TUMORS AT THE BILIARY CONFLUENCE — HOW TO CHOOSE BETWEEN EXTERNAL DRAINAGE, ENDOPROSTHESES, STENTS, AND RADIATION

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OBJECTIVES:

1. To review the surgical, endoscopic, and percutaneous (interventional) management of bifurcation lesions from the perspective of a multidisciplinary "team" approach.
2. To review the etiology of the more common benign and malignant conditions found at the biliary bifurcation.
3. To review the current interventional techniques used to treat patients with lesions at the biliary bifurcation.

I. INTRODUCTION

Optimal management of patients with lesions at the biliary bifurcation requires a multidisciplinary approach frequently involving the Primary Care Physician, Surgeon, Gastroenterologist, and Interventional Radiologist. The Radiologist is frequently involved at multiple levels in the workup of patients with lesions at the biliary bifurcation. These include:

1) Confirmation of surgically suspected obstructive jaundice using cross-sectional imaging[1] (i.e., Ultrasound [US][2-4], computed tomography [CT][5], magnetic resonance imaging [MRI][5]).
2) Precisely defining biliary anatomy to determine the severity and level of obstruction using percutaneous techniques (i.e., percutaneous transhepatic cholangiography [PTHC or PTC]).
3) Drainage of obstructed bile ducts (i.e., percutaneous transhepatic biliary drainage [PTHB or PTB][6]).

4) Obtaining tissue and/or bile to confirm a suspected diagnosis (i.e., percutaneous biopsy[7-14] and/or bile sampling for cytopathology[15]).

5) Providing unilateral or bilateral biliary access:

   a) for eventual surgical resection of the bifurcation lesion(s)followed by biliary reconstruction through creation of Roux-en-Y hepaticojejunostomies[20].

   b) as access for palliation using percutaneous interventional techniques (e.g. biliary endoprostheses[6,16,17,21-31]).

   c) a means of percutaneous biliary access for brachytherapy[32,33] (e.g. Iridium 192 seeded wires placed through the indwelling biliary drainage catheters for delivery of local radiation in the setting of malignant disease at the bifurcation).

   d) as a means of biliary access for adjunctive biliary procedures (e.g. transhepatic biliary endoscopy[34], balloon dilation of the benign biliary strictures[35-42], long-term internal/external biliary stenting in the setting of benign or malignant disease at the bifurcation[6,16], etc.).

6) In specific clinical situations, assisting the Gastroenterologist in endoscopic biliary interventions (e.g. the "rendezvous procedure"). This technique involves the Interventional Radiologist percutaneously advancing a guidewire through an obstructing biliary lesion and into the duodenum from a transhepatic approach. The

Gastroenterologist then grasps the wire tip during endoscopy. This provides "through and through" access for placement of an endoprostheses, for dilation of a high-grade stricture at the bifurcation, etc.

7) Confirming a biliary leak using radionuclide hepatobiliary scintigraphy[43].

Thus, the Radiologist plays an essential role in the diagnostic workup and management of patients with lesions at the biliary confluence.

II. ETIOLOGY OF TUMORS AT THE BILIARY CONFLUENCE

Tumors at the biliary confluence may cause obstruction due to intrinsic occlusion or extrinsic compression. Dilated intrahepatic ducts (diffuse or segmental) are seen on cross-sectional imaging studies. Depending on the degree of obstruction, clinically evident jaundice may or may not be present.

Benign "tumors" of the biliary confluence include: 1) Extrinsic compression of the confluence by enlarged lymph nodes, cysts, and inflammatory lesions. 2) Intrinsic obstruction due to stones, and infrequently tumors arising from the bile duct epithelium or wall (e.g. papillomas, adenomas, granular cell myoblastomas, hamartomas, etc.). Most benign bile duct tumors are found in the periampullary region or the common bile duct and are quite uncommon in the intrahepatic ducts[1]. Occasionally benign lesions such as a patient with an atypical "central" obstruction due to sclerosing cholangitis may appear to have a tumor at the biliary confluence.

Malignant tumors of the biliary confluence also include: 1) Extrinsic compression of the biliary duct bifurcation by metastatic disease (e.g. to lymph nodes at the bifurcation), 2) Local extension of tumors from adjacent structures (e.g. primary hepatic, pancreatic, gall bladder, duodenal, or gastric malignancies), 3) Malignant tumors arising from the bile duct epithelium or wall

(e.g. cystadenocarcinomas, cholangiocarcinoma, villous tumors, embryonal rhabdomyosarcoma [sarcoma botryoides], extension of ampullary carcinoma or carcinoid, etc.)[1,16].

Cholangiocarcinoma is a slow growing uncommon tumor with a peak incidence in the sixth and seventh decades. The tumor is two to three times more common in males than in females. Most cholangiocarcinomas are adenocarcinomas with a minority being of other histologic types such as squamous cell and anaplastic.[1] Cholangiocarcinoma infrequently spreads by lymphatic or blood borne means; occurring in only 12% of patients at the time of clinical presentation.[33] Rather cholangiocarcinoma invades hepatic parenchyma and locally invades hepatic arteries and portal veins, making surgical resection difficult.[32]

The growth patterns of cholangiocarcinoma include (1) infiltrating-scirrhous, (2) nodular, and (3) papillary.[1] The infiltrating-scirrhous pattern is most common [1-3] Characteristically, this growth pattern presents as a focal stricture, often without a mass[4] and the scirrhous reaction explains the difficulty in obtaining positive preoperative biopsies. When extensive, it may mimic sclerosing cholangitis.[1]

In about five percent of patients, a papillary form of growth of adenocarcinoma may occur.[4] This form results in expansion of the bile ducts and one finds intraluminal masses.[4] Benign conditions which predispose patients to developing cholangiocarcinoma include: inflammatory bowel disease, gallstones, hepatolithiasis, choledochal cysts, sclerosing cholangitis, and Clonorchis infection.[1,2,44-47]

III. SURGICAL, ENDOSCOPIC, AND PERCUTANEOUS (INTERVENTIONAL) MANAGEMENT OF PATIENTS WITH TUMORS AT THE BILIARY CONFLUENCE: A TEAM APPROACH

The goal of therapy for patients with benign or malignant tumors of the biliary confluence is elimination of tumor whenever possible and/or relief of symptoms (e.g. drainage of biliary infection, relief of symptomatic jaundice, etc.). This is accomplished by surgical resection of the lesion in an attempt to "cure", surgical "debulking" followed by adjunctive therapy (such as brachytherapy, chemotherapy, etc.), or palliation through endoscopic or percutaneous (interventional) techniques (e.g. placement of endoprostheses).

For benign conditions, persistent obstructive symptoms such as recurrent bouts of cholangitis associated with benign lesions at the biliary confluence and/or stones may ultimately require surgical resection of the biliary confluence followed by creation of biliary-enteric anastomoses (Roux-en-Y hepaticojejunostomies). Prior to surgery, the Gastroenterologist and/or Interventional Radiologist actively participate in patient management. After confirmation of the degree and level of biliary obstruction based on cross-sectional imaging studies, the Gastroenterologist is frequently asked to perform endoscopic retrograde cholangiopancreatography (ERCP). This defines anatomy and frequently results in some form of therapy (e.g. brush biopsy of suspicious lesions at the confluence, balloon dilation of strictures, sphincterotomy to facilitate biliary drainage, etc.) However, obstructing tumors at the confluence are not well visualized by ERCP if contrast cannot be injected

beyond the level of obstruction. Such is the case when tumors cause strictures involving central right anterior and posterior ducts, and the main left bile duct. In such instances, a percutaneous transhepatic cholangiogram (PTC), sometimes performed bilaterally, will precisely define biliary anatomy.

In general, ERCP should be used in patients with tumors of the biliary confluence when:

1) Intrahepatic bile ducts are nondilated.

2) The patient has an absolute contraindication to PTC/PBD (i.e. a coagulopathy that cannot be corrected).

3) The patient has a relative contraindication to PTC/PBD (i.e. ascites, etc.).

PTC (often followed by PBD) should be performed:

1) When ERCP fails.

2) When the patient has had a prior biliary-enteric anastomosis. Such surgical biliary reconstructions frequently prevent successful cannulation of the ampulla by ERCP.

3) If surgical resection of the tumor at the biliary confluence is planned. PBD (often bilateral) is performed to relieve obstructive symptoms (e.g. to drain infected bile). In some centers, the presence of a percutaneously placed biliary drainage catheter(s) facilitates intraoperative biliary reconstruction and aids in the surgical creation of biliary enteric anastomoses.[16-20]

4) In those patients who are not surgical candidates and who have known malignant tumors at the biliary confluence, bilateral PTC/PBD will allow palliative endoprosthesis placement[16,17,21-31]. The endoscopist may not be able

to successfully relieve obstruction from malignant tumors at the biliary confluence. An endoprosthesis placed during endoscopy is frequently deployed into either the right or the left biliary duct. This may result in inadequate biliary drainage.

To summarize, the team approach is essential in managing patients with tumors at the biliary confluence. Depending on planned therapy, the therapeutic options generally consist of either attempts at surgical resection or nonsurgical procedures (endoscopic or interventional) aimed at palliation. A review of interventional techniques and the choice of which technique to employ will be discussed next.

IV. EXTERNAL DRAINAGE, BILIARY ENDOPROSTHESES, STENTS, OR RADIATION? HOW TO CHOOSE.

Previous reported studies on PBD have reported prevalences of 4.6-25% for major complications and 0-5.6% for procedure related deaths[48-53]. Yee and Ho reviewed the medical literature and combined the results of six groups of investigators. In the combined group of 702 patients, the overall percentage of major complications was 8% and the percentage of deaths 2%. Six hundred nine of the 702 patients (87%) had malignant biliary obstruction[54]. The authors indicate that the patient's general physical condition is a major determinant of the likelihood of complications. In Yee and Ho's own series of 206 patients undergoing PBD, 54 had benign and 152 had malignant biliary disease. In the malignant group, 85 patients (56%) had one or more complications; ten of these (7%) had major complications. Five patients (3%) suffered cholangitis with hypotension, and three of these died as a result. Two patients (1%) had major bile peritonitis; one died as a result, and the other required laparotomy for evacuation of bile. Two patients (1%) had

dyspnea due to bilious pleural effusions which developed after inadvertent dislodgement of the biliary drainage catheters. Both required chest tubes. One patient (1%) had a major intraperitoneal hemorrhage due to liver laceration. This patient required surgical repair and a blood transfusion.

Of the 54 patients with benign biliary lesions, complications of PBD occurred in nine patients (17%) vs 56% in the malignant group. Of the benign group with complications, one (2%) was major vs 7% in the malignant group. The single patient with a major complication developed bile peritonitis after premature removal of his biliary drainage catheter. This patient had a benign biliary stricture from pancreatitis. No procedure related deaths occurred in the benign group. In the above retrospective study, it is apparent that patients with malignant disease are at higher risk for major complications compared to patients with benign disease. Unfortunately the data is not stratified to the percentage of patients with lesions at the biliary confluence. Similar findings regarding the patient's general state of health have been described in the surgical literature[55]. Despite this, percutaneous techniques should be used after careful consideration of treatment options (e.g. surgical, endoscopic, percutaneous). Metallic stents should be avoided in patients with benign biliary disease at the bifurcation. Such stents will become incorporated into the bile duct wall. Should surgery be eventually required, a greater length of duct may need to be resected. Patency of metallic stents is limited to approximately 6-12 months.

For patients with malignant lesions at the biliary bifurcation, the type of tumor frequently dictates management. Bilateral access is generally required to relieve obstruction and to effectively drain infected bile. Unresectable cholangiocarcinoma, often slow growing, is managed at the author's institution by palliating the patient using internal/external biliary drainage catheters. This is preferred because patients often outlive the patency of plastic endoprosthesis or metallic stents.

An added benefit of the use of internal/external biliary drainage catheters is that of using the transhepatic biliary access to deliver high doses of radiation i.e. brachytherapy. Through the indwelling biliary drainage catheters, intracavitary radiation may be delivered (e.g. use of Iridium 192 seeded wires). Encouraging results in a limited number of patients have been reported by Nunnerly et al using this method[32].

Patients with limited life expectancy and bilateral percutaneous access may experience improved quality of life through the use of biliary endoprostheses. In general, bifurcation lesions are difficult to treat using either plastic or metallic stents (endoprostheses). Though more expensive, metallic stents, e.g. Wallstents (Schneider USA Inc., Minneapolis, MN), Z stents (Cook Inc., Bloomington, IN), Palmaz stents (Johnson and Johnson Interventional Systems Co., Warren, NJ) are frequently used. At the author's institution, Wallstents are often preferred because of the smaller percutaneous deployment system (i.e. 7 French), the ability to perform transhepatic drainage and stent placements in "one step", and the avoidance of painful transhepatic tract dilation (e.g. 10-14 French) as would be required when using other metallic stents or plastic endoprostheses.

ERCP for patients with benign or malignant lesions at the bifurcation may prove inadequate. Intrahepatic bile duct anatomy may be inadequately seen and plastic or metallic stents are often difficult to deploy by ERCP. It is the opinion of the author that endoprosthesis placed during ERCP should be reserved primarily for distal common bile duct(CBD) lesions.

V. CONCLUSION:

Choosing the appropriate biliary drainage method should thus be based on 1) the patient's overall health status, 2) the etiology of the lesion at the confluence, 3) the expected length of time that biliary endoprostheses or external/internal drainage catheters will be required, 4) whether the

patient is to have surgery or palliative treatment, 5) the ability of the patient to care for himself/herself. In general, ERCP should be reserved for defining anatomy, especially in patients with nondilated ducts. External drainage alone is generally to be avoided because of the significant loss of fluids and electrolytes. Internal/external drainage is preferred for "long term" biliary access. "Long term" may generally be considered greater than 6 months. Stents are changed every 2 to 3 months on an outpatient basis.

A "common sense" team approach to the management of patients with lesions at the biliary confluence has been provided. An understanding of the etiology of the lesion, the natural history, the general condition of the patient's health, and an awareness of the surgical or nonsurgical options will hopefully simplify therapy, avoid costly duplication by medical services within the hospital, and optimize patient management.

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