ACG Clinical Guideline: Primary Sclerosing Cholangitis

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Abstract

Primary sclerosing cholangitis is a chronic cholestatic liver disease that can shorten life and may require liver transplantation. The cause is unknown, although it is commonly associated with colitis. There is no approved or proven therapy, although ursodeoxycholic acid is used by many on an empiric basis. Complications including portal hypertension, fat-soluble vitamin deficiency, metabolic bone diseases, and development of cancers of the bile duct or colon can occur.

Preamble

The writing group was invited by the Practice Parameters Committee and the Board of the Trustees of the American College of Gastroenterology to develop a practice guideline on primary sclerosing cholangitis (PSC).

Guidelines for clinical practice are intended to indicate preferred approaches to medical problems as established by scientifically valid research. Double-blind, placebo-controlled studies are preferable, but reports and expert review articles are also used in a thorough review of the literature con- ducted through the National Library of Medicine's MEDLINE. When only data that will not withstand objective scrutiny are available, a recommendation is identified as a consensus of experts. Guidelines are applicable to all physicians who address the subject, without regard to specialty training or interests, and are intended to indicate the preferable but not necessarily the only acceptable approach to a specific problem. Guidelines are intended to be flexible and must be dis- tinguished from standards of care that are inflexible and rarely violated. Given the wide range of specifics in any healthcare problem, the physician must always choose the course best suited to the individual patient and the variables in existence at the moment of decision.

Guidelines are developed under the auspices of the American College of Gastroenterology and its Practice Parameters Committee, and are approved by the Board of Trustees. Each has been intensely reviewed and revised by the Committee, other experts in the field, physicians who will use them, and specialists in the science of decision of analysis. The recommendations of each guideline are therefore considered valid at the time of their production based on the data available. New developments in medical research and practice pertinent to each guideline will

Introduction

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver and biliary tract disease that has a highly variable natural history (1). The pathogenesis of the disorder remains elusive, although the complications of the disease are a direct result of fibrosis and strictures involving intra and extrahepatic bile ducts (1). PSC may be asymptomatic for long periods but may also have an aggressive course, leading to recurrent biliary tract obstruction, recurrent episodes of cholangitis, and may

progress to end-stage liver disease. The diagnosis is now most frequently established using magnetic resonance cholangiography (MRCP), although direct cholangiography may be more sensitive (2). The typical cholangiographic findings include focal stricturing and saccular dilatation of the bile ducts, which may lead to a "beaded" appear ance (3).

The differential diagnosis of PSC includes several disorders that lead to biliary strictures such as bacterial cholangitis, intraarterial administration of floxuridine, prior biliary surgery, and AIDS- related cholangiopathy (3).

Diagnosis

Recommendations

1. MRCP is preferred over endoscopic retrograde cholangiopancreatography (ERCP) to establish a diagnosis of PSC. (Strong recommendation, moderate quality of evidence) (4,5,20)
2. Liver biopsy is not necessary to make a diagnosis in patients with suspected PSC based on diagnostic cholangiographic findings. (Conditional recommendation, low quality of evidence) (21)
3. Liver biopsy is recommended to make a diagnosis in patients with suspected small duct PSC or to exclude other conditions such as suspected overlap with autoimmune hepatitis. (Conditional recommendation, moderate quality of evidence) (22–24)
4. Antimitochondrial autoantibody testing can help exclude primary biliary cirrhosis. (Conditional recommendation, moderate quality of evidence) (25)
5. Patients with PSC should be tested at least once for elevated serum immunogloblulin G4 (IgG4) levels. (Conditional recommendation, moderate quality of evidence) (26–28)

Medical Treatment

Recommendation

1. Ursodeoxycholic acid (UDCA) in doses >28 mg/kg/day should not be used for the management of patients with PSC. (Strong recommendation and high quality of evidence) (42)

Table 1. Differential diagnosis of primary sclerosing cholangitis
Secondary sclerosing cholangitis
Cholangiocarcinoma
IgG4-associated cholangitis
Histiocytosis X
Autoimmune hepatitis
HIV syndrome
Bile duct strictures
Cholendocholithiasis
Primary biliary cirrhosis
Papillary tumors

Endoscopic Management

Recommendations

1. ERCP with balloon dilatation is recommended for PSC patients with dominant stricture and pruritus, and/or cholangitis, to relieve symptoms. (Strong recommendation, low quality of evidence) (64–68)
2. PSC with a dominant stricture seen on imaging should have an ERCP with cytology, biopsies, and fl uorescence *in-situ* hybridization (FISH), to exclude diagnosis of cholangiocarcinoma. (Strong recommendation, low quality of evidence) (69,70)
3. PSC patients undergoing ERCP should have antibiotic prophylaxis to prevent post-ERCP cholangitis. (Conditional recommendation, low quality of evidence) (71)
4. Routine stenting after dilation of a dominant stricture is not required, whereas short-term stenting may be required in patients with severe stricture. (Conditional recommendation, low quality of evidence) (68,72)

Liver Transplantation

Recommendations

1. Liver transplantation, when possible, is recommended over medical therapy or surgical drainage in PSC patients with decompensated cirrhosis, to prolong survival. (Strong recommendation, moderate quality of evidence) (94–96)
2. Patients should be referred for liver transplantation when their Model for End-Stage Liver Disease (MELD) score exceeds 14. (Conditional recommendation, moderate quality of evidence) (97)

PSC and IBD

Recommendations

1. Annual colon surveillance preferably with chromoendoscopy is recommended in PSC patients with colitis beginning at the time of PSC diagnosis. (Conditional recommendation, moderate quality of evidence) (104)
2. A full colonoscopy with biopsies is recommended in patients with PSC regardless of the presence of symptoms to assess for associated colitis at time of PSC diagnosis. (Conditional recommendation, moderate quality of evidence) (3)
3. Some advocate repeating the exam every 3–5 years in those without prior evidence of colitis. (Weak recommendation, low quality of evidence) (3)

Hepatobiliary Malignancies and Gallbladder Disease

Recommendations

1. Consider screening for cholangiocarcinoma with regular cross-sectional imaging with ultrasound or MR and serial CA 19-9 every 6–12 months. (Conditional recommendation, very low quality of evidence) (107,108)
2. Cholecystectomy should be performed for patients with PSC and gallbladder polyps >8 mm, to prevent the development of gallbladder adenocarcinoma. (Conditional recommendation, very low quality of evidence) (109)

Special Situations

Recommendations

1. Further testing for autoimmune hepatitis is recommended for patients with PSC <25 years of age or those with higher-than- expected levels of aminotransferases usually 5× upper limit of normal. (Conditional recommendation, moderate quality of evidence) (1,3)
2. MRCP is recommended for patients <25 years of age with autoimmune hepatitis, who have elevated serum ALP usually greater than 2× the upper limit of normal. (Conditional recommendation, moderate quality of evidence) (1)

General Management

Recommendations

1. Local skin treatment should be performed with emollients and/or antihistamines in patients with PSC and mild pruritus, to reduce symptoms. (Conditional recommendation, very low quality of evidence) (123,124)
2. Bile acid sequestrants such as cholestyramine should be taken (prescribed) in patients with PSC and moderate pruritus to reduce symptoms. Second-line treatment such as rifampin and naltrexone can be considered if cholestyramine is ineff ective or poorly tolerated. (Conditional recommendation, very low quality of evidence) (124–126)
3. Recommend screening for varices in patients with signs of advanced disease with platelet counts <150×10 3 /dl. (Conditional recommendation, very low quality of evidence) (127)
4. Patients with PSC should undergo bone mineral density (BMD) screening at diagnosis with dual energy X-ray absorption at diagnosis and repeated at 2- to 4-year intervals. (Conditional recommendation, moderate quality of evidence) (128)
5. Patients with advanced liver disease should be screened and monitored for fat-soluble vitamin deficiencies. (Conditional recommendation, moderate quality of evidence) (129)

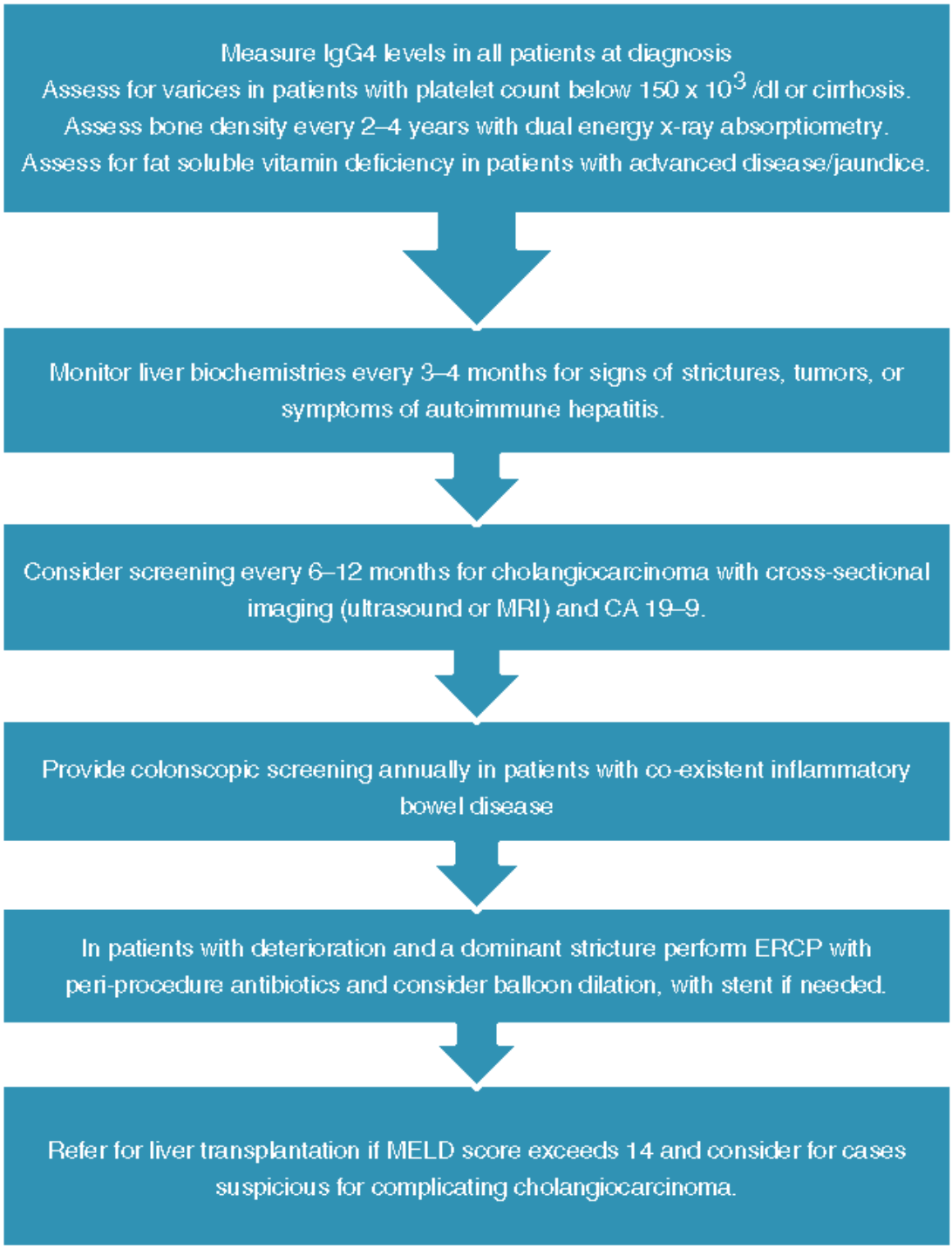

Figure 1. Management of primary sclerosing cholangitis.