ONLINE DATA SUPLEMENT

Definitions

A **malignant** PE was defined by the presence of malignant cells on PF cytology or pleural biopsy. **Paramalignant** PE was defined as a PE associated with a known malignancy, albeit malignant cells could not be detected in the PF or pleural tissue, and effusion arises from another mechanism\(^27\). PF was considered **tuberculous** when confirmed by Ziehl-Neelsen staining, culture was positive for Mycobacterium tuberculosis in sputum, PF, or pleural biopsy, or if granulomas were observed in the biopsy. **Infectious** PE was defined as that associated with bacterial pneumonia, lung abscess, or bronchiectasis. Infectious PEs were classified as simple or uncomplicated, complicated (pH <7.20 or loculated PE in an ultrasound or chest CT scan), or empyema (pus in the PF or positive PF bacterial cultures). Diagnosis of **heart failure** was based on Framingham clinical criteria, response to diuretic treatment and, if available, echocardiographic or diagnostic evidence of systolic dysfunction\(^28\). In cases of suspected heart failure, only those patients with asymmetric PE or pain or fever were punctured\(^29\). Other PEs were diagnosed based on predefined criteria\(^1\).

Variables

The **clinical variables** analyzed were age, gender, fever (temperature >37ºC), cough, dyspnea, chest pain, time of evolution of symptoms until thoracentesis (less or more than 30 days) and general syndrome (asthenia, anorexia and loss of 10% of its usual weight).

**Radiological variables** were: PE size (<1/3 of the hemithorax, >1/3 of the hemithorax but <2/3 of the hemithorax, >2/3 of the hemithorax), laterality of PE, lung lesion, and images considered as suggestive of malignancy, either on simple X-ray or on chest CT-scan (presence of lung masses, pulmonary atelectasis, or mediastinal lymph node disease).

**Analytical variables** included appearance of PF (serous, serous-bloody, bloody, purulent
and milky); total count and percentage of leukocytes (segmented, lymphocytes and eosinophils); pH, cholesterol, total proteins, albumin, lactate dehydrogenase (LDH), adenosine deaminase (ADA), interleukins 6 and 8 (IL-6, IL-8), C-reactive protein (CRP), carcinoembryonic antigen (CEA), cancer antigen 125 (CA125) and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels. **Biochemical variables** were determined in both PF and blood, with their respective ratios and/or gradients.