Using the modern Silverhawk™ atherectomy catheter to characterize biliary structures that appear malignant: review of initial experience

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Abstract

Background: Diagnosis of a biliary stricture often hinges on cytological interpretation. In the absence of accompanying stroma, these results can often be equivocal. In theory, advanced shave biopsy techniques would allow for the preservation of tissue architecture and a more accurate definition of biliary pathology.

Objectives: We sought to determine the initial diagnostic utility of the modern Silverhawk™ atherectomy (SA) catheter in the evaluation of biliary strictures that appear to be malignant.

Methods: A total of 141 patients with biliary pathology were identified during a retrospective review of medical records for the years 2006–2011. The SA catheter was employed 12 times in seven patients for whom a tissue diagnosis was otherwise lacking.

Results: Neoplasia was definitively excluded in seven specimens from four patients. These four individuals were followed for 1–5 years to exclude the development of cholangiocarcinoma (CC). Samples were positive for CC in three patients, one of whom became eligible for neoadjuvant therapy and orthotopic liver transplantation.

Conclusions: The SA catheter appears to be a useful adjunct in diagnosing patients with biliary pathology. The existence of this technique, predicated on tissue architecture, may impact therapy, allow more timely diagnosis, and exclude cases of equivocal cytology. Although the initial results of SA use are promising, more experience is required to effectively determine its clinical accuracy.

Keywords

biliary stricture, cholangiocarcinoma, diagnosis, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography

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Introduction

In the setting of a biliary stricture that appears to be malignant, a tissue diagnosis of cholangiocarcinoma (CC) informs all subsequent decision making. Although contemporary advances in endoscopic retrograde cholangiopancreatography (ERCP) technology and endoscopic accessories have made non-operative treatment a viable alternative in even the most complicated of biliary pathology, definitive evidence of neoplasia can transform an expectant management paradigm into one in which the possibility of resection or, more recently, orthotopic liver transplantation (OLT), becomes the primary focus.1 In both scenarios, outcomes are much improved by the early detection of disease.2–5 Early detection of CC, however, is a formidable challenge. Current diagnostic approaches offer suboptimal yield and must rely on a combination of serological testing, imaging modalities, cytological analyses and a high index of clinical suspicion.6 Pathological diagnosis, however, remains the reference standard. In this
context, endoscopic over-the-wire brush sampling of suspicious biliary lesions is frequently performed as the primary diagnostic procedure, allowing for the characterization of biliary epithelia as benign, atypical, or overtly malignant-appearing. However, as sensitivities range from 20% to 60%, these samples are not always confirmatory and are sometimes difficult to acquire.7–9

Because the maintenance of tissue architecture and preservation of stroma are fundamental components of pathological diagnosis, biopsy techniques incorporating greater amounts of biliary tissue have at least the potential to improve diagnostic yield when cytology is otherwise equivocal. This has been demonstrated most recently in the use of endoscopic forceps biopsy, especially when it is combined with biliary brushings, and in some cases has doubled diagnostic sensitivity.9

Interestingly, the Simpson Atherocath™ (Devices for Vascular Intervention, Inc., Redwood City, CA, USA), a device originally intended for use in the treatment of atherosclerotic occlusive disease by means of percutaneous atheroma removal, was appropriated by Kim et al. over two decades ago for biopsy of common bile duct lesions via a percutaneous transhepatic approach.10 This was followed by two demonstrations of the high diagnostic yield of the technique in the setting of biliary strictures.11,12 Since its approval in 1990 by the US Food and Drug Administration (FDA) for directional coronary plaque excision, numerous improvements in catheter design have followed,13 culminating in the present-day Silverhawk™ SXL plaque excision system (FoxHollow Technologies, Inc., Redwood City, CA, USA). This device was approved by the FDA in 2007, and is now the leading directional atherectomy catheter on the market.14 Lacking an apposition balloon, the Silverhawk™ device self-apposes using a hinge system, contains a carbide cutter with variable height, and can rotate at speeds of up to 8000 rpm. The device is utilized over a commonly available guidewire (0.014-inch) in a ‘monorail’ configuration. It is also smaller and contains a palm-sized drive unit that permits convenient single-operator use. Additionally, the hinged nose cone can act as a large depository for intraluminal contents, with collection occurring distally to the cutting mechanism. Using this, the operator can decide the extent of the application and the large chamber size can facilitate its application over longer distances.14 These improvements not only make the device more attractive in the coronary and peripheral vascular areas, but also offer theoretical advantages in hepatobiliary applications. Since 2006, we have used the Silverhawk™ atherectomy (SA) catheter in situations in which conventional diagnostic approaches to biliary lesions have proven equivocal. In this report, we catalogue the first clinical experience of use of the SA catheter for hepatobiliary indications.

Materials and methods

A total of 141 patients with suspicious biliary pathology were identified upon a retrospective review of multidisciplinary treatment conference records (diagnostic radiology, interventional radiology, hepatobiliary or transplant surgery, hepatology, pathology, medical oncology, radiation oncology) for the year 2006–2011. Of the total, 78 patients had documented CC. Of those for whom complete documentation was available, 31 were noted to have peripheral (non-hilar) CC; the remainder had either a hilar stricture with or without an associated mass (n = 29), or a malignant lesion of the extrahepatic bile ducts (n = 18). Of the patients with CC, 14% had a concomitant diagnosis of either primary sclerosing cholangitis (PSC) or inflammatory bowel disease. Patients in the non-CC group had either benign pathology (n = 23) or pancreatic cancer (n = 7). Data for the remainder showed metastatic neuroendocrine tumour (n = 1), papillary adenoma (n = 1), or were inconclusive (n = 1).

Procedural details

All patients undergoing the procedure were given antibiotics as prophylaxis against cholangitis and i.v. sedation with fentanyl citrate and midazolam hydrochloride prior to and during the procedure. Two to eight weeks prior to the biopsy procedure, an ultrasound or fluoroscopically guided percutaneous transhepatic cholangiogram (PTC) was performed. An 8–12-Fr internal/external biliary drainage catheter was advanced across the suspicious areas in the biliary tree and into the duodenum. Right- or left-sided access was selected according to clinical needs and imaging. Patients were typically admitted for overnight observation after initial percutaneous access. Prior to the biopsy procedure, all anticoagulants and antiplatelet medications were discontinued and bleeding risks were mitigated as well as possible.

To perform the procedure, the indwelling drainage catheter was removed over a 0.035-inch guidewire. A 9–10-Fr vascular sheath was then inserted through the biliary tree and into the duodenum. A pull-back cholangiogram was performed and the target lesion(s) identified. The wire was replaced with a 0.014-inch interventional-type stiff body guidewire. A large vessel Silverhawk™ LX or LM atherectomy catheter was advanced over the wire, through the sheath, and into a position distal to the target lesion. The sheath was then pulled back, exposing the cutting surface of the device to the mucosa. Contrast medium was injected as needed to delineate the target. The device was actuated by advancing it slowly over the wire and across the target. Biopsy was performed by pulling back while simultaneously rotating the device. In this manner, multiple circumferential biopsies were obtained (Fig. 1). Typically, between three and 12 passes were made depending upon the amount of tissue to be removed. Ease of removal and re-insertion was facilitated by the rapid-exchange monorail design of the device. Usually, the procedure was terminated when 0.2-cm tissue plugs totalling 5–8 cm in length had been removed (Fig. 1). Finally, a completion cholangiogram was performed through the sheath and a new 10–14-Fr internal/external biliary drain was inserted. Following the procedure, all patients were monitored every 1–4 h depending on the technical difficulty of the procedure, the patient’s clinical status, and whether haemobilia was present. Transhepatic catheters were left to drain externally and capped the next day. Criteria for discharge
post-procedure included haemodynamic stability, absence of cholangitis symptoms, and biliary drainage with no discernable signs of haemorrhage. Patients were instructed to flush the tube with 10 ml of sterile saline each day and received longterm follow-up with at least one of the clinical services referred to above.

Results

Patient overview

Table 1 presents an overview of the patient series. The SA catheter was employed 12 times in seven patients in whom malignancy was suspected, but a definitive tissue diagnosis was lacking. These individuals ranged in age from 49 years to 76 years (mean age: 62 years). Four patients were male; three were female. Three patients had known PSC. Prior to the use of the SA catheter, all patients underwent computed tomography (CT) of the abdomen and/or magnetic resonance imaging (MRI) with cholangiopancreatography as part of their workup. All but one patient lacked evidence of a hilar mass on cross-sectional imaging. According to the Bismuth – Corlette classification system,15 biliary strictures were classed as types I (n = 1), II (n = 2), IIIb (n = 2) and IV (n = 2). As in other patients with biliary pathology, ERCP with intraluminal brush cytology was the method preferred to obtain a tissue diagnosis in these individuals. However, endoscopic brushings were obtained in only two individuals because in the remaining cases, a portion of the biliary tree could not be accessed by endoscopic means. This necessitated percutaneous transhepatic intubation for biliary sampling or relief of obstruction in six individuals. Of the patients in whom percutaneous access was attempted, over-the-wire brushings prior to deploying the atherectomy device were performed in two patients. One patient (Patient 3) arrived at our institution with percutaneous biliary access already in place, which greatly facilitated an atherectomy approach as the initial diagnostic procedure.

Endoscopic or percutaneous cytological results, when obtained, were negative, equivocal or demonstrated reactive epithelial atypia. To secure a diagnosis, an atherectomy approach was employed in two individuals (Patients 1 and 2) who demonstrated clinical deterioration (new-onset pruritus, rapid weight loss, inanition) or stricture progression (Patient 7) despite normal cytology and CA 19-9 levels. A third patient with dramatically elevated CA 19-9 underwent the procedure when brush cytology was negative in the setting of equivocal fluorescence in situ hybridization (FISH) results (Patient 4). In one instance (Patient 5), the technique was
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aAtherectomy biopsy performed as first-line procedure given existing PTC access.

bMagnetic resonance imaging or computed tomography of the abdomen.

²SA catheter results: (1) abscess, acute inflammation reactive epithelial changes; (2) bile duct fibrosis and intense lymphoplasmacytic infiltrate, reactive epithelial atypia, and papillary proliferation suspicious, but not diagnostic for adenoma and (3) reactive epithelial atypia, abundant lymphoplasmacytic infiltrate and focal, acute inflammatory infiltrate.

3Readmitted on postoperative day 1 for post-procedural pain at percutaneous access site.
used to delineate the cause of biliary obstruction in a patient with a prior history of an upper gastrointestinal tract malignancy and in another to exclude neoplasia when cross-sectional imaging suggested a malignant cause of obstruction (Patient 4).

Outcome of the procedure
In all seven patients, SA catheter biopsy was the primary means of establishing or excluding a diagnosis of biliary malignancy. While corroborating earlier cytological and imaging results, neoplasia was definitively excluded in seven biopsy specimens. These four individuals were followed for 1–5 years to exclude the development of CC. Three of the patients harboured a concomitant diagnosis of PSC. Mean CA 19-9 level at the time of SA catheter biopsy in these individuals was 33.5, compared with 406.7 in patients in whom catheter biopsy was positive. The procedure was performed multiple times in one individual because of strong clinical suspicion and extensive stricturing of the biliary tree. Absence of neoplastic change was confirmed with each subsequent biopsy and this patient remains alive and well. Follow-up procedures were required in a further two patients when the initial sample was non-diagnostic. Another patient with PSC in whom negative results were obtained eventually underwent OLT for intrinsic liver disease. Malignancy was absent in the explanted liver.

Samples were positive for CC in three patients, only one of whom had a known hilar mass. One patient became eligible for neoadjuvant therapy and OLT despite several earlier false negative cytological results. The explant in this case demonstrated evidence of CC. This patient remains alive without evidence of recurrence at >1 year post-OLT (Fig. 2). In the second positive case, atherectomy biopsy uncovered evidence of severe epithelial atypia and CC was found in the second of two biopsies performed 4 days apart after review by a senior cytopathologist; this patient has since died. The technique was used in a third patient to establish a diagnosis of CC prior to resection, and employed again to document recurrence in the liver remnant after resection; this patient subsequently died. In one additional non-equivocal case, the SA catheter corroborated positive results obtained with conventional brushings (data not shown). In our series, sufficient tissue was obtained for interpretation in 10 of 12 applications.

Complications and longterm effects
Minor haemobilia resulted after two of the atherectomy biopsy attempts and was treated by irrigation or use of a larger drain. On one of these occasions (Patient 2), a particularly difficult percutaneous access procedure was complicated by inadvertent arterial puncture, requiring emergent arterial embolization of a terminal hepatic arterial branch. However, this was related to the difficulty of the percutaneous access procedure and was not a function of atherectomy catheter deployment. One patient (Patient 6) required hospital admission for pain control at 1 day post-procedure. As this patient had admitted to pain after her original PTC and prior to atherectomy, it is unclear whether this was again a function of percutaneous access in general or associated with the SA catheter. None of the patients developed infectious complications as a direct result of the procedure. However, one patient with multiple biliary instrumentations and a history of postcholecystectomy stricture (Patient 5) developed an intrahepatic abscess 4.5 months after the atherectomy procedure. It is unknown whether the atherectomy procedure in this patient contributed to abscess formation or whether the abscess represented a consequence of longstanding biliary obstruction and repeated biliary manipulation.

All of the patients in whom the SA catheter was deployed required routine tube exchanges in accordance with the standard of care for those with percutaneous biliary access. Patients were routinely stented or retained their percutaneous biliary drains post-procedure, but none appear to have incurred longterm sequelae from the procedure that would suggest progressive scarring or a further predisposition to biliary obstruction. In fact, two patients (Patients 1 and 6) evidenced an improvement in the radiographic appearance of their benign strictures, with Patient 6 demonstrating patency of the biliary tree post-procedure.

Discussion
On many occasions, a combination of methods is required to evaluate a suspicious biliary lesion. Although imaging and serological testing remain vital components of the multimodal approach to diagnosis, pathological evaluation is central to subsequent management decisions. In many cases, rendering a definitive diagnosis in the setting of suspicious biliary pathology is predicated on intraluminal brush cytology, in which discrimination between dysplasia and overt malignancy can be difficult. In reality, little may separate the two. This, coupled with a lack of uniform interpretation of diagnostic criteria, has caused reported sensitivities for brush cytology to vary widely. With sensitivities typically ranging between 20% and 60%,12 inability to secure a diagnosis with this technique can be influenced by a variety of additional factors. As CCs are tumours of the bile duct epithelium, those that fail to penetrate into the lumen (submucosal spread) will not be sampled appropriately. Sampling error may also be encountered as a result of the paucicellular, desmoplastic nature of the surrounding environment in which these tumours frequently arise. The chronic inflammatory milieu common to the biliary tree in patients with PSC can introduce further ambiguity. Well-differentiated tumours, such as mucinous and papillary types, may also generate false negatives as these tumours are difficult to interpret on cytology. Tumours may occur at sites that are difficult to access and that obviate the use of various biopsy techniques. In the end, collected material may be insufficient for analysis.12

At a cost of approximately US$3000, the SA catheter is a device readily available to most interventional radiology departments. Familiarity with its use in the peripheral vascular arena is often cultivated by interventional radiologists during fellowship and is directly transferable to hepatobiliary applications. For those who are unfamiliar with its operation, the technique is rapidly learned
and straightforward, requiring only a fundamental skill set in interventional radiology as a prerequisite. Refinements in catheter design have reduced the device profile, improved its trackability and led to better ergonomics compared with earlier atherectomy devices. These features offer the potential for enhanced sample collection and a reduced likelihood of complications. Specifically, the previous generation Atherocath™ obtained biopsy samples in a radial direction, perpendicular to the long axis of the duct. However, the contemporary SA catheter shaves parallel to the long axis, thereby reducing the potential for significant haemobilia and bile duct perforation. In addition, the SA catheter’s greater flexibility allows greater ease of access to the left-sided biliary tree.

Stricture morphology notwithstanding, our results show that the SA catheter can be utilized with a high likelihood of success to establish a tissue diagnosis when a portion of the biliary tree remains inaccessible to the endoscopist, or when histology is equivocal or inconsistent with clinical expectations. We found the technique particularly advantageous in patients with pre-existing biliary access. At our institution, patients with a dominant stricture, cellular irregularity or indeterminate results undergo repeat ERCP and follow-up cytology at 3-month intervals, or more frequently according to the degree of clinical suspicion. The continued presence of cytological atypia on these examinations or its return after an intervening normal cytological result is another common scenario in which we foresee the employment of this technique. Drawbacks to the technique include the need for percutaneous access and, by inference, interventional radiology capability. Other potential shortcomings are the increased invasiveness of the procedure and the risk for complications, of which haemobilia is the chief concern. Longterm biliary sequelae could not be convincingly demonstrated in our small subset of patients. Although such changes may be difficult to discern from the natural history of most biliary disorders, further documentation is not currently available. For these reasons, we continue to recommend conventional intraluminal brush cytology as the primary means of establishing a diagnosis when an apparently malignant biliary stricture is encountered.

Although our experience was relatively small, sensitivity and specificity were 100%. These figures are relevant given the emergence of neoadjuvant protocols to facilitate OLT in patients with CC. Given that eligibility for transplant is restricted to those with stage I and II disease, early detection is mandatory. In this context, endoluminal bile duct biopsy by SA catheter appears to be effective in excluding or diagnosing CC in patients with apparently malignant biliary strictures. Because it incorporates underlying stroma and maintains tissue architecture (Fig. 3), the availability of this technique may result in eventual cost savings by obviating the need for subsequent non-diagnostic procedures. Additionally, it may allow for earlier diagnosis, earlier opportunities for resection, and the more efficient use of limited donor resources where protocols for OLT are available.

Although surgery continues to represent the primary treatment for CC, favourable outcomes after resection or transplant begin with early detection and a multimodal approach to care. Familiarity with a wide array of diagnostic techniques is paramount to success. This analysis of our initial experience demonstrates that: (i) intraluminal biliary pathology can be accessed safely using the modern SA catheter via a percutaneous approach, and (ii) the SA catheter has a potential for higher diagnostic yield than conventional techniques. Therefore, it would be reasonable to consider its
use in the setting of diagnostic uncertainty or when a portion of the biliary tree is inaccessible to the endoscopist. Ultimately, its utility can be determined only after additional experience is gained in the clinical setting. However, awareness of this technique may prove beneficial in select cases.

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Conflicts of interest
None declared.

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