Adding Molecular Testing to the Menu of Pleural Disease

The clinical question

Are varying pleural biopsy techniques adequate for molecular testing?

Research question

What is the adequacy of various pleural biopsy techniques at providing adequate molecular diagnostic information to guide treatment in MPE?

AABIP take home message

Local anesthetic thoracoscopy has a higher diagnostic yield and ability to capture actionable history when compared to CT-guided and US-guided pleural biopsies in patients with malignant pleural effusion.

Background

- There is a need for adapting new techniques for obtaining a higher sensitivity and specificity in samples acquired for the evaluation of a malignant pleural effusion (MPE)
- Sensitivity of cytology for pleural fluid analysis is only 58.2% and molecular marker status is lower, at 53.4%
- The concept of actionable histology: adequacy of pleural biopsy techniques in achieving molecular marker status
- Various sampling methods include local anesthesic thoracoscopies (LATs), US-guided percutaneous biopsies (USGPBx) and CT-guided percutaneous biopsies(CTGPBx).

Current Practice / Guidelines

- British Thoracic Guidelines: biomarkers not necessarily offered in isolation as a diagnostic test (GRADE B), only considered with suspicious cytology in patients who are not fit for additional invasive testing (GRADE B)
- Local anesthetic thoracoscopy with pleural biopsies has high sensitivity and specificity for MPE
- Molecular testing is superior, it may help drive therapy decision and can be useful for prognostication(4)

- Therapies associated with the treatment of mesothelioma vary (e.g., from anti-angiogenesis and mesothelin-based therapies)(4)
- BAP1 (BRCA1-associated protein 1) may differentiate reactive from malignant mesothelioma (5)

Study Design

Study design

- **Type of trial:** multicenter, retrospective cohort
- **N:** 183
- **Study groups:** Patients with pleural biopsy positive for malignancy, in which molecular profiling was considered relevant
- **Settings:** Four clinical sites across three countries
- **Enrollment:** 7-year period
- **Treatment period:** 2014 -2021
- **Follow up:** none

Primary outcome:

- Adequacy for molecular marker analysis associated with different modes of biopsy.

Secondary outcome:

- Secondary outcomes included variation in procedural factors (ie, procedure type, number of biopsies, size of biopsy specimen, cancer subtype)

Population

Inclusion Criteria:

- Patient has undergone pleural biopsy via CTGPBx, LAT or USGPBx), confirmed malignancy and final diagnosis of tumor type.

Exclusion Criteria:

- Additional methods of biopsy

Baseline Characteristics:

- Median age was 71 years,
- (50%) of patients were male and patients would have had to have the presence of interventions as stated above 105 (57%) LATs,
- 12 (%) CT-guided, and 66 (36%) ultrasound-guided.

Interventions

Pleural biopsy via CT-guided, local anesthetic thoracoscopy or ultrasound-guided

Outcomes

Leading diagnoses were lung and breast cancer: 100 of 183 (55%) and 34 (19%), respectively.

Primary outcome:
Overall diagnostic adequacy
Pleural biopsy: 129/146 (88%, 95% CI, 82-93)
Pleural biopsy + pleural fluid: 92% (134 of 146; 95% CI, 86-97)
LAT having the highest yield and ultrasound guided biopsy the lowest LAT vs CT-guided vs ultrasound-guided: LAT yield, 95%; CT- guided, 86%; and ultrasound-guided, 77% [p = 0.004]

Secondary outcomes:
Univariate analysis: Found procedure type (LAT), size of biopsy specimens, sex (female), and type of cancer (breast) as factors associated with successful molecular marker analysis.

Multivariate analysis:
Type of Procedure LAT > CTGPBx ≅USGPbx
Number of biopsies (OR, 0.76; 95% CI, 0.62-0.93; P = 0 .008)
Size of biopsy (OR of 1.18 (95% CI, 1.02-1.37; P = 0.03)

Adverse events: complications procedural related including pain, hypotension, pneumothorax.
LAT had higher complication rate 24% vs USGPBx (8%), CTGPBx (0%)
Most common complication with LAT was pain.
No complication that met clinical trial criteria for “serious”.

Commentary

Strengths

- Unique assessment of diagnostic adequacy for molecular marker testing
- International and multicenter increases its external validity

Limitations

- Small study / population
- Retrospective
- Only 7% of cases (12/183) were CT-guided pleural biopsies
- Long follow up timeline – techniques might have adapted or changed
- Not all interventions were offered in each center (less ct guide biopsy)

Study Conclusion

Local anesthetic thoracoscopies offer a superior result in achieving molecular profile testing in patients with malignant pleural effusion.

Funding

No funding sources disclosed.

Suggested Reading

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Article citation

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