Role of Endoscopic Procedures in the Diagnosis of IgG4-Related Pancreatobiliary Disease

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The emergence of the disease entity of glucocorticoid-responsive systemic immunoglobulin G4 (IgG4)-related pancreatobiliary disease has generated substantial attention among the international gastroenterology society. IgG4-related pancreatobiliary disease includes type 1 autoimmune pancreatitis (AIP) and IgG4-related sclerosing cholangitis (IgG4-SC). The typical manifestations of IgG4-related pancreatobiliary disease are cholestatic liver dysfunction, obstructive jaundice, and weight loss, although it may present with no clinical symptoms. Since it mimics tumors on imaging, AIP/IgG4-SC may often be misdiagnosed as pancreatic or biliary cancer. The endoscopic armamentarium for the diagnosis of IgG4-related pancreatobiliary disease includes endoscopic ultrasonography, intraductal ultrasonography, endoscopic retrograde cholangiopancreatography, and cholangioscopy. The role of endoscopic tissue acquisition is two-fold in the diagnosis of IgG4-related pancreatobiliary disease: exclusion of cancer and procurement of histopathological proof for diagnosis of AIP/IgG4-SC, which can also be achieved by adding the immunohistochemistry for IgG4. Our review article addresses the role of various endoscopic examinations in diagnosing IgG4-related pancreatobiliary disease, focusing on the differentiation of this condition from pancreatobiliary malignancies.

Key Words: Autoimmune Pancreatitis; IgG4-Related Sclerosing Cholangitis; Endoscopy

INTRODUCTION

IgG4-related disease (IgG4-RD) is a systemic sclerosing disorder characterized by fibrotic lesions in the form of a mass-like lesion that contains dense IgG4-positive lymphoplasmacytic infiltrates. The concept of IgG4-RD was proposed by Kamisawa in 2003, based on the discovery of various systemic involvements of unique histopathologic findings of autoimmune pancreatitis (AIP).

The pathology of IgG4-RD can involve nearly every human organ system: the pancreas (type 1 AIP or IgG4-related pancreatitis), bile duct (IgG4-related sclerosing cholangitis (IgG4-SC) or IgG4-associated cholangitis), kidneys, salivary glands (Mikulicz’s syndrome), retroperitoneum, thyroid gland (Riedel’s thyroiditis), liver, gallbladder, aorta, lungs, periportal tissues, pericardium, and prostate. IgG4-RD typically presents as a subacute manifestation and relatively mild symptoms. Therefore, it is often characterized as an incidental radiologic finding. However, in clinical practice, its presentation may often mimic pancreatobiliary malignancies.

Clinicians are often fascinated by the entity of AIP/IgG4-SC because of its dramatically quick response to glucocorticoid therapy. However, its misdiagnosis as pancreatobiliary malignancy may lead to inappropriate surgical interventions. By contrast, misdiagnosis of pancreatobiliary malignancies as AIP/IgG4-SC can cause a delay in adequate treatment of this disease.

The endoscopic armamentarium for the diagnosis of AIP/IgG4-SC includes endoscopic ultrasonography (EUS), endoscopic retrograde cholangiopancreatography (ERCP), intraductal ultrasonography (IDUS), and cholangioscopy. The review article discusses the role of various endoscopic examinations in the diagnosis of IgG4-related pancreato-
biliary disease, focusing on differentiating it from pancreaticobiliary malignancies.

DIAGNOSIS OF IGG4-RELATED PANCREATOBLIARY DISEASES

Various diagnostic criteria have been proposed for the diagnosis of AIP from Japan, the United States, Italy, Germany, and South Korea. However, in 2011, the International Consensus Diagnostic Criteria for AIP (ICDC) were proposed by worldwide experts. According to the ICDC, AIP is divided into two subtypes with different diagnostic criteria. Type 1 AIP should be considered part of the spectrum of IgG4-RD and is also called IgG4-related pancreatitis. Type 2 AIP is not part of IgG4-RD, but another type of steroid-responsive pancreatitis with distinct histopathology and clinical presentations.

International consensus diagnostic criteria have not yet been proposed for IgG4-SC, and researchers commonly use the Japanese clinical diagnostic criteria for IgG4-SC or Mayo group’s HISORt diagnostic criteria. Table 1 compared these 2 diagnostic criteria. In addition, the Japanese group recently published clinical practice guidelines for IgG4-SC, which may help clinicians accurately differentiate IgG4-SC from primary sclerosing cholangitis and cholangiocarcinoma.

Although comprehensive diagnostic criteria for IgG4-RD are available, organ-based diagnostic criteria may be more useful in clinical practice. Pathologists have published a consensus statement on the pathology of IgG4-RD stating that the combination of dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterator phlebitis are highly specific for IgG4-RD when viewed in tandem with IgG4 immunohistochemistry. A three-tiered diagnostic classification for the pathological diagnosis of IgG4-RD was proposed based on these items: (1) histologically highly suggestive of IgG4-RD, (2) probable histological features of IgG4-RD, and (3) insufficient histopathological evidence of IgG4-RD.

ENDOSCOPIC EVALUATION FOR THE DIAGNOSIS OF IGG4-RELATED PANCREATOBLIARY DISEASE

Endoscopic evaluation, including EUS, EUS elastography, contrast-enhanced EUS, IDUS of the bile duct wall, ERCP, and peroral/percutaneous cholangioscopy, is crucial for diagnosing IgG4-related pancreaticobiliary disease and differentiating it from pancreaticobiliary malignancies. Pancreatobiliary endoscopists should deeply comprehend the weaknesses and strengths of these endoscopic modalities, and they must use these methods appropriately, based on individual clinical circumstances, local facilities, and expertise (Table 2).

1. Endoscopic retrograde pancreatography

AIP shows several characteristic features on endoscopic retrograde pancreatography (ERP) that are useful for differentiating it from pancreatic cancer: (1) a long stricture of the main pancreatic duct (>1/3 the length of the whole main pancreatic duct); (2) lack of upstream duct dilatation (duct diameter <5 mm); and (3) multifocal strictures with intervening normal-looking duct. By contrast, pancreatic cancer is seen as a single ductal stricture associated with

| TABLE 1. Comparison of diagnostic criteria for IgG4-related sclerosing cholangitis (IgG4-SC) between the United States and Japan |
|---|---|
| Mayo’s HISORt criteria* | Japan Pancreas Society criteria* |
| Imaging of bile duct (I) | a. One or more stricture involving intrahepatic, proximal extrahepatic, or intrapancreatic bile ducts | Diffuse or segmental narrowing of the intrahepatic and/or extrapancreatic bile ducts associated with the thickening of bile duct wall |
| Serology (S) | >140 mg/dL | ≥135 mg/dL |
| Extent of other organ involvement | a. Pancreatic lesions | a. Pancreatic lesions |
| | b. Retroperitoneal fibrosis | b. Retroperitoneal fibrosis |
| | c. Renal lesions | c. Salivary/lacrimal gland enlargement |
| | d. Salivary/lacrimal gland enlargement | a. Marked lymphoplasmacytic infiltration and fibrosis |
| | a. Marked lymphoplasmacytic infiltration and fibrosis | b. >10 IgG4-positive plasma cells/HPF |
| | c. Storiform fibrosis | c. Storiform fibrosis |
| | d. Obliterator phlebitis | d. Obliterator phlebitis |
| Response to steroid therapy | Normalization of liver enzyme levels or resolution of stricture | Option: effectiveness of steroid therapy |
| Definite diagnosis | Classic imaging findings of autoimmune pancreatitis+S | I+OOI |
| | H a+b+c | I+S+H a+b |
| | H a+b+d | H a+b+c |

*Modified from Ghazale et al. and Ohara et al.
**TABLE 2. Endoscopic tools for the diagnosis of autoimmune pancreatitis (AIP) and IgG4-related sclerosing cholangitis (IgG4-SC)**

|                                | Findings suggestive of AIP/IgG4-SC | Strengths of the test                                                                 | Limitations of the test                                                                 |
|--------------------------------|----------------------------------|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| **AIP**                        |                                  |                                                                                       |                                                                                        |
| Endoscopic retrograde pancreatography (ERP) | 1) Long stricture                | 1) Helpful in the diagnosis of AIP with atypical imaging and/or seronegative AIP.     | 1) Low sensitivity in the centers that do not routinely perform ERP.                     |
|                                 | 2) Lack of upstream dilatation    | 2) High sensitivity (70-90%) and specificity (80-90%) in the centers that routinely perform ERP. | 2) Concern of post-ERCP pancreatitis.                                                  |
|                                 | 3) Multifocal strictures         |                                                                                       | 3) Mostly supplanted by MRCP                                                          |
| Endoscopic ultrasonography (EUS)| 1) Diffuse hypoechoic pancreatic enlargement | 1) Can examine the pancreas in real-time.                                               | 1) Diverse spectrum of EUS morphologic findings in IgG4-RD of the pancreas.            |
|                                 | 2) Concentric bile duct wall thickening (homogeneous regular thickening with a hypoechoic intermediate layer and hyperechoic outer and inner layer) | 2) Allows EUS-guided FNA/biopsy.                                                      |                                                                                        |
| **IgG4-SC**                     |                                  |                                                                                        |                                                                                        |
| Endoscopic retrograde cholangiography (ERC) | 1) Multifocal strictures          | 1) ERCP is usually performed to relieve biliary obstruction.                           | 1) In cases with isolated stricture of intrapancreatic common bile duct, ERC finding of AIP is similar to that of pancreatic or distal CBD cancer. |
|                                 | 2) Mild proximal dilatation despite a long stricture | 2) Allows tissue sampling from ampulla and/or bile duct.                              |                                                                                        |
| Intraductal ultrasonography (IDUS) | 1) Thickening of the bile duct wall (>0.8 mm) on IDUS in a non-stenotic bile duct on ERC | 1) Can be performed during ERCP in a single session.                                  | 1) Expertise in ERCP and EUS is required.                                              |
|                                 | 2) Concentric wall thickening with smooth configuration of the outermost layer and a smooth luminal surface |                                                                                        |                                                                                        |
| Cholangioscopy                  | 1) Dilated and tortuous vessels, and absence of partially enlarged vessels | 1) Directly visualize the biliary lumen and guide targeted biopsy.                    | 1) Technically demanding procedure.                                                    |

ERCP: endoscopic retrograde cholangiopancreatography, MRCP: magnetic resonance cholangiopancreatography, CBD: common bile duct, EUS: endoscopic ultrason, FNA: fine needle aspiration.

apparent upstream duct dilatation. The sensitivity and specificity of ERP for differentiating AIP from pancreatic cancer have been reported to be 33-91% and 80-90%, respectively. The reported incidence of Post-ERCP pancreatitis in patients with AIP was low (1.2% in 82 patients), because AIP is under a category of chronic pancreatitis which has a protective effect against ERCP-induced pancreatitis. In 2011, ICDC recommended the tailored use of ERP because Asian pancreatobiliary endoscopists had usually performed diagnostic ERP in most patients with suspected AIP while Western endoscopists rarely performed diagnostic ERP. Diagnostic ERP could be used in the setting of indeterminate pancreatic parenchymal imaging for AIP or for seronegative AIP without other organ involvement. However, Japanese clinical diagnostic criteria for AIP from 2018 stipulate that magnetic resonance cholangiopancreatography (MRCP) can also be used to diagnose AIP, because the quality of MRC images has improved. The diagnostic use of ERP likely will be increasingly supplanted by MRCP.

2. **Endoscopic retrograde cholangiography**

IgG4-SC, which is the bile duct involvement of IgG4-RD, typically presents radiographically as concentric bile duct wall thickening with biliary strictures. According to Nakazawa et al., IgG4-SC is classified into four types according to cholangiographic findings: type 1, stenosis only in the lower part of the common bile duct (diagnostic diagnosis: pancreatic cancer, cholangiocarcinoma, and chronic pancreatitis); type 2, stenosis diffusely distributed in the intra- and extra-hepatic bile ducts (diagnostic diagnosis: primary sclerosing cholangitis and secondary sclerosing cholangitis); type 3, stenosis in both hilar and hepatic lesions and the lower part of the common bile duct (diagnostic diagnosis: cholangiocarcinoma and gallbladder cancer); and type 4, bile duct strictures only in the hilar hepatic lesions (diagnostic diagnosis: cholangiocarcinoma and gallbladder cancer). Type 1 IgG4-SC is usually associated with AIP. Isolated type 4 IgG4-SC is especially difficult to differentiate from cholangiocarcinoma. For differentiating type 4 pattern from cholangiocarcinoma, mild proximal duct dilatation despite a long stricture with concentric wall...
thickening is characteristic of IgG4-SC, whereas marked proximal duct dilatation with eccentric wall thickening is characteristic of cholangiocarcinoma.22,23

State-of-the-art MRCP displays high-resolution images of the pancreatic and biliary ducts, without exposure to invasive intervention or radiation.24 MRCP and endoscopic retrograde cholangiography showed comparable abilities to depict the biliary system to evaluate sclerosing cholangitis.25 Therefore, MRCP can be recommended as an initial modality for evaluating bile ductal abnormalities during the workup for patients with suspected IgG4-SC. By contrast, unlike MRCP, ERCP can be used to acquire tissue samples for differentiating cancer and IgG4 immunostaining and to relieve obstructive jaundice.

3. EUS

EUS can display pancreatobiliary ductal features and parenchyma in substantial detail.24,26 According to Hoki et al.,26 a diffuse hypoechoic area, diffuse enlargement, peri-pancreatic hypoechoic margins, and bile duct wall thickening are more frequently found in AIP than in pancreatic cancer. Diffuse hypoechoic pancreatic enlargement of AIP may be accompanied by hyperechoic inclusions. Concentric bile duct wall thickening of AIP/IgG4-SC may be depicted as a homogeneous thickening with hyperechoic-hypoechoic-hyperechoic (outer-intermediate-inner layer, three-layer type).27-29 However, the EUS morphologic spectrum of AIP is wide. EUS findings of atypical imaging features of AIP may include a pancreatic cancer-mimicking mass lesion.28,30 Therefore, EUS should not be used as the sole diagnostic test for AIP, but it can assist in differentiating AIP from pancreatic cancer and also guide FNA (fine needle aspiration) or fine needle biopsy (FNB).31

4. Contrast-enhanced EUS

Enhancement with a contrast agent can be concurrently performed during a conventional B-mode EUS for providing information regarding microcirculation and parenchymal perfusion.31,32 This contrast-enhanced EUS can be visualized by power or color Doppler mode or by a dedicated harmonic detection mode.32 The ultrasound contrast agents include Echovist, Albunex, Levovist, Optison, SonoVue, Definity, and Sonazoid.33 Among them, SonoVue and Sonazoid are commonly used for contrast-enhanced EUS. The contrast agent creates encapsulated air microbubbles, which provide significant alterations in the reflection pattern by increasing the backscattered acoustic signal markedly.33 Contrast-enhanced EUS may differentiate mass-forming AIP from pancreatic cancer because mass-forming AIP typically presents as a pseudotumor of hypervascularization, whereas pancreatic cancer is displayed as a hypovascular mass.34-36 A meta-analysis on the role of contrast-enhanced EUS revealed that its pooled sensitivity and specificity in the differentiation of pancreatic cancer were 94% and 89%, respectively.37 Some researchers have reported high sensitivity (96-100%) and specificity (95-100%) for differentiating AIP from pancreatic cancer by adding quantitative perfusion analysis with the time intensity curve to contrast-enhanced EUS.38,39 A recent study compared 53 patients with pancreatic cancer and 27 with focal AIP.31 The cited study discovered that hyper- to iso-enhancement in the arterial phase, homogeneous contrast agent distribution, and absent irregular internal vessels indicated focal AIP more frequently than pancreatic cancer.31 Consequently, contrast-enhanced EUS may improve the specificity in differentiating AIP from pancreatic cancer.31

5. Intraductal ultrasonography of the bile duct wall

The appearance of bile duct wall thickening on focused imaging differs between IgG4-SC and cholangiocarcinoma.44 During an ERCP session, transpapillary IDUS with a scanning frequency of 12-30 MHz can provide high-resolution images of the bile duct wall with detailed layer structure. The normal structure of the bile duct on IDUS shows an inner hypoechoic and outer hyperechoic layer.44 The characteristic IDUS findings for IgG4-SC include an even concentric ductal wall thickening with smooth inner and outer margins, whereas cholangiocarcinoma is seen as an uneven eccentric wall thickening with irregular luminal surface and indistinct outer margins.25,40-42 According to Naitoh et al.,42 the most specific IDUS finding for the diagnosis of IgG4-SC was ductal wall thickening of more than 0.8 mm in a non-stenotic area of the bile duct, whereas ductal wall thickening of cholangiocarcinoma was localized in the stenotic area of the bile duct.

6. Peroral/percutaneous cholangioscopy

Cholangioscopy can provide direct visualization of the biliary lumen, even though the biliary tree is among the most elusive structures for direct endoscopic evaluation.43 Cholangioscopy may also permit highly targeted biopsy. Itoi et al.44 were the first to examine the role of cholangioscopy in patients with IgG4-SC. The most frequent findings on cholangioscopy in patients with IgG4-SC were dilated and tortuous vessels and an absence of partially enlarged vessels.44 Differentiation of IgG4-SC from primary sclerosing cholangitis (PSC) was made based on the finding of significantly higher numbers of dilated and tortuous vessels in IgG4-SC than in PSC, whereas scarring and pseudodiverticula are more frequent in PSC than in IgG4-SC. Differentiation of IgG4-SC from cholangiocarcinoma was based on a significantly higher incidence of partially enlarged vessels in “distal” cholangiocarcinoma than in IgG4-SC, whereas the incidence of dilated vessels is significantly higher in IgG4-SC than in “ hilar” cholangiocarcinoma. Although cholangioscopy may be a technically demanding procedure, the recently developed Spy-Glass system and intraductal balloon-guided direct peroral cholangioscopy may overcome the limitations of the current cholangioscopy systems.43
**ENDOSCOPY-GUIDED TISSUE SAMPLING FOR DIAGNOSING IGG4-RELATED PANCREATOBILIARY DISEASE FROM PANCREATOBILIARY MALIGNANCIES**

The similar imaging findings between IgG4-related pancreatobiliary disease and pancreatobiliary malignancies highlight the following two roles of endoscopic sample acquisition: exclusion of pancreatobiliary malignancies and procurement of pathological evidence for IgG4-RD.24,45

1. **Diagnostic performance of endoscopy-guided tissue sampling for diagnosis of pancreatobiliary malignancies**

   EUS-FNA is the first-line diagnostic modality for preoperative pathological diagnosis of pancreatic cancer. According to a meta-analysis analyzing a total number of 4984 patients,46 the pooled sensitivity and specificity for malignant cytology was 85% (95% confidence interval (CI), 84%-86%) and 98% (95% CI, 97%-99%), respectively.

   ERCP-guided sampling is recommended for the diagnosis of bile duct cancer, especially when biliary decompression is needed for relieving obstructive jaundice.24,47 Reported mean sensitivities of ERCP-guided intraductal forceps biopsy and brush cytology for the diagnosis of bile duct cancer were 63% (6 studies involving 127 patients) and 59% (18 studies involving 306 patients), respectively.47,48 Although a combination of brushing and biopsy may increase these modest sensitivities of ERCP-based sampling, EUS-FNA can be used when ERCP-guided sampling is nondiagnostic. According to a recent meta-analysis involving 957 patients,49 pooled sensitivity and specificity of EUS-FNA for malignant biliary strictures were 80% (95% CI 74%-86%) and 97% (95% CI, 94%-99%), respectively.

2. **FNA versus FNB in the diagnosis of AIP**

   For the diagnosis of pancreatic ductal adenocarcinoma, a FNA needle may be comparable with a FNB needle in terms of diagnostic performance.50 However, the tissue amount required for the histologic diagnosis of AIP may be larger than that required for the diagnosis of pancreatic ductal adenocarcinoma.51 Yoon et al.51 recently performed a systematic review and meta-analysis to compare the diagnostic performance of EUS-guided FNA versus FNB sampling for diagnosing AIP. Based on analysis of nine studies for FNA (309 patients with AIP) and seven studies for FNB (131 patients), FNB showed superior diagnostic yields for level 1 or 2 histology criteria of AIP than FNA (56% vs. 87%) with comparable adverse events.51 Therefore, when EUS-guided pancreatic tissue acquisition is needed for the differentiation of AIP, FNB with needle size of 22G or more should be used for a high diagnostic yield for AIP.

3. **IgG4 immunostaining for supporting the diagnosis of IgG4-related pancreatobiliary disease**

   Definitive histopathological diagnosis of IgG4-RD is difficult due to the small endoscopic biopsy specimen, although pancreatic biopsies have shown moderate sensitivity for the histologic diagnosis of AIP.30,52-55 Moreover, contrary to a pancreatic core biopsy specimen, the small specimens obtained by ERCP-guided intraductal forceps biopsy cannot show the full characteristic features of histopathology of IgG4-RD.18,42,57 Given the nature of IgG4-RD, with its systemic IgG4-positive plasma cell infiltration, immunohistochemical staining for IgG4 is often used to support the diagnosis of IgG4-related pancreatobiliary disease.56,57

   For the diagnosis of IgG4-related pancreatobiliary disease, the biopsy specimens from the pancreas, bile duct, and ampulla of Vater can be used for Ig4 immunostaining.56 Given that the ampulla of Vater is a confluence of the common bile duct and the main pancreatic duct, Ig4 immunostaining of the ampillary biopsy specimen has been attempted to support the diagnosis of IgG4-RD when pancreatic/biliary tissue is neither available nor adequate.59 Although infiltration of IgG4-positive cells into the stomach, duodenum, and colon are frequently found in patients with IgG4-RD, low specificity of IgG4 immunostaining of biopsies from the gastrointestinal tract other than the ampulla may limit its clinical use in the diagnosis of IgG4-related pancreatobiliary disease.60

   Yoon et al.58 recently performed a systematic review and meta-analysis regarding the diagnostic performance of immunohistochemistry for IgG4 in diagnosing AIP. This meta-analysis was based on 20 studies comprised 346 patients with AIP and 590 with other pancreatobiliary diseases, including 371 with pancreatobiliary malignancies. IgG4 immunostaining of pancreatic, biliary, and ampullary tissue had a 64% pooled sensitivity and 93% pooled specificity.58 The pooled positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 7.66, 0.30, and 38.86, respectively.58 However, endoscopists must also remain aware of possible tissue IgG4 positivity (10%) in peritumoral pancreatitis associated with pancreatic cancer.61 The pathologic diagnosis of IgG4-RD in positive tissue IgG4 should be made together with the histopathological features and other cardinal features of IgG4-RD.10,57

**CONCLUSION**

IgG4-related pancreatobiliary disease is a relatively new disease entity with a dramatic response to glucocorticoid therapy; however, it needs to be differentiated from pancreatobiliary malignancies. Various endoscopic examinations can provide detailed images for differentiation between two entities. Endoscopic tissue acquisition is necessary to both exclude malignancy and provide the histological evidence of IgG4-RD, with immunohistochemical aid for IgG4. With knowledge of the full details of the endoscopic armamentarium, as reviewed in this article, clinicians can accurately diagnose IgG4-related pancreatobiliary disease and avoid unnecessary surgery for this benign steroid-responsive disease entity.
CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012;366:359-51.
2. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. Mod Rheumatol 2012;22:1-14.
3. Kamisawa T, Funata N, Hayashi Y, Eishi Y, Koike M, Tsuruta K, et al. A new clinicopathological entity of IgG4-related autoimmune disease. J Gastroenterol 2003;38:982-4.
4. Moon SH, Kim MH, Park DH, Hwang CY, Park SJ, Lee SS, et al. Is a 2-week steroid trial after initial negative investigation for malignancy useful in differentiating autoimmune pancreatitis from pancreatic cancer? A prospective outcome study. Gut 2008;57:1704-12.
5. Shimosegawa T, Charli ST, Frulloni L, Kamisawa T, Kawa S, Mino-Kenudson M, et al. International consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology. Pancreas 2011;40:355-8.
6. Ghazale A, Chari ST, Zhang L, Smyrk TC, Takahashi N, Levy MJ, et al. Immunoglobulin G4-associated cholangitis: clinical profile and response to therapy. Gastroenterology 2008;134:706-15.
7. Ohara H, Okazaki K, Tsuochi H, Inui K, Kawa S, Kamisawa T, et al. Clinical diagnostic criteria of IgG4-related sclerosing cholangitis 2012. J Hepatobiliary Pancreat Sci 2012;19:536-42.
8. Kamisawa T, Nakazawa T, Tazuma S, Zen Y, Tanaka A, Ohara H, et al. Clinical practice guidelines for IgG4-related sclerosing cholangitis. J Hepatobiliary Pancreat Sci 2019;26:189-203.
9. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol 2012;22:21-30.
10. Shihane V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, et al. Consensus statement on the pathology of IgG4-related disease. Mod Pathol 2012;25:1181-92.
11. Sugumar A, Levy MJ, Kamisawa T, Webster GJ, Kim MH, Enders F, et al. Endoscopic retrograde pancreatography criteria to diagnose autoimmune pancreatitis: an international multicentre study. Gut 2011;60:666-70.
12. Inoue K, Ohuchida J, Ohtsuka T, Nabea T, Yokohata K, Ogawa Y, et al. Severe localized stenosis and marked dilatation of the main pancreatic duct are indicators of pancreatic cancer instead of chronic pancreatitis on endoscopic retrograde balloon pancreatography. Gastrointest Endosc 2003;58:510-5.
13. Kamisawa T, Imai M, Yui Chen P, Tu Y, Egawa N, Tsuruta K, et al. Strategy for differentiating autoimmune pancreatitis from pancreatic cancer. Pancreas 2008;37:e62-7.
14. Kim JH, Kim MH, Byun JH, Lee SS, Lee SJ, Park SH, et al. Diagnostic strategy for differentiating autoimmune pancreatitis from pancreatic cancer: is an endoscopic retrograde pancreatography essential? Pancreas 2012;41:639-47.
15. Nishino T, Oyama H, Toki F, Shiratori K. Differentiation between autoimmune pancreatitis and pancreatic carcinoma based on endoscopic retrograde cholangiopancreatography findings. J Gastroenterol 2010;45:988-96.
16. Naitoh I, Nakazawa T, Okumura F, Takada H, Hirano A, Hayashi K, et al. Endoscopic retrograde cholangiopancreatography-related adverse events in patients with type 1 autoimmune pancreatitis. Pancreatology 2016;16:78-82.
17. Horiuchi A, Kawa S, Hamano H, Hayama M, Ota H, Kiyosawa K. ERCP features in 27 patients with autoimmune pancreatitis. Gastrointest Endosc 2002;55:494-9.
18. Kawakami H, Zen Y, Kuwatani M, Eto K, Haba S, Yamato H, et al. IgG4-related sclerosing cholangitis and autoimmune pancreatitis: histological assessment of biopsies from Vater’s ampulla and the bile duct. J Gastroenterol Hepatol 2010;25:1648-55.
19. Kawa S, Kamisawa T, Notohara K, Fujinaga Y, Inoue D, Koyama T, et al. Japanese clinical diagnostic criteria for autoimmune pancreatitis, 2018: revision of Japanese clinical diagnostic criteria for autoimmune pancreatitis, 2011. Pancreas 2020;49:e13-4.
20. Moon SH, Kim MH, Lee JK, Baek S, Woo YS, Cho DH, et al. Development of a scoring system for differentiating IgG4-related sclerosing cholangitis from primary sclerosing cholangitis. J Gastroenterol 2017;52:483-93.
21. Kamisawa T, Naitoh I, Hayashi K, Okumura F, Miyabe K, Yoshida M, et al. Diagnostic criteria for IgG4-related sclerosing cholangitis based on cholangiographic classification. J Gastroenterol 2012;47:79-87.
22. Moon SH, Kim MH. The role of endoscopy in the diagnosis of autoimmune pancreatitis. Gastrointest Endosc 2012;76:645-56.
23. Nishino T, Toki F, Oyama H, Oi I, Kobayashi M, Takasaki K, et al. Biliary tract involvement in autoimmune pancreatitis. Pancreas 2005;30:76-82.
24. Moon SH, Kim MH. Autoimmune pancreatitis: role of endoscopy in diagnosis and treatment. Gastrointest Endosc Clin N Am 2013;23:893-915.
25. Vitellas KM, Enns RA, Keog MT, Freed KS, Spritzer CE, Baillie J, et al. Comparison of MR cholangiopancreatographic techniques with contrast-enhanced cholangiography in the evaluation of sclerosing cholangitis. AJR Am J Roentgenol 2002;178:327-34.
26. Hoki N, Mizuno N, Sawaki A, Tajiuka M, Takayama R, Shimizu Y, et al. Diagnosis of autoimmune pancreatitis using endoscopic ultrasonography. J Gastroenterol 2009;44:154-9.
27. De Lisi S, Buscarini E, Arcidiacono PG, Petrone M, Menozzi F, Testoni PA, et al. Endoscopic ultrasonography findings in autoimmune pancreatitis: be aware of the ambiguous features and look for the pivotal ones. JOP 2010;11:78-84.
28. Farrell JJ, Garber J, Sahani D, Brugge WR. EUS findings in patients with autoimmune pancreatitis. Gastrointest Endosc 2004;60:927-36.
29. Hyodo N, Hyodo T. Ultrasonographic evaluation in patients with autoimmune pancreatitis. Endoscopy 2006;38 Suppl 1:L30-6.
30. Hyodo N, Hyodo T. Ultrasoundographic evaluation in patients with autoimmune-related pancreatitis. J Gastroenterol 2003;38:1155-61.
31. Cho MK, Moon SH, Song TJ, Kim RE, Oh DW, Park DH, et al. Contrast-enhanced endoscopic ultrasound for differentially diagnosing autoimmune pancreatitis and pancreatic cancer. Gut Liver 2018;12:591-6.
32. Fusaroli P, Saftoiu A, Mancino MG, Caletti G, Eloubeidi MA. Techniques of image enhancement in EUS (with videos). Gastrointest Endosc 2011;74:645-55.
33. Ignee A, Atkinson NS, Schuessler G, Dietrich CF. Ultrasound contrast agents. Endosc Ultrasound 2016;5:355-62.
34. Hocke M, Ignee A, Dietrich CF. Contrast-enhanced endoscopic ultrasound in the diagnosis of autoimmune pancreatitis. Endoscopy 2011;43:163-5.
35. Kitano M, Kudo M, Yamao K, Takagi T, Sakamoto H, Komaki T, et al. Characterization of small solid tumors in the pancreas: the value of contrast-enhanced harmonic endoscopic ultrasonography. Am J Gastroenterol 2012;107:303-10.
36. Kitano M, Sakamoto H, Komaki T, Kudo M. New techniques and future perspective of EUS for the differential diagnosis of pancreatic malignancies: contrast harmonic imaging. Dig Endosc 2011;23 Suppl 1:46-50.
37. Gong TT, Hu DM, Zhu Q. Contrast-enhanced EUS for differential diagnosis of pancreatic mass lesions: a meta-analysis. Gastrointest Endosc 2012;76:301-9.
38. Imazu H, Kanazawa K, Mori N, Ikeda K, Kakutani H, Sumiyama K, et al. Novel quantitative perfusion analysis with contrast-enhanced harmonic EUS for differentiation of autoimmune pancreatitis from pancreatic carcinoma. Scand J Gastroenterol 2012;47:853-60.
39. Matsubara H, Itoh A, Kawashima H, Kasugai T, Ohno E, Ishikawa T, et al. Dynamic quantitative evaluation of contrast-enhanced endoscopic ultrasonography in the diagnosis of pancreatic diseases. Pancreas 2011;40:1073-9.
40. Hirano K, Tada M, Isayama H, Yamamoto K, Mizuno S, Yagioka H, et al. Endoscopic evaluation of factors contributing to intra-pancreatic biliary stricture in autoimmune pancreatitis. Gastrointest Endosc 2010;71:85-90.
41. Kawasumi S, Okazaki K, Kamisawa T, Shimosugiwa T, Tanaka M; Working members of Research Committee for Intractable Pancreatic Disease and Japan Pancreas Society. Japanese consensus guidelines for management of autoimmune pancreatitis: II. Extra-pancreatic lesions, differential diagnosis. J Gastroenterol 2010;45:355-69.
42. Naitoh I, Nakazawa T, Ohara H, Ando T, Hayashi K, Tanaka H, et al. Endoscopic transpanillary intraductal ultrasonography and biopsy in the diagnosis of IgG4-related sclerosing cholangitis. J Gastroenterol 2009;44:1147-55.
43. Moon JH, Terheggen G, Choi HJ, Neuhaus H. Peroral cholangioscopy: diagnostic and therapeutic applications. Gastroenterology 2012;144:276-82.
44. Isoi T, Kamisawa T, Igarashi Y, Kawakami H, Yasuda I, Itokawa F, et al. The role of peroral video cholangioscopy in patients with IgG4-related sclerosing cholangitis. J Gastroenterol 2013;48:504-14.
45. Finkelberg DL, Sahani D, Deshpande V, Brugge WR. Autoimmune pancreatitis. N Engl J Med 2006;355:2670-6.
46. Hewitt MJ, McPhail MJ, Possamai L, Dhar A, Vlavianos P, Monahan KJ. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis. Gastrointest Endosc 2012;75:319-31.
47. Dumonceau JM. Sampling at ERCP for cyto- and histopathological examination. Gastrointest Endosc Clin N Am 2012;22:461-77.
48. Tamada K, Ushio J, Sugano K. Endoscopic diagnosis of extrapancreatic bile duct carcinoma: advances and current limitations. World J Clin Oncol 2011;2:203-16.
49. Sadeghi A, Mohamadnejad M, Ismaili F, Eshtehar A, Biglari M, Malekzadeh R, et al. Diagnostic yield of EUS-guided FNA for malignant biliary stricture: a systematic review and meta-analysis. Gastrointest Endosc 2016;83:290-8.e1.
50. Facciorusso A, Wani S, Triantafylloiu K, Tzatzios G, Cannizzaro R, Muscatelli N, et al. Comparative accuracy of needle sizes and designs for EUS tissue sampling of solid pancreatic masses: a network meta-analysis. Gastrointest Endosc 2019;90:893-903.e7.
51. Yoon SB, Moon SH, Song TJ, Kim JH, Kim MH. Endoscopic ultrasound-guided fine needle aspiration versus biopsy for diagnosis of autoimmune pancreatitis: systematic review and comparative meta-analysis. Dig Endosc 2020. doi: 10.1111/den.13866. [Epub ahead of print]
52. Detlefsen S, Mohr Drewes A, Vyberg M, Klöppel G. Diagnosis of autoimmune pancreatitis by core needle biopsy: application of six microscopic criteria. Virchows Arch 2009;454:531-9.
53. Hirano K, Fukushima N, Tada M, Isayama H, Mizuno S, Yamamoto K, et al. Diagnostic utility of biopsy specimens for autoimmune pancreatitis. J Gastroenterol 2009;44:765-73.
54. Mizuno N, Bhatia V, Hosoda W, Sawaki A, Hoki N, Haro K, et al. Histological diagnosis of autoimmune pancreatitis using EUS-guided trucut biopsy: a comparison study with EUS-FNA. J Gastroenterol 2009;44:742-50.
55. Song TJ, Kim JH, Kim MH, Jang JW, Park DH, Lee SS, et al. Comparison of clinical findings between histologically confirmed type 1 and type 2 autoimmune pancreatitis. J Gastroenterol Hepatol 2012;27:700-8.
56. Chari ST, Takahashi N, Levy MJ, Smyrk TC, Clain JE, Pearson RR, et al. A diagnostic strategy to distinguish autoimmune pancreatitis from pancreatic cancer. Clin Gastroenterol Hepatol 2009;7:1097-103.
57. Deheragoda MG, Church NI, Rodriguez-Justo M, Munson P, Sandanayake N, Seward EW, et al. The use of immunoglobulin G4 immunostaining in diagnosing pancreatic and extrapancreatic involvement in autoimmune pancreatitis. Clin Gastroenterol Hepatol 2007;5:1229-34.
58. Yoon SB, Moon SH, Kim JH, Song TJ, Kim MH. The use of immunohistochemistry for IgG4 in the diagnosis of autoimmune pancreatitis: a systematic review and meta-analysis. Pancreatology 2020;20:1611-9.
59. Moon SH, Kim MH, Park DH, Song TJ, Eum J, Lee SS, et al. IgG4 immunostaining of duodenal papillary biopsy specimens may be useful for supporting a diagnosis of autoimmune pancreatitis. Gastrointest Endosc 2010;71:960-8.
60. Rebours V, Le Baleur Y, Cazals-Hatem D, Stefanescu C, Hentic O, Maire F, et al. Immunoglobulin G4 immunostaining of gastric, duodenal, or colonic biopsies is not helpful for the diagnosis of autoimmune pancreatitis. Clin Gastroenterol Hepatol 2012;10:91-4.
61. Dhall D, Suriawinata AA, Tang LH, Shia J, Klimstra DS. Use of immunohistochemistry for IgG4 in the distinction of autoimmune pancreatitis from peritumoral pancreatitis. Hum Pathol 2010;41:643-52.