



Malignant Pleural Effusion: The Importance of pH as Prognostic Marker. A 2-Year Review

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Abstract

Malignant Pleural Effusion (MPE) is a sign of advance disease in patients with cancer. The management of these patients could present as a challenge. It is crucial to identify patients with poor prognosis and offer them alternatives to pleurodesis (a discomfort procedure that may lead to hospitalization). Although several studies have been conducted to assess the accuracy of pH as prognostic factor in MPE, its use is not validated by international guidelines. A retrospective analysis of the electronic medical records of all patients with MPE that underwent first thoracentesis in our department between June 2016 and June 2018 was done. The primary endpoint was to assess the relation between pH of MPE and survival. 62 patients were included in this study. PH mean was 7.32. Median survival in months for Group A, defined as pH less than the mean, was 1.9 months [1.3-4.9] and for Group B, defined as pH equal or superior to the mean was 4.3 [2.5-13] ($p=0.006$). We found an existence relation between pH inferior to 7.32 and lower median survival. The association between low pH and survival could be explained as tumors in advanced stage of disease may provoke the accumulation of end products of glycolysis in the pleural space.

Introduction

The presence of malignant cells in pleural fluid or parietal pleura is a sign of advance disease with concomitant reduction of life expectancy in patients with lung cancer [1]. Median survival after the diagnosis of pleural effusion is usually 4 to 7 months and quality of life is impaired by dyspnea, cough or other symptoms due to recurrent pleural effusion [2,3]. Malignant Pleural Effusion (MPE) due to lung cancer has the shortest survival time and ovarian cancer the longest [1]. The management of patients with MPE is a challenge. Pleurodesis requires the insertion of a chest tube which is a discomfort procedure many times associated with the need of hospitalization. Also, pleurodesis could lead to pleural infection. Patients with poor prognosis that are already in pain may prefer to undergo less invasive palliative measures rather than prolonging their time in the hospital [4]. Limited data exist to assist clinicians in predicting short-term survival. The use of pH in MPE as a prognostic marker is still in discussion.

Material and Methods

A retrospective analysis of the electronic medical records of all patients with MPE that underwent first thoracentesis in our department between June 2016 and June 2018 was done. The primary endpoint was to assess the relation between pH of MPE and survival. Patients that abandoned our centre during treatment were excluded. MPE was defined as positive malignant cells on cytologic examination of the effusion or in pleural biopsy. All malignancies were included. The mean pH of the MPE evaluated was 7.32 and patients were divided in two groups according to this value: A, defined as pH less than the mean, and B, defined as pH equal or superior to the mean. The results were analyzed using IBM SPSS Statistics version 25[®] (Lisbon, Portugal). Survival after first thoracentesis was assessed with Kaplan-Meier curves. Categorical variables are presented as frequencies and percentages, and continuous variables as medians and [25th percentile to 75th percentile] since all had skewed distributions. Generalized Wilcoxon test was used to compare results.

Results

62 patients were included (51.6% male). Median age in years was 70.50 [59.0-80.25]. 33 of MPE (53.2%) were secondary to lung cancer (Table 1). Overall median survival was 2.78 [1.8-9.3] months (Figure 1). pH mean value was 7.32. 25 (40.3%) of the patients had a pH inferior to the mean and 37 (59.7%) equal or superior. Median survival in months for Group A was 1.9 months [1.3-4.9] and

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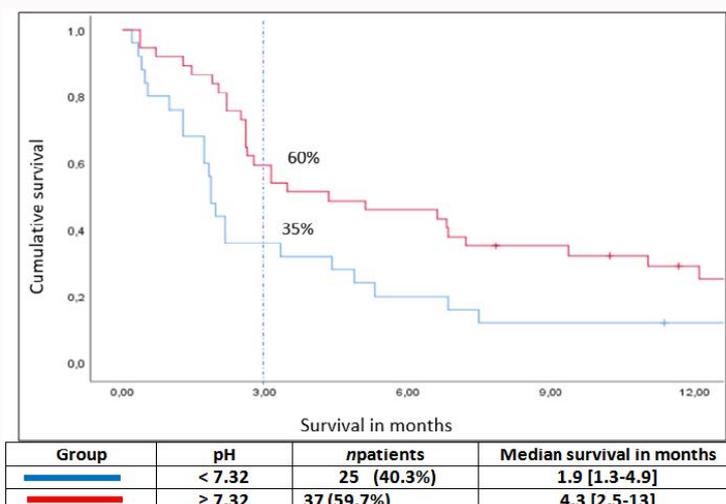


Figure 1: Survival comparison between group A (pH<7.32) and group B (pH ≥ 7.32).

Table 1: Malignant pleural effusion cancer etiology.

	n	%
Lung	33	53.2
Adenocarcinoma	22	
Squamous Cell carcinoma	7	
Small cell cancer	4	
Breast	9	14.5
Ovarian	6	9.7
Uterus	3	4.8
Gastric	2	3.2
Kidney	2	3.2
Urothelial	2	3.2
Others	5	8

for Group was 4.3 [2.5-13] months (p=0.006). Three months after first thoracentesis 35% and 60% of the patients were alive in group A and B respectively. No association was found between tumour type and pH values.

Discussion

The pH evaluation is of major importance in non-malignant pleural effusion, especially when infection is suspected, but often forgotten in MPE. The LENT score (that includes LDH in pleural fluid, performance status, neutrophil-lymphocyte ratio in the serum, and tumor type) stratifies patients into risks groups and is a validated tool in the management of MPE [5]. PH assessment is not part of this score. The use of pH as prognostic factor in MPE has been the role of diverse publications but results are still not consistent [1-5] and its use as a single marker or in a combined score is not yet approved in the 2018 European Respiratory Society statement on the management of MPE [6].

In our work we found an existence relation between pH inferior to 7.32 and low median survival, reinforcing the existing data on the potential role of pH as prognostic factor in MPE. The association between low pH and survival could be explained from accumulation of end products of glycolysis in the pleural space caused by tumors in advanced stage of disease. If approved by international societies this marker could identify patients with fewer benefits of pleurodesis in a more practical way when compared to LENT score. Prospective studies are needed to confirm our findings.

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