THE USE OF PLEURAL FLUID CHOLESTEROL IN IDENTIFYING THE TYPE OF PLEURAL EFFUSION

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introduction

- The first step in proper and adequate management of pleural effusion is correctly classifying it into exudative and transudative type
- It is the **exudative effusions that will require a gamut of follow-up diagnostic examinations** to ascertain its etiology
- The classic teaching on the origin of exudates and transudates has been that pleural effusion originated from the pleural capillaries

Broaddus VC, Light RW. What is the origin of pleural fluid transudates and exudates. *Chest* 1992; 102:658-659.

introduction

- In the 1930ês, the presence of cholesterol in pleural fluid was known

Mechanisms causing elevation of pleural fluid cholesterol in exudates:

1) Cholesterol is synthesized by pleural cells and its concentration is increased by the degeneration of leukocytes and erythrocytes
2) Increased permeability of pleural capillaries in pleural exudate patients would allow plasma cholesterol to enter the pleural space in inflammatory states

Valdes L, Pose A, Suarez J, et al. Cholesterol: a useful parameter for distinguishing between pleural exudates and transudates. *Chest 1991*; 99:1097-1102.

introduction

- **transudative pleural fluids have low levels of cholesterol** (mean=16% of simultaneous serum values) while **exudative pleural effusions had higher levels of pleural cholesterol** (mean=68% of serum values)[1]

- there was **no significant close correlation between the pleural fluid and serum cholesterol levels**. A further consideration of the pleural capillary permeability showed that the pleura is less permeable to different lipids than it is to other smaller molecules like protein[2]

1. Pfalzer B, Hamm H, Beisiegel U, et al. Lipoproteins and apolipoproteins in human pleural effusions. *J Lab Clin Med* 1992; 120:483-493.
2. Vaz MAC, Teixeira LR, Vargas F, et al. Relationship between pleural fluid and serum cholesterol levels. *Chest* 2001; 119:204-210.

introduction

- In 1972, the **Light's criteria** was conceptualized (**sensitivity= 99% & specificity= 98%** in detecting exudative effusions)

Light RW, MacGregor MI, Luchsinger PC, Ball WC. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med 1972*; 77:507-13.

general objective

To determine the usefulness of pleural f luid cholesterol in identifying the type of pleural effusion, whether exudative or transudative with Lightôs Criteria as comparison.

specific objective

To evaluate the probability of using pleural fluid cholesterol in classifying pleural effusions into exudative and transudative types with Light's criteria as the gold standard using the following measures of validity:

a) Sensitivity

b) Specificity

c) Positive predictive value (PPV)

d) Negative predictive value (NPV)

e) Overall diagnostic accuracy

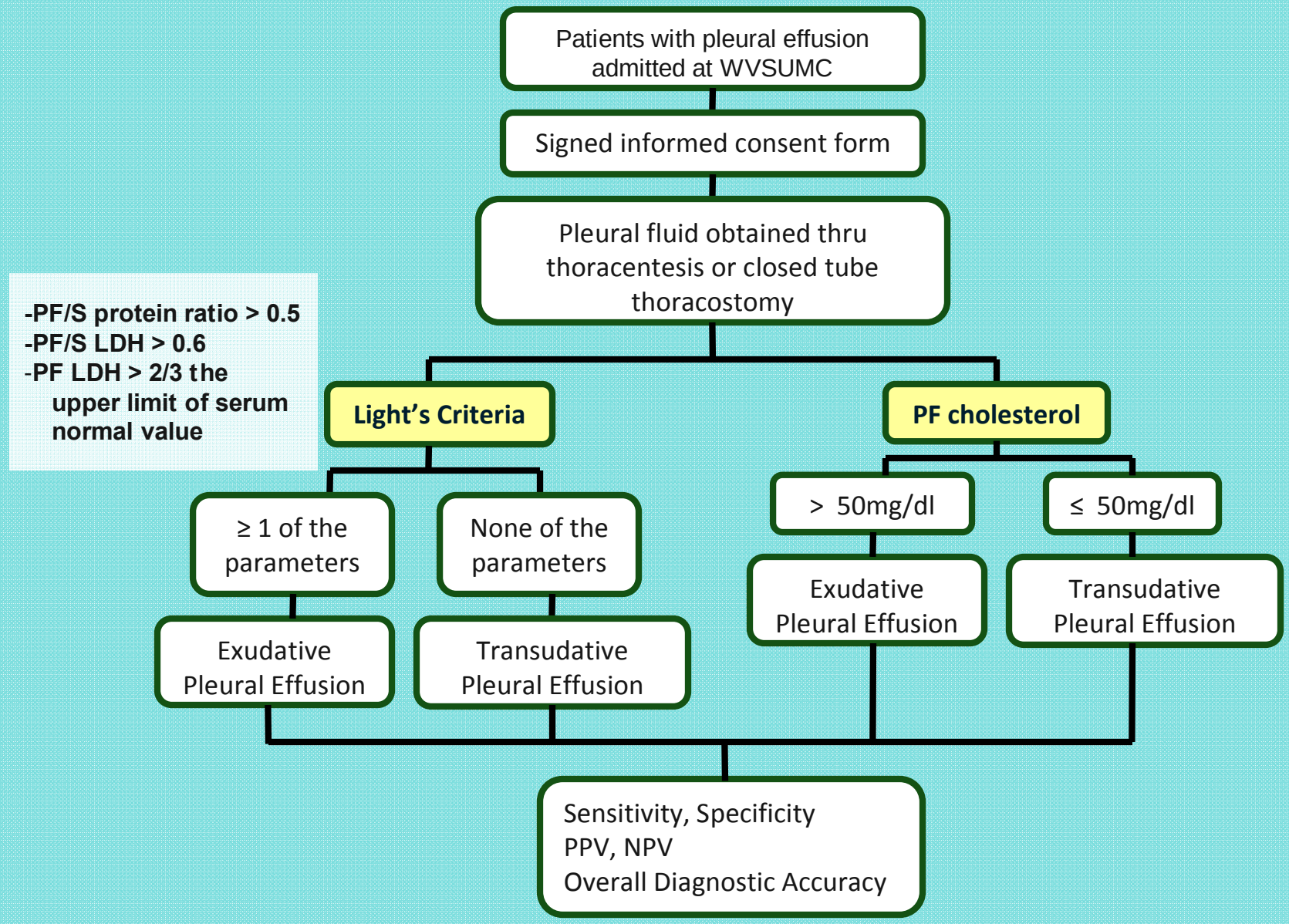

Figure 1. Study design

results

- From June to October 2009, a total of 48 patients with pleural effusions were evaluated
- 16 patients were excluded f rom the final subjects
- With the remaining **32 patients (n=32)**, the **mean age was 57± 18.2 years (range, 21 to 87 years)**

results

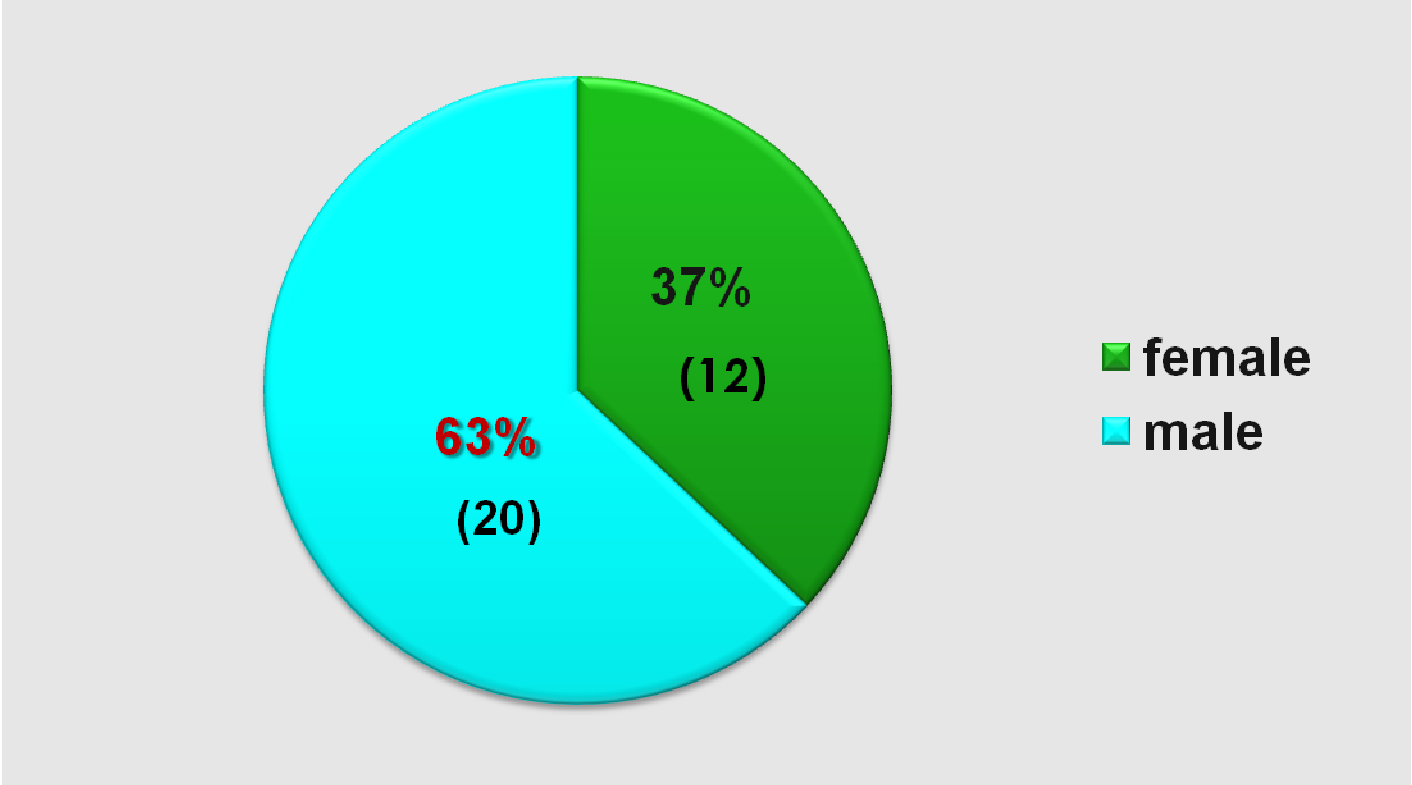

Figure 2. Proportion of gender in the sample population

results

Table 1. Concomitant conditions of patients studied

Co-morbid conditions	No. of Patients	Percentage (%)
Cigarette smoking	**9**	**28**
Hypertension	7	22
Alcohol intake	5	15
Diabetes mellitus	4	13
Malignancy	2	6
Congestive heart failure	2	6
Chronic Obstructive Lung Disease	2	6
Liver disease	1	3

results

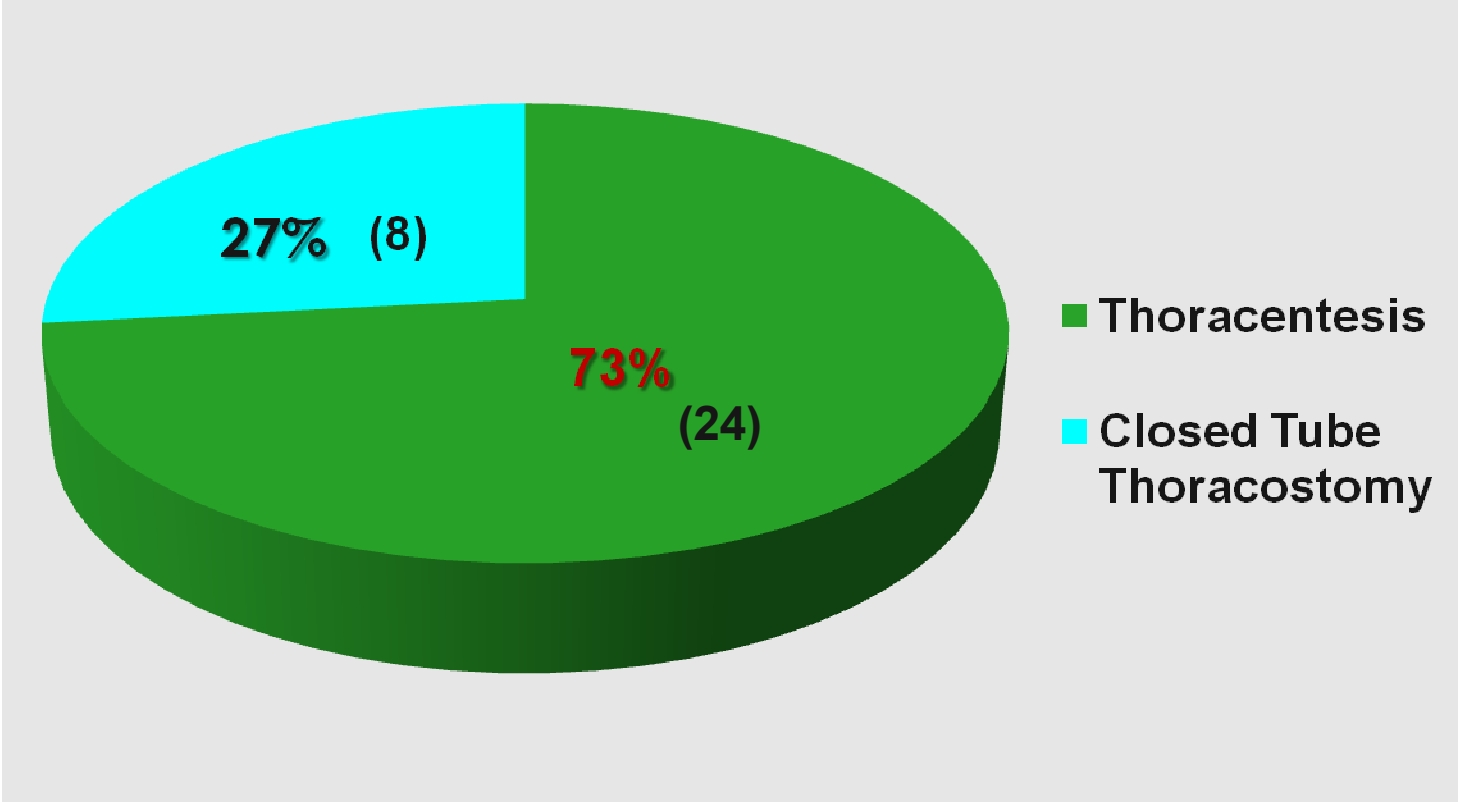

Figure 3. Method of obtaining the specimen

results

Table 2. Number of classified effusions using the parameters (n=32)

Parameters	Exudative	Transudative	Total
Light's criteria	**29 (0.91)**	3 (0.09)	32
PF cholesterol	**30 (0.94)**	2 (0.06)	32

results

Table 2. Causes of Effusion

Etiology	No. of Patients (n=32)	Percentage (%)
Transudative	**2**	**6**
Congestive Heart Failure	1	3
Liver Cirrhosis	1	3
Exudative	**30**	**94**
Tuberculous	**19**	**59**
Parapneumonic	7	22
Malignancy	4	13
TOTAL	**32**	**100**

results

- The data obtained were substituted into the 2x2 table

INDEX TEST (Pleural Fluid Cholesterol)	**GOLD STANDARD (Light's Criteria)**	
	Exudative (D+)	Transudative (D-)
Exudative (D+)	**29**	**1**
Transudative (D-)	**0**	**2**

(D+)- disease positive; (D-)- disease negative

results

OUTCOME MEASURE	PLEURAL FLUID CHOLESTEROL	LIGHT'S CRITERIA
Sensitivity (%)	**100%**	**99%**
Specificity (%)	**66.7%**	**98%**
PPV (%)	93.5%	
NPV (%)	100%	
Overall diagnostic accu racy (%)	**96.9%**	

discussion

Studies (PF cholesterol level)	Sensitivity (%)	Specificity (%)
Costa, et al[1] (> 45mg/dl)	90	100
Chibante, et al.[2] (> 48mg/dl)	83.7	94.7
Garcia-Panchion, et al.[3] (≥ 50mg/dl)	**91**	**93**
Hamm, et al.[4] (> 60mg/dl)	73	100
PRESENT STUDY	**100**	**66.7**

1. 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*; 108:1260-63.
2. Chibante A, Nieves D, Miranda S, Dias R. Cholesterol as a differential parameter to separate pleural transudates from exudates. *Rev Port Pneumol 2006*; 12(1):25.
3. Garcia-Pachon E, Padilla-Navas I, Sanchez JF, Jiménez B, Custardoy J. PF cholesterol and lactate dehydrogenase for separating exudates from transudates. *Chest 1996*;110:97ï 101.
4. Hamm H, Brohan U, Bohmer R, et al. Cholesterol in pleural effusions: a diagnostic aid. *Chest 1987*; 92:296-302.

discussion

- In the **false positive** result in 1 sample, the histopathologic findings suggested of a chronic inflammatory process as evidenced by the mesothelial hyperplasia, an indicator of chronic inflammation

conclusions

1) Determining the pleural fluid cholesterol level is a useful method of identifying the type of pleural fluid with a relatively high diagnostic accuracy

2) The test is as good as the Lightôs criteria in identifying exudates and reduces the biochemical parameters from three to one

3) No additional simultaneous serologic studies are needed to complete the work up

recommendations

- The results should be correlated with work up for pleural fluid (Gram stain, culture, KOH, AFB smear, cell count, differential count and histopathologic examination)
- A longer study period and a larger study sample should be considered in the future
- Combination of pleural fluid cholesterol with other parameters of the Lightôs criteria
- Another study on varying levels of pleural fluid cholesterol which will give the highest accuracy in detecting exudative effusions


thank you

STANDARD 2X2 TABLE

TEST OUTCOME (Pleural Fluid Cholesterol)	**GOLD STANDARD (Light's Criteria)**	
	Exudative (D+)	Transudative (D-)
Exudative (D+)	True positive (TP)	False Positive (FP)
Transudative (D-)	False Negative (FN)	True Negative (TN)

(D+)- disease positive; (D-)- disease negative

Winner L. Diagnostic tests. *Introduction to Biostatistics 2004*:21.

EQUATIONS

$$\textbf{Sensitivity} = \frac{\text{True Positive (TP)}}{\text{True Positive (TP) + False Negative (FN)}} \times 100$$

$$\textbf{Specificity} = \frac{\text{True Negative (TN)}}{\text{True Negative (TN) + False Positive (FP)}} \times 100$$

$$\textbf{PPV} = \frac{\text{True Positive (TP)}}{\text{True Positive (TP) + False Positive (FP)}} \times 100$$

$$\textbf{NPV} = \frac{\text{True Negative (TN)}}{\text{True Negative (TN) + False Negative (FN)}} \times 100$$

$$\textbf{Diagnostic Accuracy} = \frac{\text{True Positive (TP)} + \text{True Negative (TN)}}{\text{Total number of samples}} \times 100$$

Winner L. Diagnostic tests. *Introduction to Biostatistics 2004*:21.

COMPUTATIONS

- The data obtained substituted into the 2x2 table

INDEX TEST (Pleural Fluid Cholesterol)	**GOLD STANDARD (Light's Criteria)**	
	Exudative (D+)	Transudative (D-)
Exudative (D+)	29	1
Transudative (D-)	0	2

COMPUTATIONS

Sensitivity = $\frac{TP}{TP + FN} \times 100 = \frac{29}{29 + 0} \times 100 = 100\%$

Specificity = $\frac{TN}{TN + FP} \times 100 = \frac{2}{2 + 1} \times 100 = 66.7\%$

PPV = $\frac{TP}{TP + FP} \times 100 = \frac{29}{29 + 1} \times 100 = 93.5\%$

NPV = $\frac{TN}{TN + FN} \times 100 = \frac{2}{2 + 0} \times 100 = 100\%$

Overall diagnostic accurac y = $\frac{TP + TN}{n} \times 100 = \frac{29 + 2}{32} \times 100 = 96.9\%$

DEFINITIONS

Diagnostic accuracy- this is the probability that a randomly selected subject is correctly diagnosed by the test

Negative Predictive Value- the probability that a person who has tested negative on a diagnostic test (Tī) actually does not have the disease (Dī). In this study, (D-) describes the transudative type of pleural effusion

Positive Predictive Value- this is the probability that a person who has tested positive on a diagnostic test (T+) actually has the disease (D+). In this study, (D+) describes the exudative type of effusion

Winner L. Diagnostic tests. *Introduction to Biostatistics 2004*:21.

DEFINITIONS

Sensitivity- this is the probability that a person with disease (D+) will correctly test positive based on the diagnostic test (T+). In this study, (D+) describes the exudative type of effusion

Specificity- this is the probability that a person without disease (D−) will correctly test negative based on the diagnostic test (T−). In this study, (D-) describes the transudative type of pleural effusion

Winner L. Diagnostic tests. *Introduction to Biostatistics 2004*:21.