Unstandardized Diagnostic Yield Calculation: Is it ever really apples to apples?

The clinical question

When evaluating the performance of peripheral diagnostic bronchoscopy, how do different diagnostic definitions influence the interpretation of study results and limit the ability to compare findings across different studies?

AABIP take home message

When comparing two or more studies that are reporting peripheral bronchoscopy diagnostic yield, it is of paramount importance to note how diagnostic yield was defined in each of the studies.

Background

- Diagnostic accuracy is the most frequently used assessment metric, also termed diagnostic yield in bronchoscopy literature.
- There is no standardized definition of diagnostic yield.
- With recent advancements in the guidance technologies for peripheral bronchoscopy, including newer electromagnetic navigation platforms, cone-beam CT augmented fluoroscopy, digital tomosynthesis, and robot-assisted bronchoscopy; recently published studied use different definitions of DY.
- Varied definitions of DY may influence the interpretation of study results and limit the ability to compare findings across studies.
- The aim of this analysis is to illustrate and quantify the impact of different methodological approaches on DY estimates.
- Standardized definitions for study reporting is lacking in the field of peripheral diagnostic bronchoscopy
- Different methods are currently used to calculate the diagnostic yield in any study.
- There are various definitions of diagnostic yield currently used, all use true positives and true negatives. They are classified based on pathology findings. All methods classify a bronchoscopic procedure positive for malignancy as a TP. However, they vary in their approach to categorizing negative cases and handling missing data, resulting in variability in DY estimates.

Study Design

- **Type of Study:** Hypothetical Cohort Study
- **N:** 1000 procedures
- **Study groups:** All patients underwent diagnostic peripheral bronchoscopy.
- **Settings:** The data was extrapolated from a prospective study of robot-assisted bronchoscopy, which included 55 patients.
- **Follow up:** 1 year.
- **Primary outcome:** Calculation of Diagnostic Yield using models incorporating strict, intermediate and liberal classifications of a positive procedure

Population

- 1000 hypothetical peripheral diagnostic bronchoscopy procedures with longitudinal assessment.

Intervention

- Patients underwent diagnostic bronchoscopy (TO= Total Number of Procedures) with longitudinal assessment. The cases that were negative for malignancy at index were assessed at 1 year to determine a final clinical diagnosis (malignant vs benign).
- Bronchoscopy procedure positive for malignancy was considered true positive (TP).
- The cases negative for malignancy as either (1) a specific benign (SPB) diagnosis (e.g., infection, granuloma); (2) a nonspecific benign (NSB) finding (e.g., inflammation); or (3) a nondiagnostic (ND) result (e.g., atypical cells, normal alveoli).
- These patients were followed for 1 year to confirm the nonspecific benign and non-diagnostic results.
- Three methods were used to calculate diagnostic yield while the third method was subdivided into three sub-group diagnostic calculations.
- Method 1 (Strict): DY estimates are determined with data available at the time of index bronchoscopy; without the inclusion of any follow-up data.
  DY (method 1) = (TP+SBP)/TO
- Method 2 (Intermediate): DY calculation allows only for the inclusion of follow-up data for cases with an NSB finding at bronchoscopy. NSB findings are assessed longitudinally and categorized as TNs only if a subsequent biopsy or imaging confirms a nonmalignant diagnosis (NSBTN); cases in which a definitive diagnosis is not established because of lack of follow-up are considered non-diagnostic. DY is calculated as (TP + SPB + NSBTN) divided by total procedures.
  DY (method 2): (TP + SPB + NSBTN)/TO
- Method 3 (Liberal): DY calculation allows for the inclusion of follow-up data for all cases that are negative for malignancy at index bronchoscopy. Cases with either an SPB, NSB, or ND finding can be considered a TN (SPBTN þ NSBTN or NDTN) if either of the following is true: a subsequent biopsy confirms a definitive nonmalignant diagnosis or there is imaging evidence of benign disease (ie, lack of lesion progression). There are different Iterations of this approach.

- Method 3A: DY is calculated as (TP + SPBTN + NSBTN + NDTN) divided by total procedures with longitudinal data and excludes index NSB, SPB, or ND cases that lack follow-up data)
- Method 3B—patients that are lost to follow-up (LTFU) are considered ND and included only in the denominator; DY is calculated as (TP + SPBTN + NSBTN +
- NDTN) divided by total procedures.
- Method 3C—index SPB, NSB, or ND cases that are LTFU are considered as TNs; DY is calculated as (TP + SPBTN + NSBTN + NDTN + LTFU) divided by total procedures.

Outcomes

Primary outcomes:

- A total of 61.1% (611 of 1,000) were diagnosed with malignant disease, and 38.9% (389 of 1,000) were negative for malignancy, 5.6% (56 of 1,000) of which had an SPB (specific benign) diagnosis, 11.1% (111 of 1000) of which had an NSB (nonspecific benign) diagnoses and 22.2% (222 of 1000) were nondiagnostic (ND).
- A total of 9.2% (92 of 1,000) were lost to follow-up; the remaining cases that were negative for malignancy at index were assessed at 1 year to determine a final clinical diagnosis (malignant vs benign).
- Of the 111 patients with NSB findings at bronchoscopy, 74 were categorized as TNs based on subsequent biopsy or repeat imaging (labeled NSBTN) at 1 year. Of the 222 patients with ND findings at bronchoscopy, 56 were determined to have benign disease based on subsequent biopsy or repeat imaging (labeled NDTN)
- The DY estimates based on the three primary approaches were
  66.7% (Method 1)
  74.1% (Method 2)
  87.8% (Method 3A)
  79.8% (Method 3B)
  88.9% (Method 3C)

Conclusion

- Application of different approaches to calculate diagnostic yield (DY) results in widely varying estimates.
- Applying different approaches to the calculation of DY results in estimates that can differ by more than 20% on an absolute basis. The variability in DY estimates is driven by the characterization and approach to classifying nonmalignant findings at bronchoscopy.
- Rigorous methods should be used to capture follow-up information in patients without definitive results at initial bronchoscopy; follow-up periods that allow determination of the true diagnosis among patients.

Commentary

- The study highlighted different diagnostic yields using the same simulated cohort.
- Study was limited to a single simulated cohort.

- Changes in the prevalence of cancer, test sensitivities, and loss of follow-up will affect the outcomes of diagnostic yield, and different studies in different settings should be done to look at it.

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Suggested Reading

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Contributors

Author:
Muhammad Ibrar Islam, MD
University of Virginia
@Dr_MianMIbrar

Reviewer:
Sameer K. Avasarala, MD
University Hospitals – Case Western Reserve University School of Medicine
@SKAvasarala

Reviewer:
Yaron B Gesthalter, MD
University of California San Francisco