The Light Criteria
The Beginning and Why they are Useful 40 Years Later

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KEYWORDS

• Light criteria • Pleural effusion • Transudative effusion

KEY POINTS

- The Light criteria serve as a good starting point in the separation of transudates from exudates.
- The Light criteria misclassify about 25% of transudates as exudates, and most of these patients are on diuretics.
- If a patient is thought likely to have a disease that produces a transudative pleural effusion but the Light criteria suggest an exudate by only a small margin, the serum–pleural fluid protein gradient should be examined.
- If this is greater than 3.1 gm/dL, the patient in all probability has a transudative effusion.
- If the gradient is less than 3.1 gm/dL, either the NT-pro-BNP level in the pleural fluid or the serum–pleural fluid albumin gradient can be measured.
- Either an NT-pro-BNP greater than 1300 pg/mL or an albumin gradient greater than 1.2 gm/dL indicate that the effusion is a transudate.

It has been 40 years since I published the article[1] describing what came to be known as the Light criteria. I thought that it might be appropriate to begin this article by detailing how that article came about.

THE DEVELOPMENT OF THE LIGHT CRITERIA

When I was an intern in medicine at Johns Hopkins Hospital in Baltimore, Maryland, in 1968 to 1969, there was a period when a large percentage of my patients had a pleural effusion. The chief resident, Dr Richard Winterbauer, made rounds around midnight and always asked me what the thoracentesis revealed. At that time, we routinely measured the cell count and differential, glucose, and protein, and performed smears and cultures on the pleural fluid. I asked Dr Winterbauer the significance of the various pleural fluid findings and, for the most part, neither he nor anybody else had a scientific answer.

It was at this time that additional measurements were first being made on blood, such as the lactic dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). At about the same time, blood gas machines became available that would allow the accurate measurement of pH, P_{CO_2}, and P_{O_2} of body fluids. I theorized that some of these new measurements might be useful in the differential diagnosis of pleural effusions. After doing a literature review, I developed 2 hypotheses. The first was that the pH of pleural fluid would be lower in tuberculous pleural effusions than in other exudative pleural effusions. The basis for this hypothesis was an article in the *Scandinavian Journal of Respiratory Disease* that purported to show this.[2] My second hypothesis was that LDH isoenzymes would be

Disclosures: The author has nothing to disclose related to this publication.
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Clin Chest Med 34 (2013) 21–26
http://dx.doi.org/10.1016/j.ccm.2012.11.006
0272-5231/13/$ – see front matter

useful in the differential diagnosis of exudative pleural effusions. To get the absolute value of the LDH isoenzymes, I needed to have the total LDH in the pleural fluid and the serum. A previous study on pleural fluid LDH concluded that the pleural fluid LDH was increased in malignant pleural effusions compared with other pleural effusions.[3] I submitted a proposal to the Institutional Review Board and received their approval. The blood gas machine was in the pulmonary function laboratory and I could measure all of the pleural fluid pH myself. The clinical laboratory measured the protein, LDH, and glucose in the serum and pleural fluid without charge. However, I did have to come up with some funds to pay for the LDH isoenzymes. I received a small grant from Johns Hopkins Hospital to fund this.

To get called when patients with pleural effusions were admitted, I made a deal with my fellow interns and residents. If they would call me when they did a thoracentesis, I would do the cell count and differential on the pleural fluid; duties for which they would normally be responsible. I quickly found out that, with this arrangement, I got called often in the middle of the night about pleural effusions.

One of the first patients I studied was a young man with an exudative lymphocytic effusion. His pleural fluid pH was 7.40. The patient turned out to have caseating granulomas on the needle biopsy of his pleura; so much for the first hypothesis. Soon thereafter, another patient had a pleural fluid pH of 6.95. The pleural fluid was clear yellow and the pleural fluid glucose was not reduced. However, the pleural fluid grew *Streptococcus pneumoniae* and the patient eventually developed a frank pneumococcal empyema. This case was the first to suggest that a low pleural fluid pH might be an indicator of a complicated parapneumonic effusion.[4]

I subsequently studied more than 150 pleural effusions in a 2-year period. I submitted an abstract of my preliminary findings to the American Thoracic Society for their annual meeting in 1971. The abstract was rejected. I was devastated.

In early 1971, when I was a pulmonary fellow, Johns Hopkins had a reunion for some of its alumni. My mentor, Dr Wilmot C. Ball, Jr, suggested that I present something on the pleural fluid that I had been studying. At that time, transudates and exudates were usually separated by using a protein level of 3.0 gm/dL.[5] I elected to see how this would work on my set of pleural effusions. On a rainy, sleety Sunday in Baltimore, Maryland, I spent several hours with a pencil and graph paper plotting protein levels, LDH levels, and ratios of protein and LDH in the serum and pleural fluid.

When I examined my plots, it was obvious that no single value of any of these measurements correctly identified all transudates and exudates. If the cutoff was made high enough that all transudates were below the cutoff level, then some exudates would be classified as transudates. My objective at that time was to identify all exudates correctly. Therefore I elected to make the cutoff points such that no transudates were above the line. I noticed that, when I did this, some exudates were in the transudative range for each of the measurements. However, I also noticed that, if I used 3 different cutoff levels such that no transudates were above the cutoff line, I could identify almost all transudates and exudates correctly. The 3 cutoff points that I found were a protein ratio greater than 0.5, an LDH ratio greater than 0.6, and an absolute pleural fluid LDH greater than two-thirds of the upper normal limit for serum. An exudative effusion met at least 1 of these 3 criteria, whereas a transudative effusion met none.

I presented these data to the alumni and they did not seem particularly impressed. I also submitted an abstract on the separation of transudates by the criteria listed earlier to the American College of Physicians in 1972.[6] It was accepted for an oral presentation in Atlantic City. This oral presentation was the only one that I ever participated in where the audience graded the contents of the presentation. I got, at most, average marks; certainly nothing to suggest that these cutoff levels would still be in use 40 years later. Nevertheless, I wrote the article and submitted it to the *Annals of Internal Medicine*. It was accepted with minimal revisions.[1]

There are several lessons to be learned from my experience in developing the Light criteria. First, if you want people to cooperate with you on your research, you need to make it worthwhile for them. In this case, I did some of the work that they would otherwise have to do. Second, although research is best done when it is hypothesis driven, it is worthwhile to look at your data to determine whether there are other interesting findings. Third, if you initially submit your work and it is not particularly well received, do not give up. Remember that the first abstract on the Light criteria was turned down.

WHY THE LIGHT CRITERIA ARE STILL USEFUL

The first reference to use the name the Light criteria that I am aware of was published in 1989.[7] Since the original publication in 1972, there have been many studies comparing other measurements with the Light criteria for the separation of transudates and exudates, but, in general, the Light criteria have

been proved to be better than anything else. I am amazed that, after 40 years, the Light criteria are still being used.

Pleural effusions have classically been divided into transudates and exudates. By definition, a transudative pleural effusion develops when the systemic factors influencing the formation or absorption of pleural fluid are altered so that pleural fluid accumulates. The pleural fluid is called a transudate. The permeability of the capillaries to proteins is normal in the area where the fluid is formed. Examples of conditions producing transudative pleural effusions are left ventricular failure producing increased pulmonary interstitial fluid and a resulting pleural effusion, ascites caused by cirrhosis with movement of fluid through the diaphragm, and decreased serum oncotic pressure with hypoproteinemia.[8]

In contrast, an exudative pleural effusion develops when the pleural surfaces or the capillaries in the location where the fluid originates are altered such that fluid accumulates. The most common causes of exudative pleural effusions are pleural malignancy, parapneumonic effusions, and pulmonary embolism.

Why is it important to differentiate transudates from exudates? If a patient has a transudative pleural effusion, then it is only necessary to treat the cause of the effusion, such as heart failure or cirrhosis. However, if it is an exudative effusion, more investigation is indicated to identify the local problem that is causing the pleural effusion.

Why use 2 different measurements to separate transudates from exudates? The pleural fluid/serum protein ratio is an indication of the permeability of the capillaries in the area where the pleural fluid was formed. In contrast, the pleural fluid LDH level is an indication of the degree of inflammation in the pleural space. Therefore, they measure different things. However, there is no doubt that they are related because inflammation in the pleural space increases the permeability of the capillaries in the pleura.

Why are the Light criteria still useful after 40 years? I think that there are several reasons for its popularity and its usefulness, including (1) it is simple and easy to remember, (2) its measurement is readily available, (3) it is accurate.

Since the Light criteria were first presented, there have been many articles proposing alternatives. One of the measures proposed was the level of cholesterol in the pleural fluid,[9–11] or the ratio of the pleural fluid to the serum cholesterol.[11] The cholesterol measurement is unlikely to be superior to the Light criteria because the pleural fluid cholesterol level can be accurately predicted from the serum cholesterol and the ratio of the pleural fluid to the serum protein level.[12] Cholesterol measurements provide no additional information to the protein ratio. Other proposed measures have included the pleural fluid/serum bilirubin ratio,[13] the pleural fluid viscosity,[14] the level of oxidative stress markers,[15] the level of soluble leukocyte selectin,[16] the level of various cytokines,[17] the level of uric acid,[18] and the pleural fluid/serum cholinesterase ratio.[19] Subsequent articles[20,21] have shown that none of these other measures are superior to the Light criteria in separating transudates from exudates.

When the original article[1] was published, the Light criteria identified all transudates and exudates accurately. However, subsequent studies have shown that the Light criteria classify almost all exudates correctly, but falsely classify about 25% of transudates as exudates. In a study[22] of 249 patients in which there were 185 exudates and 64 transudates, the Light criteria correctly identified 99.5% of exudates but only 75% of transudates. In a recent article,[23] the Light criteria falsely classified 107 of 364 (29%) transudates caused by heart failure and 18 of 102 (18%) transudates caused by hepatic hydrothorax.

Transudates that are falsely classified as exudates usually make exudative criteria by only a slight amount. In an article[23] involving 107 falsely classified transudates, the mean pleural fluid (PF)/serum protein ratio was 0.51, the mean PF/serum LDH was 0.63, and the mean pleural fluid LDH was 0.34 the upper normal limit for serum for the transudates that were falsely classified. Most transudates are falsely classified by only 1 of the 3 elements of the Light criteria.[23] Most of the patients with transudates who are falsely classified either are receiving diuretics or have a pleural fluid red blood cell (RBC) count greater than 10,000/mm^3.[24] Romero-Candeira and colleagues[25] performed 3 thoracenteses at 48-hour intervals in 15 patients with pleural effusions caused by heart failure after they were started on diuretics. They reported that the mean pleural fluid protein increased from 2.3 to 3.3 gm/dL and the mean pleural fluid LDH increased from 177 to 288 IU/L. After diuresis, the Light criteria would have classified most of the effusions as exudates.[25]

In the original article,[1] almost all transudates were classified correctly. What is the explanation for the observation that currently about 25% of transudates are falsely classified? I think that there are probably 2 reasons for this discrepancy. First, in the original series, almost all the thoracenteses were done on patients who had just been admitted to the hospital and were not on diuretics. Second, the diuretics are more powerful now than those that were available in 1972, namely

hydrochlorothiazide and the mercurial diuretics (ie, mercury chloride; now rarely used).

An alternative approach for the identification of transudates and exudates is to select the cutoff levels that correctly identify the highest percentage of patients. Heffner and colleagues[26] analyzed data from 8 studies with a total of 1448 patients and concluded that the best cutoff levels for the different pleural fluid tests were protein ratio 0.5, LDH ratio 0.45, and LDH 0.45 of the upper limits of normal for serum. The problem with this approach is that some effusions will be misclassified but it is impossible to know whether they are misclassified wrongly as a transudate or an exudate. I still prefer the Light criteria because I want to definitely identify all exudative effusions.

TRANSUDATIVE EFFUSIONS MISCLASSIFIED BY THE LIGHT CRITERIA

When the Light criteria are used, how are those transudative pleural effusions identified that are misclassified? If a patient is clinically suspected of having a transudative effusion but exudative criteria are met by a small margin (protein ratio between 0.5 and 0.65, LDH ratio between 0.6 and 1.0, pleural fluid LDH between two-thirds and the upper normal limit for serum), attempts should be made to determine whether the patient really has a transudative effusion. The 2 main measures that have been proposed to identify these patients are a serum–pleural fluid albumin gradient greater than 1.2 gm/dL or a serum–pleural fluid protein gradient greater than 3.1 gm/dL. Romero-Candeira and colleagues[22] studied 64 patients with transudative pleural effusions and reported that the Light criteria identified 75% correctly, the serum–pleural fluid albumin gradient identified 86% correctly, and the serum–pleural fluid protein gradient identified 91% correctly. In a recent article,[23] 107 of 364 transudates (29%) caused by congestive heart failure (CHF) were misclassified as exudates. In these 107 instances, a serum–pleural fluid protein gradient greater than 3.1 gm/dL identified 55% correctly, whereas a serum–pleural fluid albumin gradient greater than 1.2 gm/dL, which was only performed in 36 patients, identified 83% correctly.[23] In the same report, 18 of 102 transudates (18%) caused by hepatic hydrothorax were misclassified with the Light criteria. The protein gradient and the albumin gradient identified 61% and 62% of these misclassified transudates correctly. An albumin ratio less than 0.6 correctly identified 77% of these transudates caused by hepatic hydrothorax.

My recommendations in view of the 2 studies discussed earlier are as follows. When evaluating a patient who could have a transudative effusion but who meets exudative criteria via the Light criteria by a small margin, I first look at the serum–pleural fluid protein gradient. If this is greater than 3.1 gm/dL, I conclude that the patient has a transudative effusion. I look at the protein gradient first because it is already available from the Light criteria. If this gradient is less than 3.1 gm/dL, I consider measuring the albumin gradient. If the patient may have a hepatic hydrothorax, I measure the albumin ratio. As an alternative, measurement of the serum or pleural fluid N-terminal probrain natriuretic peptide (NT-pro-BNP) can be performed to determine whether the pleural effusion is caused by CHF (discussed than).

Most transudates are caused by CHF. It is preferable to establish the diagnosis of CHF directly. It seems that the diagnosis of CHF as a cause of the pleural effusion can be made with measurement of the NT-pro-BNP in the pleural fluid or the serum. When the ventricles are subjected to increased pressure or volume, NT-pro-BNP and BNP are released into the circulation.[27] The biologically active BNP and the larger NT-pro-BNP are released in equimolar amounts into the circulation.[27]

Porcel and colleagues[28] first showed that the pleural fluid levels of NT-pro-BNP are increased in patients with heart failure. These researchers measured NT-pro-BNP levels in 117 pleural fluid samples with the following diagnosis: CHF, n = 44; malignancy, n = 35; tuberculous pleuritis, n = 20; hepatic hydrothorax, n = 10; and miscellaneous, n = 18. The mean pleural fluid NT-pro-BNP level in the patients with CHF was 6931 pg/mL, which was significantly higher than the 551 pg/mL in patients with hepatic hydrothorax and the 292 pg/mL in patients with exudative pleural effusions.[28] When a cutoff level of 1500 pg/mL was used, the sensitivity was 91% and the specificity was 93% for the diagnosis of CHF.[28] We compared the pleural fluid NT-pro-BNP levels in 10 patients each with effusions caused by CHF, pulmonary embolism, postcoronary artery bypass graft surgery, and malignancy.[29] All the patients with CHF had NT-pro-BNP levels greater than 1500 pg/mL, whereas none of the other patients had NT-pro-BNP levels this high. There have been several subsequent articles evaluating the accuracy of NT-pro-BNP in making the diagnosis of pleural effusion caused by heart failure. In a meta-analysis of 10 studies with a total of 1120 patients, the pooled sensitivity and specificity were 94% and 94% respectively.[30]

There is a close relationship between the levels of NT-pro-BNP in the pleural fluid and serum. Han and colleagues[31] measured the NT-pro-BNP levels in 240 patients and reported that the correlation coefficient between the pleural and serum

NT-pro-BNP was 0.928. In a second study, Kolditz and colleagues[32] measured the serum and pleural fluid NT-pro-BNP levels in 93 patients, including 25 with CHF. They confirmed the results of the study mentioned earlier in that the levels of serum and pleural fluid NT-pro-BNP were closely correlated (r^2 = 0.90). In addition, in each of the two studies,[31,32] the values in the pleural fluid and the serum were almost identical. From these latter two studies, it seems that measurement of the pleural fluid NT-pro-BNP levels provides no additional information beyond the serum measurements.

The pleural fluid NT-pro-BNP is also superior to the BNP and the protein gradient in identifying patients with heart failure who meet the Light criteria for exudates.[33] In a study of 20 patients with heart failure who met the Light criteria for exudates, 18 had NT-pro-BNP levels greater than 1300 pg/mL, 16 had NT-pro-BNP levels greater than 1500 pg/mL, but only 10 had a serum–pleural fluid protein gradient greater than 3.1 gm/dL.

The serum or pleural fluid BNP and NT-pro-BNP cannot be used interchangeably in the diagnosis of pleural effusions caused by CHF.[34] The BNP levels are only about 10% of the NT-pro-BNP levels. There is not a close correlation between the BNP levels and the NT-pro-BNP levels (r = 0.78).[33,34] Moreover, the diagnostic usefulness of the NT-pro-BNP in making the diagnosis of heart failure is superior to that of the BNP.[33,35]

SUMMARY

The Light criteria serve as a good starting point in the separation of transudates from exudates. The Light criteria misclassify about 25% of transudates as exudates, and most of these patients are on diuretics. If a patient is thought likely to have a disease that produces a transudative pleural effusion but the Light criteria suggest an exudate by only a small margin, the serum–pleural fluid protein gradient should be examined. If this is greater than 3.1 gm/dL, the patient in probably has a transudative effusion. If the gradient is less than 3.1 gm/dL, either the NT-pro-BNP level in the pleural fluid or the serum–pleural fluid albumin gradient can be measured. Either an NT-pro-BNP greater than 1300 pg/mL or an albumin gradient greater than 1.2 gm/dL indicate that the effusion is a transudate.

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