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## FREQUENCY AND CHARACTERISTICS OF PLEURAL EFFUSIONS IN PULMONARY EMBOLISM

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**Abstract:** Pulmonary embolism (PE) is the fourth cause of pleural effusions, after pneumonia, neoinfiltrates and tuberculosis. Several questions are yet unanswered: are the pleural effusions in PE exudates or transudates, what is their size, are they unilateral or bilateral, are they only haemorrhagic, etc.

The aim of this study is to determine the frequency, side, size, biochemical and cytological characteristics of pleural effusions in PE.

In this study, 100 patients with suspicion of PE were examined and treated and in all the diagnosis of PE was establish. 31 of them had pleural effusions.

Of 31 patients with PE and pleural effusions, six (9.84%), had bilateral pleural effusions, 14 (22.95%) patients had right-sided pleural effusion, and 11 (18.03%) had pleural effusion on the left side. 22 (36.07%) had small pleural effusions, 8 (13.11%) had medium and 1 (1.64%) had a large pleural effusion. 18 (29.51%) had yellowish colored pleural effusions, 12 (19.67%) had haemorrhagic pleural effusions and 1 (1.64%) had transparent pleural effusion. Values of the total protein in pleural effusions varied in the interval  $45.70 \pm 7.25$  gr/l., 30 patients had LDH an effusion/sera ratio bigger than 0.6, and 1 patient had an LDH p/s ratio  $< 0.6$ . 15 patients (24.59%) had neutrophil cells, 10 (16.39%) had lymphocytes, and eosinophil cells dominated in 5 (8.20%). One patient (1.64%) had a negative cytological finding.

We can conclude that pleural effusions secondary to PE can be found in around one third of all cases with PE. They are small, mostly unilateral, often but not always haemorrhagic. They are always exudates with a predomination of neutrofil cells.

**Key words:** pulmonary embolism, pleural effusion, unilateral, exudates, neutrofil.

### *Introduction*

Pulmonary embolism (PE) is a disorder with significant rate of morbidity and mortality. Therefore, it is of great importance to improve diagnosis of PE. PE is the fourth cause of pleural effusions, after pneumonia, neoinfiltrates and tuberculosis [1].

It is estimated that frequency of pleural effusions due to PE is to be found in 30–50% of patients with PE [2], but in some studies they occur in less than 5% of all cases with PE. This is probably because PE is not considered in patients with undiagnosed pleural effusions and because thoracentesis is not performed on these patients [3]. Also, the biochemical characteristics of pleural effusions in PE were not examined, so that they were classified as exudates or transudates [5] and rarely haemorrhagic [6].

The exact pathophysiological mechanism in forming the pleural effusion in PE remains unknown. It seems that the embolus in the peripheral pulmonary arteries is the reason for mesothelial reaction and releasing cytokines that increase the permeability of the vessels and when the lymph vessels exceed their capacity to eliminate the liquid from the pleural space pleural effusion is created [6]. Another mechanism for forming the pleural effusion seems to be increased systemic venous pressure in the parietal pleura because of pulmonary hypertension and right heart failure that leads to having transudates in PE [5]. But pulmonary hypertension is often not so serious in patients with PE as to create right heart failure. In fact it is assumed that most of the transudates in PE are the result of undiagnosed congestive heart disease [7].

Several questions are still unanswered: are the pleural effusions in PE exudates or transudates, what is their size, are they unilateral or bilateral, are they only haemorrhagic, etc.

### *Aim of the study*

The aim of this study is to determine the frequency, side, size, biochemical and cytological characteristics of pleural effusions in PE.

### *Material and Methods*

In this study, 100 patients with suspicion of PE were examined and treated in the Lung Diseases and Tuberculosis Institute, Skopje, R. Macedonia in the period from May 2006 to December 2011 and in all the diagnosis of PE was established. Thirty-one of them had pleural effusions.

As a control group we enrolled 100 patients who were treated for COPD, pneumonias, chronic cardiomyopathy and other pulmonary diseases and in all of them PE was excluded. In this group 30 patients also had pleural effusions.

Standard diagnostic procedures were performed on all patients:

Standard laboratory analyses (ESR, CBC, AST, ALT, urea, creatinine level, electrolyte status, protein status:

CXR with profile;

Blood gas analysis (AVL Compaq 3 blood gas analyser);

Clinical decision rule (Wells score);

D-dimmer levels (Latex agglutination quantitative method INNOVANCE D-dimmer, Siemens, Germany) range 170–4500 ng/ml. D-dimmer levels above 500 ng/ml, were abnormal), MDCT angiography, V/Q study;

In patients with pleural effusions the following were performed:

Chest ultrasound (CUS) (ALOKA SSD 1100 with convex probe 3,5 MHz and linear probe 7.5 MHz), thoracentesis, biochemical and cytological analysis of the pleural effusions (total protein level, LDH level, total protein level ratio in pleural fluid and sera, LDH level ratio in pleural fluid and sera)

#### *Statistical analysis*

Differences of analysed parameters in series with attributive values were tested with Pearson Chi-square ( $\chi^2$ ); in series with numeric attributes descriptive statistic was used (Mean  $\pm$  Std. Dev.,  $\pm$  95,00 CI., minimal and maximal value); in series with numerical values, differences between two independent samples were tested with the Mann-Whitney U test (U/Z).

#### *Results*

In the study group with PE, 31 patients (31%) had pleural effusion.

Thirty patients (30%) in the control group also had pleural effusion (Table 1). The distribution data for the pleural effusion showed that there was no statistical difference between the study and the control groups for  $\chi^2 = 0.02$  and  $p > 0.05$  ( $p = 0.88$ ).

Of the 31 patients with PE and pleural effusions, six (9.84%), had bilateral pleural effusion, 14 (22.95%) patients had right-sided pleural effusion, and 11 (18.03%) had pleural effusion on the left side. In the control group all patients had bilateral pleural effusions (49.18%). The distribution data for the pleural effusion sides showed that there is a significant statistical difference between the study and the control group of  $\chi^2 = 40.99$  and  $p < 0.001$  (Table 2).

Table 1

*Pleural effusions/study and control group*

| Pearson Chi-square: 0.02, df = 1, p = 0.88 |          |                     |                      |            |
|--|----------|---------------------|----------------------|------------|
|  | Group    | Pl. effusion absent | Pl. effusion present | Row Totals |
| Count                                      | Study    | 69                  | 31                   | 100        |
| Total Percent                              |          | 69.00%              | 31.00%               | 100.00%    |
| Count                                      | Control  | 70                  | 30                   | 100        |
| Total Percent                              |          | 70.00%              | 30.00%               | 100.00%    |
| Count                                      | All Grps | 139                 | 61                   | 200        |

Table 2

*Side of pleural effusions*

| Pearson Chi-square: 40.99, df = 2, p = 0.000 |          |           |        |        |            |
|--|----------|-----------|--------|--------|------------|
|  | Group    | Bilateral | Right  | Left   | Row Totals |
| Count  | Study    | 6         | 14     | 11     | 31         |
| Total Percent                                |          | 9.84%     | 22.95% | 18.03% | 50.82%     |
| Count  | Control  | 30        | 0      | 0      | 30         |
| Total Percent                                |          | 49.18%    | 0.00%  | 0.00%  | 49.18%     |
| Count  | All Grps | 36        | 14     | 11     | 61         |
| Total Percent                                |          | 59.02%    | 22.95% | 18.03% |            |

Of the 31 patients with pleural effusion, 22 (36.07%) had small pleural effusions, 8 (13.11%) had medium and 1 (1.64%) had a large pleural effusion. Of the 30 patients in the control group, six (9.84%) had small, 14 (22.95%) had medium and 10 (16.39%) had large pleural effusions. Distribution data for the size of the pleural effusion showed that there is a significant statistical difference between the study and the control groups of  $\chi^2 = 18.13$  and  $p < 0.001$  (Table 3).

In the study group, 18 (29.51%) had yellowish pleural effusions, 12 (19.67%) had haemorrhagic pleural effusion and 1 (1.64%) had a transparent pleural effusion. Of the 30 patients in the control group, 11 (18.03%) had yellow, 7 (11.48%) had haemorrhagic pleural effusions and 12 (19.67%) had

transparent pleural effusions. Distribution data for the colour of the pleural effusion showed that there is a significant statistical difference between the study and the control group of  $\chi^2 = 12.30$  and  $p < 0.01$  ( $p = 0.002$ ) (Table 4).

Table 3

*Size of pleural effusions*

| Pearson Chi-square: 18.13, df = 2, p = 0.000 |          |        |        |        |            |
|--|----------|--------|--------|--------|------------|
|  | Group    | Small  | Medium | Large  | Row Totals |
| Count  | Study    | 22     | 8      | 1      | 31         |
| Total Percent                                |          | 36.07% | 13.11% | 1.64%  | 50.82%     |
| Count  | Control  | 6      | 14     | 10     | 30         |
| Total Percent                                |          | 9.84%  | 22.95% | 16.39% | 49.18%     |
| Count  | All Grps | 28     | 22     | 11     | 61         |
| Total Percent                                |          | 45.90% | 36.07% | 18.03% |            |

Table 4

*Colour of pleural effusions*

| Pearson Chi-square: 12.30, df = 2, p = 0.002 |          |           |          |        |            |
|--|----------|-----------|----------|--------|------------|
|  | Group    | Yellowish | Haemorr. | Clear  | Row Totals |
| Count  | Study    | 18        | 12       | 1      | 31         |
| Total Percent                                |          | 29.51%    | 19.67%   | 1.64%  | 50.82%     |
| Count  | Control  | 11        | 7        | 12     | 30         |
| Total Percent                                |          | 18.03%    | 11.48%   | 19.67% | 49.18%     |
| Count  | All Grps | 29        | 19       | 13     | 61         |
| Total Percent                                |          | 47.54%    | 31.15%   | 21.31% |            |

In the study group (Fig. 1), values of the total protein in pleural effusions vary in the interval  $45.70 \pm 7.25$  gr/l.,  $\pm 95.00\%$  CI: 43,04–48,36; the minimal value is 21.10 g/l., and the maximal value is 58.10 g/l. Total proteins in effusions in the control group vary in the interval  $23.12 \pm 7.01$  gr./l.,  $\pm 95.00\%$  CI: 20,51–25,74; the minimal value is 00.00 g/l., and maximal value 32.0 g/l. (Table 5).

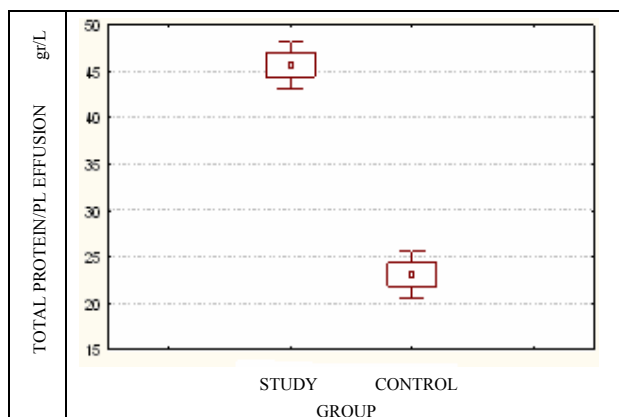


Figure 1 – Values of the total protein in pleural effusions

Table 5

Total proteins in pleural effusions/study and control group

| Total proteins/<br>group | Valid<br>N | Mean  | Confidence<br>-95.00% | Confidence<br>+95.00% | Min   | Max   | Std. Dev |
|--------------------------|------------|-------|-----------------------|-----------------------|-------|-------|----------|
| Study                    | 31         | 45.70 | 43.04                 | 48.36                 | 21.10 | 58.10 | 7.25     |
| Control                  | 30         | 23.12 | 20.51                 | 25.74                 | 0.00  | 32.00 | 7.01     |

Mean values of the total proteins in pleural effusion in the study group are bigger than in the control group,  $Z = 6.46$  and  $p < 0.001$ ; the difference is significant (Table 6).

Table 6

Total proteins in pleural effusions/ differences

| Total proteins | Rank Sum<br>Study group | Rank Sum<br>Control group | U     | Z    | p-level |
|----------------|-------------------------|---------------------------|-------|------|---------|
|                | 1409.00                 | 482.00                    | 17.00 | 6.46 | 0.000   |

In the study group, 30 patients had an LDH effusion/sera ratio greater than 0.6, and 1 patient had the LDH p/s ratio  $< 0.6$ . In the control group none of

them had LDH > 0.6. Distribution data for the LDH ratio p/s > 0.6 showed that there is a significant statistical difference between the study and the control groups,  $\chi^2 = 57.13$  and  $p < 0.001$  (Table 7).

Table 7

*LDH ratio p/s in study and control group*

| Pearson Chi-square: 57.13, df = 1, p = 0.000 |          |                   |                  |            |
|--|----------|-------------------|------------------|------------|
|  | Group    | LDH p/s > 0.6 YES | LDH p/s > 0.6 NO | Row Totals |
| Count  | Study    | 30                | 1                | 31         |
| Total Percent                                |          | 49.18%            | 1.64%            | 50.82%     |
| Count  | Control  | 0                 | 30               | 30         |
| Total Percent                                |          | 0.00%             | 49.18%           | 49.18%     |
| Count  | All Grps | 30                | 31               | 61         |
| Total Percent                                |          | 49.18%            | 50.82%           |            |

In the study group, 15 patients (24.59) had neutrophil cells, 10 had lymphocytes (16.39%), and eosinophil cells dominated in 5 (8.20%). One patient (1.64%) had a negative cytological finding. In the control group all 30 patients had negative cytological findings. Distribution data for the cytological findings in the pleural effusions showed that there is a significant statistical difference between the study and the control group,  $\chi^2 = 57,13$  and  $p < 0.001$  (Table 8).

Table 8

*Cytological characteristics of pleural effusions*

| Pearson Chi-square: 57.13, df = 3, p = 0.000 |          |          |        |       |        |            |
|--|----------|----------|--------|-------|--------|------------|
|  | Group    | Cytology |        |       |        | Row Totals |
|  |          | No       | Lympho | Eo    | Neutro |            |
| Count  | Study    | 1        | 10     | 5     | 15     | 31         |
| Total Percent                                |          | 1.64%    | 16.39% | 8.20% | 24.59% | 50.82%     |
| Count  | Control  | 30       | 0      | 0     | 0      | 30         |
| Total Percent                                |          | 49.18%   | 0.00%  | 0.00% | 0.00%  | 49.18%     |
| Count  | All Grps | 31       | 10     | 5     | 15     | 61         |
| Total Percent                                |          | 50.82%   | 16.39% | 8.20% | 24.59% |            |

*Discussion*

In the literature, the incidence of pleural effusions in PE varies between 23 and 48%, diagnosed with chest radiography [8, 9]. Data for pleural effusions described with MDCT are partial because there is still a relatively small series of patients with that pathology. In several studies pleural effusions due to PE are described as transudative or exudative, although in recent years almost all studies reject this hypothesis [10, 3]. In our study 31% with PE had pleural effusions; this data is comparable with the data published by several authors [8, 9].

In the study several aspects of the pleural effusions in PE (study group) and pleural effusion due to other conditions (control group) were examined. CUS was performed to diagnose pleural effusion; thoracocentesis under CUS was performed in every effusion greater than 1 cm., every pleural effusion was macroscopically (colour), microscopically, biochemically and cytologically examined.

There is a statistically significant difference for the side of pleural effusion between the study and the control group of  $\chi^2 = 40.99$  and  $p < 0.001$ ; in this study pleural effusions in PE are unilateral. This data matches the data of Pocol *et al.* [11].

It is characteristic that pleural effusion which are small dominate in our study, and there is a statistically significant difference between the study and the control group of  $\chi^2 = 18.13$  and  $p < 0.001$ ; these data are very similar to those of Porcel *et al.*, Candeira *et al.* and Light *et al.* [11, 3, 10].

Although many thought that pleural effusions in PE are mostly haemorrhagic, still many studies, especially that of Candeira *et al.* [3], show that the colour of the pleural effusion varies from yellowish to haemorrhagic. In our study, yellowish colour of the pleural effusions dominated in PE (29.5%), with haemorrhagic (19.67%). There is a significant difference between the study and the control group of  $\chi^2 = 12.30$  and  $p < 0,01$  ( $p = 0.002$ ).

This study shows the uniformity of the exudative character of the pleural effusions in PE. Until 1976, most authors classified the pleural effusions as exudates [12–15]. But Bynum and Wilson [4] in 1976 published a study in which one third of 26 pleural effusions in PE were transudates. This paper is cited many times, but there were no attempts to compare these data with data from other authors. The paper, however, also has several methodological restrictions; effusions are obtained with rigid thoracotomy which can alter the character of the effusion; a small group of patients was examined, outdated biochemical criteria for the exudative character of effusion were used; total protein levels and LDH levels in pleural effusion were not examined. In our study, the mean value of the total proteins is 45.7 g/l; all the pleural effusions in PE are exudates, and the total protein ratio in pleural effusions/sera is  $> 0.5$ . The mean



values of the total proteins in pleural effusions in the patients in the study group are greater than in the patients in the control group,  $Z = 6.46$  and  $p < 0.001$ , and there is a significant difference. Also, there is a significant difference between LDH levels in pleural effusions in the study and the control groups,  $\chi^2 = 57.13$  and  $p < 0.001$ . These values show that pleural effusions are exudates according to the Light LW criteria [10, 5].

In the present study, neutrophil cells dominate in the pleural effusions due to PE (in almost half the pleural effusions). These data match the data from Light LW [16] and, partially, the results from Porcel *et al.*, Candeira SR *et al.* [11, 3].

### Conclusion

In this study we have shown that pleural effusions secondary to pulmonary embolism can be found in around one third of all cases with PE. They are small, mostly unilateral, often, but not always, haemorrhagic. They are always exudates with a predomination of neutrophil cells.

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Резиме

**ЧЕСТОТА И КАРАКТЕРИСТИКИ НА ПЛЕВРАЛНИ ИЗЛИВИ  
КАЈ БЕЛОДРОБНА ТРОМБОЕМБОЛИЈА****Сандевски А.<sup>1</sup>, Јовковска Каева Б.<sup>2</sup>, Глигоровски Љ.<sup>2</sup>,  
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Белодробната тромбоемболија (БЕ) е четврта причина за појава на плеврален излив, по пневмонии, малигни болести и туберкулоза. Сè уште постојат неколку неодговорени прашања: дали плевралните изливи кај БЕ се трансудати или ексудати, каква е нивната големина, дали се унилатерални или билатерални, дали се хеморагични итн.

Целта на студијата е да се одреди фреквенцијата, страната, големината, биохемиските и цитолошките карактеристики на плевралните изливи кај БЕ.

Во студијата испитани се 100 пациенти суспектни за постоење на БЕ. Кај сите е потврдена дијагноза за БЕ, а плеврални изливи имаа 31 пациент.

Од 31 пациент со БЕ и плеврални изливи: шест (9,84%) имаа билатерални плеврални изливи, 14 (22,95%) пациенти имаа деснострани плеврален излив, и 11 (18,03%) имаа плеврален излив од левата страна. 22 (36,07%) имаа мали плеврални изливи, 8 (13,11%) имаа средни и 1 (1,64%) имаше масивен плеврален излив. Кај 18 (29,51%) плевралниот излив беше со жолта боја, 12 (19,67%) имаа хеморагичен, а еден (1,64%) имаше безбоен плеврален излив.

Вредностите на вкупните протеини во плевралните изливи варираа во интервали  $45,70 \pm 7,25$  g/l. 30 пациенти имаа LDH однос на пунктат/серум поголем од 0,6, и 1 пациент имаше LDH однос на пунктат/серум помал од 0,6. Кај 15 пациенти (24,59%) доминираа неутрофили во плевралната течност, лимфоцити имаа 10 (16,39%), и еозинофили имаше кај 5 (8,20%). Еден пациент имаше негативен цитолошки наод.

Можеме да заклучиме дека плевралните изливи поради БЕ може да се сретнат кај околу една третина од пациентите со БЕ. Тие се мали, нај-

често еднострани, често но не секогаш хеморагични. Секогаш се ексудати со преминација на неутрофили.

**Клучни зборови:** белодробна тромбоемболија, плеврален излив, едностран, ексудати, неутрофили.

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