Original Article

The Concordance between Cytological and Histological Specimens of Bile Duct and Malignancy Rates of Cytological Specimens: A Study in a Single Institution

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Background: Cytological evaluation of biliary tract specimens, especially from the common bile duct, is a procedure to identify potential malignant lesions that is less invasive than resection. Staffs of cytological service examined cytological specimens from the bile duct. Following this, tissue biopsy or resection was conducted and the diagnostic discrepancies between the two procedures were analyzed.

Objective: To investigate the diagnostic concordance rates from the histological and the cytological examination of bile duct specimens and to evaluate the malignancy rate according to the bile duct cytological diagnostic category.

Materials and Methods: Seventy-eight cytological bile duct specimens were collected between January 2011 and September 2017. In addition, 44 histological biopsied or resected specimens were retrospectively included in the present study. The Kappa coefficient was calculated and used to determine the concordance rate between the two procedures. The sensitivity and positive predictive value of cytology were calculated and compared to histological biopsied or resected specimens. The malignancy rates among the cytological diagnostic categories were identified.

Results: There was moderate concordance between the cytology and the biopsy or resected specimens (K=0.52, p=0.001), the sensitivity and specificity of which were 75% (95% CI 47.62 to 92.73) and 79% (95% CI 59.05 to 91.70), respectively. The positive predictive value was 67 (95% CI 48.24 to 81.10), and negative predictive value was 85% (95% CI 69.73 to 92.92). The malignancy rate in the negative for malignancy group was 18%.

Conclusion: The diagnostic concordance rate between the cytological results of bile duct specimens and the results of biopsy or resection was 77% (95% CI 62 to 88), with a moderate concordance rate (K=0.52, p=0.001).

Keywords: Bile cytology, Bile duct, Cytology, Histology, Concordance rate, Bile duct cancer

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Biliary stricture is a common problem in the extrahepatic bile duct. Most patients undergo endoscopic retrograde cholangiopancreatography (ERCP) to evaluate and diagnose pathological lesions of the biliary tree. The most common causes of malignant strictures are peri-ampullary cancer, pancreatic duct cancer, intraductal neoplasm, and cholangiocarcinoma[1,2]. In northeast Thailand, there is a high prevalence of cholangiocarcinoma. In many cases, the disease is considered to be locally advanced, making it unsuitable for surgery and increasing the risk of post-operative complications. Accurate diagnosis of biliary stricture is essential in the planning of treatment.

Biliary cytology is usually conducted when an ERCP is performed, and brushing is an easy, safe, and cost-effective technique. However, a previous study found that the pooled sensitivity and specificity of the biliary brushing cytology was 45% and 99%, respectively[3].

The aim of the present study was to investigate the diagnostic concordance rate between histological and cytological examination of bile duct specimens in

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Table 1. Demographic data and cytological/histological categories

Characteristic	n (%)
Age (year)	
Mean±SD	64±11
Range	39 to 78
Sex	
Male	29 (65.9)
Female	15 (34.1)
Bile cytological procedure	
Aspiration	38 (86.4)
Brushing	6 (13.6)
Diagnostic categories for cytological specimens	
Negative for malignancy	22 (50.0)
Atypical cells	4 (9.1)
Neoplastic	4 (9.1)
Suspicious for malignancy	13 (29.5)
Positive for malignancy	1 (2.3)
Diagnostic categories for histological specimens	
Negative for malignancy	28 (63.6)
Positive for malignancy	16 (36.4)

SD=standard deviation

patients with biliary stricture, as well as to evaluate the malignant rates in cytological bile duct specimens.

Materials and Methods

Study population

Patients presenting with jaundice and malignant bile duct stricture at Srinagarind Hospital between January 2011 and September 2017 were included in the present study. Seventy-eight bile duct cytological or brushing specimens were collected. In addition, 44 subsequent histological intraductal biopsy, bile duct resection, or Whipple resection specimens were included in the present study. Cases of the bile duct cytology or brushing cytology without surgical follow-up within six months and those with non-epithelial neoplasm were excluded.

Specimen preparation methods

The specimens that underwent routine cytological evaluation were prepared by using Papanicolaou staining, and those that underwent histological evaluation were prepared by using Hematoxylin and Eosin staining. No liquid-based cytology preparation or cell block preparation was performed in the present study.

Cytological interpretation

The specimens were categorized by diagnostic cytological result as negative, atypical, neoplastic, suspicious for malignancy, and positive for malignancy. The criteria for each category were described in previous publications[1,4]. The histological biopsied or resected specimens were also categorized as being either negative or positive for malignancy, which required surgical treatment.

Results

Demographic data

The mean age of the patients was 64 years old. The youngest patient was 39, and the oldest was 78. Twenty-nine were men, making the male to female ratio 1.9:1.

Cytological and histological categories

Each of the 44 cases was classified as either negative for malignancy (20 cases, 45.5%), atypical (five cases, 11.4%), neoplastic (two cases, 4.5%), suspicious for malignancy (14 cases, 31.8%), or positive for malignancy (three cases, 6.8%). The authors combined cases that were negative for malignancy and atypical into the negative cytological result group (26 cases, 59%), and those that were neoplastic, suspicious for malignancy, and positive for malignancy into the positive cytological result group (18 cases, 41%). Six of the specimens were brushing specimens (13%) and the others were bile aspiration and mixed. Surgical biopsy or resection results were classified into negative for malignancy (28 cases, 63.6%) and positive for malignancy groups (16 cases, 36.4%) (Table 1).

Diagnostic correlation, sensitivity, and specificity

The sensitivity and specificity of the cytological specimens and surgical specimens were 75% (95% CI 47.62 to 92.73) and 79% (95% CI 59.05 to 91.70), respectively. The negative predictive value and positive predictive value were 85% (95% CI 69.73 to 92.92) and 67% (95% CI 48.24 to 81.10), respectively. The diagnostic accuracy of the cytological specimens was 77% (95% CI 62.16 to 88.53). The diagnostic concordance rate between the cytologic and histologic specimens was 77% (95% CI 62 to 88, kappa=0.52) (Table 2).

Rate of malignancy among by cytological category

The malignancy rates for the surgical specimens categorized as negative, atypical, neoplastic, suspicious for malignancy, and positive for malignancy

Table 2. Diagnostic correlation, sensitivity, and specificity

Diagnosis	Histological specimen		Total	Kappa index	p-value
	Positive for malignancy	Negative for malignancy			
Cytological specimen					
Positive	12	6	18	0.52	0.001
Negative	4	22	26		
Total	16	28	44		
Sensitivity (%)	75 (95% CI 47.62 to 92.73)	Specificity (%)		79 (95% CI 59.05 to 91.70)	
Positive predictive value (%)	67 (95% CI 48.24 to 81.10)	Negative predictive value (%)		85 (95% CI 69.73 to 92.29)	
Prevalence (%)	36	Accuracy (%)		77 (95% CI 62.16 to 88.53)	

Table 3. Rate of malignancy among the cytologic categories

Cytological diagnostic categories	Histological		Total	Rate of malignancy (%)
	Negative	Positive		
Negative for malignancy	18	4	22	18
Atypical	2	2	4	50
Neoplastic	2	2	4	50
Suspicious for malignancy	6	7	13	53
Positive for malignancy	0	1	1	100

were 18%, 50%, 50%, 53%, and 100%, respectively (Table 3).

Discussion

Cholangiocarcinoma, peri-ampullary cancer, and pancreatic cancer are the biliary strictures in which malignancy is the most common. This means that it is important to differentiate these from other benign strictures using ERCP-based cytology and histological biopsy to avoid unnecessary surgery.

In the present study, the sensitivity and specificity of the cytological brushing specimens were 75% and 79%, respectively. The specificity found in the present study was lower than in a previous study (99%)[2]. This may be due to the sampling technique and inflammatory reactions interfering in the cytologic changes of the epithelial cells, which may have led to the moderate concordance between cytology and histology (K=0.52, p=0.001). The malignancy rates of specimens in the negative and atypical cytological diagnostic categories were 18% and 50%, respectively, which are higher than those found in the other studies[5]. This makes it challenging for routine cytological working groups to lower the rate of false negatives in the diagnosis of malignancy. Intraoperative mixing together of the aspiration cytology specimens and bile duct brushing specimens without using a liquid-based cytology technique lowers the cytological diagnostic accuracy[5]. In addition, further advances in diagnostic testing will be helpful in increasing diagnostic accuracy such as cytological brushing and post-brushing technique. Liquid based cytology, advances in cell block preparation, and the development of fluorescence in situ hybridization (FISH) would be particularly useful[6-8]. Specimens considered suspicious for malignancy and positive for malignancy according to cytological examination had malignancy rates of 53% and 100%, respectively, which are comparable to the rates found in other studies[5]. A previous study on fluke-related cholangitis and desmoplastic features of cholangiocarcinoma showed that inflammation may interfere cytological diagnostic accuracy[3]. However, clinical and radiological examination can lead to greater diagnostic accuracy in cytological diagnosis.

Conclusion

The diagnostic concordance rate between the cytological examination of bile duct specimens and biopsy or resection results was 77% (95% CI 62 to 88), showing a moderate concordance rate (K=0.52, p=0.001). Specimens that were considered suspicious for malignancy and positive for malignancy according to cytological examination had malignancy rates of

54% and 100%, respectively.

What is already known on this topic?

Previous studies showed the varying sensitivity, 30% to 60%, of the bile duct cytology specimen.

What this study adds?

This study has reported the higher sensitivity and 18% malignancy rate of the negative group in the cytological specimen. Even higher sensitivity and specificity and moderated concordant rate between the cytological examination of bile duct specimens and biopsy or resection, advance diagnostic technique will be helpful for raising the accuracy of the cytological diagnosis.

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Conflicts of interest

The authors declare no conflict of interest.

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