Dig Dis Sci (2009) 54:1184–1198
DOI 10.1007/s10620-008-0479-4

REVIEW

Palliation of Malignant Obstructive Jaundice

G. Garcea · S. L. Ong · A. R. Dennison ·
D. P. Berry · G. J. Maddern

Received: 28 May 2008 / Accepted: 24 July 2008 / Published online: 4 September 2008

Abstract Peri-ampullary and hepatic malignancies will frequently present with obstructive jaundice. For unresectable tumors, effective and lasting decompression of the biliary tree is essential to improve quality of life and survival. An overview of present treatment modalities for palliation of obstructive jaundice is provided, including a systematic review of the English literature regarding the optimum choice of palliation.

Keywords Malignant jaundice · Obstructive jaundice · Palliation · Surgery · Biliary bypass · Antegrade stent · Percutaneous · Endoscopic retrograde cholangiopancreatography (ERCP) · Plastic stent

Introduction

Malignant obstructive jaundice is a common problem. Obstruction can occur at any level within the biliary tree, the most common sites being at the distal common bile duct (secondary to peri-ampullary malignancies) or at the hilum (usually due to cholangiocarcinomas, or, less commonly, hepatocellular carcinomas or metastatic lesions to the liver). Clinical history, liver function profile, and ultrasonography are essential first-line investigations to differentiate between obstructive and non-obstructive jaundice, and benign from malignant causes. Magnetic resonance cholangiopancreatography (MRCP) and computed tomography (CT) are utilized to further characterize the underlying cause [1, 2]. Endoscopic retrograde cholangiopancreatography (ERCP) is no longer routinely used in a diagnostic setting [3]. Careful evaluation by combined cross-sectional imaging, including CT and MRCP, is also important in locating the position of the stricture (Fig. 1). In those patients re-presenting with jaundice following previous palliation or resection, the possibility of liver dysfunction secondary to tumor replacement must also be borne in mind as a causative factor for jaundice (Fig. 1). For those patients with unresectable disease, progressive jaundice constitutes an immediate limitation to their survival, in addition to causing significant loss to their quality of life secondary to pruritis, malaise and cholangitis [4]. Effective and lasting decompression of the biliary tree is a priority and consists of either positioning of a biliary endoprosthesis (stent) or an operative bypass. This review provides an overview of present treatment modalities for the palliation of malignant obstructive jaundice. Evidence supporting the use of pre-operative biliary drainage prior to attempted resection is not discussed.

G. Garcea (✉) · G. J. Maddern
Department of Hepatobiliary and Upper Gastrointestinal Surgery, The Queen Elizabeth Hospital, 28 Woodville Road, Adelaide, SA 5011, Australia
e-mail: gg43@le.ac.uk

S. L. Ong · A. R. Dennison · D. P. Berry
Department of Hepatobiliary and Pancreatic Surgery, Leicester General Hospital, Gwendolen Road, Leicester, LE5 4PW, UK

Hilar Versus Distal Strictures of the Common Bile Duct

Hilar strictures present a greater technical challenge than mid- to distal strictures of the common bile duct (CBD), particularly when treated endoscopically or percutaneously. Decompression of both left and right hepatic ducts ideally requires the insertion of two stents, although there is evidence that unilateral stent insertion can be attempted, with good palliation [5], particularly if MRCP is utilized to direct stent placement [6]. Despite anatomical considerations

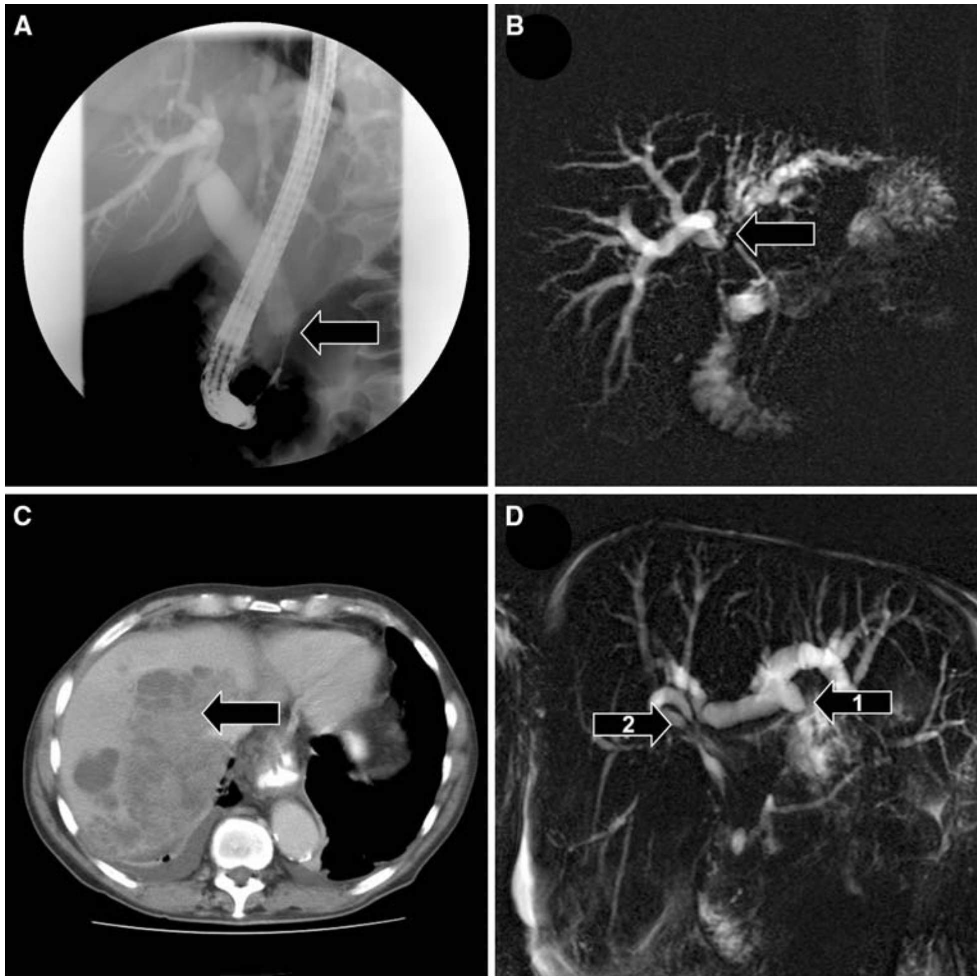

Fig. 1 Clinical examples of malignant obstructive jaundice. (**a**) ERCP image demonstrating distal common bile duct (CBD) stricture (*block arrow*) in a patient initially thought to have choledocholithiasis on pre-operative imaging. (**b**) MRCP of patient demonstrating hilar stricture (*block arrow*) with proximal biliary dilatation and normal CBD caliber. (**c**) Patient re-presenting with jaundice following ERCP for pancreatic cancer. The jaundice was thought to be due to liver dysfunction secondary to liver replacement (*block arrow*). (**d**) Recurrence of distal cholangiocarcinoma following pylorus-preserving pancreaticoduodenectomy. Multiple strictures were found, including at the hepaticojejunostomy (*block arrow 1*) and segmental ducts on right (*block arrow 2*)

suggesting that the left hepatic duct should be preferentially stented, it has been previously shown that drainage of the most technically accessible system will achieve adequate palliation in over 80% of patients [7].

Authors supporting multiple stent placements for hilar strictures claim that if a second procedure is required after unilateral stenting, there is an increased risk of septic complications, with a concomitant increase in mortality [8]. There are reports suggesting that multiples stents result in longer survival and better palliation [9]). When an endoscopic route is used for stent placement, injection of contrast agent into an hepatic segment without adequate subsequent drainage results in bacterial contamination of stagnant bile and resultant cholangitis [8]. It is unclear if this situation also holds true for percutaneous placement of stents [10]. For uncomplicated hilar strictures, one stent is probably sufficient, unless two stents can be inserted with ease. With more complex strictures, the potential benefits of multiple stent placements must be weighed against the technical difficulty of the procedure and increased costs. A significant proportion of patients with grade III–IV bismuth strictures (strictures extending up into the right/left or both secondary hepatic ducts) will not achieve significant decompression with stent placement, secondary to ‘sub-segmentalisation’ of the liver (Fig. 1). In addition, such patients with advanced disease may also demonstrate loss of inflow to areas of the liver (due to portal vein occlusion), leading to areas of atrophy; further compounding their hepatic dysfunction. In such cases, heroic attempts at biliary decompression may not be in the patient’s best interests and should be undertaken cautiously.

Historical Overview

Surgical Bypass

Initially, surgery was the mainstay of treatment for patients with obstructive malignant jaundice. Treatment options for distal CBD strictures range from definitive procedures, such as choledochojejunostomy (either alone or combined with a prophylactic gastrojejunostomy) to choledochoduodenostomy [11], cholecystojejunostomy [12], cholecystogastrojejunostomy [13], cholecystotomy [14], or insertion of T-tubes to obtain bile drainage [15]. The latter techniques have fallen largely from favor, although cholecystojejunostomy has enjoyed a resurgence with the advent of laparoscopic biliary bypass [16, 17]. For hilar strictures, an intrahepatic duct anastomosis may be employed as a palliative procedure. These include the formation of a biliary–enteric anastomosis using ducts from either segment III or IV (segment III or segment IV bypass), or from peripheral ducts passing through segment VI (right intrahepatic bypass) [18, 19]. Other single reports are present in the literature that describe the use of Dacron bypass grafting [20] and even peritoneovenous shunt pumps [21].

Palliative Resection

Recorded mortality rates following pancreaticoduodenectomy used to be as high as 25% [22–24], and, for these reasons, biliary bypass (with its lower mortality rate and zero risk of pancreatic leakage) was employed as palliation for distal CBD strictures. However, sub-specialization and improved experience in hepatobiliary surgery within high-volume centers have greatly reduced the attendant morbidity and mortality. For this reason, some centers would advocate resection in patients with pancreatic tumors, on the basis that if not curative, it offers good palliation. Pancreaticoduodenectomy undertaken as a palliative procedure has been shown to result in improved survival rates when compared with those of surgical bypass (12 months versus 9 months) [25]. However, this practice is not widespread, and its applicability for unresectable hilar lesions is unknown and probably limited.

Radiologic Advances

External biliary drainage was the first non-surgical technique described for malignant obstructive jaundice [26]. Early reports consisted predominantly of internal–external drainage catheters passing though the strictured bile duct and into the duodenum [26]. These early radiological drainage procedures were invaluable for patients who were too frail for definitive surgery and had some role in prolonging survival. Disadvantages of exteriorization of bile include pain, dislodgment of drainage catheters, and bile and ascitic fluid leakages from around the puncture sites, with associated volume depletion from this high-output drainage [27–29]. The development of long-lasting internal endoprostheses greatly improved quality of life and patient mobility following decompression [30]. Although external drainage is still used as a temporary measure in patients suffering sepsis from cholangitis, the establishment of a more permanent internal stent is now the goal of treatment. Procedure-related complications, from the method of stent placement, include sepsis from bile leakage, biliary peritonitis, intra-abdominal collections, fistula formation, pain, and duodenal perforation [9, 27–29, 31].

Endoscopic Retrograde Cholangiopancreatography

Endoscopic cannulation of the ampulla of Vater was first described in 1968, and, since that time, ERCP has become rapidly established as a valuable diagnostic and therapeutic technique [32]. It is now widely used in the palliation of malignant obstructive jaundice, and a combination of either metal or plastic stents can be deployed endoscopically. In cases where retrograde navigation of a malignant stricture with a guidewire cannot be attempted, then a combined or rendezvous procedure can be undertaken. In this procedure a percutaneous radiologic guidewire can be passed across the strictures, with endoscopic cannulation over this [33, 34]. Complications from ERCP include cholangitis, perforation, bleeding, fistulae, and acute pancreatitis [35–39].

Types of Biliary Endoprostheses and Stent Survival

Plastic Stents

Typical materials used in the composition of plastic stents include Teflon, Percufex, polyethylene, and polyurethane [40, 41]. Plastic stents are prone to early occlusion secondary to bacterial colonization and development of a biofilm over their internal surface [42]. Precipitation of bile (secondary to bacterial colonization) results in encrustation over the internal surfaces of stents, and narrows the lumen [43]. An increase in stent diameter of 0.2 mm results in a three-fold increase in the rate of bile flow [44], and so, if one presumes the reverse to be true, the decreased rate of bile flow secondary to stent narrowing further encourages precipitation of bile salts. The composition of the bile draining through the stent may also be a factor; sludge within bile increases its viscosity and causes early stent failure in up to 30% of plastic stents [45].

Plant fibers from duodenal reflux may also become incorporated into the intraluminal precipitation and further contribute to stent clogging [46]. Microscopic irregularities on the internal surfaces of stents have been shown to enhance precipitation, and attempts have been made to develop coatings which impede colonization by bacteria. These include hydrophilic polymer-coated polyurethane stents, silver-coated stents, and linings bonded with antimicrobial agents [47–50]; however, data regarding the clinical efficacy of such modifications are lacking.

In addition, the use of systemic prophylactic antibiotics has also been postulated as a method of prolonging stent patency. In vitro studies have demonstrated that quinolones such as ciprofloxacin are able to achieve high concentrations within bile and reduce bacterial adhesion [51]. Systemic antibiotic prophylaxis has been combined with ursodeoxycholic acid (USD) in a further attempt to prolong patency rates of plastic stents. USD is a bile-modifying agent, used in the treatment of primary biliary cirrhosis and occasionally indicated in the treatment of cholesterol-predominant gallstones. A Cochrane review of the combined use of systemic antibiotics and USD failed to demonstrate any improvement in stent duration following such treatment with a combination of the two, or of each agent used alone [52]. Since disruption of the sphincter of Oddi (by passage of a stent across it) allows the ascension of micro-organisms (with subsequent colonization of the endoprosthesis), it may be feasible to reduce bacterial colonization by positioning stents above the sphincter, thus allowing it to function normally. There are clinical data that suggest that stents positioned in this manner have longer patency rates and lower failure rates; however, the numbers of patients in this study were very small ($n = 16$) [53].

The only factor that has been consistently shown to reduce encrustation and prolong patency of plastic stents is its internal diameter [54, 55]. The typical size of plastic stents varies from 7 Fr to 10 Fr [40, 41]; however, stents of up to 14 Fr may be employed. The insertion of these stents is limited by the trauma of insertion and discomfort when positioned endoscopically. A further consideration is that there are few duodenoscopes that can accept stents over 12 Fr in diameter. When a radiologic route is used, the larger track size required trans-hepatically may significantly increase the risk of bleeding and bile leak after insertion.

The risk of stent occlusion increases over the period of time following insertion. For this reason, many centers employing plastic stents as palliation will undertake routine stent changes at intervals of 3 months or greater. Stent migration can also be a problem, but it appears to be more common when used for benign biliary disease with a concomitant sphincterotomy. The use of multiple stents has been previously described for benign biliary conditions but not for malignant strictures (other than hilar strictures) [56, 57]. Having additional stents in situ increases the functional diameter for biliary drainage and may also allow free drainage of bile from around the stents, should one occlude. The authors of this review, who undertake ERCP for palliation of obstructive jaundice, will frequently insert multiple stents for this reason. Data collection is currently in progress to determine if this policy prolongs median patency rates.

Metal Stents

Patency rates of plastic stents fueled the development of metal stents which are self-expanding, allowing their deployment over a narrow track if done percutaneously, or via standard delivery systems if positioned endoscopically. The internal diameter of a metallic stent when fully expanded can be up to three-times greater than that of a standard plastic prosthesis. Other purported advantages are that metal stents become covered by biliary epithelial cells and so are incorporated into the bile wall, reducing the risk of migration [31] (but also precluding their use for benign conditions), and that spaces between the supporting struts of metal stents allow further drainage of bile between them. This feature may be of particular value in allowing bilateral decompression of the biliary tree when stents are utilized for hilar strictures [29]. The main thrust behind the evolution of metal stents is the larger internal diameter, which should, in theory, increase long-term patency rates.

There are several designs of metallic stents, with variations in diameter of the expanded stent (10 mm to 12 mm), the diameter of their delivery system (7 Fr to 12 Fr) length of stent, and wall thickness [31, 58]. The most common type in use is the Wallstent, made of cobalt alloy with a fully expanded diameter of 30 Fr and delivery stems of 7 Fr [58]. The major drawback to the use of metallic stents is their price, metallic stents being 15–40 times dearer than plastic stents [59]. It can be argued that greater initial 'outlay' costs are made up for by longer survival, greater patency rates, and reduced need for re-intervention, and these considerations will be assessed further, later on in this review.

Covered Metal Stents

Whilst displaying a possible greater resistance to early occlusion than plastic stents, metallic stents can still become blocked, the mechanism for this being tumor ingrowth around and into the spaces between the metal lattice in the stent side-wall. In an attempt to counteract this problem silicone-lined stents have been designed to occlude the inter-strut spaces. In a further advance on this, covered stents with linings bounded to cytotoxic agents, such as paclitaxel, are also now available for clinical use, although there are no significant data regarding their efficacy in humans [60]. One may surmise that potential advantages gained in longer patency from such covered stents may only be fully realized for distal malignant strictures, since the loss of inter-strut spaces may impede drainage of hilar lesions.

Treating Stent Occlusion

Plastic stent occlusion, when it does occur, is relatively easily treated by repeat endoscopy and re-insertion of another metallic/plastic stent. If an endoscopic approach is no longer possible, due to duodenal compression from an advanced malignancy, then a percutaneous insertion of the stent can be employed. Occlusion of metal stents can be more problematic, since the stent cannot easily be removed after insertion and the unblocking of such stents usually requires the re-establishment of a lumen with the blocked stent in situ. Techniques described include balloon trawling of the stent endoscopically [43], and insertion of a plastic endoprosthesis or re-insertion of a second metallic stent thought the lumen of the occluded stent [43, 61]. Of these methods, it has been reported that re-insertion of a further stent, in particular a metal stent, offers the best chance of successful re-canalization [62].

Stent-Related Complications

Irrespective of the techniques employed to deploy biliary endoprosthesis, the stents themselves may also cause complications and contribute to post-procedure morbidity. Plastic stents have been reported to cause duodenal perforation by being incorrectly placed at the time of procedure, with the result that the mechanical force exerted by the tip of the plastic stent against duodenal intestinal mucosa causes necrosis over time. Inflexibility or a stent of an incorrect length may also lead to pressure necrosis [63, 64]. Perforations may also occur secondary to stent migration. Case reports exist of stents causing colovaginal fistulae [65], colovesical fistulae [65], colocutaneous fistulae [66], perforations within parastomal hernia [67], or other incarcerated herniae [68], perforations of sigmoid diverticulae [69], and small bowel perforations, usually involving the distal ileum [70–72]. In many of these cases, stent perforation occurs within the presence of other, unrelated, bowel abnormalities, including colonic diverticulae and abdominal wall herniae. Although the migration of metallic stents is less common, it may still occur in up to 6% of cases [73]. Stent fracture has been reported [74], and acute pancreatitis, duodenal perforation, upper gastrointestinal bleeding [75], and even air embolism [76], have been reported following metallic stent deployment.

Which Palliation to Choose?

The relative merits, cost benefits, and palliative efficacy of surgery versus endoscopic stenting, or percutaneous stenting, has been the subject of numerous systematic reviews and randomized controlled trials. A review of all English-language studies comparing surgery versus stents; endoscopic versus percutaneous placement of stents; plastic versus metal stents, and covered metal stents versus uncovered metal stents, was undertaken. Manuscripts included were retrospective cohort studies and randomized controlled trials. Main outcome measures were stent patency, survival, mortality, and morbidity. Secondary outcome measures were quality of life and cost effectiveness. Where possible, data regarding hilar and malignant structures were considered separately.

Surgery Versus Stents

Tables 1 and 2 summarize procedures and cost data for studies comparing surgery versus stenting for malignant jaundice [77–87]. Of the studies reviewed, five were randomized controlled trials. All studies, with the exception of those by Artifon et al. [82] and Maosheng et al. [87] compared plastic endoprosthesis with surgery. Only one study was found that compared surgery with stenting for the management of hilar strictures [83], the remainder of the studies including only patients with distal CBD occlusion. The most common pathologic condition for distal CBD strictures was pancreatic adenocarcinoma. The study by McGrath et al. [85] was the only one found to compare percutaneous stent insertion alone, rather than the endoscopic route, with surgical bypass.

A Cochrane meta-analysis of three of the randomized controlled trials (RCTs) included in Tables 1 and 2 (Anderson et al., Smith et al., and Shepard et al.) found no differences in therapeutic success between stenting and surgery, with a trend toward a reduced risk of immediate complications following stenting [59]. The relative risk of late biliary obstruction was greater for stenting than for bypass ($P < 0.00001$) [59]. The majority of studies reviewed reported longer in-patient admissions following surgery, which was associated with higher cost (even when later admissions for stent changes and stent-related complications were included). In keeping with the Cochrane review, the majority of studies in Table 2 suggested a higher degree of late readmissions following stenting than following surgery, although in many of the studies it was not made clear if these differences were statistically significant.

Although technical success following surgery was good (ranging from 70% to 100%), surgical techniques varied across the studies and even within individual studies. The lower values for technical success rate are unusual and may be accounted for by some centers undertaking cholecystjejunostomies as drainage procedures. A retrospective analysis of 218 patients with pancreatic cancer fond that only 20% of the patients had cystic ducts suitably placed and/or patent to allow such a procedure to be successful [88]. Only one study ([83]) reported better survival following bypass than following stenting. As yet unpublished data from Leicester, UK, retrospectively comparing survival of patients matched for pancreatic tumor stage, also suggest that biliary bypass may result in prolonged survival when compared with stenting. However, these data must be interpreted with caution, since patient suitability for operative intervention will almost certainly contribute to such survival advantages.

Table 1 Comparisons of success rates, morbidity, mortality and long-term survival between surgical bypass and stenting for malignant obstructive jaundice

Procedure efficacy and complications

Name	Study type	Year	Stricture		Number of patients		Success rate (%)		(Early) complications (%)		Mortality (%)		Survival time (months)	
			Hilar	Distal	Stent	Bypass	Stent	Bypass	Stent	Bypass	Stent	Bypass	Stent	Bypass
Connor et al. [83]	Prosp	2007	233	–	205	20	–	–	23.4	30	9.3	0	**4.9***	**16.3***
Artifon et al. [82]	RCT	2006	–	30	15	15	100	100	33	47	0	0	**5.8**[a]	**7.2**[a]
Maosheng et al. [87]	Retro	2001	–	60	19	41	100	100	**5***	**22***	5	0	6.6	7.5
Raikar et al. [81]	Prosp	1996	–	66	34	32	–	–	21	33	2.9	3.5	No difference	
van de Bosch et al. [86]	Retro	1994	–	107	63	44	95.2	93.2	–	–	13.6	12.7	4.7	5.5
Smith et al. [80]	RCT	1994	–	104	101	103	92.2	93.1	**11.0***	**28.7***	**3.0***	**13.9***	5.3	6.5
Anderson et al. [77]	RCT	1989	–	50	25	25	98	94	30	20	0.1	0.1	3.0	3.6
McGrath et al.[85]	Retro	1989	–	73	21	52	81	100	33	15	33	0	4.0	7.0
Shepard et al. [84]	RCT	1988	–	48	23	25	82	92	7	14	9	20	5.5	4.5
Bornman et al. [78]	RCT	1986	–	50	25	25	84	76	28	32	8	20	4.8	3.8
Leung et al. [79]	Retro	1983	–	–	64	34	–	–	21.0	33.0	3.0	4.0	–	–

* Statistically significant ($P < 0.05$)

[a] Approaching significance

– Data not available from manuscript

RCT randomized controlled trial

Retro retrospective study

Prosp prospective study

Values of interest within the table are shown in bold type

Table 2 demonstrates that up to 25% of patients undergoing endoscopic treatment of their malignant jaundice proceeded to develop gastric outlet obstruction. A major advantage to the undertaking of a biliary bypass is the option of prophylactic gastrojejunostomy to obviate such future problems. A recent RCT examining the need for prophylactic gastrojejunostomy found that it significantly reduced the risk of subsequent gastric outlet obstruction without increasing complication rates [89]. At present there are no studies comparing laparoscopic biliary bypass with endoscopic or trans-hepatic non-surgical drainage. It remains to be seen what impact laparoscopic bypass will have.

One can surmise from the data presented that non-surgical palliation can be achieved with a similar technical success to that of surgical bypass, at cheaper cost and with a trend toward a lower risk of short-term complications. However, surgical bypass would appear to provide better long-term palliation in patients, both in terms of prevention of recurrent jaundice and by including a prophylactic gastrojejunostomy to prevent future gastric outlet obstruction. Hence, a biliary endoprosthesis should, perhaps, be reserved for those patients with a shorter expected survival time. The cut-off point in survival time that determines which of these two treatment modalities should be used has often been quoted as 6 months [86, 87, 90]. Other determinants of poor survival rates include the presence of peritoneal or liver metastases and a low Karnofsky index of performance [91]. These considerations could be useful in selecting the appropriateness of cases for bypass procedures versus endoscopic stenting.

Endoscopic Placement Versus Percutaneous Placement of Stents

There are relatively few comparisons of endoscopic deployment of stents versus the trans-hepatic method. Table 3 summarizes the data [28, 92–95]. It is generally perceived that trans-hepatic drainage carries a higher risk of morbidity than does endoscopic drainage, with four of the five studies reviewed demonstrating this, although only one study by Speer et al. found this difference to be statistically significant. In addition, there is a suggestion that trans-hepatic drainage might also incur a higher mortality rate than would endoscopic drainage. Both endoscopic and trans-hepatic methods of stent placement carry a higher risk of cholangitis and other complications than does percutaneous drainage alone [93]. Hence, percutaneous drainage (whilst not a definitive solution to malignant jaundice) still has a role to play in the patient whose condition is unstable and who requires emergency decompression of the biliary tree.

Table 2 Cost, hospital stay and long-term success from surgical bypass versus stenting for malignant obstructive jaundice

Cost and resource utilization

Name	Study type	Year	Stricture (%)		Hospital stay (days)		Readmission or recurrent jaundice (%)		Patency (%)		Cost		Gastric outlet obstruction (%)	
			Hilar	Distal	Stent	Bypass	Stent	Bypass	Stent	Bypass	Stent	Bypass	Stent	Bypass
Connor et al. [83]	Prosp	2007	233	–	–	–	37.7	29.4	–	–	–	–	–	–
Artifon et al. [82]	RCT	2006	–	30	**2**[a]	**9**[a]	**26**[a]	**40**[a]	–	–	**$4,271***	**$8,321***	–	–
Maosheng et al. [87]	Retro	2001	–	60	**21***	**32***	**42***	**10***	–	–	**¥14,50912***	**¥24,13181***	–	–
Raikar et al. [81]	Prosp	1996	–	66	**7***	**14***	35.3	25	–	–	**$9,663***	**$18,325***	3	0
van de Bosch et al. [86]	Retro	1994	–	107	**27.3***	**42.8***	1.7	2.0	–	–	–	–	–	–
Smith et al. [80]	RCT	1994	–	104	19	26	**36.0**[a]	**1.0**[a]	–	–	–	–	25.2	9.7
Anderson et al. [77]	RCT	1989	–	50	26	27	–	–	–	–	–	–	0	0
McGrath et al. [85]	Retro	1989	–	73	13	12	**16**[a]	**4**[a]	–	–	–	–	–	–
Shepard et al. [84]	RCT	1988	–	48	**8***	**13***	**43**[a]	**21**[a]	–	–	–	–	9	4
Bornman et al. [78]	RCT	1986	–	50	**18***	**24***	**38**[a]	**16**[a]	–	–	–	–	14.3	0
Leung et al. [79]	Retro	1983	–	–	**14***	**30***	13	9	5% occlusion	3% occlusion	–	–	3	6

* Statistically significant ($P < 0.05$)

[a] Not stated in text if statistically significant, but marked difference in values noted

– Data not available from manuscript

RCT randomized controlled trial

Retro retrospective study

Prosp prospective study

Values of interest within the table are shown in bold type

Table 3 Comparisons of success rates, morbidity, cost, hospital stay, survival, long-term success and mortality between endoscopic and percutaneous deployment of stents

Procedure efficacy and complications

Name	Study type	Year	Number of patients		Stricture		Success rate (%)		(Early) complications (%)		Mortality (%)		Survival (months)	
			Perc	Endo	Hilar	Distal	Perc	Endo	Perc	Endo	Perc	Endo	Perc	Endo
Lee et al. [93]	Retro	2007	34	34	68	–	97.1	79.4	50	38.2	0	1.5	–	–
Pinol et al. [94]	RCT	2002	26	28	31	22	**75***	**58***	**61**	**35**	36	42	**3.7***	**2.0***
Hall et al.** [92]	Retro	1989	19	19	–	–	58	79	**47**[a]	**26**[a]	26	21	2.3	2.5
Speer et al. [28]	RCT	1987	36	39	29	46	76	89	**67***	**19***	**33***	**15***	3.1	4.3
Stanley et al. [95]	Retro	1986	34	24	Includes benign disease		98	92	30	25	**32**	**4**	4.8	3.3

Cost and resource utilization

Name	Study type	Year	Number of patients (%)		Hospital stay (Days)		Readmission or recurrent jaundice (%)		Stent patency (days)		Cost	
			Perc	Endo	Perc	Endo	Perc	Endo	Perc	Endo	Perc	Endo
Lee et al. [93]	Retro	2007	34	34	–	–	–	–	**180***	**120***	–	–
Pinol et al. [94]	RCT	2002	26	28	15.8	15.4	43	54	34% risk reduction of recurrent jaundice with percutaneous stent		$6,368	$4,767
Hall et al.** [92]	Retro	1989	19	19	–	–	–	–	–	–	–	–
Speer et al. [28]	RCT	1987	36	39	17	11	11.1	23.1	80 to 186	170	–	–

* Statistically significant ($P < 0.05$)

** Comparison of percutaneous against percutaneous and endoscopic combined (rendezvous procedure)

[a] Cholangitis within 1 week of presentation

Perc percutaneous approach

Endo endoscopic approach

RCT randomized controlled trial

Retro retrospective study

Prosp prospective study

Values of interest within the table are shown in bold type

Table 4 Comparisons of success rates, morbidity, mortality, and long-term survival between metal and plastic stenting for malignant obstructive jaundice

Procedure efficacy and complications

Name	Study type	Year	Number of patients		Stricture		Method of stent insertion		Success rate (%)		(Early) complications (%)		Mortality (%)	
			Plastic	Metal	Hilar	Distal	Perc	Endo	Plastic	Metal	Plastic	Metal	Plastic	Metal
Soderlund et al. [96]	RCT	2006	51	$49_{covered}$	–	100	All endoscopic		98.0	95.9	3.9	4.1	2.0	0
Pinol et al. [94]	RCT	2002	26	28	31	22	26	28	**58***	**75***	35	61	42	36
Prat et al. [101]	RCT	1998	33_{PRN} 34_{REG}	34	– –	–	All endoscopic		No differences between groups					
Schmassmann et al. [99]	Retro	1996	70	95	–	–	All endoscopic		88	95	–	–	2	3
Wagner et al. [97]	RCT	1993	9	11	20	0	Rendezvous procedure		88.9	100	**33.3**[a]	**9.1**[a]	0	0
Knyrim et al. [98]	RCT	1993	31	31	–	–	Endoscopic/ rendezvous		100	100	**36***	**15***	0	0
Davids et al. [100]	RCT	1992	56	49	–	–	All endoscopic		95	96	11	12	**4***	**14***

* Statistically significant ($P < 0.05$)

[a] Not stated in manuscript if statistically significant

– Data not available from manuscript

Perc percutaneous approach

Endo endoscopic approach

covered covered metal stent

PRN plastic stent changed as needed (when blocked)

REG Plastic stent changed regularly

RCT randomized controlled trial

Retro retrospective study

Prosp prospective study

Values of interest within the table are shown in bold type

Pinol et al. reported higher success rates with trans-hepatic drainage than with endoscopic means, a finding reflected by Lee et al. some years later [93, 94]. However, in the former study, all the trans-hepatic procedures involved self-expanding metal stents (and, in the paper by Lee et al., it was acknowledged that metal stents were more frequently deployed when the trans-hepatic route was used). The predominance of metal stent usage trans-hepatically, may explain the higher success rates and longer patency rates described in these studies. With increasing complexity of hilar strictures (Bilroth type IV), a percutaneous trans-hepatic technique of stent deployment may confer better long-term patency as shown by Lee et al. [93]. At present, endoscopic drainage is frequently described as the preferred choice in achieving biliary decompression and may offer a lower risk than the trans-hepatic method. It must be stressed, however, that there is a lack of comparative studies between the two techniques. Trans-hepatic drainage should certainly be considered in those patients whose endoscopic drainage fails, either alone or in the setting of a combined endoscopic/radiologic rendezvous procedure.

Metal Versus Plastic Stents

All bar one of the studies reviewed found metal insertion to result in a longer patency time, with reduced risk of recurrent jaundice when compared with plastic endoprostheses (Table 4) [94, 96–101]. A Cochrane review found no significant differences between technical success rates, survival or complications between metal and plastic stents, but confirmed that metal stents had a reduced relative risk for recurrent biliary obstruction [59]. Whilst initial costs for metal stent insertion were greater than when plastic stents were used, many studies found that overall costs (after the inclusion of repeat ERCP and re-stenting) were comparable and occasionally lower in those patients undergoing insertion of metal stents [94, 97, 98, 101]. Prat et al. are unique in that they compared ERCP and repeat-plastic stenting on an ad hoc basis, ERCP and regular changes of stents with metal stent insertion [101]. They found that symptom-free survival times were comparable between the latter two groups, suggesting that regular ERCP and change of stent might achieve as good a control of symptoms as metal stents would. In the long term, this approach was found to be more costly [101], and, one may surmise, would have a greater impact on a patient's quality of life than would metal stenting alone. With the present evidence it would appear that metal stents confer significant advantages in maintaining longer-term patency of the biliary tree, with equivalent rates of morbidity, mortality and success to those of a plastic endoprosthesis. The initial cost of deployment is greater with metal stents, but this initial expenditure may be offset by reduced post-procedure re-admissions and necessitated changes of stent. These savings, however, are only appreciable if the patient's survival is for longer than 6 months [101].

Covered Metal Versus Uncovered Metal Stents

At present there are few studies comparing covered and uncovered metal stents. Two of the three studies reviewed reported that covered metal stents were associated with a significantly longer patency than uncovered stents (Table 5) [102–104]. All studies reported a higher rate of stent migration and higher rate of acute cholecystitis with covered stents [102–104]. The higher rate of acute cholecystitis with covered stents is presumably secondary to occlusion of the cystic duct by the stent side-wall. This feature of covered stents may also reduce their efficacy in the management of hilar strictures, because the side covering could prevent adequate drainage of intrahepatic ducts. Whilst the covering prevents tumor in-growth, it may also reduce the ability of the stent to 'bed' into the epithelial lining of the bile duct and contribute to the increased risk of migration. In a report of endoscopic removal of covered and uncovered metal stents, the presence of a stent covering was the only factor predictive of successful stent extraction [105].

Photodynamic Therapy

Photodynamic therapy is a method that produces tissue necrosis, using laser therapy in conjunction with a photosensitizer. A photosensitizing agent is employed, which accumulates in proliferating tissue. Following illumination with a laser, free radicals are generated, resulting in necrosis and apoptosis of cells [106]. Tissue necrosis is typically achieved at a depth of 4–6 mm, and the destructive effect can be augmented by the delivery of systemic oxygen [106]. Photodynamic therapy can be used as primary therapy to control tumor growth and to prolong the patency rates of biliary endoprostheses.

There have been a number of studies, including a randomized controlled trial, which showed an increase in median survival time from 98 days to 493 days following photodynamic therapy [107–109]. Photodynamic therapy has been used to re-canalize blocked metal stents [110]. As discussed previously, recurrent biliary obstruction, and subsequent cholangitis secondary to stent failure, is a major cause of morbidity and limitation of survival time in patients with malignant jaundice. Hence, prolongation of stent patency may also have a significant impact on survival times.

Skin photosensitization is a major side effect of photodynamic therapy. A typical regimen following administration of the photosensitizer requires patients to be exposed to no more than 60 W of light for the first 24 h and to avoid external lighting for at least 1 week [110]. In addition, despite its potential efficacy, severe complications have been reported, including fatal liver abscesses and gallbladder empyemas [110]. A National Cancer Research Network multi-center randomized trial is presently underway (PHOTOSTENT 2), comparing photodynamic therapy and stenting with stenting alone for patients with advanced or metastatic cholangiocarcinoma. The results of this study should provide more data regarding the efficacy of this promising technique. However, at present, photodynamic therapy is not a widely adopted treatment for malignant jaundice.

Radiotherapy

Both intraductal brachytherapy and external beam radiotherapy have been evaluated in the management of advanced non-resectable cholangiocarcinoma. Data from external beam radiotherapy are limited to mostly retrospective studies involving small numbers of patients. In the context of extending stent patency, there is some evidence that external beam radiotherapy results in longer patency of metal stents, from 3.7 months to 9.8 months [111].

Intraluminal brachytherapy involves the use of iridium-192 seeds placed either percutaneously or endoscopically. [112, 113]. Intraluminal brachytherapy combined with external beam radiotherapy has been described as leading to complete resolution of biliary strictures; however ,recurrent stricturing is common, and, as a result, this treatment modality is usually used in combination with permanent insertion of a biliary endoprosthesis [114]. Intraluminal brachytherapy and stenting combined has been shown to increase stent patency and to prolong survival in hilar cholangiocarcinoma [115]. Stent patency rates of up to 14 months and 30 months have been reported with this technique for hilar and distal biliary strictures, respectively [116]. At present there are no randomized controlled trials comparing these therapies with stenting alone.

Table 5 Comparison between covered metal stents and uncovered metal stents in patients with malignant biliary obstruction

Procedure efficacy and complications

Name	Study type	Year	Number of patients		Method of stent insertion		Success rate (%)		(Early) complications (%)		Mortality (%)	
			Covered metal	Metal	Perc	Endo	Covered metal	Metal	Covered metal	Metal	Covered metal	Metal
Park et al. [104]	Retro	2006	98	108	Endoscopic		–	–	12.2	2.9	–	–
Yoon et al. [103]	Prosp	2005	36	41	Endoscopic		–	–	–	–	–	–
Isayama et al. [102]	RCT	2004	57	55	Trans-hepatic/endoscopic and rendezvous		100	100	14.0	5.5	1.8	1.8

Cost and resource utilization

Name	Study Type	Year	Numbers of patients		Survival time (months)		Patency		Cost	
			Covered metal	Metal	Covered metal	Metal	Covered metal	Metal	Covered metal	Metal
Park et al. [104]	Retro	2006	98	108	–	–	No difference in stent patency between covered and uncovered		–	–
Yoon et al. [103]	Prosp	2005	36	41	–	–	Stent patency significantly higher in covered group (398 versus 319 days)		–	–
Isayama et al. [102]	RCT	2004	57	55	9.1	8.5	Stent patency significantly higher in covered group (255 versus 237 days)		$3,901.3	$5129.1

– Data not available from manuscript

Perc percutaneous approach

Endo endoscopic approach

RCT randomized controlled trial

Retro retrospective study

Prosp prospective study

Conclusion

Effective and lasting palliation of malignant jaundice is a priority to achieve both quality of life and prolong survival. The exact method of palliation is determined by the patient's personal preferences, expected survival time, and location of stricture. For patients with distal biliary strictures, who have an expected survival period of greater than 6 months and suitable fitness, then surgical bypass should be considered with a prophylactic gastrojejunostomy. There is good evidence that metallic stents provide longer palliation than do plastic ones, with a cost benefit if patient survival is for longer than 6 months. Hence, metallic stents may be suitable alternatives for patients who are too infirm or unwilling to undergo surgical bypass. Plastic stents are appropriate for patients with limited survival times. Hilar strictures represent a unique management problem and may respond less well to palliation than distal occlusions. There are few comparative data favoring an endoscopic approach over percutaneous methods, but endoscopic stent placement appears to be safe and well tolerated and the favored route of stent insertion across all the studies reviewed. Adjuvant therapies, such as photodynamic therapy, intraluminal brachytherapy, and external beam radiotherapy, may further prolong stent patency, but published data (particularly in the form of randomized controlled trials) is lacking.

References

1. Andersson M, Kostic S, Johansson M, Lundell L, Astely M, Hellstrom M. MRI combined with MR cholangiopancreatography versus helical CT in the evaluation of patients with suspected periampullary tumours: a prospective comparative study. *Acta Radiol*. 2005;46:16–27. doi:10.1080/02841850510016018.
2. Saluja SS, Sharma R, Pal SPS, Chattopadhyay TK. Differentiation between malignant and benign hilar obstructions using laboratory and radiological investigations: a prospective study. *HPB*. 2007;9:373–382.
3. Acalovschi M. Cholangiocarcinoma: risk factors, diagnosis and management. *Rom J Intern Med*. 2004;42:41–58.
4. Bergasa NV. Medical palliation of the jaundiced patient with pruritis. *Gastroenterol Clin North Am*. 2006;35:113–123. doi:10.1016/j.gtc.2005.12.008.
5. De Palma GD, Pezzulo A, Rega M, et al. Unilateral placement of metallic stents for malignant hilar obstruction: a prospective study. *Gastrointest Endosc*. 2003;58:50–53. doi:10.1067/mge.2003.310.
6. Hintze RE, Abou-rebyeh HA, Adler A, Veltzke-Schlieker W, Felix R, Wiedenmann B. Magnetic resonance cholangiopancreatogoraphy-guided unilateral endoscopic stent placement for Klatskin tumours. *Gastrointest Endosc*. 2001;53:40–46. doi:10.1067/mge.2001.111388.
7. Polydorou AA, Chisholm EM, Romanos AA, et al. A comparison of right versus left hepatic duct endoprosthesis insertion in malignant hilar biliary obstruction. *Endoscopy*. 1989;21:266–271.
8. Chang WH, Kortan P, Haber GB. Outcome in patients with bifurcation tumours who undergo unilateral versus bilateral hepatic duct drainage. *Gastrointest Endosc*. 1998;47:354–362. doi:10.1016/S0016-5107(98)70218-4.
9. Barth KH. Percutaneous biliary drainage for high obstruction. *Radiol Clin North Am*. 1990;28:1223–1225.
10. Hii WJ, Gibson RN. Role of radiology in the treatment of malignant hilar biliary strictures 1: review of the literature. *Australas Radiol*. 2004;48:3–13. doi:10.1111/j.1440-1673.2004.01233.x.
11. DiFronzo LA, Egrari S, O'Connell TX. Choledochoduodenostomy for palliation in unresectable pancreatic cancer. *Arch Surg*. 1998;133:820–825. doi:10.1001/archsurg.133.8.820.
12. Hepp J. Place of palliative cholecystojejunostomy in therapy of inoperable duodenopancreatic cancers. *Gaz Med Fr*. 1951;58:985–989.
13. Hao C-Y, Su X-Q, Ji JF, Huang X-F, Xing BC. Stomach-interposed cholecystogastrojejunostomy: a palliative approach for periampullary carcinoma. *World J Gastroenterol*. 2005;11:2009–2012.
14. Nicoli N, Benati G, Mainette M, et al. Cholecystotomy and PTBD in the treatment of obstructive jaundice (a comparative study). *Chir Ital*. 1984;36:582–588.
15. Ono K, Hada R. Indirect cholangiojejunostomy using a latex T tube for palliation of obstructive jaundice. *Tohoku J Exp Med*. 1978;125:31–38.
16. Date RS, Siriwardena AK. Current status of laparoscopic biliary bypass in the management of non-resectable peri-ampullary cancer. *Pancreatology*. 2005;5:325–329. doi:10.1159/000086533.
17. O'Rourke RW, Lee NN, Cheng J, Swanstrom LL, Hansen PD. Laparoscopic biliary reconstruction. *Am J Surg*. 2004;187:621–624. doi:10.1016/j.amjsurg.2004.01.006.
18. Launois B, Jamieson GG. Moderative operative techniques in liver surgery. *Clin Surg Int*. 1993;18:94–97.
19. Suzuki S, Kurachi K, Yokoi Y, et al. Intrahepatic cholangiojejunostomy for unresectable biliary tumours with obstructive jaundice. *J Hepatobiliary Pancreat Surg*. 2001;8:124–129. doi:10.1007/s005340170034.
20. Osborne MP, Murray-Lyon IM, Reynolds K. Dacron bypass grafting in the relief of obstructive jaundice. *Lancet*. 1979;1:1323–1325. doi:10.1016/S0140-6736(79)91953-6.
21. Araki K, Kure M, Koboyashi M, Sugito M, Ogato T. A new method for palliation of malignant obstructive jaundice utilizing a peritoneo-venous shunt pump. *Hepatogastroenterology*. 1994;41:38–40.
22. Bergstrand O, Ahlberg J, Ewerth S, Hellers G, Holmstrom B. A retrospective study of carcinoma of the pancreas with special reference to the results of surgical treatment. *Acta Chir Scand Suppl*. 1978;482:26–28.
23. Hermreck AS, Thomas CY, Friesen SR. Importance of pathologic staging in the surgical management of adenocarcinoma of the exocrine pancreas. *Am J Surg*. 1974;127:653–657. doi:10.1016/0002-9610(74)90341-9.
24. Longmire WPJ, Longmire WPJ. The technique of pancreaticoduodenal resection. *Surgery*. 1966;59:344–352.
25. Lillemoe KD, Cameron JL, Yeo CJ, Sohn TA, Nakeeb A, Sauter PK. Pancreaticoduodenectomy Does it have a role in the palliation of pancreatic cancer? *Ann Surg*. 1996;223:718–725. doi:10.1097/00000658-199606000-00010.
26. Molnar W, Stockum AE. Relief of obstructive jaundice through a percutaneous transhepatic catheter: a new therapeutic method. *AJR Am J Roentgenol*. 1974;122:356–367.

27. Gunther RW, Schild H, Thelen M. Percutaneous transhepatic biliary drainage: experience with 311 patients. *Cardiovasc Intervent Radiol*. 1988;11:65–71. doi:10.1007/BF02577061.
28. Speer A, Cotton PB, Russell RC, et al. Randomized trial of endoscopic versus percutaneous stent insertion in malignant obstructive jaundice. *Lancet*. 1987;2:56–70.
29. Lameris JS, Stoker J, Nijs H. Malignant biliary obstruction: percutaneous use of self expandable stents. *Radiology*. 1991; 179:703–707.
30. Pereiras RV, Rheingold OJ, Huston D, et al. Relief of malignant obstructive jaundice by percutaneous insertion of a permanent prosthesis in the biliary tree. *Ann Intern Med*. 1978;89:589–593.
31. Lammer J. Biliary endoprosthesis; plastic stents versus metal stents. *Radiol Clin North Am*. 1990;28:1211–1235.
32. Cotton PB. ERCP over-view: a 30-year perspective. In: Cotton PB, Leung J, eds. *Advanced digestive endoscopy (ERCP)*. 1st edn. Oxford, Blackwell; 2005:1–10.
33. Dowsett JF, Vaira D, Hatfield AR, Cairns SR, Polydorou AA, Frost R. Endoscopic biliary therapy using the combined percutaneous and endoscopic technique. *Gastroenterology*. 1989;96: 1180–1186.
34. Shorvon PJ, Cotton PB, Mason RR, Sigel HJ, Harfield ARW. Percutaneous transhepatic assistance for duodenoscopic sphincterotomy. *Gut*. 1985;26:1373–1376. doi:10.1136/gut.26.12.1373.
35. Ferreira LE, Baron TH. Post-sphincterotomy bleeding: who, what, when and how? *Am J Gastroenterol*. 2007;102:2850–2855. doi:10.1111/j.1572-0241.2007.01563.x.
36. Bailey AA, Bourke MJ, Williams SJ, et al. A prospective randomized trial of cannulation technique in ERCP: effects on technical success and post-ERCP pancreatitis. *Endoscopy*. 2008; 40:296–301. doi:10.1055/s-2007-995566.
37. Wu HM, Dixon E, May GR, Sutherland FR. Management of perforation after endoscopic retrograde cholangiopancreatography (ERCP): a population-based review. *HPB*. 2006;8:393–399.
38. Etzel JP, Eng SC, Ko CW, et al. Complications after ERCP in patients with primary sclerosing cholangitis. *Gastrointest Endosc*. 2008;67:643–648. doi:10.1016/j.gie.2007.07.042.
39. Cotton PB, Rawlse Connor P, Romagnuolo J. Infection after ERCP, and antibiotic prophylaxis: a sequential quality-improvement approach over 11 years. *Gastrointest Endosc*. 2008;67:471–475. doi:10.1016/j.gie.2007.06.065.
40. Lammer J, Haussegger KA, Fluckiger F. Common bile duct obstruction due to malignancy: treatment with plastic versus metal stents. *Radiology*. 1996;201:167–172.
41. McLean GR, Burke DR. Role of endoprosthesis in the management of malignant biliary obstruction. *Radiology*. 1989;170: 961–967.
42. Groen AK, Out T, Huibregtse KK. Characterisation of content of occluded biliary endoprosthesis. *Endoscopy*. 1987;19:57–59.
43. Donelli G, Guaglianone E, Di Rosa R, Fiocca F, Basali A. Plastic biliary stent occlusion: factors involved and possible preventive approaches. *Clin Med Res*. 2007;5:53–60. doi:10.3121/cmr.2007.683.
44. Rey JF, Maupeti P, Greff M. Experimental study of biliary endoprosthesis efficiency. *Endoscopy*. 1985;17:145–148.
45. Huibregtse KK, Cheng J, Coene PPLO, Fockens P, Tytgat GNJ. Endoscopic placement of expandable metal stents for biliary strictures: a preliminary report with 33 patients. *Endoscopy*. 1989;21:280–282.
46. van Berkel AM, van Marle J, Groen AK, Bruno MJ. Mechanisms of biliary stent clogging: confocal laser scanning and scanning electron microscopy. *Endoscopy*. 2005;37:729–734. doi:10.1055/s-2005-870131.
47. Sung YY, Shaffer EA, Lam K, Rususka I, Costerton JW. Hydrophobic bile salt inhibits bacterial adhesion on biliary stent material. *Dig Dis Sci*. 1998;39:999–1006. doi:10.1007/BF02087551.
48. Rees EN, Tebbs SE, Elliott TS. Role of anti-microbial-impregnated polymer and Teflon in the prevention of biliary stent blockage. *J Hosp Infect*. 1998;39:323–329. doi:10.1016/S0195-6701(98)90298-5.
49. Leung JW, Lau GT, Sung JJ, Costerton JW. Decreased bacterial adherence to silver-coated stent material: an in vitro study. *Gastrointest Endosc*. 1992;38:338–340.
50. Jansen B, Goodman LP. D. R. Bacterial adherence to hydrophilic polymer-coated stents. *Gastrointest Endosc*. 1993;39: 670–673.
51. Leung J, Liu WY, Desta TD, Libby ED, Inciardi JF, Lam K. In vitro evaluation of antibiotic prophylaxis in the prevention of biliary stent blockage. *Gastrointest Endosc*. 2000;51:296–303. doi:10.1016/S0016-5107(00)70358-0.
52. Galandi D, Schwarzer G, Bassler D, Allgaier HP. Ursodeoxycholic acid and/or antibiotics for prevention of biliary stent occlusion. Cochrane Database Syst Rev. 2002;3:CD003043.
53. Uchida N, Tsutsui K, Ezaki T, et al. Estimation of the stent placement above the intact sphincter of Oddi against malignant bile duct obstruction. *J Gastroenterol*. 2005;40:291–296. doi:10.1007/s00535-004-1535-2.
54. Speer A, Cotton PB, Macrae KD. Endoscopic management of malignant biliary obstruction; stents 10 French gauge are preferable to stents eight French gauge. *Gastrointest Endosc*. 1988;34:412–417.
55. Kuvshinoff BW, Armstron JG, Fong Y. Palliation of irresectable hilar cholangiocarcinoma with biliary drainage and radiotherapy. *Br J Surg*. 1995;82:1522–1525. doi:10.1002/bjs.1800821122.
56. Pozsar J, Sahin P, Laszlo F, Topa L. Endoscopic treatment with sphincterotomy-associated distal common bile duct strictures by using sequential insertion of multiple plastic stents. *Gastrointest Endosc*. 2005;62:85–91. doi:10.1016/S0016-5107(05)00547-X.
57. Kuzela L, Oltman M, Sutka J, Hrcka R, Novotna T, Vavrecka A. Prospective follow-up of patients wit bile duct strictures secondary to laparoscopic cholecystotomy treated endoscopically with multiple stents. *Hepatogastroenterology*. 2005;52:1357–1361.
58. Laberge JM, Doherty M, Gordon RL, Ring EJ. Hilar malignancy: treatment with an expandable metallic transhepatic biliary stent. *Radiology*. 1990;177:793–797.
59. Moss AC, Morris E, MacMathuna P. Palliative biliary stents for obstructing pancreatic carcinoma. *Cochrane Collaboration*. 2006;2:1–32.
60. Suk KT, Kim JW, Kim HS, et al. Human application of a metallic stent covered with a paclitaxel-incorporated membrane for malignant biliary obstruction: a multicenter pilot study. *Gastrointest Endosc*. 2007;66:798–803. doi:10.1016/j.gie.2007.05.037.
61. Togowo O, Kawabe T, Isayama H, et al. Management of occluded uncovered metallic stents in patients with malignant distal biliary obstruction using covered metallic stents. *J Clin Gastroenterol*. 2008;42(5):546–549.
62. Bueno JT, Gerdes H, Kurtz RC. Endoscopic management of occluded biliary Wallstents: a cancer center experience. *Gastrointest Endosc*. 2003;58:879–884. doi:10.1016/S0016-5107(03)02309-5.
63. Smith FT, O'Connor HJ, Downing R. An endoscopic technique for stent recovery used after duodenal perforation by a biliary stent. *Endoscopy*. 1991;23:244–245.
64. Schuster D, Achong DW, Knox TA, Fawaz KA. Duodenal perforation by a biliary endoprosthesis: evaluation by hepatobiliary scintigraphy. *J Clin Gastroenterol*. 1992;15:177–179. doi:10.1097/00004836-199209000-00031.

65. Blake AM, Monga N, Dunn EM. Biliary stent causing colovaginal fistula: a case report. *JSLS*. 2004;8:73–75.
66. Figuerias RG, Echart MO, Figuerias AG, Gonzalez GP. Colocutaneous fistulae relating to the migration of a biliary stent. *Eur J Gastroenterol Hepatol*. 2001;13:1251–1253. doi:10.1097/00042737-200110000-00021.
67. Levey JM. Surgical Endoscopy. *Surg Endosc*. 2002;16:1636–1637. doi:10.1007/s00464-002-4506-9.
68. Mastorakos DP, Milman PJ, Cohen R, Goldenburg SP. An unusual complication of a biliary stent-small bowel perforation of an incarcerated hernia sac. *Am J Gastroenterol*. 1998;93:2533–2535.
69. Klein U, Weiss F, Wittkugel O. Migration of a biliary Tannebaum stent with perforation of a sigmoid diverticulum. *Rofo Fortschr Geb Rontgenstr Neuen BildgebVerfahr*. 2001;173:1057.
70. Mistry BM, Memon MA, Silverman R, Burton FR, Varma CR, Solomon H, et al. Small bowel perforation from a migrated biliary stent. Surg Endosc. 2001;15:1043.
71. Mofidi R, Ahmed K, Mofidi A, Joyce WP, Khan Z. Perforation of ileum: an unusual complication of distal biliary stent migration. *Endoscopy*. 2000;32:S67.
72. Baillie J, Mergener K. Gut perforation caused by biliary endoprosthesis. *Endoscopy*. 2000;32:738–739.
73. Manouras A, Archodovassilis F, Lagoudiankis EE, et al. Vertical rotation and impaction to the choledochal duct of a migrated biliary self-expanding metal stent. *Surg Laparosc Endosc Percutan Tech*. 2007;17:416–417.
74. Yoshida H, Mamada Y, Taniai N, et al. Fracture of an expandable metallic stent placed for biliary obstruction due to common bile duct carcinoma. *J Nippon Med Sch*. 2006;73:164–168. doi:10.1272/jnms.73.164.
75. Marano BJ, Bonanno CA. Metallic biliary endoprosthesis causing duodenal perforation and acute gastrointestinal bleeding. *Gastrointest Endosc*. 1994;40:257–258.
76. Rabe C, Balta Z, Wullner U, et al. Biliary metal stents and air embolism: a note of caution. *Endoscopy*. 2006;38:648–650. doi:10.1055/s-2006-925053.
77. Anderson JR, Sorenson SM, Kruse A, Rokkjaer M. Randomised trial of endoscopic endoprosthesis versus operative bypass in malignant obstructive jaundice. *Gut*. 1989;30:1132–1135. doi:10.1136/gut.30.8.1132.
78. Bornman PC, Harries-Jones EP, Tobias R, Stiegmann GV, Terblanche J. Prospective controlled trial of transhepatic biliary endoprosthesis versus bypass surgery for incurable carcinoma of head of pancreas. *Lancet*. 1986;1:69–71. doi:10.1016/S0140-6736(86)90719-1.
79. Leung JW, Emery R, Cotton PB, Russell RC, Vallon AG, Mason RR. Management of malignant obstructive jaundice at the Middlesex Hospital. *Br J Surg*. 1983;70:584–586. doi:10.1002/bjs.1800701006.
80. Smith AC, Dowsett JF, Russell RC, Hatfield AR, Cotton PB. Randomised trial of endoscopic stenting versus surgical bypass in malignant low bile duct obstruction. *Lancet*. 1994;344:1655–1660. doi:10.1016/S0140-6736(94)90455-3.
81. Raikar GV, Melin MM, Ress A, et al. Cost-effective analysis of surgical palliation versus endoscopic stenting in the management of unresectable pancreatic cancer. *Ann Surg Oncol*. 1996;3:470–475. doi:10.1007/BF02305765.
82. Artifon EL, Sakai P, Cunha JE, et al. Surgery or endoscopy for palliation of biliary obstruction due to metastatic pancreatic cancer. *Am J Gastroenterol*. 2006;101:2031–2037. doi:10.1111/j.1572-0241.2006.00764.x.
83. Connor P, Barron E, Redhead DN, et al. Palliation for suspected unresectable hilar cholangiocarcinoma. *Eur J Surg Oncol*. 2007;33:341–345. doi:10.1016/j.ejso.2006.11.005.
84. Shepard HA, Royle G, Ross AP, Diba A, Arthur M, Colin-Jones D. Endoscopic biliary endoprosthesis in the palliation of malignant obstruction of the distal common bile duct: a randomized trial. *Br J Surg*. 1988;75:11661–11668.
85. McGrath PC, McNeill PM, Neifild JP, et al. Management of biliary obstruction in patients with unresectable carcinoma of the pancreas. *Ann Surg*. 1989;209:284–288. doi:10.1097/00000658-198903000-00006.
86. van den Bosch RP, van der Schelling GP, Klinkenbijk JH, Mulder PGH, Blankenstein MV, Jeekel J. Guidelines for the application of surgery and endoprosthesis in the palliation of obstructive jaundice in advanced cancer of the pancreas. *Ann Surg*. 1994;219:18–24. doi:10.1097/00000658-199401000-00004.
87. Maosheng D, Ohtsuka T, Ohuchida J, et al. Surgical bypass versus metallic stent for unresectable pancreatic cancer. *J Hepatobiliary Pancreat Surg*. 2001;8:367–373. doi:10.1007/s005340170010.
88. Tarnasky PR, England RE, Lail LM, Pappas TN, Cotton PB. Cystic duct patency in malignant obstructive jaundice. *Ann Surg*. 1995;221:265–271.
89. Van Heek N, De Catro SM, va Eijck CH, et al. The need for a prophylactic gastrojejunostomy for unresectable periampullary cancer. *Ann Surg*. 2003;238:894–905. doi:10.1097/01.sla.0000098617.21801.95.
90. Sunpawervong S, Ovarlarnporn B, Khwo-ean U, Soontraprnchai P, Charoonratan V. Endoscopic stenting versus biliary bypass in advanced malignant bile duct obstruction: cost-effectiveness analysis. *Asian J Surg*. 2005;28:262–265.
91. Bakkevold KE, Kambstad B. Morbidity and mortality after radical and palliative pancreatic cancer surgery. *Ann Surg*. 1993;217:356–368. doi:10.1097/00000658-199304000-00007.
92. Hall RI, Denyer ME, Chapman AH. Palliation of obstructive jaundice with a biliary endoprosthesis. Comparison by insertion of the percutaneous-transhepatic and the combined percutaneous endoscopic routes. *Clin Radiol*. 1989;40:186–189. doi:10.1016/S0009-9260(89)80089-3.
93. Lee SH, Park JK, Yoon WJ, et al. Optimal biliary drainage for inoperable Klatskin tumour based on Bismuth type. *World J Gastroenterol*. 2007;13:3948–3955. doi:10.3748/wjg.13.6296.
94. Pinol V, Castells A, Bordas JM, et al. Percutaneous self-expanding metal stents versus endoscopic polyethylene endoprostheses for treating malignant biliary obstruction: randomized clinical trial. *Radiology*. 2002;225:27–34. doi:10.1148/radiol.2243011517.
95. Stanley J, Gobien RP, Cunningham J, Andriole J. Biliary decompression: an institutional comparison of percutaneous and endoscopic means. *Radiology*. 1986;158:195–197.
96. Soderlund C, Linder S. Covered metal stent versus plastic stents for malignant common bile duct stenosis: a prospective randomized, controlled trial. *Gastrointest Endosc*. 2006;63:986–995. doi:10.1016/j.gie.2005.11.052.
97. Wagner HJ, Knyrim K, Kose KJ. Plastic endoprostheses versus metal stents in the palliative treatment of malignant hilar biliary obstruction. A prospective randomized trial. *Endoscopy*. 1993;25:213–218.
98. Knyrim K, Wagner HJ, Pausch J, Vakil N. A prospective randomized controlled trial of metal stents for malignant obstruction of the common bile duct. *Endoscopy*. 1993;25:207–212.
99. Schmassmann A, von Gunten E, Knuchel J, Scheurer U, Fehr HF, Halter F. Wallstents versus plastic stents in malignant biliary obstruction: effects of stent patency of the first and second stent on patient compliance and survival. *Am J Gastroenterol*. 1996;91:654–659.
100. Davids PH, Groen AK, Rauws EA, Tytgat GNJ, Huibregtse KK. Randomised trial of self-expanding metal stents versus

polyethylene stent for distal malignant biliary obstruction. *Lancet*. 1992;340:1488–1492. doi:10.1016/0140-6736(92)92752-2.
101. Prat F, Chapat O, Ducot B, et al. A randomized trial of endoscopic drainage methods for inoperable malignant strictures of the common bile duct. *Gastrointest Endosc*. 1998;47:1–7. doi: 10.1016/S0016-5107(98)70291-3.
102. Isayama H, Komatsu Y, Tsujino T, et al. A prospective randomised study of "covered" versus "uncovered" diamond stents for the management of distal malignant biliary obstruction. *Gut*. 2004;53:729–734. doi:10.1136/gut.2003.018945.
103. Yoon WJ, Lee JK, Lee HK, et al. A comparison of covered and uncovered Wallstents for the management of distal malignant biliary obstruction. *Gastrointest Endosc*. 2006;63:996–1000. doi:10.1016/j.gie.2005.11.054.
104. Park Do H, Kim MH, Choi JS, et al. Covered versus uncovered wallstent for malignant extrahepatic biliary obstruction: a cohort comparative analysis. *Clin Gastroenterol Hepatol*. 2006;4:790–796. doi:10.1016/j.cgh.2006.03.032.
105. Familiari P, Buljaic M, Mutignani M, Lee LS, Spera G, Spada C. Endosopic removal of malfunctioning biliary self-expandable metallic stents. *Gastrointest Endosc*. 2005;62:903–910. doi: 10.1016/j.gie.2005.08.051.
106. Stern N, Sturgess R. Endoscopic therapy in the management of malignant biliary obstruction. *Eur J Surg Oncol*. 2008;34:313–317. doi:10.1016/j.ejso.2007.07.210.
107. Zoepf T, Jakobs R, Arnold JC, Apel D, Riemann JF. Palliation of nonresectable bile duct cancer: improved survival after photodynamic therapy. *Am J Gastroenterol*. 2005;100:2426–2430. doi:10.1111/j.1572-0241.2005.00318.x.
108. Ortner MA, Leibruth J, Schreiber S. Photodynamic therapy of nonresectable cholangiocarcinoma. *Gastroenterology*. 1998; 114:536–542. doi:10.1016/S0016-5085(98)70537-2.
109. Harewood GC, Baron TH, Rumalla A. Pilot study to assess patient outcomes following endoscopic application of photodynamic therapy for advanced cholangiocarcinoma. *J Gastroenterol Hepatol*. 2005;20:415–420. doi:10.1111/j.1440-1746.2005.03582.x.
110. Pereira S, LAyaru L, Rogowska A, Mosse A, Hatfield AR, Bown SG. Photodynamic therapy of malignant biliary strictures using meso-tetrahydroxyphenylchlorin. *Eur J Gastroenterol Hepatol*. 2007;19:479–485. doi:10.1097/MEG.0b013e328013c0bd.
111. Schinchi H, Takao S, Nishida H, Aikou T. Length and quality of survival following external beam radiotherapy combined with expandable metallic stents for unresectable hilar cholangiocarcinoma. *Gut*. 2000;39:852–855.
112. Venu RP, Geenen JE, Hogan WJ. Intraluminal radiotherapy for biliary tract malignancy: an endoscopic approach. *Gastrointest Endosc*. 1987;33:236–237.
113. Ikeda H, Kuroda C, Uchida E. Intraluminal radiotherapy with iridium-192 wires for extrahepatic bile duct carcinoma: a preliminary report. *Nippon Igaku Hoshasen Gakkai Zasshi*. 1979;25:1256–1358.
114. Ishii F, Furuse J, Nagase M. Relief of jaundice by external beam radiotherapy and intraluminal brachytherapy in patients with extrahepatic cholangiocarcinoma: results without stenting. *Hepatogastroenterology*. 2004;51:954–957.
115. Kubota Y, Takaoka M, Kinekawa F, et al. Endoscopic irrigation and parallel arrangements of Wallstents for hilar cholangiocarcinoma. *Hepatogastroenterology*. 1998;45:415–419.
116. Bruha R, Petrtyl J, Kubecova M, et al. Intraluminal brachytherapy and self-expandable stents in nonresectable biliary malignancies the question of long-term palliation. *Hepatogastroenterology*. 2001;48:631–637.