failure with left ventricle dysfunction in 6, interstitial lung disease in 1, bronchiectasis in 1, and chronic renal failure in 2) although they had thrombus on CT-angiography and elevated NT-pro-BNP.

NT-pro-BNP levels were found significantly higher in patients who had right heart dysfuntion in our study as stated in the article. The ratios of centrally located thrombus in patients who had dilatation of right heart chambers, septal hypochinesia, pulmonary hypertension on echocardiogram were as follows; 81.5%, 87.6%, 82.3%, respectively.

Elevated natriuretic peptides, including NT-pro-BNP, have been shown to be predictive of adverse short-term outcomes in acute pulmonary embalism. Submassive embolism that causes right heart dysfunction and elevation of NT-pro-BNP may be considered for thrombolytic treatment.[4]

Computed tomography angiography may not be available in all hospitals' emergency department around the country. Of course solely, evaluation of the level of NT-pro-BNP is not enough to decide treatment strategy, but it would be useful in combination with echocardiogram. Otherwise, the evaluation of NT-pro-BNP is not so-much time-consuming when considering other diagnostic procedures such as D-dimer.

In conclusion, NT-pro-BNP is an useful biomarker showing right heart dysfunction, adverse outcomes in acute pulmonary embolism. Further, larger studies are necessary to decide its exact cut-off levels in determination of treatment strategies.

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