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Accuracy of brush cytology in biliopancreatic strictures: a single-center cohort study

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Abstract

Objective: False positive and negative results are associated with biliary tract cell brushing cytology during endoscopic retrograde cholangiopancreatography (ERCP). The causes are uncertain. The purpose of this study was to evaluate the accuracy of diagnoses made via cell brushing in our center, and to explore the factors influencing diagnosis.

Methods: The clinical data of patients who underwent cell brushing at our center from January 2016 to August 2019 were retrospectively analyzed. These included age, gender, stricture location, thickness of the bile duct wall in the narrow segment, maximum diameter of the biliary duct above the stricture, number of cell brush smears, carbohydrate antigen 19-9, and carcinoembryonic antigen. Positive brush cytology results were compared with results of surgical histology or tumor biopsy as well as with the patient's clinical course.

Results: Of the 48 patients who underwent cell brushing cytology, 27 (56.3%) had positive results. The sensitivity and specificity of biliary duct cell brushing was 79.4%, and 85.7%, respectively. None of the above-mentioned factors were associated with positive cytology brushing results.

Conclusions: Cell brushing cytology remains a reliable method for diagnosis of pancreaticobiliary malignancies.

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Introduction

Biliary duct cell brushing during endoscopic retrograde cholangiopancreatography (ERCP), a safe and practicable method for diagnosis of hepatobiliary and pancreatic malignancies,[1] was first described in 1975 by Osnes.[2] Currently, the technique is widely used as the bridge between radiological imaging and surgical intervention. However, the diagnostic value of biliary duct cell brushing was challenged recently because of high frequencies of false positive and negative results.[3–5] High false negative rates were associated with sampling errors and technical faults,[6] and false positive cytological diagnoses occurred most often in patients with primary sclerosing cholangitis, IgG4-related cholangitis and autoimmune pancreatitis.[4] Moreover, the desmoplastic reaction around the tumor also limits the sensitivity of this technique.[7] Therefore, it is still strongly advised that patients suspected of malignant hepatobiliary and pancreatic diseases with or without obstructive jaundice should undergo cell brushing on initial ERCP.[5] These patients are at a high risk of misdiagnosis, and if an uncovered biliary stent is placed through ERCP without pathological support, irreversible consequences may occur.

The frequency of positive cell brushing results ranged from 30% to 80% in previous studies.[1,4,8–13] The variables associated with positive brushing cytology results are complex and stochastic. Cell brushing experience, skills, brushed cell yield, interobserver variability of pathologists, patient age, mass size, and stricture length were all potentially associated with the likelihood of obtaining positive results.[4,14,15]

The objective of this study was to evaluate the accuracy of cell brushing cytology in our center and to explore factors influencing positive results over a 2.7-year period from January 2016 to August 2019.

Materials and methods

This was a retrospective study at Shulan (Hangzhou) Hospital, which is affiliated to Zhejiang Shuren University, Shulan International Medical College. The study was conducted from January 2016 until August 2019. Patients undergoing ERCP cell brushing because of biliary stricture, biliary dilation or suspected pancreaticobiliary neoplasia during the study period were eligible. Data on age, gender, stricture location, thickness of the bile duct wall in the narrow segment (at least three measurements by enhanced computed tomography or magnetic resonance imaging were averaged), maximum diameter of the biliary duct above the stenotic segment, number of cell brush smears, carbohydrate antigen (CA)19-9 and carcinoembryonic antigen (CE)A were collected from medical records. The same medical records of patients (except for the number of cell brush smears) with suspected extrahepatic cholangiocarcinoma (including gallbladder cancer) who underwent surgery during the same period were also collected and analyzed. The positive rate of cell brushing

for diagnosis of malignant tumors and its relationships with age, gender, number of cell brush smears, CA19-9, CEA, stenosis site, thickness of the bile duct wall at stenosis, and maximum transverse diameter of the bile duct above stenosis were examined. The study was approved by the ethics committee of Zhejiang Shuren University, Shulan International Medical College (number: 2020016). The requirement for informed consent was waived because of the retrospective nature of the study.

After successful intubation of the papillary bile duct, the stricture segment was clearly visible by contrast medium. The cell brush was placed within the narrowing range and the cell brush was rubbed back and forth under fluoroscopy for at least 10 passes. The above procedure was repeated twice. We do not routinely perform biopsies with forceps unless there is a significant mass lesion of the duodenal papilla. When malignancy was considered but the cytological pathology of cell brushings was negative, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) was used to distinguish the nature of the mass.

Immediately after obtaining cell brushing samples using a Cook cytology brush, slide cytology smears were prepared (4–7 smears) and fixed with 95% alcohol for routine diagnostic cytology (Papanicolaou or hematoxylin-eosin staining). Cytopathologic evaluation in our center did not include fluorescence *in situ* hybridization. Cytology samples were classified as normal epithelial cells, mildly atypical cells, severely atypical cells for which malignancy could not be excluded, suspected cancer cells, or cancer cells. We defined normal epithelial cells and mildly atypical cells as negative, while severely atypical cells and suspected or clearly malignant cells were defined as negative. The final diagnosis was confirmed following postoperative pathological diagnosis, histopathological diagnosis by EUS-FNA or extracorporeal ultrasound-guided puncture, and radiological infiltration of adjacent organs or metastases. Final diagnosis was made after at least a 3-month follow-up combined with the patient's clinical course. Patients with benign pathology were advised to reassess tumor markers and hepatobiliary ultrasonography or computed tomography every 3 to 6 months in the first 2 years. The follow-up duration ranged from 3 months to 17 months.

Sensitivity was calculated as true positive (TP)/(TP + false negative (FN)). Specificity was calculated as true negative (TN)/(TN + false positive(FP)). Positive predictive value (PPV) was calculated as TP/(TP + FP), and negative predictive value (NPV) was calculated as TN/(TN + FN). Analyses were performed using IBM SPSS for Windows version 19.0 (IBM, Armonk, NY, USA). Independent sample T tests, non-parametric tests and binary logistic regression were used for further analysis. Values of $p<0.05$ were considered statistically significant.

Results

Brushing cytology was performed in 51 patients from January 2016 until August 2019 at our center. A group of 32 patients with suspected extrahepatic cholangiocarcinoma who underwent surgery during the same period served as a comparison group. Three patients were excluded. One patient only underwent pancreatic duct cell brushing because of chronic pancreatitis. One patient had suspected hilar cholangiocarcinoma by imaging examination and cancer cells were detected by ERCP cell brushing; the patient was excluded because of lack of tumor markers such as CA19-9 and CEA and loss of in-hospital follow-up. One patient underwent a biliary tract smear for jaundice after liver transplantation. The mean age of the patients undergoing cell brushing was 63.1 years (range 34–84 years) and the male:female ratio was 1.4:1. Table 1 shows the

Table 1. All variables studied in patients undergoing brush and cytology analysis of diagnostic parameters.

	n = 48
Age (years, range)	63.1 (34–84)
Sex (male)	28
Thickness of strictured bile duct wall (mm, mean)	3.55
Maximum diameter of biliary duct above stenotic segment (mm, mean)	13.9
CA19-9 (U/mL, mean)	1746.7
CEA (ng/mL, mean)	250.4
Number of cell brush smears (range)	4–7
Location of stricture	
Hilar bile duct	18
Mild + lower common bile duct	30
True positive	27
False positive	2
True negative	12
False negative	7
Sensitivity	79.40%
Specificity	85.70%
Positive predictive value	93.10%
Negative predictive value	63.20%

The criteria for the confirmation of true positive brush cytology results in this study was surgical pathology or autopsy, accompanied by peripheral organ invasion, abdominal and pelvic lymph node metastasis or distant metastasis and long-term follow-up.

distributions of true/false positive and true/false negative results of cell brushing. The sensitivity of biliary duct cell brushing was 79.4%, the specificity was 85.7%, the positive predictive value was 93.1%, and the negative predictive value was 63.2%.

Malignancy was detected in 27 of 48 patients (for cytological results see Figure 1). The mean age of patients with true positive cell brushing results was 63.9 years (range 34–84 years), and the male: female ratio was 1.2:1. The 27 patients with true positive cell brushing cytology results were confirmed to have the following malignant neoplasms: hilar cholangiocarcinoma (n = 8; two cases were confirmed by postoperative pathology, one was confirmed by liver biopsy, and the remaining five were confirmed by clinical course), gallbladder cancer (n = 3, confirmed by clinical course), carcinomas of the middle and lower segment of the common bile duct (n = 12; eight cases were confirmed by postoperative pathology, one was confirmed by liver biopsy, and the remaining three were confirmed by clinical course), pancreatic adenocarcinoma (n = 2,

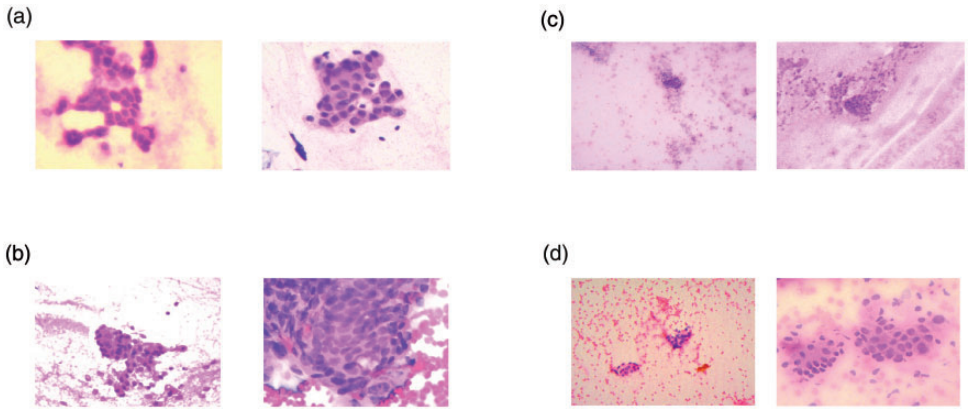

Figure 1. Cell brushing cytology results of the biliary tract. (a) True positive cases: hilar cholangiocarcinoma and lower common bile duct adenocarcinoma. (b) False positive cases: two cases of autoimmune cholangiopancreatic diseases. (c) True negative cases: pyogenic cholangitis and chronic pancreatitis. (d) False negative cases: pancreatic adenocarcinoma and lower common bile duct adenocarcinoma.

confirmed by clinical course), hepatocellular carcinoma (n = 1, confirmed by postoperative pathology), and ampullary cancer (n = 1, confirmed by duodenal papilla forceps biopsy). None of age, gender, stricture location, thickness of the bile duct wall in the narrow segment, maximum diameter of the biliary duct above the stenotic segment, number of cell brush smears, CA19-9 or CEA were associated with positive results of cytology brushing (Table 2). The mean level of CEA in the brush positive group was much higher than in the surgery group, because this was because of the surprisingly high CEA level in one patient (11444.4 ng/mL).

There were two cases of false positive cell brushing results (for cytological results see Figure 1). One patient was a 51-year-old man. Imaging examinations showed abnormal thickening and stenosis of the lower part of the common bile duct. Cholangiocarcinoma was possible and autoimmune cholangitis was difficult to distinguish. IgG4 was 0.38 g/L (range: 0.03–2.01 g/L), CA19-9 was 27.1 U/mL (range: 0–37 U/mL), and CEA was 8.5 ng/mL (range: 0–5 ng/mL). Brush cytology revealed atypical cells that were possibly malignant. Ultrasound endoscopic fine needle aspiration biopsy showed no evidence of tumors. The patient was reluctant to receive steroid therapy, and imaging findings after 3 months were like those in the anterior photograph. The other false positive case was a 67-year-old man. Brush cytology revealed atypical cells, and malignant tumors could not be excluded. However, imaging findings suggested IgG4-related cholangitis and autoimmune pancreatitis. IgG4 was 2.43 g/L, antinuclear antibody was 1:320, total bilirubin was 474 μmol/L, and direct bilirubin was 415 μmol/L. The patient received steroid therapy. A review after 2 months showed that the level of IgG4 was 0.8 g/L, total bilirubin was 108 μmol/L, and direct bilirubin was 95 μmol/L.

Overall, 12 patients had a variety of benign diagnoses including local fat invasion of the head of the pancreas (n = 1), bilateral gallbladder (n = 1), pyogenic cholangitis (n = 3), primary sclerosing cholangitis (n = 1), chronic pancreatitis (n = 2), autoimmune pancreatitis (n = 1), and post cholecystectomy (n = 3). There were seven false negative diagnoses including pancreatic adenocarcinoma (n = 3), postoperative recurrence of gallbladder cancer (n = 1), ampullary cancer (n = 2), and hilar cholangiocarcinoma (n = 1) (for cytological results see Figure 1).

The mean age of patients undergoing direct surgery was 60.9 years (range: 34–81 years) and the male:female ratio was 1.5:1 (Table 3). The underlying conditions of the 32 patients were as follows: hilar cholangiocarcinoma (n = 24), gallbladder cancer

Table 2. Analysis factors associated with true positive brush cytology results.

	n = 27	P value
Age (years, range)	63.9 (34–84)	>0.05
Sex (male)	15	>0.05
Thickness of strictured bile duct wall (mm, mean)	3.67	>0.05
Maximum diameter of biliary duct above stenotic segment (mm, mean)	13.15	>0.05
CA19-9 (U/mL, mean)	3002.4	>0.05
CEA (ng/mL, mean)	432.8	>0.05
Number of cell brush smears (range)	4∼7	>0.05
Location of stricture		>0.05
Hilar bile duct	12	–
Mild + lower common bile duct	15	–

Table 3. All variables studied in patients undergoing direct surgery.

	n = 32
Age (years, range)	60.9 (34–81)
Sex (male)	19
Thickness of strictured bile duct wall (mm, mean)	3.44
Maximum diameter of biliary duct above stenotic segment (mm, mean)	13.07
CA19-9 (U/mL, mean)	1542.2
CEA (ng/mL, mean)	12.9
Location of stricture	
Hilar bile duct	27
Mild + lower common bile duct	5

(n = 4), pancreatic adenocarcinoma (n = 2), middle and lower segment of the common bile duct carcinoma (n = 2). There were no significant differences in any of the above-mentioned factors including age, gender, thickness of the bile duct wall in the narrow segment, maximum diameter of the biliary duct above the stenotic segment, CA19-9 or CEA between the true positive cell brushing group and the surgery group (Figure 2).

Discussion

Biliary strictures are caused by a variety of conditions including inflammatory diseases and malignant pancreaticobiliary tumors.[3] Brushing cytology is the most common diagnostic technique used in patients with suspected pancreaticobiliary malignancies. It is simple to perform and highly specific. It was reported that the specificity of brushing cytology varied between 95% and 100%.[16,17] However, in this study we found a relatively low specificity of 85.7%. There are several potential explanations of this finding. First, although biliary tract cell brushing during ERCP is safe and easy to perform, it is more expensive than magnetic resonance cholangiopancreatography and other imaging examinations. Physicians requesting imaging examinations are not always suspicious of malignant diseases, and we do not perform them casually. Second, it is necessary to treat diseases with obvious clinical symptoms that have the possibility of secondary malignant tumors, such as chronic pancreatitis. However, the incidence of chronic pancreatitis and autoimmune pancreatitis is not high. As a result, few patients are genuinely negative.

The sensitivity of brushing cytology has always been unsatisfactory (resulting from limited cellularity) according to the published literature.[18] In this study, we found a relatively high sensitivity of 79.4%. There are several potential explanations of the discrepancy. First, we have the patience to brush the bile duct cells in suspected lesions. The time of brushing is not of great importance but making sure that the cell brush is within the narrow range and rubbing the cell brush back and forth under fluoroscopy is essential. Second, when we do biliary brushing, we hope to see that the brush is bloodstained; the results from our center suggest that bloodstained brushes seem to have more positive results. Finally, our hospital is a tertiary referral center, and patients generally have advanced malignancies or metastatic cancers. Especially patients with hilar cholangiocarcinoma have often lost the opportunity for surgical intervention. The stricture of the bile duct is significant and obstructive jaundice is often serious in these patients. They are admitted in our department for liver transplantation or to obtain pathological results before undergoing chemotherapy after jaundice diminishes. Therefore, it is generally easy to obtain sufficient cancer cells.

We tried to identify factors associated with positive results of brush cytology. Factors including age, gender, stricture location, thickness of the bile duct wall in the narrow segment, maximum diameter of the biliary duct above the stenotic segment,

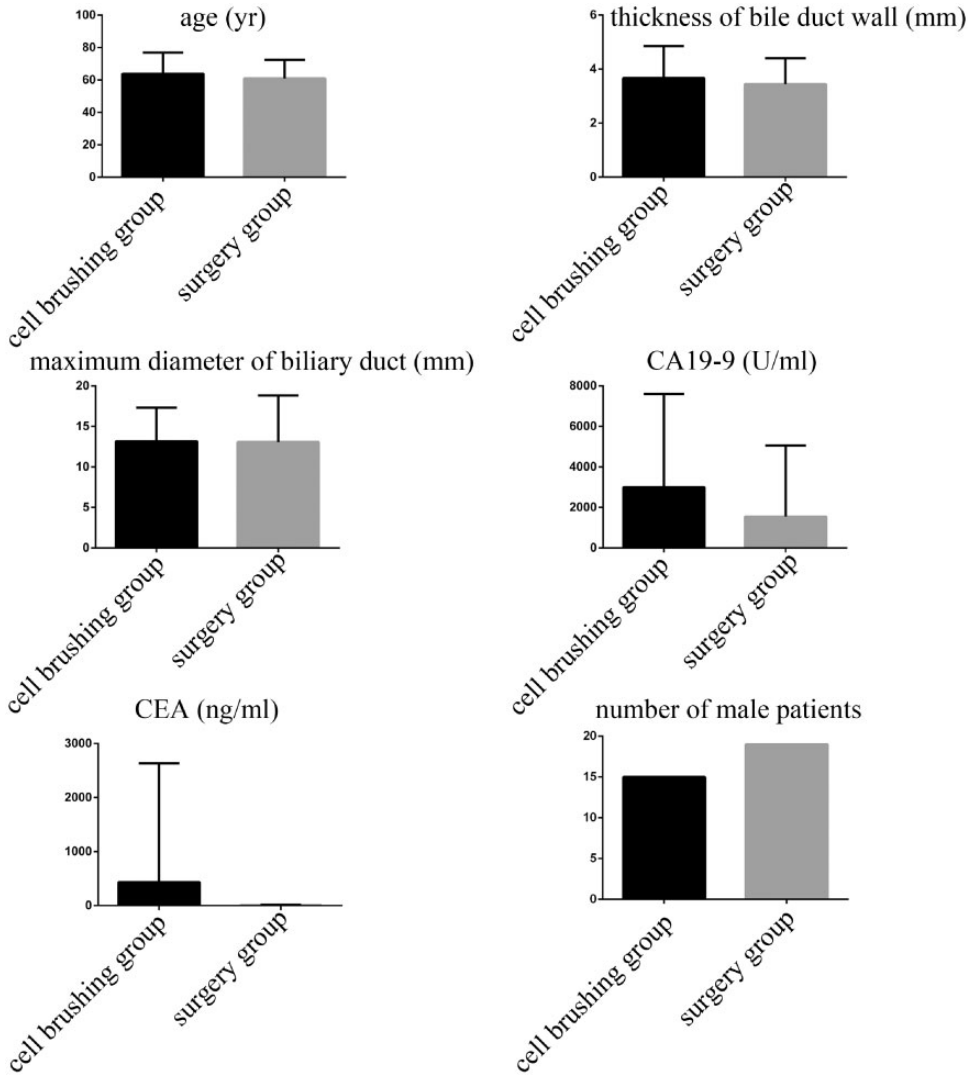

Figure 2. Comparison of age, thickness of the bile duct wall in the narrow segment, maximum diameter of the biliary duct above the stenotic segment, carbohydrate antigen (CA)19-9 and carcinoembryonic antigen (CEA) between the true positive cell brushing group and the surgery group.

number of cell brush smears, CA19-9 and CEA were analyzed. None of the above-mentioned factors were associated with true positive brushing cytology.

We collected and assessed the medical records of patients (excluding number of brushing smears) with suspected extrahepatic cholangiocarcinoma (including gallbladder cancer) who underwent direct surgery during the same period. There were no differences in age, gender, thickness of the bile duct wall in the narrow segment, maximum diameter of the biliary duct above the stenotic segment, CA19-9, or CEA between the ERCP cell brushing group and direct surgery group.

EUS-FNA can evaluate the size, character, location of abdominal masses and their relationships with blood vessels. Currently, it has been strongly advised to use EUS-FNA for evaluation of indeterminate biliary strictures in patients.[19] It is a safe medical instrument with morbidity and mortality rates $< 1\%$.[20] It has also been shown that EUS-FNA is superior to ERCP with brush cytology for diagnosing malignant biliary strictures.[19,21,22] However, EUS-FNA also has low negative post-test probabilities. In addition, the positive rate of EUS-FNA is greatly limited by the size, location, and non-cystic nature of the tumor, as well as the ability of the operator. Conversely, the success of ERCP cell brushing mainly depends on the degree and length of the bile duct stricture. Compared with EUS, the difficulty of ERCP cell brushing is greatly reduced. Therefore, ERCP cell brushing biopsy can be combined with EUS-FNA to improve the positive rate when conditions permit.

Single-operator peroral cholangioscopy (sPOCS) also has significant advantages in the diagnosis of indeterminate biliary diseases. For example, sPOCS enables direct visualization of lesions in the bile duct (even minimal biliary mucosal lesions) and has specific miniature biopsy forceps allowing for substantial tissue acquisition.[23] was is reported that sPOCS-guided biopsies had moderate sensitivity for the diagnosis of malignant biliary strictures.[24] However, sPOCS-guided biopsy is much more expensive than ERCP cell brushing, limiting its widespread use in clinical practice.

This study had several limitations. First, this was a single center retrospective study and the sample size was relatively small. Second, we did not identify risk factors related to true positive cell brushing cytology results. Third, the follow-up duration of patients with benign pathology was relatively short. It remains possible that risk factors could be identified using larger numbers of cases. Alternatively, we may need to upgrade the cytopathological examination technologies in our center, for instance by adopting fluorescence *in situ* hybridization technique.

In conclusion, biliary duct cell brushing can provide clear results from a patient and skilled examination. To obtain a true positive result, it is necessary to work closely with radiologists, pathologists, and endoscopy nurses. Biliary tract cell brushing should also be timely combined with EUS-FNA/forceps biopsy.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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References

1. Stewart C, Mills P, Carter R, et al. Brush cytology in the assessment of pancreaticobiliary strictures: A review of 406 cases. *J Clin Pathol* 2001; 54: 449–455.
2. Osnes M, Serck-Hanssen A and Myren J. Endoscopic retrograde brush cytology (ERBC) of the biliary and pancreatic ducts. *Scand J Gastroenterol* 1975; 10: 829–831.
3. Abbasi MR, Ghazi Mirsaeed SM and Mohammad Alizadeh AH. Diagnosis of malignant biliary strictures: Conventional

or negative pressure brush cytology? *Asian Pac J Cancer Prev* 2016; 17: 4563–4566.
4. Mahmoudi N, Enns R, Amar J, et al. Biliary brush cytology: Factors associated with positive yields on biliary brush cytology. *World J Gastroenterol* 2008; 14: 569–573.
5. Sethi R, Singh K, Warner B, et al. The impact of brush cytology from endoscopic retrograde cholangiopancreatography (ERCP) on patient management at a UK teaching hospital. *Frontline Gastroenterol* 2016; 7: 97–101.
6. Alizadeh MAH, Mousavi M, Salehi B, et al. Biliary brush cytology in the assessment of biliary strictures at a tertiary center in Iran. *Asian Pacific J Cancer Prev* 2011; 12: 2793–2796.
7. Harada T, Baril P, Gangeswaran R, et al. Identification of genetic alterations in pancreatic cancer by the combined use of tissue microdissection and array-based comparative genomic hybridisation. *Br J Cancer* 2007; 96: 373–382.
8. Kocjan G and Smith AN. Bile duct brushings cytology: Potential pitfalls in diagnosis. *Diagn Cytopathol* 1997; 16: 358–363.
9. Sawada Y, Gonda H and Hayashida Y. Combined use of brushing cytology and endoscopic retrograde pancreatography for the early detection of pancreatic cancer. *Acta Cytol* 1989; 33: 870–874.
10. Sachdev A, Duseja A, Bhalla A, et al. Efficacy of endoscopic wire guided biliary brushing in the evaluation of biliary strictures. *Trop Gastroenterol* 2003; 24: 215–217.
11. McGuire DE, Venu RP, Brown RD, et al. Brush cytology for pancreatic carcinoma: An analysis of factors influencing results. *Gastrointest Endosc* 1996; 44: 300–304.
12. Kurzawinski T, Deery A, Dooley J, et al. A prospective controlled study comparing brush and bile exfoliative cytology for diagnosing bile duct strictures. *Gut* 1992; 33: 1675–1677.
13. Foutch PG. Diagnosis of cancer by cytologic methods performed during ERCP. *Gastrointest Endosc* 1994; 40: 249–252.
14. Temiño López-Jurado R, Cacho Acosta G, Argüelles Pintos M, et al. Diagnostic yield of brush cytology for biliary stenosis during ERCP. *Rev Esp Enferm Dig* 2009; 101: 385–394.
15. Sugimoto S, Matsubayashi H, Kimura H, et al. Diagnosis of bile duct cancer by bile cytology: Usefulness of post-brushing biliary lavage fluid. *Endosc Int Open* 2015; 15: 394–403.
16. Foutch PG, Kerr DM, Harlan JR, et al. Endoscopic retrograde wire-guided brush cytology for diagnosis of patients with malignant obstruction of the bile duct. *Am J Gastroenterol* 1990; 85: 791–795.
17. Furmanczyk PS, Grieco VS and Agoff SN. Biliary brush cytology and the detection of cholangiocarcinoma in primary sclerosing cholangitis evaluation of specific cytomorphologic features and CA19-9 levels. *Am J Clin Pathol* 2005; 124: 355–360.
18. Salomao M, Gonda TA, Margolskee E, et al. Strategies for improving diagnostic accuracy of biliary strictures. *Cancer Cytopathol* 2015; 123: 244–252.
19. De Moura DTH, De Moura EGH, Bernardo WM, et al. Endoscopic retrograde cholangiopancreatography versus endoscopic ultrasound for tissue diagnosis of malignant biliary stricture: Systematic review and meta-analysis. *Endosc Ultrasound* 2018; 7: 10–19.
20. Wang KX, Ben QW, Jin ZD, et al. Assessment of morbidity and mortality associated with EUS-guided FNA: A systematic review. *Gastrointest Endosc* 2011; 73: 283–290.
21. Moura DTH, De Moura EGH, Matuguma SE, et al. EUS-FNA versus ERCP for tissue diagnosis of suspect malignant biliary strictures: A prospective comparative study. *Endosc Int Open* 2018; 6: E769–E777.
22. De Moura DTH, Ryou M, De Moura EGH, et al. EUS-guided fine needle aspiration and ERCP-based tissue sampling in suspected malignant biliary strictures: A meta-analysis of same-session procedures. *Clin Endosc* 2019. doi:10.5946/ce.2019.053.
23. De Moura EGH. Limited diagnostic accuracy and clinical impact of single-operator peroral cholangioscopy for indeterminate biliary strictures. *Endoscopy* 2020; 52: 90–91.
24. Navaneethan U, Hasan MK, Lourdusamy V, et al. Single-operator cholangioscopy and targeted biopsies in the diagnosis of indeterminate biliary strictures: A systematic review. *Gastrointest Endosc* 2015; 82: 608–614.