The value of use of amino-terminal brain natriuretic peptide as marker in cases of pleural effusion of different etiologies

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KEYWORDS
Pleural effusion; Transudate; Exudate; Amino-terminal brain natriuretic peptide (NT-proBNP); Thoracentesis

Abstract Background: The criteria of Light et al. have been used to make the differentiation between transudate and exudate effusion for the past 25 years. The main problem with those criteria is that although they identify nearly all exudates correctly, they misidentify about 20–25% of transudates as exudates.

The plasma NT-proBNP level is a sensitive marker of cardiac dysfunction and has proved to be a useful tool for the identification and management of systolic and diastolic cardiac dysfunction.

Objective: The aim of this work was to study the value of pleural NT-pro brain natriuretic peptide in the diagnosis of pleural effusion of different causes in comparison to the conventional diagnostic procedures in cases of pleural effusion.

Subjects and methods: The present study was conducted on 32 patients who suffered from pleural effusion, they were classified according to Light’s criteria into two groups namely transudate, exudate, and the third group of 10 normal healthy subjects as control group.

Results: The levels of both serum and pleural fluid pro-BNP in group I patients with transudate effusion were significantly higher than group II patients with exudate effusion (P > 0.001, 0.003) respectively.

Conclusion: The results support the feasibility of using the pleural fluid amino terminal proBNP measurement in thoracentesis that would enhance discrimination among the different causes of pleural effusion especially for heart failure patients. Serum and pleural fluid levels of NT-pro

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Introduction

Traditionally, pleural effusions have been separated into transudative and exudative pleural effusions [1]. The primary reason to separate transudative from exudative pleural effusions is that if a patient has a transudative pleural effusion, no investigations need to be directed toward the pleural effusion and the systemic condition can be treated with the expectation that the effusion will resolve. In contrast, if the patient has an exudative pleural effusion it is important to determine the local disease that is responsible for the effusion. Accordingly, additional laboratory tests and at times invasive tests are indicated to demonstrate the etiology of the pleural effusion [2].

Amino-terminal brain natriuretic peptide precursor (NT-proBNP) is a member of a family of vasoactive peptides produced by the heart and circulate as hormones to act in various tissues in the body. The synthesis of this peptide is stimulated by the increased wall tension or stretching of cardiac chambers. The plasma NT-proBNP level is a sensitive marker of cardiac dysfunction and has proved to be a useful tool for the identification and management of systolic and diastolic cardiac dysfunction [3,4,5].

The criteria of Light’s [2] have been used to make the differentiation between transudate and exudate effusion for the past 25 years. The main problem with those criteria is that although they identify nearly all exudates correctly, they misidentify about 20–25% of transudates as exudates [6,7].

The aim of this work was to study the value of pleural NT-pro brain natriuretic peptide in the diagnosis of pleural effusion of different causes in comparison to the conventional diagnostic procedures in cases of pleural effusion.

Subjects and methods

This study enrolled 32 patients with symptomatic pleural effusion admitted to the chest department, Alexandria University Hospital and 10 normal healthy subjects as control group.

Patients were divided into two groups according to Light’s criteria [8]:

1. Group I contains 16 patients who were diagnosed as transudative pleural effusion.
2. Group II contains 16 patients who were diagnosed as exudative pleural effusion.

Each patient signed an informed consent before inclusion in the study. The study protocol was approved by the local ethics committee of the Alexandria faculty of medicine.

All patients were subjected to the following: complete history taking, clinical examination, radiological evaluation (plain chest X-ray, computed tomography of the chest, US chest/abdomen and or pelvis), routine laboratory investigations and serum NT-proBNP level.

Thoracentesis: [9] The pleural fluid analysis was carried out including: biochemical (pH, LDH, protein and glucose content), bacteriological (AFS, C&S), cytological for detection of abnormal cells, and NT-proBNP level determination.

ECG/Echocardiography, thoracoscopy, pleural biopsy and bronchoscopy were done if needed.

Measurements of NT-BNP; serum and pleural fluid NT-pro BNP level was determined using N-terminal pro-Brain Natriuretic Peptide ELISA Kit Product No.: E20111 018033 – 96 test.

Principle of assay

The NT-proBNP enzyme linked immunosorbent assay (ELISA) kit is used for the estimation of N-terminal Pro BNP level in serum and biological fluids. A purified antibody was coated on a microwell plate and fully adsorbed on the microwell wall to make a solid-phase carrier. Enzyme conjugation solution affinity material contains the enzyme labeled antigen. During the experiment, by adding the sample under test and enzyme-linked affinity material and coated on the porous incubated with antibody response to be fully integrated in the porous walls, a common competition coated on the porous solid phase antibody, the formation of labeled antigen complex. Unbonded samples were washed off upon the reaction, and a substrate was added for reaction, the substrate developed a blue color in the presence of enzyme, and finally developed a yellow color in the presence of acid. A standard curve was drawn by reading absorbance values, and concentrations of the samples to be assayed were obtained [10].

Results

The demographic data of the three studied groups as regards age and sex is showed in Table 1.

In group I, 11 patients (68.8%) were suffering from diabetes mellitus, 7 patients (43.8%) presented with heart failure, 7 patients (43.8%) presented with liver failure and 4 patients (25%) presented with renal impairment.

In group II, 3 patients (18.8%) were suffering from diabetes mellitus, 8 patients presented with malignancy (50%), and six patients (37.5%) presented with pneumonia. There was one case (6.3%) of extrapulmonary TB and one patient (6.3%) presented with pulmonary embolism (Table 2).

Table 3 shows that the mean pleural fluid protein was 2.09 ± 0.75 g/dl ranging between 1.2 and 4.2 g/dl in group I, while it was 4.87 ± 1.03 g/dl ranging between 3.1 and 6.8 in group II. There was a statistically significant increase in pleural fluid protein in group II than in group I ($F = 14.098$, $p = 0.001^*$).

Applying Light’s criteria on the two studied groups we found that:

1. There was a statistically significant increase in pleural fluid protein in group II than in group I ($p = 0.001$).
2. Pleural fluid/serum protein ratio, there was a statistically significant increase in group II than in group I ($p = 0.001$).
There was a statistically significant increase in F/S LDH ratio in group II than in group I ($p = 0.001$).

S/F gradient was increased in group I than in group II and it was statistically significant ($p = 0.001$).

### Table 1: Demographic data of the three studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th></th>
<th>Group II</th>
<th></th>
<th>Control</th>
<th></th>
<th>$\chi^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>75.0</td>
<td>9</td>
<td>56.2</td>
<td>5</td>
<td>50.0</td>
<td></td>
<td>0.371</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>25.0</td>
<td>7</td>
<td>43.8</td>
<td>5</td>
<td>50.0</td>
<td></td>
<td>1.981</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>33–72</td>
<td>21–67</td>
<td>26–62</td>
<td>51.13 ± 14.46</td>
<td>46.70 ± 11.11</td>
<td>0.457</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± S.D</td>
<td>52.94 ± 10.73</td>
<td>51.13 ± 14.46</td>
<td>46.70 ± 11.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD = standard deviation, $p$ is significant at $\leq 0.05$.

### Table 2: The prevalence of co-morbidities among the studied patient groups.

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Group I ($n = 16$)</th>
<th>Group II ($n = 16$)</th>
<th>Test of sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11</td>
<td>68.8</td>
<td>3</td>
</tr>
<tr>
<td>Heart failure</td>
<td>7</td>
<td>43.75</td>
<td>-</td>
</tr>
<tr>
<td>Malignancy</td>
<td>-</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>7</td>
<td>43.75</td>
<td>0</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>4</td>
<td>25.0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>-</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

$p$: $p$ value for comparing the two studied groups. $\chi^2$: Chi Square test. FE: Fisher Exact test.

$p_1$: Statistically significant at $p \leq 0.05$.

### Table 3: Light’s criteria among the pleural effusion patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th></th>
<th>Group II</th>
<th></th>
<th>$F(P)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural fluid protein g/dl</td>
<td>M ± SD</td>
<td>2.09 ± 0.75</td>
<td>4.87 ± 1.03</td>
<td></td>
<td>14.098(0.001*)</td>
</tr>
<tr>
<td>F/S protein ratio M ± SD</td>
<td>0.32 ± 0.12</td>
<td>0.67 ± 0.12</td>
<td></td>
<td>11.079(0.001*)</td>
<td></td>
</tr>
<tr>
<td>F/S LDH ratio M ± SD</td>
<td>0.43 ± 0.128</td>
<td>3.37 ± 2.24</td>
<td></td>
<td>12.069(0.001*)</td>
<td></td>
</tr>
<tr>
<td>S/F protein gradient M ± SD</td>
<td>0.30 ± 0.65</td>
<td>2.40 ± 0.85</td>
<td></td>
<td>15.048(0.001*)</td>
<td></td>
</tr>
</tbody>
</table>

$p$: $p$ value for $F$ test (ANOVA).

$p$ is significant at $\leq 0.05$. M = mean; LDH = lactate dehydrogenase. F/S = fluid/serum.

### Table 4: Comparison between the different studied groups according to serum pro BNP.

<table>
<thead>
<tr>
<th></th>
<th>Group I ($n = 16$)</th>
<th>Group II ($n = 16$)</th>
<th>Control ($n = 10$)</th>
<th>$F(P)$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum pro BNP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min.–Max.</td>
<td>404.0–3393.0</td>
<td>246.0–874.0</td>
<td>186.40–223.60</td>
<td>14.437 &lt; 0.001</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1587.88 ± 1091.90</td>
<td>615.50 ± 199.66</td>
<td>205.47 ± 12.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$p_1$</td>
<td>0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$p_2$</td>
<td>0.346</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$p$: $p$ value for $F$ test (ANOVA) for comparing between the three studied groups.

$p_1$: $p$ value for Post Hoc test (Scheffe) for comparing between group I and each other group.

$p_2$: $p$ value for Post Hoc test (Scheffe) for comparing between group II and control.

Statsitically significant at $p \leq 0.05$.
Table 5 Comparison between the two studied groups according to fluid pro BNP.

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 16)</th>
<th>Group II (n = 16)</th>
<th>t (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid pro BNP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min.-Max.</td>
<td>392.0–3412.0</td>
<td>282.0–849.0</td>
<td>3.541* (0.003)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1600.18 ± 1095.48</td>
<td>617.81 ± 187.07</td>
<td></td>
</tr>
</tbody>
</table>

* p value for Student t-test.
* Statistically significant at p ≤ 0.05.

Table 6 Correlation between serum pro BNP and fluid pro BNP.

<table>
<thead>
<tr>
<th></th>
<th>Serum pro BNP</th>
<th>Fluid pro BNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid pro BNP</td>
<td>r</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>0.995*</td>
<td>0.001*</td>
</tr>
</tbody>
</table>
| r: Pearson coefficient. * Statistically significant at p ≤ 0.05.

Table 7 Median values of pro BNP among patients of group I and group II.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Serum pro BNP</th>
<th>Fluid pro BNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>7</td>
<td>2890</td>
<td>2897</td>
</tr>
<tr>
<td>Liver failure</td>
<td>6</td>
<td>659</td>
<td>654</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>2</td>
<td>1122</td>
<td>1124</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>8</td>
<td>785</td>
<td>789.5</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6</td>
<td>447</td>
<td>455.5</td>
</tr>
</tbody>
</table>

Table 8 Correlation between serum pro BNP and pleural fluid pro BNP and Light’s criteria.

<table>
<thead>
<tr>
<th></th>
<th>Serum pro BNP</th>
<th>Fluid pro BNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural fluid protein</td>
<td>−0.440*</td>
<td>0.012</td>
</tr>
<tr>
<td>F/S protein ratio</td>
<td>−0.448*</td>
<td>0.010</td>
</tr>
<tr>
<td>S/F protein gradient</td>
<td>0.485*</td>
<td>0.005</td>
</tr>
<tr>
<td>F/S LDH</td>
<td>−0.383*</td>
<td>0.030</td>
</tr>
</tbody>
</table>

* 0.383*, 0.448*, 0.485*, 0.390*, 0.445*,
* 0.012, 0.010, 0.005, 0.011, 0.009, respectively.

Discussion

Brain natriuretic peptide (BNP) and N-proBNP are indicator and prognostic factors for left heart failure and valuable markers for risk stratification in acute coronary syndrome. Moreover natriuretic peptide has been demonstrated to be useful for the differential diagnosis of acute dyspnea in emergency department and identification of acute heart failure in particular [5,10].

Table 4 shows that serum pro BNP in group I ranged between 404 and 3393 pg/ml with a mean of 1587.88 ± 1091.90 pg/ml.

As regards group II the range was 246–874 pg/ml with a mean of 205.47 ± 12.09 pg/ml.

There was a significant increase in serum pro BNP in group I than in group II and control group (t = 0.346) (Table 4).

The mean value of pro BNP in pleural effusion patients of group I was 1600.18 ± 1095.48 pg/ml ranging between 392 and 3412 pg/ml (Table 5).

While, the mean was 617.81 ± 187.07 pg/ml ranging between 282 and 849 pg/ml among patients of group II. There was a statistically significant difference in pro BNP among the two studied groups (P = 0.003) (Table 5).

It was found that the level of proBNP was closely correlated in serum and pleural fluid in both group I and group II (Pearson coefficient r 1.000 and 0.995, respectively) (Table 6).

The median value of serum pro BNP among patients of heart failure was 2890 and 659 pg/ml in patients of liver failure while the median was 1122 pg/ml in patients with renal impairment. Among patients of group II the median value of serum pro BNP was 785 pg/ml in patients with malignancy while the median was 447 pg/ml among patients with pneumonia.

The median value of pleural pro BNP among patients of heart failure was 2897 pg/ml and 654 pg/ml in patients of liver failure with hepatic hydrothorax, while the median was 1124 pg/ml in patients with renal impairment. Among patients of group II the median value of pleural pro BNP was 789.5 pg/ml in patients with malignancy while the median was 455.5 pg/ml among patients with pneumonia (Table 7).

Table 8 shows that there was a statistically significant negative correlation between pleural fluid protein and serum and pleural fluid pro BNP (r: −0.440, −0.445 and P = 0.012, 0.011, respectively).
The value of use of amino-terminal brain natriuretic peptide

Porcel and associates [11] first demonstrated in 2004 that the measurement of the levels of N-terminal pro-brain natriuretic peptide (NT-pro-BNP) in the pleural fluid was useful in identifying patients with congestive heart failure.

Burgess and associates [12] proposed that an albumin gradient (serum albumin-pleural fluid albumin) of >1.2 g/dL should be used to identify the misclassified transudates.

The present study was conducted on 32 patients. All patients suffered from pleural effusion, they were classified according to Light’s criteria [24] into two groups namely transudate, exudate, and the third group of 10 normal healthy subjects as control group.

It has been shown consistently in several studies that NT-proBNPare related to sex, with higher values in females, and to age, with higher values in older individuals. The sex relation is thought to be caused by differences in metabolism [13].

In the current study we found a positive not significant correlation of NT-pro BNP in serum and pleural fluid and age which may be because the mean age was younger in our study population (mean age was 52.94 ± 10.73 years) and 75% of the studied patients were males.

In accordance with our study Cincin et al. [14] who studied the amino-terminal brain natriuretic peptide (NT-proBNP) levels in pleural fluid of two groups, group I with heart failure related pleural effusion and group II non heart failure effusion. They found no statistical significant differences between the different studied groups regarding age.

In contrast Stolz et al. [15] observed significant correlations between BNP levels on hospital admission and age in patients with acute exacerbation of COPD (r = 0.425, p = 0.001).

In the present study the levels of both serum and pleural fluid pro-BNP were significantly higher in group I patients with transudate effusion than in group II patients with exudate effusion (p > 0.001, 0.003), respectively.

In accordance with our study Cincin et al. [14] found that, patients with HF related pleural effusion had significantly higher pleural NT-proBNP levels than other patients (p < 0.001). Pleural and serum NT-proBNP measures were closely correlated. An NT-proBNP cut-off value of ≥2300 pg/mL in pleural fluid had a sensitivity of 70.8%, and specificity of 97.6% for discriminating transudates caused by HF from exudates.

In agreement with our study Kolditz et al. [16] evaluated the diagnostic accuracy of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) levels, measured simultaneously in serum and pleural fluid, in identifying pleural effusions due to heart failure. They found that levels of NT-proBNP in serum and pleural fluid were significantly elevated, 10-fold, in patients with acute decompensated left heart failure compared to patients with noncardiac effusions. Moreover, elevated NT-proBNP levels displayed a high sensitivity and specificity in detecting cardiac transudates in the patient group over a relatively large range of cut-off values.

In accordance with our study Porcel et al. [11] retrospectively examined 117 patients with pleural effusion, of whom 44 (38%) were diagnosed as having pleural effusion due to heart failure. The pleural fluid levels of NT-proBNP were significantly higher in patients with cardiac transudates than in patients with effusion due to other causes. The pleural fluid NT-proBNP or BNP cut-off values for discriminating pleural effusion with heart failure are variable from 1176 to 4000 pg/mL [4,21].

In agreement with our study Tomcsanyi et al. [17] compared NT-proBNP levels in serum and pleural fluid in 14 patients with pleural effusion due to congestive heart failure and 14 patients with pleural exudates of various causes. They found significantly higher levels of NT-proBNP in both serum and pleural fluid from patients with cardiac effusions (median 6,295 versus 277 ng/L in pleural fluid; 5713 versus 236 ng/L in serum) and suggested a diagnostic cut-off point for detecting cardiac transudates of 599–1457 ng/L.

Gegenhuber et al. [18] evaluated the diagnostic accuracy of NT-proBNP measured in serum and pleural fluid for the identification of pleural effusions caused by heart failure in 93 patients referred for thoracentesis.

Both were significantly higher in patients with effusions caused by heart failure than in patients with pleural effusions attributable to other causes.

Among the studied population we found that median levels of pleural fluid NT-proBNP were higher in heart failure patients (2897 pg/ml) than in renal impairment patients (1124 pg/ml), malignant effusions (789.5 pg/ml), liver failure patients (668 pg/ml) and parapneumonic effusion (445.5 pg/ml).

Another study [13] evaluated the clinical utility of pleural fluid NT-proBNP in patients with pleural effusion. They found that median levels of pleural fluid NT-proBNP among patients with heart failure were significantly higher (3310 pg/mL) than in those patients with hepatic hydrothorax (531 pg/mL), malignant pleural effusions (733 pg/mL), tuberculous pleural effusions (214 pg/mL), and parapneumonic pleural effusions (294 pg/mL).

In our study we found that the levels of NT-pro BNP was closely correlated in serum and pleural fluid in both group I and group II (Pearson coefficient r 1.000, 0.995, respectively) and (p < 0.001).

Han et al. (2008) [13] found that, levels of NT-proBNP measurement in pleural and in serum were closely correlated (Spearman’s coefficient of rank correlation 0.928; p < 0.001) for pleural effusion patients.
The study by Kolditz et al. [16] demonstrated a strong correlation of NT-proBNP concentrations in serum and pleural fluid and equal diagnostic accuracies for serum and pleural fluid NT-proBNP measurements for the discrimination of pleural effusions attributable to heart failure.

This close correlation between pleural fluid and serum NT-proBNP may be explained by that serum NT-proBNP is derived from cardiac ventricular myocytes. Due to its small size (8.5 kDa), the peptide can easily diffuse from the blood into the pleural space. Because there is no evidence that NT-proBNP is synthesized by mesothelial cells, they assume that pleural NT-proBNP levels are proportional to serum NT-proBNP levels [13].

Therefore, Gegenhuber et al. [18] claimed that it may not be necessary to perform diagnostic thoracentesis in patients with serum NT-proBNP concentrations exceeding a cut-off value, making the diagnosis of heart failure as the underlying cause of pleural effusion is very likely in these patients. However, in all other patients with serum NT-proBNP concentrations below such a cut-off value, early diagnostic thoracentesis may be necessary to determine whether the effusion is exudative or transudative in nature.

Porcel et al. [19] suggested two potential cutoff values for NT-proBNP, 1300 and 1500 pg/mL. A cutoff value of 1300 provided a sensitivity of 95.6% (95% CI, 0.89–0.988) and a specificity of 87.9% (95% CI, 0.794–0.938), whereas a cutoff value of 1500 pg/mL demonstrated a sensitivity of 93.3% (95% CI, 0.861–0.975) and a specificity of 89% (95% CI, 0.807–0.946). Previously recommended cutoff values vary from 1176 to 4000 pg/mL for pleural fluid NT-proBNP [13].

Ann et al. [20] found a NT-proBNP value of 2000 pg/mL to have a sensitivity of 80% (95% CI, 0.58–0.92) and a specificity of 73% (95% CI, 0.61–0.83), whereas a cutoff value of 5000 pg/mL had a sensitivity of 45% (95% CI, 0.26–0.66) and a specificity of 97% (95% CI, 0.89–0.99). The discrepancy between these studies regarding both the degree of correlation as well as sensitivity and specificity may relate to a specific immunoassay.

In agreement with Light’s criteria in our study population we found that, there was a statistically significant increase of pleural fluid protein in group II than in group I (P < 0.001), F/S protein ratio showed a statistically significant increase in group II than in group I (P < 0.001), finally S/F protein gradient showed a statistically significant increase in group I than in group II (p < 0.001), fluid/serum LDH ratio showed a statistically significant increase in group II than in group I (P < 0.001).

In the study population of Cincin et al. [14], they found eight HF patients were classified as exudates by Light’s criteria, 5 of which received diuretics before thoracentesis. All misclassified patients had pleural NTproBNP levels higher than 1165 pg/mL, which predicted HF associated transudates with 95.8% sensitivity and 85.7% specificity [18].

Romeo-Candeira et al. [21] asserted that if pleural fluid meets exudative Light’s criteria but the effusion is thought to be due to heart failure, the serum to pleural fluids protein gradient should be examined. And if this gradient is greater than 3.1 g/dL, the pleural fluid in all probability is due to heart failure and additional diagnostic studies are not indicated. But other studies showed that pleural fluid NT-proBNP is more accurate than protein gradient [13,17].

In our study we found a statistically significant negative correlation between both serum and pleural fluid proBNP and ejection fraction in patients of group I with transudate effusion (r = 0.582, 0.572, respectively and P 0.018*, 0.020*, respectively).

In accordance Inoue et al. [22] found a significant correlation between plasma BNP level and % ejection fraction (r = −0.41, p = 0.0197).

Simon et al. [23] showed a significant negative correlation between N terminal BNP levels and LVEF and a significant positive correlation between N terminal BNP and LV end-diastolic dimension.

Viscente et al. [24] found a good correlation of NT-proBNP plasma levels with LV two-dimensional cavity areas (LVEDA, LVESA).

Bay et al. [25] found that the concentrations of NT-pro BNP increase with decreasing left ventricular ejection fraction (LVEF).

Groenning et al. [26] found a statistically significant negative correlation between N terminal BNP and LV ejection fraction (r = −0.75; P < 0.0001). They concluded that NT-proBNP is a powerful marker for LV dimensions and systolic function in patients with heart failure.

Conclusion

Measurement of Pleural fluid NT-pro BNP levels is probably the best way to identify patients with pleural effusion due to heart failure that meet exudative criteria by lights.

The results support the feasibility of using the pleural fluid amino terminal proBNP measurement in thoracentesis that would enhance discrimination among the different causes of pleural effusion especially for heart failure patients.

Serum and pleural fluid levels of NT-pro BNP were closely correlated and measurement of NT-pro BNP in serum showed equally good diagnostic properties. Serum and pleural fluid levels of NT-proBNP showed a significant negative correlation with ejection fraction and the parameters of Light’s criteria.

References

The value of use of amino-terminal brain natriuretic peptide


