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Advanced endoscopic imaging for biliary strictures: Review of current technologies

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ABSTRACT

Conventional diagnostic techniques for indeterminate biliary strictures using endoscopic retrograde cholangiopancreatoscopy based ductal brushings and biopsy alone remains insensitive with inconsistent yields. There are multiple technologies, both established and novel, including peroral cholangioscopy, endoscopic and intraductal ultrasound, probe-based confocal laser endomicroscopy, and volumetric laser endomicroscopy with evolving data to support their use in the workup of indeterminate biliary strictures. Implementation of such technologies remains hindered by steep operator learning curves, device cost, and a dirth of comparative literature to support evidence based practice using one device over the other or adjunctively with the current gold standard of endoscopic retrograde cholangiopancreatoscopy. In this review, we focus on the aforementioned modalities, their technical specifications and operator considerations, and the available literature for use in evaluating indeterminate biliary strictures.

1. Introduction

Advanced imaging of the biliary tree remains an area of active interest with the development of multiple modalities for the investigation and assessment of the biliary tree. Modern imaging techniques allow high-resolution scans of biliary structures, allow direct visualization of the biliary mucosa, and can perform directed biopsies of suspect tissues through the use of a peroral endoscope; some technologies can even provide microscopy of tissues enabling “virtual biopsies” with rapid diagnostic and analytical power. Most of these endoscopic techniques have low rates of complications, and often provide a cost-effective and less invasive alternative to surgical interventions. Endoscopic imaging and diagnosis have, therefore, become an essential component of pancreaticobiliary medicine, forming the basis of many standard diagnostic algorithms. Nevertheless, the data provided by these advanced modalities is often subject to operator interpretation, and strict standardization of diagnostic thresholds and identification of imaging features is essential to making accurate and consistent conclusions. As a result, consistent and accurate diagnosis of indeterminate bile duct strictures remains a contentious issue even for expert endoscopists at specialized centers.

In this review, we explore the limitations of current imaging modalities, complexities of diagnosing indeterminate biliary strictures, and the potential of frontier imaging technologies, including peroral cholangioscopy (POC), endoscopic and intraductal ultrasound (IDUS), confocal laser endomicroscopy (CLE), and optical coherence tomography (OCT). We discuss what makes these modalities worth consideration and examine the currently existing limitations from the professional perspective of providing accurate, safe, and timely evaluation of bile duct disease. Further, we examine the specific strengths and weaknesses of various imaging modalities contingent on diagnosis type, which include postoperative stenosis, chronic pancreatitis, primary sclerosing cholangitis (PSC), autoimmune pancreatitis, malignancy, and inflammatory stricture. Ultimately, the various technologies are framed through the following 3 critical features: (1) the self-evident importance of distinguishing benign from malignant disease; (2) provision of timely diagnoses and interventions; and (3) avoidance of unnecessary surgery.

2. Background

Biliary duct obstruction can occur within the intrahepatic or extrahepatic biliary tree. There is a critical need to differentiate malignant from benign strictures in a timely and accurate manner, but indeterminate bile duct strictures are diagnostically challenging because of low yields from standard sampling techniques. The differential diagnosis generally includes postoperative complications, choledocholithiasis, and etiologies that range from

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inflammation to malignancies with primary or metastatic origins. Currently, multiple noninvasive modalities are available for the study of biliary disease including computed tomography (CT), magnetic resonance imaging or magnetic resonance cholangioscopy (MRI or MRCP), and abdominal ultrasound (US), and these have been well studied to characterize their strengths and weaknesses. Despite excellent detection rates for biliary stricture with some noninvasive modalities (eg, MRCP); detailed mucosal examination currently requires endoscopic retrograde cholangiopancreatoscopy (ERCP) with the added challenge of identifying hilar lesions of the indeterminate stricture.

Decades of development and refinement have established ERCP as highly reliable and the most common method for biliary decompression. However, despite the regular use of ERCP for the purposes of endoscopic therapy, ERCP as a diagnostic tool continues to face issues of reliability and consistency in assessing the malignant potential of biliary strictures. One recent meta-analysis found that combination of both ERCP-derived intraductal biopsies and brushings showed a meager sensitivity rate of 59.4% (albeit with high specificity 100%) with comparable individual sensitivity and specificities [1].

Use of diagnostic ERCP as a “stand-alone” modality has decreased as advancements in noninvasive MR and CT modalities have evolved to become increasingly sensitive, specific, and accurate tools of diagnosis. This has relegated ERCP as a supplementary tool for provision of index pathology [2]. Estimated sensitivity of ERCP with brush cytology remains disappointing at 54%-71% [3] with an increase in sensitivity rates of 10%-20% by adding fluorescence in situ hybridization (FISH). Unfortunately, other modifications, including augmentation of brush style and improving access using duct dilation, have proven less effective. Repeated brushings results in a modest increase in sensitivity, with one study demonstrating improved diagnostic capability of combining predilation (34.5%) and postdilation (31%) brushing specimens for an amalgamated sensitivity of 44% ($P = 0.001$) [4,5].

To address some of these concerns, Tamada et al have proposed standardized diagnostic protocols that formalize the use of non-invasive diagnoses with follow-up ERCP and surgery as necessary [6]. Standardized procedural therapies of this kind can be considered to be the current state-of-the-art. The frontier modalities to be discussed in this article represent potential alternatives to the contemporary diagnostic paradigm, and may well obviate some of the steps required for successful diagnosis and treatment of biliary strictures in the future.

3. Cholangioscopy

3.1. Background

Common bile duct endoscopy was introduced as an intraoperative technique for detection of stone retention after cholecystectomy in the 1940s and entered the gastrointestinal (GI) endoscopy realm in 1976 when Rosch and Koch [7] and Urakami et al [8] independently described endoscopic methods for peroral cholangioscopy. Early cholangioscopes required operation by 2 endoscopists with a mother-baby platform and were limited by the fragility of the endoscopic tools. These early systems were cumbersome, resource intensive, and limited mechanistically in other ways; for example, mobility was restricted to only one degree-of-freedom steering, and a lack of working channels or irrigation ports constrained treatment or diagnostic options. The next generation of peroral cholangioscopes by Olympus and Pentax featured reusable fiber optic and video formats designed to pass through the working channel of a duodenoscope. The widest diameter cholangioscope (3.4 mm) had a 1.2 mm working channel large enough to accommodate 3 Fr electrohydraulic lithotripsy fibers, 0.035-in. guidewire and biopsy forceps [9]. These versions remained standard before the introduction of single operator cholangiopancreatoscopy (POCP) systems, however, widespread implementation was encumbered by technical factors including the bulky 2 operator mother-daughter design, limited tip deflection (2 way) and limited irrigation capacities [10]. Additionally the cholangioscopes were prone to breaking in part due to the acute angle at the duodenoscope's orifice and resulting force applied to forceps or lithotripsy fibers within the cholangioscope channel [11]. The development of the SpyGlass™ peroral cholangiopancreatoscopy system (Boston Scientific Corp) eliminated many of these limitations and was heralded as a landmark development in the long-hindered cholangioscopy arena [10,12].

3.2. Single operator cholangioscopy and derived systems

There are 2 commonly employed methods for cholangioscopy, the first of which includes peroral single-operator (video) systems reliant on the working channel of a duodenoscope. In these systems, a narrow catheter cholangioscope advances through the endoscopic channel into the biliary tree. A second, more recent approach is peroral direct (video) cholangioscopy (PDCS), in which ultraslim gastroscopes are advanced in monorail fashion over a guidewire or with balloon assistance into the biliary tree. This approach normally requires sphincterotomy or distal duct dilation for advancement of the cholangioscope through the biliary sphincter. For both methods, the duct is irrigated with sterile saline solution through the working channel of the cholangioscope for adequate visualization, followed by slow withdrawal of the scope, allowing inspection of the ductal mucosa and lumen. Cholangioscope position can be ascertained fluoroscopically. These technologies have been refined with an indication primarily for cases of indeterminate biliary strictures or intraluminal lesions or atypical stone cases wherein direct intraductal visualization is an advantage. The approach allows targeted biopsy of mucosal abnormalities or direct treatment of stone disease.

SpyGlass™ (Boston Scientific) is a peroral single-operator, video cholangiopancreatoscopy system based on the original mother-baby platform. It features a reusable fiber optic probe with disposable SpyScopetm access (10 Fr diameter, 2 irrigation channels, and 1.2 mm diameter working channel), delivery catheter, and biopsy forceps. The novel, mounting device used in SpyGlass™ is what enables single operator control of both duodenoscope and POC. Advantages include fewer required personnel, 4-way (2 degree-of-freedom) tip deflection for improved maneuverability and ductal cannulations, and separated working (1.2 mm) and irrigation channels (0.6 mm) [13].

The SpyGlass™ DS Direct Visualization system was released February 2015 (Boston Scientific) featuring an integrated digital sensor with improved visual resolution and wider field of view. The entirely disposable single-use system addresses previous concerns about degradation of visual quality because of the reusable optic probe. Additionally, the simplified set-up includes a “plug and play” design for ease-of-use. One group has recently presented the first US multicenter experience with this fully disposable, catheter-based, digital single operator cholangiopancreatoscope with 71 cases for indeterminate strictures (121 total patients) [14]. All 121 cases evaluated were technically successful and directed tissue sampling provided novel neoplastic diagnoses in $> 90\%$ of patients (22/24 new neoplastic diagnosis confirmed with SpyBite™ tissue acquisition). Furthermore, authors were able to describe features of benign disease: concentric stenosis or normal or erythematous changes ($n = 17$), low papillary mucosal projections ($n = 9$), coarse granular mucosa ($n = 8$), and nodular