Magnetic Resonance Imaging in Primary Sclerosing Cholangitis

Rezonans magnetyczny w pierwotnym stwardniającym zapaleniu dróg żółciowych

Julia Tuchalska-Czuroń[*1], Aldona Wybraniec-Zaręba[1], Gabriela Półtorak-Szymczak[1], Mariusz Furmanek[1], Jerzy Walecki[1], Katarzyna Sklinda[1]*

[1] *Department of Radiology, Centre of Postgraduate Medical Education, Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw, Poland*

KEYWORDS:

- magnetic resonance imaging
- primary sclerosing cholangitis
- imaging

ABSTRACT

Primary sclerosing cholangitis (PSC) is a chronic liver disease in which there are inflammation and scarring of the bile ducts leading to fibrosis, destruction and narrowing of the bile ducts, resulting in cholestasis. In the long run, PSC can cause liver cirrhosis and failure. In clinical practice, the diagnosis of PSC is generally based on blood tests and imaging studies (currently preferably magnetic resonance cholangiopancreatography). To make a diagnosis of PSC it is necessary to exclude secondary causes of sclerosing cholangitis. The most common MRI features of PSC concerning bile ducts are: bile duct dilatation, beading, extrahepatic bile duct stenosis, wall enhancement and thickening. The most common MRI features of PSC concerning hepatic parenchyma are: rounded shape of the liver caused by hypertrophy of caudate lobe and left liver lobe, atrophy of the right lobe, enlargement of portal and/or portacaval lymph nodes, peripheral parenchymal inflammation, wedge-shaped confluent fibrosis, heterogeneity of the liver parenchyma, periportal oedema, cirrhosis with indirect signs of portal hypertension such as splenomegaly, ascites and collateral vasculature.

SŁOWA KLUCZOWE:

- rezonans magnetyczny
- pierwotne stwardniajace zapalenie dróg żółciowych
- obrazowanie

STRESZCZENIE

Pierwotne stwardniające zapalenie dróg żółciowych jest przewlekłą chorobą wątroby, w której dochodzi do procesu zapalnego i bliznowacenia w obrębie dróg żółciowych, co prowadzi do ich włóknienia, destrukcji i zwężeń, skutkujących cholestazą. Ostatecznie, pierwotne stwardniające zapalenie dróg żółciowych prowadzi zwykle do marskości i niewydolności wątroby. W praktyce klinicznej, do postawienia rozpoznania niezbędne jest wykonanie badań krwi oraz badań obrazowych (obecnie metodą z wyboru jest cholangiopankreatografia rezonansu magnetycznego). Postawienie rozpoznania pierwotnego stwardniającego zapalenia dróg żółciowych wymaga wykluczenia wtórnych przyczyn stwardniającego zapalenia dróg żółciowych. W obrazowaniu metodą rezonansu magnetycznego, u pacjentów z pierwotnym stwardniającym zapaleniem dróg żółciowych obserwuje się: odcinkowe poszerzenia i zwężenia dróg żółciowych ("obraz korali"), pogrubienie i wzmocnienie kontrastowe ścian dróg żółciowych, zaokrąglony obrys wątroby spowodowany powiększeniem płatów lewego i ogoniastego, atrofia płata prawego, powiększenie węzłów chłonnych okolicy żyły wrotnej i żyły głównej dolnej, obwodowo widoczne cechy zapalenia w obrębie miąższu, zlewające się obszary włóknienia klinowatego kształtu, niejednorodność miąższu, obrzęk okołowrotny, marskość wątroby z pośrednimi objawami nadciśnienia wrotnego, takimi jak powiększenie śledziony, wodobrzusze i naczynia krążenia obocznego.

Introduction

Bile duct anatomy

The bile ducts are a number of tube-like structures that carry bile from the liver to the duodenum. There are intra- and extrahepatic bile ducts. The intrahepatic bile ducts consist of bile canaliculi, segmental bile ducts, sectoral bile ducts, left and right hepatic bile ducts. Bile canaliculi merge to form segmental bile ducts which drain each liver segment. The segmental ducts from segments 6. and 7. unite to create right posterior sectoral duct (RPSD). The segmental ducts from segments 5. and 8. combine to make right anterior sectoral duct (RASD). Right anterior and posterior sectoral ducts

*Address for correspondence: *Julia Tuchalska-Czuroń , Department of Radiology, Centre of Postgraduate Medical Education, Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw, Wołoska 137 Street, 02-507 Warsaw, Poland, e-mail: tuchalska@gmail.com.*
ISSN 2657-9669/ This work is licensed under a Creative Commons Attribution 4.0 International License.
Published and financed by Centre of Postgraduate Medical Education; https://doi.org/10.36553/wm.92.

merge to form right hepatic duct (RHD). The segmental ducts from segments 2.,3. and 4. unite to create left hepatic duct (LHD). The common hepatic duct (CHD) arises from the union of right and left hepatic ducts. The angle of their union is the point of the exit of a bile duct (or ducts) from segment 1. of the liver. The extrahepatic bile ducts consist of common hepatic duct, gallbladder, cystic duct, and common bile duct. The gallbladder stores an excess of the bile. Cystic duct from the gallbladder merge with common hepatic duct and together they form common bile duct. The common bile duct combines with main pancreatic duct and form major duodenal papilla, a conical structure, where the bile and pancreatic juice get to the duodenum (1).

Primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is a chronic liver disease in which there are inflammation and scarring of the bile ducts leading to fibrosis, destruction and narrowing of the bile ducts, resulting in cholestasis (2). In the long run, PSC can cause liver cirrhosis and failure (3). At present, the etiology of the disease is unknown. It is supposed that autoimmune factors, genetic susceptibility and incorrect composition of the gut flora play a key role in pathomechanism of PSC (4). This is supported by the observation, that 50-80% of PSC patients have inflammatory bowel disease (4). Primary sclerosing cholangitis is a rare disease, affecting mostly men aged 30 to 50, with prevalence range from 3.85 to 16.2 cases per 100,000 person-years (5). In clinical practice, the diagnosis of PSC is generally based on blood tests (like alkaline phosphatase, aminotransferases, bilirubin) and imaging studies (cholangiography via endoscopic retrograde cholangiopancreatography or magnetic resonance cholangiopancreatography) (3). This paper presents current and brief review concerning magnetic resonance imaging of the primary sclerosing cholangitis.

PSC Diagnosis

To make a diagnosis of PSC it is necessary to exclude secondary causes of sclerosing cholangitis such as: toxic, infectious, traumatic, obstructive, ischemic or potential other inflammatory factors (6). The most useful tools for detecting PSC are magnetic resonance cholangiopancreatography (MRCP, in most cases the modality of choice) and endoscopic retrograde cholangiopancreatography (ERCP).

ERCP is a technique that incorporate endoscopy and fluoroscopy. During ERCP, an endoscope is inserted through the upper gastrointestinal tract into the duodenum. Next, the catheter or cannula is inserted through the major duodenal papilla and radiocontrast is injected to visualize bile ducts and/or pancreatic duct. Thus, ERCP is an invasive technique with potential serious complications including pancreatitis, cholangitis, perforation and bleeding (7).

Magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP) is the imaging modality of choice to workup of patients with suspected PSC (7, 8) as recommended by both American Association for the Study of Liver Diseases (AASLD) and European Association for the Study of the Liver (EASL) guidelines (6, 7) and widely used for surveillance purposes (6). MRCP has high diagnostic sensitivity (86%) and specificity (94%) for detection of PSC (6) and is superior to ERCP for initial screening of suspected cases in terms of cost effectiveness. However, diagnostic accuracy of early-stage PSC is 90% for MRCP compared with 97% for ERCP (8). ERCP is preferred in non-diagnostic cases and in patients with early small duct PSC, who have normal MRCP, despite clinical, biochemical and histological findings (6). In comparison to ERCP, MRCP is more limited in visualization of the peripheral intrahepatic branches. Also, the detection of PSC in patients with cirrhotic liver is reduced in MRCP (8). In these patients cirrhotic nodules may compress the bile duct lumen that may mimic sclerotic bile duct changes.

An abdominal ultrasound (US), which is still a very sensitive examination especially for detecting intrahepatic calculi, cannot provide complete morphological results in the event of cholangitis. Otherwise, patients with unrecognized PSC are more likely to be evaluated with computed tomography (CT), as it is usually first modality for the assessment of upper abdominal syndromes (6). However, similar to US, the role of CT is limited in the assessment of biliary strictures, especially of small peripheral bile ducts that can be missed in early stages of disease.

MRI and MRCP features in PSC

Technical overview

MRCP can be performed at 1,5 or 3 T scanners, but 3T MRI exam is preferred because of the better visualization of the biliary system. A recent recommendation from the International PSC Study Group requires at least 1,5 T MR scanner for the diagnosis (8).

Acquisition is performed in a fasted state (often at least 4 hours), to reduce signal overlap from fluid in the surrounding stomach and duodenum, reduce peristalsis and promote gallbladder distension. Some centres use a negative oral contrast agent, such as 200-400 ml of pineapple juice, 20-30 min prior MRCP (7).

The main principle of MRCP is use of T2-weighted (T2w) imaging sequences that provide high signal of biliary system and pancreatic duct with suppression of background signal from abdominal structures (7, 8). The images can be performed with both two-dimensional (2D) and three-dimensional (3D) images. Common additional sequences obtained during whole abdominal MRI protocol include traditional axial T2w, Diffusion-weighted images (DWI), in and out of phase, precontrast T1w and multiphasic postcontrast T1w series (6). The best images in the diagnosis of PSC with this method are obtained with the complementary evaluation of MRCP images obtained with several (usually 2-3) different MRCP techniques.

MRI imaging contrast agents can be either extracellular (ECM) or hepatobiliary contrast agents (HBCAs). ECM (such as Gadovist, Dotarem) are used when general evaluation of liver and vascular structures is needed in examination of liver disease. HBCA (such as Multihance, Eovist) behaves like ECM but portion of contrast agent is taken up by functioning hepatocytes and excreted via bile ducts that is seen as bright signal on T1w images. The difference of standard MRCP and HBCA-MRCP is that the latter requires injection of intravenous contrast and uses T1w images, whereas standard MRCP uses bile high signal on T2w images. HBCA-MRCP is less susceptible to motion artifacts (images are obtained in only one or two breath holds), but smaller peripheral ducts are not well delineated with this technique (6). Depending on the contrast agent used, post-contrast images are acquired in different phases

including arterial, portal venous, equilibrium (parenchyma), delayed and hepatobiliary phases (7).

According to Arive L et al. performing the sequences after contrast injection is not needed in all cases. It is unnecessary for detecting of bile duct abnormalities in cases where liver function tests have altered, if the previous exam has shown nothing. In PSC it can be useful in the initial examination, to detect heterogeneous enhancement of the liver parenchyma and contrast uptake by the wall of the bile ducts. It is not certain that it is essential in regular monitoring of PSC. Contrast injection can also be used in suspicion of cholangiocarcinoma (CCC) even though contrast uptake by CCC is generally similar to uptake by a local fibrous stenosis (9).

To sum up, the complete workup for performing MRI /MRCP in PSC should consists of:

- **bile duct imaging:** T2w MRCP preferred over T1w and 3D MRCP over 2D MRCP to improve visualization of biliary ducts;
- **liver parenchyma imaging:** cross sectional T2w and T1w acquisition is recommended. T2w coronal plane acquisitions cover most of the liver from anterior to posterior, they are important to evaluate the peripheral intrahepatic ducts. Fat-suppressed T1w images add information about liver parenchyma. Contrast enhanced images form part of complete workup to detect and differentiate mass lesions and inflammation (7).

The examination should be interpreted according to the plan that includes:

1) examination of the bile ducts, describing any stenosis and dilatations if present;
2) systemic search for any intrahepatic calculus;
3) examination of the heterogeneity of the liver parenchyma;
4) investigation to find signs of liver hypertension;
5) analysis of the enhancement of the liver parenchyma and enhancement of the wall of the bile ducts (9).

MRI/MRCP bile ducts features

The features of PSC vary in different stages of the disease. In the early stages, multifocal annular short segmental strictures in the intrahepatic and/or extrahepatic biliary ducts alternating with normal ducts or focal mildly dilated ducts (beaded appearance so called "string of pearls appearance") is the typical MRCP manifestation. A problem may arise in the early stages of the disease, especially in healthy patients, concerning visualization of small peripheral biliary ducts as they're filled with only small amount of intraductal bile. However, peripheral bile ducts in PSC patients are more recognizable owing to biliary dilatation, and there are characteristic features at cholangiography. Long segmental intrahepatic biliary strictures are not common and are concerning features of superimposed cholangiocarcinoma (CCA). The strictures are usually located at the biliary bifurcations and are out of proportion to their upstream dilatations (6). This is likely because of periductal fibrosis and inflammation, that prevent the biliary ducts from dilating. In more advanced stages peripheral biliary ducts may not be well visualized and may have a "pruned-tree" appearance (6, 9) owing to the progression of fibrosis and advanced strictures obliterating small peripheral ducts. Moreover, an obtuse angle instead of acute between the central and more peripheral ducts is suggestive of PSC (6).

Both MRI and MRCP are good tools for evaluation of biliary stones, that can coexist with PSC. T2-weighted images are superior to T1-weighted images for detection of biliary stones, as they illustrate focal areas of signal-intensity-void filling defects among the background of high-signal-intensity bile. Biliary stones can be iso- or hyperintense at T1w imaging.

To be precise in the interpretation of PSC changes on MRCP images, Arrive L et al. proposed the description details of the hepatic bile ducts morphological changes. According to them, the stenosis is moderate when it is less than 75%, and severe when greater than 75%, short when it is less/or equal to 2 mm, long when exceeds 10 mm, intermediate when between 2-10 mm; involvement of the bile ducts is localised when less than 25% of the intrahepatic bile ducts are involved and diffuse when more than 25% are affected (9).

Summing up, the most common MRI features of PSC concerning bile ducts are: bile duct dilatation (77%) – usually moderate, beading (36%), extrahepatic bile duct stenosis (50%), wall enhancement (67%) and thickening (50%) (6).

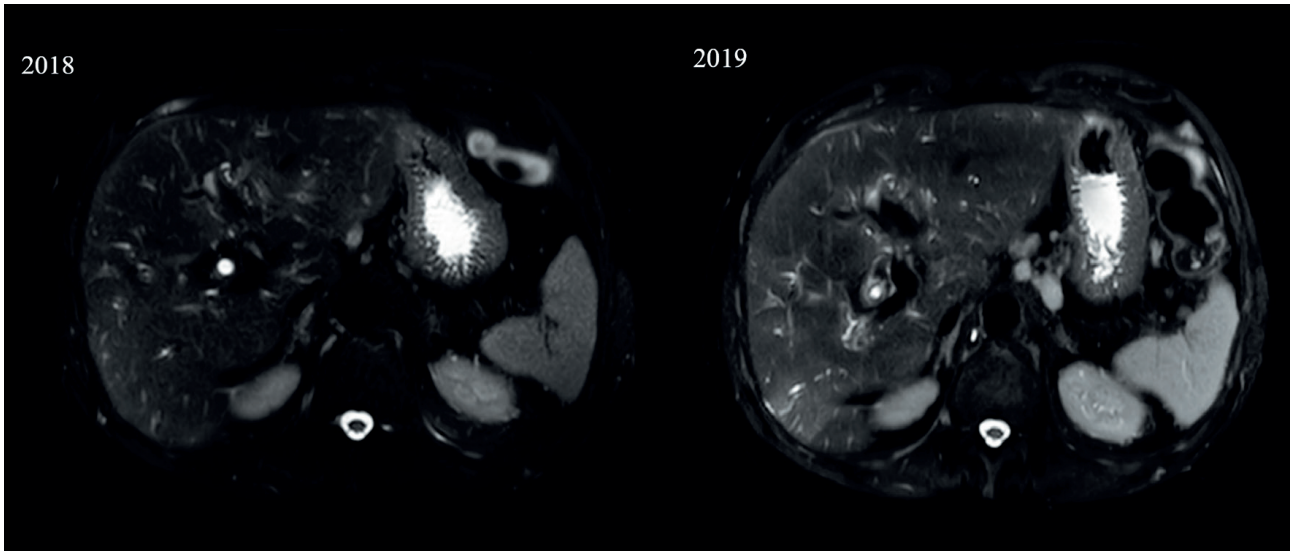

Figure 1. Axial scans show a progression of the disease (stricture of the common hepatic duct, progressive periportal fibrosis and inhomogenity of the liver parenchyma) in case of a patient suffered from colitis ulcerosa.

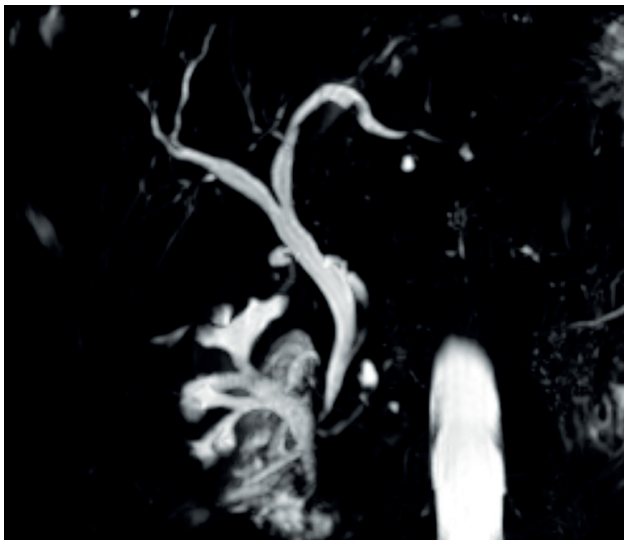

Figure 2. MRCP image of the patient suffered from Crohn disease shows multiple dilatations and strictures of the biliary tree.

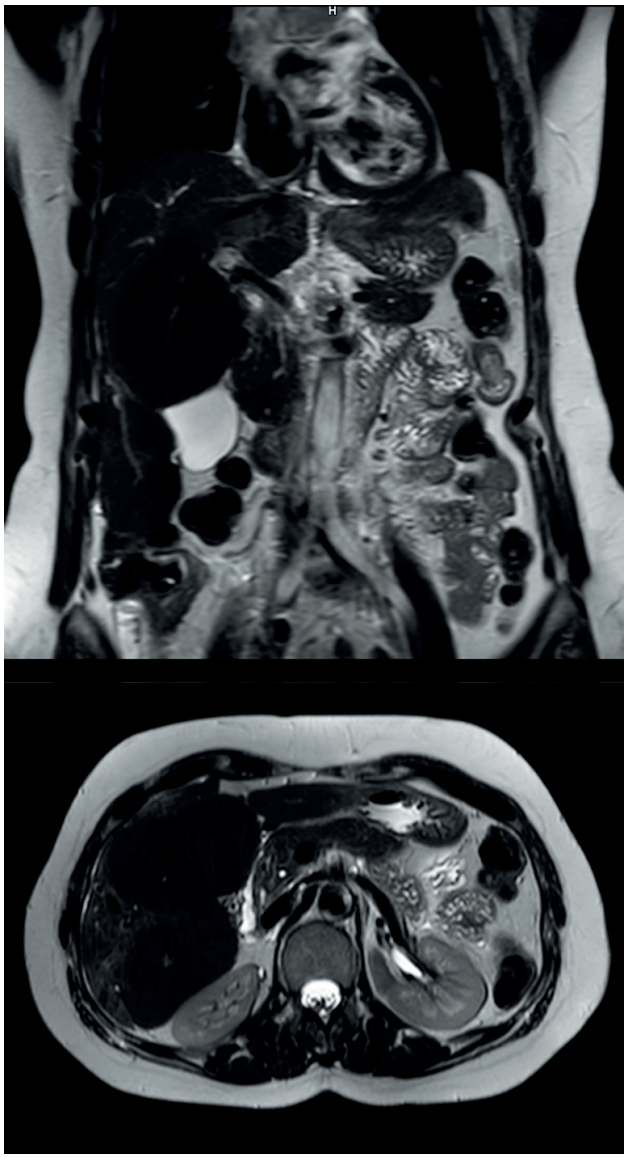

Figure 3. T2w MRCP scans in coronal and axial planes depict regeneration tumors. Radiological findings were confirmed in histopathological examination (a chronic fibro-inflammatory changes, an infiltration of lymphocytes and eosinophils).

MRI liver parenchyma features

Aside from bile ducts changes, several hepatic parenchymal features can be observed in PSC, such as: rounded/spherical shape of the liver caused by hypertrophy of caudate lobe and left liver lobe, atrophy of the right lobe, enlargement of portal and/or portocaval lymph nodes, peripheral parenchymal inflammation, wedge-shaped confluent fibrosis, heterogeneity of the liver parenchyma (reticular, nodular parenchyma), periportal oedema, cirrhosis with indirect signs of portal hypertension such as splenomegaly, ascites and collateral vasculature (6).

The characteristic findings of liver parenchyma in PSC are:

- **T1-weighted imaging:** atrophied, peripheral wedge-shaped areas present hypoenhancement in early contrast-enhanced phases and hyperenhancement in more delayed contrast-enhanced phases. Arterial phase peribiliary enhancement with focal, segmental or diffuse distribution can be seen as another enhancement pattern of PSC, related to ongoing cholangitis;
- **T2-weighted imaging:** wedge-shaped peripheral confluent hepatic fibrosis is seen as areas of high signal in T2w images. The signal abnormalities are due to parenchymal oedema and hyperperfusion due to parenchymal inflammation. Periportal oedema is seen as high T2w signal and is seen in 40-68% of cases in different studies (6);
- **diffusion-weighted imaging:** some authors has reported high sensitivity and specificity of apparent diffusion coefficient (ADC) values in the detection of liver parenchymal fibrosis, however, the utility of DWI and ADC remains controversial in this purpose (6, 7). On the other hand, DWI imaging is helpful in distinguishing acute bacterial cholangitis from abscess, as they both can be the complications of PSC. In abscess DWI signal intensity is expected to increase with higher b-values. In cases of acute cholangitis without abscess formation the signal is decreasing (6).

Conclusions

- Primary sclerosing cholangitis (PSC) is a chronic liver disease in which there are inflammation and scarring of the bile ducts.
- Eventually, PSC can cause liver cirrhosis and failure.
- It is supposed that autoimmune factors, genetic susceptibility and incorrect composition of the gut flora play a key role in pathomechanism of PSC.
- In clinical practice, the diagnosis of PSC is generally based on blood tests and imaging studies (currently preferably magnetic resonance cholangiopancreatography).
  - magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP) is the imaging modality of choice to workup of patients with suspected PSC as recommended by both American Association for the Study of Liver Diseases (AASLD) and European Association for the Study of the Liver (EASL) and widely used for surveillance purposes. It is a cost-effective tool and has high sensitivity and specificity for diagnosis and assessment of PSC progression;

  - recent recommendation from the International PSC Study Group requires at least 1,5 T MR scanner for the diagnosis.
- Minimum recommended standard protocol MRI /MRCP in PSC includes: T2-weighted liver axial, T1-weighted liver axial, T2-weighted MRCP, 3D MRCP, dynamic contrast-enhanced MRI. MRI imaging contrast agents can be either extracellular (ECM) or hepatobiliary contrast agents (HBCAs). The best images in the diagnosis of PSC with this method are obtained with the complementary evaluation of MRCP images obtained with several (usually 2-3) different MRCP techniques.
- The examination should be interpreted according to the plan that includes:
  - examination of the bile ducts, describing any stenosis and dilatations if present;
  - systemic search for any intrahepatic calculus;
  - examination of the heterogeneity of the liver parenchyma;
  - investigation to find signs of liver hypertension;
  - analysis of the enhancement of the liver parenchyma and enhancement of the wall of the bile ducts.
- The features of PSC vary in different stages of the disease. The most common MRI features of PSC concerning bile ducts are: bile duct dilatation (77%) – usually moderate, beading (36%), extrahepatic bile duct stenosis (50%), wall enhancement (67%) and thickening (50%).
- Long segmental intrahepatic biliary strictures are not common and are concerning features of superimposed cholangiocarcinoma (CCA).

References

(1) Frierson HF Jr. The gross anatomy and histology of the gallbladder, extrahepatic bile ducts. Vaterian system, and minor papilla. Am J Surg Pathol 1989; 13(2):146-162. DOI:10.1097/00000478-198902000-00008.

(2) Karlsen TH, Folseraas T, Thorburn D, Vesterhus M. Primary sclerosing cholangitis – a comprehensive review. J Hepatol 2017; 67(6):1298-1323. DOI:10.1016/j.jhep.2017.07.022.

(3) Fricker ZP, Lichtenstein DR. Primary Sclerosing Cholangitis: A Concise Review of Diagnosis and Management. Dig Dis Sci 2019; 64(3):632-642. DOI: 10.1007/s10620-019-05484-y.

(4) Ricciuto A, Kamath BM, Griffiths AM. The IBD and PSC Phenotypes of PSC-IBD. Curr Gastroenterol Rep 2018; 20(4):16. DOI:10.1007/s11894-018-0620-2.

(5) Tanaka A, Takikawa H. Geoepidemiology of primary sclerosing cholangitis: a critical review. J Autoimmun 2013; 46:35-40. DOI:10.1016/j.jaut.2013.07.005.

(6) Khoshpouri P, Habibabadi RR, Hazhirkarzar B, et al. Imaging Features of Primary Sclerosing Cholangitis: From Diagnosis to Liver Transplant Follow-up. Radiographics 2019; 39(7):1938-1964. DOI:10.1148/rg.2019180213.

(7) Selvaraj EA, Culver EL, Bungay H, Bailey A, Chapman RW, Pavlides M. Evolving role of magnetic resonance techniques in primary sclerosing cholangitis. World J Gastroenterol 2019; 25(6):644-658. DOI:10.3748/wjg.v25.i6.644.

(8) Zenouzi R, Welle CL, Venkatesh SK, Schramm C, Eaton JE. Magnetic Resonance Imaging in Primary Sclerosing Cholangitis-Current State and Future Directions. Semin Liver Dis 2019; 39(3):369-380. DOI:10.1055/s-0039-1687853.

(9) Arrivé L, Ruiz A, El Mouhadi S, Azizi L, Monnier-Cholley L, Menu Y. MRI of cholangitis: traps and tips. Diagn Interv Imaging 2013; 94(7-8):757-770. DOI:10.1016/j.diii.2013.03.006.