The use of pleural fluid and serum biochemical parameters in the differentiation of transudates and exudates

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Introduction

Pleural effusions develop in thoracic or systemic diseases and based on their underlying pathophysiology are classified into transudate or exudate. The differentiation of a pleural effusion as either transudate or exudate is useful when investigating the cause of a pleural effusion. Identification of a fluid as transudate implies that there is no pleural disease and an exudate suggests involvement of the pleura in an inflammatory or malignant process.

In 1972 Light et al.1 established the ‘gold standard’ criteria for identifying exudates and transudates using both serum and fluid total protein (TP) and lactate dehydrogenase (LDH). Although Lights’ original criteria demonstrated excellent discrimination, further studies have shown poorer diagnostic accuracy.2

The use of protein zone electrophoresis of pleural effusion was studied by Chen et al.,3 who proposed that the pattern of specific low and high molecular weight proteins and the ratio of fluid β2-macroglobulin to albumin could be used to differentiate transudates and exudates.

The aim of this study was to assess the diagnostic value of various fluid and serum biochemical parameters (TP, LDH, total cholesterol, β2-macroglobulin:albumin ratio) and to compare their diagnostic efficiency to that of Light’s original criteria.

Methods

Patient Samples:

54 patients with pleural effusion of well-defined aetiology, as determined by retrospective notes review, were studied. Of these, 21 were transudates and 33 were exudates. Pleural fluid and serum samples were collected within 24 hours of each other.

Analysis:

Pleural fluid and serum samples were analysed for TP, LDH and total cholesterol on an Olympus AU600, using Olympus methodology. Protein sub-fractions, β2-macroglobulin, and albumin were estimated by protein zone electrophoresis (PZE) on agarose gel using the Sebia Hydrasys system and scanned by densitometry (figure 1).

Statistical Analysis:

The effectiveness and optimum cut-off values of individual tests and combinations of tests in distinguishing a transudate from an exudate were determined using Receiver Operator Characteristic (ROC) curves. Statistical analysis was undertaken using Analyse-IT for Microsoft Excel (University Of Leeds, UK).

Results

Performance indices of the various combinations of serum and fluid parameters are shown in table 1. An example of protein zone electrophoresis and densitometry for a fluid exudate is shown in figure 1.

The performance of a combination of fluid total biochemical parameters was evaluated by dividing each parameter by its optimum cut-off level so that a value of greater than 1.0 was indicative of an exudate and less than 1.0 a transudate. The 3 individual scores for fluid TP, fluid cholesterol and fluid LDH were then added together and divided by 3 to give an overall score.

Table 1: Performance indices of various combinations of fluid and serum parameters for identification of pleural effusion as an exudate (AUC area under the curve; PPV: positive predictor value)

<table>
<thead>
<tr>
<th>Combination</th>
<th>Optimum Cut-off</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>AUC %</th>
<th>PPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light’s criteria</td>
<td>0.75</td>
<td>90</td>
<td>90</td>
<td>0.94</td>
<td>0.90</td>
</tr>
<tr>
<td>Fluid Cholesterol</td>
<td>1.5</td>
<td>85</td>
<td>91</td>
<td>0.84</td>
<td>0.93</td>
</tr>
<tr>
<td>Fluid (TP + Chol + LDH)</td>
<td>1.0</td>
<td>84</td>
<td>86</td>
<td>0.86</td>
<td>0.91</td>
</tr>
<tr>
<td>Fluid/serum TP ratio</td>
<td>0.5</td>
<td>85</td>
<td>91</td>
<td>0.63</td>
<td>0.93</td>
</tr>
<tr>
<td>Fluid/serum Chol ratio</td>
<td>0.38</td>
<td>79</td>
<td>86</td>
<td>0.91</td>
<td>0.90</td>
</tr>
<tr>
<td>Fluid β2-macro:albumin ratio</td>
<td>0.13</td>
<td>70</td>
<td>57</td>
<td>0.74</td>
<td>0.72</td>
</tr>
<tr>
<td>Fluid β2-macro:albumin ratio</td>
<td>0.6</td>
<td>91</td>
<td>100</td>
<td>0.98</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Discussion

In this study, we found that the optimum cut-off points for fluid TP (0.5) and fluid/serum LDH (0.6) compared well to those previously reported by Light et al., but differed for fluid cholesterol. The optimum cut-off for fluid cholesterol was 0.3mmol/l which again differed from previous reports1 and gave a reduced sensitivity when compared with Light’s criteria.

The test combination of fluid TP, LDH and cholesterol/fluid/LDH ratio gave significantly better AUC of 0.91 (figure 4) compared to other parameters measured and gave similar performance indices to Light’s criteria. Fluid β2-macroglobulin:albumin ratio showed a significantly worse AUC of 0.74.

We recommend the use of a combination of fluid TP, LDH and cholesterol in the differentiation of transudates and exudates. This test combination gave similar performance indices to Light’s criteria, with the added advantage of avoiding simultaneous collection of a blood sample.

In order to simplify reporting we propose to calculate a combined score for the fluid parameters using the optimum cut-off for the differentiation between transudate and exudate derived from this study. When reporting pleural fluid results a comment is generated by the Pathology computer system to aid interpretation (figure 4).

Figure 1: Protein zone electrophoresis of matched serum and pleural fluid exudate. From the densitometer scan of the fluid sample, the relative area of each protein fraction is obtained and the ratio of fluid β2-macroglobulin to albumin calculated.

Figure 2: Distribution of exudates and transudates by combined fluid TP, cholesterol and LDH score.

Figure 3: Receiver operating characteristic (ROC) curve analysis for fluid total protein + LDH + cholesterol. Area under curve = 0.983 (95% C.I. 0.957 - 1.000, p = <0.0001).}

References