Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis

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Background: Evaluation of indeterminate biliary strictures typically involves collection and analysis of tissue or cells. Brush cytology and intraductal biopsies that are routinely performed during ERCP to assess malignant-appearing biliary strictures are limited by relatively low sensitivity.

Objective: To study the comparative effectiveness of brushings for cytology and intraductal biopsies in the etiology of biliary strictures.

Design: Meta-analysis.

Setting: Referral center.

Patients: PUBMED and Embase databases were reviewed for studies published to April 2014 where diagnostic correlation of histology was available.

Intervention: Database and review of study findings.

Main Outcome Measurements: Sensitivity and specificity.

Results: The pooled sensitivity and specificity of brushings for the diagnosis of malignant biliary strictures was 45% (95% confidence interval [CI], 40%-50%) and 99% (95% CI, 98%-100%), respectively. The pooled diagnostic odds ratio to detect malignant biliary strictures was 33.43 (95% CI, 14.29-78.24). For intraductal biopsies, the pooled sensitivity and specificity were 48.1% (95% CI, 42.8%-53.4%) and 99.2% (95% CI, 97.6%-99.8%), respectively. The pooled diagnostic odds ratio to detect malignant biliary strictures was 43.18 (95% CI, 19.39-95.83). A combination of both modalities only modestly increased the sensitivity (59.4%; 95% CI, 53.7%-64.8%) with a specificity of 100% (95% CI, 98.8%-100.0%). The Begg-Mazumdar and Egger tests indicated a low potential for publication bias.

Limitations: Inclusion of low-quality studies.

Conclusion: Our study suggests that both brushings and biopsy are comparable and have limited sensitivity for the diagnosis of malignant biliary strictures. A combination of both only modestly increases the sensitivity. (Gastrointest Endosc 2015;81:168-76.)

Abbreviations: CCA, cholangiocarcinoma; CI, confidence interval; DOR, diagnostic odds ratio; LR, likelihood ratio; LR+, positive likelihood ratio; LR−, negative likelihood ratio.

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Biliary strictures are challenging to diagnose and manage.[1] Malignant strictures of the bile duct are commonly caused by periampullary cancer, cholangiocarcinoma (CCA), or pancreatic cancer. These strictures commonly manifest in their advanced stages and are often unresectable.[1-3] When early diagnosis of malignancy is possible, the prognosis might improve with aggressive management.[4] Surgery is often associated with high postoperative morbidities.[5-7] Approximately 7% to 10% of patients undergoing surgery for suspected malignancy are found to have benign pathology.[8,9] Confirming malignancy through cytological/tissue diagnosis is essential before considering aggressive surgical management.

ERCP is commonly performed to rule out malignancies in suspicious strictures, and cytological/tissue diagnosis of malignancies can be made with brush cytology or intraductal biopsies. Brush cytology is routinely done to diagnose malignant biliary strictures because it is easier to perform, associated with fewer adverse events, but is limited by its low sensitivity.[10,11] Endobiliary forceps biopsies often require biliary sphincterotomy, and their advantage over brush cytology is not clearly established. Also, use of intraductal forceps would be difficult in narrow bile ducts. An ERCP-based diagnosis of indeterminate biliary strictures is important, particularly at centers where there is limited access to EUS. With the increasing costs of health care, if a second procedure (EUS) could be avoided through appropriate use of resources at the time of the ERCP for biliary drainage, it could result in a huge impact. We wanted to study the utility of the commonly used techniques when encountering a biliary stricture during ERCP to determine the optimal diagnostic approach. To our knowledge, no formal quantitative review of the available evidence has been published that comprehensively examined the diagnostic performance of biliary brushings for cytology and intraductal biopsies in the diagnosis of biliary strictures. The aim of this study was to perform a structured meta-analysis of all eligible studies to evaluate the comparative effectiveness of biliary brush cytology and intraductal biopsies in diagnosing malignant biliary strictures.

METHODS

Medical literature search

A comprehensive search of the medical literature was performed to identify peer-reviewed articles that examined the diagnostic accuracy of endoscopic retrograde biliary brush cytology and intraductal biopsies to detect malignancy as the etiology of biliary strictures. We systematically searched the PUBMED and Embase databases for studies published from January 1980 to April 2014 by using the following search terms: "ERCP brush cytology and forceps biopsy," "bile duct brush cytology," and "endobiliary forceps biopsy." We searched for additional references by cross checking bibliographies of retrieved full-text papers. Two reviewers (V.L. and B.N.) independently screened the titles and abstracts of all the articles according to predefined inclusion and exclusion criteria. Any differences were resolved by mutual agreement and in consultation with the third reviewer (U.N.).

Selection criteria

Only studies involving both ERCP brushing and biopsies in the identification of biliary strictures with availability of data for the construction of 2×2 contingency tables were included. None of the studies included in our meta-analysis used cholangioscopy techniques for sampling the biliary stricture. Studies with insufficient data and a sample size of less than 10 were excluded from the analysis. The standard criterion for the confirmation of malignancy in the studies was the surgical pathology or autopsy and long-term clinical follow-up.

Index test

The index test was the use of brushings for cytology and intraductal biopsies with studies reporting positive for malignancy included in our analysis.

Quality of studies

Currently there are no consensus or criteria to evaluate the quality of studies without a control arm.[12] The quality of studies was interpreted based on Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 criteria.[13]

Statistical analysis

Meta-analysis for the accuracy of biliary brush cytology and intraductal biliary biopsy to diagnose malignancy was performed by calculating the pooled estimates of sensitivity, specificity, likelihood ratios (LRs), and diagnostic odds ratio (DOR). Pooling was performed by using the Der Simonian-Laird method (random-effects model). Forest plots were constructed to show the point estimates in each study in relation to the summary pooled estimate. The width of the point estimates in the Forest plots corresponded to the assigned weight of the study. Heterogeneity was assessed by using χ^2 statistics, I^2 measure of inconsistency, and Cochran's Q test.

A summary receiver-operating characteristic was constructed based on the Moses-Shapiro-Littenberg method as a way to summarize the true-positive and false-positive rates from different studies. The proximity of the area under the receiver-operating characteristic curve to 1 is a well-validated overall representation of the diagnostic accuracy of a test.

The robustness of the meta-analysis to publication bias was assessed by funnel plots and bias indicators, including the Begg-Mazumdar test and the Harbord–Egger test.[14,15]