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MR imaging features of primary sclerosing cholangitis: a comprehensive overview of image-based scoring systems for assessment of disease severity and prognosis

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Summary

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease marked by inflammation, fibrosis, and narrowing of the bile ducts, leading to cholestasis. Magnetic resonance cholangiopancreatography (MRCP) is the gold standard for the diagnosis of PSC allowing insight into biliary duct changes. The typical presentation of PSC includes multifocal anular and short-segmental strictures alternating with normal or slightly dilatated biliary ducts. Besides cholangiographic findings, magnetic resonance (MR) allows the assessment of liver parenchymal changes which might indicate the severity of the disease. The scoring systems based on MR findings, such as the ANA-LI score, and new computer-based software analysis termed MRCP+, provide a prediction of the course of disease and identify high-risk patients. Thus, MR with MRCP is a promising diagnostic tool for the integrative evaluation of PSC patients allowing not only initial diagnosis and detection of complications but also has prognostic significance.

Key words: liver, primary sclerosing cholangitis, magnetic resonance cholangiopancreatography

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INTRODUCTION

PSC is a chronic immune-mediated cholestatic liver disease characterized by inflammation and obliterative fibrosis of large bile ducts with subsequent development of multifocal biliary strictures. Even though PSC is a rare condition, typically seen in young and middle-aged men with slow progression, it eventually leads to cirrhosis and many associated complications (1, 2). There is a strong correlation between PSC and inflammatory bowel disease (IBD), particularly ulcerative colitis, but Crohn's disease can also be found (3). To date, there is no effective medical therapy for PSC and liver transplantation remains, the only proven life-extending treatment (4). The average transplant-free survival is estimated to be 20 years (5). There are a few prognostic models predominantly based on biochemical and clinical findings aiming to aid in predicting disease progression and time to transplant, but none of them has been widely accepted (7).

The precise etiopathogenesis of PSC remains unknown. Different factors such as autoimmune, genetic, and environmental contribute to the development of multifocal, patchy peribiliary inflammation pathognomonic for PSC (4). Histologically, concentric periductal fibrosis (onion skinning) in medium- and large-size bile ducts is a characteristic finding, accompanied by minimal inflammatory cells (7). However, this histological pattern is observed in less than 20% of patients and may also be present in secondary sclerosing cholangitis (7). Thus, liver biopsy alone is insufficient for PSC diagnosis and must be assessed in conjunction with clinical and imaging findings.

Diagnosis and follow-up of patients with PSC

The diagnosis of PSC is usually suspected due to elevation of cholestatic liver enzymes, alkaline phosphatase in particular (8). Nevertheless, elevated cholestatic biochemical markers are not mandatorily present, their values may spontaneously fluctuate and could also be normal (8). Transaminase levels are commonly slightly elevated, while the significant increase is seen during episodes of acute ascending cholangitis and also in patients with an overlap with AIH (6). Serum bilirubin levels are usually normal in PSC patients (6). Hyperbilirubinemia might be seen in cases of severe benign or malignant strictures or late stage of the disease with the development of hepatic dysfunction (6, 8). The diagnosis of PSC can be made only after the exclusion of all secondary causes of sclerosing cholangitis (8).

Since PSC is a disease of the biliary tract, the diagnosis relies on cholangiography findings obtained by endoscopic retrograde cholangiopancreatography (ERCP) or more commonly magnetic resonance cholangiopancreatography (MRCP) (8,9). MRCP exhibits high sensitivity (85%) and specificity (98%) for detection of bile duct irregularities in patients with PSC (9). Nowadays, MRCP is also used for surveillance of PSC patients and should be performed once a year (9). MRCP has superseded ERCP which was previously the only method for biliary duct evaluation (10). Although ERCP allows very good visualization of the biliary tract, it has serious post-procedural complications and also doesn't allow visualization of the lumen above the stenosis (9). ERCP is advised only when there is a need for therapeutic biliary stent placement (10). The diagnosis of PSC might be made on cholangiography if typical findings consisting of multiple strictures with or without dilatations are seen (11). However, the assessment of the presence of the strictures is made qualitatively, leading to high interobserver variability in MRCP interpretation (11). Therefore, there is an obvious need for a more quantitative approach in the analysis of MRCP findings.

Liver biopsy is generally unnecessary for the diagnosis of the most common type of PSC, large-bile duct PSC. In cases where the small bile duct type is suspected or PSC-AIH overlap syndrome liver biopsy should be performed (12). The small bile duct type is suspected when a patient with IBD presents with cholestatic laboratory findings, normal cholangiographic imaging features, and a negative antimitochondrial antibody profile (13). PSC is histologically characterized by the presence of an inflammatory infiltrate in a large intra- and extra-hepatic bile duct wall in conjunction with an obliterative concentric periductal fibrosis called "onion skin fibrosis" (12). As the disease progresses there is a gradual loss of small- and medium-sized bile ducts (ductopenia) (8, 12). Eventually, chronic inflammation leads to portal and periportal fibrosis and the development of biliary cirrhosis (8). Although liver biopsy may precisely depict the progression of the disease through different stages, it is not routinely used in everyday clinical practice due to its invasive nature and the possibility of sampling error (5,6).

MR IMAGING FEATURES OF PSC

The typical MRCP presentation of PSC consists of diffuse, multifocal strictures affecting both intra- and extrahepatic bile ducts in the majority of patients. The pathognomonic"beaded" appearance of the bile ducts is created by multiple, diffusely distributed, short, annular strictures associated with normal or slightly dilatated segments (**Figure 1**) (14). Isolated intrahepatic bile duct involvement is seen in 15% of patients, while only extrahepatic bile duct involvement is the rarest manifestation occurring in 8% of cases (11). The strictures in PSC are described as band-like strictures if the length is less than 2mm, segmental strictures if the length is from 2 mm up to 10 mm, and confluent strictures are commonly seen on bile duct bifurcations (11). In the early stages of PSC,



Figure 1. Primary sclerosing cholangitis in 33-year old man. (A) MRCP shows multiple short band-like strictures and slight luminal dilatation (*solid arrows*). In another 36-year-old patient with PSC (B), there is a classical "beaded appearance" of bile ducts - multiple short segmental and annular strictures with slightly dilated bile ducts between them. Note also the stricture of the middle third of the common bile duct (*dotted arrow*).

multiple strictures are seen in the absence of biliary dilatation (11, 15). With the progression of the disease, dilatation might be detected, but due to periductal fibrosis and inflammation the dilatation is rarely prominent (15).

Further disease progression may lead to complete obliteration of small peripheral ducts, resulting in a "pruned tree" appearance where only central ducts are visualized, while peripheral ducts are completely obliterated (Figure 2) (15). If significant dilatation is detected, complications of PSC like cholangiocarcinoma or ascending suppurative cholangitis should be suspected (16). Diverticular outpouchings are observed in up to 20% of cases. The least common feature is the presence of pigmented stones (15). Rarely, abnormalities might also be seen in the main pancreatic duct (15).

In addition to bile duct changes, MRI reveals associated parenchymal liver changes, including liver dysmorphy, confluent liver fibrosis, and parenchymal heterogeneity. A



Figure 2. Advanced primary sclerosing cholangitis. (A) MRCP reveals obliterated peripheral bile ducts, resulting in a "pruned tree" appearance and multiple diverticular outpouchings (*solid arrows*). Moreover, note the stricture of the common hepatic duct (*dotted arrow*). In another case (B), MRCP in a 44-year-old patient with primary sclerosing cholangitis displays very irregular bile ducts, multiple strictures combined with diverticular biliary dilatation (*solid arrows*).



Figure 3. Primary sclerosing cholangitis in 44-year old man. (**A**) An axial T2-weighted image displays hyperintense areas in peripheral, atrophic regions within the right liver lobe, correlating with sites of parenchymal inflammation and increased water content (*solid arrows*). Additionally, observe the enlarged caudate lobe (*asterisks*). Axial T1-weighted image from the same patient, acquired after intravenous administration of gadolinium chelates during arterial (**B**) and portal-venous phase (**C**), depicts increased enhancement of peripheral liver areas, indicative of intrahepatic perfusion abnormalities (*solid arrows*).

spherical liver shape is a typical finding for PSC and develops as the consequence of caudate lobe hypertrophy and atrophy of left lateral and right posterior segments (Figure 3A) (17). The most frequent type of liver cirrhosis in PSC patients is macronodular cirrhosis, with large regenerative nodules predominantly located in central liver parts (14, 15). This could be explained by the more severe inflammation in subcapsular regions of the liver, while central parts are partly spared and undergo hypertrophy. The severity of liver fibrosis could be assessed non-invasively with MRI using MR elastography (MRE) or diffusion-weighted MRI measurements (18). Among these two methods, liver stiffness measurement using MRE has been validated in many studies showing a significant correlation with other non-invasive markers of disease progression (8). Areas of increased T2-weighted signal intensity, wedgeshaped or reticular, with peripheral distribution are common findings in PSC (14). As this feature is explained by intense inflammation in highly fibrotic areas, increased enhancement on arterial phase contrast-enhanced MR which persists in delayed phases is also seen (Figure 3B) (14, 17). Hilar lymphadenopathy and periportal hyperintensity are also common findings, occurring due to edema and inflammation in the periportal space (14, 18). However, they are not pathognomonic for PSC as they are also seen in other cholestatic liver diseases.

Image-based scoring systems for assessment of PSC severity and prognosis

Based on clinical and laboratory findings, two prognostic risk models have been developed, including the Mayo risk model (MRS) and the Amsterdam-Oxford model (AOM) (19, 20). Both have shown great performance in estimating prognosis and survival in PSC patients. However, the results of large studies investigating the role of these scoring systems in predicting the prognosis of PSC are conflicting (20, 21). Recently, serum markers that reflect fibrosis and inflammation are increasingly being investigated in PSC patients (21). Based on these markers the enhanced liver fibrosis score was developed and evaluated in PSC (21). Additionally, the role of liver stiffness measurement using transient elastography and magnetic resonance elastography has been systematically evaluated and was found to correlate significantly with the fibrosis stage (22).

Taking into account that PSC is the disease of bile ducts, it would be expected that cholangiographic findings should be used to stage the disease and assess its prognosis. The first scoring system based on imaging findings was developed by Li-Yeng and Goldman in 1984. and was later modified by Majoie et al. and Ponsioen et al. (23-25). This classification scheme was employed by a Dutch gastroenterologist for the development of Amsterdam cholangiographic score. Amsterdam score was developed based on ERCP features found in 174 patients with PSC (25). According to the modified Amsterdam score, all patients could be classified in three stages depending on the abnormalities of intrahepatic bile ducts: I - multiple strictures without biliary dilatation; II multiple strictures associated with saccular dilatations and decreased arborization; III- pruning of peripheral bile ducts with good visualization of only central ducts with adequate filling pressure (24). Concerning findings in extrahepatic bile ducts patients might be divided into four stages according to modified Amsterdam score: Islight irregularities of contour without strictures; II- the presence of segmental stricture (the stricture 3-10mm in length); III- stricture of almost whole extrahepatic bile ducts; IV - extreme irregularities of bile duct contours and the presence of diverticulum-like outpouchings (24). Using this classification system and the age of the patient at the time of initial ERCP, a prognostic model was created showing that the sum of intrahepatic and extrahepatic scoring was a significant predictor in determining the prognosis (26). Namely, patients with high overall scores had significantly lower survival rates (26). To overpass the disadvantages of the scoring system developed by Majoie et al. and Ponsioen et al. which was based on qualitative assessment and therefore had very poor interobserver agreement, Craig et al. introduced quantitative measurements of bile duct changes on ERCP performed in patients with PSC (27). The novel classification system included the following measurements: the grade of bile duct narrowing, the length of strictures, the extent of stricturing (localized or diffused), the diameter of the common bile duct, right and left main hepatic duct, and secondary intrahepatic ducts (27). Among all measurements, two variables were found to have prognostic significance. Namely, patients with high-grade intrahepatic duct strictures had a 19% decrease, while patients with diffuse intrahepatic strictures had a 16% decrease in transplant-free survival at three years follow-up (27).

Although ERCP has the potential to accurately depict the state of the biliary tract in PSC patients since biliary ducts are filled with contrast media under pressure, it is an invasive diagnostic modality and carries the risk of many possible post-procedural complications (28). That is the reason why MRCP as a non-invasive and non-ionizing diagnostic modality has largely replaced ERCP for the initial diagnosis and follow-up of patients with PSC (29). After the introduction of MRCP in the evaluation of PSC patients, efforts were made to adapt Amsterdam score to MRCP. Nevertheless, it has been shown that there was a 5% overestimation of intrahepatic biliary changes and a 10% discrepancy in staging extrahepatic disease when Amsterdam score was applied to MRCP findings (30). These discrepancies might be explained by different acquisition protocols. Thus, in ERCP biliary ducts are filled with contrast media under pressure, while in MRCP biliary tree is examined in a resting state without distension (30). Therefore, it is much more difficult to evaluate strictures on MRCP than on ERCP (31).

Considering that MRI provides not only insight into bile duct changes but also delineates morphological changes in the liver parenchyma, Ruiz et. al introduced a new score for staging and prognostic purposes in PSC, termed ANALI score (32). This classification system is based on quantitative measurements of MRCP, including the garde of intrahepatic biliary duct dilatation, length of strictures in main intrahepatic ducts and peripheral ducts, and morphological changes of liver parenchyma such as parenchymal enhancement heterogeneity, portal hypertension, and liver dysmporphy (32). Liver dysmorphy was defined as severe right or left lobe atrophy occurring as a consequence of severe biliary dilatation, or an abnormal caudate to right lobe volume ratio (32). Concerning parenchymal enhancement heterogeneity, peribiliar enhancement was assessed implying the severity of peribiliary parenchymal inflammation (32). Intrahepatic biliary duct dilatation was scored as 0 (less than 4mm), 1 (4mm), or 2 (more than 4mm), where other variables were either present or absent. Using the abovementioned variables, the following two scores were developed:

Score (MRI without gadolinium): 1 x intrahepatic bile duct dilatation + 2 x dysmorphy + 1 x portal hypertension

Score (MRI with gadolinium) = 1 x dysmorphy + 1 x parenchymal enhancement heterogeneity

Subsequent studies have shown that the ANALI score has good prognostic value in patients with PSC and that it is significantly correlated with existing biochemical and clinical scores like MRS and PRESTO (33, 34). According to a large retrospective multicenter study on 238 PSC patients, the predictive accuracy of ANALI score without and with gadolinium was 0.89% IC 95%, and 0.75% IC 95% (34). In another large study evaluating the value of MR and MRCP in the prediction of PSC progression, multivariate logistic regression analysis showed that liver dysmorphy, signs of portal hypertension, and perihepatic lymph nodes were significantly associated with transplant-free survival and adverse clinical outcomes in long-standing PSC (35). Accordingly, a modified MRCPrisk score was developed as an upgrade of the ANALI score. Nevertheless, the evaluation of PSC changes remains a challenge for radiologists since subtle irregularities are hardly detectable and the evaluation is quite subjective (36). Taking into account the importance of detecting PSC early and close monitoring of disease progression, a more objective approach to disease staging with limited variability in reporting is necessary (37).

In the era of artificial intelligence, several deep learning models have been developed for the automatic detection of PSC-compatible cholangiography alterations (38). Ringe et al. reported a great diagnostic accuracy of these models with sensitivity, specificity, positive and negative predictive values higher than 90% (38). Recently, a quantitative biliary tree analysis software (MRCP+, Perspectum Diagnostics Limited) was developed allowing semi-automatic quantification of bile duct changes in PSC (39, 40). After uploading the 3D MRCP examination, the MRCP+ post-processing tool provides multiple measurements of biliary ducts. Among many quantitative variables that can be generated, the following metrics have been highlighted as the most important: sum of relative severity of dilatations; proportion of dilatated biliary tree; biliary tree dilatation score; and total stricture severity score (33, 34). Bile duct dilatation was considered to be present if the lumen of the bile duct is at least 1mm increased in comparison to the diameter of the closest duct (41). The dominant stricture was defined as the diameter of the common bile duct less than 1.5mm, and less than 1mm for the left and right hepatic duct (41). Currently, there are a few published studies implying the value of the new computer-based system suggesting its high diagnostic accuracy in the diagnosis of PSC (41-44). Among different variables obtained by the 3D-biliary analysis tool in PSC patients, increased gallbladder volume and higher dilatation metrics were found to be significant predictors of survival (43). Distension of the gallbladder in PSC patients has previously been described as a characteristic finding, occurring probably due to lower levels of hydrophobic serum bile acids (45). It has been hypothesized that gallbladder has a protective role in PSC, as PSC patients who had cholecystectomy develop more severe cholangiographic findings (45). Furthermore, Selvaraj et al. have shown that dilatation metrics had a significant correlation with non-invasive biochemical markers of disease severity and were also significantly higher in the high-risk PSC group defined by MRS (42). In contrast to dilatation variables, stricture metrics did not differ significantly among high-risk and low-risk PSC groups. No significant correlation between biliary stricture severity score and advanced stages of liver fibrosis in PSC patients was also found in the study by Song et al. (46). Similar results were reported by another group that tested the correlation between intrahepatic stricture severity and disease stage assessed by magnetic resonance elastography (47). In opposite, Ismail et al. reported that the stricture severity index was significantly correlated with biochemical prognostic

scores indicating that also stricture metrics derived from MRCP+ may have a prognostic purpose (44). The generally low sensitivity of stricture metrics might be explained by technical limitations of MRCP which is unable to assess the severity of strictures due to examining non-distended biliary ducts. Furthermore, MRCP images often have artifacts disabling adequate measurement of the bile duct lumen (9). It should be pointed out that even with ERCP, the prognostic significance of stricture severity and dominant stricture is questionable as no correlation with biochemical markers of cholestasis was demonstrated (48). On the other hand, the importance of biliary dilatation was also stressed by Ruiz et al. who incorporated this parameter in the ANALI score (32). Opposite to the index of biliary dilation severity, biliary tree volume obtained from MRCP+ analysis did not show an association with bad outcomes in PSC patients (33, 34). It could be explained by the fact that biliary tree volume is increased in an intermediate stage of disease but it often decreases in advanced disease due to reduction of peripheral ducts and atrophy of liver segments with severe dilatation (49). Nevertheless, although the most important cholangiographic finding obtained by the computer-based 3-dimensional model of the biliary tree is the severity of biliary dilatation, other metrics might also have a role in the evaluation of disease severity (42).

DIFFERENTIAL DIAGNOSIS OF PSC

Differential diagnosis of primary sclerosing cholangitis includes IgG4-sclerosing cholangitis (IgG4-SC), primary biliary cirrhosis, ischemic cholangitis, and AIDS cholangitis (11, 15). Characteristic cholangiographic findings, young age, male patients, and association with IBD favor the diagnosis of PSC (11, 14). IgG4-SC, which is more commonly seen in elderly men, is characterized by long segmental strictures with prestenotic dilation (50). Moreover, it is frequently associated with autoimmune pancreatitis and other disorders from the IgG4 disease spectrum (50). If classical cholangiographic findings are absent and papillary stenosis is the predominant imaging feature in cholangiography, AIDS cholangitis should be considered (51). Further correlation with clinical and laboratory findings allows the correct differential diagnosis among these two types of cholangitis. Ischemic cholangitis is typically seen in posttransplant patients due to ischemic injury and is characterized by strictures of the middle third of the common bile duct and the hilar part of the biliary tree (52). Together with PSC, primary biliary cirrhosis comprises a spectrum of primary cholestatic liver diseases (53). In contrast to PSC, PBS is typically seen in middle-aged women without characteristic cholangigraphic findings. Furthermore, laboratory data adds additional information necessary for distinguishing among these two entities (53).

Complications of PSC

Cholangiocellular carcinoma (CCC) represents the most severe complication arising from long-standing PSC, and affecting approximately 10-14% of patients (54). The exact pathogenesis of cholangiocarcinoma in PSC patients is still not elucidated, but chronic inflammation probably plays the most important role. The detection of cholangiocarcinoma in the early stage is a challenge for radiologists as there are no pathognomonic cholangiographic features (55). The majority of cholangiocarcinomas originate in the perihilar area, but some develop in intrahepatic bile ducts. The tumor is usually seen as an indistinct hypovascular mass with progressive delayed enhancement in imaging studies (Figure 4) (56, 57). However, findings may be more discrete, and a stricture accompanied by prominent wall thickening, alongside significant proximal biliary dilatation, might be the only indicator of CCC (58). To facilitate early CCC detection, regular screening of PSC patients is advocated, involving CA 19-9 measurements every six months and MRCP annually. Elevated CA 19-9

levels have high diagnostic accuracy, with a sensitivity of 75% and specificity of 80% for a cutoff value of 100 U/ml (59). From a clinical standpoint of view sudden worsening of symptoms in PSC patients, characterized by cholestasis and weight loss, should raise the suspicion of CCC. Unfortunately, CCC development in the context of PSC carries a poor prognosis, even after resection or liver transplantation, with 3-year survival rates ranging from 0% to 42% (58, 60). The radiologist should bear in mind that the progression of the dominant stricture with subsequent biliary dilatation does not necessarily mean the development of CCC, but it can also occur due to the worsening of inflammation (15). In doubtful cases further check-out with cholangioscopy if available is recommended.

Another complication in long-standing PSC is acute ascending cholangitis with superimposed biliary sepsis (54). It usually occurs in patients with severe strictures of the common bile duct, left or right hepatic duct. In such cases, after medicamentous treatment of acute infection, therapeutic endoscopic dilatation should be performed.



Figure 4. Cholangiocellular carcinoma complicating long-standing primary sclerosing cholangitis in a 52-year-old male patient. (**A**) An axial T2-weighted image displays a large irregular, moderately hyperintense mass in the right liver (*solid arrows*). Bile ducts are irregularly dilated in both lobes due to primary disease. Multiple intrahepatic calculi are also present (*dotted arrows*). (**B**) An axial T1-weighted fat-saturated image reveals a hypointense mass with a central necrotic part (*solid arrow*). Intrahepatic calculi are also visible as hyperintense lesions within dilated bile ducts (*dotted arrow*). (**C**) On the portal-venous phase T1-weighted fat-saturated image, the tumor appears as a hypovascular lesion (*solid arrows*). (**D**) A thick slab MRCP demonstrates multifocal alternating strictures of intrahepatic bile ducts with loss of bile duct visualization in segment V corresponding to tumor infiltration (*asterisks*).

Medical therapy for PSC has limited value, and liver transplantation remains the only life-expanding treatment, offering a 75-85% five-year post-transplant survival (61). However, recurrence of PSC after transplantation is observed in up to 25% of cases, necessitating careful differential diagnosis due to various potential causes of post-transplant biliary strictures (61). Diagnosing recurrent PSC after liver transplantation is quite difficult due to the various causes responsible for post-transplant biliary strictures, such as ischemia, rejection, allograft reperfusion injury, recurrent biliary sepsis, ABO incompatibility, or technical issues with biliary reconstruction (61, 62). To make a diagnosis of recurrent PSC the non-anastomotic strictures occurring three months post-transplantation must be detected (62). However, distinguishing between chronic rejection and recurrence remains challenging. Certain imaging features have been previously described to aid in this differentiation (62). An additional feature that favors the diagnosis of recurrent PSC instead of chronic rejection is an enlarged liver with a slightly nodular contour, whereas, in chronic rejection, it typically maintains a normal size (62). Furthermore, MRCP findings in recurrent disease often reveal multiple non-anastomotic strictures with mildly dilated bile ducts, while cholangiograms in

chronic rejection patients show peripheral arterial insufficiency-induced reduction of the peripheral biliary tree (61, 62). A liver biopsy is recommended when a non-invasive differential diagnosis cannot be established (62).

CONCLUSION

In conclusion, the role of MR and MRCP in evaluating patients with PSC is evolving. Although there are a few disadvantages of MRCP in comparison to ERCP, its non-invasive nature, and the possibility of repeating examinations without adverse effects make it the gold standard for the diagnosis and follow-up in PSC patients. In addition to cholangiography findings, MRCP allows the assessment of liver parenchymal changes which might indicate the severity of the disease. The scoring systems based on MR findings, such as the ANALI score, and new computer-based software analysis termed MRCP+, provide a prediction of the course of disease and identify high-risk patients. Thus, MR with MRCP is a promising diagnostic tool for the integrative evaluation of PSC patients allowing not only initial diagnosis and detection of complications but also has prognostic significance.

REFERENCES

- Lewin M, Vilgrain V, Ozenne V, Lemoine M, Wendum D, Paradis V, et al. Prevalence of sclerosing cholangitis in adults with autoimmune hepatitis: a prospective magnetic resonance imaging and histological study. Hepatology 2009; 50(2): 528-537. doi: 10.1002/hep.23024.
- Sohal A, Kayani S, Kowdley KV. Primary Sclerosing Cholangitis: Epidemiology, Diagnosis, and Presentation. Clin Liver Dis 2024; 28(1): 129-141. doi: 10.1016/j.cld.2023.07.005.
- Eksteen B. <u>The Gut-Liver Axis in Primary Sclerosing Cholangitis</u>. Clin Liver Dis 2016; 20(1): 1-14. doi: 10.1016/j.cld.2015.08.012.
- Cullen S, Chapman R. Aetiopathogenesis of primary sclerosing cholangitis. Best Pract Res Clin Gastroenterol 2001; 15: 577-589. doi: 10.1053/bega.2001.0206.
- Silveira MG, Lindor KD. Primary sclerosing cholangitis. Can J Gastroenterol 2008; 22(8): 689-98. doi: 10.1155/2008/824168.
- Lazaridis KN, LaRusso NF. Primary Sclerosing Cholangitis. N Engl J Med 2016; 375(25): 2501-2502. doi: 10.1056/NEJMc1613273.
- Yu S, Vidal B, Peric M, Rosenbaum MW, Cates JMM, Gonzalez RS. Comparative histologic features among liver biopsies with biliary-pattern injury and confirmed clinical diagnoses. Hum Pathol 2024: 146: 8-14. doi: 10.1016/j.humpath.2024.03.003.
- Tow CY, Chung E, Kaul B, Bhalla A, Fortune BE. Diagnostic Tests in Primary Sclerosing Cholangitis: Serology, Elastography, Imaging, and Histology. Clin Liver Dis 2024; 28(1): 157-169. doi: 10.1016/j. cld.2023.07.007.
- Dave M, Elmunzer BJ, Dwamena BA, Higgins PD_Primary sclerosing cholangitis: meta-analysis of diagnostic performance of MR cholangiopancreatography. Radiology 2010; 256: 387-396. doi: 10.1148/radiol.10091953.
- Aabakken L, Karlsen TH, Albert J, Arvanitakis M, Chazouilleres O, Dumonceau J-M, et al. Role of endoscopy in primary sclerosing cholangitis: European Society of Gastrointestinal Endoscopy (ESGE) and European Association for the Study of the Liver (EASL) Clinical Guideline. Endoscopy 2017; 49(6): 588-608. doi: 10.1055/s-0043-107029.

- Pria HD, Torres US, Faria SC, Velloni FG, Caiado AHM, Tiferes DA, et al. Practical Guide for Radiological Diagnosis of Primary and Secondary Sclerosing Cholangitis. Semin Ultrasound CT MR 2022; 43(6): 490-509. doi: 10.1053/j.sult.2022.06.007.
- Sarcognato S, Sacchi D, Grillo F, Cazzagon N, Fabris L, Cadamuro M, et al. Autoimmune biliary diseases: Primary biliary cholangitis and primary sclerosing cholangitis. Pathol J Ital Soc Anat Pathol Diagn Cytopathol 2021; 113: 170–184. doi: 10.32074/1591-951X-245.
- Björnsson E, Olsson R, Bergquist A, Lindgren S, Braden B, Chapman RW, et al. The natural history of small-duct primary sclerosing cholangitis. Gastroenterology 2008; 134: 975-980. doi: 10.1053/j.gastro.2008.01.042.
- Kovač JD, Ješić R, Stanisavljević D, Kovač B, Maksimovic R. <u>MR</u> imaging of primary sclerosing cholangitis: additional value of diffusion-weighted imaging and ADC measurement. Acta Radiol 2013; 54(3): 242-248. doi: 10.1177/0284185112471792.
- O'Brien C, Malik M, Jhaveri K. MR Imaging in Primary Sclerosing Cholangitis and Other Cholangitis. Radiol Clin North Am 2022; 60(5): 843-856. doi: 10.1016/j.rcl.2022.05.007.
- Kovač JD, Janković A, Đikić-Rom A, Grubor N, Antić A, Dugalić V. Imaging Spectrum of Intrahepatic Mass-Forming Cholangiocarcinoma and Its Mimickers: How to Differentiate Them Using MRI. Curr Oncol 2022; 29(2): 698-723. doi: 10.3390/curroncol29020061.
- Düşünceli E, Erden A, Erden I, Karayalçin S. Primary sclerosing cholangitis: MR cholangiopancreatography and T2-weighted MR imaging findings. Diagn Interv Radiol 2005; 11: 213-218. PMID: 16320228.
- Kovač JD, Daković M, Stanisavljević D, Alempijević T, Ješić R, Seferović P, et al. <u>Diffusion-weighted MRI versus transient elastography in quantification of liver fibrosis in patients with chronic cholestatic liver diseases</u>. Eur J Radiol 2012; 81(10): 2500-2506. doi: 10.1016/j.ejrad.2011.10.024.
- Kim WR, Therneau TM, Wiesner RH, Poterucha JJ, Benson JT, Malinchoc M, et al. A revised natural history model for primary sclerosing cholangitis. Mayo Clin Proc 2000; 75: 688-94. doi: 10.4065/75.7.688.

- de Vries EM, Wang J, Williamson KD, Leeflang MM, Boonstra K, Weersma RK, *et al.* A novel prognostic model for transplant-free survival in primary sclerosing cholangitis. Gut 2018; 67: 1864-1869. doi: 10.1136/gutjnl-2016-313681.
- 21. Vesterhus M, Hov JR, Holm A, Schrumpf E, Nygard S, Godang K, et al. Enhanced liver fibrosis score predicts transplant-free survival in primary sclerosing cholangitis. Hepatology 2015; 62: 188-197. doi: 10.1002/hep.27825.
- 22. Corpechot C, Gaouar F, El Naggar A, Kemgang A, Wendum D, Poupon R, et al. Baseline values and changes in liver stiffness measured by transient elastography are associated with severity of fibrosis and outcomes of patients with primary sclerosing cholangitis. Gastroenterology 2014; 146: 970-979. doi: 10.1053/j.gastro.2013.12.030.
- Chen LY, Goldberg HI. Sclerosing cholangitis: Broad spectrum of radiographic features. Gastrointest Radiol 1984; 9: 39-47. doi: 10.1007/ BF01887799.
- Majoie CB, Reeders JW, Sanders JB, Huibregtse K, Jansen PL. Primary sclerosing cholangitis: A modified classification of cholangiographic findings. AJR Am J Roentgenol 1991; 157: 495-497. doi: 10.2214/ajr.157.3.1651643.
- Ponsioen CY, Vrouenraets SM, Prawirodirdjo W, Rajaram R, RauwsEA, Mulder CJ, et al. Natural history of primary sclerosing cholangitis and prognostic value of cholangiography in a Dutch population. Gut 2002; 51: 562-566. doi: 10.1136/gut.51.4.562.
- Ponsioen CY, Reitsma JB, Boberg KM, Aabakken L, Rauws EA, Schrumpf E. Validation of a cholangiographic prognostic model in primary sclerosing cholangitis. Endoscopy 2010; 42: 742-747. doi: 10.1055/s-0030-1255527.
- Craig DA, MacCarty RL, Wiesner RH, Grambsch PM, LaRusso NF. Primary sclerosing cholangitis: Value of cholangiography in determining the prognosis. AJR Am J Roentgenol 1991; 157: 959-964. doi: 10.2214/ajr.157.5.1927817.
- Aabakken L, Karlsen TH, Albert J, Arvanitakis M, Chazouilleres O, Dumonceau J-M, et al. Role of endoscopy in primary sclerosing cholangitis: European Society of Gastrointestinal Endoscopy (ESGE) and European Association for the Study of the Liver (EASL) Clinical Guideline. Endoscopy 2017; 49: 588–608. doi: 10.1055/s-0043-107029.
- Chazouilleres O, Beuers U, Bergquist A, Karlsen TH, Levy C, Samyn M, et al. EASL Clinical Practice Guidelines on sclerosing cholangitis. J Hepatol 2022; 77: 761–806. doi: 10.1016/j.jhep.2022.05.011.
- 30. Tenca A, Mustonen H, Lind K, Lantto E, Kolho KL, Boyd S, et al. The role of magnetic resonance imaging and endoscopic retrograde cholangiography in the evaluation of disease activity and severity in primary sclerosing cholangitis. Liver Int 2018; 38(12): 2329-2339. doi: 10.1111/liv.13899.
- Moff SL, Kamel IR, Eustace J, Lawler LP, Kantsevoy S, Kalloo AN, et al. Diagnosis of primary sclerosing cholangitis: a blinded comparative study using magnetic resonance cholangiography and endoscopic retrograde cholangiography. Gastrointest Endosc 2006; 64(2): 219-223. doi: 10.1016/j.gie.2005.12.034.
- Ruiz A, Lemoinne S, Carrat F, Corpechot C, Chazouilleres O, Arrive L. Radiologic course of primary sclerosing cholangitis: Assessment by three-dimensional magnetic resonance cholangiography and predictive features of progression. Hepatology 2014; 59: 242-250. doi: 10.1002/hep.26620.
- 33. Trivedi PJ, Arndtz K, Abbas N, Telford A, Young L, Banerjee R, et al. Quantitative MRCP and metrics of bile duct disease over time in patients with primary sclerosing cholangitis: A prospective study. Aliment Pharmacol Ther 2024. doi: 10.1111/apt.17944.
- 34. Cazzagon N, Lemoinne S, El Mouhadi S, Trivedi P, Dohan A, Fankem AK, et al. Two simple magnetic resonance scores are able to predict survival in patients with primary sclerosing cholangitis. Hepatology 2018; 68(Suppl 1): 29A-30A. doi: 10.1007/s00261-023-04051-4.
- 35. Muir AJ. Is Magnetic Resonance Cholangiopancreatography Worth a Thousand Words in Determining Prognoses of Patients With Primary Sclerosing Cholangitis? Clin Gastroenterol Hepatol 2019; 17(13): 2654-2656. doi: 10.1016/j.cgh.2019.04.067.

- 36. Zenouzi R, Liwinski T, Yamamura J, Weiler-Normann C, Sebode M, Keller S, et al. Follow-up magnetic resonance imaging/3D-magnetic resonance cholangiopancreatography in patients with primary sclerosing cholangitis: challenging for experts to interpret. Alimentary pharmacology & therapeutics 2018; 48(2): 169-178. doi: 10.1111/ apt.14797.
- 37. Schramm C, Eaton J, Ringe KI, Venkatesh S, Yamamura J; MRI working group of the IPSCSG. Recommendations on the use of magnetic resonance imaging in PSC-A position statement from the International PSC Study Group. Hepatology 2017; 66(5): 1675-1688. doi: 10.1002/hep.29293.
- Ringe KI, Vo Chieu VD, Wacker F, Lenzen H, Manns MP, Hundt C, et al. Fully automated detection of primary sclerosing cholangitis (PSC)-compatible bile duct changes based on 3D magnetic resonance cholangiopancreatography using machine learning. Eur Radiol 2021; 31(4): 2482-2489. doi: 10.1007/s00330-020-07323-5.
- 39. Cazzagon N, El Mouhadi S, Vanderbecq Q, Ferreira C, Finnegan S, Lemoinne S, et al. Quantitative magnetic resonance cholangiopancreatography metrics are associated with disease severity and outcomes in people with primary sclerosing cholangitis. JHEP Reports 2022; 4(11):100577. doi: 10.1016/j.jhepr.2022.100577.
- 40. Cristoferi L, Porta M, Bernasconi DP, Leonardi F, Gerussi A, Mulinacci G, et al. A quantitative MRCP-derived score for medium-term outcome prediction in primary sclerosing cholangitis. Digestive and Liver Disease. 2023; 55(3): 373-380. doi: 10.1016/j.dld.2022.10.015.
- McCrary J, Trout AT, Mahalingam N, Singh R, Rojas CC, Miethke AG, et al. Associations Between Quantitative MRI Metrics and Clinical Risk Scores in Children and Young Adults With Autoimmune Liver Disease. AJR Am J Roentgenol 2022; 219(1): 142-150. doi: 10.2214/AJR.21.27204.
- 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.
- 43. Goldfinger MH, Ridgway GR, Ferreira C, Langford CR, Cheng L, Kazimianec A, et al. Quantitative MRCP Imaging: Accuracy, Repeatability, Reproducibility, and Cohort-Derived Normative Ranges. J Magn Reson Imaging 2020; 52(3): 807-820. doi: 10.1002/jmri.27113.
- 44. Ismail MF, Hirschfield GM, Hansen B, Tafur M, Elbanna KY, Goldfinger MH, et al. Evaluation of quantitative MRCP (MRCP+) for risk stratification of primary sclerosing cholangitis: comparison with morphological MRCP, MR elastography, and biochemical risk scores. Eur Radiol 2022; 32(1): 67-77. doi: 10.1007/s00330-021-08142-y.
- 45. Cazzagon N, Gonzalez-Sanchez E, El-Mourabit H, Wendum D, Rainteau D, Humbert L, et al. Protective potential of the gallbladder in primary sclerosing cholangitis. JHEP Reports 2023; 5(4): 100649. doi: 10.1016/j.jhepr.2022.100649.
- 46. Song C, Lewis S, Kamath A, Hectors S, Putra J, Kihira S, et al. Primary sclerosing cholangitis: diagnostic performance of MRI compared to blood tests and clinical scoring systems for the evaluation of histopathological severity of disease. Abdom Radiol (NY) 2020; 45: 354-364. doi: 10.1007/s00261-019-02366-9.
- 47. Grigoriadis A, Morsbach F, Voulgarakis N, Said K, Bergquist A, Kartalis N. Inter-reader agreement of interpretation of radiological course of bile duct changes between serial follow-up magnetic resonance imaging/3D magnetic resonance cholangiopancreatography of patients with primary sclerosing cholangitis. Scand J Gastroenter-ol 2020; 55(2): 228-235. doi: 10.1080/00365521.2020.1720281.
- Björnsson E, Lindqvist-Ottosson J, Asztely M, Olsson R. Dominant strictures in patients with primary sclerosing cholangitis. Am J Gastroenterol 2004; 99(3): 502-508. doi: 10.1111/j.1572-0241.2004.04106.x.
- 49. Schulze J, Lenzen H, Hinrichs JB, Ringe B, Manns MP, Wacker F, et al. An imaging biomarker for assessing hepatic function in patients with primary sclerosing cholangitis. Clin Gastroenterol Hepatol 2019; 17: 192–199. doi: 10.1016/j.cgh.2018.05.011.
- Tokala A, Khalili K, Menezes R, Hirschfield G, Jhaveri KS. Comparative MRI analysis of morphologic patterns of bile duct disease in IgG4-related systemic disease versus primary sclerosing cholangitis. Am J Roentgenol 2014; 202(3): 536–543. doi: 10.2214/AJR.12.10360.

- Tonolini M, Bianco R. HIV-related/AIDS cholangiopathy: pictorial review with emphasis on MRCP findings and differential diagnosis. Clin Imaging 2013; 37(2): 219-226. doi: 10.1016/j.clinimag.2012.03.008.
- Katabathina VS, Dasyam AK, Dasyam N, Hosseinzadeh K. <u>Adult bile</u> duct strictures: role of MR imaging and MR cholangiopancreatography in characterization. Radiographics 2014; 34(3): 565-586. doi: 10.1148/rg.343125211.
- 53. Kovač JD, Ješić R, Stanisavljević D, Kovač B, Banko B, Seferović P, et al. Integrative role of MRI in the evaluation of primary biliary cirrhosis. Eur Radiol 2012; 22(3): 688-694. doi: 10.1007/s00330-011-2296-y.
- Azizi L, Raynal M, Cazejust J, Ruiz A, Menu Y, Arrivé L. MR Imaging of sclerosing cholangitis. <u>Clin Res Hepatol Gastroenterol</u> 2012; 36(2): 130-138. doi: 10.1016/j.clinre.2011.11.011.
- Bowlus CL, Arrivé L, Bergquist A, Deneau M, Forman L, Ilyas SI, et al. AASLD practice guidance on primary sclerosing cholangitis and cholangiocarcinoma. Hepatology 2023; 77(2): 659-702. doi: 10.1002/ hep.32771.
- 56. Kovač JD, Galun D, Đurić-Stefanović A, Lilić G, Vasin D, Lazić L, et al. Intrahepatic mass-forming cholangiocarcinoma and solitary hypovascular liver metastases: is the differential diagnosis using diffusion-weighted MRI possible? Acta Radiol 2017; 58(12): 1417-1426. doi: 10.1177/0284185117695666.

- 57. Kovač JD, Daković M, Janković A, Mitrović M, Dugalić V, Galun D, et al. The role of quantitative diffusion-weighted imaging in characterization of hypovascular liver lesions: A prospective comparison of intravoxel incoherent motion derived parameters and apparent diffusion coefficient. PLoS One 2021; 16(2): e0247301. doi: 10.1371/journal.pone.0247301.
- Saca D, Flamm SL. Cholangiocarcinoma Surveillance Recommendations in Patients with Primary Sclerosing Cholangitis. Clin Liver Dis 2024; 28(1): 183-192. doi: 10.1016/j.cld.2023.07.010.
- 59. Charatcharoenwitthaya P, Enders FB, Halling KC, Lindor KD. Utility of serum tumor markers, imaging, and biliary cytology for detecting cholangiocarcinoma in primary sclerosing cholangitis. Hepatology 2008; 48(4): 1106-1117. doi: 10.1002/hep.22441.
- Bonato G, Cristoferi L, Strazzabosco M, Fabris L. <u>Malignancies in</u> <u>Primary Sclerosing Cholangitis--A Continuing Threat</u> Dig Dis 2015; 33: 140-148. doi: 10.1159/000440826.
- Prokopič M, Beuers U. Management of primary sclerosing cholangitis and its complications: an algorithmic approach. Hepatol Int 2021; 15(1): 6-20. doi: 10.1007/s12072-020-10118-x.
- Henson JB, King LY. Post-Transplant Management and Complications of Autoimmune Hepatitis, Primary Biliary Cholangitis, and Primary Sclerosing Cholangitis including Disease Recurrence. Clin Liver Dis 2024; 28(1): 193-207. doi: 10.1016/j.cld.2023.07.009.

MR KARAKTERISTIKE PRIMARNOG SKLEROZIRAJUĆEG HOLANGITISA: PREGLED SKORING SISTEMA ZASNOVANIH NA IMIDŽING KARAKTERISTIKAMA KOJI SE KORISTE ZA PROCENU TEŽINE I PROGNOZE

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Sažetak

Primarni sklerozirajući holangitis (PSC) je hronično, holestatsko oboljenje jetre koje se odlikuje hroničnom inflamacijom, fibrozom i stenozom žučnih puteva. Magnetno rezonantna holangiopankreatiografija (MRCP) predstavlja zlatni standard za dijagnozu PSC-a i omogućava uvid u promene na bilijarnom stablu. Tipična radiološka slika PSC-a obuhvata multifokalne anularne i kratke-segmente strikture u kombinaciji sa normalnim ili lako dilatiranim žučnim vodovima. Pored holangiografskog prikaza, magnetna rezonanca (MR) pruža uvid i u morfološke promene parenhima jetre koje mogu ukazivati na težinu bolesti. Savremeni skoring sistemi zasnovani na MR nalazima, uključuju ANALI skor i novu softversku analizu zvanu MRCP+, omogućavaju procenu težine bolesti i identifikovanje visoko-rizičnih pacijenata. Stoga, MR sa MRCP-om predstavlja dijagnostičku metodu koja pruža sveobuhvatnu evaluaciju pacijenata sa PSC-om, uključujući inicijalnu dijagnozu, praćenje pacijenata radi rane detekcije komplikacija uz prognostički značaj.

Ključne reči: jetra, primarni sklerozirajući holangitis, magnetno rezonantna holangiopankreatografija

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