REVIEW ARTICLE

Primary Sclerosing Cholangitis

Diagnosis and Treatment

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SUMMARY

Background: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease that involves progressive destruction of the bile ducts. Its prevalence is 4 to 16 cases per 100,000 persons. Its incidence has risen over the last 20 years, with a more than 35% increase in the last 10 years alone. PSC tends to arise in patients with chronic inflammatory bowel diseases. It is associated with an increased risk of various types of cancer (13%–14%), most prominently cholangiocellular carcinoma (CCC).

Method: This review is based on a selective search in PubMed for original articles, meta-analyses, and review articles about PSC that appeared from January 1980 to May 2013.

Results: The diagnosis is generally established with a bile duct imaging study—typically, magnetic resonance cholangiopancreatography (MRCP): this test is more than 80% sensitive and more than 90% specific for the diagnosis of PSC. The time from diagnosis to death or liver transplantation is 12 to 18 years, and the risk that a patient with PSC will die of cancer is 40% to 58%. Options for drug treatment are limited. Randomized, controlled trials have not shown any improvement of outcomes from the administration of ursodeoxycholic acid (UDCA). Interventional endoscopy is used to treat dominant stenoses and cholangitis, even though this method of treatment is supported only by low-level evidence. Liver transplantation results in a 10-year survival rate above 80%.

Conclusions: There is no causally directed treatment for PSC. Early diagnosis, complication management, and the evaluation of an optimally timed liver transplantation are the main determinants of outcome.

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The optimal treatment of primary sclerosing cholangitis (PSC) requires early diagnosis and ongoing clinical surveillance in accordance with the existing guidelines. The manifestations of this disease are often relatively mild and nonspecific even when the bile ducts have already been extensively destroyed, or even when cholangiocellular carcinoma is already present; thus, there is typically a long interval between the clinical onset and the diagnosis (median, 46 months) (1). The typical cholestatic pattern of increased liver-enzyme concentrations leads all too rarely to the initiation of a differential diagnostic evaluation. In this review article on PSC, we present the main facts about the etiology, epidemiology, natural course, and clinical surveillance of this disease, with particular attention to the risk of malignancy; we then discuss current developments and clinical recommendations regarding medical, endoscopic, and surgical treatment. To these ends, we selectively searched the PubMed database for original publications and meta-analyses about PSC that appeared from January 1980 (when the cholangiographic diagnostic pattern of PSC was first described by Chapman et al.) (2) to May 2013.

Etiology, epidemiology, and pathogenesis

Cholestatic liver diseases of unclear origin are commonly seen in clinical practice and have a broad differential diagnosis. Once a skeletal disease has been ruled out (absence of the typical isolated elevation of the alkaline phosphatase [AP] concentration), PSC is an important potential diagnosis to consider. This is a chronic cholestatic disease with a prevalence of 4–16/100 000 and an increasing incidence (with a recent 35.1% increase over a period of 10 years alone) (e1). PSC involves progressive destruction of the intra- and/or extrahepatic bile duct system. It affects men more commonly than women (62%–70% of patients are male), generally in middle age (the reported median age at diagnosis ranges from 35 to 51) (e2). PSC is strongly associated with chronic inflammatory bowel diseases (CIBD), particularly ulcerative colitis (60%–80% of patients with PSC) but also Crohn's disease (7%–21% of patients with PSC) (1, 3, 4). Liver function tests should be performed in all patients with CIBD. If the values are abnormal, the patient should undergo further evaluation for PSC.

The exact etiology and pathogenesis of this disease remain unclear. The International PSC Study

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TABLE 1

Overview of prognostic parameters in primary sclerosing cholangitis as reported in large-scale follow-up studies

	Wiesner (36) 1989 174 patients	Farrant (37) 1991 126 patients	Broomé (38) 1996 305 patients	Kim (39) 2000 405 patients	Ponsioen (40) 2002 174 patients	Tischendorf (1) 2007 273 patients	Tanaka (e25) 2008 391 patients
Age	+	+	+	+	+	+	+
Sex	n.s.	+/-	+/-	+/-	+/-	+/-	+/-
Bilirubin	+	+	+	+	n.s.	+	+
AST/ALT	+/-	+/-	+	+	n.s.	+	+/-
Albumin	+	n.s.	+	+	n.s.	+	n.s.
AP	+	+	+	+	n.s.	n.s.	+/-
Anemia	+	+/-	n.s.	+	n.s.	+	n.s.
CIBD	+	+/-	+/-	+/-	+/-	+/-	+/-
Variceal bleeding	+	+/-	+	+	n.s.	+	n.s.
Hepatomegaly	+	+	n.s.	+	n.s.	+	n.s.
Splenomegaly	+	+	n.s.	+	n.s.	+	n.s.
Histology	+	+	+	n.s.	n.s.	n.s.	+/-
Intra- and extrahepatic involvement	n.s.	+/-	+	n.s.	+	+	+/-

+, The presence or elevation of this parameter is associated with poorer outcomes in univariate analysis. **Bold-face type** indicates that this was found in multivariate analysis as well. +/-, the parameter is not prognostic. n.s., not studied; AST, aspartate aminotransferase; ALT, alanine aminotransferase; AP, alkaline phosphatase; CIBD, chronic inflammatory bowel disease.

Group (IPSCSG) and the German PSC Study Group are now investigating its pathogenesis with respect to possibly contributory infectious agents, immunological factors, and genetic associations. One study has shown a higher risk of developing PSC (odds ratio up to 4.8; 95% confidence interval, 3.6–6.5) in first-degree relatives of patients, in persons with an HLA type known to be associated with the disease (e.g., B8, Dr2, Dr3, Dr3w52a), and in persons with certain non-HLA haplotypes (5). A further reason to suspect a genetic basis is the fact that PSC is more common in Scandinavia (e3).

Natural course and prognosis

The mean interval from the diagnosis of PSC to death in patients who do not undergo liver transplantation is 12 to 18 years (1). The typical manifestations of the disease are poor general condition, fatigue, weight loss, pruritus, jaundice, and pain in the right upper quadrant of the abdomen (e4). As the destruction of the bile ducts progresses, liver involvement does as well, and hepatic fibrosis or cirrhosis arises. The course of the disease varies markedly from one patient to another (1). An overview of published studies on prognostication in PSC is given in *Table 1*.

The serious complications of PSC that can lead to poor outcomes include (biliary) cirrhosis and cholangiocellular carcinoma (CCC). PSC patients with an elevated concentration of the tumor marker carbohydrate antigen 19-9 (CA 19-9; value above 129 U/L), even if they do not have CCC, tend to have

more rapidly progressive disease and shorter survival times (without transplantation) than PSC patients with a normal CA 19-9 value (6).

So-called small-duct PSC may be an early form of PSC. This is a liver disease with the typical histologic findings of PSC, but with a normal cholangiogram. While about 20% of patients with small-duct PSC go on to develop PSC in the classic sense, most do not develop destructive disease of the bile ducts and are not at any increased risk of cancer (7).

Primary sclerosing cholangitis and the risk of cancer

Cancer surveillance, early detection, and treatment are vital elements of the clinical management of PSC patients, whose risk of developing hepatobiliary carcinoma is 13%–14% (e5). In pertinent studies, the overall risk that a PSC patient will die of cancer has been found to range from 40% to 58% (1, e5–e7). The various types of cancer that make up this figure will be discussed in the following sections. An overview of PSC-associated carcinomas is given in *Figure 1*, and surveillance recommendations are summarized in *Table 2*.

Cholangiocellular carcinoma

The cumulative incidence of CCC among PSC patients is markedly elevated, being higher than 10% (e6, e8). The simultaneous presence of ulcerative colitis in a patient with PSC probably increases the risk of CCC, but the available data on this question do not permit a definitive conclusion (e9). Up to half of all cases of CCC in PSC patients are diagnosed simultaneously

FIGURE 1

The risk of developing PSC-associated cancers. The underlying studies are based on varying patient populations and follow-up periods. CRC (colorectal carcinoma) – 9% at 10 years and 31% at 20 years in patients with both PSC and chronic inflammatory bowel disease (CIBD). CCC (cholangiocellular carcinoma) – ca. 11% cumulative incidence in population studies; up to 26% in patients with dominant stenoses with 9 years of follow-up. HCC (hepatocellular carcinoma). GB (gall-bladder carcinoma). PC (pancreatic carcinoma) – only a single study indicates elevated risk (significance unclear).

with, or within a year of, the diagnosis of PSC; this reflects the fact that previously undiagnosed PSC sometimes becomes symptomatic through the development of CCC (8). Thus, whenever PSC is diagnosed, a possible dominant bile duct stenosis or CCC should be actively sought. Although CA 19-9 is a tumor marker for CCC, it cannot be used to detect CCC in an early stage.

CCC often manifests diffuse, infiltrative growth and is therefore only rarely resectable, e.g., in cases of early carcinoma of the distal portion of the common bile duct. If CCC is not resectable, gemcitabine/cisplatin-based chemotherapy can moderately prolong survival (11.7 months) (9). Patients with hilar and distal bile duct carcinomas who are treated palliatively with metal stenting and/or photodynamic therapy were found in one study to have a median survival time of 12.4 months (e10).

As the risk of recurrent CCC is high, only a minority of selected patients are suitable candidates for liver transplantation (e11). The prerequisites include the documented absence of distant metastases and the elimination of the possibility of lymphatic spread by abdominal lymphadenectomy. Once the latter procedure has been performed, neo-adjuvant radiotherapy and chemotherapy are given according to the Mayo Clinic Protocol. Liver transplantation can only be considered if the patient remains free of metastases. After transplantation, the 5-year-survival rate of these patients is very high (current figure: 70%). In Germany at present, a trial of adjuvant gem-

TABLE 2

Clinical surveillance of PSC patients, as recommended by the EASL (4) and AASLD (3)

Lab tests (LFT, blood counts, inflammatory parameters)	every three months
CA 19-9	once per year
Ultrasonography	every six months
Colonoscopy	every 1–2 years in CIBD or s/p LTx
MRCP	depending on course; every 1–2 years in advanced or progressive PSC
ERCP (e26)	only if CCC is suspected (CA 19-9 values > 129 U/l) (17); not a "screening test"
Urine proteome analysis (18)	only experimental to date

AASLD, American Association for the Study of Liver Diseases. CA, carbohydrate antigen. CCC, cholangiocellular carcinoma. CIBD, chronic inflammatory bowel disease. EASL, European Association for the Study of the Liver. ERCP, endoscopic retrograde cholangiopancreatography. LTx, liver transplantation. LFT, liver-function tests. MRCP, magnetic resonance cholangiopancreatography; s/p, status post.

citabine chemotherapy after liver transplantation in patients with proximal bile duct carcinoma is being carried out; patients with PSC can also be included in this trial (DRKS00000805, product 001).

Colorectal carcinoma

Cholestatic liver diseases increase the amount of secondary bile acids in bile. It has been postulated that these substances are responsible for the increased incidence of cancers of the right colon in such patients. It is unclear, however, whether PSC patients can be protected against colorectal carcinoma (CRC) by the administration of ursodeoxycholic acid (UDCA), a drug that lowers the concentration of secondary bile acids (10). Moreover, there are conflicting data as to whether PSC patients have an elevated risk of CRC (e6). A number of studies have revealed a 10% to 30% risk of developing CRC over a variable follow-up interval (5 to 15 years). In any case, PSC patients who also have CIBD should undergo colonoscopy with stepwise biopsy every 1–2 years both before and after liver transplantation, as these patients have been shown to have a markedly elevated risk of CRC (25 % in 5 years) (10–12, e7).

Hepatocellular carcinoma

The risk of hepatocellular carcinoma (HCC) among PSC patients apparently lies in the range of 2%–4%, but the data on this question are sparse (8). The risk depends on the extent of the accompanying cirrhosis and is lower than the risk of CCC.

FIGURE 2

Diagnostic algorithm for suspected primary sclerosing cholangitis. ERC, endoscopic retrograde cholangiography; MRCP, magnetic resonance cholangiopancreatography. ERC (endoscopic retrograde cholangiopancreatography) is indicated when transabdominal ultrasonography or MRCP reveals stenosis with proximal dilatation of the bile ducts requiring endoscopic treatment. If the MRCP findings are normal or unclear, liver biopsy should be performed to complete the diagnostic evaluation.

Carcinoma of the gall bladder

PSC patients are at increased risk of developing polyps and cancer of the gall bladder. An adenoma-carcinoma sequence is likely in such cases (e12). In PSC patients with unclear gall-bladder structures, the prevalence of carcinoma is high (greater than 50 %) (e13). If multiple gall-bladder polyps are found, or if a polyp is found that is increasing in size (above 0.8 cm), cholecystectomy is indicated (13). The EASL, in its guidelines, recommends cholecystectomy whenever gall-bladder polyps are present, regardless of size (4). For small, solitary polyps, frequent follow-up (e.g., every three months) is recommended as a minimum.

Diagnostic evaluation

In patients with cholestatic liver disease of unclear origin, PSC should always be included in the differential diagnosis. Various PSC subtypes must be considered, as well as other diseases that only resemble PSC, as the difference can have implications for treatment (e14).

The recommended diagnostic algorithm, shown in Figure 2, begins with the usual laboratory tests and percutaneous ultrasonography. If cholestasis is found, further diagnostic and therapeutic steps are taken. Magnetic resonance cholangiopancreatography (MRCP) is now the standard procedure for visualizing the intra- and extrahepatic bile ducts (sensitivity 86% and specificity 94% for the detection of PSC [14]). If ultrasonography reveals bile duct distention, then this is presumably due to dominant stenosis, and treatment will

be needed; in such cases, endoscopic retrograde cholangiography (ERC) should be performed directly, rather than MRCP (see Figure 3).

5% to 20% of dominant stenoses are due to CCC. Thus, whenever a dominant stenosis is found, an additional, targeted diagnostic evaluation should be performed (see also Table 3) (15, 16). Brush cytology or forceps biopsy of the stenosis are standard methods in this situation and have been shown to be 60%–83% sensitive and 89%–95 % specific (e15, e16). Biopsy can also be supplemented with a fluorescent-in-situ-hybridization (FISH) study to detect chromosome anomalies, if this technique is available (17). Further diagnostic methods for determining the cause of dominant stenosis include intraductal ultrasonography and ductal cholangioscopy (15, 16). Proteome analysis of bile and urine is under evaluation as a complementary method but has not yet been adequately validated (18, 19). Endosonography of the extrahepatic bile ducts can also provide diagnostic help in unclear cases (20). Liver biopsy is not routinely necessary; it is indicated only when visualization of the bile ducts has not yielded any abnormal findings and cholestatic liver disease still needs further evaluation, or when there is clinical suspicion of an overlap syndrome with autoimmune hepatitis or primary biliary cirrhosis (PBC, up to 10% of cases). Table 2 contains a detailed presentation of the differential diagnostic evaluation for these and other types of cholestatic liver disease.

Drug treatment of PSC

The treatment of PSC with drugs is problematic, as no specific or effective form of pharmacotherapy has yet been identified. Immune suppressants and modulators and anti-fibrotic drugs have been found to have essentially no effect and are therefore not routinely used (e17).

There is a longstanding tradition of treating PSC with ursodeoxycholic acid (UDCA), a hydrophilic bile acid. The clinical benefit of this drug has been under debate in recent years. In the 1990s, two single-center trials and one multicenter, randomized, placebo-controlled trial of low-dose UDCA (10–15 mg/kg body weight [BW]) revealed an improvement of laboratory values, disease manifestations, and, in some cases, histological findings (21, 22, e18). When further trials (23–25) with higher UDCA doses (17–23 mg/kg BW, 10–30 mg/kg BW, 25–30 mg/kg BW) also yielded positive findings, a randomized, double-blinded, placebo-controlled, multicenter trial with a UDCA dose of 28–30 mg/kg BW was initiated. That trial, however, was stopped before its completion, because the patients in the treatment arm, despite the improvement of their laboratory values, more commonly reached the predefined negative endpoints than the patients in the placebo group. These endpoints were death, liver transplantation, and the development of varices (26).

There is also controversy about whether UDCA can help to prevent CCC and/or colorectal carcinoma in PSC patients. In two small-scale trials, patients treated with 13–15 mg/kg BW of UDCA had a lower frequency

TABLE 3

The differential diagnosis and treatment of cholestatic hepatopathies

	Bili-rubin	gGT	AP	AST	ALT	AMA	ANA	ANCA	IgG	IgM	IgG 4	Cholangio-graphy	Histology	Treatment ^{*1} (Source)
PSC	↔- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↔- (↑)	↔- (↑)	↔	↔- ↑	↔- ↑↑	↔- ↑	↔- ↑	↔- ↑	multifocal strictures and rarefaction of bile ducts	"onion-skin" periductal fibrosis (rare)	clinical surveil- lance, antibiotics, endoscopy, (UDCA) (3, 4)
Small-duct PSC	↔- ↑↑	↑- ↑↑	↑- ↑↑	↔- (↑)	↔- (↑)	↔	↔- ↑	↔- ↑↑	↔- ↑	↔- ↑	↔- ↑	normal	"onion-skin" periductal fibrosis (rare)	(UDCA) (3, 4)
PSC-AIH overlap	↔- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↔	↑- ↑↑↑	↔- ↑	↑- ↑↑	↔	↔-↑	typical changes of PSC and interface hepatitis	typical changes of PSC and interface hepatitis	clinical surveil- lance, antibiotics, endoscopy, (UDCA), im- mune suppres- sion (3, 4, e27)
IgG4 autoimmune cholangio- pathy	↔- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↔- (↑)	↔- ↑	?	?	?	?	?	↑↑- ↑↑↑	one or more strictures, variable course	lymphoplas- matic infiltra- tion, transmu- ral fibrosis, infiltration of IgG4-positive plasma cells	immune suppression (steroids) (e28)
SSC	↔- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↔- ↑	↔- ↑	↔	↔	↔	↔	↔	↔	casts, stenoses	nonspecific inflammation ranging to chronic bile duct obstruction	endoscopic treatment, antibiotics, (UDCA) (e29)
PBC	↔- ↑↑	↑- ↑↑	↑- ↑↑	↔- ↑	↔- ↑	↑- ↑↑	↔- ↑	↔	↔	↑↑↑	↔	normal	inflammatory destruction of small bile ducts	UDCA in early stages (4)
PBC-AIH overlap	↔- ↑↑	↑- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↑- ↑↑↑	↑- ↑↑	↑- ↑↑↑	↔- ↑	↑- ↑↑	↑↑↑	↔	normal	PBC and interface hepatitis	clinical surveil- lance, antibi- otics, endos- copy, UDCA in early stages (4, e27)
Familial intrahepatic liver diseases (e.g., ABCB4 defects) ^{*2}	↔- ↑↑	(↑)- ↑↑	(↑)- ↑↑	↔- ↑↑	↔- ↑↑	↔	↔	↔	↔	↔	↔	variable; typically, hepatolithiasis	nonspecific changes, intra- canalicular cholestasis	depending on phenotype (e30, e31)
Embryologic diseases of the ductal plate (e.g., Caroli syndrome) ^{*2}	↔- ↑↑↑	↔- ↑↑↑	↑- ↑↑↑	↔- ↑↑	↔- ↑↑	↔	↔	↔	↔	↔	↔	(cystic) dilatation of bile ducts, hepatolithiasis	dilatation of bile ducts	endoscopy, surgery, anti- biotics (e32)
Granuloma- tous hepato- pathies ^{*2}	↔- ↑↑	↑- ↑↑	↑- ↑↑	↔- ↑	↔- ↑	↔	↔	↔	↔	↔	↔	normal	epithelioid cell granulomas	depending on underlying disease
Druc-induced/ toxic hepato- pathies ^{*2}	↔- ↑	(↑)- ↑↑	(↑)- ↑↑	↔- ↑↑	↔- ↑↑	↔	↔- ↑	↔	↔	↔	↔	normal	nonspecific	discontinuation of offending substance

ABCB, ATP-binding cassette (subfamily B); AIH, autoimmune hepatitis; ALT, alanine aminotransferase; ANA, antinuclear antibodies; ANCA, antineutrophilic cytoplasmic antibodies; AMA, antimitochondrial antibodies; AP, alkaline phosphatase; AST, aspartate aminotransferase; gGT, gamma-glutamyltransferase; Ig, immunoglobulin; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; SSC, secondary sclerosing cholangitis; UDCA, ursodeoxycholic acid

Arrows (typical laboratory findings for the disease in question): ↔, not elevated; ↑, mildly elevated; ↑↑, moderately elevated; ↑↑↑, markedly elevated.

^{*1}Liver transplantation should be considered as a treatment option for patients with any of these diseases in an advanced stage.

^{*2} These groups of diseases comprise multiple subentities. Clinical variability thus depends not only on the severity of the condition, but on its subtype as well.

Figure 3: Primary sclerosing cholangitis (PSC) with involvement of the intra- and extrahepatic bile duct system in a 35-year-old man. a) Magnetic resonance pancreatography (MRCP) reveals the caliber fluctuations and irregular walls of the common bile duct (CBD) and the intrahepatic bile ducts. There is narrowing of a long segment of the distal portion of the CBD. b) similar findings are seen in this image of the bile ducts obtained by endoscopic retrograde pancreatography (ERCP).

of colorectal dysplasia, but the frequency of colorectal dysplasia and colon carcinoma in patients with both PSC and ulcerative colitis was actually higher in the treatment arm (these patients were given 28–30 mg/kg BW of UDCA) (27–29). A recent long-term follow-up study of patients treated with UDCA did not reveal any reduction of the risk of colon carcinoma (10). The available data on the putative prevention of CCC by UDCA are similarly inconsistent (e19).

In consequence, the American Association for the Study of Liver Diseases (AASLD) has taken a stand against the use of UDCA in any patient with PSC, while the European guidelines contain a recommendation to consider giving UDCA (15–20 mg/kg BW) if the patient has a positive family history of colorectal carcinoma, a previously diagnosed colorectal neoplasia, or a longstanding CIBD (recommendation grade II, evidence level C) (3, 4). In its current guidelines, the German Society of Gastroenterology and Digestive and Metabolic Diseases (Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten, DGVS) states that UDCA can be given for chemoprevention (evidence grade A, strong consensus).

Another potential therapeutic option for the future that still needs further evaluation is the administration of nor-ursodeoxycholic acid (norUDCA), a substance arising from a chemical modification of UDCA in which a side chain is shortened. norUDCA undergoes cholehepatic shunting; this, in turn, results in the induction of a bicarbonate-rich choluresis and has additional anti-inflammatory and antifibrotic effects (30). After the successful completion of a phase I trial, a European multicenter phase II trial was initiated in early 2013.

Endoscopic treatment

The evidence level for endoscopic treatment is low, as large-scale studies are lacking. Just under 60% of PSC patients develop a dominant bile-duct stenosis over the course of their illness (1, 31); the endoscopic treatment of such stenoses improves the outcomes (e20). In particular, many of these patients have bacterial colonization of their bile ducts requiring both endoscopic treatment and appropriate antibiotic therapy (after identification of the responsible pathogen, whenever possible) (e21). The available treatment options include bougie dilatation, balloon dilatation, stenting, and combinations of these. Stenting, if performed, is best done only over the short term (e.g., for two to four weeks), as the risk of stent occlusion rises significantly thereafter (32, e22). The risk that ERC will lead to a complication such as cholangitis or pancreatitis increases with the complexity and length of the procedure (33, 34). According to the current guidelines, peri-interventional antibiotics (e.g., sulfamonomethoxazole) should always be given to prevent ascending cholangitis whenever a PSC patient undergoes ERC (3, 4).

Liver transplantation

Liver transplantation (LTx) is the only curative treatment option for PSC patients. The optimal timing of LTx is debated; for each patient, the timing should be based on the individual prognosis. Many studies have been performed with the intention of determining valid markers of prognosis (see Table 1). At the very latest, a patient should be put on the LTx waiting list when he or she is found to have severe, progressive liver disease with persistent elevation of the bilirubin concentration or recurrent cholangitis, with or without the development of dominant stenoses, despite optimal endoscopic

treatment and despite having lost weight to lower the body-mass index (BMI) by at least 10% over a period of 1 year.

Organ distribution for PSC patients is not regulated solely according to the Model of End-Stage Liver Disease (MELD) score, because the latter does not adequately reflect the true urgency of LTx in these patients. PSC patients are given points according to the so-called “standard exceptions”: from March 2012 onward, PSC patients fulfilling the criteria for LTx have been taken directly onto the LTx waiting list on reaching a MELD score of 22 points. They are then automatically assigned a higher urgency level every 3 months, corresponding to an assumed 10% mortality, regardless of their laboratory findings. After receiving a liver transplant, PSC patients tend to do very well: 5- and 10-year survival rates of 87.4% and 83.2 % have been reported (e23). Recurrent PSC after LTx has been said to arise in 20% or more of all cases, but recurrent PSC is hard to distinguish from secondary changes in the bile ducts, and the data on this question are inconsistent (35, e24). For the LTx criteria in patients with CCC, see the section on cholangiocellular carcinoma, above.

Overview

Optimal patient care depends on the early diagnosis of PSC and its differentiation from other cholestatic liver diseases. Although the options for drug treatment are limited, adequate clinical surveillance of these patients is essential for the early detection and treatment of further complications, above all cholangitis and cancer. Moreover, the indication for liver transplantation must be continually re-evaluated. For all these reasons, patients with PSC should be followed in clinical centers with the relevant expertise.

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Conflict of interest statement

The authors state that they have no conflicts of interest.

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KEY MESSAGES

- Elevated liver enzyme concentrations in a typical cholestatic pattern, without any known cause, should arouse the suspicion of primary sclerosing cholangitis (PSC).
- PSC takes a variable course and is associated with a high risk of developing various kinds of carcinoma—in particular, cholangiocellular carcinoma (CCC).
- The options for pharmacotherapy are limited. Current guidelines carry a weak recommendation (at most) for the administration of ursodeoxycholic acid in low doses. Endoscopy is used to treat dominant stenoses. Dilatation is preferable to long-term stenting.
- Patients with advanced PSC should be evaluated for liver transplantation, which is the only curative treatment for this disease.
- As there is no easy way to screen for CCC, patients with PSC should be treated in centers that possess the relevant experience.

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REVIEW ARTICLE

Primary Sclerosing Cholangitis

Diagnosis and Treatment

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