

ORIGINAL ARTICLE

Percutaneous transhepatic cholangiographic endobiliary forceps biopsy versus endoscopic ultrasound fine needle aspiration for proximal biliary strictures: a single-centre experience

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Abstract

Background: Endoscopic ultrasound fine needle aspiration (EUS-FNA) and percutaneous transhepatic cholangiographic endobiliary forceps biopsy (PTC-EFB) are valid procedures for histological assessment of proximal biliary strictures (PBS), but their performances have never been compared. This study aimed to compare the diagnostic performance of these two techniques.

Method: The diagnostic performances of EUS-FNA and PTC-EFB were compared in a retrospective cohort of patients assessed for PBS from 2011 to 2015 at a single tertiary centre. An inverse probability of treatment weighting (IPTW) was performed to adjust for covariate imbalance.

Results: A total of 102 EUS-FNAs and 75 PTC-EFBs (performed in 137 patients) were compared. Patients in the PTC-EFB group had higher preoperative bilirubin (243 versus 169 $\mu\text{mol/l}$, $p = 0.005$) and a higher incidence of malignancy (87% versus 67%, $p = 0.008$). Both techniques showed specificity and positive predictive value of 100%, and similar sensitivity (69% versus 75%, $p = 0.45$), negative predictive value (58% versus 38%, $p = 0.15$) and accuracy (78% versus 79%, $p = 1.00$). After IPTW, the diagnostic performance of the two techniques remained similar.

Conclusion: Compared to EUS-FNA, PTC-EFB provides similar sensitivity, negative predictive value and accuracy. It should therefore be considered as the preferred tissue-sampling procedure, if biliary drainage is indicated.

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Introduction

Proximal biliary strictures (PBS) represent a challenging diagnostic and therapeutic dilemma. In most cases, such strictures are related to hilar cholangiocarcinoma, but in 10%–25% of cases, they could be related to benign lesions or other malignancies, which may mimic the clinical and radiological pattern of hilar cholangiocarcinoma.^{1–5} While the management of resectable

hilar cholangiocarcinoma relies on bile duct excision combined with major liver resection, other malignant hilar lesions such as metastatic lymph nodes or malignant lymphomas and benign hilar strictures should not be treated surgically.^{6–9} Therefore, despite some controversies regarding their utility, invasive tissue-sampling explorations are generally advocated prior to the therapeutic decision in order to choose the adequate treatment.^{10–13}

Several tissue-sampling techniques have been reported for the assessment of PBS,^{13–17} most of which have shown modest sensitivities ranging from 25% to 86% as a result of the fibrotic nature of hilar cholangiocarcinomas.^{10,12–14,18} Among the various techniques, endoscopic ultrasound fine needle aspiration

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(EUS-FNA) has become the standard tissue-sampling technique since it limits the risk of peritoneal seeding as compared to other techniques of transperitoneal biopsy, and its superiority compared to endoscopic retrograde cholangiopancreatography (ERCP)-guided biopsy has been demonstrated.^{13,18} However, EUS-FNA has been mainly assessed for distal common bile duct lesions, and concerns have been raised regarding its performance for lesions located at the hilum level.^{14,16}

Percutaneous transhepatic cholangiographic endobiliary forceps biopsy (PTC-EFB) may represent a valuable alternative since it could be performed simultaneously at the time of biliary drainage – a mandatory step for most patients with PBS – and in case of positivity, the need for additional invasive procedures such as EUS-FNA can be avoided.¹⁹ Albeit described more than 3 decades ago, PTC-EFB failed to gain popularity for assessing PBS owing to its poor sensitivity for hilar lesions.^{20,21} However, recent studies have reported some technical refinements for PTC-EFB procedures, which resulted in increased sensitivities of 75%–92% when performed for hilar lesions.^{22,23}

Overall, only a few studies on biliary tissue-sampling methods have specifically focused on PBS, and to date, there has been no study comparing the performance of EUS-FNA and PTC-EFB. In this context, the aim of the present study was to compare the performance of EUS-FNA versus PTC-EFB in patients with PBS.

Patients and method

The reporting of this study is in accordance with the updated 2015 STARD statements on diagnostic accuracy studies standards.²⁴ The dedicated STARD checklist was provided to the editorial office of the journal at the time of manuscript submission.

Study population

The study population consisted of consecutive patients referred to liver unit regional multidisciplinary team meeting of the Queen Elizabeth Hospital (Birmingham, United Kingdom) for a PBS between January 2010 and December 2015. Biliary strictures at the level of the hepatic hilum or of the proximal third of main bile duct were defined as PBS. The following patients were excluded from analysis: patients who no preoperative histological study, patients who had a histological study other than PTC-EFB or EUS-FNA, patients with biliary stricture of the intermediate or distal bile duct after radiological reassessment, patients with evidence of benign disease with no hilar mass, patients presenting with recurrence of a formerly treated malignant disease, and patients who had a tissue-sampling performed on an extra-hilar location of the disease such as regional lymph node or intrahepatic metastasis.

Study design

A comparative analysis was conducted between EUS-FNA and PTC-EFB. Each procedure was considered separately and thus,

patients who had both techniques or who had repeated EUS-FNA procedures were considered as multiple cases. This retrospective study was part of an internal audit under the supervision of the institution governance (registration number CARMS-12133), and it was approved by the editorial review board. Written consent for research was obtained from all patients included and the study conformed to the precept of the 1975 Helsinki declaration.

Tissue-sampling procedures

All decisions for tissue-sampling procedures were undertaken during multidisciplinary team meetings in the presence of oncologists, experienced interventional radiologists, endoscopists and hepatobiliary surgeons. The choice of one particular procedure was decided on a case-by-case setting, after review of the relevant cross sectional imaging. Patients who required biliary decompression for significant jaundice, were referred preferentially for PTC-EFB. The latter procedure could also be proposed to patients with altered upper gastrointestinal anatomy. All others were referred for EUS-FNA, including those that may have already had a biliary stent placed at ERCP. Written consent was obtained for all patients.

• Endoscopic ultrasound guided – fine needle aspiration

All procedures were performed under conscious sedation using a curved linear array echoendoscope (Olympus GF-UCT240-AL5; Olympus Corp., Tokyo, Japan). After positioning of the transducer and visualization of the hilar mass, a needle catheter system (EchoTip, 22-gauge needle or Procore 22 gauge; Wilson-Cook Medical, Inc., Winston-Salem, NC, USA) was inserted through the echoendoscope working channel, and the fine needle was advanced under ultrasound guidance into the target lesion. A negative pressure was applied to the needle using a 40 ml syringe and the needle was then carefully moved back and forth within the lesion. The aspirate was then expressed onto glass slides and both air-dried and alcohol-fixed smears were prepared by the endoscopist. A further aspirate was usually expressed into 15 ml of CytoRich Red fixative. One to four needle passes were generally performed to achieve an adequate sample.

• Percutaneous transhepatic cholangiographic – endobiliary forceps biopsy

All procedures were performed under combination of intravenous sedation and local anesthesia and according to a previously reported technique.²³ In brief, access to the biliary system was preferentially obtained from the right biliary duct; however, depending on local anatomy, access from the left side could also be considered. Percutaneous transhepatic cholangiography was performed in a standard fashion using a 21-gauge access system (AccuStick, Boston Scientific, Marlborough, MA)

followed by a change to a 0.97 mm diameter system under ultrasound and fluoroscopic guidance. Access to the biliary tree was secured using either a standard (11 cm) 7-Fr Brite-tip sheath or a long (23 cm) 7-Fr sheath (Cordis Europe, Waterloo, Belgium). After identifying the level of obstruction on the cholangiogram, the biliary stricture was crossed and a 0.97 mm diameter wire was placed within the duodenum to maintain access, and the sheath was further advanced over the wire up to the proximal limit of the stricture. A flexible cup biopsy forceps (Cook 5.2-Fr 60-cm myocardial biopsy forceps with a standard 2.25 mm³ cup [Cook Medical, Bloomington, IN]) was passed through the sheath alongside the guide wire. The forceps was opened upon exiting the sheath and advanced within the stricture. The cup of the forceps was closed and a sample was obtained and placed in a histology pot. Further samples could be taken in a similar fashion if required. The sheath remained in situ throughout the procedure to allow safe exchange of the biopsy forceps between samples. The procedure was generally completed with placement of an internal/external biliary drain or a metallic stent.

Test performance assessment

Tissue-sampling tests showing evidence of adenocarcinoma, lymphoma or any other malignant lesions were considered as positive tests. All other results, including negative, inconclusive or atypical cells were considered as negative tests. For post-operative patients, pathology of surgical specimen was considered as the reference standard. For non-operated patients, the reference standard was based on the clinical and imaging follow-up of patients. Patients with negative results who were found to have an evidence of malignant disease during follow-up (such as a growing mass, or liver and/or extrahepatic metastasis) were considered as false negatives.

Statistical analysis

Continuous variables were expressed as median values and interquartile ranges, whereas categorical variables were expressed as counts and percentages. To overcome covariate imbalance between the 2 groups, an inverse probability of treatment weighting (IPTW) was conducted using a propensity score. The propensity score was calculated using a non-parsimonious

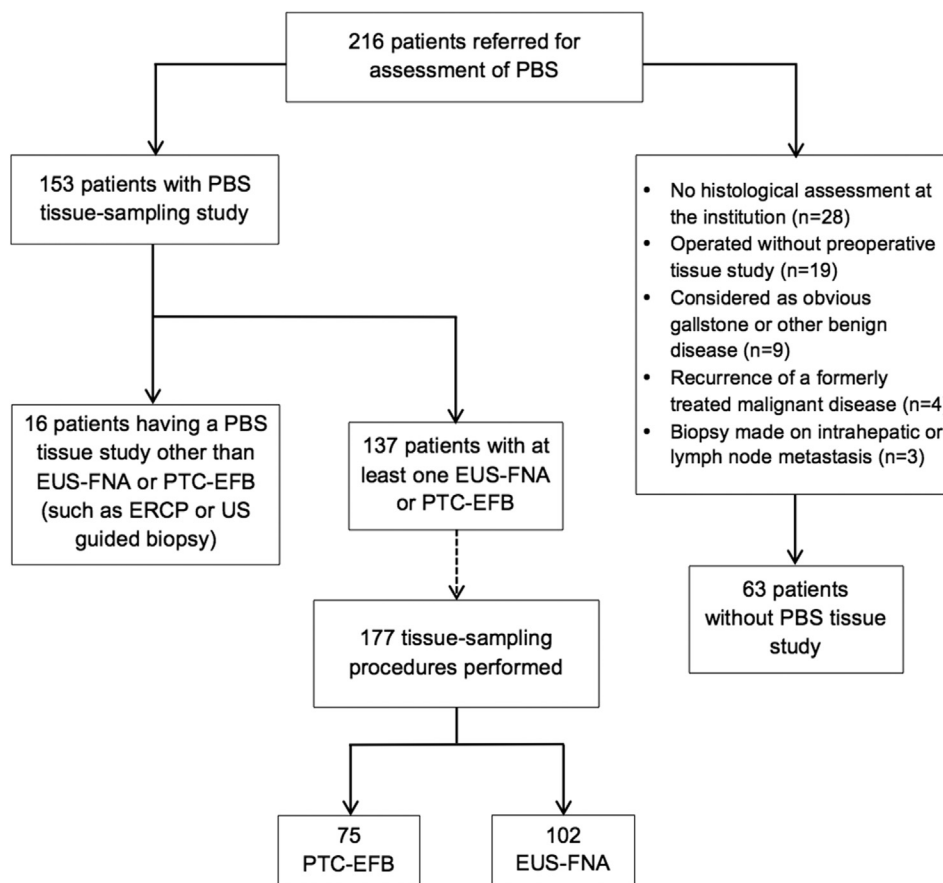


Figure 1 Study flowchart depicting the number of patients included and the number of tissue-sampling procedures performed. PBS, proximal biliary stricture; EUS-FNA, endoscopic ultrasound fine needle aspiration; PTC-EFB, percutaneous transhepatic cholangiographic endobiliary forceps biopsy; ERCP, endoscopic retrograde cholangiopancreatography; US, ultrasound

binary logistic regression model including 7 variables deemed to possibly influence the choice for one particular histology technique. Those variables comprised: age, sex, existence of clinical jaundice, Bismuth classification (dichotomized in below and above/equal to type III), total level of bilirubin, final diagnosis of malignancy, and surgical intervention. For unadjusted data, comparison between categorical variables was performed using Pearson's Chi-square test or Fisher's exact test, as appropriate, whereas continuous variables were compared using the Mann-Whitney test. Sensitivity, specificity, negative predictive value, positive predictive value and accuracy (calculated as the sum of true positives and true negatives divided by the sum of all tests) were expressed as percentages and 95% confidence intervals (calculated using binomial distribution) and were compared using Fisher's exact test.

After IPTW adjustment, baseline variable balance was assessed by the absolute value of the standardized difference, and variables with a standardized difference below 0.10 were considered well-balanced.²⁵ Sensitivity, specificity, negative predictive value, positive predictive value and accuracy were expressed as percentages and 95% confidence intervals using a robust variance estimator and were compared using the adjusted F, a variant of the Rao-Scott adjusted Pearson's Chi-square statistic.²⁶ Additional details for statistical analysis are provided in a [Supplementary file](#). All statistical tests were two-tailed and significance was considered for $p < 0.05$. All calculations were performed with SPSS software version 20.0 (IBM corp., Armonk, NY, United States).

Results

Over the study period, 216 patients with PBS had their case discussed at the institution's multidisciplinary team meeting. Of these, 69 did not fulfill the inclusion criteria and were excluded, and a total of 137 patients who had at least one procedure of EUS-FNA or PTC-EFB on the suspected hilar lesion were included for analysis (Fig. 1). Of these, 62 patients had an EUS-FNA, 56 had a PTC-EFB and 19 had both techniques. Moreover, 18 of the 62 patients who had an EUS-FNA had a repeated procedure (of which 15 patients had 2 procedures, and 3 patients had 3 procedures). Thus, a total of 102 EUS-FNA were compared to 75 PTC-EFB.

Baseline patient characteristics

Baseline clinical features of patients are reproduced in Table 1, showing a significantly higher level of total bilirubin (before any drainage) and a higher rate of malignant lesion in the PTC-EFB group, while there was a trend toward a higher number of male patients in the EUS-FNA group. The assessment of potential confounders in the original sample showed significant

Table 1 Comparison of clinical features between EUS-FNA and PTC-EFB

	EUS-FNA N = 102	PTC-EFB N = 75	P
Age (yr)	65 (54–71)	67 (59–73)	0.17
Gender			0.07
Male	72 (70.6)	43 (57.3)	
Female	30 (30.6)	32 (42.7)	
Presenting symptoms			0.28
Painless jaundice	61 (59.8)	50 (66.7)	
Jaundice and abdominal pain	15 (14.7)	15 (20.0)	
Abdominal pain without jaundice	7 (6.9)	3 (4.0)	
Other symptoms	9 (8.8)	5 (6.7)	
Non-symptomatic	10 (9.8)	2 (2.7)	
Previous knowledge of underlying hepatic or biliary disease			0.12
None	88 (86.3)	70 (93.3)	
Primary sclerosing cholangitis	13 (12.7)	4 (5.3)	
Cirrhosis	0 (0.0)	1 (1.3)	
Steato-hepatitis	1 (1.0)	0 (0.0)	
Total bilirubin level ($\mu\text{mol/l}$)	90 (39–223)	193 (79–310)	0.005
CA 19.9 (U/ml)	169 (41–851)	243 (60–963)	0.61
Bismuth type			0.24
I or II	15 (14.7)	6 (8.0)	
IIIa	19 (18.6)	17 (22.7)	
IIIb	15 (14.7)	5 (6.7)	
IV	43 (42.2)	38 (50.7)	
Undetermined	10 (9.8)	9 (12.0)	
Metastatic disease on preoperative assessment			0.26
None	96 (94.1)	66 (88)	
Liver metastases	3 (2.9)	3 (4.0)	
Extrahepatic metastases	3 (2.9)	6 (8.0)	
Surgical procedure			0.35
Not operated	79 (77.5)	60 (80.0)	
Resected	16 (15.7)	7 (9.3)	
Operated but not resected	7 (6.9)	8 (10.7)	
Final diagnosis			0.008
Malignant	71 (69.6)	65 (86.7)	
Benign	31 (30.4)	10 (13.3)	

Categorical variables are expressed in counts (percentages); continuous variables are expressed in median values (interquartile range). EUS-FNA, endoscopic ultrasound fine needle aspiration; PTC-EFB, percutaneous transhepatic cholangiographic endobiliary forceps biopsy.

imbalances between the two groups for age, sex, lesions above or equal to Bismuth type III, total level of bilirubin, and rate of malignancy (Table 2). After IPTW, all those covariates appeared to be well-balanced (all standardized differences were below 0.10).

Diagnostic performance of EUS-FNA and PTC-EFB

In the EUS-FNA group, 49 procedures had a positive result and 53 had a negative result. All positive results were found to be true positives according to the surgical specimen ($n = 8$) or patient follow-up ($n = 41$). Among the negative test results, 31 were confirmed to be true negatives (23 according to their follow-up, 8 based on surgical specimen), whereas 22 were found to be false negatives (15 according to their follow-up, 7 based on surgical specimen).

In the PTC-EFB group, 49 procedures had a positive result and 26 had a negative result. All positive test results were found to be true positives according to the surgical specimen ($n = 12$) or patient follow-up ($n = 37$). Among the negative test results, 10 were confirmed to be true negatives (9 according to their follow-up, 1 based on surgical specimen), whereas 16 were found to be false negatives (14 according to their follow-up, 2 based on surgical specimen).

The diagnostic performances of the two tissue-sampling methods are reproduced in Table 3. Specificity and positive

predictive values were of 100% for both techniques. Comparison between the two techniques before and after IPTW-adjustment showed no significant difference in terms of sensitivity, negative predictive value and accuracy.

Overall contribution of tissue-sampling tests on patient management

Table 4 reproduces the final management of the 137 patients included for analysis. Among the 31 patients who were surgically explored, a surgical excision was performed in 18 patients, while intraoperative findings precluded resection in 13 patients due to locally advanced disease ($n = 9$), evidence of stone disease ($n = 2$), liver cirrhosis undiagnosed on preoperative workup ($n = 1$), or peritoneal carcinomatosis ($n = 1$). Among the 18 patients who had a surgical excision, 5 were found to have a benign disease, including 3 who had a liver transplant for primary sclerosing cholangitis and 2 who had a major liver resection.

In 92 patients, the preoperative workup precluded surgical exploration regardless of the tissue-sampling test results because of the evidence of locally advanced disease ($n = 81$), extrahepatic metastases ($n = 4$), liver metastases ($n = 2$), or poor general condition ($n = 5$). In 14 patients, surgery was avoided as a direct consequence of the tissue-sampling test, which showed a benign disease (4 patients with primary

Table 2 Balance assessment of patient clinical features before and after IPTW

	Unadjusted			After IPTW		
	EUS-FNA	PTC-EFB	Standardized difference	EUS-FNA	PTC-EFB	Standardized difference
Age (yr, median)	65.0	67.0	0.24	65.0	66.0	0.03
Male sex (%)	70.6	57.3	0.28	67.3	64.1	0.07
Clinical jaundice (%)	78.4	89.3	0.30	83.3	82.6	0.02
Total bilirubin ($\mu\text{mol/l}$, median)	60.0	192.0	0.52	80.0	103.0	0.08
Bismuth \geq III (%)	75.5	80.0	0.11	77.8	78.8	0.02
Operated (%)	22.5	20.0	0.06	19.9	19.1	0.02
Malignant (%)	69.6	86.7	0.42	77.1	77.2	0.003

EUS-FNA, endoscopic ultrasound fine needle aspiration; PTC-EFB, percutaneous transhepatic cholangiographic endobiliary forceps biopsy; IPTW, inverse probability of treatment weighting.

Table 3 Comparison of the diagnostic performance of EUS-FNA and PTC-EFB before and after IPTW

	EUS-FNA	PTC-EFB	P	EUS-FNA	PTC-EFB	P ^a
Sensitivity, % (95% CI)	69 (57–79)	75 (63–85)	0.45	67 (52–79)	75 (62–85)	0.33
Specificity, % (95% CI)	100 (89–100)	100 (69–100)	1.00	–	–	–
Positive predictive value, % (95% CI)	100 (93–100)	100 (93–100)	1.00	–	–	–
Negative predictive value, % (95% CI)	58 (44–72)	38 (20–59)	0.15	47 (32–63)	55 (34–74)	0.59
Accuracy, % (95% CI)	78 (69–86)	79 (68–87)	1.00	74 (62–84)	81 (70–89)	0.36

^a Adjusted Chi-square statistic using the adjusted F. EUS-FNA, endoscopic ultrasound fine needle aspiration; PTC-EFB, percutaneous transhepatic cholangiographic endobiliary forceps biopsy.

Table 4 Patient management

Type of procedure	Number of patients (%)
No surgery	106 (77)
Surgical resection	
ALPPS	1
Central hepatectomy	1
Right extended hepatectomy	9
Left extended hepatectomy	3
Liver transplant	4
Surgery without resection	
Palliative double bypass	1
Palliative gastrojejunostomy	1
Palliative hepaticojejunostomy	2
Exploratory laparotomy (open-close)	5
Staging laparoscopy	1
Common bile duct exploration	3

EUS-FNA, endoscopic ultrasound fine needle aspiration; PTC-EFB, percutaneous transhepatic cholangiographic endobiliary forceps biopsy; ALPPS, associated liver partition and portal vein ligation for staged-hepatectomy.

sclerosing cholangitis, 3 with IgG4-related disease, and 2 with unspecified benign inflammatory disease) or a malignant disease other than hilar cholangiocarcinoma (4 patients with lymphoma, 1 with hepatocellular carcinoma).

Discussion

The management of PBS represents a diagnostic and therapeutic dilemma owing to the lack of strong preoperative methods for the differentiation between malignant and benign lesions.¹² Consistently with former reports,^{2,3,5} this single-centre study reported a sensitivity for tissue-sampling tests ranging from 69% to 75% and an accuracy of 78%–79%, which may be considered as quite poor. However, despite those relatively disappointing diagnostic performances, only 2 out of 137 patients underwent a major hepatectomy for a benign disease whereas an unnecessary surgical exploration was avoided in 14 patients as a direct consequence of the preoperative biopsy. These findings support the practice of systematic tissue-sampling tests for the assessment of PBS, even in operable patients.

Various tissue-sampling methods for PBS have been reported, most of which could be divided into two categories: endobiliary and transperitoneal approaches. Endobiliary approaches can be either performed through a percutaneous transhepatic or a transpapillary pathway, and they used to represent the standard procedure until the early 2000's.¹⁰ PTC-EFB was first described in 1980, but only a few centres have reported this technique, with sensitivities ranging from 27% to 100%, and most of these did not specifically focus on PBS (Table 5).^{19–23,27} ERCP-guided biopsy leads to a very satisfactory sensitivity for distal and intermediate common bile duct lesions, but its performance tends to dramatically decrease as the lesions become distant from the

Table 5 Main series reporting the performance of endoscopic ultrasound fine needle aspiration or percutaneous transhepatic cholangiographic tissue-sampling for the assessment of proximal biliary strictures

Authors, year of publication	No. of procedures for hilar lesions	No. of malignancies (%)	Se	Sp	PPV	NPV	Acc.
<i>Series on PTC-biopsy</i>							
Jung, 2002 ²¹	53	51 (96)	86	100	100	22	87
Tapping, 2012 ²⁷	24	NA	78 ^a	100	100	30 ^a	63
Ierardi, 2014 ²²	24	16 (67)	75	100	100	NA	83
Patel, 2015 ²³	26	24 (96)	92	100	100	33	92
<i>Series on EUS-FNA</i>							
Rosch, 2004 ¹⁸	11	4 (36)	25	100	100	NA	NA
Fritscher-Ravens, 2004 ³⁰	44	31 (70)	86 ^b	100	100	62 ^b	89 ^b
Eloubeidi, 2004 ¹⁴	15	8 (53)	86 ^a	100	100	57 ^a	88 ^a
Dewitt, 2006 ¹⁵	24	22 (92)	77	100	100	29	79
Mohamadnejad, 2011 ¹⁶	27	27 (100)	59	NA	NA	NA	NA
Weilert, 2014 ¹³	7	7 (100)	86	100	100	NA	80 ^a
<i>Present series</i>							
EUS-FNA	102	71 (70)	69	100	100	58	78
PTC-EFB	75	65 (87)	75	100	100	38	79

^a Values expressed for both proximal and distal biliary strictures, since values for hilar lesions were not reported.

^b Values differ from the ones reported by authors because result for inadequate material were excluded, while we consider such results as negative. Se, sensitivity; Sp, specificity; PPV, predictive positive value, NPV, negative predictive value; Acc., accuracy; NA, not available; EUS-FNA, endoscopic ultrasound fine needle aspiration; PTC-EFB, percutaneous transhepatic cholangiographic endobiliary forceps biopsy.

papilla of Vater, with reported sensitivity of approximately 40% for hilar lesions.^{10,12} On the other hand, transperitoneal approaches may increase the sensitivity of tests, but they expose to the risk of intraperitoneal seeding and therefore must be avoided when a curative treatment is planned.²⁸ As an alternative, the use of fine needle aspiration instead of conventional biopsy may limit the risk of tumor seeding, and it has been demonstrated that EUS-FNA could provide satisfactory performance with no impact on survival due to tumor seeding.²⁹ Therefore, EUS-FNA has become the method of choice for the assessment of PBS over the last decade.^{13,18} However, former series supporting the evidence of the efficacy of EUS-FNA are limited and based on small cohorts (Table 5). Moreover, most of these studies were not focusing on PBS only, but on all types of biliary lesions, including distal ones, thus limiting the conclusion that can be drawn from these studies regarding the management of PBS. To the best of our knowledge, the present study represents the largest series of EUS-FNA for the assessment of PBS; all tissue-sampling tests were performed by 3 experienced endosonographers of which 2 were highly experienced in a high-volume tertiary centre, but despite this, a sensitivity of only 69% was achieved with EUS-FNA.

One argument against the use of tissue-sampling tests during the assessment of PBS is that it may add additional invasive procedures to the management process of patients with PBS. To address this issue, the use of a percutaneous transhepatic route for tissue-sampling may represent a valuable option. In fact, up to 90% of patients with PBS will need a percutaneous transhepatic biliary drainage, regardless of whether they will be operated or not.^{6,9} Moreover, recent technical refinement of the performance of PTC-EFB have resulted in encouraging increase of sensitivity, but to our knowledge, there has been no study comparing the performance of PTC-EFB with EUS-FNA, the reference method. Herein, after adjusting for potential confounders, we demonstrated that PTC-EFB showed identical specificity, PPV, and accuracy, and at least comparable sensitivity when compared to EUS-FNA.

This study had some limitations. Indeed, it was a retrospective study and the comparative analysis of EUS-FNA versus PTC-EFB could subsequently be biased. The two groups were not strictly comparable, and caution should be taken while interpreting data. However, we used a robust statistical methodology in order to reduce the effects of potential confounders, and after IPTW, the comparison of the two techniques did not show any difference in terms of performance characteristics, thus supporting the fact that PTC-EFB was equivalent to EUS-FNA for the histological diagnosis of PBS.

In conclusion, the current modalities of tissue-sampling for PBS still lack sensitivity and accuracy. However, an unnecessary surgical exploration may be avoided thanks to the preoperative biopsy in a substantial number of patients, which underscores the interest of non-operative tissue-sampling methods. Moreover, when compared to EUS-FNA, PTC-EFB provides similar sensitivity, negative predictive value and accuracy, without

requiring additional invasive endoscopic procedures such as EUS-FNA or ERCP-guided biopsy, and with no risk of tumor seeding. Therefore, PTC-EFB could be considered as the best possible first-line tissue-sampling method for the diagnostic management of patients with PBS, especially when a preoperative drainage is required. Further prospective randomized studies are warranted to confirm these findings.

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Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.hpb.2017.02.001>.