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TECHNICAL NOTE

Improved Accuracy of Percutaneous Biopsy Using "Cross and Push" Technique for Patients Suspected with Malignant Biliary Strictures

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Abstract
Purpose Various methods have been used to sample biliary strictures, including percutaneous fine-needle aspiration biopsy, intraluminal biliary washings, and cytological analysis of drained bile. However, none of these methods has proven to be particularly sensitive in the diagnosis of biliary tract malignancy. We report improved diagnostic accuracy using a modified technique for percutaneous transluminal biopsy in patients with this disease.
Materials and Methods Fifty-two patients with obstructive jaundice due to a biliary stricture underwent transluminal forceps biopsy with a modified "cross and push" technique with the use of a flexible biopsy forceps kit commonly used for cardiac biopsies. The modification entailed crossing the stricture with a 0.038-in. wire leading all the way down into the duodenum. A standard or long sheath was subsequently advanced up to the stricture over the wire. A Cook 5.2-Fr biopsy forceps was introduced alongside the wire and the cup was opened upon exiting the sheath. With the biopsy forceps open, within the stricture the sheath was used to push and advance the biopsy cup into the stricture before the cup was closed and the sample obtained. The data were analysed retrospectively.
Results We report the outcomes of this modified technique used on 52 consecutive patients with obstructive jaundice secondary to a biliary stricture. The sensitivity and accuracy were 93.3 and 94.2 %, respectively. There was one procedure-related late complication.
Conclusion We propose that the modified "cross and push" technique is a feasible, safe, and more accurate option over the standard technique for sampling strictures of the biliary tree.

Keywords Non-vascular interventions · Biopsy · Bile duct/gallbladder/biliary · Cancer · Diagnostic

Introduction

Ultrasound (US)-guided fine-needle aspiration (FNA) biopsies [1, 2] and automated biopsy gun samples [3] have yielded improved sensitivity and specificity for several sites in the body except the biliary tree. Sampling the biliary tree in suspected malignant obstruction has historically proven problematic for two main reasons. First, the tumours are often small and visualisation of them as a biopsy target by US is technically difficult or impossible [4]. Second, these tumours are often accompanied by a significant desmoplastic response, making any sort of sampling unreliable [5–7].

Endoluminal techniques used for obtaining biliary samples can be broadly divided into those that require a percutaneous or an endoscopic access tract. Percutaneous-based methods include percutaneous transhepatic cholangiogram (PTC) brush cytology and cholangioscopy [8], whereas endoscopy-based methods include endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS).

Whilst EUS-FNA in recent years has become an established method for sampling pancreatic lesions with a sensitivity approaching 100 %, it is less sensitive (79 %) for

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hilar strictures [9, 10]. When accessing the biliary tree using ERCP- and PTC-based methods, either washings or brushings can be taken and sent for cytology. Brush cytology has been popular and probably the most used method despite its low specimen yield and variable accuracy, with studies showing sensitivity ranging from 30 to 75 % [11–13].

Since the 1980 s biopsy forceps have been used via the percutaneous tract to sample the biliary tree and obtain histology in suspected malignant obstruction as reported by a few centres [14]. Two smaller studies with fewer than 25 patients showed a wide range in sensitivity: as low as 30 % [15] and up to 100 % [16]. Jung et al. [17] reported a large study, comprising 130 patients, where they employed a specific type of forceps (Cordis Corporation, Miami, FL) to obtain biopsy samples and the sensitivity was 78.4 %. Tapping et al. [18] compared cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage in 119 patients with suspected malignant inoperable obstructive jaundice. Histological diagnosis with forceps biopsy was more successful than with cytology: Sensitivity was 78 versus 61 % and the negative predictive value was 30 versus 19 %. Cytology results were never positive when the forceps biopsy was negative.

We evaluated our results of a modified biopsy technique used sample biliary strictures in patients with suspected malignant biliary obstruction.

Materials and Methods

We have retrospectively reviewed the data from 52 consecutive patients who had a biliary stricture biopsy performed at a major hepatobiliary centre by one hepatobiliary interventional radiologist who used the "cross and push" technique between October 2007 and March 2012. The decision to perform PTC with or without drainage was made for all patients who had obstructive jaundice suspected as secondary to a malignant obstruction, following approval at a multidisciplinary team review meeting at our institution. This study reports the sensitivity, specificity, and accuracy of this method of biliary sampling as well as any complications encountered during or after the procedure as a result of the biopsy. Informed consent was obtained from all individual participants included in the study.

Technique

All procedures were performed under intravenous sedoanalgesia and local anaesthesia at the puncture site. Initial percutaneous access to the biliary system was achieved with a 21-gauge access system (AccuStick™, Boston Scientific, Marlborough, MA) followed by a change to a 0.038-in. system in conventional fashion under US and fluoroscopic guidance. A cholangiogram to identify the level of obstruction was performed and access to the biliary tree was secured using a standard (11 cm long) 7-Fr Brite-tip sheath (Cordis) or a long (23 cm) 7-Fr sheath (Cordis). Thereafter, attempts were made to cross the biliary stricture using standard interventional radiology techniques with a variety of catheters and wires. It is imperative to cross the stricture with a 0.038-in. wire leading all the way down into the duodenum. The sheath is then 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 size (2.25 cc) cup (Cook Medical, Bloomington, IN)] was then passed through the sheath alongside the guide wire. The cup was opened upon exiting the sheath, with the tip of the sheath remaining resident just proximal to the stricture. With the biopsy forceps open in this manner, within the stricture we used the sheath to push and advance the open biopsy forceps into the stricture before the cup was closed and thus the sample was obtained (Fig. 1A). Up to five samples were taken and sent for histological analysis. The sheath always remained in situ to allow safe exchange of the biopsy forceps between samples. The procedure was completed with a control cholangiogram following placement of a biliary drain or a metallic stent in a conventional manner.

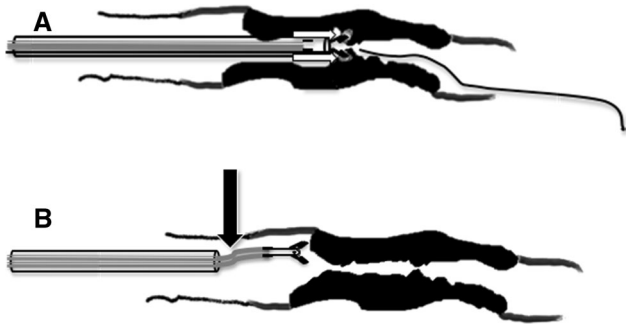

Fig. 1 **A** Schematic of biopsy performed in patients where a modified "cross and push" technique was employed. The sheath is placed within the substance of the stricture and the leading edge is used to push the open cup of the biopsy forceps (*open arrows*), enabling more stricture sample to be obtained. **B** Schematic of biopsy where a 5.2 Fr biopsy needle is passed within the sheath, but the cup is proximal to the stricture and sheath, well short of the cup, leading to retroflexion (*solid arrow*)

The modified "cross and push" technique was used in 52 patients. Data were collected retrospectively and included age, sex, prebiopsy liver functions, biopsy characteristics, and location and histology of the lesion. The results of the final diagnosis and the complications are also presented. Probability of survival was determined using the Kaplan–Meier method. The correlation of

Table 1 Patient characteristics and overall data

No. of patients	52
Age [mean (95 % CI)] (years)	68.8 (±3)
Age range (years)	38.2–87.8
Male:female ratio	1.9:1
Prebiopsy liver functions [mean (95 % CI)]	
Bilirubin (μmol/L)	284 (±50)
GGT (IU/L)	330 (±91)
AST (IU/L)	119 (±25)
ALT (IU/L)	119 (±28)
ALP (IU/L)	1562 (±326)
Biopsy characteristics	
Median number of cores	3
Median length of cores (mm)	2
Crush artefacts	4/52 (8 %)

Histology and location of stricture		Intrahepatic		Extrahepatic			
Benign histology on PTEB (true negatives)	$n = 7$	Hilar	Main RHD	Distal CBD	Mid CBD	Proximal CBD	BEA
Benign (all inflammatory)	7	1		3	1	1	1
Benign histology on PTEB (false negatives)	$n = 3$						
Solitary metastasis from previously resected gastric adenocarcinoma*	1			1			
Solitary metastasis from previously resected gall bladder adenocarcinoma*	1	1					
de novo colorectal metastasis (CRM)*	1	1					

Malignant histology on PTEB	$n = 42$	Hilar	Main RHD	Distal CBD	Mid CBD	Proximal CBD	BEA
Cholangiocarcinoma	28	17	1	5	1	4	
Pancreatic adenocarcinoma	11	2					
Hepatocellular carcinoma (HCC)	1	1					
Neuroendocrine tumour (NET)	2	2					
Test reliability to pick up malignant biliary strictures							
Sensitivity (%)	93.3						
Specificity (%)	100						
Positive predictive value (%)	100						
Negative predictive value (%)	70						
Accuracy (%)	94.2						
Procedure-related complication	1 (hepatic artery pseudoaneurysm						
Median follow-up (months)	8.5						
Median overall survival (months) since biopsy with benign histology	31.0						
Median overall survival (months) since biopsy with malignant histology	6.8						

* False negatives

RHD right hepatic duct, *CBD* common bile duct, *BEA* biliary enteric anastomosis

biopsy results to the final diagnosis was established through either subsequent follow-up (both radiological and clinical) or surgical histology. A 2 × 2 table statistics was performed to derive sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and accuracy.

Results

Fifty-two patients who presented with obstructive jaundice presumed secondary to a suspected malignant stricture in the biliary tree based on clinical presentation and findings at PTC cholangiogram were included in the study. The results are presented in Table 1. All biopsies obtained samples reliable enough to make a histological diagnosis. None of the samples obtained were found to be suspicious, inadequate, necrotic, or containing fibrinous materials. There were 4 (8 %) crush artefacts, but the cytopathological assessment was possible as the largest dimension amongst these samples was 1–2 mm. Forty-two of the 52 (81 %) biopsies resulted in a correct diagnosis of malignancy. The specific histological diagnosis correlated with the clinical diagnosis in 49 cases (accuracy of 94.2 %). The remaining three cases were confirmed to have an underlying malignancy (false negatives), although the exact histological type on PTC biopsy was reported as benign (inflammatory changes). One of these three patients had stricture secondary to primary gallbladder carcinoma and the other two had primary gastric and colorectal cancer respectively, causing extrinsic compression of the biliary tree from secondary lymph nodes. There were seven true-negative diagnoses and no false-positive diagnoses. For the diagnosis of malignant biliary obstruction, transluminal forceps biopsy using the "cross and push" technique had a sensitivity of 93.3 % and a specificity of 100 %. Although the positive predictive value was 100 %, the negative predictive value was only 70 %. The median overall survival in patients with malignant biliary strictures following primary decompression and histology was 4.8 months.

We noticed one procedure-related complication: haemobilia 2 months after the procedure. Computed tomography (CT) showed a hepatic artery pseudoaneurysm located in the periphery of the liver at the access point for the PTC. This was anatomically distant from the biopsy site, which was at the distal CBD. It was treated successfully with embolisation.

Discussion

We present an accurate and safe way to sample the biliary tree in suspected malignant obstruction using a readily available kit.

We favour the 5.2-Fr flexible biopsy forceps and used it in all 52 patients as it permitted deployment alongside a guide wire within the sheath. We recommend that the biopsy forceps be advanced inside a long 7-Fr sheath with the tip placed in the stricture (Fig. 2A, B). This is possible alongside a 0.038-in. wire after the stricture has been crossed. It seems logical that the leading edge of the sheath

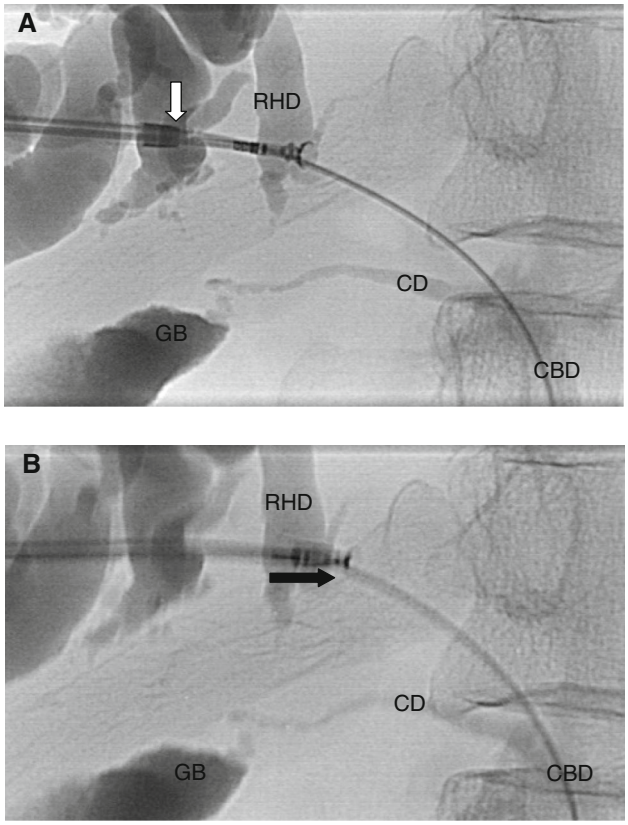

Fig. 2 Images obtained from a patient with jaundice. **A** Percutaneous transhepatic cholangiogram shows a stricture in the proximal common hepatic duct. The biopsy forceps lies open proximal to the stricture and is beyond the leading edge of the sheath (*open arrow*), alongside a guide wire that lies distal to CBD. **B** The sheath is advanced over the biopsy forceps alongside the guide wire into the stricture (*solid arrow*) with an open biopsy cup to secure a good amount of tissue within the stricture (cross and push technique). *RHD* right hepatic duct, *CD* cystic duct, *CBD* common bile duct, *GB* gallbladder

can help push the open cup of the biopsy forceps into the substance of the stricture (Fig. 1A) thereby resulting in better sampling. We believe retroflexion (Fig. 1B) of the biopsy cup results in a poor tissue yield and could be prevented by using the "cross and push" technique.

The procedure-related complication (hepatic pseudoaneurysm) that occurred in one of the patients was due to the PTC access and not the biopsy since it was anatomically far away from the pseudoaneurysm. Such complications are often reported in patients who have only a PTC; hence, we believe it is not due solely to the biopsy technique [20].

We recognise that differentiating true from false negatives is difficult. There were 10 patients with a negative biopsy for malignancy, of which 3 (5.7 %) were regarded as false negatives based on clinical and radiological corroboration during subsequent follow-up and histocytopathological evidence where available. The overall limitations of the modified technique lie in the low negative predictive value of

70 %. However, given the nature of the disease process and desmoplastic response associated with cholangiocarcinoma, a higher false-negative rate may be expected. Extrinsic compression of the biliary tree, which is usually extrahepatic, is generally managed by ERCP and stenting at our institution; hence, we had only two patients with this situation. In both cases the histological analysis of the percutaneous endoluminal biopsy (PTEB) was benign. We also recognise that such patients are more prone to a false-negative result so the biopsy results are unreliable in extrinsic lesions [21]. There were some crush artefacts but decent quality histology was achieved despite the small cup size.

We believe that our modified technique is more sensitive and has better accuracy than FNA biopsy [22], bile cytology [23], brush cytology [11–13], and previously described forceps biopsy techniques [8, 18] for sampling the biliary tree in obstructive jaundice. Patients often present with severe liver dysfunction and the referring institution usually drains the biliary tree. We believe a rapid diagnosis is imperative in patients suspected with malignant strictures as overall survival is poor.

The overall sensitivity of the technique reported here was comparable to that of the largest reported study that used intraluminal forceps biopsies to sample the biliary tree [17]. However, our modified technique yielded better sensitivity and accuracy of sampling suspected malignant biliary strictures. The reluctance to pursue histological confirmation in all cases is understandable. NCCN guidelines do recommend taking a biopsy in certain situations [19]. However, we are in favour of a biopsy whenever possible in patients with suspected malignant biliary obstruction based on clinical, imaging, and laboratory criteria for the following reasons. First, we have found a 13.5 % incidence of true negative in cases presumed to be malignant (Table 1). Second, 8 % of the cases had unexpected malignant histology such as NET, HCC, and CRM, which had an entirely different course of therapy. Finally, histological confirmation may be required to enrol patients in appropriate clinical trials. Hence, we recommend that this modified technique be used for all cases where PTC is undertaken for suspected bile duct malignancy.

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Conflict of Interest Kamarjit Mangat: recieved professional fees from Cook Medical, to present the study findings at the CIRSE 2012 and SIR 2013 meetings. Cook Medical has patented a Transluminal Biliary Biopsy Forceps Set (BBFS-100) with royalties paid to Kamarjit Mangat. Prashant Patel and Balaji Rangarajan have no conflicts of interest to disclose.

Statement of Human and Animal Rights and Informed Consent The reported study is a technical note and did not require ethics committee approval. The study was logged as an Institutional audit. Informed consent was obtained from all individual participants included in the study.

References

1. Al-Sindi K, Kamal N, Golbahar J (2009) Efficacy of fine-needle aspiration biopsy in diagnosis of breast cancer: a retrospective study of 303 cases in Bahrain. Diagn Cytopathol 37(9):636–640
2. Kim DW, Lee EJ, Kim SH, Kim TH, Lee SH, Kim DH, Rho MH (2009) Ultrasound-guided fine-needle aspiration biopsy of thyroid nodules: comparison in efficacy according to nodule size. Thyroid 19(1):27–31
3. Burbank F, Kaye K, Belville J, Ekuan J, Blumenfeld M (1994) Image-guided automated core biopsies of the breast, chest, abdomen, and pelvis. Radiology 191(1):165–171
4. Baron RL, Stanley RJ, Lee JK, Koehler RE, Melson GL, Balfe DM, Weyman PJ (1982) A prospective comparison of the evaluation of biliary obstruction using computed tomography and ultrasonography. Radiology 145(1):91–98
5. Singh P, Patel T (2006) Advances in the diagnosis, evaluation and management of cholangiocarcinoma. Curr Opin Gastroenterol 22(3):294–299
6. Van Beers BE (2008) Diagnosis of cholangiocarcinoma. HPB 10(2):87–93
7. Ierardi AM, Mangini M, Fontana F, Floridi C, De Marchi G, Petrillo M et al (2014) Usefulness and safety of biliary percutaneous transluminal forceps biopsy (PTFB): our experience. Minim Invasive Ther Allied Technol 23(2):96–101
8. Li TF, Ren KW, Han XW, Li WC, Ren JL, Jiao DC, Li Z, Ma J (2014) Percutaneous transhepatic cholangiobiopsy to determine the pathological cause of anastomotic stenosis after cholangiojejunostomy for malignant obstructive jaundice. Clin Radiol 69(1):13–17
9. Zaheer A, Anwar MM, Donohoe C, O'Keeffe S, Mushtaq H, Kelleher B et al (2013) The diagnostic accuracy of endoscopic ultrasound in suspected biliary obstruction and its impact on endoscopic retrograde cholangiopancreatography burden in real clinical practice: a consecutive analysis. Eur J Gastroenterol Hepatol 25(7):850–857
10. Weilert F, Bhat YM, Binmoeller KF, Kane S, Jaffee IM, Shaw RE et al (2014) EUS-FNA is superior to ERCP-based tissue sampling in suspected malignant biliary obstruction: results of a prospective, single-blind, comparative study. Gastrointest Endosc 80(1):97–104
11. Cropper LD Jr, Gold RE (1983) Simplified brush biopsy of the bile ducts. Radiology 148(1):307–308
12. Xing GS, Geng JC, Han XW, Dai JH, Wu CY (2005) Endobiliary brush cytology during percutaneous transhepatic cholangiodrainage in patients with obstructive jaundice. Hepatobiliary Pancreat Dis Int 4(1):98–103
13. Weber A, von Weyhem C, Fend F, Schneider J, Neu B, Meining A et al (2008) Endoscopic transpapillary brush cytology and forceps biopsy in patients with hilar cholangiocarcinoma. World J Gastroenterol 14(7):1097–1101
14. Elyaderani MK, Gabriele OF (1980) Brush and forceps biopsy of biliary ducts via percutaneous transhepatic catheterization. Radiology 135(3):777–778
15. Savader SJ, Prescott CA, Lund GB, Osterman FA (1996) Intraductal biliary biopsy: comparison of three techniques. J Vasc Interv Radiol 7(5):743–750
16. Terasaki K, Wittich GR, Lycke G, Walter R, Nowels K, Swanson D, Lucas D (1991) Percutaneous transluminal biopsy of biliary strictures with a bioptome. AJR Am J Roentgenol 156(1):77–78

17. Jung GS, Huh JD, Lee SU, Han BH, Chang HK, Cho YD (2002) Bile duct: analysis of percutaneous transluminal forceps biopsy in 130 patients suspected of having malignant biliary obstruction. Radiology 224(3):725–730
18. Tapping CR, Byass OR, Cast JE (2012) Cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage and analysis of factors predicting success. Cardiovasc Intervent Radiol 35(4):883–889
19. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Hepatobiliary Cancers version 2, 2014. Available at http://www.nccn.org/professionals/physician_gls/f_guidelines.asp
20. Lokich JJ, Kane RA, Harrison DA, McDermott WV (1987) Biliary tract obstruction secondary to cancer: management guidelines and selected literature review. J Clin Oncol 5(6):969–981
21. Cohan RH, Illescas FF, Braun SD, Newman GE, Dunnick NR (1986) Fine needle aspiration biopsy in malignant obstructive jaundice. Gastrointest Radiol 11(2):145–150
22. Hall-Craggs MA, Lees WR (1986) Fine-needle aspiration biopsy: pancreatic and biliary tumors. AJR Am J Roentgenol 147(2):399–403
23. Muro A, Mueller PR, Ferrucci JT Jr, Taft PD (1983) Bile cytology. A routine addition to percutaneous biliary drainage. Radiology 149(3):846–847