Key Concepts

- Laparoscopic cholecystectomy is the procedure of choice for symptomatic gallstones in the cirrhotic population
- Many cirrhotic patients have reduced gallbladder emptying and a thickened wall making evaluation of acalculous cholecystitis challenging
- There is little evidence that endoscopic intervention alters the natural history of PSC
- MRI with MRCP and CA 19-9 are the recommended studies to survey patients with PSC
- ERCP is indicated in patients with PSC who present with rising alkaline phosphatase, jaundice and a dominant biliary stricture.

Introduction

Cirrhosis is a causative factor for gallbladder disease whereas it is usually an end-stage effect of biliary disease. The primary aim of this section is to cover gallbladder and bile disease associated with cirrhosis. Toward this end, we will cover the cause and management of gallstones and will also discuss gallbladder dysfunction associated with cirrhosis. The predominant biliary tract disease associated with cirrhosis is primary sclerosing cholangitis (PSC). This section will cover the diagnosis, surveillance and management of PSC with an emphasis on the role of endoscopy. A rare biliary tract disease associated with cirrhosis, portal biliopathy, will also be discussed.

Gallbladder

Cirrhosis is a well-established risk factor for the development of gallstones with an estimated prevalence of 25 to 30%. Unlike the standard population where cholesterol is the primary component of gallstones, when associated with cirrhosis, the stones tend to be black pigment type. It is thought that this is related to altered pigment secretion combined with abnormal gallbladder motility. The diagnosis of gallstones in the cirrhotic population is made by a combination of clinical symptoms and abdominal ultrasound. While the management options are the same for a cirrhotic population compared to a standard population, the risks of surgery are greater. The risks of surgery are related to the severity of the cirrhosis as judged by the Child – Pugh score. Most cirrhotic patients undergoing cholecystectomy are Child class A and B and the morbidity and mortality increases with the severity of the liver disease. In a large review of laparoscopic cholecystectomy in cirrhotics, the conversion rate was 4.58% with a morbidity and mortality of 17% and 0.45% respectively for all Child grades. A recent study has suggested that the MELD score may be a better measure to predict morbidity after cholecystectomy than the Child-Pugh classification. Because of the increased risks in this...
population, with the advent of laparoscopic cholecystectomy, numerous studies have been conducted comparing open to laparoscopic cholecystectomy in the cirrhotic population. While there are few randomized controlled trials and the studies tend to be small and heterogeneous, the results of a systematic review of outcomes and meta-analysis of randomized trials shows that laparoscopic cholecystectomy is associated with shorter operative time, reduce complication rates and reduced length of stay of hospital stay.5,8 The take home message is that cirrhotic patients with symptomatic gallstones should undergo laparoscopic cholecystectomy when there liver disease is most compensated. Alternatively, there is no data to support prophylactic cholecystectomy in the cirrhotic population.

There are some circumstances where patients develop symptoms with end stage cirrhosis and possibly waiting for liver transplantation. This is a high risk situation and the Denver group reported on the results of endoscopic stenting of the gallbladder. They reported on 23 patients most with acute calculous cholecystitis or recurrent biliary colic. All patients underwent ERCP with placement of a transpapillary plastic stent into the gallbladder. All patients experienced resolution of their symptoms and 87% were asymptomatic 5 days to 3 years after the procedure until transplantation, death or the completion of the study period. An emerging endoscopic approach to gallbladder drainage employs EUS guidance and transduodenal placement of a lumen apposing covered metal stent.10

The determination of gallbladder disease in the cirrhotic population may be more difficult when compared to a normal population. Gallbladder contractility has been used as a method of determining gallbladder disease not associated with gallstones. However, in the cirrhotic population, it has been shown that gallbladder bladder contractility is reduced and is thought to be related to portal hypertension and hepatic failure.11 This reduced contractility is also felt to play a role in gallstone formation. A recent study has also shown the cirrhotic patients have increased gallbladder wall thickness which is another finding, when present in a normal population, can indicate gallbladder disease.11 The take-home message is that when evaluating patients with cirrhosis and suspected gallbladder disease, gallbladder wall thickness and reduced contractility are poor indicators of actual disease.

**Bile Duct**

Long-standing biliary obstruction can lead to secondary biliary cirrhosis. With modern day laboratory and imaging assessment, secondary biliary cirrhosis is uncommon in the Western world except in the population with PSC. In other parts of the world such as Asia, where biliary infections are common, secondary biliary cirrhosis is much more commonly encountered.

Primary sclerosing cholangitis is a chronic, progressive inflammatory disease involving the biliary tract and is often associated with inflammatory bowel disease. Most patients with PSC will progress to cirrhosis from the chronic obstruction and/or infection. The natural history is quite variable making investigation of interventions quite difficult. Medical and endoscopic interventions have been employed to alter the course of the disease. PSC is associated with cholangiocarcinoma (CCA) as well as gallbladder cancer and it is theorized that the chronic ongoing inflammation is important as a causative agent. Management of PSC involves methods to establish the diagnosis, medical management of chronic obstruction and infection, treatment of dominant strictures and surveillance for CCA.

In the past, the diagnosis of PSC was made by a finding of an elevated alkaline phosphatase and then corroborated with ERCP. With the advent of MRCP, this noninvasive imaging technique has completely supplanted ERCP for the diagnosis of PSC. Some patients present with only intrahepatic disease and diagnosis is established by liver biopsy. Once the diagnosis is established, there are no proven medical therapies that alter the natural course of the disease.12 However, if patients present with the rising alkaline phosphatase and/or bilirubin, MRI with MRCP is used to establish the presence or absence of a dominant stricture. If present, current guidelines from the EASL and AASLD recommend biliary dilation with or without short-term stenting.12 As with medical therapy, endoscopic intervention has also not been proven to alter the course of the disease. The potential benefit of ERCP but be balanced by the risk of introducing infection which can result in ongoing, unremitting infectious cholangitis and progressive deterioration of hepatic function.

Cholangiocarcinoma is a common malignancy complicating PSC and PSC patients have a lifetime prevalence of 5 to 10%.13 The prognosis for CCA is quite poor with a 5 year survival below 10%.14 Management of PSC is made more complicated by the fact that we have little data on the risk factors and surveillance strategies for detecting CCA in this cohort of patients. Older age at time of diagnosis, smoking, alcohol use and elevated bilirubin have all been suggested as risk factors for the development of CCA in PSC patients.15

MRCP visualizes the biliary tree very well, is noninvasive and does not subject the patient to radiation
exposure. For these reasons, it is been that proposed as the best method for screening and surveillance for CCA in PSC. MRCP alone has a sensitivity of 78% and a specificity of 76% with an overall accuracy of 76% for CCA. Another method of surveillance is to use biomarkers. The most useful biomarker is carbohydrate antigen 19-9 (CA 19-9). The use of CA 19-9 in conjunction with MRI improves overall accuracy in the detection of CCA with the usual conundrum of lower levels of CA 19-9 improving sensitivity at the expense of specificity and increasing the cut off improves specificity at the expense of sensitivity.16

ERCP with biliary brushing and/or biopsies may be considered as a component of the surveillance strategy. It can be notoriously difficult to differentiate reactivate atypia from malignancy on cytology. Fluorescence in situ hybridization (FISH) analysis may add to the value of conventional cytology.17,18,19 The use of intraductal ultrasound and/or cholangioscopy for viewing and to direct biopsies may enhance ERCP in the detection of CCA.20,21 For the most part, ERCP is too invasive to advocate as a routine surveillance modality. In summary, MRI and CA 19-9 represents the current recommendation for surveillance in patients with PSC with ERCP reserved for those with increasing alkaline phosphatase, rising CA 19-9, and a dominant stricture.

Patients with PSC are at increased risk for developing gallbladder cancer (GBCA) as well. Interestingly, GBCA in PSC has a male predominance which is strongly opposite from that seen in the general population.22 The risk factors for the development of GBCA is unknown but likely reflects the same factors seen with CCA. The only known risk factor is a gallbladder polyp and it is especially worrisome if the polyp is greater than .8 cm, is sessile and rapidly growing.3,24 Patients with PSC have a prevalence of mass lesions in the gallbladder of 3-14% versus 0.35% of the general population.24 Because of the poor prognosis for gallbladder cancer and because almost 60% of mass lesions in the gallbladder harbor either cancer or dysplasia, the general consensus is to recommend cholecystectomy for all gallbladder lesions in PSC patients.25

Portal hypertensive biliopathy (PHB) causes anatomical and functional abnormalities of the intra-and extra hepatic bile ducts and is seen primarily in patients with portal hypertension associated with extra hepatic portal vein obstruction but is seen in patients with cirrhosis. The pathology consists of dilation and stenosis of the biliary tree due to extensive venous collaterals which develop in an attempt to decompress the portal venous blockage. The clinical result in more advanced stages include cholestasis, jaundice, bile duct stones, cholangitis and finally, secondary biliary cirrhosis. The diagnosis is made after a clinical suspicion is combined with imaging. MRCP is currently the noninvasive modality of choice because it allows characterization of the location and extent of biliary obstruction and provides vascular information as well.

No treatment is recommended for those who are asymptomatic.26 The most common symptoms are recurrent abdominal pain, fever, jaundice and cholangitis. For those presenting with abdominal pain, the use of therapeutic doses of Ursodeoxycholic acid is the first choice for treatment. In cases of jaundice and cholangitis, decompression of the biliary tree is indicated and ERCP can be employed to dilate the bile duct, remove stones or implant a stent. Endoscopic biliary drainage is likely to help in the short term but does not permanently treat of the biliary obstruction. The ideal treatment for PHB is decompression of the portal system with either a surgical porto-systemic shunt or interventional radiology placement of the TIPS. Neither of these interventions may be possible depending on the extent the portal vein obstruction.

References


