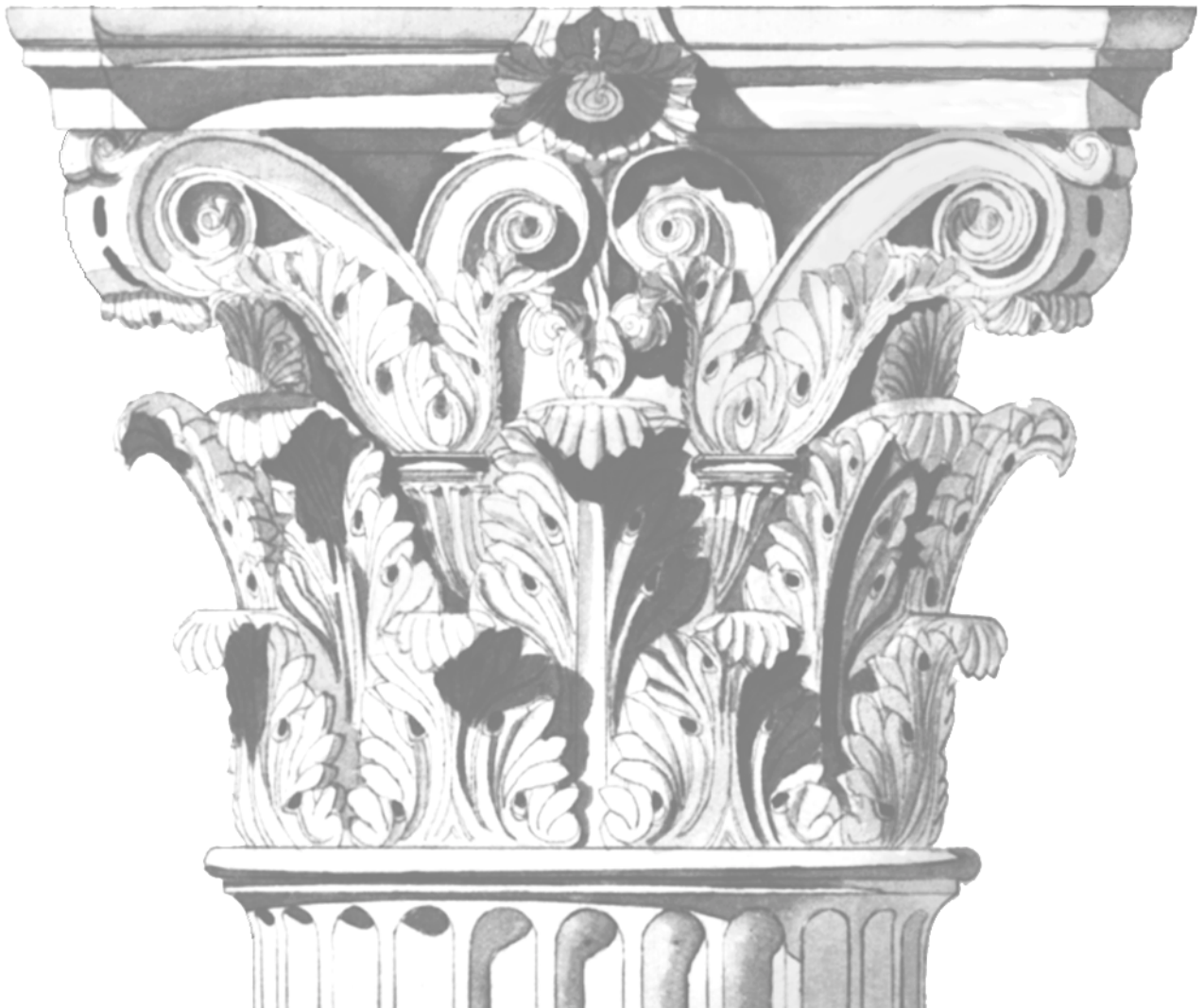


**IMAGING OF BILIARY CARCINOMA,
FISTULA AND PRIMARY
SCLEROSING CHOLANGITIS AND
PERCUTANEOUS METALLIC
STENTING IN MALIGNANT
BILIARY OBSTRUCTION**

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OULU 2001



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FISTULA AND PRIMARY SCLEROSING
CHOLANGITIS AND PERCUTANEOUS
METALLIC STENTING IN MALIGNANT
BILIARY OBSTRUCTION**

Academic Dissertation to be presented with the assent of the Faculty of Medicine, University of Oulu, for public discussion in the Auditorium 7 of the University Hospital of Oulu, on March 23rd, 2001, at 12 noon.

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Abstract

Biliary carcinoma, biliary fistula with occasional gallstone ileus and primary sclerosing cholangitis (PSC) are serious diseases and present specific diagnostic and therapeutic challenges. Stenting of biliary obstruction has also involved problems, but the reports are contradictory and partly limited. The aim of the present work was to evaluate and compare various imaging modalities in biliary diseases. The study also aimed to evaluate the usefulness of metallic stents in malignant biliary obstruction.

The study population consisted of 210 patients with gallbladder carcinoma, bile duct carcinoma, biliary fistula, PSC or malignant biliary obstruction and eight control patients with various hepatobiliary diseases. The imaging findings of 80 patients with gallbladder carcinoma, 58 patients with bile duct carcinoma, and 16 patients with biliary fistula were reviewed. Nine patients with PSC underwent magnetic resonance cholangiography (MRC) and magnetic resonance imaging (MRI) of the liver, ultrasonography (US) of the liver and the bile ducts and endoscopic retrograde cholangiography (ERC). Eight control patients had had MRC and MRI of the liver and ERC. The medical records and radiographs of 39 patients with malignant biliary obstruction treated with percutaneously inserted metallic stents were also analysed. The stents included 48 Wallstents and seven Memotherm stents.

In cases of gallbladder carcinoma, US visualised the primary tumour in 68 % and computed tomography (CT) in 57 % of the cases examined, but both methods were insufficient for accurate staging. In bile duct carcinoma, US revealed the primary tumour in 63 % and CT in 44 % of the cases examined. Both methods were sensitive in diagnosing peripheral intrahepatic cholangiocarcinoma, but inaccurate for more distal bile duct carcinoma or abdominal spread. The infiltrating type of gallbladder carcinoma and bile duct carcinoma were difficult to detect. US and CT were sensitive in revealing bile duct obstruction.

The patients with biliary fistula and gallstone ileus had undergone various examinations with pathological, but not diagnostic results, and there was often a delay to diagnosis. Imaging did not reveal any of the ten spontaneous fistulas, but CT showed one of the five cases of gallstone ileus, and Gastrografin® meal revealed the single case of Bouveret's syndrome. Fistulography or cholangiography revealed all but one of the six iatrogenic fistulas. A nonvisualised or shrunken gallbladder at US should raise a suspicion of biliary enteric fistula in an appropriate clinical setting.

MRC-MRI depicted the changes of PSC correctly in nine patients (radiologist 1) and in eight patients with one false positive finding (radiologist 2) in a blinded analysis. In the segmental comparison MRC missed especially bile duct dilatations. MRC was too pessimistic in the evaluation of the predictors of poor outcome. US detected features suggestive of PSC in eight patients (radiologist 3). US was unable to indicate the predictors of poor outcome.

Of the patients with metallic stents in malignant biliary obstruction, 30 % had early and 66 % late complications, including stent obstructions, which occurred in 27 % of the patients at a mean of 4.4 months. The cause was mostly tumour ingrowth or overgrowth. The 25-week and 50-week patency rates were 71 % and 42 %. The patency rates of the patients with cholangiocarcinoma were significantly the lowest. There was also a tendency towards lower patency with less dilatation of the stents, an increasing number of the stents, longer strictures and hilar strictures. Many other complications were infectious. 31 % of the patients had late reinterventions.

Keywords: primary sclerosing cholangitis, biliary carcinoma, biliary fistula, diagnostic imaging, metal stents, cholestasis

*To Aarne,
Raine and Iiro*

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Oulu, March 2001

Heljä Oikarinen

Abbreviations

AIDS	acquired immunodeficiency syndrome
CE	contrast-enhanced
CEA	carcinoembryonic antigen
CT	computed tomography
2 D / 3 D	2-dimensional / 3-dimensional
ERC	endoscopic retrograde cholangiography
ERCP	endoscopic retrograde cholangiopancreatography
F	French
FNB	fine-needle biopsy
HIDA	hepatoiminodiacetic acid
MR	magnetic resonance
MRA	magnetic resonance angiography
MRC	magnetic resonance cholangiography
MRCP	magnetic resonance cholangiopancreatography
MRI	magnetic resonance imaging
pANCA	perinuclear antineutrophil cytoplasm antibodies
PSC	primary sclerosing cholangitis
PTC	percutaneous transhepatic cholangiography
PTCD	percutaneous transhepatic cholangio drainage
RARE	rapid acquisition relaxation enhancement
SSD	shaded surface display
SSFP	steady-state free procession
TE	time of echo
TR	time of repetition
TSE	turbo spin echo
US	ultrasonography

List of original papers

This thesis is based on the following articles, which are referred to in the text by their Roman numerals:

- I Oikarinen H, Päivänsalo M, Lähde S, Tikkakoski T & Suramo I (1993) Radiological findings in cases of gallbladder carcinoma. *Eur J Radiol* 17: 179–183.
- II Päivänsalo M, Oikarinen H, Tikkakoski T, Puumala K & Suramo I (1993) Radiological findings in bile duct carcinoma. *Fortschr Röntgenstr* 159: 4–9.
- III Oikarinen H, Päivänsalo M, Tikkakoski T & Saarela A (1996) Radiological findings in biliary fistula and gallstone ileus. *Acta Radiol* 37: 917–922.
- IV Oikarinen H, Pääkkö E, Suramo I, Päivänsalo M, Tervonen O, Lehtola J & Aukee J (2001) Imaging and estimation of the prognostic features of primary sclerosing cholangitis by ultrasonography and magnetic resonance cholangiography. Accepted for publication in *Acta Radiol*.
- V Oikarinen H, Leinonen S, Karttunen A, Tikkakoski T, Hetemaa T, Mäkelä J & Päivänsalo M (1999) Patency and complications of percutaneously inserted metallic stents in malignant biliary obstruction. *J Vasc Interv Radiol* 10: 1387–1393.

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1 Introduction

Carcinoma of the gallbladder is the fourth most common malignant tumour of the gastrointestinal tract. The incidence of carcinoma of the bile duct has also been increasing. Biliary tumours present specific diagnostic challenges. (Wei & Gadacz 1996, van Leeuwen & Fockens 1999.)

Gallbladder carcinoma spreads early in its course, and preoperative diagnosis of early-stage cancer is therefore rare. The carcinoma is actually often found incidentally in a resected cholecystectomy specimen. It is either asymptomatic or presents with nonspecific symptoms, and it may be fairly advanced before jaundice develops. The prognosis of the cancer greatly depends on the initial stage. Accurate staging would also be important for the selection of the best possible therapy. (Wei & Gadacz 1996, Demachi *et al.* 1997, Haribhakti *et al.* 1997, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.) The abilities of various imaging modalities to facilitate the diagnosis and staging of gallbladder cancer have been variable.

Cholangiocarcinoma has also had a poor prognosis. The symptoms are usually nonspecific gastrointestinal complaints, unless jaundice develops. The diagnosis of early cholangiocarcinoma is often difficult, especially in the case of peripheral intrahepatic and hilar cancers. Some cancers may present as only a thickening of the wall of the bile duct. The stage of the carcinoma at the time of diagnosis is one of the most important prognostic factors. Cholangiocarcinoma usually spreads to the adjacent organs and tissues. Radiologic assessment should identify the patients for whom resection might be possible. (Guthrie *et al.* 1996, Wei & Gadacz 1996, Keogan *et al.* 1997, Sherlock & Dooley 1997a.) Preoperative evaluation is often extensive, requiring several types of imaging.

The adverse sequelae of malignant biliary obstruction warrant serious consideration of biliary drainage, which can be done by a surgical or interventional procedure (Spivack & Jacobson 1999). Bypass surgery involves considerable mortality and morbidity, catheter drainage has problems, and plastic stents are often occluded by sludge or displaced (Barth 1990, Davids *et al.* 1992, Smith *et al.* 1994). Although metallic self-expandable stents have certain advantages, there have also been disappointments, such as occlusion of the stents by tumour ingrowth or overgrowth and other complications (Rossi *et al.* 1994,

Tesdal *et al.* 1997). However, the reports of patency rates with regard to the level and cause of obstruction, of early and especially late complications and of reinterventions have been limited and contradictory.

Biliary enteric fistulas are rare and often difficult to diagnose. The symptoms are nonspecific, and the diagnosis is often made during cholecystectomy. (Knol *et al.* 1996, Colizzo & Farraye 1999.) Fistulas with bowel obstruction cause up to 25 % of all cases of non-strangulated intestinal obstruction in the elderly. Mortality from this disease is still high, partly due to the diagnostic delay. (Sherry & Gadacz 1996, Sherlock & Dooley 1997c.) The risk for iatrogenic biliary fistula is more likely with laparoscopic cholecystectomy than with the open method. The injury often goes unrecognised during surgery, and the clinical manifestations may be nonspecific, but lead to serious complications. (Lu & Kaplowitz 1991, Kastrinakis & Brooks 1999.) Reported series with diagnostic imaging of biliary fistulas, especially spontaneous fistulas, are rare and limited. Early recognition of biliary fistulas would be critical in decreasing morbidity and mortality.

Primary sclerosing cholangitis (PSC) is a chronic cholestatic disease of relatively young people leading to liver transplantation or death. It may be complicated by bile duct carcinoma. PSC should be diagnosed in the early phase, when treatment would be most beneficial, but there is often a delay of years before the diagnosis. Apart from biochemical and hepatic histologic findings, detailed evaluation of the biliary tree is essential for the final diagnosis. However, endoscopic retrograde cholangiopancreatography (ERCP) is invasive and may cause serious complications, and it is difficult to opacify the ducts proximal to a high-grade stenosis. Liver biopsy is also invasive and rarely definitive. (Lu & Kaplowitz 1991, Lee & Kaplan 1995, Broomé *et al.* 1996, Ernst *et al.* 1998, Ponsioen & Tytgat 1998, Zakko 1999.) Reports of non-invasive ultrasonography (US) and magnetic resonance cholangiography (MRC) in the diagnosis and follow-up of PSC are rare.

The purpose of the present work was to compare the respective abilities of certain imaging methods to diagnose biliary carcinoma and its abdominal spread and to evaluate the efficacy and the problems of percutaneously inserted metallic stents in malignant biliary obstruction. The study also aimed to compare imaging methods in the diagnostics of biliary fistula and gallstone ileus, and to assess the efficacy of US and MRC in the diagnostics of PSC.

2 Review of the literature

2.1 Anatomy and function of the biliary tract

The gallbladder lies in a depression on the inferior surface of the liver at the boundary between the right and left lobes. This interface between the gallbladder and the liver usually contains some loose connective tissue, which is traversed by small lymphatics, veins and sometimes small accessory bile ducts. The surface of the gallbladder not attached to the liver is covered by the peritoneum and is in intimate contact with the duodenum, the head of the pancreas, and the hepatic flexure of the colon. (Pellegrini & Duh 1991.)

The gallbladder has four anatomic parts: the fundus, the body, the infundibulum and the neck. The arterial supply of the gallbladder is usually from a single cystic artery originating from the proximal right hepatic artery. There is no major cystic vein, but a venous net, and the lymphatic drainage parallels the venous drainage. The gallbladder has four layers: the mucosa, the muscularis, the perimuscularis connective tissue layer, and the serosa. In the gallbladder, the bile is concentrated by absorption of water. (Ganong 1991, Pellegrini & Duh 1991.)

Bile is secreted by hepatocytes into the biliary canaliculi, which drain into the biliary ductules. The latter unite to form the segmental bile ducts. In 95 % of cases, the left and right hepatic ducts join outside the liver, just below the porta hepatis, to form the common hepatic duct. In 5 % of cases, they join inside the liver. The lengths of the right and left hepatic ducts vary from 0.5 to 2.5 cm, the left one being usually longer. The length of the common hepatic duct varies from 2 to 6.5 cm. It joins the cystic duct to form the common bile duct. (Pellegrini & Duh 1991.)

The cystic duct is 0.1 to 0.4 cm in diameter and 0.5 to 8 cm in length. Its course and entrance into the common hepatic duct are variable. The spiral valves of Heister are crescent-shaped folds of the mucosa that project into the lumen, spanning the entire length of the duct. The common bile duct, the hepatic artery and the portal vein run in the hepatoduodenal ligament. The common bile duct varies from 5 to 17 cm in length, and its diameter varies from 0.3 to 1.5 cm and may become markedly distended by biliary obstruction. The duct contains scanty smooth muscle arranged in a circular fashion. It has a fibroareolar coat. The lumen is lined by columnar epithelium that is continuous with

that of the gallbladder and the other extrahepatic bile ducts. The common bile duct is divided into four segments: supraduodenal, retroduodenal, pancreatic, and intraduodenal. The pancreatic segment lies in a groove on the undersurface of the pancreas or may be completely surrounded by pancreatic tissue. (Menuck & Amberg 1976, Pellegrini & Duh 1991, Vandervoort *et al.* 1999.)

Usually, the lumens of the common bile duct and the main pancreatic duct join to form the ampulla of Vater. In about 30 % of cases, however, these ducts drain separately into the duodenum, or the ampulla is very short. Each lumen narrows as it passes through the duodenal wall. The terminal parts of the common bile duct and the pancreatic duct, the common channel, and the major duodenal papilla of Vater form the sphincter of Oddi segment. (Menuck & Amberg 1976, Pellegrini & Duh 1991, Vandervoort *et al.* 1999.)

The human liver secretes 600–1200 ml of bile a day into the duodenum. Bile contains bile salts, bile pigments (e.g. bilirubin), cholesterol, phospholipids and proteins and serves a number of important functions. Bile salts play an important role in the intestinal absorption of lipid. Bile salts are conjugates of bile acids, which are derived from cholesterol and thus constitute a path for its excretion. Biliary secretion is also an important route for the excretion of bilirubin from the body. In biliary obstruction, both conjugated and unconjugated bilirubin accumulate in plasma, and their proportion changes in favour of conjugated bilirubin. (Tso 1995, Sauter *et al.* 1999.)

During the interdigestive period, the sphincter of Oddi is normally contracted and the gallbladder is relaxed, storing most of the hepatic bile. After the ingestion of a meal, cholecystokinin is released into the blood stream, causing contraction of the gallbladder and resulting in the delivery of bile into the duodenum. (Tso 1995.)

2.2 Biliary tumours and obstruction

Benign tumours of the biliary tract are rare. The gallbladder may contain polyps (papilloma), adenomas, myomas, lipomas and fibromas. Most of the benign tumours of the common bile duct are papillomas or cystadenomas. Adenomyomas, fibromas, and granular cell tumours have also been found. However, most biliary tumours are malignant. Their presentation may vary, and it is partially determined by the location of the tumour. Tumours that arise from the papilla of Vater or the distal common bile duct may be symptomatic at the early stage of disease in contrast to intrahepatic biliary tumours or gallbladder carcinomas, which may be at a much more advanced stage before causing symptoms of obstruction. (Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

2.2.1 Carcinoma of the gallbladder

Most malignant tumours of the gallbladder are adenocarcinomas, although squamous cell, anaplastic and oat cell carcinomas, sarcomas, carcinoid tumours and metastases (e.g. from melanoma or breast cancer) have also been reported. Adenocarcinoma of the gallbladder is the fourth most common malignant tumour of the gastrointestinal tract in

the West. Northern Europeans are at an especially high risk. It is most common in women and in the elderly. Adenocarcinoma may be scirrhous, papillary or colloid. (Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

Predisposing factors include gallstone disease, calcification of the gallbladder wall, congenital biliary cysts, adenomatous polyps and some infections. An anomalous union between the bile duct and the pancreatic duct outside the duodenal wall has been suspected to predispose to cancer formation by producing harmful effects due to pancreatic juice reflux. Racial, genetic, and cultural differences may explain geographic differences. Mirizzi syndrome and biliary papillomatosis may also have an association with the carcinoma. (Townsend 1991, Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

Carcinoma is associated with gallstones in 80 % of cases. However, the cancer risk has not been considered high enough to warrant prophylactic cholecystectomy. The duration of gallstone disease and chronic irritation of the mucosa, the size of the stones (large stones appear to carry a greater risk than small ones), the possible carcinogenic components of the gallstones or bile, and the patient's age may play a role. Chronic inflammation may irritate the epithelium and cause it to change through dysplasia into carcinoma *in situ* and further into invasive carcinoma. (Way & Altman 1989, Townsend 1991, Wei & Gadacz 1996, van Leeuwen & Fockens 1999.)

The tumour usually arises in the fundus or the neck. The rich lymphatic and venous drainage of the gallbladder facilitates early spread into lymph nodes, which may cause jaundice and widespread dissemination. The liver bed is invaded, and there may be local spread to the duodenum, stomach and colon and metastases in the peritoneum and lungs. Because of the various nonspecific symptoms, there is often a delay in diagnosis. Patients may also present with chronic cholecystitis or cholangitis. Jaundice is a poor prognostic sign, reflecting obstruction of the extrahepatic duct. Symptomatic cancer is nearly always an advanced, incurable disease. (Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

Only about 5 % of the carcinomas are diagnosed preoperatively. The carcinoma is most often found incidentally in the resected cholecystectomy specimen. With the advent of laparoscopic techniques for cholecystectomy, a small carcinoma may not be evident. The median survival from diagnosis is three months, and 14 % of the patients are alive at one year. Survival is related to the depth of invasion and, thus, staging and histologic type. If the tumour invasion involves only the mucosa or the muscle layer (stage I), the 2-year survival rate is 45 %. A stage II tumour invades the perimuscular tissue, and a stage III tumour perforates the serosa, invades an adjacent organ or metastasises to the regional lymph nodes. Stage IV implies distant regional lymph node or distant organ metastasis and is associated with a 5-year survival rate of 2 %. (Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

The majority of carcinomas are inoperable at the time of diagnosis. The only long-term survivors are those in whom the tumour is found incidentally as carcinoma *in situ*. In general, recovery is possible in the patients whose tumour is confined to the gallbladder or is locally resectable. The treatment consists of cholecystectomy, resection of the gallbladder bed and removal of all surrounding lymph nodes. If the diagnosis is made only after a pathologic examination, a radical second operation may improve the cure rate in some patients. The carcinoma may be radiosensitive. Intraoperative radiation therapy is

still experimental. Chemotherapy does not improve 5-year survival. Palliative decompression is performed surgically or by stents. Palliation of jaundice by radiation therapy has also been reported. (Townsend 1991, Wei & Gadacz 1996, Sherlock & Dooley 1997a.)

2.2.2 Carcinoma of the bile duct

The incidence of bile duct carcinoma has been increasing. Most of the tumours are adenocarcinomas, but papillary, mucinous, squamous and oat cell carcinomas and sarcomas have also been reported. Carcinoma of the bile duct is more common in men and occurs in the older age group. Predisposing factors include congenital anomalies (e.g. choledochal cysts and Caroli's disease), a long common channel, and various conditions associated with chronic inflammation (e.g. primary sclerosing cholangitis, colitis ulcerosa and infestation by parasites). Papillomatosis is a rare condition, which is considered premalignant. Bile duct cancer is associated with gallstones in about 40 % of cases. (Townsend 1991, Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

Carcinoma may occur in intrahepatic ducts, at the confluence of the right and left hepatic ducts (Klatskin tumour) or anywhere in the extrahepatic bile duct below the confluence. Tumours derived from the intrahepatic bile duct may be classified as primary hepatic carcinoma. Carcinoma of the cystic duct is rare and most likely to be found at operation for an obstructed gallbladder or discovered incidentally in a cholecystectomy specimen. Approximately 20 %–30 % of the tumours are intrahepatic, 50 % occur in the proximal common hepatic duct or at the confluence and 20 %–30 % occur in the distal common bile duct. Some tumours may present as merely a thickening of the wall. Approximately 70 % are mucin-producing, sclerosing tumours, and the more distal tumours are more likely to be papillary. (Tompkins 1990, Townsend 1991, Baron 1997, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

Carcinomas are characterised by local extension into the liver, portal vessels, pancreas and duodenum. Metastases may involve the peritoneum, lymph nodes, diaphragm and gallbladder. The symptoms are nonspecific gastrointestinal complaints. Painless jaundice is the most prominent sign. In the case of extrahepatic carcinomas, jaundice may be caused by a small tumour. (Wei & Gadacz 1996, Sherlock & Dooley 1997a.)

The extent and stage of the carcinoma, the type and grade of the histology and the location of the tumour are the most important prognostic factors. The patients with a stage I tumour (invading the mucosa or muscularis) have a 2-year survival rate of 27 %. Those with stage II (invading perimuscular connective tissue) and III tumours (metastasis in regional lymph nodes) have 2-year survival rates between 12 and 17 %, and those with a stage IV tumour (invading adjacent organs or distant metastasis) have a 2-year survival rate of 4 %. (Townsend 1991, Wei & Gadacz 1996.)

The extent of surgery is determined by the location of the tumour as well as the surrounding invasion. The tumours located distally are more likely to be resectable than those at the hilum. After a systematic preoperative diagnostic evaluation, a proper diagnosis should be made, resectability should be determined, and optimal treatment

should be carried out. In general, a tumour involving the distal common bile duct and the ampullary area should be treated by pancreaticoduodenectomy if there is no evidence of spread outside the biliary tract, while a tumour in the middle portion of the common bile duct should be resected if there is no local invasion. A Klatskin tumour is considered unresectable for cure if there is evidence of extensive or multifocal disease proximal to the secondary intrahepatic ducts, invasion of the portal vein or hepatic artery and vascular involvement of one lobe of the liver and bile duct involvement of the opposite lobe. Liver resection is the only chance for effective treatment of intrahepatic bile duct derived tumour. (Wei & Gadacz 1996, Sherlock & Dooley 1997a.)

There is a need to identify the patients for whom resection might be possible, since surgical treatment, even if not curative, may prolong survival and result in a better quality of life. In patients unfit for surgery or with unresectable tumours, palliative decompression of the bile ducts should be performed operatively or by stents. Radiotherapy, chemotherapy and hepatic transplantation have been used, but the response has been poor or unproven. (Wei & Gadacz 1996, Sherlock & Dooley 1997a, van Leeuwen & Fockens 1999.)

2.2.3 Tumours of the ampulla

Ampullary tumours are uncommon. They occur at all ages, but mostly between 50 and 70 years, and males are affected more frequently than females. Benign tumours represent the minority and include villous adenomas, leiomyomas, lipomas, hemangiomas, lymphangiomas, and neurogenic tumours. Malignant ampullary tumours are invariably adenocarcinomas. Most arise from the mucosa of the ampulla of Vater, but they may arise from the pancreas or the pancreatic duct epithelium, the epithelium of the terminal portion of the common bile duct or the duodenal mucosa. (Sherlock & Dooley 1997b, Isenberg & Wong 1999.)

Adenoma is considered a premalignant lesion, which may be transformed into carcinoma *in situ* or invasive carcinoma. Carcinogens in bile or pancreatic secretions may also have a role in the development of carcinomas. Gallstones are present in 35–50 % of these patients, but no convincing association has been found. Aetiological factors may include cigarette smoking, diet, partial gastrectomy and diabetes mellitus. (Sherlock & Dooley 1997b, Isenberg & Wong 1999.)

Ampullary tumours are rarely more than 2 to 3 cm in diameter, soft and polypoid. They are often of low-grade malignancy, do not usually metastasise, but infiltrate locally and sometimes spread into the local lymph nodes or the liver. The patients present nonspecific symptoms and early jaundice, which may fluctuate. Many patients are initially misdiagnosed. (Sherlock & Dooley 1997b, Isenberg & Wong 1999.)

Ampullary carcinoma is the most curable of all cancers of the upper gastrointestinal tract. It is usually treated with pancreaticoduodenectomy or local resection in selected patients. Endoscopic treatment is reserved for high-risk surgical patients. The 5-year survival rate after treatment is 10–40 %. The survival rates correlate with staging and the epithelium of origin. (Sherlock & Dooley 1997b, Isenberg & Wong 1999.)

2.2.4 Malignant biliary obstruction

Malignant obstruction of the extrahepatic biliary tract is a common consequence of carcinoma of the pancreas, ampulla, bile duct or gallbladder, but it may also result from metastases or lymphoma. Metastases usually arise from carcinoma of the colon, gallbladder, pancreas, small intestine, stomach, breast, ovary or lung or from renal cell carcinoma or melanoma. (Way & Sleisenger 1989, Spivack & Jacobson 1999.)

Obstruction may occur at any level from the hilum to the papilla. Obstruction results in cholestasis and reduced excretion of bile into the small intestine. Steatorrhea and fat-soluble vitamin deficiencies may result, with malnutrition, weight loss and coagulopathy. Pruritus may be related to excess bile acids and jaundice and acholic stools to bilirubin. Impaired cholesterol excretion may lead to xanthelasma, xanthomas and alterations in the erythrocyte membrane. Prolonged obstruction may cause hepatic failure, biliary cirrhosis and portal hypertension. (Spivack & Jacobson 1999.)

Painless jaundice is a characteristic hallmark of malignant biliary obstruction. However, there are no absolute distinguishing signs between benign and malignant obstruction. About 80 % to 90 % of patients with cancer of the head of the pancreas present with jaundice, and patients with ampullary cancers and cholangiocarcinomas almost always present with jaundice, whereas jaundice is a late symptom of cancer of the gallbladder. (van Leeuwen & Fockens 1999, Spivack & Jacobson 1999.)

Appropriate management relies on accurate staging of the primary lesion and determination of resectability. Unfortunately, fewer than 20 % of patients have resectable disease at the time of presentation. The adverse sequelae of obstruction warrant serious consideration of biliary drainage, which can be done as a surgical or interventional procedure. (Spivack & Jacobson 1999.)

2.3 Biliary fistulas and gallstone ileus

Fistulous connections may occur between the biliary tract and various structures, e.g. the enteric tract, bronchial tree, skin and vessels. They may develop as a complication of chronic cholelithiasis or infection, peptic ulcer or malignancy or result from abdominal or operative trauma. (Lu & Kaplowitz 1991.)

Spontaneous biliary enteric fistulas have been found in 0.9 % of patients undergoing biliary tract surgery. In fact, most spontaneous fistulas result from complications of gallstone disease. Biliary enteric fistulae occur in about 1 % of patients with acute cholecystitis. Chronic inflammation of the gallbladder may follow acute cholecystitis, but usually develops insidiously. An association with stones is almost always present. The gallbladder is usually contracted and has a thickened, sometimes calcified wall. The most common communication of the fistula is cholecystoduodenal, followed by cholecystocolic and cholecystogastric. A fistulous connection between the common bile duct and the enteric tract as a result of stones is much less common. The majority of choledochoduodenal fistulas are caused by peptic ulcer, but stones usually cause the fistulas located in the parapapillary area. Biliobiliary fistulas rarely develop as a complication of gallstones. They may be caused by Mirizzi's syndrome. A fistula may

also develop between the colon and the biliary tract in ulcerative colitis or Crohn's disease. Very rarely, spontaneous fistulas are external. (Lu & Kaplowitz 1991, Knol *et al.* 1996, Sherlock & Dooley 1997c.)

Biliary enteric fistulas are more common in women and the elderly. The symptoms are usually nonspecific (e.g. cholangitis, weight loss, malabsorption and bleeding), and the diagnosis is often made during cholecystectomy based on an intraoperative cholangiogram. About 50 % of the patients with biliary enteric fistulas are diagnosed preoperatively. The fistula may manifest as a mechanical bowel obstruction. Gallstone ileus causes 25 % of all cases of non-strangulated intestinal obstruction in patients aged over 65 years. The gallstone that causes ileus is usually larger than 2.5 cm. The most common site for stone impaction is the ileum, followed by the jejunum, duodenum, colon or rectum. In patients with small bowel disease or previous surgery, the stone may lodge at any site of narrowing. The impacted stone may cause an inflammatory reaction in the intestinal wall or intussusception. Multiple stones may also be found. (Lu & Kaplowitz 1991, Knol *et al.* 1996, Sherlock & Dooley 1997c, Colizzo & Farraye 1999.)

The prognosis of gallstone ileus is poor and worsens with age. The mortality rate in gallstone ileus is 15 %–20 %, partly because of the late recognition of this disease. Preoperative diagnosis is made variably, and the diagnosis is often only made at laparotomy. The obstruction should be relieved surgically. Whether fistula repair and cholecystectomy are done at the time of the first operation depends upon the operative feasibility and the clinical status of the patient. (Roslyn & DenBesten 1990, Sherry & Gadacz 1996, Sherlock & Dooley 1997c.)

Most external biliary fistulas and peritoneal bile leaks are complications of operations on the liver or the biliary tree. Injury to the bile duct during cholecystectomy may result in bile duct fistulas. The injury often goes unrecognized during surgery. About one third of the patients with a fistula present, early in the postoperative period, with an external cutaneous fistula or an internal biliary-peritoneal fistula resulting in peritonitis or an abscess. Bile duct injuries that occur during laparoscopic cholecystectomy range from small bile collections to major ductal disruption. The risk for the latter is two to five times higher with the laparoscopic method than the open method. Complications may be secondary to either the laparoscopic technique or removal of the gallbladder. Early suspicion, recognition and treatment are critical in decreasing morbidity and mortality. Postoperative biliary strictures may also be complicated by fistula formation, usually hepatico-duodenal or hepatico-gastric. Cholecystostomy, transhepatic drainage, T-tube choledochotomy or trauma may cause external fistulas. Bile leaks have been treated by endoprosthesis, sphincterotomy or surgery. (Lu & Kaplowitz 1991, Knol *et al.* 1996, Sherlock & Dooley 1997c, Kastrinakis & Brooks 1999.)

2.4 Primary sclerosing cholangitis

PSC is a chronic cholestatic liver disease of unknown cause characterised by inflammation, destruction of the bile ducts and fibrosis. Sclerosing cholangitis may be either primary or secondary to a variety of disorders, including surgical trauma, bile duct stones, ischemia, cholangiocarcinoma, histiocytosis X, chronic pancreatitis and toxic agents. (Lu & Kaplowitz 1991, Zakko 1999.)

70 % to 80 % of the patients with PSC have a concomitant disorder. These disorders include inflammatory bowel disease (ulcerative colitis (UC), Crohn's disease), fibrosing diseases (e.g. retroperitoneal or mediastinal fibrosis), immunodeficiency syndromes (e.g. acquired immunodeficiency syndrome (AIDS)) and other miscellaneous disorders (e.g. recurrent pancreatitis, diabetes mellitus, rheumatoid arthritis). The most common associated disorders are UC, AIDS and pancreatitis, and UC occurs in 50 % to 75 % of patients. Colonic disease usually precedes the diagnosis of PSC, but PSC may occur before the colitis is clinically evident. Although the course of PSC does not parallel that of colitis, its presence seems to be a risk for increased mortality, dysplasia, and colorectal cancer. The etiology for PSC in patients with AIDS may be infectious. Some patients with PSC have a history of acute or chronic pancreatitis. The prevalence of abnormal pancreatograms has ranged widely, including irregularities of the main pancreatic duct and the side branches, which may result from cholestasis. Magnetic resonance imaging (MRI) of the pancreas has also shown changes. (Lu & Kaplowitz 1991, Lee & Kaplan 1995, Ponsioen & Tytgat 1998, Ito *et al.* 1999a, Zakko 1999.)

Several factors have been proposed to play etiologic roles in PSC: portal bacteremia, viral infections, toxic bile acid metabolites, toxins produced by enteric bacteria and copper. Yet, immune and genetic factors appear more likely to be involved in the pathogenesis. (Lu & Kaplowitz 1991, Lee & Kaplan 1995, Zakko 1999.)

Seventy percent of patients are men, and two thirds are under 45 years old. In one study, the mean age of patients was 39.9 years at diagnosis. Pediatric cases have also been described. Most patients suffer from symptoms for years before diagnosis. Progressive fatigue and pruritus followed by jaundice, abdominal pain and unexplained elevation of the alkaline phosphatase value are common symptoms. Most symptomatic patients have an advanced and medically irreversible disease. PSC can be subclinical and nonprogressive or variable, with exacerbations and remissions. Some patients may remain asymptomatic for many years and yet have a surprisingly advanced disease. Most often, however, PSC shows slow progression, leading to portal hypertension, cirrhosis and death from liver failure. There are reports of 12-year median survival until death or liver transplantation and a 5-year survival rate of 78 %. Age, serum bilirubin concentration and histological stage at the time of diagnosis are independent predictors of an unfavourable prognosis. (Lu & Kaplowitz 1991, Lee & Kaplan 1995, Broomé *et al.* 1996, Ponsioen & Tytgat 1998.)

PSC may involve the intrahepatic or extrahepatic bile ducts or both. There is also a variety called small-duct PSC. The gallbladder and cystic duct are involved in 15 %. In one series, 87 % had involvement of both the intrahepatic and extrahepatic ducts, 11 % of the intrahepatic ducts alone and 2 % of only the extrahepatic ducts. The bifurcation of the hepatic duct is macroscopically involved in the majority of patients. Enlarged lymph

nodes may be present throughout the porta hepatis. Biliary stasis secondary to multiple strictures may account for calculus formation. (Yeo & Cameron 1990, Lee & Kaplan 1995, Majoie *et al.* 1997, Zakko 1999.)

Liver biopsy is rarely definitive, but it is useful in staging and determining the prognosis. The changes seen in liver biopsy consist of periductal fibrosis and inflammation, portal edema and fibrosis, focal proliferation or obliteration and loss of bile ducts, deposition of copper and cholestasis. Four histologic stages have been identified. Stage 1 represents the initial lesion, while the other stages presumably develop over time and progression, leading to the end stage 4 characterized by obvious cirrhosis. (Way & Sleisenger 1989, Lee & Kaplan 1995.)

Complications of PSC may relate to cholestasis or to the underlying disease. Cholangiocarcinoma complicates PSC in 6–30 % of cases. The carcinoma is most commonly located at the hepatic bifurcation and may be multicentric in origin. After the diagnosis of cholangiocarcinoma, the median survival has been only 5 months. (Lu & Kaplowitz 1991, Ponsioen & Tytgat 1998, Zakko 1999.)

The management of PSC is a real challenge. PSC should be treated early in its course. Once the bile ducts have been destroyed, they do not regenerate or do so only ineffectively. No specific therapy apart from liver transplantation has been beneficial. PSC is the fourth leading indication for liver transplantation in adults in the United States. Three-year survival after liver transplantation is 85 %. One post-transplantation problem is the development of strictures. Immunosuppressants, cupruritic agents, antifibrogenic agents and oral bile acid therapy have been tried. The most widely used agent is ursodeoxycholic acid. To treat cholestasis and complications of PSC, reconstructive or interventional procedures (e.g. balloon dilatation and stenting) of the biliary tract are used. (Lu & Kaplowitz 1991, Lee & Kaplan 1995, Ponsioen & Tytgat 1998, Zakko 1999.)

2.5 Diagnosis of malignant biliary tumours and obstruction

In the case of malignant biliary tumours, the laboratory findings are usually related to abnormalities associated with bile duct obstruction. Tumour markers (carcinoembryonic antigen (CEA), CA-19) may be elevated. Fine-needle biopsy and bile cytology may also be helpful in diagnostics. Endoscopy with a biopsy is the most accurate test for ampullary carcinoma. (Townsend 1991, Isenberg & Wong 1999.) However, imaging methods play a crucial role in the diagnosis.

2.5.1 Carcinoma of the gallbladder

2.5.1.1 Conventional methods

Most conventional radiologic methods have failed to produce a definite diagnosis because of the lack of specific findings and the inability to delineate the gallbladder. Oral cholecystography has resulted in nonfilling or poor concentration even in early lesions.

I.v. cholangiography may show early stages, but the incidence has been very low. Intraluminal filling defects or protrusions or a deformed gallbladder may be found. A failure to visualise the gallbladder may raise a suspicion of abnormality. (Itai *et al.* 1980, Chijiwa *et al.* 1991.)

Percutaneous transhepatic cholangiography (PTC) and ERCP are quite accurate for the evaluation of the bile ducts and sometimes also disclose important information of the gallbladder. However, obstruction of the cystic or extrahepatic duct hinders the diagnosis in many cases. (Itai *et al.* 1980.)

Angiography has been reported to have an accuracy of up to 72 %. It was earlier useful in the detection, differentiation and determination of the local extent of the tumour, but has been later used in assessing the local extension of an already known or suspected tumour. The findings may include enlargement of the cystic artery, irregular and interrupted arteries in the wall of the gallbladder and uneven thickness of the wall. Superselective angiography has also been helpful. (Itai *et al.* 1980, Hederström & Forsberg 1987.)

2.5.1.2 Ultrasonography

Sonographic diagnoses of the primary gallbladder tumour currently range from 28 % to 98 % in various series, with the technical development of US equipment. Three US patterns of gallbladder cancer have been described. *A mass replacing the gallbladder* is the most common form seen in 40 %–65 % of cases. The cancer fills the entire lumen and appears as a heterogeneous mass. It may cause difficulties to locate the gallbladder. The mass may appear as diffuse weak echoes, sometimes with additional strong central echoes representing gallstones, air or necrosis. *Thickening of the gallbladder wall* secondary to tumour infiltration and inflammation is seen in 20 %–30 % of cases. The wall may be hyperechoic or hypoechoic, and the thickening may be diffuse or focal. The third pattern is *an intraluminal mass* within the gallbladder with a fungate appearance and an irregular border. (Suramo *et al.* 1983, Hederström & Forsberg 1987, Nilsson *et al.* 1989, Rooholamini *et al.* 1994, Bach *et al.* 1998.) In a study of 40 patients with macroscopic gallbladder carcinoma, US revealed 30 of them: a mass filling the gallbladder in 15, a wall thickening in nine and a polypoid or fungating tumour in six cases (Soiva *et al.* 1987).

Associated findings may include involvement of the adjacent liver or spread to lymph nodes, hepatic and common bile ducts, portal veins, pancreas, colon or duodenum. Obstruction of the biliary tree or intraperitoneal seeding or other distant metastases may be found. There are reports of liver involvement occurring in 34 %–89 % of cases and nodal metastasis in 26 %–75 %. Discontinuous calcification in the gallbladder wall may also be found. (Daly *et al.* 1993, Rooholamini *et al.* 1994, Bach *et al.* 1998.)

In a study comparing the sonographic findings of gallbladder cancer and benign gallbladder conditions, solitary gallstones, displaced stones (lifted from the gallbladder wall by a mass or a focal wall thickening), intraluminal mass, gallbladder-replacing or invasive mass and discontinuity of the mucosal echo were all statistically significantly more common in patients with cancer (Wibbenmeyer *et al.* 1995).

In 40 macroscopic primary carcinomas, the sensitivity of US was 75 % prospectively and 92 % retrospectively. There were 25 false positive diagnoses in approximately 40,000 patients. (Soiva *et al.* 1987.) There are also reports of sensitivity of 50 %, 59 % and 70 % (Frank *et al.* 1989, Nilsson *et al.* 1989, Daly *et al.* 1993).

In a study of 35 patients with gallbladder carcinoma, the extent of disease and staging as revealed by sonography (including colour and duplex Doppler of portal veins) were compared to the operative and surgical pathologic findings. Masses in the gallbladder or gallbladder fossa were visualised by US in 85 %. US identified 67 % of the liver metastases, 79 % of the bile duct involvements, 67 % of the portal venous involvements, 36 % of the lymph node metastases and none of the cases with peritoneal metastases. US correctly identified 94 % of the 16 patients with potentially resectable disease and 37 % of the 19 patients with advanced disease. Twelve patients with advanced disease were understaged. US seemed to be reliable in the detection of a primary gallbladder mass or a local extension of tumour into the liver, but limited in the diagnosis of metastases in the peritoneum and lymph nodes. Many normal-size nodes may contain metastases. (Bach *et al.* 1998.)

In a prospective study of 26 patients with carcinoma of the gallbladder, US had limitations in staging, the accuracy being 38 %. Only one patient was overstaged, while 15 patients were understaged due to missed distant metastases and missed advanced local infiltrations. The sensitivity was 50 % in detecting liver infiltration, 50 % in lymph node metastasis and 8 % in liver metastasis. (Haribhakti *et al.* 1997.)

US is also helpful in diagnosing metastatic tumours in the gallbladder. Suspicion should be raised in the presence of a focal wall thickening associated with nonshadowing intraluminal soft-tissue masses. Cholelithiasis is usually absent. Metastatic melanoma has been identified as single or multiple hyperechoic masses more than 1 cm in diameter and attached to the gallbladder wall. (Phillips *et al.* 1982, Stutte *et al.* 1989, Holloway & King 1997.)

Colour Doppler US has helped to differentiate carcinomas from debris and metastatic and benign lesions of the gallbladder. Endoscopic US has also been used in the staging of gallbladder carcinomas and shown to be 100 % accurate in detecting hepatic invasion. Intraoperative or laparoscopic US may also be helpful. (Li *et al.* 1994, Ueno *et al.* 1996, Dill *et al.* 1997, Haribhakti *et al.* 1997.)

US-guided fine-needle aspiration is safe, rapid, reliable, cost-effective and accurate in diagnosing gallbladder carcinoma. It has a diagnostic accuracy of 95 % as compared to 60 % on blind aspiration. (Shukla *et al.* 1997.)

2.5.1.3 Computed tomography

The sonographic findings of gallbladder carcinoma can be applied to computed tomography (CT). The findings may include a mass replacing the gallbladder, a wall thickening or a fungate mass within the gallbladder. Extrahepatic biliary obstruction caused by metastatic lymph nodes, encasement of the common hepatic duct, invasion into the adjacent structures, liver metastases, distant metastases, thickening of the hepatoduodenal ligament or protrusion of the quadrate lobe may also occur. The latter

finding and the presence of lymphadenopathy have been reported to be unique to gallbladder carcinoma. Cholelithiasis or calcification of the gallbladder wall may also be found. (Rooholamini *et al.* 1994.)

Itai *et al.* reported 20 out of 27 cases (74 %) of gallbladder cancer to have been diagnosed correctly by CT. They concluded that a discontinuous wall thickening, a highly enhanced mass with an ill-defined contour and a solid mass surrounded by a narrow zone of low density are suggestive of gallbladder cancer. Contrast enhancement was occasionally useful in assessing whether the tumour originates in the gallbladder or the liver. Direct hepatic extensions were easy to reveal by CT, except in minimal lesions. Bile duct dilatation was often noticed. Lymph node metastases and bile duct extension were difficult to distinguish. (Itai *et al.* 1980.)

In a study of ≤ 2 cm polypoid lesions, the density of the lesions compared with the liver parenchyma on enhanced CT was not specific. However, CT has been able to differentiate between neoplastic and nonneoplastic ≤ 3 cm polypoid lesions. When a lesion was demonstrated on unenhanced CT or was sessile in shape, it could be cancerous and invade the subserosa or beyond with an associated risk of lymph node metastases. When it was demonstrated on unenhanced CT and was pedunculated in shape, it could be an adenoma or carcinoma limited to the mucosa. (Furukawa *et al.* 1995, Furukawa *et al.* 1998.)

According to Engels *et al.*, CT is reliable in demonstrating lymphatic or other extrahepatic spread of biliary cancers. The study included 20 patients with gallbladder cancer, and CT demonstrated correctly liver metastases in 5 out of 6 cases, lymph nodes in 13 out of 14, peritoneal spread in 7 out of 9, and direct invasion (to the hepatoduodenal ligament or duodenum) in all the six cases. The study had, however, some limitations. (Engels *et al.* 1989.)

Ohtani *et al.* studied the ability of CT to detect gallbladder carcinoma and its spread in 59 patients. CT found 92 % of the primary tumours, 65 % and 100 % of the instances of direct spread into the liver of less than 2 cm or more than 2 cm, respectively, 75 % of the liver metastases, 50 % of the instances of spread into the extrahepatic bile duct, 36 % and 47 % of N1 and N2 nodal involvement, respectively, and 57 % of invasions into the gastrointestinal tract or pancreas. CT failed to detect direct spread into the omentum or peritoneal seedings. (Ohtani *et al.* 1996.)

Comparative studies: There are some studies comparing different modalities. Chijiwa *et al.* studied 11 resected cases of gallbladder carcinoma. US and CT were valuable in detecting carcinoma preoperatively, while direct cholangiography and angiography were useful in assessing the site of bile duct involvement and vessel involvement, respectively. The sensitivity of US was 82 % and that of CT 60 %. All carcinomas located in the mucosal layer, muscularis propria and subserosal layer seemed to be polypoid. Endoscopic US – used only in one patient in this study – provided information of the depth of tumour invasion into the gallbladder wall and invasion into the liver and bile duct. (Chijiwa *et al.* 1991.)

There is an evaluation of different modalities to detect the hepatic invasion of gallbladder carcinoma in 21 patients. US, CT and angiography failed to detect intrahepatic invasion in one, one and six cases, respectively, and US was superior to CT or angiography in defining the extent of invasion. Preoperative US had a diagnostic value almost comparable to intraoperative US. (Iida *et al.* 1995.)

2.5.1.4 Magnetic resonance imaging

There are only a few reports of MRI in gallbladder carcinoma. Nineteen patients with gallbladder carcinoma were studied by MRI. The primary tumour as well as its spread beyond the gallbladder were hyperintense on T2 images and hypointense on T1 images when compared with the liver parenchyma. Liver invasion and metastases could be depicted by MRI, unless the tumours were small or the invasion was minimal. Duodenal invasion was difficult to detect. T1 images visualised extension into the hepatoduodenal ligament, para-aortic region and blood vessels. MRI demonstrated the primary tumour in all the 19 cases, direct liver invasion in 11 out of 13 cases and metastatic liver changes in 5 out of 8 cases. It overstaged duodenal invasion, and the other findings were only partly explored and confirmed on operation. However, in the 15 cases also examined with CT, CT was no better than MRI. (Sagoh *et al.* 1990.)

T1 images may also show extension into fat and the head of the pancreas. MRI is also able to show the bile duct dilatation occasionally caused by gallbladder carcinoma. (Rooholamini *et al.* 1994, Soto *et al.* 1997.)

Dynamic MRI with a spoiled gradient pulse sequence may differentiate benign from malignant gallbladder lesions. Malignant lesions demonstrate early and prolonged enhancement for all the three types: polypoid masses, diffuse wall thickening and exophytic masses, whereas benign lesions show different patterns. Dynamic MRI can also be useful for the differentiation of chronic cholecystitis from carcinoma and for the evaluation of whether the tumour invades beyond the serosa. (Demachi *et al.* 1997, Yoshimitsu *et al.* 1997.)

2.5.2 Carcinoma of the bile duct

2.5.2.1 Cholangiography

Proper management of patients with bile duct carcinoma requires a complete and accurate evaluation of the location, morphology and extent of the disease. Cholangiography performed either percutaneously or endoscopically provides a detailed view of the anatomy of the biliary tree. (Nichols *et al.* 1983, Shlansky-Goldberg & Weintraub 1997.)

Bile duct carcinoma may appear as a ductal stricture of variable length. Less frequently, it may visualise as a polypoid filling defect or a diffuse sclerosing change. The carcinoma may locally obstruct the duct. The accuracy of cholangiography in detecting the level of obstruction ranges within 92–100 %, while the accuracy of determining the cause has been reported to range within 75–87 %. (Nichols *et al.* 1983, Shlansky-Goldberg & Weintraub 1997, Kumar *et al.* 1998.) In a study of 111 patients with biliary obstruction, PTC revealed obstruction in 94 %, its site in 92 %, and the correct cause in 87 % (Gibbons *et al.* 1983).

There is a report of rotational cine cholangiography in 26 patients with bile duct carcinoma and obstructive jaundice. The modality seemed to be reliable in detecting the confluence of the bile ducts and in diagnosing the longitudinal extent of cancer spread along the bile duct wall. (Miura *et al.* 1999.) Cholangioscopy has also been used to define tumour extension (Nimura 1993).

2.5.2.2 Ultrasonography

US is valuable in the initial identification of cholangiocarcinoma, tumour staging and the prediction of resectability. When ever cholangiocarcinoma is suspected, the following aspects should be assessed: biliary dilatation, level of obstruction, presence of mass, focal or diffuse thickening of the bile duct wall, hepatic tumours, local lymph nodes, portal vein thrombosis and cholelithiasis. (Mittelstaedt 1997, Bloom *et al.* 1999.)

The most frequently seen abnormality in patients with ductal cholangiocarcinoma at US is dilatation of the intrahepatic ducts. With the modern technology, it is possible to visualise the central intrahepatic structures that represent normal bile ducts. They are considered normal if they measure 2 mm or less in diameter. Colour Doppler is helpful in distinguishing between vessels versus dilated ducts. The diameter of the common hepatic duct and the common bile duct may exceed the threshold of 6 mm without obstruction, especially in elderly subjects and after cholecystectomy. (Mittelstaedt 1997, Bloom *et al.* 1999.)

There has been variation in the reported accuracy of US in defining the level and cause of obstruction in patients with surgical obstructive jaundice, ranging within 23–95 % and 38–81 %, respectively. Differential diagnosis for the cause is related to the anatomic level of the obstruction. (Mittelstaedt 1997, Kumar *et al.* 1998.) US indicated the level of dilatation in 92 % and suggested the correct cause in 71 % of 110 patients with biliary dilatation caused by benign or malignant diseases. Benign disease processes were most often responsible for distal dilatation. (Laing *et al.* 1986.) In fact, malignancy is reported to be the most common cause of obstruction at the suprapancreatic level or at or proximal to the level of porta hepatis. Metastatic adenopathy or lymphoma may form extensive lobulated masses that surround rather than fill the bile ducts. Occasionally, a metastasis may be seen as a polypoid intraluminal mass. Gallbladder cancer extending to porta hepatis is often indistinguishable from cholangiocarcinoma. (Laing *et al.* 1986, Bloom *et al.* 1999.)

In a study of 120 patients, US differentiated obstructive from non-obstructive jaundice in 96 % of the patients, comparing well with the results of ERCP. US defined correctly the cause in 90 % of the patients with tumoural duct obstruction (19 malignant tumours), while ERCP did so in 79 %. (Rigauts *et al.* 1992.)

Carcinoma of the bile duct may be classified according to the anatomic level of the tumour: Klatskin tumour, extrahepatic tumour and peripheral cholangiocarcinoma.

Klatskin tumours may show segmental dilatation and nonunion of the right and left ducts. The point of caliber alteration or ductal occlusion should be located. The tumour may be: 1. papillary, resembling polypoid intraluminal masses, 2. nodular, i.e. a discrete smooth mass with associated mural thickening and possible tumoural shouldering, or 3.

infiltrating. The latter type may show a central porta hepatis mass, a “mass effect“, subtle alterations in liver echogenicity, pressure effects on adjacent vascular structures or focal irregularity of the ducts. The infiltrating type is most difficult to appreciate at US. The masses in Klatskin tumours may be iso-, hypo-, or hyperechoic. Subtle lobar atrophy may also be seen. Vascular involvement may be assessed with gray-scale, colour Doppler or spectral Doppler US. The vessels may be in close proximity to the tumour or invaded, encased or obliterated by the tumour. US may also show lymphadenopathy. US seems to be valuable in the identification of hilar cholangiocarcinoma and the prediction of tumours that are unresectable. (Yeung *et al.* 1988, Hann *et al.* 1997, Mittelstaedt 1997, Bloom *et al.* 1999.)

Extrahepatic bile duct tumours (involving the common bile duct) resemble Klatskin tumours and may show a short stricture or a polypoid mass. Carcinomas of the distal duct are usually small. *Peripheral cholangiocarcinoma* is often nodular or infiltrating. The former may be a solitary mass, while the latter may show diffusely abnormal liver echotexture. Tumours less than 3 cm in diameter often visualise as hypoechoic, whereas larger tumours tend to be hyperechoic. A papillary tumour may produce mucin and present as a cystic mass. Peripheral carcinoma may cause dilatation of the bile ducts peripheral to the tumour. Satellite nodules and calcification may also be seen. (Mittelstaedt 1997, Bloom *et al.* 1999.)

The accuracy of US in the diagnosis of cholangiocarcinoma depends on tumour location. US is more accurate for lesions involving the bifurcation and the common hepatic duct than for those involving the common bile duct. The sensitivity and specificity of US in the detection of Klatskin tumours have risen lately. (Mittelstaedt 1997, Bloom *et al.* 1999.)

In a report of 39 Klatskin tumours, US with Doppler revealed the extent of bile duct involvement in 87 % and depicted 86 % of the 21 involved portal veins (Hann *et al.* 1997). Another study also reported US to be valuable in the preoperative staging of Klatskin tumours, especially in predicting ductal and portal involvement. In 25 (out of 35) patients, hilar vessels were also evaluated with the image-directed and colour Doppler techniques. However, US had poor sensitivity in detecting infiltration of the hepatic artery (43 %) and metastases in the regional lymph nodes (37 %) and the peritoneum (33 %). US identified 66 % of liver infiltrations. (Neumaier *et al.* 1995.)

Laparoscopic, endoscopic and intraductal US have also been used for detecting or staging bile duct tumours. Fine-needle biopsy (FNB) is helpful in characterising the lesion. (Tio & Tytgat 1986, Ros *et al.* 1988, Kuroiwa *et al.* 1994, Mittelstaedt 1997.)

2.5.2.3 Computed tomography

CT has achieved success in evaluating abnormalities of the bile ducts. When a conventional scanner is used, it may be necessary to re-scan through the zone of transition of a dilated duct to search for details, while reconstructions can be helpful following helical acquisition. The latter technique has the advantage of maintaining

optimal tissue contrast by obtaining images during the initial contrast bolus. It also minimizes data misregistration and partial volume averaging when single breath-hold acquisition is used. (Baron 1997, Keogan *et al.* 1997, Kim *et al.* 1997, Tillich *et al.* 1998.)

The current technology has allowed the occasional visualisation of small intrahepatic ducts. Very few ducts should be seen, and they should be minimal in size (< 2 mm) and not confluent. The common bile duct lumen appears to be of near-water attenuation. The duct wall is “pencil line“ thin and it shows contrast enhancement. The normal duct diameter is generally accepted as 8 mm or less and there is gradual tapering distally. Three-dimensional spiral CT cholangiography following intravenous infusion of a biliary contrast agent can use maximum intensity projections and shaded surface display projections. The accuracy of CT in determining the level and cause of obstruction has been 88–97 % and 70–94 %, respectively. (Stockberger *et al.* 1994, Baron 1997, Kumar *et al.* 1998.)

Klatskin tumours and extrahepatic tumours can be subtle and show abrupt termination of bile duct dilatation. The mass is seen in about 70 % of cases. It may be difficult to differentiate extrinsic masses from an intrinsic mass. However, thin-section CT may show thickening of the duct wall just proximal to the mass. Hilar cholangiocarcinoma may appear as infiltrating, exophytic, polypoid or diffuse lesions. (Choi *et al.* 1989, Baron 1997, Han *et al.* 1997, Tillich *et al.* 1998.)

Peripheral intrahepatic cholangiocarcinoma is usually exophytic, although sometimes papillary. It may appear as a parenchymal liver mass of nonspecific appearances, e.g. as a low-attenuation mass with wide variations in homogeneity. The tumour can enhance and usually reaches a level of isoattenuation or less during portal venous phase imaging. The optimal time of delayed images with retention of contrast is 10 to 20 minutes. This is helpful for tumour characterisation and for the differentiation of peripheral cholangiocarcinoma from hepatocellular carcinoma. A study of 25 patients with peripheral intrahepatic or hilar cholangiocarcinoma using dynamic CT showed the true extent of the tumour to be most apparent by viewing the dynamic and delayed images together. The features of peripheral carcinoma also include calcification, mild biliary dilatation, invasion of veins, hepatic lobar atrophy or lymphadenopathy. (Ros *et al.* 1988, Baron 1997, Keogan *et al.* 1997, Kim *et al.* 1997, Loyer *et al.* 1999, Zhang *et al.* 1999.)

When two-phase spiral CT was used in 34 patients with peripheral cholangiocarcinoma, the typical findings were thin, mild, incomplete rim-like contrast enhancement at the tumour periphery and markedly low intratumoural attenuation with amorphous areas of slightly higher attenuation during both phases of scanning (Kim *et al.* 1997). Spiral CT during arterial portography has also been used to evaluate peripheral and central cholangiocarcinomas. All the 17 tumours were seen as hypoattenuating masses, being homogenous in 11 cases. (Soyer *et al.* 1994.)

The sensitivity of conventional CT in the detection of hilar cholangiocarcinoma has varied from 40 % to 90 % (Tillich *et al.* 1998). CT may also be useful in staging. However, although dynamic CT is valuable in tumour identification, it is not considered accurate when evaluating bile ducts or vascular involvement. Feydy *et al.* reported helical CT to identify hilar carcinoma in 91 % and to aid in the assessment of parenchymal, biliary intrahepatic and portal involvement, but not to be effective in the assessment of biliary extrahepatic, arterial and lymph node involvement. (Feydy *et al.* 1999.) Another report of spiral CT in hilar cholangiocarcinoma also showed it to be valuable in diagnosis,

but less accurate in the evaluation of intraductal tumour extent (Han *et al.* 1997). A study of 29 patients also evaluated multiphasic helical CT in the staging of hilar cholangiocarcinoma. The accuracy of helical CT in assessing resectability was 60 %. The exact proximal tumour extent tended to be underestimated. The artery phase enabled better detection of infiltrating stenotic lesions and involvement of hepatic artery, and the venous phase improved the detection of exophytic tumours and portal vein involvement. (Tillich *et al.* 1998.)

Comparative studies: Some older reports have shown US and CT to be complementary to cholangiography in biliary malignancies (von Triller *et al.* 1985, Nesbit *et al.* 1988). One study compared CT with US in 51 cases of hilar cholangiocarcinoma. With CT, infiltrating tumours were more difficult to depict than the other types, while with US, infiltrating and exophytic tumours were difficult. CT and US were of comparable accuracy in determining the level of obstruction, but CT was superior in depicting the tumour and in demonstrating associated findings, e.g. lymphadenopathy and lobar atrophy. (Choi *et al.* 1989.)

Another study reported US and CT arterial portography in 19 patients with malignant hilar obstruction (15 were cholangiocarcinomas). US with colour and duplex Doppler was comparable to CT arterial portography in determining the extent of portal venous and hepatic parenchymal invasion, the presence of atrophy and the level of bile duct obstruction, revealing best the latter two findings. Both methods were unreliable in the detection of metastatic disease. (Hann *et al.* 1996.)

The diagnostic accuracy of US, CT and cholangiography in defining the level of obstruction in 50 patients with surgical obstructive jaundice has been 86 %, 86 % and 95 %, respectively. To evaluate the cause of obstruction, the accuracy was 84 %, 86 % and 75 %, respectively. Sensitivity in the diagnosis of malignant disease (29 cases) was 100 % for US and CT, whereas specificity was 90 % and 81 %, respectively. (Kumar *et al.* 1998.) In an older report of US, CT, cholangiography and angiography in 65 patients with bile duct obstruction, the resectability of 56 malignant tumours was correctly predicted in 71 %, 42 %, 58 %, and 25 % of the cases, respectively (Gibson *et al.* 1986).

2.5.2.4 Magnetic resonance cholangiography and magnetic resonance imaging

MRC has its rationale in the acquisition of heavily T2-weighted images that result in increased contrast between stationary fluids, such as bile, and background. As a consequence, bile appears to have very high signal intensity, whereas the background appears to have low signal intensity. Different techniques have been used, initially based on gradient-echo (GRE) sequences, but more recently replaced by fast spin-echo (FSE) sequences. (Pavone *et al.* 1999.)

There are numerous trials using different techniques of MRC in assessing the biliary tree and its abnormalities, including the breath-hold and non-breath-hold techniques, the 2-dimensional (2D) and 3-dimensional (3D) techniques, rapid acquisition relaxation enhancement (RARE), half-Fourier acquisition single-shot turbo spin-echo (HASTE), single slice and multislice and steady-state free precession (SSFP). Most techniques

produce multiple contiguous thin slices, “source images”, which then undergo postprocessing, such as maximum intensity pixel projection (MIP), shaded surface display (SSD) and multiplanar reformatting (MPR). Interpretation requires that both sets of reformatted and individual source images should be evaluated at the same time. A review of pertinent T1 and T2 images may also be useful. (Barish & Soto 1997, Becker *et al.* 1997, Soto *et al.* 1997, Yamashita *et al.* 1997, Fulcher & Turner 1998, Lee *et al.* 1998, van Epps & Regan 1999, Pavone *et al.* 1999.)

MRC is able to image a common bile duct of normal caliber, the common hepatic duct and the right and left hepatic ducts. Intrahepatic segmentary ducts are visible only up to the first-order branches. More peripheral ducts can be visualised only in case of dilatation. A distended gallbladder and cystic duct are also visible. Many trials report MRC to offer diagnostic value comparable to cholangiography in suspected biliary diseases, e.g. in dilatation, choledocholithiasis and strictures. (Soto *et al.* 1996a, Bearcroft *et al.* 1997, Lee *et al.* 1997b, Holzknecht *et al.* 1998, Takehara 1998, Lomas *et al.* 1999, Pavone *et al.* 1999, Varghese *et al.* 1999.)

The MRC finding of cholangiocarcinoma is a sudden biliary stricture or obstruction with dilatation above. The technique can provide a detailed map of the biliary tree, also demonstrating isolated segmental ducts. The morphology and the length of the strictures are usually clearly evaluated by MRC, but occasionally the strictures are seen as short segments of signal dropout. On T1-weighted MRI, hilar tumours appear hypointense or isointense, while on T2-weighted images their appearance is variable. Scirrhus tumours may have central low signal intensity and variable high signal intensity in the periphery. Well-differentiated tumours may have a higher signal on T2 images. After enhancement with a gadolinium-based contrast agent, the tumour initially remains hypointense, but later shows slow and progressive enhancement. (Guthrie *et al.* 1996, Reinhold & Bret 1996, Soto *et al.* 1997, Pavone *et al.* 1999.)

Peripheral intrahepatic cholangiocarcinoma may present as an isointense or hypointense mass on T1 images. Segmental hyperintensity on T1-weighted MRI may also occur, indicating segmental cholestasis. On T2 images the tumour is usually hyperintense, sometimes with a hypointense central scar. Gadolinium may define the margins, and there may be delayed enhancement of the scar. The enhancing pattern has not been typical in small tumours. (Adjei *et al.* 1995, Gabata *et al.* 1997, Soto *et al.* 1997, Pavone *et al.* 1999, Zhang *et al.* 1999.)

Spread into the bile ducts or vessels, satellite lesions in the liver, regional lymphadenopathy, peritoneal spread, and lobar atrophy can be demonstrated with a combination of MRC and MRI. Magnetic resonance angiography (MRA) or dynamic magnetic resonance may also be helpful in assessing vascular involvement. MR imaging has been comparable to angiography in the evaluation of vascular spread. (Guthrie *et al.* 1996, Becker *et al.* 1997, Fulcher & Turner 1997, Soto *et al.* 1997.)

The accuracy of MRC in diagnosing the presence of obstruction ranges within 91–100 %, whereas the level of obstruction can be correctly evaluated in 85–100 %. It can visualise the bile ducts above and below the obstruction. The cause of obstruction is more difficult to predict on the basis of the MRC sequences alone. The accuracy in the differentiation of benign from malignant obstructions has varied within 30–98 %. The use of a combination of MRI and MRC improves diagnostic accuracy. T1- and T2-weighted MRI may also reveal extrabiliary malignant lesions causing obstruction. (Guibaud *et al.*

1995, Barish & Soto 1997, Soto *et al.* 1997, Mendler *et al.* 1998, Pavone *et al.* 1999, Kim *et al.* 2000.) In a report of six patients with hilar cholangiocarcinoma, HASTE MRC (with T1 and T2 images and MRA) delineated the duct both proximal and distal to the stricture, showed isolated ductal obstructions and helped to assess resectability (Fulcher & Turner 1997).

Comparative studies: Dynamic CT has been better than dynamic MRI for demonstrating vascular involvement and extrahepatic invasion in intrahepatic peripheral cholangiocarcinoma (Zhang *et al.* 1999). In a comparison of MRI with CT in 11 patients with peripheral cholangiocarcinoma, MRI was slightly superior to CT in detecting the tumours, equal to CT in assessing the extent of the tumours, but inferior to CT in delineating the focal ductal dilatation around them (Choi *et al.* 1995).

2.5.3 Carcinoma of the ampulla

2.5.3.1 Endoscopy

Ampullary carcinomas tend to be small at the time of diagnosis. They may be subtle or completely invisible at endoscopy, but may also look like a prominent papilla or an apparent submucosal mass. More commonly, a portion of the tumour extends into the duodenum and has an irregular surface and ulcerations. Endoscopy provides access for biopsy and cytology. (Hayes *et al.* 1987, Buck & Elsayed 1993.)

2.5.3.2 Cholangiography

Antegrade cholangiography demonstrates either a complete obstruction or a lesion in the most distal segment of the common bile duct causing proximal ductal dilatation. The lesion appears as an irregular polypoid filling defect or only as a stenosis. (Buck & Elsayed 1993, Shlansky-Goldberg & Weintraub 1997.)

ERCP allows a direct look at the ampulla and demonstrates findings identical to those of percutaneous cholangiography. It can also outline the intraduodenal portion of the tumour. It also provides a pancreatogram. Dilatation of both the common bile duct and the pancreatic duct, which is called the “double-duct sign”, is typical of ampullary tumours. (Hayes *et al.* 1987, Buck & Elsayed 1993.)

2.5.3.3 Ultrasonography and computed tomography

At US, there may be dilatation of the common bile duct or pancreatic duct, but the mass itself is either completely invisible or seen as an intraluminal polypoid mass or a sharply delineated mass (Robledo *et al.* 1988, Mittelstaedt 1997).

Endoscopic US is useful with distal ductal obstruction and small intraampullary tumours. It may show the anatomy of the ampulla, the surrounding duodenal wall, and the adjacent pancreas. The layers of the wall of the papilla together with the adjacent common bile duct and the pancreatic duct can be imaged. Invasion into the adjacent major blood vessels can also be evaluated. Abdominal US can be used for the assessment of distant metastases. (Tio *et al.* 1990, Buck & Elsayed 1993, Mittelstaedt 1997.) In a study of 24 patients, the accuracy of endoscopic US was 87 % in the classification of ampullary carcinoma and 54 % in the diagnosis of regional lymph nodes (including 80 % accuracy in metastatic lymph nodes). Endoscopic US seemed to be accurate in the evaluation of the location, size and extent of the tumour, but it was not accurate in assessing distant metastases, especially liver or peritoneal metastases. (Tio *et al.* 1990.) Intraductal US is also a useful method for polypoid tumours, but not for the detection of distant metastases (Menzel *et al.* 1999).

At CT, the double-duct sign may be obvious, but the tumour is often inapparent. A mass is sometimes seen protruding into the duodenum. The sensitivity of CT in detecting ampullary tumours has been 58 %. Bolus injections and spiral scanners with thin sections might also be helpful. (Buck & Elsayed 1993, Midwinter *et al.* 1999.) Two cases of CT hypotonic duodenography have also been reported. The tumours were clearly seen as bulging into the air-filled lumen of the duodenum. (Pandolfo *et al.* 1990.)

2.5.3.4 Magnetic resonance imaging and magnetic resonance cholangiography

Ampullary carcinoma, especially when intraductal, is a challenge for magnetic resonance cholangiopancreatography (MRCP). Detailed examination of the ampulla is difficult because of the limited spatial resolution and artifacts. When MRC reveals common bile duct dilatation to the level of the ampulla, evaluation of the source data and conventional MR images is necessary. (Reinhold & Bret 1996, Barish & Soto 1997.)

Nine patients with known ampullary carcinoma were examined by MR (T1 spoiled GRE, T1 fat-suppressed, and T1 contrast-enhanced (CE) spoiled GRE for all, and MRC for three). The carcinomas were demonstrated as small masses arising at the ampulla, and they were well defined with contrast medium. The tumours were low in signal intensity relative to normal pancreatic tissue in the first and second sequences and enhanced less than the pancreas. Tumour conspicuity was greatest on the immediate CE images. MRC demonstrated the double-duct sign with abrupt termination of the ducts. (Semelka *et al.* 1997.)

Comparative studies: Endoscopic US has been superior to US, CT and angiography in the detection of ampullary tumours and superior to US, CT, angiography and MRI in staging (Buck & Elsayed 1993, Cannon *et al.* 1999). However, there is also a report of helical CT being better than endoscopic US in determining resectability (Howard *et al.* 1997). With tumours of the ampullo-pancreatico area, the ability of endoscopic US and spiral CT to detect involvement of the superior mesenteric vein, portal vein and lymph nodes was similar, but US was less effective in evaluating the superior mesenteric artery

(Midwinter *et al.* 1999). Intraductal US has been reported to be the most effective method in visualising, diagnosing and staging polypoid tumours of the major duodenal papilla compared with endoscopic US and CT (Menzel *et al.* 1999).

2.6 Diagnosis of biliary fistula and gallstone ileus

2.6.1 Iatrogenic fistula

The diagnosis of a biliary fistula is dependent on its mode of presentation. The clinical manifestations of bile leaks are nonspecific. Laboratory tests may show leukocytosis and abnormal liver tests, and abdominal films may reveal an ileus. Radiologic imaging plays an important role in the diagnosis and management of iatrogenic bile duct injuries. (Horattas *et al.* 1994, Kastrinakis & Brooks 1999.)

2.6.1.1 Cholangiography

The optimal mode of imaging to define any biliary tract trauma is cholangiography, which is able to delineate the location and anatomy of the fistula. Cholangiography can be performed intraoperatively, via a T tube, endoscopically (endoscopic retrograde cholangiography (ERC)) or via a percutaneous transhepatic approach (PTC). (Ghahremani *et al.* 1991, Horattas *et al.* 1994.)

I.v. cholangiography is rarely helpful. Intraoperative cholangiography and cholangiography performed via a T tube are particularly valuable in detecting the precise location, extent and cause of operative biliary tract injuries. The use of intraoperative cholangiography may help to reduce the frequency of complications of laparoscopic cholecystectomy. (Kissin & Grundy 1987, Ghahremani *et al.* 1991, Trerotola *et al.* 1992.)

PTC is rarely needed to demonstrate the presence of a leak, but it may, however, localise the source of leakage and identify any cause of persistent leakage, such as obstruction. It is also useful in defining the length of a stricture or anomalous anatomy or in the evaluation of the biliary-enteric anastomosis. PTC visualises biliary anatomy well, and it is a reliable technique, although it is often difficult in patients with nondilated ducts. Transhepatic treatment of bile leaks has also been used. (Kissin & Grundy 1987, Ponchon *et al.* 1989, Trerotola *et al.* 1992.)

ERCP allows visualisation of bile leaks, but may not always fully depict the extent of a possible stricture, may neglect to show anomalous intrahepatic bile duct anatomy, and may not show all of the proximal biliary tree. It may also be technically complex or impossible if gastric surgery has been performed. Endoscopy offers an invaluable modality for the management of iatrogenic biliary leaks by nasobiliary tubes, endoprotheses, sphincterotomy, and balloon dilatation of a stricture. (Kissin & Grundy 1987, Ponchon *et al.* 1989, Trerotola *et al.* 1992, Sherman *et al.* 1993, Hoff *et al.* 1998.)

Twenty-four biliary fistulas, 23 of them iatrogenic, were evaluated by ERC and treated endoscopically. Twenty-two patients presented with a persistent cutaneous leak, and three patients had internal fistulas. ERC showed extravasation of contrast material in 22 patients. Leaks were managed by sphincterotomy, nasobiliary drainage, or insertion of an endoprosthesis resulting in prompt resolution in 16 patients. (Ponchon *et al.* 1989.)

Sherman *et al.* report 18 patients with liver transplantation having bile peritonitis and 13 patients having biliary fistula after other hepatobiliary operations. ERCP revealed a biliary fistula at the T tube insertion site into the bile duct in all liver transplant patients and demonstrated contrast extravasation from the biliary tree in 12 patients in the latter group. All the patients were treated endoscopically with a fistula closure rate of over 90 %. (Sherman *et al.* 1993.)

After cholecystectomy and bile duct exploration, 35 patients had iatrogenic biliary complications, including biliary ruptures, lacerations and perforations, malposition of T tubes, choledochoduodenal fistulas, biliovenous fistulas and bilomas. Cholangiograms revealed collections of bile and extravasated contrast material. In some patients CT was also demonstrative. (Ghahremani *et al.* 1991.)

2.6.1.2 Ultrasonography and computed tomography

US and CT can be useful adjuncts in revealing the presence, location and extent of a bile leak, but they do not differentiate bile from other fluid accumulations. The usual presentation of an actual biloma is that of a unilocular, well encapsulated, extraorgan fluid collection. Percutaneous drainage of biliary leaks can be achieved under US or CT guidance, and they are also useful in demonstrating the parenchyma of the liver. US is used in the follow-up of fluid collections. Access and visualisation by US may, however, be limited in the immediate post-operative period. (Weissmann *et al.* 1979, Mueller *et al.* 1983, Kissin & Grundy 1987, Horattas *et al.* 1994, Wicky *et al.* 1999.)

Eleven bilomas caused by abdominal surgery, PTC or blunt abdominal trauma were demonstrated by US, and all patients underwent percutaneous needle aspiration under US or CT control, followed by catheter drainage. Although all trauma and surgery had occurred in the right upper or mid-quadrant, four patients had a left-sided subhepatic or subphrenic collection. Needle aspiration seemed to be essential in confirming the diagnosis of biloma. Four patients presented with abscesses and five patients demonstrated continuous bile leaks. (Mueller *et al.* 1983.)

2.6.1.3 Other modalities

Retrograde injection of contrast medium along a fistulous tract, if present, or along a surgical drain, is able to demonstrate the site of communication with the biliary system, but the presence of debris may prohibit delineation of the entire extent of the tract (Kissin & Grundy 1987).

Hepatobiliary scintigraphy utilizing hepatoiminodiacetic acid (HIDA) is a sensitive test for identifying biliary leaks and fistulas. However, it remains nonspecific, its resolution is poor and it cannot provide precise anatomical localisation of the site of leakage. It can be helpful in the follow-up of a biloma. (Weissmann *et al.* 1979, Kissin & Grundy 1987, Horattas *et al.* 1994.)

MRI has demonstrated intrahepatic biloma in two patients. The biloma was heterogeneously intense on T1-weighted images and homogeneously hyperintense on T2-images. (Shigemura *et al.* 1995.)

Comparative studies: The biliary tract complications following laparoscopic cholecystectomy in 13 patients included biliary leaks, strictures, obstructions and a transection. Cholescintigraphy appeared most helpful in screening, supplemented by ERCP and / or PTC for definitive diagnosis. CT and US frequently allowed the detection of nonspecific fluid collections but were unable to demonstrate the presence of a bile leak. (Trerotola *et al.* 1992.) ERC or PTC have been considered suitable methods for diagnosing biliary leakage after conventional and laparoscopic cholecystectomy (Hoffmann & Neuhaus 1993). HIDA scan has also been recommended as the first method when suspecting bile leakage after laparoscopic cholecystectomy. Positive scans should be followed with ERC or PTC. (Morgenstern *et al.* 1993.)

2.6.2 Biliary enteric fistula

2.6.2.1 Abdominal plain film and barium studies

Patients with biliary enteric fistula may have symptoms similar to those with chronic cholecystitis and cholelithiasis or other nonspecific symptoms, and the diagnosis is often made during cholecystectomy (Lu & Kaplowitz 1991, Colizzo & Farraye 1999).

The diagnosis is to be suspected whenever air is demonstrated within the biliary system on roentgenographic examination. However, the presence of air in the biliary tree is nonspecific. Infection, gas-containing gallstones, neoplasia, trauma, an incompetent sphincter of Oddi and congenital anomalies have been implicated as factors in the production of pneumobilia. Air can also be present in too small, unrecognized amounts. (Piedad & Wels 1972, Safaie-Shirazi *et al.* 1973, Glenn *et al.* 1981.) Of the 267 cases of spontaneous internal biliary fistula reported by Borman and Rigler, 30 % had air in the biliary tree (Borman & Rigler 1937).

Further investigations might include barium studies, which outline the stomach, duodenum and small intestine and demonstrate the passage of barium into the gallbladder or the ductal system through a fistula. A failure to demonstrate a fistula by this procedure could be an indication for a barium enema. Endoscopy may also reveal a fistula. (Stitt *et al.* 1967, Glenn *et al.* 1981, Grumbach *et al.* 1986, Clavien *et al.* 1990, Romano *et al.* 1997.)

A report of 55 patients with spontaneous biliary fistula during the period from 1950 to 1970 showed some improvement in the preoperative diagnosis of both the nonobstructive and obstructive types over the 20-year period. In the former type, however, the diagnostic accuracy was only 17 % as compared to 63 % in gallstone ileus. Preoperative recognition

is more difficult in the nonobstructive type. In six of the 36 nonobstructive cases, a fistula was suspected based on the abdominal plain film and confirmed by radiography with contrast medium. All six showed air in the biliary tree in the plain films, which finding is often only recognized in retrospect. The remaining 30 nonobstructive cases were found incidentally in a total of 4720 cholecystectomies. (Piedad & Wels 1972.)

Of the 92 patients with spontaneous enterobiliary fistulas from the 30-year period until 1970, 37 patients had an oral cholecystogram, and the gallbladder was not visualised in 33. Air or barium was visualised in the biliary tree by means of abdominal plain films or barium studies in 31 patients. Seventy patients (all the 40 patients with gallstone ileus) had a cholecystoduodenal fistula. (Safaie-Shirazi *et al.* 1973.)

A study of 105 patients with biliary enteric fistula from a period of 46 years until 1978 revealed 45 correct diagnoses preoperatively. The accuracy increased from 30 % in the earlier period (1932–1956) to 51 % in the latter period. The most common location of the fistula was cholecystoduodenal followed by cholecystocolic. Twenty-two patients had gallstone ileus. (Glenn *et al.* 1981.)

2.6.2.2 Endoscopic retrograde cholangiopancreatography

ERCP provides a detailed image of the biliary duct system, which may permit precise localisation of a fistula and evaluation of the extrahepatic anatomy, to exclude conditions that may impede successful fistula closure (e.g. biliary stricture, inflammation). In addition, endoscopic access to the common bile duct permits endoscopic treatment. (Hoff *et al.* 1998.)

The precise detection of a postoperative bilioenteric fistula is often difficult (Hoff *et al.* 1998). However, there is a report of 14 choledochoduodenal fistulas demonstrated by ERCP. Two fistulas occurred spontaneously caused by stones located in the distal common bile duct. The stones were removed endoscopically. The twelve remaining cases were iatrogenic, occurring after surgical papillotomy. (Jorge *et al.* 1991.) A choledochogastric or cholecystogastric fistula may also be revealed by ERCP (Nakamura *et al.* 1997, Hoff *et al.* 1998).

2.6.2.3 Computed tomography and ultrasonography

There are only a few reports of CT and US in biliary enteric fistulas. At CT, the location of air and contraction of the gallbladder have been useful signs to differentiate gallbladder-enteric fistulas from common bile duct-enteric fistulas (Shimono *et al.* 1998). CT revealed cholecystoenteric fistulas in three patients with gallstone ileus. All had a greatly distorted gallbladder containing air and being in direct continuity with a thickened duodenal wall. (Lorén *et al.* 1994.) There is also a report of abnormal gas in the gallbladder fossa, a cholecystoduodenal fistula and an abnormal duodenum at CT in three of four patients with gallstone ileus. The region of the gallbladder fossa should be viewed with wide window settings to reveal subtle gas. The same technique may help to identify

the fistulous tract. (Swift & Spencer 1998.) According to a case report, a duodeno-cholecystic fistula complicating a duodenal ulcer was revealed by CT and US (Fournier *et al.* 1994).

2.6.3 Gallstone ileus

2.6.3.1 Abdominal plain film and barium studies

The classic triad of small bowel obstruction, ectopic gallstone and air in the biliary tree on abdominal plain film should be diagnostic of gallstone ileus. The presence of two of the signs of the triad has been considered pathognomonic and is encountered in 40–50 % of the cases. The change of location of a previously observed stone has been added to the set of criteria. In serial views, one may recognise the progression of the degree of obstruction and changes in its level. A review of previous radiographs is also often helpful. (Rigler *et al.* 1941, Stitt *et al.* 1967, Clavien *et al.* 1990.)

However, the majority of gallstones are not sufficiently calcified to permit detection on abdominal radiography. Visualisation of stones outside the biliary region is also often difficult because of the superimposition of gaseous or bony contours. Air in the biliary tree is not specific to gallstone ileus. Plain radiographs are also insensitive for small quantities of biliary air, and gallbladder gas or biliary gas may be absent if the underlying biliary enteric fistula closes. (Grumbach *et al.* 1986, Clavien *et al.* 1990, Davies *et al.* 1991.)

In a study of 37 patients with gallstone ileus, the most frequent finding on the admission radiographs was mechanical obstruction (70 %), followed by pneumobilia (54 %) and the presence of an abnormally located gallstone (35 %). These radiographs were diagnostic in 46 %. (Clavien *et al.* 1990.)

Bryk *et al.* developed a fluid gas index for plain abdominal films. Gallstone ileus had a significantly higher index than simple distal small bowel obstruction. (Bryk *et al.* 1977.) An additional radiological sign associated with gallstone ileus may be two adjacent small air-fluid levels in the right upper quadrant, the medial collection being in the duodenal bulb and the lateral in the gallbladder (Balthazar & Schechter 1978). In a study of 19 cases of gallstone ileus, 10 out of the 12 diagnosed cases were revealed by plain films (Piedad & Wels 1972).

The use of contrast medium is valuable as a means of identifying the level of bowel obstruction and the radiolucent stone. It may also reveal the fistula. (Stitt *et al.* 1967, Clavien *et al.* 1990.) In a study of 105 patients with biliary enteric fistula, 22 had gallstone ileus, and 16 were diagnosed correctly before surgery (Glenn *et al.* 1981).

2.6.3.2 *Computed tomography and ultrasonography*

CT is increasingly used to investigate acute abdomen, including cases of small bowel obstruction. CT is capable of revealing all signs of Rigler's triad, as in the report of three patients with gallstone ileus diagnosed by CT (Lorén *et al.* 1994). There are some other case reports of CT in gallstone ileus.

The diagnosis of gallstone ileus was made preoperatively with CT in three of four patients. CT also revealed the fistula. The presence of small bowel dilatation, the luminal transition point and the distally collapsed small bowel were clearly seen in all the four cases. The CT features of the intraluminal gallstones were variable. CT was considered to have a role in excluding complications and being a complementary investigation. (Swift & Spencer 1998.)

There are some reports of US in the diagnostics of gallstone ileus. In a study covering a period of over 30 years and 108 patients with gallstone ileus, US provided an exact diagnosis in 10 out of 15 cases since 1992 (Freitag *et al.* 1998). Among the 74 patients with gallstone ileus, the preoperative diagnosis was made by abdominal radiography or US in 31 %. US is recommended as a complementary investigation. (Schutte *et al.* 1992.)

One study reports four patients diagnosed by US. Ectopic gallstone was demonstrated as an intraluminal semicircular reflex with strong echoes and a sonic shadow in all the patients. Lacking visibility of the gallbladder in the clinical setting of ileus or subileus proved to be a sonographic clue to gallstone ileus. (Manner & Stickel 1998.) There are some case reports of US revealing features of Rigler's triad. A stone with thickening of the intestinal wall was also shown. The patient was successfully treated with shock wave lithotripsy. (Pedersen *et al.* 1988, Davies *et al.* 1991, Elewaut *et al.* 1993.)

In most series, the diagnosis of gallstone ileus has been made preoperatively in less than half of the patients (Day & Marks 1975, van Hillo *et al.* 1987). In the study of Clavien *et al.* with 37 patients, the diagnosis was made before the operation in 73 %. US provided useful diagnostic information for six patients, gastrointestinal contrast studies for three patients and CT for one patient. Gastroduodenoscopy demonstrated duodenal obstruction in two patients. (Clavien *et al.* 1990.) In another report, 82 % of the cases of gallstone ileus were correctly diagnosed preoperatively (Stitt *et al.* 1967).

2.6.3.3 *Bouveret's syndrome*

Bouveret's syndrome is a rare entity consisting in a duodenal obstruction due to the passage of gallstones from the gallbladder to the duodenum through a cholecystoduodenal or cholecystogastric fistula. The fistula is likely to be a large, patulous opening, creating a confluence of the gallbladder and the duodenal bulb. The preoperative diagnosis of Bouveret's syndrome is not easy. Endoscopy has been the main diagnostic procedure according to an extensive literature review. The diagnosis was made endoscopically in more than 90 % of the cases. Endoscopy allows visualisation of the stone and often the fistula way, too. Fragmentation and removal of the stone endoscopically is also a therapeutic option. (Cooper *et al.* 1987, Romano *et al.* 1997.)

Plain abdominal film is also used in diagnostics. Rigler's triad may be seen, but gastric distention will be evident in most instances. Plain films were obtained of almost all patients reviewed until 1995. Most films revealed evocative information about the situation. (Cooper *et al.* 1987, Romano *et al.* 1997.)

Barium study may also reveal duodenal obstruction and repletion defects, and US or CT may be helpful in revealing aerobilia and lithiasis. CT has demonstrated the gallbladder and the duodenum not to be separate and distinct structures. (Cooper *et al.* 1987, Kasano *et al.* 1997, Romano *et al.* 1997, Farman *et al.* 1998.)

In the evaluation of 52 reported cases from 1985 to 1995, the preoperative diagnosis was made by endoscopy in 20 patients, by barium meal in five, by US in two, and by CT and plain abdominal film in one (Romano *et al.* 1997).

2.7 Diagnosis of primary sclerosing cholangitis

2.7.1 General

The diagnosis of PSC can be made on the basis of a cholestatic liver chemistry profile and a typical cholangiogram or liver histology, when all other secondary causes of sclerosing cholangitis have been excluded. Liver biopsy is almost always abnormal, but mostly nonspecific. It is only diagnostic when fibrous obliterative cholangitis is seen, i.e. in less than 40 % of patients. The disease may not be evenly and diffusely spread, and the most characteristic lesions can easily be missed. Histology may also be used for staging. Tests for perinuclear antineutrophil cytoplasm antibodies (pANCA) and other antibodies and hepatobiliary scintigraphy with technetium-99m-labeled IDA analogues have been used. Copper metabolism is also virtually always abnormal. In diagnosing cholangiocarcinoma complicating PSC, tumour markers (CEA, CA 19-9) and cytology are used. (Lu & Kaplowitz 1991, Lee & Kaplan 1995, Ponsioen & Tytgat 1998, Zakko 1999.)

2.7.2 Direct cholangiography

Visualisation of the biliary tract is essential for the diagnosis of PSC. ERCP has been the method of choice. Good intrahepatic studies are best obtained by advancing the catheter deeply into a position above the cystic duct, which may require use of the balloon occlusion technique. PTC has been considered technically more difficult, as the intrahepatic bile ducts are often attenuated or reduced in number, and it has only been performed if ERCP fails. The characteristic findings of PSC include multifocal strictures and dilatations. Diffuse strictures with short intervening segments of normal or dilated bile duct produce the beaded appearance. In early stages, the only abnormality may be fine or deep ulcerations of the common bile duct. In the small-duct variant of PSC, the

affected bile ducts may be too small to be detected by cholangiography. Cholangiography may also show calculi. However, cholangiography has shown the fewest calculi compared to US and CT. (Lee & Kaplan 1995, Dodd *et al.* 1997, Majoie *et al.* 1997.)

In the report of MacCarty *et al.*, multifocal strictures involving both intra- and extrahepatic ducts were the most common findings. They were diffusely distributed, short (1–2 cm) and annular, alternating with normal or slightly dilated segments. Very short (1–2 mm) band-like strictures and diverticulum-like outpouchings were also found. These two findings appeared to be specific for PSC. In more advanced disease, long, confluent strictures were seen. There were also mural irregularities, which, when severe, produced a shaggy appearance and were more often seen in the extrahepatic ducts. Some patients also had cystic duct abnormalities. (MacCarty *et al.* 1983.)

Majoie *et al.* proposed the modified classification of cholangiographic findings in 1991. This was based on the extent and severity of bile duct narrowing, contour abnormalities, prestenotic dilatation, decreased arborization, diverticula and pruning of the bile ducts. The classification had special clinical implications. In this study, the intrahepatic ducts were involved in 93 % of the 40 patients and the extrahepatic ducts in 95 %. (Majoie *et al.* 1991.) In 1991, Craig *et al.* reported a cholangiographic classification predicting the clinical outcome of PSC. It could be useful in treating and counseling patients. It was based on the grade, length and extent of strictures, the degree of dilatation and the distribution of lesions. Intrahepatic duct disease was found to have greater prognostic significance than extrahepatic disease. (Craig *et al.* 1991.)

The presence of a severe stricture with marked ductal dilatation, progression in a stricture, and a polypoid mass of over 1 cm are suggestive of malignant change. In cases of segmental or diffuse stenosis of the common bile duct, differentiation from cholangiocarcinoma may be difficult. Brushing and biopsies of suspicious strictures may be obtained during ERCP. ERCP also has an important therapeutic capability. (Majoie *et al.* 1997, Campbell *et al.* 1998, Varghese *et al.* 1999, Zakko 1999.)

ERCP and PTC are relatively time-consuming and costly. There is also small but significant associated morbidity (including sepsis, cholangitis, pancreatitis, instrumental injury and drug reactions) and mortality. Cannulation of the common bile duct or pancreatic duct for ERCP fails in 3–9 % of cases. ERCP is also often limited by the opacification of the ducts proximal to a high-grade stenosis and, in PSC, by the multiplicity of strictures. Also, underfilling of the ducts can give the radiographic appearance of strictures, falsely suggesting PSC. ERCP may also result in progressive cholestasis in patients with advanced PSC. (Bilbao *et al.* 1976, Reinhold & Bret 1996, Bearcroft *et al.* 1997, Lomas *et al.* 1999, Zakko 1999, Fulcher *et al.* 2000.) In the report of Bilbao *et al.* of 10,000 cases of ERCP, the procedure failed in 30 %, complications occurred in 3 %, and the patient died in 0.2 % (Bilbao *et al.* 1976).

2.7.3 Magnetic resonance studies

MRC is a relatively new, non-invasive imaging technique for the evaluation of the biliary tract without contrast agents or radiation. Heavily T2-weighted fat-suppressed sequences are used to produce images in which the static fluid is hyperintense and the background

signal is suppressed. The published data – some of the studies also including patients with PSC – have demonstrated high accuracy in the depiction of bile duct strictures, dilatation, and the level and extent of obstruction. Half-Fourier RARE MRC has produced diagnostic images of the pancreatobiliary tract in more than 99 % of patients. However, it may not properly delineate the peripheral intrahepatic ducts. (Reinhold & Bret 1996, Soto *et al.* 1996a,b, Barish & Soto 1997, Bearcroft *et al.* 1997, Becker *et al.* 1997, Fulcher *et al.* 1998, Varghese *et al.* 1999, Fulcher *et al.* 2000.)

There are some reports of MRC in PSC. In a case-control study of 34 patients with PSC and 68 controls, MRC was accurate in detecting PSC (the sensitivities and specificities for the two readers were 88 % and 85 % and 97 % and 92 %, respectively) and in defining the extent of disease. The study evaluated multiple segmental strictures, alternating ductal strictures and dilatations as well as mural irregularities. The location of PSC noted at ERCP was used as the standard of reference in the 24 patients whose ERCP images were available. The presence of cirrhosis and PSC limited to the peripheral intrahepatic bile ducts led to some false-positive and false-negative diagnoses. (Fulcher *et al.* 2000.)

According to another report, MRC could be useful in the diagnosis of PSC. Slightly dilated peripheral bile ducts unconnected to the central ducts were considered a characteristic MRC sign of PSC. Biliary abnormalities suggesting PSC were shown in all the nine patients with PSC. MRC depicted strictures, beaded appearance and dilatations of the intrahepatic ducts and strictures and mural irregularities of the extrahepatic ducts. Staging of the intrahepatic abnormalities (using the classification of Majoie *et al.*) at MRC and direct cholangiography was similar for eight of the nine patients and that of the extrahepatic ducts for seven patients. Slightly dilated peripheral bile ducts above the central stenoses were only depicted by MRC. (Ernst *et al.* 1997, Ernst *et al.* 1998.)

The MRC features of 22 patients with PSC have been reported. Abnormal bile duct findings were seen in all patients; the most common finding was intrahepatic bile duct dilatation, followed by intrahepatic stenosis, extrahepatic wall enhancement, wall thickening, stenosis and intrahepatic beading. No significant differences were found between the ERC and MRC findings of the 15 patients examined with both methods, with the exception of intrahepatic ductal stenosis, which was more commonly shown with ERC. (Ito *et al.* 1999b.) In a study of 20 patients with PSC, MRC visualised intrahepatic ducts that were nonopacified at ERC. MRC could be an adjunct to ERC for the primary diagnosis of PSC and an alternative method for follow-up. (Oberholzer *et al.* 1998.)

MRC can be used to reliably estimate the degree of intrahepatic stenoses, but it may be insensitive to subtle ectasiae of the common duct. MRC correlates well with direct cholangiography in the identification of dominant strictures. A lack of dilatation proximal to an area of stenosis may be a sign of a diffuse or multifocal process, such as PSC, and strictures may also appear as segments of complete signal dropout. Follow-up of PSC could be a possible indication for MRC. MRC can also identify intrahepatic calculi, but may underestimate their number. (Barish & Soto 1997, Feldman *et al.* 1997.)

MRI changes of the liver in PSC may include abnormal hyperintensity of the parenchyma on T1-weighted images, periportal high signal intensity on T2-weighted images, increased enhancement of the liver parenchyma, predominantly in the peripheral areas of the liver, on dynamic arterial-phase images, hypertrophy of the caudal lobe and atrophy of the other segments. Abnormally high signal intensity of the parenchyma may

correspond to the areas of intrahepatic bile duct dilatation. Peripheral wedge-shaped areas of high T2 signal intensity, a reticular pattern, portal hypertension or periportal lymphadenopathy may also be found. Contrast-enhanced dynamic MRI sequences should also be used for patients with suspected PSC. (Ito *et al.* 1999b, Revelon *et al.* 1999.)

Cholangiocarcinoma associated with PSC has exhibited masses with low signal intensity on spin-echo T1-weighted images and high signal intensity with T2 weighting in a limited number of the cases studied. An intrahepatic mass and eccentric thickening of the bile duct wall have also been reported. (Campbell *et al.* 1998, Ito *et al.* 1999b.)

Pancreatic changes of PSC have also been depicted by MRI: a decreased signal on T1-weighted images, an increased signal on T2-weighted images, decreased contrast enhancement, enlargement of the pancreas, narrowing of the pancreatic ducts and peripancreatic edema or fluid (Ito *et al.* 1999a).

Although MR has certain advantages – e.g. the rate of failure of MRCP is less than that of ERCP and MRCP is not limited by altered anatomy – there are also some limitations. It is possible to underestimate duct caliber, MRCP has limited spatial resolution, which restricts its ability to provide a detailed analysis of stricture morphology, and no therapeutic interventions can be performed. (Reinhold & Bret 1996, Fulcher & Turner 1998.)

2.7.4 Ultrasonography

There are only a few reports about the sonographic manifestations of PSC. Features suggestive of PSC at US include mural thickening of the extrahepatic ducts, segmental dilatation, intrahepatic stones, and gallbladder wall thickening. Marked dilatation of the intrahepatic ducts is usually absent, but discontinuous dilatation or nonvisualisation of the intrahepatic ducts is usually found. (Carrol & Oppenheimer 1982, Vrla *et al.* 1986, Brandt *et al.* 1988, Majoie *et al.* 1995, Dodd *et al.* 1997, Majoie *et al.* 1997, Zakko 1999.) US can also show hepatic morphologic and parenchymal changes and signs of portal hypertension and be used to guide needle biopsies. Parenchymal changes may include diffuse increased echogenicity and a loss of fine detail or focal increased periportal or intrahepatic echogenicity. (Majoie *et al.* 1997, Zakko 1999.)

In a study of 23 patients with PSC, extrahepatic disease, mural thickening of the common bile duct and advanced disease manifested as signs of portal hypertension were well demonstrated by US. Mural thickening of the extrahepatic ducts was considered the clue to the diagnosis in an appropriate clinical setting, and the liver parenchymal change was taken to suggest intrahepatic involvement. The major limitation of US was its inability to exclude intrahepatic duct disease. (Majoie *et al.* 1995.)

Thickening of the wall of the extrahepatic bile duct of more than 6 mm, seen at US (or CT), has been considered highly suspicious of carcinoma. Marked intrahepatic duct dilatation or a hypoechoic, hyperechoic or heterogenic mass may also be signs of cholangiocarcinoma. Endoscopic US has been useful to stage cholangiocarcinoma, to detect encasement of vessels by colour Doppler imaging and to sample tissues. (Majoie *et al.* 1995, Campbell *et al.* 1998, Zakko 1999.)

2.7.5 Computed tomography

Helical CT cholangiography is a useful method for visualising the biliary tree. General features suggestive of PSC, liver parenchymal changes and portal hypertension can be depicted by CT. Guided needle biopsies are also possible. The finding of focal discontinuous areas of minimal intrahepatic bile duct dilatation without an associated mass lesion is highly suggestive of sclerosing cholangitis. CT may also reveal bile duct calculi. (Ament *et al.* 1983, Rahn *et al.* 1983, Stockberger *et al.* 1994, Dodd *et al.* 1997, Zakko 1999.)

The CT findings of 20 patients with PSC revealed abnormalities of the common hepatic duct or the common bile duct (duct stenosis, mural nodularity, duct dilatation, wall thickening and mural enhancement) in 16 out of 19 cases having extrahepatic duct disease demonstrated with cholangiography, and CT showed intrahepatic disease in all of the 20 cases (dilatation, stenosis, pruning and beading). It also demonstrated extrabiliary complications and cholangiocarcinomas. CT could provide valuable information about the extent and complications of PSC. (Teefey *et al.* 1988.)

Cholangiocarcinoma with PSC may show as hypoattenuating masses, delayed contrast enhancement, progressive biliary dilatation and a thickened bile duct wall (Campbell *et al.* 1998). Hepatic morphology seen at CT seems to be significantly different in patients with PSC-induced end-stage cirrhosis versus that in patients with end-stage cirrhosis due to other causes (Dodd *et al.* 1999).

2.8 Palliative treatment of malignant biliary obstruction

Malignant biliary obstruction can be treated by surgery, percutaneous transhepatic cholangio drainage (PTCD) or plastic or metallic stents inserted endoscopically or percutaneously.

2.8.1 Bypass surgery, percutaneous transhepatic cholangio drainage, endoscopic endoprosthesis

Adequate palliation of the biliary obstruction is desirable, as prolonged obstructive jaundice causes pruritus, malabsorption and progressive hepatocellular and renal dysfunction. It is also important to treat or avoid cholangitis. (Davids *et al.* 1992, Schöfl *et al.* 1994.) There are several treatment modalities available.

Biliary bypass surgery is effective, and surgical drainage can create a large biliary intestinal anastomosis and has the advantage of allowing additional preventive or therapeutic gastrojejunostomy. However, surgery involves considerable, although decreasing, mortality and morbidity. Anastomotic strictures or tumor invasion may also occur. (Barth 1990, Davids *et al.* 1992, Schöfl *et al.* 1994, Smith *et al.* 1994.)

With the advances in percutaneous catheterization techniques in the mid-1970s, percutaneous biliary drainage became popular as a preoperative risk-reducing measure and as palliation for the patients who were not surgically drainable. An internal-external catheter is easy to place, but it has a major potential for infection and dislodgement, and it is associated with problems of the long-term catheter maintenance and patient discomfort. Endotoxemia, loss of electrolytes, bleeding and sludge accumulation may also occur. There is a need for regular catheter flushing and dressing, and bile leakage, infection and pain at the catheter entry site may occur. (Barth 1990, Coons 1990, Lammer 1990.)

The advancement in endoscopic techniques led to more frequent successful retrograde drainage via plastic endoprostheses. Avoidance of the transhepatic approach reduced the incidence of immediate infections and bleeding complications. (Barth 1990.) The ideal plastic prosthesis should have a small outer diameter, to ensure minimal insertion trauma, and its inner diameter should be as large as possible to maintain bile flow for a long period. The wall of the prosthesis should be as thin as possible without kinking or being easily compressed by the tumour, and the encrustation rate should be low. (Lammer 1990.)

The major problem with plastic stents has been occlusion of the endoprosthesis with sludge, which happens in about 20–30 % of the patients with polyethylene stents within three months of insertion. The clogging sequence includes protein adherence, subsequent biofilm formation, and final entrapment of bile crystals and food fibres. In fact, plastic stents should be replaced every three months. An obstructed endoprosthesis can be removed and exchanged endoscopically. (Barth 1990, Davids *et al.* 1992, Knyrim *et al.* 1993, O'Brien *et al.* 1995.) Displacement of plastic stents is well recognized, too. A stent may migrate from its initial position or it may sometimes be primarily misplaced via a false track. (Nicholson & Martin 1997.) The passage of nonexpanding large-bore stents is also limited by the diameter of the strictures and the size of the instrumentation channel of the endoscope. It has been problematic to steer a catheter or guide wire in a retrograde manner through the obstructed duct in high or proximal biliary obstructions. (Barth 1990, Davids *et al.* 1992.)

There are reports of a combined percutaneous-endoscopic technique of inserting plastic stents. The endoscopist and the interventional radiologist work together on selected patients with complex or unusual biliary problems. (Gordon & Ring 1990, Knyrim *et al.* 1993, Wagner *et al.* 1993.)

Trials of endoscopic stent placement versus surgical bypass report stenting to involve less procedural mortality, a shorter hospital stay and a better cost-effectiveness ratio. However, despite the efforts to prolong patency by changing stent design and material or by administering antibiotics or aspirin, stent clogging has been an important problem. Occasional duodenal obstructions also occur. (Davids *et al.* 1992.) Endoscopic stenting with plastic endoprostheses (100 patients) was compared to surgical bypass (101 patients) in malignant low bile duct obstruction. Both methods were effective, the former resulting in fewer early treatment-related complications and the latter in fewer late complications. (Smith *et al.* 1994.)

Self-expanding metal stents may also be inserted endoscopically, and a combined percutaneous-endoscopic technique has been used, too (Knyrim *et al.* 1993, Schöfl *et al.* 1994, O'Brien *et al.* 1995). Metal stents have been considered superior to plastic stents in many uncontrolled and randomised controlled trials. There are reports of the technical

success rate being high, complications rare, the primary clinical success rate high, patency markedly prolonged in comparison with plastic stents, and the need for further interventions small. However, the occlusion of metal stents by tumor growth has been substantial. (Davids *et al.* 1992, Huibregtse *et al.* 1992, Knyrim *et al.* 1993, Wagner *et al.* 1993.) In the study of Carr-Locke *et al.*, the stent occlusion rates of endoscopically placed Wallstents and plastic stents were similar, but the causes were different. The duration of stent patency was better in Wallstents. (Carr-Locke *et al.* 1993.) Davids *et al.* considered polyethylene stents to be the treatment of choice in metal stent obstruction (Davids *et al.* 1992).

2.8.2 Percutaneously inserted endoprostheses

Transhepatic stenting has become a valuable alternative to surgical bilioenteric bypass. The main drawback of plastic endoprostheses, regardless of whether a percutaneous or endoscopic route has been chosen, is eventual clogging due to biliary sludge. Percutaneous drainage with plastic stents also causes pain and discomfort. (Mueller & Dawson 1991.) A comparison of endoscopic insertion of plastic stents with the percutaneous technique showed the endoscopic method to have a significantly higher success rate for the relief of jaundice and a lower 30-day mortality (Speer *et al.* 1987). There is a review of previous studies of plastic stents in malignant biliary obstruction in Table 1. The results are not directly comparable, as the study designs vary.

Metallic self-expandable endoprostheses have been designed to circumvent the limitations of plastic endoprostheses. They have advantages over plastic stents, as they can be introduced on a small delivery catheter, have a large inner diameter and have a fixed position after release. (Stoker & Laméris 1993.) Various types of stents differing in material, design and implantation technique have been designed for enhanced clinical efficacy. The material characteristics of endoprostheses must be evaluated for three major properties: biocompatibility, stability and handling. The first feature includes chemical surface interaction with the surrounding tissue and bile. The two other features depend on the mechanical properties of stent: length, wall thickness, surface friction and elasticity. (Lammer 1990.)

The Wallstent, the Gianturco stent and the Palmaz metallic stent are constructed of a thin wire-type material shaped into different specific designs. The Wallstent is like a thin wire mesh made of stainless steel monofilaments, which, when fully expanded, has a diameter of 10 mm. When compressed, it fits onto a 7-French (F) introducer catheter. The stent is covered by a membrane that is removed upon insertion. The length of the stents is variable. There are also nitinol, tantalum and spiral stents. (Lammer 1990, Mueller & Dawson 1991, Bezzi *et al.* 1994, von Friedrich *et al.* 1995, Lee *et al.* 1997a.) The standard method for percutaneous introduction of metallic stents varies only slightly with the different types of stents used. Dilatation of the tract should be performed to allow placement of a 7–9-F biliary drainage catheter. When placing a Wallstent, the catheter that contains the stent is placed across the stricture, and the stent is deployed by slowly withdrawing the plastic membrane. It can be placed with a single-step procedure. There is

some controversy about the use of a dilatation balloon, both prior to the placement to dilatate the stricture and after the stent has been placed to accelerate the expansion of the metallic stent. (Mueller & Dawson 1991.)

Table 1. A review of previously published results of plastic stents in malignant biliary obstruction.

Study	Succession rate %	Procedure-related deaths %	Re-obstruction %	Dislocation %	Patency months	Re-intervention %	Complication early %
Mueller <i>et al.</i> 1985, 113 patients (109 malignant)	92		25 (late)	6 (late)		15 (late)	17/31 early/late
Lammer & Neumayer 1986, 162 patients (156 malignant)		3.7	6	3			20 (cholangitis) late
Lammer & Neumayer 1986, 525 patients, 7 studies*			1.5–25	0–6			
Tytgat <i>et al.</i> 1986, 2458 patients, 5 studies*	80–90		21–31				
Speer <i>et al.</i> 1987, 75 patients	89 (endoscopic insertion), 76 (percutaneous)						19 67
Siegel <i>et al.</i> 1988, 183 patients	91	0	1	2	6.3 (mean)		
Wagner & Knyrim 1993, 969 patients						35	
Doctor <i>et al.</i> 1999, 54 patients	89	0	22	0	4 (mean)		24
England <i>et al.</i> 2000, 134 patients	99	1			teflon: 6 (median) polyethylene: 4.4 (median)		7
Terruzzi <i>et al.</i> 2000, 57 patients					teflon: 3.2 (median) polyethylene: 2.5 (median)		

*review.

Stents have an effect on the surrounding tissues. The normal bile duct mucosa becomes edematous between the struts of the stent within 24 hours after stent placement, probably due to mechanical irritation. Mucosal hyperplasia may develop after four weeks, being most marked at the proximal and distal edges. However, hyperplasia ultimately subsides. Destruction of normal epithelium, nonspecific inflammatory reactions and slight necrotic reactions may also occur. Necrosis and inflammation may involve the epithelium,

including tumour cells, and the inner layer of muscularis. After one year, the whole lumen of the stent may be lined by tissue. There may also be invasion of tumour cells. The main reaction to the stent has been connective tissue formation. (Lammer 1990, Boguth *et al.* 1994.)

Metallic stents have many advantages. Their design allows a small track through the liver parenchyma, which should reduce the complications associated with the percutaneous procedure. Once in place, the stents extend to their large lumen, which might reduce the reocclusion rates, as the patency of a stent should be directly related to the stent diameter. The internal lumen of metallic stents is 20–30 times larger than the lumen of plastic stents. The open wire mesh allows drainage of biliary side-branches and plays an important role in the management of hilar obstructions. The variety of different combinations allows treatment of complicated strictures and complete drainage of several isolated hepatic ducts, which should reduce the risk of cholangitis and septicemia. The small surface area of the wire mesh in Wallstents might also reduce bacterial growth and encrustation. Multiple stent placements in both liver lobes can be achieved via uni-, bi- or multilateral percutaneous approaches, and the stents may be arranged side-to-side, one through the struts of the other, or two or even three into one. There are also several anatomic configurations that may be treated only by the percutaneous technique, and finally, the lumen of metallic stents can be evaluated with US and CT. (Coons 1990, Cwikiel *et al.* 1990, Gordon & Ring 1990, Lammer 1990, Mueller & Dawson 1991, Nicholson *et al.* 1992, Wagner *et al.* 1993, Rossi *et al.* 1994.)

There are numerous reports of percutaneously inserted metallic stents in malignant biliary obstruction. Numerical comparisons between different studies are difficult, as the study design, the number of patients, the duration of follow-up, the type of stents, the definitions and the listed complications are variable.

In a multicenter study of 240 patients with malignant biliary obstruction, 300 Wallstents, 35 nitinol Strecker stents, 40 Gianturco stents and 13 tantalum Strecker stents were used. Average follow-up was 8 months, and the longest observation period was 28 months. The overall 25- and 50-week survival rates were 42 % and 16 %, respectively. Eight percent had major complications. The 25-week patency rate was significantly higher for the nitinol Strecker stents (78 %) and the Wallstents (67 %) than for the Gianturco stents (30 %) and the tantalum Strecker stents (20 %). Average patency was 8.3, 5.9, 2.3, and 4.0 months, respectively. Stent occlusion was mostly caused by tumour ingrowth or overgrowth but debris, duodenal stenosis, blood clots and mucosal hyperplasia also occurred. Reintervention due to stent obstruction was necessary in 53 patients (22 %). No cases of long-term migration occurred. With Wallstents, the patency rates were not affected by the type of tumour, but the patency of the stents placed at the level of the biliary-enteric anastomoses was lower than that of the stents placed either in the common bile duct or at the hilar confluence. (Rossi *et al.* 1994.)

In another study, 176 patients were treated with Wallstents. Early complications occurred in 7 %, predominantly cholangitis and reobstruction. Thirty-day mortality was 12 %, and in three patients the death was procedure-related. Late complications, predominantly reobstruction, occurred in 20 %. Reocclusion was seen in altogether 33 patients (19 %) after a median period of 4.5 months. Tumour overgrowth was the major cause of reobstruction (n = 19), tumour ingrowth caused obstruction in three patients. Occlusion was most frequent in patients with a hilar stenosis caused by cholangio-

carcinoma or gallbladder carcinoma. Reintervention was performed in 25 patients (14 %), and it caused complications in four patients. Multiple reinterventions for reobstruction were performed in six patients. The authors considered the Wallstent to be preferable to a plastic stent, as the reobstruction is not stent-related predominantly, but is caused by tumour progression. (Stoker & Laméris 1993.)

A hundred patients with malignant biliary obstruction were treated with various metallic stents: 64 Gianturco and 39 Hanaro spiral stents, 16 Wallstents, two tantalum Strecker stents, one Endocoil stent and one Memotherm nitinol stent. The average follow-up was 7.3 months. The median patency was 360 days, being much longer in the patients with hilar obstruction than in those with common bile duct obstruction. Twenty-one percent developed recurrent jaundice or cholangitis. The causes for the former were tumour overgrowth, encrustation of bile sludge, duodenal obstruction, stent impaction into the bile duct wall, stent malposition and tumour ingrowth. (Lee *et al.* 1997a.)

Either percutaneously or endoscopically placed metal stents in 82 patients involved problems with stent deployment in 19 out of 82 Wallstents (23 %) and 6 out of 34 Strecker stents (18 %) (Bethge *et al.* 1992).

A review of 15 other studies, most of them with fewer patients than the above series, is included in Table 2. The studies are not directly comparable. Some conclusions of the authors can be highlighted. The long-term patency of Wallstents has been excellent in common duct obstruction, but significantly lower in hilar obstruction (Becker *et al.* 1993). However, there are results indicating that Wallstents offer moderate results in malignant hilar obstructions regardless of the type of obstruction according to the Bismuth classification (Schima *et al.* 1997). Adequate peripheral purchase and overstenting are thought to be necessary to prevent tumour overgrowth when stenting hilar lesions, and drainage of only one system in patients with multisegmental obstruction risks subsequent development of cholangitis (Lee *et al.* 1993, Lee *et al.* 1994). A conclusion of no great clinical advantages in prolonged patency in metal stents compared to plastic stents has also been reported (Gordon *et al.* 1992). (Table 2)

Apart from cholangitis, the serious problems encountered with metal stents have included duodenal ulcer, bile duct perforation, abscess, pleural empyema, cholecystitis and arteriobiliary fistula (Laméris *et al.* 1991, Becker *et al.* 1993, Stoker & Laméris 1993, Wagner & Knyrim 1993).

The occlusion rate of polyurethane-covered Wallstents in 30 patients was 37 %. The 12-month patency rate was 31 %. Tumour ingrowth was observed in two patients, causing stent obstruction in one patient. (Hausegger *et al.* 1998.) Polyurethane-covered nitinol Strecker stents had a mean patency of 9.5 months in 18 patients (Kanasaki *et al.* 2000).

Table 2. A review of 18 previously published results concerning metal stents in malignant biliary obstruction.

Study	Stent	Reobstruction (at mean) cause* n	Reinter- vention n	Procedure- related deaths %	Mean patency months	Complica- tion early/ late %
Laméris <i>et al.</i> 1991, 69 patients	Wallstent	10, overgrowth 7, ingrowth 3	6			
Gordon <i>et al.</i> 1992, 50 patients	Wallstent	12, overgrowth 10	12		5.8	18 minor/ 8 major
Salomonowitz <i>et al.</i> 1992, 80 patients, percutaneous/ endoscopic	Wallstent	14, overgrowth 5	5	0		
Becker <i>et al.</i> 1993, 58 patients (39 hilar, 19 dis- tal obstruction)	Wallstent		15	3.4	46% hilar, 89% distal (12-month)	24/35
Lee <i>et al.</i> 1993, 22 patients (hilar)	Wallstent Gianturco	6 (2.5 months), overgrowth 4	6			
Mygind & Hennild 1993, 10 patients (8 malignant)	Gianturco Strecker	2	1			
Stoker <i>et al.</i> 1993a, 45 patients (hilar)	Wallstent	17, overgrowth 11	14	4		16/7
Stoker <i>et al.</i> 1993b, 75 patients (distal)	Wallstent	4	2	1		21/3
Stoker & Laméris 1993, 176 patients	Wallstent	33, overgrowth 19, ingrowth 3	25	2		7/20
Wagner & Knyrim 1993, 42 patients, percutaneous/ endoscopic	Wallstent Strecker	3	3			
Bezzi <i>et al.</i> 1994, 19 patients	Nitinol	3	2	0	7	
Boguth <i>et al.</i> 1994, 59 patients, percutaneous/endoscopic	Wallstent	12 (6.5 months), debris 5, overgrowth 4, ingrowth 3	12	1.7	5.2	27 (early + late)
Lee <i>et al.</i> 1994, 69 patients	Wallstent	10 (4 months), overgrowth 8	8			
Rossi <i>et al.</i> 1994, 240 patients	Wallstent Nitinol Gianturco Strecker		53		5.9 (Wallstent) 8.3 (Nitinol) 2.3 (Gianturco) 4.0 (Strecker)	8 (major)
Friedrich <i>et al.</i> 1995, 17 patients	Nitinol				4.8	
Lee <i>et al.</i> 1997a, 100 patients	Gianturco Hanaro Wallstent Strecker Endocoil Nitinol				12 (median)	
Schima <i>et al.</i> 1997, 41 patients (hilar)	Wallstent	11 (2.9 months)	9	2	3.2	37/0
Tesdal <i>et al.</i> 1997, 157 patients	Wallstent Strecker Nitinol	34 (4.1 months), ingrowth 17, over- growth 8	28	0		

* cause reported if ≥ 3 cases recognised.

A review of various studies comparing plastic and metal stents is presented in Table 3.

Table 3a. A review of comparative studies of plastic and metallic stents in malignant biliary obstruction.

Study	Stent occlusion % metal/plastic	Dislocation % metal/plastic	Complication % metal/plastic
Lammer 1990 *	11 / 6–12 (various plastic)	0 / 1.2–5.5	8 / 0–9
Carr-Locke <i>et al.</i> 1993	13 / 13 (at median 3.7 / 2.1 months)		
Lammer <i>et al.</i> 1996 – distal obstruction	19 / 27		

Table 3b. A review of comparative studies of plastic and metallic stents in malignant biliary obstruction.

Study	Stent failure % metal/plastic	Median patency months metal/plastic	Cholangitis % metal/plastic	Re- intervention	Early results
Dauids <i>et al.</i> 1992 – distal obstruction	33 / 54	9.1 / 4.2			
Knyrim <i>et al.</i> 1993 – distal obstruction	22 / 43 (late) (at mean 6.2 / 4.6 months)		15 / 36 (late)	metal < plastic	no difference
Wagner <i>et al.</i> 1993 – hilar obstruction	18 / 50 (late)		9 / 33 (late)	metal < plastic	

* plastic: 297 patients (289 malignant), metal: 37 patients (31 malignant).

Apart from reobstruction and other complications, one of the disadvantages of metallic prostheses is their permanence. They become incorporated into the mucosa and cannot be removed. It is important to assess the resectability of the tumour before inserting a metal stent. Metal stents are also expensive, the price being about 5 000 FIM (800 Euro).

There are many different strategies for the management of metallic stent occlusion. Debris can be managed by sweeping the lumen with an inflated balloon catheter or drainage catheters may be left *in situ*. Tumour overgrowth or ingrowth is treated by further metallic stent insertion or catheter drainage. Endoscopic plastic stents, cleaning, diathermal cleaning and laser ablation are also used. (Becker *et al.* 1993, Lee *et al.* 1993, Rossi *et al.* 1994.)

3 Purpose of the study

1. To evaluate and compare the efficacies of various imaging methods in the diagnosis of biliary carcinoma and its abdominal spread.
2. To assess the ability of different imaging modalities to reveal biliary fistula and gallstone ileus.
3. To evaluate the ability of US and MRC to reveal bile duct changes caused by primary sclerosing cholangitis seen at ERC.
4. To analyse the patency, complications and reinterventions of percutaneously inserted metallic stents in malignant biliary obstruction.

4 Subjects and methods

The retrospective material of the Papers I–III and V consisted of 193 patients and the prospective material of Paper IV of 17 patients examined or treated (Paper V) at the Department of Diagnostic Radiology, Oulu University Hospital, Oulu. The radiological investigations were done during the years 1980–2000. The number of patients, the confirmation of the diagnosis and the sex and age (and age range) of the patients in different Papers are presented in Table 4. The evaluation concerning the retrospective material (Papers I–III and V) was done by using radiographs and their original reports and other hospital records and that concerning the prospective material (Paper IV) by analysing the imaging findings.

Table 4. Description of the patients in Papers I–V.

Paper	N (male/female)	Age, years mean (range)	Diagnosis by operation, histology / cytology / other*
I	80 (22 / 58)	69 (30 – 88)	59 / 21 / –
II	58 (20 / 38)	68 (29 – 83)	52 / 6 / –
III	16 (4 / 12)	68 (54 – 92)	12 / – / 4
IV	9 (5 / 4) + 8 controls (4 / 4)	40 (24 – 52); 42 (33 – 50)	– / – / 9 + 8
V	39 (15 / 24)	66 (46 – 84)	** / ** / 16

* clinical, radiological, endoscopy, biochemical, ** 23 patients by operation / histology / cytology.

In the Papers I and II, the accuracy of the current methods to detect biliary tumours and their abdominal involvement was analysed. In Paper I, the imaging findings relating to 80 patients treated for carcinoma of the gallbladder at Oulu University Hospital between 1983 and 1990 were reviewed. The order of the radiological examinations is presented in Table 5. In cases without surgery or autopsy the most evident imaging finding was taken as the reference for tumour spread. Of the 80 patients, 67 had abdominal metastases. Forty-one had bile duct obstruction caused by tumour spread, 38 had regionally enlarged lymph nodes, 33 had liver infiltration or metastases and 19 had metastases in other abdominal areas.

Table 5. Order of radiological examinations in 80 patients with gallbladder carcinoma (Paper I).

Method	N	Order of examination				
		1.	2.	3.	4.	5.
US	79	77	1	1		
CT	37	1	28	6	2	
PTC	26		5	18	3	
ERCP	17	1	14		1	1
Arteriography	9		2	4	3	

In Paper II, the imaging findings of 58 patients treated for carcinoma of the bile duct or the papilla of Vater at Oulu University Hospital during 1983–1990 were analysed. The order of the radiological investigations is presented in Table 6. In cases without operation or autopsy, the most evident imaging finding was taken as the reference. Eleven patients had peripheral intrahepatic cholangiocarcinoma, 15 had a tumour of the hepatic duct, 15 had a choledochal carcinoma, and 17 patients had a carcinoma of the papilla of Vater. Intrahepatic cholangiocarcinomas were multiple in seven patients and single in four. There was a total biliary obstruction in 18 patients and stenosis in 29 patients. Of the 17 patients with abdominal metastases, five had liver metastases or infiltration, 11 had regional enlarged lymph nodes and three had metastases elsewhere in the abdominal area.

Table 6. Order of imaging methods in 58 cases of bile duct carcinoma (Paper II).

Method	N	Order of examination				
		1.	2.	3.	4.	5.
US	57	54	3			
CT	27	1	18	6	2	
PTC	19		4	10	4	1
ERCP	28	3	20	2	3	
Arteriography	12			3	2	7

In Paper III, the ability of different imaging methods to detect biliary fistula and gallstone ileus was analysed. The imaging findings of all the 16 patients treated for biliary fistula at Oulu University Hospital in 1980–1995 were reviewed. Ten patients had a spontaneous fistula. Nine of them were internal bilioduodenal and one was external. Six patients had an iatrogenic fistula, one being internal bile ascites and five being external biliocutaneous fistulas. Five patients with a spontaneous fistula also had gallstone ileus, and one patient had a gastric outlet obstruction caused by a gallstone (Bouveret's syndrome). Table 7 presents the types of fistula and the radiological examinations used, and Table 8 presents the examinations for gallstone ileus.

Table 7. *Fistula types and radiological examinations and their results in 16 patients with biliary fistulas (Paper III).*

Patient No.	Diagnosis	Plain film	US (+ drainage)	CT/CT + fistulography	T-drain c-graphy	I.v. c-graphy	ERCP	Fistulography	C-graphy via cholecystostomia	UGI series
Spontaneous										
Internal										
1.	CDF	-	-	-						-
2.	CDF		+	+				+		
3.	CDF	-	-			-				
4.	CDF	-	+							
5.	CDF	-	+							
6.	CDF	+	+	+						
7.	CDF					+				
8.	CDF	-	-							-
9.	CDF	-	+							-
External										
10.	CCF		+							
Iatrogenic										
Internal										
11.	BAF	-	+		+					
External										
12.	BCF		+		+		++			
13.	BCF	+	+	+	-	+		++		
14.	BCF		+				+	++		
15.	BCF	+	+					+	++	
16.	BcyCF		+	++				++		

CDF = cholecystoduodenal fistula, CCF = cholecystocutaneous fistula, BAF = bile duct / abdominal cavity fistula (biloma), BCF = bile duct cutaneous fistula, BcyCF = biliocystic cutaneous fistula, UGI = upper gastrointestinal, c-graphy = cholangiography; - negative, normal; + pathological, but not definitive; ++ definitive diagnosis.

Table 8. *Imaging methods and their results in the patients with gallstone ileus and Bouveret's syndrome (Paper III).*

Patient No.	Diagnosis	Plain film	US (+ drainage)	CT	I.v. c-graphy	UGI series
4.	Gallstone ileus	+	+			
5.	Gallstone ileus	+	-			
6.	Gallstone ileus	+	+	++		
7.	Gallstone ileus				-	
8.	Gallstone ileus	+	+			+
9.	Bouveret's syndrome	+	+			++

UGI = upper gastrointestinal; c-graphy = cholangiography; - negative, normal; + pathological, but not definitive; ++ definitive diagnosis.

In Paper IV, the ability of US and MRC to detect bile duct changes and prognostic signs of PSC seen at ERC was studied. The study consisted of all the nine patients with an established diagnosis of PSC treated at Oulu University Hospital in 1997. The patients underwent MRC and MRI of the liver, US of the liver and the bile ducts and ERC. Eight age and sex-matched controls with hepatobiliary diseases other than PSC had also had MRC and MRI of the liver and ERC within a period of three months. The duration of the disease in the PSC patients had varied between 2–15 years (mean 6.3 years), and eight patients an inflammatory bowel disease. ERC was used as a standard of reference. If any segment of the biliary tree was not filled with contrast, it was excluded from the evaluation.

A detailed evaluation was made by analysing the grade, length and extent of the strictures and the degree of the dilatations in all the separate anatomical segments of the biliary tree, using the criteria of Craig *et al.* and also including wall thickening and erosions. The capability of MRC and US to show predictors of poor outcome in PSC was evaluated as well. (Craig *et al.* 1991, Table 9.) We tried to analyse the MRC-MRI and ERC findings blindly, but it proved to be difficult to define exactly all the anatomical segments of the biliary tree of the PSC patients in both ERC and MRC. The detailed analysis was therefore done non-blinded by two radiologists. We also evaluated blindly in random order the presence of PSC in the MRC-MRI images of the PSC patients and the control patients.

Table 9. Craig's prognostic predictors of a poor outcome in patients with primary sclerosing cholangitis used in a detailed evaluation of diagnostic modalities in Paper IV (by courtesy of Craig et al., Am J Roentgenol 1991;157:959–964).

Duct location	Predictors	
	Statistically significant (p)	Trend indicated ^a (p)
Intrahepatic	Grade 4 strictures (.050)	Confluent strictures (.140)
	Diffuse strictures (.012)	Marked dilatation (.069)
Extrahepatic	None	Grade 4 strictures (.088)
		Confluent strictures (.170)
		Diffuse strictures (.128)

a Decreased survival observed, but $p > .05$.

Definitions: Grade 4 strictures = > 75 % narrowing of duct; Confluent strictures = > 10 mm involvement; Diffuse strictures = > 25 % of ducts involved; Marked dilatation = ≥ 5 mm luminal diameter (in secondary intrahepatic ducts).

In Paper V, the medical records of 39 patients with malignant biliary obstruction treated with metallic stents at Oulu University Hospital during 1990–1996 were analysed in order to assess the patency rates and complications of the stents and the need for reinterventions. The patients were followed until death based on the records and radiographs available at the hospital where they had been treated or any other hospital or health center after the insertion of the stents. There were 42 malignant bile duct strictures or obstructions. The cause and level of obstruction are presented in Table 10.

Table 10. Cause and level of obstruction in 39 patients with malignant biliary obstruction treated with metallic stents (Paper V).

	Number of patients	Number of strictures/obstructions
Cause of obstruction		
Pancreatic carcinoma	16	16
Cholangiocarcinoma	9	9
Metastatic lymphadenopathy	5	6
Metastatic liver disease	5	5
Gallbladder carcinoma	4	4
Secondary strictures due to hepatic metastases	2	2
Level of obstruction		
Hilar	24	25
Common bile duct	16	16
Biliary-enteric anastomosis	1	1

Fifty-five metallic stents were placed in 38 patients, with a failure in one case. Forty-eight were Wallstents and seven were Memotherm stents. In four patients, the stents were placed in a tandem fashion, in one patient in a T fashion, and in nine patients in a Y fashion. Thirty patients received prophylactic antibiotics after stent placement. Primary patency was defined as the interval between the initial insertion and the recurrence of symptoms due to the first occlusion. If there was no evidence of obstruction, the patency period was considered equal to the survival period, but censored.

US was performed with real-time equipment (Toshiba SAL 20 A or SSA 77 / 90 / 100 in Papers I and II; Toshiba SAL 20 A or SSA 77 / 90 / 100 / 270 or SSH 140 or Aloka 2000 MultiView in Paper III; Toshiba PowerVision 7000 in Paper IV).

The CT examinations for the Papers I and II were done with a Siemens Somatom 2 or Toshiba TCT 80 A scanner with a scan time of 4 or 5 s and a slice thickness of 8 or 10 mm. Both plain and enhanced scans (100 ml 60 % sodium meglumin amidotrizoate or iopromide or iopamidol 300 mg I / ml) were obtained. The examination was usually completed with 4 mm / 10 s scans focused at the level of the bile duct obstruction. For Paper III, CT or CT fistulography was done with a Siemens Somatom 2 or a High Speed Advantage GE scanner.

The arteriographies in the Papers I and II were started with aortography and completed with selective coeliac and superior mesenteric arteriography if necessary.

ERCP was performed via gastroduodenoscopy under fluoroscopy for the Papers I–IV. PTC for the Papers I and II was made under US and fluoroscopy guidance.

In Paper V, all patients had PTC before stent insertion. The PTC was left in place for 6–145 days (mean, 29 days). Three patients also had at least one catheter with stents. The stent was inserted using standard techniques (Becker *et al.* 1993). Fourteen patients required more than one stent. Before stent insertion, balloon dilatation of the stenotic portion was performed on 37 patients, and a second dilatation after stent implantation was done on nine patients. The stents were placed during one session in 37 patients. The route

of insertion was right transhepatic in 19 patients, left transhepatic in 10 and bilateral in nine patients. The Wallstents were 34, 52 or 103mm x 10 mm and the Memotherm stents 30, 50 or 100 mm x 10 mm.

In Paper IV, MRI was performed by using a 1.5 T scanner and a torso phased-array coil (Signa, EchoSpeed, General Electric Medical Systems, Milwaukee, Wis.). T2-weighted fast-spin echo (time of repetition (TR) 6000, time of echo (TE) 100, 7 mm slice, 2 mm gap, respiratory triggering) transverse images were obtained with frequency-selected fat suppression together with T1-weighted spin echo transverse images (TR 620, TE 14, 7 mm slice, 2 mm gap, respiratory compensation). MRC was performed with the single-shot fast-spin echo technique (TE 1000). Single, 2-cm-thick overlapping slices with breath hold were obtained in the coronal and sagittal plane through the entire liver. A 30-cm field of view (FOV) was used with a 256x256 matrix.

In Paper V, patient survival and stent patency rates were calculated using the Kaplan-Meier survival analysis and the statistical significance was evaluated by the log rank test. A p value of less than 0.05 was considered statistically significant.

5 Results

5.1 Radiological findings in carcinomas of the gallbladder and the bile duct

The accuracy of the different imaging modalities to assess the spread of tumour in gallbladder carcinoma and bile duct carcinoma was evaluated in the Papers I and II, respectively.

The number of imaging methods and the order in which they were used in the patients with gallbladder carcinoma (Paper I) are presented in Table 5. US was the first examination in 77 out of 79 cases and CT was the second in 28 out of 37 cases.

US visualised the primary tumour in 68 % and CT in 57 % of the patients. When the tumour had spread abdominally, US showed either the primary tumour and / or a metastasis in 76 % of the cases, the gallbladder carcinoma in 73 % and a metastasis in 69 %. The corresponding rates for CT were 80, 54 and 60 %. The sensitivity of both modalities was lower for infiltrative tumours than for polypoid or exophytic tumours.

Table 11 shows the US and CT findings of gallbladder tumour and secondary tumours examined by US or US and CT. US showed 73 % of the spread to the liver, and in the cases examined by both US and CT, the percentages were 63 and 68 %, respectively. US showed metastatic lymph nodes in 70 % and CT in 52 %, and US showed metastases in other abdominal areas in 33 % and CT in 10 % of the cases examined. US showed bile duct obstruction in 95 % and CT in 91 %.

ERCP was performed as a second imaging examination in 14 out of 17 patients. It showed a suspicion of a tumour in 76 % and failed in 24 %. PTC was performed as a third investigation in 18 out of 26 patients, and it revealed a tumorous change in 96 %. Nine patients underwent angiography. Tumours or liver metastases were seen or suspected in eight patients.

The number of different imaging modalities used in the patients with bile duct carcinoma and the order of the investigations (Paper II) are presented in Table 6. US was the first investigation in 54 out of 57 examinations, and CT was the second in 18 out of 27 examinations.

Table 11. US and CT findings in 80 patients with gallbladder carcinoma examined by US or both US and CT (Paper I).

Site of tumour	US cases (79)		US and CT cases (37)		
	N	US +	N	US +	CT +
Gallbladder tumour	79	54 (68%)	37	31 (84%)	21 (57%)
Secondary tumours	67	46 (69%)	35	27 (77%)	21 (60%)
secondary obstructing tumour	37	14 (38%)	20	8 (40%)	4 (20%)
lymph node metastases	37	26 (70%)	21	16 (76%)	11 (52%)
liver infiltration or metastases	33	24 (73%)	19	12 (63%)	13 (68%)
metastases in other abdominal areas	18	6 (33%)	10	4 (40%)	1 (10%)

US showed bile duct obstruction in all the 46 cases in which US was used and identified the level correctly in 85 %. CT revealed obstruction in 17 out of 18 cases and identified the level correctly in 83 %. The US and CT findings in the cases of bile duct carcinoma examined by US or both US and CT are presented in Table 12. US showed the primary tumour in 63 %, the percentage increasing towards the periphery of the biliary tree, and CT showed the primary tumour in 44 %, revealing best the peripheral intrahepatic cholangiocarcinomas. The sensitivity of US was poorer for infiltrative choledochal or hepatic duct tumours than for polypoid or exophytic tumours, and the sensitivity of CT was poorest for infiltrative and exophytic tumours. When the tumour was spread abdominally, US showed either the primary or the secondary tumour in 94 %, the primary tumour in 75 % and the secondary tumour in 63 %. The corresponding percentages for CT were 17, 17 and 17 %.

Table 12. US and CT findings in 58 patients with bile duct carcinoma examined by US or both US and CT (Paper II).

Site of tumour	US cases (57)		US and CT cases (27)		
	N	US +	N	US +	CT +
Bile duct tumours	57	36 (63%)	27	20 (74%)	12 (44%)
intrahepatic cholangiocarcinomas	11	11 (100%)	9	9 (100%)	9 (100%)
choledochal and hepatic duct tumours	30	18 (60%)	13	9 (69%)	2 (15%)
tumours of the papilla of Vater	16	7 (44%)	5	2 (40%)	1 (20%)
Secondary tumours	16	10 (63%)	6	3 (50%)	1 (17%)
lymph node metastases	11	6 (55%)	4	1 (25%)	0
liver infiltration or metastases	5	4 (80%)	3	2 (67%)	1 (33%)
metastases in other abdominal areas	3	2 (67%)	1	0	0

US showed metastatic lymph nodes in 55 %, liver infiltration or metastases in 80 % and metastases in other abdominal areas in 67 % of the cases examined. The corresponding percentages for CT were 0, 33 and 0 %.

ERCP was performed as a second investigation in 20 out of 28 patients. It failed to fill the biliary tract in three cases. ERCP showed tumorous changes in 89 %. PTC was mostly done as the second, third or fourth investigation. It showed obstruction or narrowing in all

the 19 patients. Angiography was positive in all the five patients with intrahepatic cholangiocarcinoma examined with angiography, and in two of the seven more distal tumours examined.

5.2 Radiological findings in biliary fistula and gallstone ileus

The ability of the imaging methods to find biliary fistulas and gallstone ileus was evaluated in Paper III. The tables 7 and 8 show the types of fistula and gastrointestinal obstruction. All the nine patients with a cholecystoduodenal fistula had cholecystitis as a predisposing factor. One patient with a spontaneous fistula had an external, cholecystocutaneous fistula with chronic cholecystitis and stones passing through a subcutaneous abscess.

The ability of different imaging methods to detect the fistula or gastrointestinal obstruction is presented in the Tables 7 and 8. Various imaging modalities were used and imaging did not show the fistula itself in any of the spontaneous cases, although imaging was pathological in many instances. The gallbladder was examined by US in eight patients. In three of them the gallbladder was not visualised. In five cases US showed either a thick-walled gallbladder shrunken around gallstones, an area of echodensity or a shadow. CT showed gallstone ileus in one patient, and Gastrografin® meal gave the diagnosis of Bouveret's syndrome.

Four of the iatrogenic external fistulas were bile duct cutaneous and one was biliocystic cutaneous as a result of attempted cyst sclerotherapy. The internal fistula was a bile duct abdominal cavity fistula. Four fistulas occurred after biliary surgery and one after a liver resection. The imaging methods provided a correct diagnosis in all the external iatrogenic fistulas: fistulography in three cases (with CT fistulography in one), ERCP in one case and cholangiography via cholecystostoma in one case.

The delay from the first hospital admission (spontaneous fistulas) or the predisposing operation or intervention (iatrogenic fistulas) till the diagnosis varied between one day and eight months and 23 days.

5.3 Imaging and estimation of the prognostic features of primary sclerosing cholangitis by US and MRC

The ability of US and MRC to detect PSC seen at ERC and the ability of these non-invasive techniques to show the described predictors of poor outcome of PSC were studied in Paper IV.

In the non-blinded detailed analysis, eight and one non-diagnostic segments existed in the PSC group and in the control group, respectively. These segments were excluded from the evaluation. In the PSC group, MRC-MRI showed features of PSC as well as ERC did in the common bile duct, common hepatic duct and secondary intrahepatic ducts, but missed the lesions in the left and right main hepatic ducts in two patients each. There was one false positive stricture at MRC. US missed several pathological changes in all the

segments (Table 13). ERC showed erosions in two patients. MRC depicted five correct signs of poor prognosis, but also gave five false positive findings. US was unable to detect any signs of poor outcome (Table 14).

Table 13. Results of ERC, MRC and US in different segments of the biliary tree in nine PSC patients and eight control patients (Paper IV).

Bile duct segment	Number of PSC patients with features of PSC* (n=9)					Number of control patients with strictures or dilatations (n=8)						
	ERC			MRC-MRI	US	ERC			MRC			
	+	nd	-			+	nd	-	MRC=ERC	False posit.	False negat.	nd
Common bile duct	9	0	0	9	7	2	1	5	7	0	0	0
Common hepatic duct	8	1	0	8	5	3	0	5	6	0	2	0
Left main duct	6	2	1	4	1	4	0	4	3	0	4	1
Right main duct	6	3	0	4	0	3	0	5	4	0	3	1
Sec.intrahep.ducts	7	2	0	7	4	6	0	2	4	0	4	0

* = a stricturous change, dilatation, wall thickening or erosion, + = findings, - = no findings, nd = nondiagnostic.

Table 14. Number of patients in the groups of statistically significant poor prognostic findings in ERC, MRC and US (Paper IV).

Finding in secondary intrahepatic ducts	ERC	MRC	US
Grade 4 stricture (>75%)	4	6	0
Diffuse stricture (>25%)	1	4	0

In the control group, the right and left main hepatic ducts of one patient were non-diagnostic. There were strictures in five segments in the controls. MRC missed two of them, but it did not show any false positive strictures. MRC missed 12 out of 15 dilatations (Table 13).

In the blinded analysis to evaluate the presence of PSC, radiologist 1 depicted all true positive cases and radiologist 2 depicted one false positive and one false negative cases. In the primary evaluation of US, the radiologist had not detected any features suggestive of PSC in one of the PSC patients. In this patient, all but the secondary intrahepatic ducts had appeared to be narrower than usually.

5.4 Patency and complications of percutaneously inserted metallic stents in malignant biliary obstruction

Patency, complications and the need for reinterventions with the percutaneously inserted self-expandable metallic stents were studied in Paper V.

A total of 55 stents were inserted in 38 patients. In one patient, insertion in the stricture in the common hepatic duct behind an abrupt curve failed. One patient was lost from follow-up. Thirty-seven patients were followed up until death. The mean survival was 6.4 months (range 6–713 days). Twenty-one patients had problems with the drainage catheters, and six patients had some minor problems during the stent insertion. Of all the stents, eight dilated to 9–10 mm, 28 to 7–8 mm and 18 to 5–6 mm at their narrowest during the first 0–5 days.

Eight patients died within 30 days of stent insertion (range 6–29 days, mean 20 days). In one of them, the stent procedure was considered to be a predisposing factor, as the patient died of sepsis. Two patients had marked jaundice of undefined cause before death. Nine patients had other problems during the first 30 days: cholangitis, fever, sepsis, pancreatitis or cholecystitis. One stent obstruction developed on day 28, and its cause was unknown.

Late complications occurred in 66 %, and they are presented in Table 15. In nine patients, the stent was obstructed after 30 days (during the days 33 – 337, mean 4.8 months). The cause was tumor ingrowth in three patients, ingrowth and growth above or below the stent in two, growth above the stent in one, debris in two, and an obvious clinical obstruction without exact knowledge of the cause in one patient.

The 25-week patency was 71 % and the 50-week patency 42 %. The mean patency was 12.4 months. The patency rates of the patients with cholangiocarcinoma were significantly lower than the patency rates of the patients with other diagnoses ($p = 0.0128$). Although the difference was not significant, there was a tendency towards lower patency rates with less dilatation of the stents. Y, T or tandem style stenting ($p = 0.05$), an increasing number of stents and an increasing length of strictures also decreased patency. Hilar strictures seemed to have a tendency towards poorer prognosis in the first ten months than non-hilar ones. The distribution of the disease and cytostatic or radiation therapy did not affect the patency rates. Nineteen patients had other late complications shown in Table 15. Three of the four jaundiced patients had undefined jaundice before death.

There was a need for late reinterventions in 31 %. They are presented in Table 16. Eight of the nine patients had some reintervention after the primary stent obstruction: a drainage catheter was placed through the stent in three patients and an endoscopic plastic stent inside the metallic stent in four patients, and one patient had two new metallic stents inserted. The reinterventions required for reasons other than primary stent occlusion are also listed in Table 16.

Table 15. Late complications associated with 54 percutaneously inserted metallic stents in 37 patients with malignant biliary obstruction (Paper V). – 19 / 29 patients (66%).

Late complications	Patients	Periods
Stent obstruction 9 / 29 patients (31%)		
Other late complications 19 / 29 patients (66%)		
Cholangitis	10	13
Fever	10	13
Jaundice	4	5
Sepsis	1	1
Progression of disease *	1	1
Occlusion of plastic stent (with cholangitis in 6)	4	7
Occlusion of drainage catheter	3	5
Occlusion of some other metallic stent (I)	2	2
Occlusion of new metallic stents (II)	1	2
Stent migration	1	1 piece
Stent shortening	1	1
Plastic stent through the mesh of Wallstent	1	1
Drainage catheter through the mesh of Wallstent	1	1

* leading to further stenting, I = stents inserted initially, not obstructed as the first, II = stents inserted to treat complications.

Table 16. Late reinterventions associated with 54 percutaneously inserted metallic stents in 37 patients with malignant biliary obstruction (Paper V). – 9 / 29 patients (31%), 5 had multiple reinterventions.

Late reinterventions	Patients	Pieces
After primary stent occlusion		
Drainage catheter (with b.d.*)	4	4
Attempt		1
Plastic stent	4	5
New metallic stents (II) ** (with drainage and b.d.*)	1	2
Other reinterventions		
New metallic stents (II)** (with drainage and b.d.*)	3	8
Changing of plastic stent	3	4
Attempt		1
Routine		2
Drainage catheter (with b.d.*)	2	3
Cleaning of drainage catheter	2	3

* b.d. = balloon dilatation, ** II = stents inserted to treat complications.

6 Discussion

Four studies of the present work deal with the diagnostics of various biliary diseases, whose early diagnosis would be important to improve prognosis. The diagnostic work is difficult, however, and the stage of the disease is often advanced at the time of a correct diagnosis. The fifth study evaluated metallic stents in malignant biliary obstruction.

6.1 Problems

The comparison of imaging modalities and scientific studies concerning the relatively rare biliary diseases is difficult. The fast development of the equipment, the limited resources and the variable interests as well as the slow accumulation of data make much of the problem. However, evaluation of the real use and value of different modalities in everyday clinical practice is important.

Since the first three diagnostic studies of this work were accomplished, there has been fast development of the US methodology: improved quality of the image, Doppler, power Doppler, contrast agents, harmonic imaging, laparoscopic, endoscopic and intraductal US and real-time spatial compound imaging. Helical and multislice helical CT are also fast and have the best advantage of contrast agent and enable reconstructions of good quality, and virtual CT is under research.

Biliary carcinoma, biliary fistula, gallstone ileus and primary sclerosing cholangitis are relatively rare but serious diseases, whose early diagnosis is difficult. They may be asymptomatic or present with nonspecific symptoms. Gallbladder carcinoma and intrahepatic cholangiocarcinoma are often at an advanced stage when they cause jaundice, and some bile duct cancers present as only a thickening of the bile duct wall. (Lee & Kaplan 1995, Wei & Gadacz 1996, Sherlock & Dooley 1997a,b,c.)

Early diagnosis of biliary carcinomas would be important to improve the prognosis, and accurate staging would help to select the best possible treatment. Gallbladder carcinoma spreads early in its course. Median survival from the diagnosis is three months. (Demachi *et al.* 1997, Sherlock & Dooley 1997a.) Cholangiocarcinoma has also had a poor prognosis, but recent surgical advances have resulted in higher rates of resection and led to a need for improved detection and staging (Keogan *et al.* 1997).

Early recognition of biliary fistulas would also be critical in decreasing morbidity and mortality, as gallstone ileus causes up to 25 % of all cases of non-strangulated intestinal obstruction in the elderly and involves 15–20 % mortality (Sherry & Gadacz 1996, Sherlock & Dooley 1997c), and iatrogenic fistulas may lead to serious complications (Lu&Kaplowitz 1991). PSC should also be found in the early phase, when medical intervention would be most beneficial. However, most patients suffer symptoms for years before diagnosis, and the usual diagnostic methods, i.e. liver biopsy and ERCP, are invasive investigations, and the biopsy is rarely definitive. (Ernst *et al.* 1998, Ponsioen & Tytgat 1998, Zakko 1999.)

The adverse sequelae of prolonged obstructive jaundice warrant serious consideration of biliary drainage. Biliary bypass surgery carries considerable mortality and morbidity, catheter drainage has problems, and the major problems with plastic stents have been limited insertion, occlusion with sludge and displacement of the endoprosthesis. (Barth 1990, Davids *et al.* 1992, Smith *et al.* 1994, Spivack & Jacobson 1999.) Although metallic self-expandable endoprostheses have been designed to circumvent these limitations and they do have advantages, there have also been disappointments. (Rossi *et al.* 1994) The reports of patency rates, complications and reinterventions have, however, been limited, variable and contradictory.

6.2 Carcinoma of the gallbladder

In our study, gallbladder carcinoma had spread to the other organs in 84 % of the patients, and 51 % had biliary obstruction. US and CT were comparable in revealing the obstruction. We also recognised the three described types of tumour: polypoid, exophytic and infiltrating (Chijiwa *et al.* 1991, Rooholamini *et al.* 1994). The infiltrating tumour was the most difficult to detect, and US was more sensitive than CT in detecting all the three types. US was more sensitive than CT in revealing the primary tumour (68 % versus 57 %) and its spread (69 % versus 60 %), but both methods were insufficient for accurate staging.

Later on in 1998, using newer equipment, Bach *et al.* have reported US with Doppler to be reliable in the detection of the primary tumour (85 % sensitivity) and local extension into the liver, but still limited in the detection of lymph node or peritoneal metastases. US revealed poorly the patients with advanced disease. (Bach *et al.* 1998.) Haribhakti *et al.*, using newer equipment, also had problems with understaging (Haribhakti *et al.* 1997). Iida *et al.* showed US to be sensitive in detecting hepatic invasion and to be able to reveal the extent of invasion. However, there has been discussion of the limitations of this report. (Iida *et al.* 1995, Haribhakti *et al.* 1997.) Colour Doppler has been claimed to help to differentiate carcinoma from other findings (Li *et al.* 1994, Ueno *et al.* 1996). Thus, advances in the US technique have improved the sensitivity for the primary tumour and enabled radiologists to assess portal veins and bile ducts by US, but US still seems to have its limitations in staging.

In comparison with our results, Itai *et al.* reported the sensitivity of CT in detecting the primary tumour to be 74 %. Contrast agent seemed to be helpful in assessing the origin of the tumour. (Itai *et al.* 1980.) Later on, CT has been more sensitive in detecting the

primary tumour and quite reliable in cases of liver invasion, but it has been less accurate than US in assessing the extent of liver invasion (Iida *et al.* 1995, Ohtani *et al.* 1996). The results of Engels *et al.* were better than ours, but the study had limitations: although laparotomy was performed on the majority of patients, the surgeon was not always able to confirm the precise findings of preoperative CT (Engels *et al.* 1989).

CT may be helpful in assessing polypoid lesions, especially in detecting probable malignancies and being helpful in choosing the optimal treatment. All cancers located in the mucosa, muscularis or subserosa seem to be polypoid. (Chijiwa *et al.* 1991, Furukawa *et al.* 1998.) The development of CT equipment might also improve the results in staging. According to Ohtani *et al.*, CT has low to moderate sensitivity for the spread of gallbladder carcinoma (Ohtani *et al.* 1996).

Our study demonstrated PTC and ERCP to reveal tumorous changes in 96 % and 76 % of cases, respectively. However, direct cholangiography is of little value in detecting gallbladder carcinoma and these modalities are restricted to the evaluation of the bile ducts.

There are some promising results of MRI in diagnosing and staging of gallbladder cancer, especially in detecting the primary tumour and hepatic invasion. MRI might also be helpful in assessing spread into the adjacent areas, e.g. blood vessels, but reports are few. Dynamic MRI has been promising in differentiating malignant from benign lesions and evaluating the depth of tumour invasion. (Sagoh *et al.* 1990, Rooholamini *et al.* 1994, Demachi *et al.* 1997, Yoshimitsu *et al.* 1997.)

For successful treatment of gallbladder carcinoma, it would be important to detect the tumour as early as possible. High-resolution US detects > 5 mm polypoid lesions. There are reports of 98 % of the early carcinomas presenting as polypoid, and 88 % of the carcinomas exceeding 10 mm in diameter. US is also a useful modality due to its ease of performance, low cost and common availability, and it might thus be the initial modality, although the presence of gallstones may cause some difficulties. Colour Doppler may give additional information of the tumorous changes and also be helpful in staging. However, US alone is inaccurate in staging, and the detection of metastatic lymph nodes is difficult with any modality, as normal-sized nodes may contain metastases. (Sagoh *et al.* 1990, Chijiwa *et al.* 1991, Ueno *et al.* 1996, Bach *et al.* 1998.) US is also helpful in detecting biliary obstruction and in guiding FNB. Endoscopic US is useful in assessing hepatic invasion, but it is an invasive modality. Laparoscopic US could be used during laparoscopic cholecystectomy for the detection of unsuspected cancer. (Iida *et al.* 1995, Dill *et al.* 1997, Shukla *et al.* 1997.)

CT is sensitive in detecting gallbladder carcinoma, but still insufficient in staging, and CT includes radiation and often contrast agent, too (Ohtani *et al.* 1996). However, it has been complementary and may be useful in problematic cases, e.g. to assess spread to liver. In the future, however, MRI might replace CT in many instances, but more comparative studies are needed. Dynamic MRI, MRA and MRC may also give additional information. The ability of any modality to recognise metastatic nodes would greatly improve staging. Direct cholangiography may still be needed in special cases, especially to relieve jaundice.

6.3 Carcinoma of the bile duct

Eighty-one percent of the 58 patients with bile duct carcinoma had either obstruction or stenosis of the biliary tract in our study, and the tumour was spread in 29 %. US detected the obstruction and its level in 100 % and 85 %, respectively, and CT in 94 % and 83 %, respectively. Our study proved US and CT to be accurate – both having 100 % sensitivity – in the case of peripheral intrahepatic cholangiocarcinoma, but inaccurate for defining more distal tumours and most of the metastases. US detected 63 % of the primary tumours and CT only 44 %, and US was more sensitive than CT with the distal cancers. This contrasts to the older reports, which consider CT more successful (Nesbit *et al.* 1988, Choi *et al.* 1989). Later on, however, US has been 94–96 % sensitive with Klatskin tumours or cholangiocarcinoma and CT has been 91 % sensitive with Klatskin tumours (Garber *et al.* 1993, Bloom *et al.* 1999, Feydy *et al.* 1999).

We detected the three types of cholangiocarcinoma, polypoid, exophytic and infiltrative, as also described elsewhere (Nesbit *et al.* 1988, Choi *et al.* 1989, Han *et al.* 1997, Bloom *et al.* 1999). The sensitivity of US was poorer for infiltrative hepatic duct and choledochal tumours than for polypoid or exophytic tumours, and that of CT was poorest for infiltrative and exophytic tumours. The sensitivity of US was better than that of CT for all the types.

US was more sensitive than CT also with the abdominal spread, although both methods were quite inaccurate (sensitivities of 63 % and 17 %, respectively). US detected liver invasion well, but other metastases less well. CT was poor in all the metastases analysed. However, the number of patients in the CT group was limited. There are only a few later reports of US in staging bile duct tumours, and they include only hilar tumours. Anyhow, poor sensitivity has been reported in detecting spread to the lymph nodes, peritoneum and hepatic artery, but better in detecting the extent of bile duct involvement and hepatic metastases. The colour Doppler technique has been valuable in assessing the hilar vessels, especially portal involvement. Laparoscopic, endoscopic and intraductal US have been helpful in detecting and staging. (Neumaier *et al.* 1995, Hann *et al.* 1997, Mittelstaedt 1997.)

Helical CT, contrast studies, multiphase techniques, spiral CT during arterial portography and spiral CT cholangiography with intravenous infusion of biliary contrast have renewed CT examinations (Hann *et al.* 1996, Baron 1997, Kim *et al.* 1997). There are some later reports of the staging of hilar carcinomas with modern equipment. However, the accuracy of multiphasic helical CT for assessing resectability has been only 60 %. Although the sensitivity for the primary tumour and liver involvement has increased and the accuracy for portal venous involvement has been good, CT has not been accurate in assessing bile duct, arterial or lymph node involvement. (Han *et al.* 1997, Tillich *et al.* 1998, Feydy *et al.* 1999.)

In our patients, PTC revealed tumorous changes in all the 19 patients examined and ERCP in 89 % of the cases. The reported accuracy of cholangiography for detecting the level and cause of obstruction varies within 92–100 % and 75–87 %, respectively, and cholangiography has been better than US in detecting the length of the involved ductal segment (Mittelstaedt 1997, Kumar *et al.* 1998).

Our study did not include MRC or MRI in cholangiocarcinoma. The accuracy of MRC to reveal obstruction and its level has been good and it is able to visualise the bile ducts above and below the obstruction and demonstrate isolated segmental ducts. The morphology and the length of strictures may also be visualised. The cause is more difficult to predict on the basis of MRC alone. MRCP has, however, been 80–86 % sensitive and 96–98 % specific in predicting a malignant cause of obstruction. (Guibaud *et al.* 1995, Barish & Soto 1997, Mendler *et al.* 1998, Pavone *et al.* 1999.)

Careful evaluation of bile duct carcinoma requires, apart from individual source images and reformatted images of MRC, also a review of T1- and T2-images. Gadolinium-based contrast agent, dynamic MRI and MRA may also be valuable in assessing the spread of the cancer. Spread into the bile ducts, vessels, liver, lymph nodes and peritoneum and lobar atrophy can be demonstrated. (Guthrie *et al.* 1996, Becker *et al.* 1997, Soto *et al.* 1997.) The usual contraindications to MR imaging also apply to MRCP. The failure rate due to contraindications and claustrophobia is less than that of ERCP, and MRC is not limited by altered anatomy, either. Problems may include imaging artifacts due to surgical clips and duodenal peristalsis, a signal loss for various reasons, underestimation of duct caliber and limited spatial resolution. (Reinhold & Bret 1996) Anyhow, there will be a shortage of capacity for MR examinations at least in the near future in Finland.

Ampullary carcinoma may be subtle and difficult to reveal. In our study, the patients with carcinoma of the papilla of Vater were evaluated as a separate group for the results of US and CT. Both methods seemed to be inaccurate, CT being even poorer than US. However, these neoplasms may show an obstruction or stenosis in the most distal segment of the common bile duct. Cholangiography, US and CT may detect the obstruction, but have been less sensitive with the tumour itself. Endoscopy provides a look at the ampulla and access for biopsy. Endoscopic US has been superior to US, CT and angiography in the detection and staging and highly accurate in the assessment of the location, size and extent of the tumour, although better results of CT have also been reported. Intraductal US has also been considered valuable, but neither endoscopic nor intraductal US is suitable for the detection of distant metastases. MRC and MRI have also been useful methods. (Tio *et al.* 1990, Buck & Elsayed 1993, Howard *et al.* 1997, Mittelstaedt 1997, Semelka *et al.* 1997, Cannon *et al.* 1999, Menzel *et al.* 1999, Midwinter *et al.* 1999.)

The role of imaging in cholangiocarcinoma is to assist in the diagnosis and to provide an accurate assessment of surgical resectability. US could be the initial method in obstructive jaundice. The use of US may obviate more invasive procedures and help to identify the patients for whom further investigation would be contributory. In combination with Doppler techniques, it may also be helpful in staging, although US alone is inaccurate. (Hann *et al.* 1997, Mittelstaedt 1997, Bloom *et al.* 1999.) Endoscopy with biopsy, endoscopic US and intraductal US are valuable, especially in ampullary carcinomas. These US modalities are able to reveal the local extent of the tumour, but are not helpful in distant metastases. US-guided FNB is helpful in characterising a tumorous change, but may be hazardous in hilar tumours. (Buck & Elsayed 1993, Guthrie *et al.* 1996, Menzel *et al.* 1999.)

CT is also valuable in assessing obstruction and has recently been equally sensitive as US in detecting hilar carcinomas, but no better than US in staging despite the developments in the equipment (Han *et al.* 1997, Tillich *et al.* 1998, Feydy *et al.* 1999).

Cholangiography is a definitive technique for evaluating the intraluminal component of biliary tumours. However, the main indication is decompressive treatment of jaundice. (Neumaier *et al.* 1995, Feydy *et al.* 1999.) Nowadays, cholangiography can be performed by noninvasive MRC. MRC with MRI and MRA may demonstrate not only the obstruction and the tumour, but also the spread of the malignancy. The images may facilitate the planning of surgery, palliative drainage and radiation therapy. More comparative studies of MR imaging are still needed, and it has also some limitations, e.g. the ampullary area being difficult to visualise. Anyhow, the double-duct sign may lead to further investigations. Any imaging modality seems to have difficulties in distinguishing malignant from benign lymph nodes. (Guibaud *et al.* 1995, Fulcher & Turner 1997, Soto *et al.* 1997, David *et al.* 1998, Mendler *et al.* 1998, Cannon *et al.* 1999.) In the near future, the use of MR may decrease the total cost of the diagnostic workup by eliminating the need for multiple studies. It is also helpful in cases where ERC fails. Intervention-compatible MR scanners and instruments are being developed, too. (Soto *et al.* 1997, Takehara 1998.)

6.4 Biliary fistulas

In our study, most of the spontaneous fistulas were internal, i.e. cholecystoduodenal, which has been reported to be the most common communication (Lu & Kaplowitz 1991), and only one fistula was external, i.e. cholecystocutaneous. All the nine patients with internal fistulas had acute or chronic cholecystitis as a predisposing factor, and only one of them did not have any stones left in the gallbladder at operation. The patient with the external fistula also had stones passing through a subcutaneous abscess. In fact, most spontaneous fistulas are produced by gallstones (Knol *et al.* 1996).

About 50 % of biliary enteric fistulas are diagnosed preoperatively (Knol *et al.* 1996). Our patients had gone through various investigations with many pathological, but not definitely diagnostic results, and the delay to diagnosis varied from 1 day to 4 ½ months.

Air in the biliary tree should raise a suspicion of a biliary enteric fistula, although it is a nonspecific finding and may only be visible in 30 % of the patients according to the old reports. Air was found in only one of our patients with a biliary enteric fistula, but a review of the films also revealed faint pneumobilia in another patient. Barium studies might also visualise the fistula or confirm the diagnosis, which did not happen with our patients. The patients had not gone through ERC, either, which has been helpful in both diagnosis and treatment. (Borman & Rigler 1937, Piedad & Wels 1972, Safaie-Shirazi *et al.* 1973, Glenn *et al.* 1981, Clavien *et al.* 1990, Hoff *et al.* 1998.)

CT has also been able to reveal biliary enteric fistulas. CT and US have shown air in the gallbladder or the biliary tree and abnormalities of the gallbladder or the duodenum, although the later reports included only few patients. (Fournier *et al.* 1994, Lorén *et al.* 1994, Shimono *et al.* 1998, Swift & Spencer 1998.) A nonvisualised or shrunken gallbladder at US often coexisted with spontaneous fistulas in our patients.

Iatrogenic fistulas are often external (Feretis *et al.* 1990). Most of the iatrogenic fistulas in our study were also external and occurred after biliary surgery. The delay to diagnosis varied from 1 day to over 8 months, as calculated from the predisposing operation or intervention.

Fistulography can delineate an external fistula. The modern optimal study to define biliary trauma is cholangiography. It may be performed intraoperatively, via a T tube, endoscopically or percutaneously. Nowadays it is also used in the treatment of iatrogenic biliary leaks. (Kissin & Grundy 1987, Ghahremani *et al.* 1991, Hoffmann & Neuhaus 1993, Morgenstern *et al.* 1993, Sherman *et al.* 1993, Horattas *et al.* 1994.) In our study, a variety of imaging modalities had been used. Fistulography yielded a correct diagnosis in three cases, including the one also diagnosed with CT fistulography, and cholangiography via cholecystostoma yielded it in one case. Surprisingly, ERCP revealed the diagnosis only in one case, and only one patient had received biliary endoprosthesis. The internal biloma was diagnosed at operation.

US and CT can be useful adjuncts in revealing the presence, location and extent of bile leaks, as especially US did in our study. They also help in guiding percutaneous drainage and demonstrate the parenchyma of the liver, and US may be useful in the follow-up. (Trerotola *et al.* 1992, Horattas *et al.* 1994, Wicky *et al.* 1999).

All our six patients with gastrointestinal obstruction had a fistula between the gallbladder and duodenum. This connection has been reported to be the most common in cases of gallstone ileus (Stitt *et al.* 1967). The sizes of the stones varied from 2 to 6 cm, the biggest one being found in the patient with Bouveret's syndrome. The most common site for stone impaction is the distal ileum (Illuminati *et al.* 1987, Lu & Kaplowitz 1991), but only two patients had the stone in the lower ileum. The delay in diagnosis varied from one to 11 days, which is close to the usual delay of 4–7 days (Khaira & Thomas 1994). Although gallstone ileus is usually diagnosed preoperatively in less than 50 % of the patients, as with our patients, there are also better results of even 73 % and 82 % (Stitt *et al.* 1967, Clavien *et al.* 1990). The patients had many positive, but not definitive examinations. The diagnosis was revealed preoperatively in two cases.

The classic triad of Rigler was not present in any of our cases, even when plain film showed intestinal obstruction or an ileal stone. The triad is reported to be present variably, as air or stones may be difficult to detect on plain film. The most frequent finding on admission radiographs has been mechanical obstruction. (Grumbach *et al.* 1986, Clavien *et al.* 1990, Davies *et al.* 1991.)

Contrast medium or endoscopy may reveal the level of obstruction and the stone, as in the case of Bouveret's syndrome in our study (Clavien *et al.* 1990, Romano *et al.* 1997). Lately, CT and US have also shown the triad of Rigler or aerobilia and lithiasis in Bouveret's syndrome. CT yielded the diagnosis in one of our patients, and five of the six patients had US, which revealed gallbladder pathology and signs of obstruction, which may be a clue to the diagnosis. (Lorén *et al.* 1994, Kasano *et al.* 1997, Romano *et al.* 1997, Manner & Stickel 1998, Swift & Spencer 1998.)

The diagnosis of an enterobiliary fistula should be suspected whenever air is shown within the biliary system in an appropriate clinical setting. Abdominal plain film may give a hint of the diagnosis. Today, ERCP may localise a fistula and permit endoscopic

treatment. CT and US are also able to reveal the fistula. (Fournier *et al.* 1994, Hoff *et al.* 1998, Shimono *et al.* 1998.) A nonvisualised or shrunken gallbladder should raise a suspicion of biliary enteric fistula and lead to a careful survey of this area.

Radiological studies also play a crucial role in the diagnosis and management of iatrogenic biliary injuries. The optimal study is cholangiography. Intraoperative cholangiography might reduce complications of laparoscopic cholecystectomy. It is important to determine whether the leak stems from a major extrahepatic duct or a minor intrahepatic duct and whether there is free flow of bile or a stable biloma. Fistulography may be diagnostic in cases where a fistulous tract or a surgical drain exists. CT, US and MRI are still complementary investigations. (Kissin & Grundy 1987, Ghahremani *et al.* 1991, Trerotola *et al.* 1992, Horattas *et al.* 1994, Shigemura *et al.* 1995.)

Gallstone ileus should be suspected especially in elderly patients with intestinal obstruction. Plain film is often the initial investigation and may permit a diagnosis. Contrast studies, endoscopy, US or CT may confirm the diagnosis. US is often done in the early phase and may alone reveal adequate clues. (Rigler *et al.* 1941, Clavien *et al.* 1990, Romano *et al.* 1997, Freitag *et al.* 1998, Swift & Spencer 1998.)

The near future will show the efficacy of multislice CT, virtual examinations and MRI in fistulas and gallstone ileus.

6.5 Primary sclerosing cholangitis

Our study concerning the diagnostics of PSC is, to our knowledge, the first to include both non-invasive methods, MRC-MRI and US. It proved to be difficult to define all the anatomical segments of the biliary tree in both ERC and MRC of the PSC patients. In ERC, there were many non-filled bile duct segments – which is a problem with this method in PSC – and the restricted spatial resolution of MRC caused problems in the case of narrow branches. Hence, in order to compare reliably the same segments, we were forced to do the detailed analysis non-blinded, but later on, we further made a blind evaluation of the presence of PSC in the MRC-MRI images of the PSC patients and the controls.

The diagnosis of PSC in our patients was based on ERC. In the blinded analysis, radiologist number 1 depicted changes of PSC in all the nine patients and radiologist number 2 in eight patients. In the previous studies, MRC showed biliary abnormalities suggestive of PSC in all patients (Ernst *et al.* 1998, Ito *et al.* 1999b). In a recent case-control study of a larger series, the sensitivity of MRC was 88 % and 85 % for the two readers, and there were six false negative diagnoses (Fulcher *et al.* 2000).

ERC was used as a golden standard in our study. The eight segments that were not filled with contrast in PSC patients were excluded. It is worth mentioning, however, that in seven of these segments both US and MRC would have shown features of PSC. Abnormal intrahepatic segments have been demonstrated more completely at MRC than at ERC also earlier (Fulcher *et al.* 2000). In our study, there was one false positive finding of PSC and one false positive stricture, but no false positive dilatations. In a recent study, there were five false positive diagnoses of PSC (Fulcher *et al.* 2000). Both in our PSC patients and especially in the control patients, the dilatations were detected better by ERC

than by MRC. This contrasts with some earlier results (Oberholzer *et al.* 1998, Ito *et al.* 1999b). The possible difference in injection pressure at ERC as well as the different diagnostic criteria may play a role. Many dilatations in the control group were, however, mild.

US revealed features of PSC in eight of the nine cases and obviously narrow bile ducts in the ninth patient in our study. There were altogether 17 narrow bile ducts, which were not considered pathologic. US was unable to reveal any strictures in the secondary intrahepatic ducts. This is a drawback, as according to Craig *et al.*, a grade 4 or diffuse stricture in a secondary intrahepatic duct is the only significant predictor of poor outcome in PSC (Craig *et al.* 1991). Such insufficiency has also been reported earlier. However, liver parenchymal changes have been assumed to suggest intrahepatic involvement. (Majoie *et al.* 1995.) The cholangiographic criteria used in our study are not optimal for US, either.

The advantage of US is its ability to show wall thickening, which was seen in nine segments in our patients with PSC. In fact, wall thickening has been reported to be a clue to the diagnosis of PSC in an appropriate clinical setting, such as in patients with inflammatory bowel disease, increased alkaline phosphatase activity or other hepatobiliary symptoms. However, thickening of the wall of the common bile duct is a nonspecific finding. (Majoie *et al.* 1995.)

US serves as a noninvasive screening method for hepatobiliary symptoms, and modern US equipment may give a hint of PSC if the possibility is kept in mind. It might be also valuable in the follow-up of PSC. US has demonstrated especially extrahepatic duct disease adequately, it shows the liver parenchyma and morphology, and it may reveal features of cholangiocarcinoma as well. Doppler US is helpful in the assessment of the portal veins. (Majoie *et al.* 1995, Majoie *et al.* 1997.) One should also be more suspicious of the only slightly narrowed bile ducts.

MRC is another noninvasive method without radiation that usually offers a diagnostic value equivalent to that of ERC for the main biliary tree and has been quite reliably able to reveal PSC, as it also did in our series. (Ernst *et al.* 1998, Fulcher *et al.* 2000.) There were differences in the detailed analysis and when looking for the poor prognostic signs of PSC, but it is problematic to compare MRC and ERC, which is not necessarily able to fill all the ducts with contrast in this disease. The cholangiographic classification was not planned for MRC, either. More comparative and follow-up studies are needed to outline the role of MRC in this rare disease. Anyhow, contrast-enhanced dynamic MR sequences may help to show wall thickening, and MRI reveals parenchymal and morphological changes of the liver and may demonstrate carcinomatous changes as well, which add to the importance of MR investigations (Ernst *et al.* 1998, Ito *et al.* 1999b, Revelon *et al.* 1999). MR imaging might also screen patients for ERC and interventions, when needed, and it could be a procedure of choice for patients in whom ERCP is unsuccessful or incomplete.

6.6 Metallic stents in malignant biliary obstruction

Stent insertion was successful in 97 % of the patients in our study when percutaneously inserted metallic stents were used in malignant biliary obstruction. In general, there has been a success rate of up to 95 %–100 %, although there are also early reports of different technical failures (Bethge *et al.* 1992, Stoker & Laméris 1993, Wagner & Knyrim 1993, Boguth *et al.* 1994, Rossi *et al.* 1994, Lee *et al.* 1997a, Kaskarelis *et al.* 1999). The 30-day mortality was 22 % in our series, but the stent procedure was considered a predisposing factor in only one case. The incidence of procedure-related deaths has not been reported in every study, and it has varied within 0–4 % (Salomonowitz *et al.* 1992, Stoker *et al.* 1993a).

The analysis of the patency period of a biliary stent in malignant biliary obstruction is difficult. The occlusion rate is expressed as the percentage of stents occluded during the period of study, and it depends on the duration of the study and the survival rate. Assessment of average primary patency is also problematic, as death may occur before the stent has been in place long enough to occlude. A real estimation of stent patency can be obtained in the patients in whom stent occlusion occurs and can be estimated by life-table analysis, which produces an actuarial curve for the stents remaining patent at given intervals. (Rossi *et al.* 1994, Lee *et al.* 1997a.) In order to get reliable results, the patients in our study were followed up until death, and we also used life-table analysis.

Stent obstruction was found in 10 out of 37 patients between the days 28 and 337. The occlusion rates for metallic stents have varied within 5–38 % (Stoker *et al.* 1993a,b). In the studies where the mean time of obstruction has been reported, it has varied within 2.5–6.5 months (Lee *et al.* 1993, Boguth *et al.* 1994). Many trials report recurrent jaundice instead of occlusions, and the results cannot be compared (Gillams *et al.* 1990, Lee *et al.* 1997a). Our result of 27 % obstruction at a mean of 4.4 months compares well to many other reports. Five more patients in our study had marked jaundice near death without a known definite cause.

The mean duration of patency in our patients, 12.4 months, was much longer than the few reported patency times varying within 2.3–8.3 months with different stents, but our median patency of 11.2 months was comparable to the 12 months in the report of Lee *et al.* (Bezzi *et al.* 1994, Rossi *et al.* 1994, Lee *et al.* 1997a, Schima *et al.* 1997). Our 25- and 50-week patency rates of 71 % and 42 % also compare well to the reported rates of 81 % and 53 %, respectively, concerning several types of stents (Lee *et al.* 1997a) and to the rates of 67 % and 51 %, respectively, concerning Wallstents (Rossi *et al.* 1994).

In our study, the patency rates of the patients with cholangiocarcinoma were significantly lower than those in the patients with other malignancies. There was also a tendency toward a poorer prognosis of the stent in the first 10 months in hilar strictures compared with nonhilar ones. There are earlier contradictory results of these aspects (Becker *et al.* 1993, Stoker & Laméris 1993, Rossi *et al.* 1994, Lee *et al.* 1997a, Schima *et al.* 1997). The poor dilatation of the stents in the hilar area might explain this result, as the narrower the diameter of the stent remained, the more it became occluded.

The cause of obstruction has usually been tumour overgrowth or ingrowth rather than sludge, as also found in our study. Overgrowth can be prevented to a certain extent by overstenting. (Rossi *et al.* 1994.) Ingrowth has been a disappointment with metallic stents. Although the mesh of the stents has the advantage of being expandable and allowing

drainage of side branches, it has the problem of tumour ingrowth. However, obstruction may be a result of a combination of partial ingrowth and bile encrustation. (Nicholson *et al.* 1992, Rossi *et al.* 1994.) The recent trials of covering the stent to prevent ingrowth have been disappointing. Covering occludes the side branches, and the cystic duct and the pancreatic duct may also become occluded. Polyurethane itself may cause obstruction, too. (Hausegger *et al.* 1998.)

Thirty percent of our patients had some early complications, and as many as 66 % had one or more late complications. Apart from stent obstructions, many of the problems were infections despite prophylactic chemotherapy. Ten patients had cholangitis in the late period. Many other studies report lower rates of complications, and some studies do not give a full report. Anyhow, the rate of complications has varied, but the results are not comparable, as there are reports of the overall rate of complications or minor / major complications, and some studies do not include obstructions or include only them in the percentages. (Gordon *et al.* 1992, Lee *et al.* 1992, Becker *et al.* 1993, Boguth *et al.* 1994, Rossi *et al.* 1994.) In fact, the frequency of late biliary complications is determined by the length and thoroughness of follow-up. We followed our patients until death and also registered unknown fever as a complication. Some stents could only be dilated to 5–6 mm, which may have caused some of the complications. The stents in the common bile duct expand to or near their maximum diameter, but in the hilar region, incomplete expansion up to 7–8 mm is not uncommon, though better dilatation has also been reported (Huibregtse *et al.* 1992, Stoker & Laméris 1993).

Thirty-one percent of the patients had one or more late reinterventions, which is more than in many previous reports (Laméris *et al.* 1991, Stoker *et al.* 1993b). However, there are also reports of 20 %–30 % reinterventions (Becker *et al.* 1993, Stoker *et al.* 1993a). Eight of the patients with primary stent obstruction were treated by the usual alternatives, which, in turn, caused new problems. Two-thirds of the late problems were associated with stent obstructions or reinterventions.

The aim in the treatment of malignant biliary obstruction is to reopen the ducts and to keep them patent. The procedure should have a low rate of complications and provide the patient a good quality of life. The stent should be easily insertable, and it should remain in place and stay open until death. Because these patients have a very short life expectancy, the procedure should be safe, effective, and performed only once. (Cwikiel *et al.* 1990, Laméris *et al.* 1991, Stoker *et al.* 1993a.)

Many studies of plastic and metallic stents show comparable results. The results of metallic stents seem to be better in view of stent failure, cholangitis and reinterventions in some comparative studies. Due to many flaws in study design and evaluation, length of follow-up and variation in patient population, the studies do not allow easy comparison. Our study with careful follow-up showed numerous early and late complications and a need for reinterventions with metallic stents.

According to Lammer, a metallic stent would be the most useful device for treatment if the occlusion rate could be kept under 10 % (Lammer 1990). Technical improvements of the stents would be welcome in order to prevent infections and tumour ingrowth. There have been several means under research: combination of brachytherapy with a stent, an electrolytic stent or a coating of angiogenesis inhibitor, silicone or polyurethane (Hausegger *et al.* 1998).

It would be important to choose the best suitable drainage for each patient. According to our results, the most suitable recipient for metallic stents would be a patient with a malignancy other than cholangiocarcinoma, who has a short stricture in the common bile duct and who can be treated with a single stent, which can be dilated maximally. However, drainage of hilar strictures may also be problematic with plastic stents. Patients with a very short life expectancy might be treated with a cheaper plastic stent or sometimes even with a catheter, if possible. Metallic stents are expensive, and stenting becomes much more expensive if multiple stents are inserted. Numerous complications and reinterventions reduce the quality of life and make for even more costs. Catheters instead of further expensive metal stents might be used for palliation of stent obstruction.

7 Conclusions

1. US is more sensitive than CT in revealing gallbladder carcinoma and its spread, but both methods are insufficient for accurate staging. US and CT are sensitive methods for diagnosing peripheral intrahepatic cholangiocarcinoma, but inaccurate for more distal bile duct carcinoma and most of the abdominal spread, US being more sensitive than CT. However, US is quite sensitive to detect spread to the liver. The infiltrating types of both gallbladder carcinoma and bile duct carcinoma are difficult to detect. US and CT are accurate and comparable methods in revealing bile duct obstruction. PTC and ERCP are restricted to the evaluation of the bile ducts.
2. Patients with biliary fistula and gallstone ileus undergo a variety of imaging modalities with pathological, but not definitely diagnostic results, and there is often a delay to diagnosis. Iatrogenic fistula, however, is often revealed by fistulography or cholangiography, but spontaneous fistula and gallstone ileus are difficult to diagnose. Anyhow, CT is able to reveal gallstone ileus. Nonspecific findings of various examinations should raise a suspicion of biliary fistula or gallstone ileus, and a nonvisualised or shrunken gallbladder at US could raise a suspicion of biliary enteric fistula in an appropriate clinical setting.
3. MRC and US are useful methods in the detection of PSC. US is unable, and MRC is too pessimistic to estimate the outcome of PSC.
4. About one third of the patients with percutaneously inserted metallic stents in malignant biliary obstruction have early complications and two thirds of the patients have late complications, including occlusion of the stent, which occurs in 27 % at a mean of 4.4 months. The patency rates of the patients with cholangiocarcinoma are significantly lower than those of the patients with other malignancies. There is also a tendency towards the occlusion of a stent with less dilatation or an increasing number of stents, longer strictures, and hilar strictures. One third of the patients have late reinterventions.

8 References

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