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# Dominant Strictures in Primary Sclerosing Cholangitis: A Multicenter Survey of Clinical Definitions and Practices

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Dominant strictures (DSs) of the biliary tree occur in approximately 50% of patients with primary sclerosing cholangitis (PSC) and may cause significant morbidity. Nevertheless, the definition and management of DSs lacks consensus. We aimed to better understand current perceptions and practices regarding PSC-associated DSs. We conducted an anonymous, 23-question, survey-based study wherein electronic surveys were distributed to 131 faculty in the Division of Gastroenterology and Hepatology at the three Mayo Clinic campuses (Rochester, Scottsdale, and Jacksonville) as well as the affiliated practice network. Responses were aggregated and compared, where applicable, to practice guidelines of the American Association for the Study of Liver Diseases and European Association for the Study of the Liver. A total of 54 faculty (41.2%) completed the survey, of whom 24 (44.4%) were hepatologists, 21 (38.9%) gastroenterologists, and 9 (16.7%) advanced endoscopists. One of the major study findings was that there was heterogeneity among participants' definition, evaluation, management, and follow-up of DSs in PSC. The majority of participant responses were in accordance with societal practice guidelines, although considerable variation was noted. *Conclusion:* Despite the prevalence and morbidity of DSs in PSC, clinical perceptions and practices vary widely among hepatologists, gastroenterologists, and advanced endoscopists who manage these patients, even within a single health care system. Further studies are needed to address these variations, develop general and evidence-based consensus, and increase adherence to societal guidelines. (*Hepatology Communications* 2018;2:836-844)

**P**rimarily sclerosing cholangitis (PSC) is an idiopathic, fibro-inflammatory, cholestatic liver disease that can affect both the intrahepatic and extrahepatic biliary ductal systems.<sup>(1-3)</sup> PSC follows a progressive course that can culminate in cirrhosis, portal hypertension, liver failure, and/or cholangiocarcinoma (CCA). Median transplant-free survival from time of PSC diagnosis is variable, ranging from

approximately 12-21 years in most studies, with more recent estimates being toward the top end of this range.<sup>(4-8)</sup> It has been reported that 40%-58% of patients with PSC will develop focal high-grade strictures, referred to as a "dominant stricture" (DS), during the course of disease.<sup>(5,9-12)</sup> Patients with a DS may remain asymptomatic or may present with worsening serum liver tests, abdominal pain, and/or

*Abbreviations:* AASLD, American Association for the Study of Liver Diseases; CA 19-9, carbohydrate antigen 19-9; CCA, cholangiocarcinoma; DS, dominant stricture; EASL, European Association for the Study of Liver Diseases; ERC, endoscopic retrograde cholangiography; FISH, fluorescence in situ hybridization; PSC, primary sclerosing cholangitis.

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cholangitis.<sup>(9)</sup> Even if asymptomatic, a DS may not be without clinical consequence; indeed, studies suggest that its mere presence is associated with poorer prognosis in PSC.<sup>(13,14)</sup>

Despite the prevalence and clinical significance of DSs in PSC, consensus is lacking regarding the definition of a DS, the indications for and optimal means of endoscopic intervention, and periprocedural management and follow-up. Even within our own institution, a major referral center for patients with PSC, considerable variation among clinicians has been observed in this regard. Therefore, in the present multicenter study, we surveyed practicing hepatologists, gastroenterologists, and advanced endoscopists to assess current clinical perceptions and practices employed in managing DSs. Where applicable, we compared survey responses to societal guidelines published by the American Association for the Study of Liver Diseases (AASLD) and European Association for the Study of Liver Diseases (EASL).

## Materials and Methods

A 23-question, anonymous, electronic survey of DS-related definitions, perceptions, and practices as well as participant characteristics was developed by a multidisciplinary panel comprised of the study investigators (Table 1). The survey was electronically distributed to 131 faculty in the Division of Gastroenterology and Hepatology at the three major Mayo Clinic campuses (Minnesota, Arizona, and Florida) and to the Mayo affiliated practice network, which included hepatologists, gastroenterologists, and advanced endoscopists. Responses were securely downloaded for descriptive and statistical analyses. This study was

approved by the Mayo Clinic Institutional Review Board.

## STUDY VARIABLES

The survey contained the following questions regarding professional information and background: primary institution site, primary subspecialty, years in practice after fellowship training, number of patients with PSC cared for in the previous 12 months, number of endoscopic retrograde cholangiography (ERCs) requested for patients with PSC in the previous 12 months, number of ERCs performed on patients with PSC in the previous 12 months, and percentage of time spent in patient care and research activities. The remainder of the 23 survey questions were directly related to DSs in PSC.

## DATA ANALYSIS

Descriptive analyses were performed for the overall study cohort. Participant responses were examined in aggregate and, where applicable, compared to practice guidelines of the AASLD and EASL.

## Results

A total of 54 faculty completed the survey. In the following subsections, we summarize and present responses to survey questions grouped by topic.

## PARTICIPANT CHARACTERISTICS

Forty-three participants (82%) were employed at one of the three major Mayo Clinic sites, while 12% of respondents worked at sites within the affiliated

### ARTICLE INFORMATION:

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TABLE 1. SURVEY QUESTIONS AND RESPONSES

Question	Responses
1. Please select your primary institutional affiliation.	
a. Mayo Clinic Rochester	26 (49%)
b. Mayo Clinic Scottsdale	13 (25%)
c. Mayo Clinic Jacksonville	4 (8%)
d. Mayo affiliated practice network	10 (19%)
2. Which of the following best represents your primary subspecialty?	
a. Gastroenterology	21 (39%)
b. Hepatology	24 (44%)
c. Advanced Endoscopy	9 (17%)
3. How many years have you been in practice (post-fellowship training)?	18 (10-25)
4. Over the past 12 months, how many PSC patients have you cared for in clinic or in the hospital?	2.5 (4-30)
5. Over the past 12 months, how many endoscopic retrograde cholangiograms (ERCs) have you ordered on patients with PSC?	12.5 (26.9)*
6. Over the past 12 months, how many ERCs have you performed on patients with PSC?	11.9 (39.0)*
7. Over the past 12 months, what percentage of your time have you spent in patient care activities?	82.5% (47.5%-90%)
8. Over the past 12 months, what percentage of your time have you spent in research activities?	12.5% (5%-25%)
9. Which of the following features would you consider necessary in order to consider a biliary stenosis a "dominant stricture"? (Select all that apply).	
a. Stenosis diameter of less than 1.5 mm in the common bile duct or less than 1 mm in a hepatic duct.	52.17%
b. Stenosis length greater than 1 cm.	28.26%
c. Upstream (i.e. proximal) bile duct dilatation.	58.7%
d. New or worsening cholestatic serum biochemical profile.	58.7%
e. Pruritis.	19.57%
f. Fever.	21.74%
g. Jaundice	26.09%
10. Would you consider the following a reasonable definition of a dominant stricture: "An extrahepatic, hilar, or intrahepatic duct stenosis, regardless of length or diameter, with upstream bile duct dilatation and new or worsening cholestatic serum liver tests."	
a. Yes.	84.78%
b. No.	15.22%
11. Should serum carbohydrate antigen 19-9 (CA 19-9) be measured in PSC patients with a dominant stricture?	
a. Yes.	84.78%
b. No.	15.22%
12. Should PSC patients with incidental (i.e. asymptomatic) dominant strictures on cross-sectional imaging undergo initial management with ERC?	
a. Yes.	61.70%
b. No.	38.30%
13. Should PSC patients with dominant strictures on cross-sectional imaging and signs and/or symptoms of biliary obstruction (e.g. new pruritis) undergo initial management with ERC?	
a. Yes.	97.83%
b. No.	2.17%
14. Which one of the following therapeutic options should a PSC patient with a dominant stricture have performed during ERC?	
a. Stricture dilation only.	2.17%
b. Stricture stenting only.	2.17%
c. Stricture dilation with or without stenting.	95.65%
15. In a PSC patient with a dominant stricture undergoing ERC, which of the following would you order/perform to rule out underlying hepatobiliary malignancy?	
a. Biliary brush cytology.	91.30%
b. Biliary ductal biopsy.	78.26%
c. Fluorescence in situ hybridization (FISH) on brushing specimens.	84.78%
d. Cholangioscopy.	30.43%
e. Probe-based confocal laser endomicroscopy.	2.17%
f. Other advanced imaging modality.	2.17%
16. Should biliary brush cytology and/or endoscopic biopsy be obtained before or after biliary balloon dilation during ERC?	
a. Before.	28.26%
b. After.	15.22%
c. There is insufficient evidence to support one over the other.	56.52%

TABLE 1. CONTINUED

Question	Responses
17. If multiple dominant strictures located in separate areas of the biliary tree (e.g. right and left hepatic ducts) are present and brushed, should the brush cytology specimens be placed in separate containers?	
a. Yes.	80.00%
b. No.	4.44%
c. There is insufficient evidence to support one over the other.	15.56%
18. Should pre-procedural antibiotics be prescribed to all PSC patients undergoing ERC?	
a. Yes.	75.56%
b. No.	24.44%
19. Should post-procedural antibiotics be prescribed to all PSC patients undergoing ERC?	
a. Yes.	77.78%
b. No.	22.22%
20. Which of the following is the most appropriate duration of post-procedural antibiotics in PSC patients without overt acute cholangitis who undergo ERC?	
a. 3 days.	24.44%
b. 5 days.	31.11%
c. 7 days.	4.44%
d. 10 days.	0.00%
e. The duration should vary depending on the circumstance, i.e. there is no single standard.	40.00%
21. Which of the following would influence the duration of post-ERC antibiotics? (Select all that apply).	
a. Location of the dominant stricture.	20.00%
b. Degree of residual biliary obstruction at the end of the ERC.	71.11%
c. Severity of underlying liver disease (e.g. fibrosis stage).	20.00%
d. Degree of endoscopic manipulation (e.g. extent of contrast injection, aggressiveness of balloon dilation).	64.44%
e. Presence of acute cholangitis or pyobilia.	88.89%
f. History of prior post-ERC cholangitis.	73.33%
g. Other (please specify): depends on the endoscopist	2.22%
22. Which of the following intervals should PSC patients with a dominant stricture and negative biliary brush cytology and FISH results undergo a repeat ERC (assuming successful balloon dilation and no biliary stent placement)?	
a. Repeat ERC is not indicated based on these results.	51.11%
b. 1 month.	8.89%
c. 3 months.	15.56%
d. 6 months.	17.78%
e. 12 months.	6.67%
23. In PSC patients with a dominant stricture who have undergone placement of a 10 French plastic biliary stent, at which of the following interval should a repeat ERC be performed (assuming no prophylactic pancreatic duct stent)?	
a. 7 days.	0.00%
b. 14 days.	6.82%
c. 3-4 weeks.	18.18%
d. 2-4 months.	75.00%

Data reported as median (interquartile range) or n (%) unless otherwise specified.

\*Reported as mean (SD).

practice network. Twenty-four participants (44%) self-identified as hepatologists, while 21 (39%) identified as gastroenterologists and 9 (17%) as advanced endoscopists. The median number of years in practice after fellowship was 18 (interquartile range, 10-25 years). Participants devoted an average of 82.5% of their time to direct patient care activities. The average number of patients with PSC cared for differed significantly between gastroenterologists and advanced endoscopists (9.95 versus 50). The average number of ERCs ordered by hepatologists was significantly higher than the number ordered by gastroenterologists (23.8 versus 2.26). There were no significant differences in the average number of patients with PSC cared for, ERCs

ordered, or ERCs performed among the different Mayo affiliations. Additional participant characteristics are shown in Table 1.

## DEFINITION AND FEATURES OF A DS

Participants were asked which of the following endoscopic and clinical features were necessary to define a biliary stenosis as a DS: i) stenosis diameter  $\leq 1.5$  mm in the common bile duct or  $\leq 1$  mm in a hepatic duct; ii) stenosis length  $> 1$  cm, iii) upstream (i.e., proximal) bile duct dilatation; iv) new or worsening cholestatic serum biochemical profile; v) pruritus;

vi) jaundice; or vii) fever. A majority of participants indicated that stenosis diameter (52%), proximal bile duct dilatation (59%), and new or worsening cholestatic biochemistries (59%) were necessary in defining a DS, and 85% concurred that the following represented a reasonable definition of a DS in PSC: "An extrahepatic, hilar, or intrahepatic duct stenosis, regardless of length or diameter, with upstream bile duct dilatation and new or worsening cholestatic serum liver tests."

## EVALUATION OF AND PERIPROCEDURAL CONSIDERATIONS IN DSs

Twenty-nine participants (62%) indicated that they would recommend ERC in patients with PSC and an asymptomatic DS detected on cross-sectional imaging, and 45 participants (98%) indicated they would proceed with ERC if signs or symptoms of biliary obstruction were present. Fifty-two participants (96%) would perform both endoscopic dilatation and stenting of a DS, while 2% would perform endoscopic dilatation only and 2% would perform stenting only.

Seventy-six percent of participants favored administering antibiotics to patients with PSC prior to performing ERC, and 78% indicated they would recommend administering postprocedural antibiotics to patients with PSC. Forty percent of participants indicated that the optimal duration of antibiotics depends on the circumstances, while the remainder practiced a standardized approach (24% recommended a 3-day course, 31% a 5-day course, and 4% a 7-day course of postprocedural antibiotics). Factors considered when deciding the length of antibiotics were (in descending order): presence of acute cholangitis or pyobilia (89%), history of prior post-ERC cholangitis (73%), degree of residual biliary obstruction at completion of ERC (71%), degree of endoscopic manipulation (e.g., extent of contrast injection, aggressiveness of balloon dilatation) (64%), location of the DS (20%), and severity of the underlying liver disease (20%). Assuming successful balloon dilatation and no biliary stent placement, 23 respondents (51%) indicated they would not repeat ERC in patients with PSC and a DS with negative biliary brush cytology and fluorescence *in situ* hybridization (FISH) results, whereas the remainder would recommend a repeat ERC at some point between 1 and 12 months later. Following placement of a 10-French plastic biliary stent (without prophylactic pancreatic stent placement), 33 respondents (75%)

indicated they would recommend a repeat ERC between 2 and 4 months later, 18% 3-4 weeks later, and 7% 2 weeks later.

## DIAGNOSTIC TESTING TO RULE OUT UNDERLYING MALIGNANCY IN DSs

Thirty-nine participants (85%) replied that their practice is to assess levels of serum carbohydrate antigen 19-9 (CA 19-9) in patients with PSC and a DS. Biliary brush cytology (91%), biliary ductal biopsy (78%), and FISH (85%) were the most commonly recommended endoscopic tests employed to rule out underlying malignancy. Cholangioscopy (14%), probe-based confocal laser endomicroscopy (1%), and other advanced endoscopic imaging modalities (1%) were infrequently recommended. The majority of participants (57%) indicated that there was insufficient evidence to recommend obtaining biliary brush cytology/biopsy before as compared to after biliary balloon dilatation.

## SURVEY RESULTS COMPARED TO SOCIETAL GUIDELINES

Six of the questions in the study survey had components addressed by AASLD and/or EASL practice guideline recommendations. Participant responses and corresponding societal guidelines are shown in Table 2.

### Definition of a DS

Both AASLD and EASL guidelines define a DS as a "stenosis <1.5 mm in diameter in the common bile duct and <1 mm in the right and left hepatic ducts."<sup>(10,11,15)</sup> While most participants agreed with these diameter cutoffs, nearly 48% did not deem them necessary to consider a biliary stenosis a DS and instead placed emphasis on other factors (e.g., upstream ductal dilation).

### Evaluation and Management of DSs

AASLD and EASL guidelines both recommend (endoscopic) therapy for DSs in patients with significant cholestasis or other symptoms secondary to a DS (e.g., pruritus, cholangitis). AASLD guidelines specify that brush cytology and/or endoscopic biopsy should be obtained as part of endoscopic intervention in order to exclude superimposed malignancy; these were

TABLE 2. SURVEY RESPONSES COMPARED TO SOCIETAL PRACTICE GUIDELINES

	AASLD	EASL
3. Should serum carbohydrate antigen 19-9 (CA 19-9) be measured in patients with PSC with a dominant stricture? 84.8% yes	Check if clinical suspicion for hilar CCA.	Serum CA 19-9 combined with cross-sectional liver imaging may be useful as a screening strategy.
4. Should patients with PSC with: a. incidental (i.e., asymptomatic) dominant strictures undergo initial management with ERC? 61.7% yes b. dominant strictures on cross-sectional imaging and signs and/or symptoms of biliary obstruction (e.g., pruritus) undergo initial management with ERC? 97.8% yes	It is generally agreed that patients with symptoms from dominant strictures, such as cholangitis, jaundice, pruritus, right upper quadrant pain, or worsening biochemical indices, are appropriate candidates for therapy.	Dominant bile duct strictures with significant cholestasis should be treated with biliary dilatation.
6. In a PSC patient with a dominant stricture undergoing ERC, which of the following would you order/perform to rule out underlying hepatobiliary malignancy? 91.3% biliary brush cytology 84.8% FISH on biliary brushings 78.3% biliary biopsy 30.4% cholangioscopy 2.2% probe-based confocal laser endomicroscopy	In patients with clinical suspicion of hilar CCA (e.g., dominant stricture), CA 19-9 serum analysis, ERC, and conventional as well as FISH analysis (where available) of endoscopically obtained biliary brushings of suspicious areas should be performed.	Brush cytology sampling, and biopsy when feasible, during ERC adds to the diagnostic accuracy of CCA in PSC, but methodological refinement, including validation of digital image analysis (DIA) and fluorescence <i>in situ</i> hybridization (FISH) of cell samples is needed.
9a. Should pre- or post-procedural antibiotics be administered in the setting of ERC? 75.6% yes	Because injecting contrast agent into an obstructed duct may precipitate cholangitis, perioperative antibiotics should be administered.	Prophylactic antibiotic coverage is recommended in this setting [of ERC].
9b. Should post-procedural antibiotics be administered in the setting of ERC? 77.8% yes		

recommended by 93.5% and 80.4% of participants, respectively. Both societal guidelines acknowledge the effectiveness of balloon dilatation and recommend stent insertion only in those cases that are refractory to dilatation, given the need for stent exchange and increased risk of complications; 95.7% of participants appeared to concur with this recommendation. Both societal guidelines also recommend administration of periprocedural antibiotics but do not specify duration; notably, nearly a quarter of survey participants indicated that they would not administer preprocedural or postprocedural antibiotics.

## Detection of CCA in DSs

AASLD and EASL guidelines both recommend multimodal approaches to detect CCA in patients with PSC and DSs. Both guidelines acknowledge limitations in the use of CA 19-9 as a screening modality for CCA in PSC. EASL guidelines conclude from these limitations that although “median levels of the serum tumor marker carbohydrate antigen 19-9 are higher in PSC patients with CCA than in those without. . .in the individual case, CA 19-9 cannot be relied

upon in the differential diagnosis between PSC with and without CCA.” AASLD guidelines assert utility of CA 19-9 in assessing for CCA in symptomatic patients where CCA is suspected. According to these guidelines, appropriate evaluation of patients with clinical suspicion of hilar CCA consists of serum CA 19-9 analysis in combination with cross-sectional magnetic resonance imaging and ERC with brushing for conventional cytology and FISH analysis where available. EASL guidelines more generally recommend that “ERC with brush cytology (and/or biopsy) sampling should be carried out when clinically indicated.” At least 85% of participants responded in agreement with societal recommendations pertaining to these aspects of CCA detection in DSs.

## Discussion

Development of a DS is a common complication of PSC that can portend a diagnostic challenge as well as significant morbidity and mortality.<sup>(16-18)</sup> Nevertheless, consensus on the definition of a DS, indications for and means of further evaluation and treatment, and appropriate follow-up has yet to be established. The goal of this

study was to better define and understand perceptions regarding and management approaches to DSs in PSC among hepatologists, gastroenterologists, and advanced endoscopists. The findings of this study demonstrate heterogeneity in clinical practice with respect to: (1) criteria required to define a DS, (2) evaluation and periprocedural management of a DS, (3) methods used to assess for underlying CCA, and (4) adherence to specific aspects of societal practice guidelines.

The AASLD and EASL largely concur on the definition of a DS as a stenosis with a diameter  $<1.5$  mm in the common bile duct or  $<1$  mm in a hepatic duct. The present study reveals a tendency in clinical practice to also rely on additional parameters to qualify a biliary stenosis in PSC as a DS; indeed, many of the clinicians surveyed considered stricture length and the presence of proximal biliary dilatation, cholestatic laboratory profile, pruritus, fever, and/or jaundice as important features when qualifying a biliary stenosis as a DS (although these are not required by societal guidelines). How the reliance on these additional parameters impacts the accuracy of designating a biliary stricture as a true DS is unknown, as is any potential impact on management, but it is conceivable that it would increase specificity. To this end and in light of the apparent heterogeneity in clinicians' perceptions, a more widely applied consensus definition may well be beneficial for both patient care and research studies.

Beyond the question of whether a biliary stenosis represents a DS, the diagnostic difficulty posed in detecting potential underlying CCA in a DS remains a clinical challenge. ERC with biliary balloon dilatation and/or stenting as well as biliary cytology brushing is frequently employed in the evaluation and management of DSs and may yield clinical benefit and valuable diagnostic information.<sup>(9,19-26)</sup> Indeed, a study by Baluyut et al.<sup>(18)</sup> of 63 asymptomatic and symptomatic patients with PSC and a DS who underwent endoscopic therapy with balloon dilatation revealed improved 5-year survival as estimated by the Mayo Risk Score; this study and others<sup>(18,27)</sup> suggest that endoscopic intervention for DSs may confer a sustained benefit and potentially alter the natural history of PSC. As such, there is general recommendation that endoscopic intervention be undertaken in patients with a DS in the presence of worrisome signs or symptoms, such as cholangitis, new or worsening pruritus, jaundice, right upper quadrant pain, or cholestatic laboratory profile.<sup>(15,25,26,28)</sup> The role of endoscopic intervention for asymptomatic DSs (i.e., in the absence of related signs or symptoms) is less clear, although it is not uncommon to see patients undergo multiple ERCs in this clinical

scenario. However, given the risk of ERC in PSC (7.3%-20%)<sup>(18,29)</sup> and the uncertain benefits (at least in patients without signs or symptoms of DS), additional studies are needed to determine the impact of endoscopic therapy on the natural history and survival in PSC, especially in the absence of biliary obstructive symptoms.<sup>(30)</sup>

Patients with PSC are at increased risk for hepatobiliary cancers, especially CCA,<sup>(31)</sup> with recent studies reporting a 10-year cumulative incidence of 7%-9%.<sup>(32-34)</sup> As CCA may present morphologically and clinically as a DS, such lesions must be thoroughly investigated to rule out underlying malignancy. Multimodal approaches, including a combination of laboratory tests, cross-sectional imaging, and endoscopic testing, are frequently required for this purpose. Use of serum CA 19-9 in combination with ultrasonography, computed tomography, or magnetic resonance imaging has been reported to have a sensitivity of 91%, 100%, and 96%, respectively (when at least one modality is positive).<sup>(35)</sup> Conversely, individual tests generally have suboptimal performance characteristics. For example, conventional brush cytology has excellent specificity (nearly 100%) but limited sensitivity (ranging from 18%-40%) in diagnosing CCA.<sup>(15,35-39)</sup> Similarly, while serum CA 19-9 has a reported sensitivity and specificity of 79% and 98%, respectively, at a cut-off value of 130 U/mL,<sup>(40)</sup> its levels may become elevated in the setting of nonmalignant obstruction or acute cholangitis, and it is undetectable in Lewis blood antigen-negative patients (and remains so even in the presence of CCA).<sup>(41)</sup> Based on the aforementioned, both AASLD and EASL guidelines recommend obtaining endoscopic biliary brushings if CCA is suspected in patients with PSC.<sup>(15)</sup> In addition, EASL guidelines recommend supplementing biliary brushings with serum CA 19-9 and FISH analysis (where available) given their ancillary value.<sup>(42)</sup> The present study reveals general acceptance of this recommendation in clinical practice, with 91%, 78%, and 85% of participants recommending biliary brush cytology, biopsy, and FISH analysis, respectively, in patients with PSC and a DS. Further studies and guidelines regarding appropriate evaluation of DSs to rule out CCA will be needed with the advent of new endoscopic and cytologic techniques, including but not limited to digital cholangioscopy and touch imprinting cytology.<sup>(26,43-45)</sup> Recent studies suggest that patients with PSC with isolated biliary FISH polysomy have better clinical outcomes compared with patients with polysomy on repeat FISH testing,<sup>(34)</sup> suggesting that FISH analysis may be useful in risk stratification and designation of appropriate follow-up. Importantly, societal practice guidelines are currently



lacking regarding the need and appropriate interval for repeat ERC in patients with PSC and a DS after negative biliary brush cytology and FISH results. Our study reveals significant heterogeneity of practice in this regard, with 51% of participants indicating that repeat ERC is not indicated and 49% of participants recommending a repeat study between 1 to 12 months later.

Instrumentation of the biliary tree and injection of contrast have the potential to precipitate infection, particularly in PSC. Both AASLD and EASL guidelines therefore recommend periprocedural antibiotics in the setting of endoscopic dilatation with or without stent placement.<sup>(15)</sup> Optimal antibiotic choice and duration of treatment are not specified in the guidelines, and the present study reveals heterogeneity in practice. A majority of participants favored administration of either preprocedural or postprocedural antibiotics (75.6% and 77.8%, respectively), although the duration of antibiotics recommended varied from 3 to 7 days. Given the emergence of resistant isolates in cholangitis<sup>(46)</sup> and the prevalence of recurrent infection in PSC, standardization of practice is merited.

The limitations of our study include that it surveys practices in PSC management among physicians in the Division of Gastroenterology and Hepatology at a referral center with a relatively high volume of patients with PSC. Therefore, the responses may not reflect more widespread practices and perceptions; however, we would expect the findings of this study to provide a conservative estimate of practice variations. Physicians at multiple sites in the Mayo Clinic Health System were surveyed, and this expands the variability of training and experience among those surveyed. Even within a single health care system, this study revealed considerable heterogeneity in perceptions and practices that may be even greater when expanded to a larger population of physicians. The sample size and response rate were limited, although to our knowledge, this is the first study of its kind on the important topic of DSs in PSC. The low response rate may reflect the fact that only a minority of Gastroenterology and Hepatology faculty have expertise or interest in PSC, even at a tertiary referral center. The low proportion of participants identified as advanced endoscopists is consistent with the fact that they comprise a small proportion of all gastroenterologists and hepatologists. Finally, a majority of questions were multiple choice and did not allow for alternative options or free text comments.

In summary, the optimal definition and management of DSs in patients with PSC remains a

challenging area of clinical uncertainty. The study herein reveals heterogeneity in numerous perceptions and practices regarding DSs in PSC, even within a health system with relatively high overall expertise in PSC research and care, and calls attention to the need for further work to clarify the optimal definition of a DS, diagnostics, periprocedural management, and follow-up. This may be best achieved by developing a revised consensus regarding the definition of and clinical approach to DSs in PSC and wide adoption of such a consensus as part of expected practice protocols.

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