Revisiting Light's criteria: a validated blood-free triple combination matches diagnostic accuracy in over 7000 patients

José M. Porcel [1], Laura Porcel[2], Rosa Palma[1] and Silvia Bielsa[1]

[1]Pleural Medicine and Clinical Ultrasound Unit, Department of Internal Medicine, Arnau de Vilanova University Hospital, IRBLleida, Lleida, Spain. [2]Department of Internal Medicine, Hospital Universitario Príncipe de Asturias, Alcalá de Henares, Madrid, Spain.

Corresponding author: José M. Porcel (josemporcel@icloud.com)

Shareable abstract (@ERSpublications)
A pleural fluid combination of protein, LDH and cholesterol matches Light's criteria in diagnostic accuracy, avoids serum sampling, safely identifies exudates and reclassifies more transudates. This supports revisiting current diagnostic standards. https://bit.ly/475Wzkg

Cite this article as: Porcel JM, Porcel L, Palma R, *et al*. Revisiting Light's criteria: a validated blood-free triple combination matches diagnostic accuracy in over 7000 patients. *ERJ Open Res* 2026; 12: 00821-2025 [DOI: 10.1183/23120541.00821-2025].

This article has an editorial commentary: https://doi.org/10.1183/23120541.01362-2025

Received: 15 June 2025
Accepted: 7 Sept 2025

Abstract

Background Light's criteria remain the standard for distinguishing exudative from transudative pleural effusions, but require serum sampling and lack specificity. We assessed whether a pleural fluid-only approach could match the diagnostic accuracy.

Methods We analysed 7280 diagnostic thoracenteses from a single centre, divided into derivation (n=5000) and validation (n=2280) cohorts. We compared Light's criteria with a triple (protein >3 g·dL^{-1}, lactate dehydrogenase (LDH) >250 IU·L^{-1} or cholesterol >55 mg·dL^{-1}) and a double (LDH >250 IU·L^{-1} or cholesterol >55 mg·dL^{-1}) combination using sensitivity, specificity, likelihood ratios and area under the curve (AUC). AUCs were assessed using the DeLong method with multiple imputations from a mixed model. McNemar's test examined discordant classifications.

Results The triple combination showed no significant AUC difference *versus* Light's criteria in either cohort and had equivalent sensitivity (99% *versus* 98% in derivation; both 98% in validation). In the derivation cohort, McNemar's test showed a small but statistically significant excess of false negative exudates with the triple combination ($p<0.001$), whereas no significant difference was found in the validation cohort ($p=0.241$). The triple combination correctly reclassified 19–20% of transudates misclassified by Light's criteria, while the reverse occurred in 11–14%. The double combination yielded the highest AUCs but missed more exudates, limiting its clinical safety.

Conclusion A pleural fluid-only triple combination matches Light's criteria in diagnostic accuracy, avoids serum sampling and improves specificity with minimal sensitivity loss in one cohort. This approach may be a practical alternative for the initial classification of pleural effusion when blood sampling is unavailable or undesirable.

Introduction

Differentiating between pleural exudates and transudates is a critical initial step in the diagnostic evaluation of pleural effusion. A transudate is an ultrafiltrate of plasma that occurs through intact pleural membranes, with heart failure being the predominant cause. Consequently, the presence of transudates typically indicates the need for diuretic therapy. Conversely, exudates result from the increased permeability of an inflamed or tumour-invaded pleura. Identifying an exudate, which may arise from various etiologies, requires further diagnostic investigations, potentially including invasive procedures such as pleural biopsy [1].

Light's criteria remain the gold standard for exudate–transudate differentiation [2]. Although Light's criteria have been extensively evaluated, previous studies were based on relatively small series, often with a limited number of transudates. The largest single-centre study to date included 1490 patients (298 transudates) [3], and the most comprehensive meta-analysis gathered data from 1448 patients

(377 transudates) [4]. Most studies have not incorporated a validation cohort, and in instances where they have, the cohort has typically comprised a limited number of patients (*e.g.* 112 fluid samples in the study of Lépine *et al*. [5]). In addition, several studies have assumed that the combination of lactate dehydrogenase (LDH) and cholesterol in pleural fluid has a similar accuracy to Light's criteria, with the advantage of avoiding a simultaneous blood sample [5–12]. However, this assertion was based on patient series ranging from 32 [10] to a maximum of 108 transudates [12]. These limitations highlight the need for updated analyses based on larger and better-structured populations to reassess the diagnostic accuracy of Light's criteria and its potential alternatives. This was the aim of the present study.

Methods

Study population and design

We conducted a retrospective review of the demographics, blood biochemistry, pleural fluid analyses and final diagnoses of all consecutive patients who underwent diagnostic thoracentesis at our hospital between January 1994 and March 2025. The study protocol was approved by the local ethics committee (CEIC-1960).

Diagnostic criteria

The diagnosis of pleural transudate or exudate was based on the underlying etiology of pleural effusion, which was established according to standard criteria [13]. Heart failure was diagnosed on clinical grounds (*i.e.*, typical symptoms and signs, chest radiography, electrocardiography, echocardiography, pleural fluid chemistry, serum and pleural fluid natriuretic peptide levels, response to diuretics and exclusion of other potential causes of pleural fluid accumulation) [14–16]. Malignant pleural effusion was diagnosed when pleural cytology or pleural biopsy showed malignant cellularity or when the patient had a known tumour and an exudate with negative cytology that could not be justified by any other cause. The diagnosis of pleural tuberculosis was based on the identification of *Mycobacterium tuberculosis* in pleural fluid samples (cultures or nucleic acid amplification tests), the presence of caseating granulomas in a pleural biopsy, or the existence of a lymphocytic exudate with elevated adenosine deaminase levels and resolution with anti-tuberculosis treatment. Infectious pleural effusions were those associated with pneumonia or attributable to primary pleural infection due to bacteraemia. Idiopathic pleural effusion was defined as an exudative effusion of unknown cause despite comprehensive pleural fluid and imaging investigations that resolved spontaneously and was followed for at least 24 months after resolution without evidence of an underlying disorder. Cases in which no definitive etiological diagnosis was reached and that did not meet the above criteria for idiopathic effusion were excluded from the database; these represented <3% of the overall population. In patients in whom dual mechanisms were suspected (*e.g.* pneumonia or malignancy with secondary decompensated heart failure), the effusion was attributed to the primary or precipitating cause that was considered responsible for the fluid accumulation. The final diagnoses were determined by two senior investigators (J.M. Porcel and S. Bielsa) using clinical, laboratory, imaging and follow-up data. Discrepancies were resolved by consensus, and cases with insufficient information were excluded from the database.

Data collection

All pleural fluid and serum parameters were obtained at the time of thoracentesis and were prospectively entered into a dedicated pleural disease database. No samples were stored or reanalysed in this study. The values of protein, albumin and LDH in both serum and pleural fluid, along with pleural fluid cholesterol levels, were recorded when available. Missing data were infrequent for most variables, except for pleural fluid cholesterol (unavailable in ∼44% of the derivation cases). This was because systematic measurement of pleural fluid cholesterol at our centre was only implemented in the past 2–3 years; in earlier periods, the request was variable. Serum LDH was missing in ∼20% and serum protein in ∼10% of patients, with substantially lower rates for other parameters. Light's criteria and alternative criteria that did not require blood samples were applied. Biochemical analyses of pleural fluid were performed using Hitachi automatic analysers. In our laboratory, the upper limit of the normal LDH level is 378 $IU \cdot L^{-1}$.

Statistical analysis

Categorical and continuous variables were expressed as numbers and percentages and medians and 25th and 75th quartiles, respectively. The measures of test performance for Light's criteria and the alternative criteria included sensitivity, specificity, likelihood ratios (LRs) and area under the curve (AUC). The study population was randomly split into derivation and validation cohorts using the SPSS software (version 24.0). Differences between the derivation and validation populations were analysed using χ^2 tests for categorical variables (sex and etiologies) and Mann–Whitney tests for continuous variables (age).

Two pleural fluid-only diagnostic strategies were evaluated alongside Light's criteria, with the aim of identifying models that avoid the need for a simultaneous blood sample. The "triple combination" was defined as pleural fluid protein >3 $g \cdot dL^{-1}$, LDH >250 $IU \cdot L^{-1}$ (more than two-thirds of the upper limit of the laboratory's normal serum LDH) or cholesterol above a given cut-off value. Several "double combinations" were also explored, including protein >3 $g \cdot dL^{-1}$ or LDH >250 $IU \cdot L^{-1}$, protein >3 $g \cdot dL^{-1}$ or cholesterol, and LDH >250 $IU \cdot L^{-1}$ or cholesterol. For all combination tests, an "or" rule was applied, meaning that the presence of a pleural fluid value above the cut-off for any of the included parameters classified the effusion as exudate.

The cut-off points for pleural fluid protein (>3 $g \cdot dL^{-1}$) and LDH (>250 $IU \cdot L^{-1}$) were selected because they are widely recognised in prior research [1, 2] and were confirmed in our derivation cohort to yield the highest Youden indices (0.68 and 0.71, respectively). For cholesterol, thresholds ranging from 40 to 60 $mg \cdot dL^{-1}$ were systematically explored in the derivation cohort, and the most appropriate cut-off was selected based on the overall diagnostic performance for inclusion in the final combination models.

The McNemar and DeLong tests were used to compare the accuracy and AUC between Light's criteria and the best alternative criteria that did not require a serum sample. The McNemar test was based on a 2×2 contingency table, focusing on the off-diagonal elements, which represent discordant pairs. AUC comparisons were performed using the multiple imputation extension of the DeLong method [17]. This approach accommodates missing values through a multivariate mixed-model framework, allowing valid receiver operating characteristic comparisons even when some parameters are unavailable for a subset of patients.

Results

Study patients

The study population, comprising 7280 patients, was stratified into a derivation cohort of 5000 patients and a validation cohort of 2280 patients, maintaining a comparable relative distribution of exudates and transudates in both cohorts. Table 1 presents the demographic characteristics and etiologies of pleural

TABLE 1 Characteristics of the study population

Characteristics	All patients	Derivation cohort	Validation cohort	p-value[#]
Patients, n	7280	5000	2280	
Age, years	73 (59–83)	73 (59–83)	73 (59–84)	0.30
Female sex	2962 (41)	2058 (41)	904 (40)	0.22
Transudates	2627 (36)	1783 (36)	844 (37)	0.26
Exudates	4653 (64)	3217 (64)	1436 (63)	0.26
Etiology of transudates				0.69
Heart failure	2254 (86)	1531 (86)	723 (86)	
Cirrhosis	175 (7)	122 (7)	53 (6)	
Others	198 (7)[¶]	130 (7)	68 (8)	
Etiology of exudates				0.68
Malignancy	1894 (41)[+]	1314 (41)	580 (40)	
Infection	1178 (25)[§]	802 (25)	376 (26)	
Tuberculosis	405 (9)	284 (9)	121 (8)	
Post-surgery	335 (7)	230 (7)	105 (7)	
Pericardial diseases	245 (5)	172 (5)	73 (5)	
Idiopathic	160 (3)	105 (3)	55 (4)	
Trauma	141 (3)	107 (3)	34 (2)	
Pulmonary embolism	88 (2)	57 (2)	31 (2)	
Others	207 (4)[f]	146 (5)	61 (4)	

Data are presented as n (%) or median (interquartile range), as appropriate. [#]: for comparison between the derivation and validation cohorts; [¶]: other transudates included hypoalbuminaemia (64), non-expandable lung (32), pulmonary arterial hypertension (26), nephrotic syndrome (23), peritoneal dialysis (18) and miscellaneous (35); [+]: main causes of malignant effusions were lung (779, 41%), breast (258, 13%), gastrointestinal (213, 11%), haematological (185, 10%) and gynaecological (152, 8%) cancers; [§]: infectious effusions included complicated parapneumonics (497, 42%), empyema (286, 24%), noncomplicated parapneumonics (377, 32%) and pleural infection unrelated to pneumonia (18, 2%); [f]: other exudates included systemic autoimmune diseases (36), pancreatitis (21), uraemia (20), abdominal abscesses (18), drug-related (10), oesophageal perforation (9), sarcoidosis (6), ovarian hyperstimulation syndrome (5) and miscellaneous (82).

effusions. The median age of the population was 73 years, and 41% were women. Heart failure accounted for 86% of transudates, whereas malignancy (41%) and pleural infection (25%) were the most common causes of exudates.

Selection of the cholesterol cut-off value

Exploratory analyses in the derivation cohort evaluated pleural cholesterol thresholds of 40, 45, 50, 55 and 60 $mg \cdot dL^{-1}$, which yielded Youden indices of 0.70, 0.70, 0.68, 0.62 and 0.58, respectively. Although the lower thresholds (40–45 $mg \cdot dL^{-1}$) provided the highest Youden indices, incorporating them into the pleural fluid-only triple rule resulted in significantly lower AUCs than Light's criteria, indicating an inferior overall performance. A threshold of 60 $mg \cdot dL^{-1}$ was also suboptimal as a single test because of its reduced sensitivity. In contrast, both 50 $mg \cdot dL^{-1}$ and 55 $mg \cdot dL^{-1}$ preserved the AUC equivalence with Light's criteria when used within the triple combination. Among these, 55 $mg \cdot dL^{-1}$ was selected for the final model because it offered the most balanced diagnostic profile, maintaining 99% sensitivity across both cohorts while improving specificity, even though it showed a slightly higher number of missed exudates than Light's criteria in the McNemar test in the derivation cohort (as shown in detail below), a difference that was not reproduced in the validation cohort.

Diagnostic accuracy of individual and combined tests

Tables 2 and 3 show the diagnostic accuracies of the individual and combined tests for identifying exudates in the derivation and validation populations. In the derivation cohort, Light's criteria showed a sensitivity of 98%, specificity of 71%, positive LR of 3.4, negative LR of 0.02 and AUC of 0.847 for identifying exudates. These operating characteristics were similar to those obtained with the combination in an "or" rule of protein >3 $g \cdot dL^{-1}$, LDH >250 $IU \cdot L^{-1}$ (two-thirds the upper limit of normal for serum LDH) and cholesterol >55 $mg \cdot dL^{-1}$ in pleural fluid (sensitivity 99%, specificity 72%, positive LR 3.6, negative LR 0.02 and AUC 0.846).

Comparing the AUCs of different diagnostic tests

Using the modified DeLong method [17], the triple combination (pleural fluid protein, LDH and cholesterol) showed no significant difference in AUC compared with Light's criteria in either the derivation or validation cohort (p=0.6875 and p=0.2909, respectively) (table 4). The double combination (pleural fluid LDH and cholesterol) demonstrated significantly higher AUCs than both Light's criteria and the triple combination in the derivation cohort (p=0.0114 and p<0.001, respectively); however, the difference *versus* Light's criteria did not reach statistical significance in the validation cohort (p=0.085).

Comparing diagnostic tests (binary matched-pairs data)

McNemar's test revealed that the triple combination classified significantly fewer exudates than Light's criteria in the derivation cohort (103 *versus* 54 false negatives; p<0.001), whereas no significant difference was observed in the validation cohort (50 *versus* 38 false negatives; p=0.241) (table 5). Despite this, the triple combination reclassified 20% (95% CI: 17–24%) of the transudates incorrectly labeled as exudates by Light's criteria in the derivation cohort and 19% (95% CI: 14–24%) in the validation cohort. Conversely, only 11% (95% CI: 8–14%) and 14% (95% CI: 10–20%) of transudates were better classified by Light's criteria than by the triple combination criteria. Among transudates misclassified as exudates, heart failure accounted for the vast majority (92% in the derivation cohort and 87% in the validation cohort), with hepatic hydrothorax and other conditions being much less common. Conversely, most exudates mislabeled as transudates were malignant (59% and 56% in the derivation and validation cohorts, respectively), followed by pericardial diseases. These proportions specifically refer to patients who were simultaneously misclassified by both Light's criteria and the triple combination.

The double combination showed significantly poorer sensitivity than both Light's criteria and the triple combination in both cohorts (p<0.001), missing 240 and 113 exudates in the derivation and validation cohorts, respectively. Notably, the double combination failed to identify any exudates that were not already captured by the triple combination, confirming the superior sensitivity of the latter (p<0.001 in both cohorts).

Discussion

Light's criteria have served as the cornerstone of pleural fluid analysis for over five decades, providing high sensitivity but only modest specificity as consistently demonstrated in the literature [4, 5, 16, 18–21]. Although their ease of use and robust validation have secured their status as the diagnostic reference standard, they require simultaneous serum sampling and often misclassify transudates as exudates, leading to unnecessary investigations.

TABLE 2 Measures of diagnostic accuracy for tests identifying exudative pleural effusions (derivation cohort)

Test	No. of transudates/ exudates	Sensitivity, % (95% CI)	Specificity, % (95% CI)	LR^+ (95% CI)	LR^- (95% CI)	AUC (95% CI)
Need for serum samples						
PF/S protein >0.5	1696/2800	87 (85–88)	86 (84–87)	6.0 (5.3–6.7)	0.16 (0.14–0.17)	0.861 (0.849–0.873)
PF/S LDH >0.6	1568/2430	89 (87–90)	84 (83–86)	5.7 (5.1–6.4)	0.14 (0.12–0.15)	0.865 (0.853–0.878)
S-PF protein ⩽2.5 $g \cdot dL^{-1}$	1696/2800	70 (68–71)	95 (93–96)	12.9 (10.5–15.7)	0.32 (0.30–0.34)	0.822 (0.810–0.834)
S-PF albumin ⩽1.2 $g \cdot dL^{-1}$	1327/841	72 (69–75)	90 (89–92)	7.4 (6.3–8.8)	0.31 (0.28–0.41)	0.810 (0.790–0.831)
PF protein >3 $g \cdot dL^{-1}$ or PF/S LDH >0.6	1605/3076	96 (95–97)	74 (72–76)	3.7 (3.4–4.0)	0.06 (0.05–0.07)	0.850 (0.837–0.864)
PF/S protein >0.5 or PF/S LDH >0.6	1572/2783	96 (95–97)	76 (73–78)	4.0 (3.6–4.3)	0.05 (0.04–0.06)	0.859 (0.846–0.873)
PF/S protein >0.5 or PF LDH >250 $IU \cdot L^{-1}$	1701/3138	97 (96–97)	78 (76–80)	4.4 (4.1–4.9)	0.04 (0.03–0.05)	0.875 (0.863–0.888)
PF/S protein >0.5 or PF/S LDH >0.6 or PF LDH >250 $IU \cdot L^{-1}$ (Light's criteria)	1587/3125	98 (98–99)	71 (69–73)	3.4 (3.1–3.7)	0.02 (0.02–0.03)	0.847 (0.836–0.858)
Serum samples not required						
PF protein >3 $g \cdot dL^{-1}$	1783/3192	84 (83–85)	84 (82–86)	5.3 (4.8–5.9)	0.19 (0.18–0.21)	0.841 (0.829–0.853)
PF LDH >250 $IU \cdot L^{-}$[#]	1781/3158	82 (81–83)	89 (88–91)	7.6 (6.6–8.7)	0.20 (0.19–0.22)	0.856 (0.845–0.868)
PF cholesterol >55 $mg \cdot dL^{-1}$	1443/1343	67 (65–70)	95 (94–96)	13.9 (11–17.5)	0.34 (0.32–0.37)	0.812 (0.795–0.829)
PF protein >3 $g \cdot dL^{-1}$ or PF LDH >250 $IU \cdot L^{-1}$	1781/3189	96 (96–97)	77 (75–79)	4.2 (3.9–4.6)	0.04 (0.04–0.06)	0.868 (0.855–0.880)
PF protein >3 $g \cdot dL^{-1}$ or PF cholesterol >55 $mg \cdot dL^{-1}$	1504/2935	93 (92–93)	80 (78–82)	4.7 (4.2–5.2)	0.09 (0.08–0.11)	0.864 (0.851–0.877)
PF LDH >250 $IU \cdot L^{-1}$ or PF cholesterol >55 $mg \cdot dL^{-1}$	1460/2842	96 (96–97)	84 (82–86)	5.9 (5.3–6.7)	0.04 (0.04–0.05)	0.861 (0.851–0.872)
PF protein >3 $g \cdot dL^{-1}$ or PF LDH >250 $IU \cdot L^{-1}$ or PF cholesterol >55 $mg \cdot dL^{-1}$	1510/3128	99 (98–99)	72 (70–75)	3.6 (3.3–3.9)	0.02 (0.02–0.03)	0.846 (0.835–0.857)

LR: likelihood ratio; AUC: area under the curve; PF/S: pleural fluid-to-serum ratio; LDH: lactate dehydrogenase; S-PF: serum-to-pleural fluid gradient; PF: pleural fluid. [#]: this value represents two-thirds of the upper limit of normal for serum LDH.

TABLE 3 Measures of diagnostic accuracy for tests identifying exudative pleural effusions (validation cohort)

Test	No. of transudates/ exudates	Sensitivity, % (95% CI)	Specificity, % (95% CI)	LR^+ (95% CI)	LR^- (95% CI)	AUC (95% CI)
Need for serum samples						
PF/S protein >0.5	801/1237	85 (83–87)	86 (83–88)	6.1 (5.1–7.2)	0.18 (0.15–0.20)	0.855 (0.837–0.873)
PF/S LDH >0.6	738/1085	88 (86–90)	83 (80–85)	5.0 (4.3–5.9)	0.15 (0.13–0.17)	0.852 (0.832–0.871)
S-PF protein ⩽2.5 $g{\cdot}dL^{-1}$	801/1237	67 (64–69)	93 (91–95)	10.1 (7.8–13.1)	0.36 (0.33–0.39)	0.801 (0.781–0.820)
S-PF albumin ⩽1.2 $g{\cdot}dL^{-1}$	609/356	68 (63–73)	91 (89–93)	8.0 (6.1–10.4)	0.35 (0.30–0.41)	0.797 (0.765–0.829)
PF protein >3 $g{\cdot}dL^{-1}$ or PF/S LDH >0.6	753/1365	96 (95–97)	71 (68–74)	3.3 (3.0–3.7)	0.06 (0.04–0.07)	0.836 (0.816–0.857)
PF/S protein >0.5 or PF/S LDH >0.6	738/1232	96 (95–97)	74 (71–77)	3.7 (3.3–4.2)	0.06 (0.04–0.07)	0.849 (0.829–0.869)
PF/S protein >0.5 or PF LDH >250 $IU{\cdot}L^{-1}$	803/1398	96 (95–97)	77 (74–80)	4.2 (3.7–4.8)	0.05 (0.04–0.06)	0.868 (0.850–0.886)
PF/S protein >0.5 or PF/S LDH >0.6 or PF LDH >250 $IU{\cdot}L^{-1}$ (Light's criteria)	745/1392	98 (97–99)	69 (66–73)	3.2 (2.9–3.6)	0.03 (0.02–0.04)	0.841 (0.826–0.857)
Serum samples not required						
PF protein >3 $g{\cdot}dL^{-1}$	844/1421	82 (80–84)	83 (80–85)	4.8 (4.1–5.6)	0.21 (0.19–0.24)	0.826 (0.807–0.853)
PF LDH >250 $IU{\cdot}L^{-}$[#]	843/1401	82 (80–84)	89 (87–91)	7.5 (6.1–9.0)	0.20 (0.18–0.22)	0.856 (0.839–0.873)
PF cholesterol >55 $mg{\cdot}dL^{-1}$	671/600	66 (62–70)	94 (92–96)	11.4 (8.4–15.6)	0.36 (0.32–0.40)	0.803 (0.777–0.828)
PF protein >3 $g{\cdot}dL^{-1}$ or PF LDH >250 $IU{\cdot}L^{-1}$	843/1416	96 (94–97)	75 (72–78)	3.9 (3.4–4.3)	0.06 (0.05–0.08)	0.854 (0.835–0.872)
PF protein >3 $g{\cdot}dL^{-1}$ or PF cholesterol >55 $mg{\cdot}dL^{-1}$	698/1294	92 (91–94)	78 (75–81)	4.3 (3.7–4.9)	0.10 (0.08–0.12)	0.853 (0.833–0.873)
PF LDH >250 $IU{\cdot}L^{-1}$ or PF cholesterol >55 $mg{\cdot}dL^{-1}$	680/1269	96 (95–97)	82 (79–85)	5.4 (4.6–6.4)	0.04 (0.03–0.06)	0.856 (0.841–0.871)
PF protein >3 $g{\cdot}dL^{-1}$ or PF LDH >250 $IU{\cdot}L^{-1}$ or PF cholesterol >55 $mg{\cdot}dL^{-1}$	704/1382	98 (98–99)	70 (66–73)	3.3 (2.9–3.7)	0.02 (0.02–0.04)	0.834 (0.818–0.850)

LR: likelihood ratio; AUC: area under the curve; PF/S: pleural fluid-to-serum ratio; LDH: lactate dehydrogenase; S-PF: serum-to-pleural fluid gradient; PF: pleural fluid. [#]: this value represents two-thirds of the upper limit of normal for serum LDH.

TABLE 4 Comparison of AUCs between diagnostic strategies using a modified DeLong test [17]

Strategy comparison	Cohort	AUC (95% CI): Light's criteria	AUC (95% CI): triple combination[#]	AUC (95% CI): double combination[¶]	AUC difference (95% CI)	p-value
Light's criteria *versus* triple combination	Derivation	0.847 (0.836–0.858)	0.846 (0.835–0.857)	–	0.0014 (−0.0077 to 0.0106)	0.6875
	Validation	0.841 (0.826–0.857)	0.834 (0.818–0.850)	–	0.0075 (−0.0065 to 0.0216)	0.2909
Light's criteria *versus* double combination	Derivation	0.847 (0.836–0.858)	–	0.861 (0.851–0.872)	−0.014 (−0.0249 to −0.0032)	0.0114
	Validation	0.841 (0.826–0.857)	–	0.856 (0.841–0.871)	−0.0142 (−0.0305 to 0.0019)	0.085
Triple *versus* double combination	Derivation	–	0.846 (0.835–0.857)	0.861 (0.851–0.872)	−0.0153 (−0.023 to −0.0076)	<0.001
	Validation	–	0.834 (0.818–0.850)	0.856 (0.841–0.871)	−0.0216 (−0.033 to −0.0104)	<0.001

AUC: area under the curve. [#]: triple combination=pleural fluid protein >3 g·dL^{-1} or LDH >250 IU·L^{-1} or cholesterol >55 mg·dL^{-1}; [¶]: double combination=pleural fluid LDH >250 IU·L^{-1} or cholesterol >55 mg·dL^{-1}.

In this study, the largest single-centre analysis in the literature with over 7000 thoracenteses, we compared Light's criteria with alternative diagnostic approaches based on pleural fluid biochemistry. Unlike previous studies and meta-analyses that relied on aggregated data from heterogeneous sources, our investigation included both a large derivation cohort and an independent validation cohort, allowing for rigorous, internally consistent comparisons.

Although the combination of pleural fluid LDH >250 IU·L^{-1} and cholesterol >55 mg·dL^{-1} achieved the highest AUC in the derivation cohort, McNemar's analysis (applied against the underlying clinical diagnosis) failed to identify a significantly higher number of exudates than Light's criteria did. Given the clinical importance of avoiding false negative diagnoses of exudates, this double combination cannot be recommended for routine use despite its superior overall discriminative ability. Additionally, the double combination did not capture exudates missed by the triple combination. Although other pleural fluid-only double combinations (*e.g.* protein with LDH or cholesterol) were considered, they showed notably lower sensitivities (tables 2 and 3), resulting in a higher rate of missed exudates. Therefore, only the LDH/cholesterol pairing was retained for a detailed AUC comparison.

In contrast, the pleural fluid–only triple combination (protein >3 g·dL^{-1}, LDH >250 IU·L^{-1}, or cholesterol >55 mg·dL^{-1}) demonstrated a diagnostic performance comparable to that of Light's criteria according to the AUCs, with virtually identical sensitivities in both cohorts (99% *versus* 98% in the derivation cohort and 98% for both strategies in the validation cohort). However, McNemar's test detected a statistically significant excess of exudates missed by the triple combination in the derivation cohort. This apparent discrepancy arises because McNemar's test evaluates only discordant classifications; therefore, even small absolute differences in misclassified exudates can reach statistical significance, even though the overall

TABLE 5 McNemar analysis: diagnostic agreement between Light's criteria and alternative strategies

Comparison	Cohort	A^+/B^+	A^-/B^+	A^+/B^-	A^-/B^-	McNemar p-value
Light's criteria *versus* triple combination[#]	Derivation	3377	103	54	925	<0.001
	Validation	1512	50	38	410	0.241
Light's criteria *versus* double combination[¶]	Derivation	2955	240	10	958	<0.001
	Validation	1332	113	8	433	<0.001
Triple *versus* double combination	Derivation	2979	0	184	1139	<0.001
	Validation	1345	0	89	515	<0.001

A^+/B^+=both tests positive for exudate; A^-/B^+=Test B (reference; Light's criteria) positive, Test A negative; A^+/B^-=Test A positive, Test B negative; A^-/B^-=both tests negative. In comparison with Light's criteria, the alternative strategy is Test A. In the comparison between triple and double combinations, the triple strategy was Test A. [#]: triple combination=pleural fluid protein >3 g·dL^{-1} or LDH >250 IU·L^{-1} or cholesterol >55 mg·dL^{-1}; [¶]: double combination=pleural fluid LDH >250 IU·L^{-1} or cholesterol >55 mg·dL^{-1}.

sensitivities are almost identical. The few exudates misclassified by both strategies typically had borderline biochemical values, and future studies focusing on these discordant cases may help refine the diagnostic algorithms. In practical terms, the triple combination missed slightly more exudates but also correctly reclassified 19–20% of transudates mislabeled as exudates by Light's criteria (*versus* 11–14% in the opposite direction), thereby reducing the number of false positive classifications. Given the minimal sensitivity loss, gain in specificity and advantage of avoiding serum sampling, this approach may be acceptable in selected clinical settings where a rapid pleural fluid-only classification is desirable. Nevertheless, alternative serum-based strategies, such as the serum–pleural fluid albumin gradient [18] or the BANCA score [16], are more effective than pleural fluid-only rules for reclassifying mislabeled transudates, although they require blood sampling and thus fall outside the scope of our analysis.

These findings provide robust confirmation of the longstanding hypothesis that pleural fluid-only strategies can match the diagnostic performance of Light's criteria without the need for serum data. While this concept was previously suggested in Heffner's 1997 meta-analysis [4] and later adopted in some practice guidelines [15], prior support relied on pooled estimates from methodologically diverse and underpowered studies without validation in large independent cohorts. Furthermore, previous comparisons often relied on overlapping confidence intervals of the AUCs, which is a statistically weak approach. Our study overcame these limitations by applying formal statistical testing (DeLong and McNemar), using robust cohort sizes, and performing internal validation.

From a practical standpoint, the triple combination offers tangible benefits. It simplifies the workflow by eliminating the need for blood draws, reduces potential preanalytical errors and avoids the redundancy inherent in Light's criteria, which combine pleural LDH with its ratio to serum LDH, a correlated metric that may not provide an independent value. While it is true that most patients with pleural effusion undergo blood testing, in routine practice, serum LDH is often omitted (~20% in our cohorts), results may be delayed (*e.g.* weekend procedures) or blood sampling may be technically difficult. Under these circumstances, a pleural fluid-only rule that yields immediate results represents a clinically sound and pragmatic alternative.

This study had some limitations. Although the study was retrospective, the data were prospectively collected and reflected real-world diagnostic decision-making. The reference standard for transudates and exudates was clinical and etiological, and invasive confirmation was not routinely performed in all patients. Nevertheless, these criteria align with accepted practices and are unlikely to undermine the robustness of our findings. In addition, the study was conducted at a single centre, which may limit the generalisability of the results to other settings. However, the large sample size and concordance of our findings for Light's criteria, pleural fluid cholesterol and the LDH–cholesterol pairing with those from previous reports [3, 5–12, 22], and for the triple combination with the findings of Heffner's meta-analysis [4], support their external validity. Because LDH cut-off values were derived as two-thirds of the upper limit of normal serum LDH, the absolute threshold may vary across laboratories, but the principle remains broadly applicable. Finally, we acknowledge that alternative pleural cholesterol thresholds (*e.g.* 50 $mg \cdot dL^{-1}$) may also be acceptable. However, we selected 55 $mg \cdot dL^{-1}$ as the final cut-off because it provided a balanced diagnostic profile and was supported by prior literature [23–25], thereby ensuring methodological consistency.

Some articles have previously pointed out that efforts to find a way to differentiate exudates from transudates other than Light's criteria should be abandoned [26, 27]. Yet, this article embraces the wisdom of the Spanish Nobel laureate Santiago Ramón y Cajal, who eloquently mused that "there are no exhausted questions, only people exhausted by the questions." In conclusion, we demonstrated that a pleural fluid-only triple combination is diagnostically equivalent to Light's criteria for classifying pleural effusions while offering greater operational simplicity and a potential reduction in false positive exudate diagnoses, albeit at the expense of a slightly higher number of misclassified exudates. These results support the adoption of the triple combination as a valid first-line strategy for the biochemical evaluation of pleural effusions, as acknowledged in recent review articles [28, 29].

Acknowledgments: We thank Dr Montse Martínez-Alonso from the Biostatistics Unit of IRBLleida (Lleida, Spain) for performing the statistical analyses.

Provenance: Submitted article, peer reviewed.

Ethics statement: This retrospective observational study was conducted in accordance with the Declaration of Helsinki and approved by the Clinical Research Ethics Committee of the Arnau de Vilanova University Hospital

(Lleida, Spain) (approval number 1960). The requirement for informed consent was waived due to the use of anonymised, routinely collected data.

Author contributions: J.M. Porcel contributed to data interpretation and design, and wrote the manuscript. L. Porcel and R. Palma collected data. S. Bielsa had full access to the data, takes responsibility for the integrity of the data, and performed the data analysis. All authors have read and approved the final version of this manuscript.

Conflict of interest: J.M. Porcel is an Associate Editor of *ERJ Open Research*. He was excluded from the editorial decision-making related to the acceptance of this article for publication. The remaining authors have no conflicts of interest to disclose.

References

1 Mercer RM, Corcoran JP, Porcel JM, *et al.* Interpreting pleural fluid results. *Clin Med* 2019; 19: 213–217.
2 Light RW, Macgregor MI, Luchsinger PC, *et al.* Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med* 1972; 77: 507–513.
3 Porcel JM, Peña JM, Vicente de Vera C, *et al.* Reappraisal of the standard method (Light's criteria) for identifying pleural exudates. *Med Clin* 2006; 126: 211–213.
4 Heffner JE, Brown LK, Barbieri CA. Diagnostic value of tests that discriminate between exudative and transudative pleural effusions. Primary Study Investigators. *Chest* 1997; 111: 970–980.
5 Lépine PA, Thomas R, Nguyen S, *et al.* Simplified criteria using pleural fluid cholesterol and lactate dehydrogenase to distinguish between exudative and transudative pleural effusions. *Respiration* 2019; 98: 48–54.
6 Costa M, Quiroga T, Cruz E. Measurement of pleural fluid cholesterol and lactate dehydrogenase. A simple and accurate set of indicators for separating exudates from transudates. *Chest* 1995; 108: 1260–1263.
7 Garcia-Pachon E, Padilla-Navas I. Pleural fluid cholesterol and lactate dehydrogenase for separating exudates from transudates. *Chest* 1996; 110: 1375–1376.
8 Romero S, Martinez A, Hernandez L, *et al.* Light's criteria revisited: consistency and comparison with new proposed alternative criteria for separating pleural transudates from exudates. *Respiration* 2000; 67: 18–23.
9 Yilmaz A, Tunaboyu IK, Akkaya E, *et al.* A comparative analysis of the biochemical parameters used to distinguish between pleural exudates and transudates. *Respirology* 2000; 5: 363–367.
10 Porcel JM, Vives M, Vicente de Vera MC, *et al.* Useful tests on pleural fluid that distinguish transudates from exudates. *Ann Clin Biochem* 2001; 38: 671–675.
11 Jiménez Castro D, Díaz Nuevo G, Pérez-Rodríguez E. Comparative analysis of Light's criteria and other biochemical parameters to distinguish exudates from transudates. *Rev Clin Esp* 2002; 202: 3–6.
12 Leers MP, Kleinveld HA, Scharnhorst V. Differentiating transudative from exudative pleural effusion: should we measure effusion cholesterol dehydrogenase? *Clin Chem Lab Med* 2007; 45: 1332–1338.
13 Porcel JM, Light RW. Pleural effusions. *Dis Mon* 2013; 59: 29–57.
14 Porcel JM, Ferreiro L, Civit C, *et al.* Development and validation of a scoring system for the identification of pleural exudates of cardiac origin. *Eur J Intern Med* 2018; 50: 60–64.
15 Sundaralingam A, Grabczak EM, Burra P, *et al.* ERS statement on benign pleural effusions in adults. *Eur Respir J* 2024; 64: 2302307.
16 Porcel JM, Trujillano J, Porcel L, *et al.* Development and validation of a diagnostic prediction model for heart failure-related pleural effusions: the BANCA score. *ERJ Open Res* 2025; 11: 01030–2024.
17 Zou L, Choi YH, Guizzetti L, *et al.* Extending the DeLong algorithm for comparing areas under correlated receiver operating characteristic curves with missing data. *Stat Med* 2024; 43: 4148–4162.
18 Bielsa S, Porcel JM, Castellote J, *et al.* Solving the Light's criteria misclassification rate of cardiac and hepatic transudates. *Respirology* 2012; 17: 721–726.
19 Ferreiro L, Sánchez-Sánchez R, Valdés L, *et al.* Concordant and discordant exudates and their effect on the accuracy of Light's criteria to diagnose exudative pleural effusions. *Am J Med Sci* 2016; 352: 549–556.
20 Porcel JM, Light RW. Pleural fluid analysis: are Light's criteria still relevant after half a century? *Clin Chest Med* 2021; 42: 599–609.
21 Vives M, Porcel JM, Vicente de Vera M, *et al.* A study of Light's criteria and possible modifications for distinguishing exudative from transudative pleural effusions. *Chest* 1996; 109: 1503–1507.
22 Gázquez I, Porcel JM, Vives M, *et al.* Comparative analysis of Light's criteria and other biochemical parameters for distinguishing transudates from exudates. *Respir Med* 1998; 92: 762–765.
23 Valdés L, Pose A, Suàrez J, *et al.* Cholesterol: a useful parameter for distinguishing between pleural exudates and transudates. *Chest* 1991; 99: 1097–1102.
24 Gil Suay V, Martínez Moragón E, Cases Viedma E, *et al.* Pleural cholesterol in differentiating transudates and exudates. A prospective study of 232 cases. *Respiration* 1995; 62: 57–63.
25 Wilcox ME, Chong CA, Stanbrook MB, *et al.* Does this patient have an exudative pleural effusion? The Rational Clinical Examination systematic review. *JAMA* 2014; 311: 2422–2431.

26 Bartter T, Santarelli RJ, Pratter MR. Transudate vs exudate: genug! *Chest* 1996; 109: 1419–1421.
27 Lee YCG, Davies RJO, Light RW. Diagnosing pleural effusion: moving beyond transudate-exudate separation. *Chest* 2007; 131: 942–943.
28 Heffner JE. Pleural fluid analysis in adults with a pleural effusion. In: UptoDate. Date last accessed: 11 November 2025. Wolters Kluwer, 2025. www.uptodate.com/contents/pleural-fluid-analysis-in-adults-with-a-pleural-effusion
29 Chopra A, Hu K, Feller-Kopman D, *et al.* Pleural fluid analysis: maximizing diagnostic yield in the pleural effusion evaluation. *Chest* 2025; 168: 828–838.