Primary Sclerosing Cholangitis With Features of Autoimmune Hepatitis: Exploring the Global Variation in Management

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Patients with primary sclerosing cholangitis (PSC) frequently manifest features of autoimmune hepatitis (AIH). We sought to understand factors affecting expert management, with the goal of facilitating uniformity of care. A Survey Monkey questionnaire with four hypothetical cases suggesting a potential AIH/PSC variant was sent to hepatologists spanning global practices. Eighty responses from clinicians in 23 countries were obtained. Most of the respondents would request a liver biopsy, and stated that the cases presented could not be appropriately managed without a biopsy. Despite the fact that histology did not unequivocally support an AIH/PSC variant in three of the four cases, this diagnosis was reached by most of the respondents for all cases, except case 1, in which 49% were diagnosed with AIH/PSC. There was a wide variation of suggested medical treatment. For three cases, the most commonly chosen treatment options did not exceed 35%, indicating a lack management consensus. Most respondents would treat with ursodeoxycholic acid, despite current American Association for the Study of Liver Diseases guidelines, either alone or in combination with immunosuppression. European clinicians recommended ursodeoxycholic acid more frequently than their counterparts in North America (P < 0.05 in three out of four cases), who advocated the use of immunosuppression alone more commonly than Europeans (P = 0.005 in case 2).

Conclusions: We document a wide variation in clinical decision making in the context of managing patients with a potential AIH/PSC variant. Guidance, likely based on systematic studies arising from prospective registries, is needed to better address this difficult clinician problem.

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Primary sclerosing cholangitis (PSC) is a challenging disease for patients and clinicians. Its etiology remains unclear, and although underlying immunological mechanisms play an important role, there are a number of observations supporting nonautoimmune factors in disease course.1 Magnetic resonance cholangiopancreatography is used most commonly to diagnose PSC, usually alongside cholestatic serum liver tests. A varying proportion of patients with PSC will also over time show features of autoimmune hepatitis (AIH).2 Some patients will be diagnosed with an AIH/PSC variant (with treatment impact); however, criteria for diagnosis remain poorly defined.2-6 Interpretation of liver biopsy findings can vary. Portal inflammation and interface hepatitis, features used in the histological diagnosis of AIH, can be

Abbreviations: AIH, autoimmune hepatitis; AILD, autoimmune liver disease; AZA, azathioprine; IAIHG, International Autoimmune Hepatitis Group; IgG, immunoglobulin G; PSC, primary sclerosing cholangitis; UDCA, ursodeoxycholic acid.

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regarded as part of the normal spectrum of PSC, with a lack of guidelines concerning the nature and severity of histological inflammatory activity to suggest a diagnosis of AIH in a patient with PSC. The distinction between PSC and AIH/PSC variant is important in terms of management of a patient, and further adds complexity (and barriers) to the involvement of patients with PSC in clinical trials. To help evolve more consistency in the approach taken by clinicians, we report herein the factors presently affecting expert management.

Materials and Methods

STUDY DESIGN

Questionnaire

A survey questionnaire, applying the online Survey Monkey tool (https://www.surveymonkey.co.uk/r/psc_patients), was designed by a process of iterative review and consensus. Four clinical scenarios were provided describing adult patients with a definite cholangiographic diagnosis of PSC and features to suggest a potential AIH/PSC variant. Cases were designed with information about the clinical course, liver biochemistry, and histology. Summary data for clinical features and histology are given in Tables 1 and 2, and a full version of the questionnaire is found in Supporting Information 1. Participants were asked to respond to 29 questions. For each case, responses to standardized questions included the following:

(i) Would you request liver biopsy? If not, what is the reason?
(ii) Do you think the patient can be treated reliably without liver biopsy?
(iii) Would you perform elastography (FibroScan)?
(iv) How would you treat this patient? (For cases 1-3 there were nine treatment options; for case 4 there were six treatment options.)
(v) If you decide to treat this patient with corticosteroids, would you consider giving the patient budesonide?

For questions (i), (iii), (iv), and (v), participants had the option to make additional comments (Supporting Table S1). Respondents were also asked the following four additional, more general questions (Supporting Table S2):

(i) Do you broadly agree that AIH/PSC exists?
(ii) Do you broadly believe that immunosuppression can be clinically beneficial in AIH/PSC?
(iii) If you treat AIH/PSC, do you commit your patient to long-term immunosuppression?
(iv) Does your practice, to a large extent, reflect the unit where you were trained?

Respondents

A total of 196 members of the International Primary Sclerosing Cholangitis Study Group (IPSCSG)
were invited to participate in the survey; respondents were restricted to clinicians responsible for treatment decisions. Additional invitations were also sent to 20 hepatologists with a recognized special interest in autoimmune liver diseases (AILD) not on the IPSCSG e-mail list. Data were collected anonymously.

**TABLE 1. PATIENT DESCRIPTIONS**

| Characteristics          | Case 1       | Case 2       | Case 3       | Case 4       |
|--------------------------|--------------|--------------|--------------|--------------|
| Age (years)              | 32           | 26           | 34           | 32           |
| Gender                   | Male         | Female       | Male         | Female       |
| PSC on MRCP              | Yes          | Yes          | Yes          | Yes          |
| IBD; therapy             | Ulcerative colitis; 5ASA | Crohn’s disease; 5ASA | No, NA       | Ulcerative colitis; 5ASA |
| AST (U/L, n = 3-30)      | 45           | 345          | 445*/235†    | 205†/435§    |
| ALT (U/L, n = 3-30)      | 70           | 420          | 520†/270¹    | 235†/571‡    |
| ALP (U/L, n = 30-120)    | 196          | 222          | 622*321†     | 462*382§     |
| GGT (U/L, n = 3-30)      | 134          | 198          | 598*118†     | 397*217‡     |
| Bilirubin (mg/dL, n = 0.2-1.0) | Normal | Normal       | 7.8*/1.8†    | 1.3†/1.4§    |
| IgG (mg/dL, n = 700-1600) | 1960        | 2290         | 2390*2190²   | 1890†/2490³  |
| ANA (n < 1:80)           | 1:1200       | Negative     | 1:640*1:320³ | 1:160*1:320³ |
| SMA (n < 1:80)           | 1:160        | Negative     | 1:320*1:160³ | 1:80*1:640³  |

Note: Albumin, international normalized ratio, and IgG4 were normal in all patients. Antimitochondrial antibody and anti-liver kidney microsomal antibody were negative in all patients.

*Prior to endoscopic retrograde cholangiopancreatography.
†Two weeks after endoscopic retrograde cholangiopancreatography.
‡At the diagnosis of PSC 4 years ago.
§Current results.

Abbreviations: 5ASA, 5-aminosalicylic acid; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AMA, antimitochondrial antibody; ANA, antinuclear antibody; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; IBD, inflammatory bowel disease; LKM, anti-liver kidney microsomal antibody; MRCP, magnetic resonance cholangiopancreatography; NA, not applicable; PSC, primary sclerosing cholangitis; SMA, anti-smooth muscle antibody.

**TABLE 2. LIVER BIOPSY DESCRIPTIONS**

| Characteristic          | Case 1       | Case 2       | Case 3       | Case 4*       |
|--------------------------|--------------|--------------|--------------|--------------|
| Length                   | 26 mm        | 30 mm        | 32 mm        | 28 mm        |
| Number of portal tracts  | 18 portal tracts | 22 portal tracts | 24 portal tracts | 24 portal tracts |
| Biliary features         | Focal periductal fibrosis and bile duct loss consistent with PSC | Bile duct loss and features of chronic cholestasis consistent with PSC | Bile duct loss and features of chronic cholestasis consistent with PSC | Focal periductal fibrosis and bile duct loss consistent with PSC |
| Portal inflammatory changes | Moderately dense inflammatory infiltrate composed predominantly of lymphocytes | Moderately dense inflammatory infiltrate, which included a mixed population of lymphocytes and plasma cells | Moderately dense inflammatory infiltrate composed predominantly of lymphocytes | Dense infiltrate of inflammatory cells, which included large numbers of plasma cells |
| Interface activity and lobular changes | Moderate lymphocytic interface activity without obvious hepatocyte rosettes or emperipolesis | Moderate lymphocytic interface activity without obvious hepatocyte rosettes or emperipolesis | Moderate lymphocytic interface activity with occasional hepatocyte rosettes and focal emperipolesis | Moderate interface hepatitis with hepatocyte rosettes affecting 30% of the liver parenchyma and focal emperipolesis |
| Ludwig stage             | Ludwig stage 2: periporal fibrosis without bridging | Ludwig stage 3: periporal fibrosis with bridging | Ludwig stage 2: periporal fibrosis without bridging | Ludwig stage 3: periporal and bridging fibrosis falling short of progression to cirrhosis |

*Biopsy was reported as showing features compatible with PSC-AIH “overlap syndrome.”
DATA PRESENTATION AND ANALYSIS

The data obtained were analyzed using the graphical and analytical features of www.surveymonkey.com, Adobe Illustrator CS6 (Adobe Systems Inc., San Jose, CA), and Microsoft Excel 2016 (Microsoft Corp., Redmond, WA). Results are presented as counts and percentages for categorical variables. Fisher’s exact test was used for the analysis of contingency tables.

ETHICAL CONSIDERATIONS

This study was conducted according to the Declaration of Helsinki.

Results

In total there were 80 respondents from 23 countries spanning five continents (Fig. 1). Sixty-one respondents (76%) were male. Most worked either in tertiary hepatology transplant centers (n = 43; 54%) or in tertiary hepatology centers with no transplant program (n = 22; 28%). The remaining clinicians worked as hepatologists (n = 2; 3%), gastroenterologists (n = 3; 4%) in district general hospitals, or as office-based general gastroenterologists/hepatologists (n = 9; 11%). One respondent did not specify. Thirty-two (40%) physicians had more than 20 years of independent practice, and 25 (31%) practiced independently over a period of 11–20 years. The remaining 23 (29%) had
fewer than 10 years of independent practice. Female respondents had a significantly shorter period of independent practice (37% < 10 years and 16% > 20 years vs. 26% < 10 years and 48% > 20 years for males \( P = 0.002 \)). Fifty-eight (73%) respondents looked after up to 100 patients with PSC, and the remaining 22 (27%) looked after more than 100 patients, including 12 (15% of all respondents) who looked after more than 200 patients.

**LIVER BIOPSY AND ELASTOGRAPHY (FIBROSCAN)**

Responses related to the decision to request liver biopsy and whether analyzed cases could be managed reliably without biopsy were requested after initial clinical and laboratory features were presented (Fig. 2). For all four cases presented, most of the respondents indicated that they would request a liver biopsy, ranging from 56% in cases 1 and 3 to 95% in case 4 (Fig. 2A). Most of the respondents also stated that these patients could not be appropriately managed without liver biopsy, ranging from 51% in case 1 to 85% in case 4 (Fig. 2B). Some participants made additional comments indicating that they would need to follow the patient after initial treatment before they would decide to request a liver biopsy. Others suggested the need for a repeated biopsy during immunosuppressive treatment (Supporting Table S1).

Responses on the use of elastography are given in Table 3. Although most respondents indicated that they would use liver elastography as a tool for the estimation of fibrosis, they also emphasized a lack of validation of this method in patients with PSC. Several respondents suggested that high liver enzyme values reflecting inflammation and/or cholestasis could limit the accuracy of elastography (Supporting Table S1).

**FINAL DIAGNOSIS**

Participants were asked to provide a final diagnosis after they obtained all clinical, biochemical, serological, and histological data. These data are summarized in Fig. 2C. In case 1, the opinions regarding final diagnosis were divergent: 51% of participants diagnosed PSC, whereas the remaining 49% reached a diagnosis of AIH/PSC variant. For cases 2 and 3, a higher proportion of respondents diagnosed AIH/PSC variant (83% in case 2 and 76% in case 3), even though liver biopsy did not show all of the histological features considered to be typical of AIH according to the simplified International AIH Group (IAIHG) criteria. In case 4, in which liver biopsy showed the typical
features of AIH (interface hepatitis, rosettes, emperipolesis), virtually all respondents diagnosed AIH/PSC variant.

MANAGEMENT

After establishing a final diagnosis, respondents were asked to consider treatment options (Fig. 3 and Supporting Table S1). For all cases, most respondents indicated that they would treat patients with ursodeoxycholic acid (UDCA), either alone or in combination with immunosuppression (corticosteroids/azathioprine [AZA]). In terms of immunosuppression, prednisolone at a dose up to 30 mg in combination with AZA was mostly advocated. Among respondents who favored treating patients with corticosteroids, between 60% in case 4 and 71% in case 3 stated that they would consider budesonide instead of prednisolone, either from the beginning or in the future.

GENERAL QUESTIONS

Respondents broadly agreed that AIH/PSC variant exists (95%) and believed that immunosuppression can be clinically beneficial in such cases (80%) (Supporting Table S2). Most of the participants (76%) stated that they would treat the patients with long-term immunosuppression; however, they tended to withdraw corticosteroids and maintain their patients on AZA only. Some comments suggested mycophenolate mofetil as a therapeutic option. Others underlined the need for close follow-up to avoid side effects of immunosuppression.

RESPONSES ACCORDING TO CLINICIAN EXPERIENCE

Comparison between respondents (Supporting Fig. S1) with more than 20 years of experience and those with less than 10 years of experience showed

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**TABLE 3. USE OF ELASTOGRAPHY**

| Would You Perform FibroScan in This Patient? | Case 1 (%) | Case 2 (%) | Case 3 (%) | Case 4 (%) |
|---------------------------------------------|------------|------------|------------|------------|
| Yes, I consider it a reliable diagnostic tool in this patient | 23 | 17 | 18 | 14 |
| Yes, although the role of FibroScan in PSC has not yet been established | 61 | 39 | 37 | 44 |
| I would do it but have no access to FibroScan | 5 | 4 | 4 | 4 |
| No, this patient has high transaminases, which could make readings unreliable | 0 | 31 | 31 | 30 |
| No, FibroScan would not bring any clinically important information about this patient | 11 | 9 | 10 | 8 |

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**Final diagnosis and treatment**

| Final diagnosis and treatment | Case 1 (%) | Case 2 (%) | Case 3 (%) | Case 4 (%) |
|------------------------------|------------|------------|------------|------------|
| Stick to the diagnosis of PSC; no treatment | 12.5% | 5% | 8.9% | NA |
| Stick to PSC diagnosis; treat with UDCA 13-15 mg/kg.b.w. | 6.2% | 15% | 3.8% | 0% |
| Stick to PSC diagnosis; treat with UDCA 20-25 mg/kg.b.w. | 32.5% | 10% | 16.2% | 1.3% |
| AIH/PSC variant diagnosis; treat with UDCA 13-15 mg/kg.b.w., prednisolone up to 30 mg/daily | 6.2% | 15% | 3.8% | 0% |
| AIH/PSC variant diagnosis; treat with UDCA 13-15 mg/kg.b.w., prednisolone 60 mg/daily | 15% | 16.2% | 13.9% | 6.3% |
| AIH/PSC variant diagnosis; treat with prednisolone up to 30 mg/daily | 5% | 16.3% | 15.2% | 6.3% |
| AIH/PSC variant diagnosis; treat with prednisolone up to 60 mg/daily | 3.8% | 7.5% | 6.3% | 6.3% |
| AIH/PSC variant diagnosis; treat with prednisolone up to 30 mg/daily and azathioprine up to 2 mg/kg/b.w. | 0% | 1.3% | 1.3% | 3.8% |
| AIH/PSC variant diagnosis; treat with prednisolone up to 30 mg/daily and azathioprine up to 2 mg/kg/b.w. | 7.5% | 8.8% | 10.1% | 15.2% |
| Other suggestions | 17.5% | 32.5% | 29.1% | 39.2% |

**FIG. 3.** Final diagnosis and related treatment options.
that for case 1, those more experienced were less likely to do a liver biopsy (44% vs. 78%; P = 0.01) and thought that the patient could be reliably managed without biopsy (62% vs. 30%; P = 0.03). A minority of experienced hepatologists diagnosed AIH/PSC variant in this patient (42%) versus 70% of less-experienced clinicians (P = 0.06). For cases 2 and 4, the responses regarding the use of liver biopsy and final diagnosis were more consistent between the groups with different levels of experience. The vast majority of respondents would perform liver biopsy, regardless of professional experience (over 80% in case 2 and near 100% in case 4). For case 3, the opinions were more divided. About half of the experts would perform liver biopsy, but another half would not, regardless of years of experience (data not shown).

There was also no difference with respect to the final diagnosis in cases 2-4, in which mostly AIH/PSC variant would be diagnosed by both subgroups of professionals. Treatment with budesonide in case 4 was considered by 71% of more experienced, and only 39% of less experienced respondents (P = 0.02).

RESPONSES DEPENDING ON PRACTICE FEATURES

North American and European respondents indicated that they would use liver biopsy and elastography as diagnostic tools in similar proportions. Comparison between respondents from Europe and North America showed that European experts were more likely to use UDCA, regardless of the final diagnosis (PSC or AIH/PSC variant). The proportions were as follows: 81% versus 50% (P = 0.015) in case 1, 83% versus 50% (P = 0.011) in case 2, and 78% versus 50% (P = 0.034) in case 4 (Supporting Fig. S2). In addition, in case 2, North American respondents were significantly more likely to treat with corticosteroids with or without AZA only (44% vs. 11%; P = 0.005).

Comparison of responses provided by participants working in transplant units versus those working in nontransplant centers showed no difference in management decisions. Respondents who looked after more than 200 patients, when compared with those who looked after fewer than 50, were less likely to do a biopsy in case 1 (25% vs. 71%; P = 0.007).

Discussion

Patients with typical cholangiographic features of PSC may present with, or develop over time, variable features more classically seen in AIH. Efforts to improve the clinical management of patients would be augmented by more agreement on approaches to the diagnosis of overlap syndromes. Formal evaluation of physician perspectives is lacking, adding challenges to those charged with writing guidelines to provide advice that mirrors practice.

The persistent confusion regarding AILD overlap variants is inherent to a disease area in which etiology is not known; clinicians therefore reach a diagnosis of exclusion and apply a Bayesian approach to test the interpretation (inference begets inference), at the same time recognizing the inherent variation within-AILD and between-AILD for relevant markers such as serum liver test profiles, immunoprofiles, and liver histology. Additionally, as variants are considered infrequently, added complex investigations are requested only in a selected patient population (i.e., skewed), in whom there is a clinical deviation from “normal” presentation. This ensures that a true denominator of the pattern of disease manifestations is not necessarily recognized or used when subsequently interpreting results. This is particularly the case for PSC, for which routine use of liver biopsy is not practiced diagnostically; thus, clinicians are not exposed potentially to the normal range of interface hepatitis severity seen in PSC. Equally, liver biopsy remains an important investigation that, within its own limitations (e.g., localization of disease, heterogeneous disease features, sample size), is often used as the arbiter of diagnosing variant syndromes.

Our study raises important observations concerning the role of liver biopsy in this setting. In clinical practice there is likely to be a hierarchy in the interpretation of investigations (particularly the wording of pathology reports), and it is possible that liver biopsy findings are weighted more heavily than other investigations. This may reflect a carryover from the use of histology in diagnosing malignancy, in which the pathological diagnosis is usually absolute. It is inappropriate to apply this paradigm to AILD, which lacks a single diagnostic criterion. Although liver biopsy provides information concerning the nature, location, and severity of inflammation, which cannot be obtained by noninvasive investigations, it is not clear
how histological findings should inform decisions relating to the diagnosis and management of AIH-like features in patients with PSC. Of note, although significant pathology input existed in the study team, this survey did not involve pathologists. In furthering efforts to improve the consistency of approaches to managing AIH/PSC variants, greater collaboration between pathologists and clinicians is needed, to combine the details, context, and commentary that help clinicians maximize the use of biopsy findings that are pertinent to treatment decisions. The hypothetical liver biopsies described in the four cases presented here were all adequate in terms of recommended guidelines for portal tract numbers. Many liver biopsies obtained in practice are suboptimal in this respect, which may cause additional problems with sampling variability related to disease heterogeneity.

Case 4 had the strongest indication for obtaining a liver biopsy; indeed, almost all respondents indicated that they would request a liver biopsy in this scenario. However, in the three other cases in which all patients could be confidently diagnosed with PSC according to current guidelines, a large proportion of respondents also stated that they would request a biopsy. Interestingly, in all three of these cases, the liver biopsy findings did not show all three of the features that are regarded as being typical of AIH according to the simplified criteria proposed by the IAIHG (i.e., interface hepatitis, hepatocyte rosettes, and emperipolesis). The simplified IAIHG criteria were devised for patients with classical AIH, and the extent to which these may be relevant for diagnosing AIH-like features in patients with a primary diagnosis of chronic biliary disease (primary biliary cholangitis or PSC) is unclear.

Case 1 is of particular interest, as it showed a significant difference in the clinical approach between very experienced clinicians (more than 20 years of independent practice) and those who were less experienced (less than 10 years of independent practice). Not only did it show that very experienced practitioners tend to refer their patients for liver biopsy significantly less frequently (discussed subsequently), but also that most of them stated that this patient can be reliably managed without biopsy. More experienced hepatologists also differed in their final diagnosis in this patient, as only a minority of them diagnosed AIH/PSC variant (42%) compared to 70% of practitioners with less experience. This case highlights well the clinical impact of the practical difficulties related to the differential between PSC and AIH/PSC variant. All of the cases presented had an elevated immunoglobulin G (IgG), and this parameter is not of particular use as it can be elevated in both AIH and PSC.

Our results confirm that existing guideline advice for clinicians is inadequate for patients, as evidenced by the overt heterogeneity in responses. Guideline definitions remain a challenge, and this is largely due to a lack of true comparative studies. According to guidelines, “AIH/PSC variant can be diagnosed in a patient with cholangiographic or histological features of PSC alongside robust biochemical, serological and histological features of AIH”. Clearly, what is robust for one clinician is not necessarily robust for another. The subjectivity we demonstrate matters for patients at risk of receiving therapy without necessarily gaining benefit but potentially with risk, and equally may disqualify them from trials of new therapies aimed at changing the outcome of the PSC. At each point in the patient’s evaluation, clinician interpretation and bias is evident; resolving such bias by better understanding practice is therefore of practical relevance to improving care in the long term, alongside improving diagnostic markers of autoimmune liver injury.

Overlap features generate concern for less-specialized gastroenterologists and hepatologists, which frequently leads to referral to tertiary programs. For this reason, although the survey was broad in its remit, we ensured an appropriate level of expertise in the respondents. This approach has been used for AIH in a similar manner. A total of 80 responses were obtained from 23 countries and five continents; thus, this analysis reflects a global view. In fact, all cases would grossly fulfill the criteria for diagnosing PSC alone, as the presence of autoantibodies (in up to 90% of patients), elevated IgG (in up to 60% of patients), and elevation of transaminases are all considered to be a part of the normal clinical course of PSC.

Our survey also showed that the most experienced respondents (i.e., those who work as independent practitioners for more than 20 years and look after more than 200 patients) were significantly less likely to request a biopsy. The reason for this is unclear. It may reflect the fact that older and more experienced physicians tend to request fewer investigations. Alternatively, more experienced physicians may be more pragmatic in treatment decision making or
have personal experience with biopsy not being contributory and/or treatment based on biopsy findings not being apparently successful. It would appear that less-experienced respondents were more likely to rely on liver biopsy to establish their final diagnosis.

Interpretation of liver elastography in patients with liver inflammation remains the subject of discussion and controversy. It has been found that the presence of inflammation may make readings artificially high. This controversy has been reflected in our survey. In cases with significantly elevated transaminases, about one-third of the respondents would not perform elastography. Between 34% and 60% of participants would perform elastography; however, they acknowledge the fact that the role of this diagnostic modality remains to be fully elucidated. Across all cases, around one-tenth of the respondents stated that they would not request elastography at all and that they did not find it useful in this setting. Previous studies on using elastography in both PSC and AIH focused primarily on establishing thresholds for diagnosing liver cirrhosis.

We found that most respondents use UDCA in their treatment of PSC, which is not in keeping with American Association for the Study of Liver Disease Guidelines. Experts from Europe were more likely to use UDCA in all analyzed cases, with around 80% of them choosing this therapy as compared to 50% respondents from North America; these differences reached statistical significance in three out of four analyzed scenarios. Interestingly, the same guidelines recommend using corticosteroids and other immunosuppressive agent with no UDCA for medical therapy in AIH/PSC variants. Only a minority of participants would follow this recommendation: 11% in case 1, 18% in cases 2 and 3, and 25% in case 4. In the latter, almost half of the experts from North America would choose this option as compared with only one-tenth of European respondents. As this is indicative of the clinical challenges seen in practice, our analysis shows that many respondents do believe that AIH/PSC variant exists and that immunosuppression may be of benefit in patients. Two-thirds of respondents would treat their patients with long-term immunosuppression. Our study showed that a significant proportion of respondents who decided to treat their patients with corticosteroids would use budesonide instead of prednisolone. This option was more frequently chosen by more experienced respondents, particularly in case 4. This observation suggests that specialists treating larger groups of patients are clearly equally cognizant of corticosteroid side effects.

In conclusion, we report a global survey on the management of patients with PSC and features of AIH that demonstrates marked variability in practice. Inevitably, our study is limited by its design. Nevertheless, it contains important real-world data on approaches to care, and highlights the need for more standardized approaches to managing patient unmet need. The variations in practice demonstrated by our study have an ongoing impact on routine patient care as well as the design and delivery of international clinical trials of primary therapy for PSC. Systematic studies, based on prospectively collected data in adequately designed registries, could be of potential help in solving this important clinical issue.

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Supporting Information

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