REVIEW

Endoscopic assessment and management of biliary strictures

M F Dawwas,[1,2] K W Oppong,[2] G J Webster[3]

[1]Division of Digestive Diseases and Nutrition, Department of Medicine, University of Kentucky Medical Center, Lexington, Kentucky, USA
[2]Department of Gastroenterology, Freeman Hospital, Newcastle upon Tyne, UK
[3]Department of Gastroenterology, University College Hospital, London, UK

Correspondence to
Dr K W Oppong, Hepato-Pancreato-Biliary Unit, Freeman Hospital, Freeman Road, Newcastle upon Tyne NE7 7DN, UK; kofi.oppong@nuth.nhs.uk

Received 20 January 2015
Accepted 20 May 2015
Published Online First 17 June 2015

To cite: Dawwas MF, Oppong KW, Webster GJ. *Frontline Gastroenterology* 2016;**7**:170–175.

INTRODUCTION

Strictures of the biliary tract represent a common diagnostic and management problem in pancreaticobiliary practice, often requiring close multidisciplinary collaboration among endoscopists, surgeons, radiologists, pathologists and oncologists. The underlying aetiologies, clinical manifestations and prognostic significance are protean, encompassing both benign and malignant entities; single and multifocal disease distributions; extrahepatic and intrahepatic site involvement; silent and symptomatic presentations, and clinically indolent as well as rapidly progressive natural histories. From a practical standpoint, however, the most critical distinction to make, both accurately and expeditiously, is between benign and malignant aetiologies since timely surgical resection of early-stage malignant disease remains the only route to cure. Definitive differentiation, however, is not always feasible, and many cases remain indeterminate even after extensive investigation.

The differential diagnosis of biliary strictures is predominantly a function of geography and consequent variations in disease epidemiology. In the Western world, most biliary strictures are secondary to malignant disease in the form of pancreatic cancer, cholangiocarcinoma, gallbladder cancer, malignant hilar lymphadenopathy and hepatocellular carcinoma. Important benign aetiologies include iatrogenic causes (usually in the setting of bile duct injury during cholecystectomy) chronic pancreatitis, primary sclerosing cholangitis (PSC) and immunoglobulin G-subfraction 4 (IgG4)-related sclerosing cholangitis (IgG4-SC). Other causes of benign biliary strictures include gallstone disease (choledocholithiasis or Mirizzi syndrome); ischaemic and non-ischaemic injury in the setting of liver transplantation; anastomotic disease after biliary tract surgery; abdominal trauma; percutaneous therapy of hepatocellular carcinoma (radiofrequency or ethanol ablation and chemoembolisation); radiotherapy; portal bilopathy, vasculitides; and miscellaneous infections (such as recurrent pyogenic cholangitis, cytomegalovirus infection and human immunodeficiency virus).

The clinical manifestations of biliary strictures are equally diverse, principally dictated by the severity of luminal obstruction and nature of causative disease process, ranging from being entirely asymptomatic with or without biochemical or radiological features of cholestasis, as in many post-cholecystectomy bile duct injuries, to those of biliary obstruction; sepsis (recurrent cholangitis, liver abscesses or stone formation); secondary biliary cirrhosis; and/or underlying disease (such as malabsorption in chronic pancreatitis). The finding of a clinically palpable gallbladder in the setting of jaundice and extreme elevations in serum bilirubin (>350 μmol/L) or carbohydrate antigen 19-9 levels (>1000 U/mL) are all highly suggestive of, but poorly sensitive for, malignant obstruction. Similarly, grossly elevated serum IgG4 levels strongly favour a diagnosis of IgG4 disease.

In concert with other modalities, extracorporeal imaging plays an important role in the detection of biliary strictures, differentiation of benign from malignant causes, definition of stricture(s) length, and guidance of subsequent tissue acquisition and stent deployment. Transabdominal ultrasound, typically the initial imaging modality, is simple, non-invasive, cheap and highly sensitive for the detection of large-duct biliary obstruction and localisation of its site, but has a widely variable accuracy for defining the underlying cause; is highly operator-dependent and has less favourable sensitivity in individuals with low bilirubin levels. Cross-sectional imaging facilitates more precise definition of the site and

extent of the segment involved; improved (albeit by no means optimal) differentiation of benign from malignant causes; and staging of malignant involvement of the portal vein, hepatic artery and regional lymph nodes. Imaging features favouring malignancy on multiphase contrast-enhanced computed tomography and magnetic resonance cholangiopancreatography include delayed-phase hyper-enhancement wall thickness of >1.5 mm; greater stricture length; marked upstream biliary dilatation; irregular, asymmetric, abrupt or shouldered stricture morphology; and presence of a discrete mass lesion, vascular invasion, lymphadenopathy or liver metastases. However, with the exception of the latter, none of these features is considered pathognomic for malignant disease and, despite extensive additional investigation, up to 25% of patients undergoing surgical resection for suspected cholangiocarcinoma will ultimately prove to harbour benign,[1] often autoimmune, disease with high probability of complete response to immunosuppressive therapy. While early reports suggested impressive sensitivity and specificity for differentiating malignant from benign biliary strictures, positron emission tomography (PET) is now believed to have modest utility in the diagnosis of cholangiocarcinoma with variable performance according to the anatomical location, growth pattern and pathological characteristics.[2]

In this article, we discuss the role of endoscopy in the evaluation and management of biliary strictures and highlight some promising imaging innovations and emerging endoscopic therapies in this arena.

ENDOSCOPIC EVALUATION

Endoscopic retrograde cholangio-pancreatography

Endoscopic retrograde cholangio-pancreatography (ERCP) has long played a fundamental role in the evaluation and management of biliary strictures, facilitating high-quality fluoroscopic imaging of the biliary tree, diagnostic tissue acquisition and therapeutic biliary drainage. More recently, the advent of direct intraductal mucosal visualisation (cholangioscopy), intraductal endosonography and palliative ablative therapies (such as photodynamic and radiofrequency ablation) has further enhanced the diagnostic and therapeutic capabilities of the procedure.

Cholangiographic morphology of biliary strictures, such as irregularity, asymmetry, shouldering and extent, is known to have an unsatisfactory accuracy (of the order of 72–80%) in discriminating malignant from benign strictures.[3] For example, cholangiography alone is an unreliable means to differentiate between PSC, IgG4-SC and hilar cholangiocarcinoma, even in expert hands.[4] This highlights the need for tissue sampling, which is usually accomplished at ERCP by brush cytology and intraductal forceps biopsy. A recent meta-analysis concluded that these two modalities have near-perfect specificity but comparably limited sensitivity (of 45% and 48.1%, respectively) for the diagnosis of malignant biliary strictures, which is modestly enhanced to 59.4% when used in combination.[5] The advent of advanced cytological techniques such as fluorescence in situ hybridisation (FISH) and, to a lesser extent, digital image analysis, exploiting the correlation between malignancy and both chromosomal aneusomy and nuclear DNA content, respectively, has been shown to enhance tumour detection by approximately 10–30%. Although not widely employed, their use has been advocated in cases of indeterminate biliary strictures where both cytology and biopsy are negative. However, the combined sensitivity of these techniques remains <70% in most series and the specificity of FISH is compromised in the setting of PSC, as is that of brush cytology.[3 6] More recently, the combination of brush cytology and quantitative PET to investigate PSC-related dominant biliary strictures was shown to have a sensitivity for malignant disease of 100% and a specificity of 88%.[7] In the setting of suspected IgG4-SC, biopsy of the duodenal papilla, even if appearing normal, and/or measurement of IgG4 levels in bile aspirates may be diagnostically useful.[8 9]

Endoscopic ultrasonography

Endoscopic ultrasonography (EUS) has emerged as a key tool for investigating and, more recently, managing biliary strictures. The capacity to identify a mass lesion that had escaped detection by other imaging modalities; to provide high-definition imaging of stricture morphology (such as irregularity and wall thickness); to stage regional lymph node and portal vein involvement; and to facilitate diagnostic tissue acquisition are all important attributes of endosonography in this setting. EUS-guided fine-needle aspiration (EUS-FNA) is currently considered the standard of care for characterisation of solid pancreatic masses and, increasingly, plays an important role in the evaluation of suspected biliary tract malignancy. A recent meta-analysis reported that the pooled sensitivity of EUS-FNA for extrahepatic cholangiocarcinoma was 66%; 81% when the analysis was confined to proximal strictures; 80% when a mass lesion was detected on EUS; 45% when no mass lesion was evident at cross-sectional imaging and 59% when brush cytology was negative.[10] In a series of patients with unresectable hilar cholangiocarcinoma undergoing assessment for liver transplantation, EUS-FNA but not EUS morphology correctly identified all patients with regional lymph node involvement.[11]

Some shortcomings are noteworthy, however. The risk of bile contamination as a result of FNA mandates the administration of prophylactic antibiotics and/or stent placement at the same sitting or shortly thereafter. The presence of biliary stents can confound EUS interpretation of both stricture morphology and vascular staging. The suboptimal negative predictive value of EUS-FNA for excluding malignancy (reported

to range from 29% to 67%)[12] may consign a significant proportion of patients to additional investigation, including exploratory surgery. Most importantly, tissue acquisition with EUS-FNA from potentially surgical candidates with proximal biliary strictures has been strongly discouraged by some authorities in view of the potential risk of tumour seeding of the needle track which, in contrast to distal lesions, is typically not included in the surgical resection.[6] This recommendation, however, is predicated on a single, retrospective, unadjusted analysis that reported a substantially higher rate of peritoneal disease at staging laparotomy among liver transplant candidates with unresectable cholangiocarcinoma who had undergone transperitoneal FNA or biopsy compared with those who had not.[13] It should be noted that most of these specimens were obtained percutaneously rather than by EUS-FNA, which in other sites has been associated with a substantially lower risk of seeding,[14] possibly as a result of use of smaller calibre needles and shorter needle track. Indeed, a recent risk-adjusted single-centre study of 150 patients with cholangiocarcinoma reported that preoperative EUS-FNA did not adversely affect either overall or progression-free survival.[15]

However, it probably remains prudent to limit the use of EUS-FNA in the setting of suspected, potentially operable cholangiocarcinoma to cases where other modalities of tissue acquisition have failed to verify the diagnosis.

Intraductal ultrasound

Intraductal ultrasound (IDUS) is a valuable, albeit uncommonly used, imaging modality for indeterminate biliary strictures. Utilising a wire-guided mini-probe that can be easily advanced into the bile duct at the time of ERCP, it provides high-resolution (including three-dimensional) imaging of the entire extrahepatic bile duct, portal vein, right hepatic artery and ampulla.[16–19] In the setting of indeterminate biliary strictures, IDUS has been shown to significantly outperform EUS in terms of accuracy of differentiation of malignant from benign disease (89% vs 76%); determination of the resectability of malignant tumours (82% vs 76%); and staging of local tumour extent (78% vs 54%). The diagnostic superiority of IDUS compared with EUS was greatest for proximal biliary lesions,[19] which are often not well-visualised endosonographically. Another study reported that adding IDUS to ERCP and tissue sampling substantially improves the overall diagnostic performance without significantly compromising the specificity.[20] However, IDUS is limited by the lack of capacity for tissue acquisition, inferior utility for staging regional adenopathy, requirement for undertaking ERCP at the same sitting and less favourable diagnostic performance in the aftermath of biliary stent placement.[16 17]

Cholangioscopy

Intraductal mucosal visualisation (cholangioscopy) has been performed for >25 years, but there has been a recent resurgence of interest and use. Peroral cholangioscopy is now most commonly accomplished, following biliary shincterotomy, using a single-operator cholangioscope (Spyglass, Boston Scientific, Natick, Massachusetts, USA), which is inserted down the working channel of therapeutic duodenoscope. The system allows four-way steerability, water irrigation and tissue biopsy (via a 1.2 mm biopsy channel). Visualisation is achieved using a 6000 pixel fibre-optic probe inserted down the cholangioscope. An international, multicentre study of the utility of single-operator cholangioscopy among patients with indeterminate biliary strictures reported an 89% overall procedure success rate, securing histologically adequate tissue specimens in 88% of those who underwent biopsy with an overall sensitivity for diagnosing malignancy by visual impression and cholangioscopy-directed biopsy of 78% and 49%, respectively.[21] Similar results were reported by a multicentre UK study.[22] Emphasising the multimodality approach to stricture assessment, EUS evaluation in patients with indeterminate biliary strictures has been shown to obviate the need, cost and adverse events of standard single-operator cholangioscopy in 60% of patients, yielding the correct clinical diagnosis in 94% of patients with minimal adverse events.[23] However, this high diagnostic yield for EUS requires verification in other studies. Interobserver agreement for standard single-operator cholangioscopy has been shown to be modest at best, highlighting the need for validated scoring criteria.[24] The more recent use of ultra-slim endoscopes for cholangioscopy shows promise,[25] facilitating superior white-light image quality, larger biopsy specimens and multimodal chromendoscopy, autofluorescence and narrow band imaging. Validation of the utility of these innovations in adequately powered prospective trials is awaited.

Probe-based confocal laser endomicroscopy

The advent of probe-based confocal laser endomicroscopy (pCLE) has equipped biliary endoscopists with an exciting new tool providing high-resolution in vivo histology, thereby potentially allowing real time differentiation of malignant from benign biliary strictures. A multicentre study of the diagnostic utility of pCLE for identifying malignancy among patients with indeterminate pancreaticobiliary strictures reported excellent sensitivity and negative predictive value, as well as superior overall accuracy when combined with ERCP compared with ERCP and tissue acquisition.[26] A recent series found a sensitivity of 100%, specificity of 69%, positive predictive value of 60%, negative predictive value of 100% and overall accuracy of 79% for discriminating malignant from benign biliary strictures when pCLE is combined with endobiliary and

EUS-guided tissue acquisition.[27] However, given recent reports of significant interobserver variation,[28] these findings remain to be replicated in adequately designed randomised studies.

ENDOSCOPIC THERAPY

Symptomatic relief, prevention of complications of prolonged biliary obstruction and facilitation of definitive therapy, be it palliative or curative, are the goals of effective biliary decompression. In practice, the necessity and timing of stent placement are determined by a number of factors including the patient's candidacy for curative surgery and/or chemotherapy, severity and site of biliary obstruction, presence of biliary sepsis, requirement for endobiliary tissue acquisition and/or availability of local expertise. The utility of preoperative biliary drainage among patients with potentially resectable malignant disease has been controversial. A multicentre, randomised, controlled trial reported higher morbidity and similar mortality among individuals with pancreatic head cancer undergoing placement of plastic biliary stent prior to surgical resection compared with those proceeding to surgery without preoperative drainage.[29] However, the results of this trial may not be generalisable to several patient groups it had excluded including: deeply jaundiced patients with bilirubin levels >250 μmol/L; those with evidence of biliary sepsis or requirement for neoadjuvant chemoradiation; or those undergoing metal stent placement, propofol sedation or biliary cannulation by endoscopists with average success rates exceeding 75%. In addition, preoperative biliary drainage of the future liver remnant is indicated among patients with proximal cholangiocarcinoma undergoing resection, and stent placement with or without stricture dilatation remains the mainstay of management for patients with both benign and unresectable malignant disease.

Biliary stents can be placed endoscopically at ERCP or percutaneously (by an interventional radiologist), are either plastic or metal (which may be fully covered, partially covered or uncovered), and, in the case of hilar strictures, can be deployed bilaterally or within a single obstructed lobar segment. Stent selection is determined by stricture aetiology, location, length, ductal anatomy, nature and timing of anticipated subsequent therapy (be it surgical resection and/or chemotherapy) and likely patient longevity. In general, metal stents are more durable than their plastic counterparts as a result of substantially greater calibre leading to higher patency rates and lower requirement for subsequent hospitalisation and reintervention. A recent meta-analysis comparing plastic and metal stents in the setting of malignant biliary obstruction concluded that the latter are the treatment of choice for patients with distal as well as proximal disease.[30] Similarly, multiple versus single plastic stenting has been shown to afford more durable drainage for both benign and, more recently, malignant strictures.[31] The patency and patient survival rates associated with covered and uncovered metal stents are similar, but, in contrast to the uncovered variety, covered stents are removable and therefore preferable in benign disease; more liable to spontaneous migration; associated with higher rates of cholecystitis and possibly acute pancreatitis (as a result of obstruction of the openings of the cystic and pancreatic ducts, respectively);[32] and best avoided in proximal strictures given the risk of both contralateral duct and ipsilateral radicle occlusion. A large, recently published, international, multicentre study reported successful resolution of benign distal biliary strictures in 75% of patients undergoing short-term placement of fully covered metal stents.[33] Whether malignant hilar strictures are best managed with unilateral or bilateral stent placement (using side-by-side, stent-in-stent or Y-shaped prostheses) and whether this should be accomplished endoscopically or percutaneously are debatable. In general, however, the percutaneous route in these cases tends to be technically easier (albeit at the cost of frequent requirement for multiple sessions), and the procedure should always be guided by prior high-quality, cross-sectional imaging aiming to both drain at least 50% of the normal liver volume and minimise the attendant risk of infection by avoiding excessive contrast injection, sparing atrophic segments and achieving effective drainage of all other opacified segments. These complex cases should be discussed in a multidisciplinary setting involving specialist hepatopancreatobiliary radiologists, surgeons and endoscopists. Quite apart from the relative pros and cons of plastic versus metal stents, or the route of insertion, of fundamental importance is a clear policy to insert uncovered mesh metal biliary stents only in the setting of (pathologically) proven malignancy. With an increased recognition of benign diseases that may mimic pancreaticobiliary malignancy,[34] the injudicious insertion of uncovered stents (which are then unremovable) may have severe prognostic consequences, related to tissue in-growth long-term. Even in the setting of malignancy, uncovered stents across the liver hilum may present a difficult (and avoidable) surgical challenge in those patients deemed to have potentially resectable tumours and may also complicate the long-term management of patients with potentially curable lymphomas or indolent disease (eg, islet cell metastasis) with expected longevity exceeding that of the patency of uncovered prostheses.

In recent years, the deployment of EUS-guided biliary drainage, via the transpapillary (retrograde or antegrade), tranduodenal or transgastric routes, has been shown to be feasible and safe, potentially obviating the need for percutaneous drainage among patients with biliary obstruction in whom standard ERCP was unsuccessful or not possible. Indeed, recent series have suggested comparable, if not

superior, success rates and lower morbidity with EUS-guided versus percutaneous biliary drainage.[35 36] However, routine use of this approach in clinical practice should probably await the performance of a randomised controlled trial.

The recent development of a number of novel ablative endoscopic therapies promises the prospect of loco-regional control and improved palliation of biliary obstruction secondary to inoperable cholangiocarcinoma. These innovations include photodynamic therapy, radiofrequency ablation and brachytherapy, and can be either delivered during index ERCP in combination with stent placement or used to recanalise occluded, previously placed stents. Randomised studies comparing photodynamic therapy combined with biliary stenting to stenting alone have been inconsistent in showing a benefit in terms of patient survival and stent patency.[37–39] Retrospective series of patients with inoperable malignant strictures have reported superior patient survival in those who had undergone radiofrequency ablation and stent placement compared with stenting alone;[40 41] the results of ongoing randomised trials are keenly awaited.

Contributors MFD wrote the first draft; all authors contributed to the final manuscript.

Competing interests None declared.

Provenance and peer review Commissioned; internally peer reviewed.

REFERENCES

1 Koea J, Holden A, Chau K, *et al*. Differential diagnosis of stenosing lesions at the hepatic hilus. *World J Surg* 2004;28:466–70.
2 Sharma B, Martin A, Zerizer I. Positron emission tomography-computed tomography in liver imaging. *Semin Ultrasound CT MR* 2013;34:66–80.
3 Yoon WJ, Brugge WR. Endoscopic evaluation of bile duct strictures. *Gastrointest Endosc Clin N Am* 2013;23:277–93.
4 Kalaitzakis E, Levy M, Kamisawa T, *et al*. Endoscopic retrograde cholangiography does not reliably distinguish IgG4-associated cholangitis from primary sclerosing cholangitis or cholangiocarcinoma. *Clin Gastroenterol Hepatol* 2011;9:800–3.e2.
5 Navaneethan U, Njei B, Lourdusamy V, *et al*. Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. *Gastrointest Endosc* 2015;81:168–76.
6 Levy MJ, Heimbach JK, Gores GJ. Endoscopic ultrasound staging of cholangiocarcinoma. *Curr Opin Gastroenterol* 2012;28:244–52.
7 Sangfelt P, Sundin A, Wanders A, *et al*. Monitoring dominant strictures in primary sclerosing cholangitis with brush cytology and FDG-PET. *J Hepatol* 2014;61:1352–7.
8 Kawakami H, Zen Y, Kuwatani M, *et al*. IgG4-related sclerosing cholangitis and autoimmune pancreatitis: histological assessment of biopsies from Vater's ampulla and the bile duct. *J Gastroenterol Hepatol* 2010;25:1648–55.
9 Vosskuhl K, Negm AA, Framke T, *et al*. Measurement of IgG4 in bile: a new approach for the diagnosis of IgG4-associated cholangiopathy. *Endoscopy* 2012;44:48–52.
10 Navaneethan U, Njei B, Venkatesh PG, *et al*. Endoscopic ultrasound in the diagnosis of cholangiocarcinoma as the etiology of biliary strictures: a systematic review and meta-analysis. *Gastroenterol Rep (Oxf)* Published Online First: 27 Aug 2014. doi:10.1093/gastro/gou057
11 Gleeson FC, Rajan E, Levy MJ, *et al*. EUS-guided FNA of regional lymph nodes in patients with unresectable hilar cholangiocarcinoma. *Gastrointest Endosc* 2008;67:438–43.
12 Strongin A, Singh H, Eloubeidi MA, *et al*. Role of endoscopic ultrasonography in the evaluation of extrahepatic cholangiocarcinoma. *Endosc Ultrasound* 2013;2:71–6.
13 Heimbach JK, Sanchez W, Rosen CB, *et al*. Trans-peritoneal fine needle aspiration biopsy of hilar cholangiocarcinoma is associated with disease dissemination. *HPB (Oxford)* 2011;13:356–60.
14 Wani S, Muthusamy VR, Komanduri S. EUS-guided tissue acquisition: an evidence-based approach (with videos). *Gastrointest Endosc* 2014;80:939–59.e7.
15 El Chafic AH, Dewitt J, Leblanc JK, *et al*. Impact of preoperative endoscopic ultrasound-guided fine needle aspiration on postoperative recurrence and survival in cholangiocarcinoma patients. *Endoscopy* 2013;45:883–9.
16 Menzel J, Domschke W. Intraductal ultrasonography (IDUS) of the pancreato-biliary duct system, Personal experience and review of literature. *Eur J Ultrasound* 1999;10:105–15.
17 Levy MJ, Vazquez-Sequeiros E, Wiersema MJ. Evaluation of the pancreaticobiliary ductal systems by intraductal US. *Gastrointest Endosc* 2002;55:397–408.
18 Stavropoulos S, Larghi A, Verna E, *et al*. Intraductal ultrasound for the evaluation of patients with biliary strictures and no abdominal mass on computed tomography. *Endoscopy* 2005;37:715–21.
19 Menzel J, Poremba C, Dietl KH, *et al*. Preoperative diagnosis of bile duct strictures—comparison of intraductal ultrasonography with conventional endosonography. *Scand J Gastroenterol* 2000;35:77–82.
20 Farrell RJ, Agarwal B, Brandwein SL, *et al*. Intraductal US is a useful adjunct to ERCP for distinguishing malignant from benign biliary strictures. *Gastrointest Endosc* 2002;56:681–7.
21 Chen YK, Parsi MA, Binmoeller KF, *et al*. Single-operator cholangioscopy in patients requiring evaluation of bile duct disease or therapy of biliary stones (with videos). *Gastrointest Endosc* 2011;74:805–14.
22 Kalaitzakis E, Webster GJ, Oppong KW, *et al*. Diagnostic and therapeutic utility of single-operator peroral cholangioscopy for indeterminate biliary lesions and bile duct stones. *Eur J Gastroenterol Hepatol* 2012;24:656–64.
23 Nguyen NQ, Schoeman MN, Ruszkiewicz A. Clinical utility of EUS before cholangioscopy in the evaluation of difficult biliary strictures. *Gastrointest Endosc* 2013;78:868–74.
24 Sethi A, Doukides T, Sejpal DV, *et al*. Interobserver agreement for single operator choledochoscopy imaging: can we do better? *Diagn Ther Endosc* 2014;2014:730731.
25 Pohl J, Ell C. Direct transnasal cholangioscopy with ultraslim endoscopes: a one-step intraductal balloon-guided approach. *Gastrointest Endosc* 2011;74:309–16.
26 Meining A, Chen YK, Pleskow D, *et al*. Direct visualization of indeterminate pancreaticobiliary strictures with probe-based confocal laser endomicroscopy: a multicenter experience. *Gastrointest Endosc* 2011;74:961–8.
27 Caillol F, Bories E, Autret A, *et al*. Evaluation of pCLE in the bile duct: final results of EMID study: pCLE: impact in the

management of bile duct strictures. *Surg Endosc* Published Online First: 10 Dec 2014. doi:10.1007/s00464-014-3986-8
28 Talreja JP, Sethi A, Jamidar PA, *et al*. Interpretation of probe-based confocal laser endomicroscopy of indeterminate biliary strictures: is there any interobserver agreement? *Dig Dis Sci* 2012;57:3299–302.
29 van der Gaag NA, Rauws EA, van Eijck CH, *et al*. Preoperative biliary drainage for cancer of the head of the pancreas. *N Engl J Med* 2010;362:129–37.
30 Sawas T, Al Halabi S, Parsi MA, *et al*. Self-expandable metal stents versus plastic stents for malignant biliary obstruction: a meta-analysis. *Gastrointest Endosc* Published Online First: 13 May 2015. doi:10.1016/j.gie.2015.03.1980
31 Lawrence C, Romagnuolo J. Double plastic stents for distal malignant biliary obstruction: preliminary evidence for a novel cost-effective alternative to metal stenting. *Am J Gastroenterol* 2014;109:295–7.
32 Lee JH, Krishna SG, Singh A, *et al*. Comparison of the utility of covered metal stents versus uncovered metal stents in the management of malignant biliary strictures in 749 patients. *Gastrointest Endosc* 2013;78:312–24.
33 Devière J, Nageshwar Reddy D, Püspök A, *et al*. Benign Biliary Stenoses Working Group. Successful management of benign biliary strictures with fully covered self-expanding metal stents. *Gastroenterology* 2014;147:385–95.
34 Erdogan D, Kloek JJ, ten Kate FJ, *et al*. Immunoglobulin G4-related sclerosing cholangitis in patients resected for presumed malignant bile duct strictures. *Br J Surg* 2008;95:727–34.
35 Khashab MA, Valeshabad AK, Afghani E, *et al*. A Comparative Evaluation of EUS-Guided Biliary Drainage and Percutaneous Drainage in Patients with Distal Malignant Biliary Obstruction and Failed ERCP. *Dig Dis Sci* 2015;60:557–65.
36 Bapaye A, Dubale N, Aher A. Comparison of endosonography-guided vs. percutaneous biliary stenting when papilla is inaccessible for ERCP. *United European Gastroenterol J* 2013;1:285–93.
37 Ortner ME, Caca K, Berr F, *et al*. Successful photodynamic therapy for nonresectable cholangiocarcinoma: a randomized prospective study. *Gastroenterology* 2003;125:1355–63.
38 Zoepf T, Jakobs R, Arnold JC, *et al*. Palliation of nonresectable bile duct cancer: improved survival after photodynamic therapy. *Am J Gastroenterol* 2005;100:2426–30.
39 Pereira SP. Photodynamic therapy for pancreatic and biliary tract cancer: the United Kingdom experience. *J Natl Compr Canc Netw* 2012;10(Suppl 2):S48–51.
40 Kallis Y, Phillips N, Steel A, *et al*. Analysis of Endoscopic Radiofrequency Ablation of Biliary Malignant Strictures in Pancreatic Cancer Suggests Potential Survival Benefit. *Dig Dis Sci*. 2015 Jun 3. [Epub ahead of print]
41 Sharaiha RZ, Natov N, Glockenberg KS, *et al*. Comparison of metal stenting with radiofrequency ablation versus stenting alone for treating malignant biliary strictures: is there an added benefit? *Dig Dis Sci* 2014;59:3099–102.