

Are the days of closed pleural biopsy over? Yes

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ABSTRACT

In the modern management of pleural diseases, thoracoscopy has a clear advantage over closed pleural biopsy. By way of its high yield, both in malignant pleural disease and pleural Tuberculosis – the two commonest cause of undiagnosed pleural effusion, thoracoscopy has the added advantage of faster symptom relief and offering effective pleurodesis. This makes it an attractive diagnostic and therapeutic procedure of choice and features high in the algorithms of many international guidelines on the approach to pleural diseases.

KEY WORDS: Closed pleural biopsy, malignant pleural effusion, pleural tuberculosis, thoracoscopy

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“And slowly answered Arthur from the barge: ‘The old order changeth, yielding place to new, And God fulfils Himself in many ways, Lest one good custom should corrupt the world’.”

From *Idylls of the King: The Passing of Arthur* by Lord Tennyson.

A 64-year old farmer and a smoker with chronic obstructive pulmonary disease (COPD) and hypertension, presents with right-sided chest pain, breathlessness, and weight loss. He has clinical features of a right pleural effusion and his chest x-ray confirms this. Aspiration yields a hemorrhagic, exudative, lymphocytic effusion with an adenosine deaminase (ADA) of 24 U/L, and no malignant cells demonstrated on cytology analysis. A contrast computed tomography (CT) of the thorax reveals massive right effusion with compressed underlying right lung and no pleuroparenchymal or mediastinal abnormality. An Abram’s closed pleural biopsy (CPB) was carried out and the histopathology report was a “small whiff of pleural tissue with the majority of tissue comprising fibroconnective tissue. Pleura has not been represented in the present specimen.”

Under ordinary circumstances, the champions of CPB will possibly subject the patient to a further CPB in the belief that a similar repeat biopsy will increase the chances of a conclusive report.^[1,2] In fact, they may even consider making as many as six blind passes to get a positive result,^[3] notwithstanding the mental anguish of the patient to undergo a repeat diagnostic procedure, the uncertainty of being told with confidence that an answer to his illness will now be obtained, or the small but definite possibility of developing complications with each repeat procedure. However, to the advocates of the more reliable, effective, safe, and dependable pleural procedure such as thoracoscopy, the inconclusive CPB result does not come as a surprise at all as in a single center experience of 348 patients, 15.5% histological examinations revealed skeletal muscles and tissue from other internal organs while in an analysis of 414 cases, CPB failed to provide adequate tissue in 13.3%^[4,5] In the same large retrospective study, only 7% of the patients with malignant pleural effusion had a positive CPB when the fluid cytology was negative.^[5] Loddenkemper and Boutin in their series of patients on the analysis of different pleural biopsy techniques for malignant effusions showed that at a sensitivity of 62%, cytology of the pleural fluid was in fact better than CPB, which gave only a 44% yield.^[6] A total of 22 case series have reported diagnostic yield of medical thoracoscopy for malignant disease. On pooling results from all these studies, thoracoscopy has 92.6% diagnostic sensitivity for malignant pleural disease.^[7] On pooling results from only those eight studies in which a prior “blind” pleural biopsy was negative, thoracoscopy had a similarly high

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sensitivity of 90.1%.^[7] Owing to this high yield coupled with its attractive therapeutic potential of giving prompt symptomatic relief by evacuating large volumes of fluid safely and offering, by way of pleurodesis, the only effective palliative management in stage IV diseases, thoracoscopy in suspected malignancy is the diagnostic procedure of choice and has clearly and unanimously replaced CPB.^[8-10]

“Bigger is better” and “tissue is the issue” appear to be the slogans of the modern day pathologist as he/she is required to give a complete histological and molecular diagnosis in lung and pleural cancers. In the era of immunochemistry and molecular pathology, there is often a demand for adequate biopsy and though there have been no studies assessing the adequacy of CPB specimens for these purposes, intuitively, a good, large sample as obtained via thoracoscopy *viz-a-viz* CPB would undoubtedly fulfill all the requirements of the histology laboratory.

With these innumerable shortcomings of CPB and the decreasing incidence of tuberculosis (TB) in most of the developed countries, one is not surprised that only 48% of the USA pulmonary intervention programs are offering the number of CPB to achieve competency and that “there is a significant reduction in operator experience among respiratory physician to the point where even experienced pulmonologists have become reluctant to utilize blind CPB even in settings where the anticipated diagnostic yields are high.”^[11,12]

PLEURAL BIOPSY IN TUBERCULOSIS

This brings us to the role of CPB in pleural TB and for this indication too it comes a distant second with a diagnostic yield of around 75% as compared to the near-100% sensitivity of thoracoscopy.^[6,13] Pleural biopsy is hardly needed to diagnose TB as the pleural fluid characteristics of an exudative lymphocytic rich content with a high ADA continues to be a robust way of diagnosing most, if not all, cases of pleural TB.^[14] The need for a biopsy arises in three situations: 1) Equivocal pleural fluid analysis, 2) suspected resistant pleural TB, and 3) differentiating TB and bacterial empyema. In all these situations, culturing the mycobacteria becomes clinching diagnostic evidence, of which CPB falls short as evident in Table 1.

Even the molecular studies on pleural tissue have a low yield as demonstrated by Christopher *et al.* in their 96

Table 1: Yield of culture positivity in pleural biopsy specimens obtained by closed pleural biopsy

Author	MTB* culture positive (%)
James <i>et al.</i> ^[1]	9.5
Hira ^[15]	10.5
Diacon <i>et al.</i> ^[16]	48
Christopher <i>et al.</i> ^[17]	29

*MTB: *Mycobacterium tuberculosis*

consecutive patients, out of which 33 were diagnosed with TB based on two composite reference scores with none demonstrating Xpert positivity.^[18] This low positivity rate of culturing *Mycobacterium tuberculosis* (MTB) in pleural tissue by either the conventional way or the more recent genotyping makes it an unattractive option of sampling it in suspected resistant pleural TB.

For differentiating empyemas most of which are loculated, thoracoscopy, by way of adhesiolysis, offers the therapeutic advantage of effective drainage. In addition, this procedure gives overall (histology and culture) 100% sensitivity and specificity in the diagnosis of pleural TB, prompting the British Thoracic Society to recommend in its guidelines that local anesthetic thoracoscopy as the investigative modality as it has a high yield for TB pleuritis and a greater yield than blind pleural biopsy even in high-prevalence TB areas.^[7]

COST

Undoubtedly, the health economics of an undiagnosed pleural effusion favor CPB over thoracoscopy but when one does a more detailed analysis of the cost of carrying out several procedures in the traditional nonthoracoscopic diagnostic pathway (1–2 pleura aspirations, CPB, image-guided biopsy and a chest drain and talc pleurodesis in case of malignant effusion), one comes to the clear conclusion that this margin significantly reduces and in some situations may even turn out to be more expensive than carrying out a thoracoscopy upfront. Based on their prospective analysis in a UK tertiary hospital center, Melford *et al.* have in fact shown that a local anesthetic video-assisted thoracoscopy (LAVAT) can theoretically save £1,527/patient, in addition to saving between 2-3 days in the hospital bed.^[19]

The health economics of a procedure has to not only take the cost of the procedure into account but also the mental anguish of the patient on being told of an inconclusive procedure and that he/she would have to undergo yet another one. Unfortunately, there are no yardsticks to assess this intangible but most vital aspect of patient care.

THE FUTURE

So, should the baby be thrown away with the bath water? Not yet, and coming to the rescue of CPB is recent evidence suggesting that it has a role when done under image guidance rather than blind and in very specific conditions such as a pleural thickening of >10 mm, diaphragmatic pleural thickening of >7 mm, pleural nodules and masses of >20 cm, and in solid pleural tumors.^[20] Recent publications have highlighted that image guidance may be used before thoracoscopy as it significantly increases the yield and reduces the complications of blind CPB, with both ultrasound and CT guidance having been utilized for this purpose.^[21-23]

However, the authors do not fail to hesitate in stating that primary medical thoracoscopy may still be the choice in patients with only pleural fluid appearance on CT without any pleural abnormality as is seen in a large number of patients and as illustrated in the above case report. The value of image-guided CPB is less well-defined in this situation.

A diagnostic algorithm for any disease should take into consideration a step that gives the maximum diagnostic yield and is unequivocally conclusive. This would then obviate the act of proceeding to a next test, which would not only add to the time taken to diagnose but also to the cost and agony of the patient to undergo yet another procedure. Nowhere are these caveats more important than in India where a majority of the patients seek private health care at considerable costs; thus, one should resort to tests that give answers effectively, safely, promptly, and economically. Practicing evidence-based medicine has therefore, become all the more crucial and the current evidence is unanimous about thoracoscopic pleural biopsy being the clear choice.^[7]

Science continues to be ever-changing and what may be good at one time may have to give way to a better alternative. Let us not allow the repetitive noise of lack of resources, expertise, and economic constraints to deafen our ears and make us ignore the symphony of scientific advancements. A prudent society, in its quest for truth, should welcome the “new order” while accepting the relevance of its past.

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