Primary Sclerosing Cholangitis: The role of endoscopy

Sharan Rambarran
Liver Transplant Lead

WITS TRANSPLANT
Wits Donald Gordon Medical Centre

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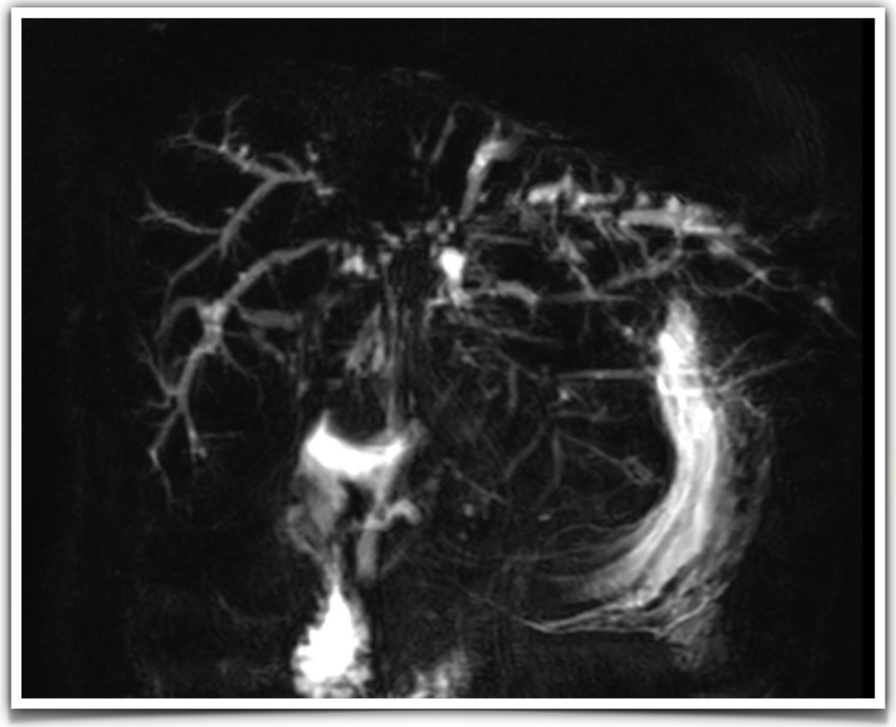
Progressive medicine, exceptional care.



SSA
GASTROENTEROLOGY FOUNDATION OF SUB-SAHARAN AFRICA

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GASTROENTEROLOGY & HEPATOLOGY ASSOCIATION OF SUB-SAHARAN AFRICA

Endoscopy Interest Group Meeting

Saturday 21 June 2025

Gautrain Radisson Blu, Johannesburg

Endo-Hepatology a new dimension

Current role for endoscopy in PSC

Cheat sheet!

ERCP

- No longer for diagnosis! (although sometimes still needed - resources)
- Cholangitis or severe sepsis with a dominant stricture
- Bile duct stone disease
- Worrisome features for malignancy stricture - sampling (CCA 400 fold risk)

Colonoscopy

- UC surveillance (right side predisposing with rectal sparing)

Gastroscopy

- Portal HPT / VBL / gastropathy

Brief history of PSC and Cholangiography

Where does ERCP fit?

- Profound biliary inflammation fibrosis narrowing the lumen described in German literature by ***Hoffman*** in 1867 (Hoffman CEE: Verschluss der Gallenwege durch Verdickung der Wandungen. Arch Pathol Anat Physiol 1867;39:206-215.}
- ***Delbert and Lafourcade*** in 1924 revisited the concept of bile duct inflammation (extra-hepatic)
- ***Klemperer*** identified “intra-hepatic cholangitis” with the same process 1937
- ***Castleman*** coined the phrase “sclerosing cholangitis” in 1954 and then again by ***Schwarz and Dale*** in 1958 - phrase stuck!

*Over the course of a 100 years after the first report, less 100 patients published in literature until the 1970’s when IV cholangiography / cholecystography / **ERCP developed!***

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REVIEW

ERCP: a very personal history

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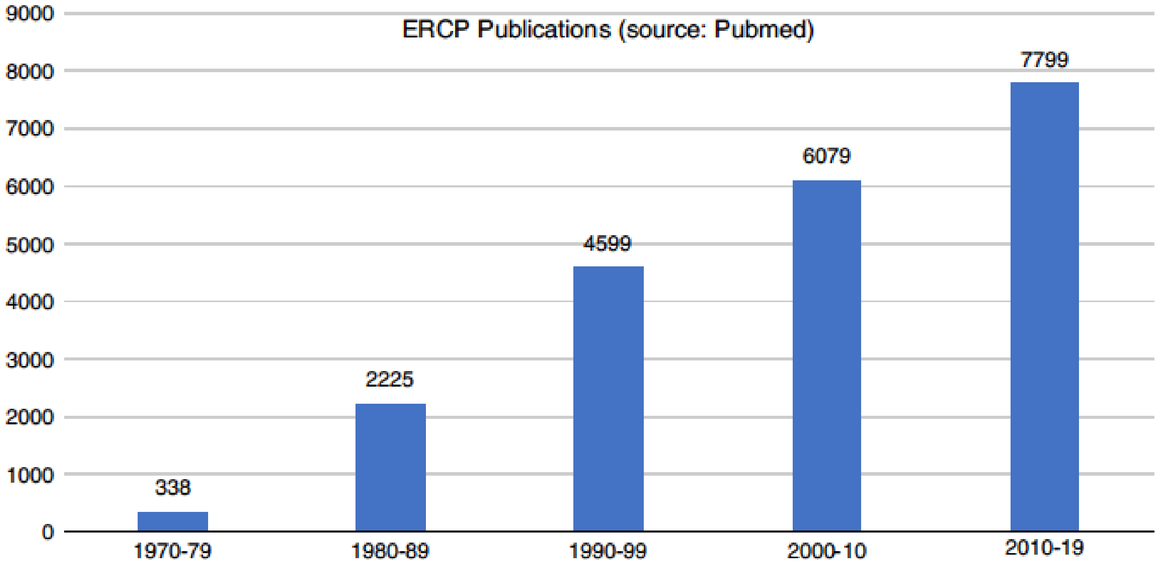

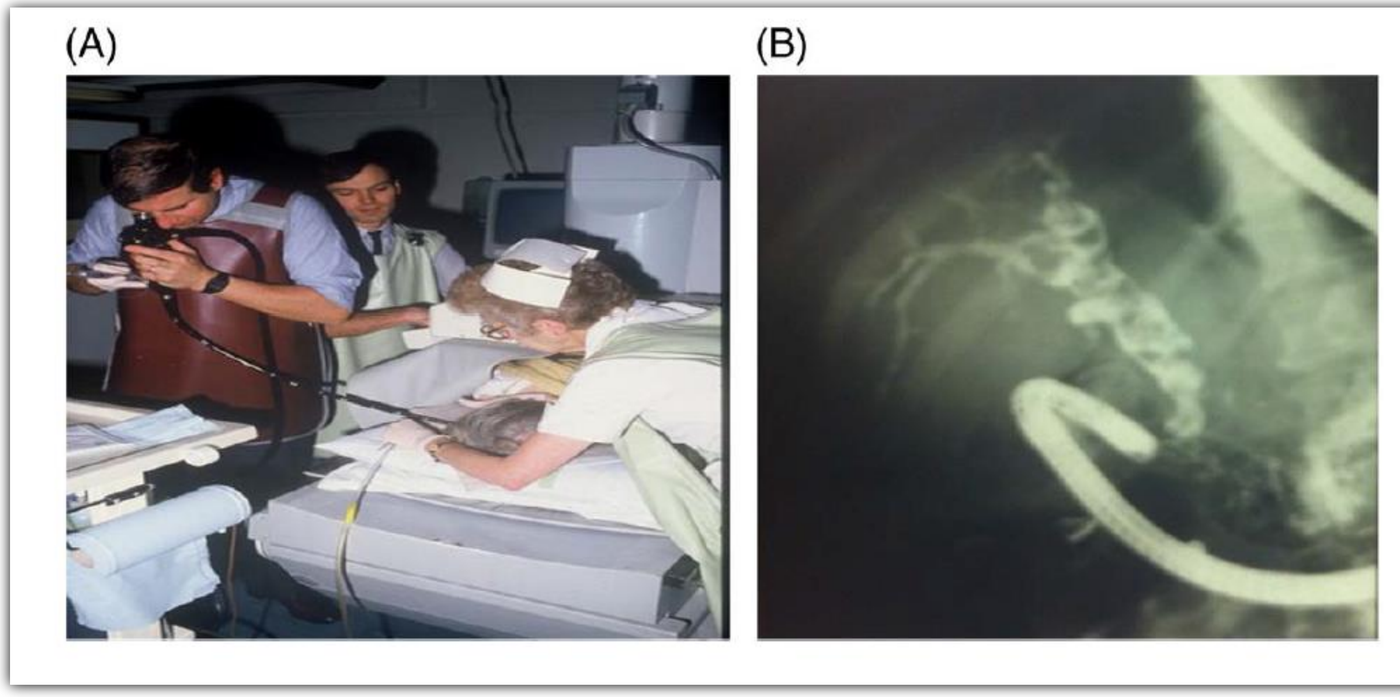

Contents lists available at ScienceDirect

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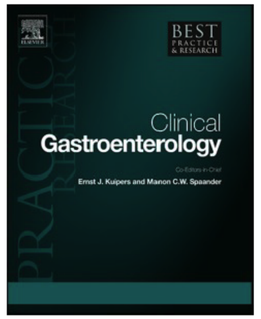

How to measure quality in ERCP?

Franco Ana Rita [a], Arvanitakis Marianna [b], Teles de Campos Sara [b,*]

Pre-procedure PI (structural)	Intra-procedure PI (process)	Post-procedure PI (outcome)	Patient-reported outcomes
• Appropriate indication for ERCP • Informed consent • Adequate antibiotic prophylaxis	• Bile duct cannulation • Clearance of bile duct stones • Stent placement in biliary obstruction • Measurement and documentation of fluoroscopy time and radiation dose	• Post-ERCP pancreatitis • Clinically significant bleeding • Perforation • Complete ERCP report	E.g. PAN-PROMISE instrument

Fig. 1. Summary of ERCP Performance Indicators (PI). ERCP = Endoscopic Retrograde CholangioPancreatography. As an international prospective cohort study, PAN-PROMISE = Patient-reported outcome scale in acute pancreatitis [24].

4 D’s approach to ERCP in PSC

Isn’t it cute?!

ANNALS of Hepatology
The Official Journal of the Mexican Association of Hepatology, the Latin-American Association for Study of the Liver and the Canadian Association for the Study of the Liver

CONCISE REVIEW
November-December, Vol. 16 No. 6, 2017: 842-850

Endoscopic Management of Primary Sclerosing Cholangitis

Jodie A. Barkin,* Cynthia Levy,** Enrico O. Souto*

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** University of Miami, Leonard M. Miller School of Medicine, Department of Medicine, Division of Hepatology. Miami, Florida, USA.

- **D**ominant stricture diagnosis and assessment
- **D**ilatation off strictures
- **D**ysplasia vs cholangiocarcinoma - choledochoscopy (cyto/FISH / biopsies)
- **D**osing of antibiotics pre and post procedure

Complications of ERCP in PSC patients

Higher risk then other cohorts! But not by much…

JOURNAL OF HEPATOLOGY

Table 5. Complications of endoscopic retrograde cholangiopancreatography (ERCP) in primary sclerosing cholangitis (PSC) patients.

First author, year [Ref.] Country	Study design	Patients/ERCPs	Complications, % of procedures		
			Total	Pancreatitis	Cholangitis
Lee, 1995 [49] USA	Retrospective	53/175	13.7	7	8
van den Hazel, 2000 [57] The Netherlands	Retrospective	83/106	9	3	2
Baluyut, 2001 [44] USA	Retrospective	63/63	1.8	1.26	0.6
Stiehl, 2002 [33] Germany	Retrospective	106/ERCP yearly, median 5 years	9	5.2	3.3
Enns, 2003 [58] Canada	Retrospective	104 patients	17	5	7.5
Gluck, 2008 [35] USA	Retrospective	106/317	7.3	3.8	0.95
Etzel, 2008 [62] USA	Retrospective	PSC: 30/85 Non-PSC: 45/70	12.9 8.6	2.4 2.9	5.9 1.4
Bangarulingam, 2009 [59] USA	Retrospective	PSC: 168 Non-PSC: 981	11 8	5 4	3.6 0.2
Alkhatib, 2011 [60] USA	Retrospective	75/185	8	5	1
Ismail, 2012 [54] Finland	Retrospective	441/441	9	7	–
Navaneethan, 2015 [55] USA	Retrospective	294/697	4.3	1.2	2.4
von Seth. 2015 [61] Sweden	Retrospective, national registry study	PSC: 141/141 Non-PSC: 8791	18.4 7.3	7.8 3.2	7.1 2.1

Endoscopic Dilatation of Dominant Strictures in Primary Sclerosing Cholangitis

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Phillipus C Bornman
Professor and Head
Surgical Gastroenterology E23
Groote Schuur Hospital
Observatory, Cape 7925
South Africa

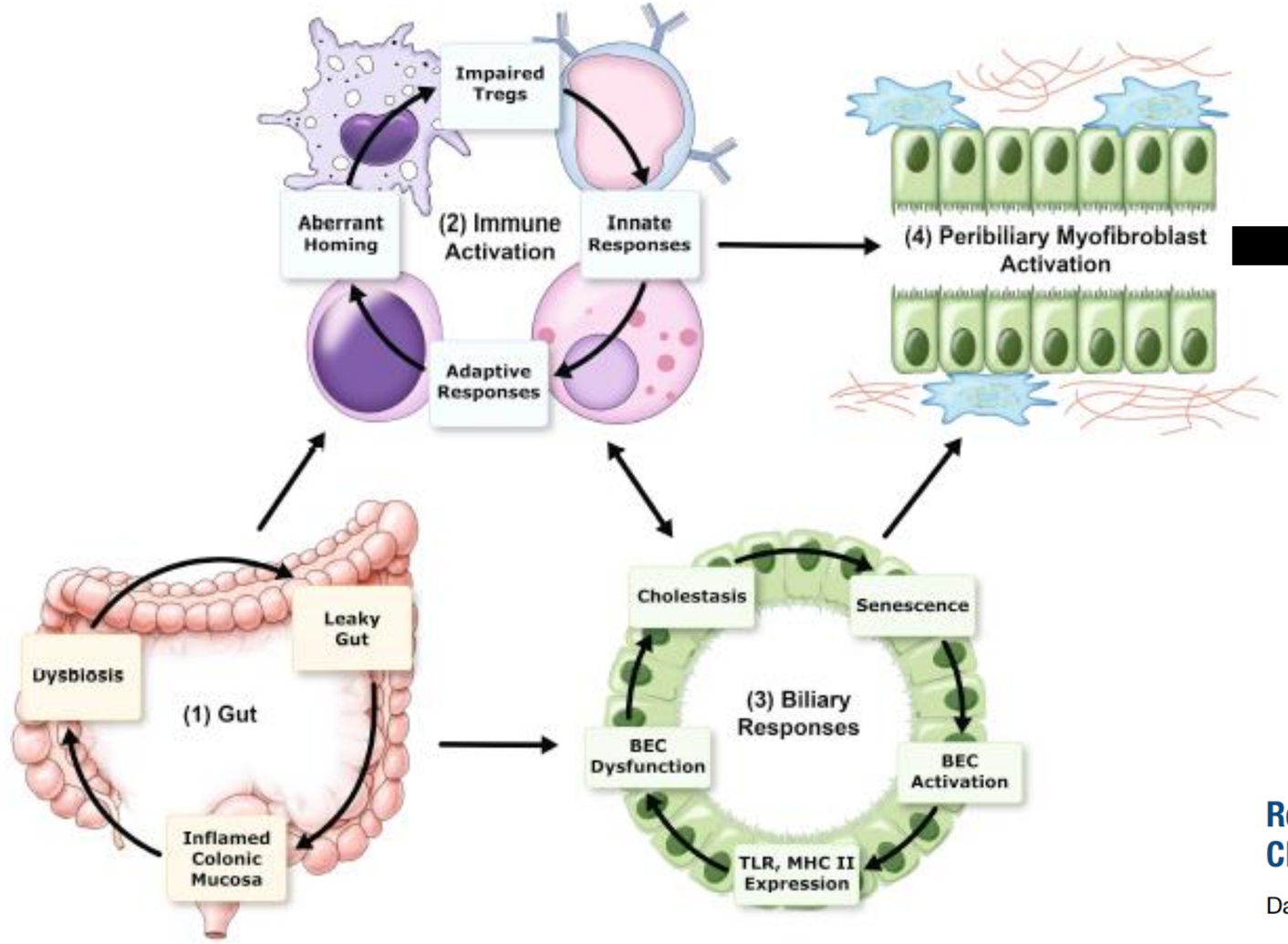
ABSTRACT

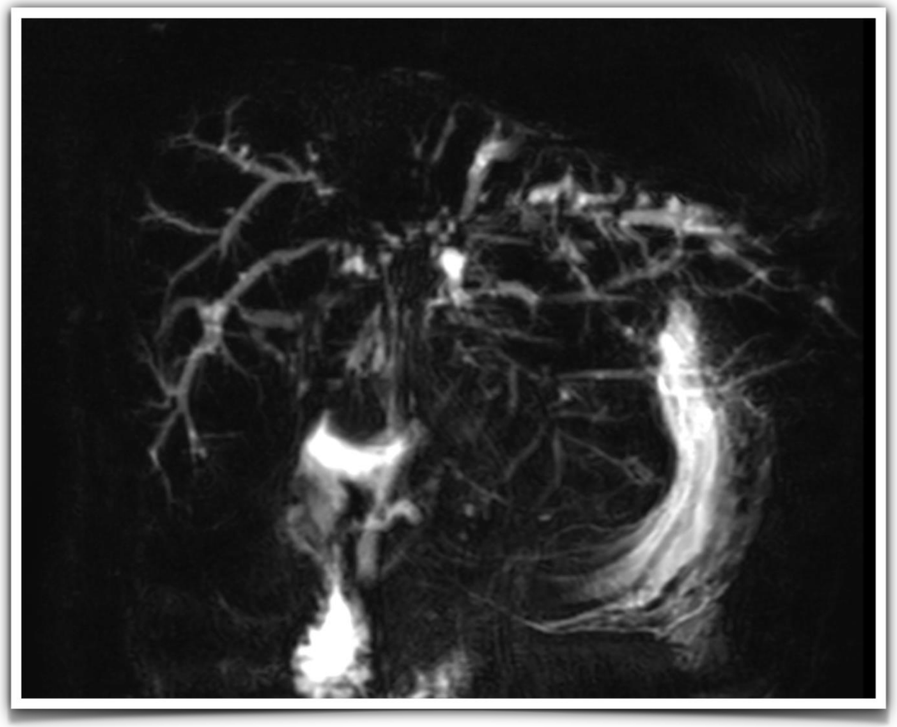
Wagner, S.,, Gebel, M.,, Meier, P.,, Trautwein, C.,, Bleck, J.,, Nashan, B., and *Manns, M. P., (1996) Endoscopic Management of Biliary Tract Strictures in Primary Sclerosing Cholangitis. Endoscopy; 28: 546–551.*

Keywords: Primary sclerosing cholangitis, bile duct strictures, ERCP dilatation

"We would caution against any biliary manipulations in PSC patients with **end-stage biliary cirrhosis**, as the injection of contrast into a poorly drained biliary system may set up a vicious cycle of biliary sepsis and further interventional procedures, and the patient may forego the chance of a transplant due to uncontrolled sepsis."

Pathophysiology theories

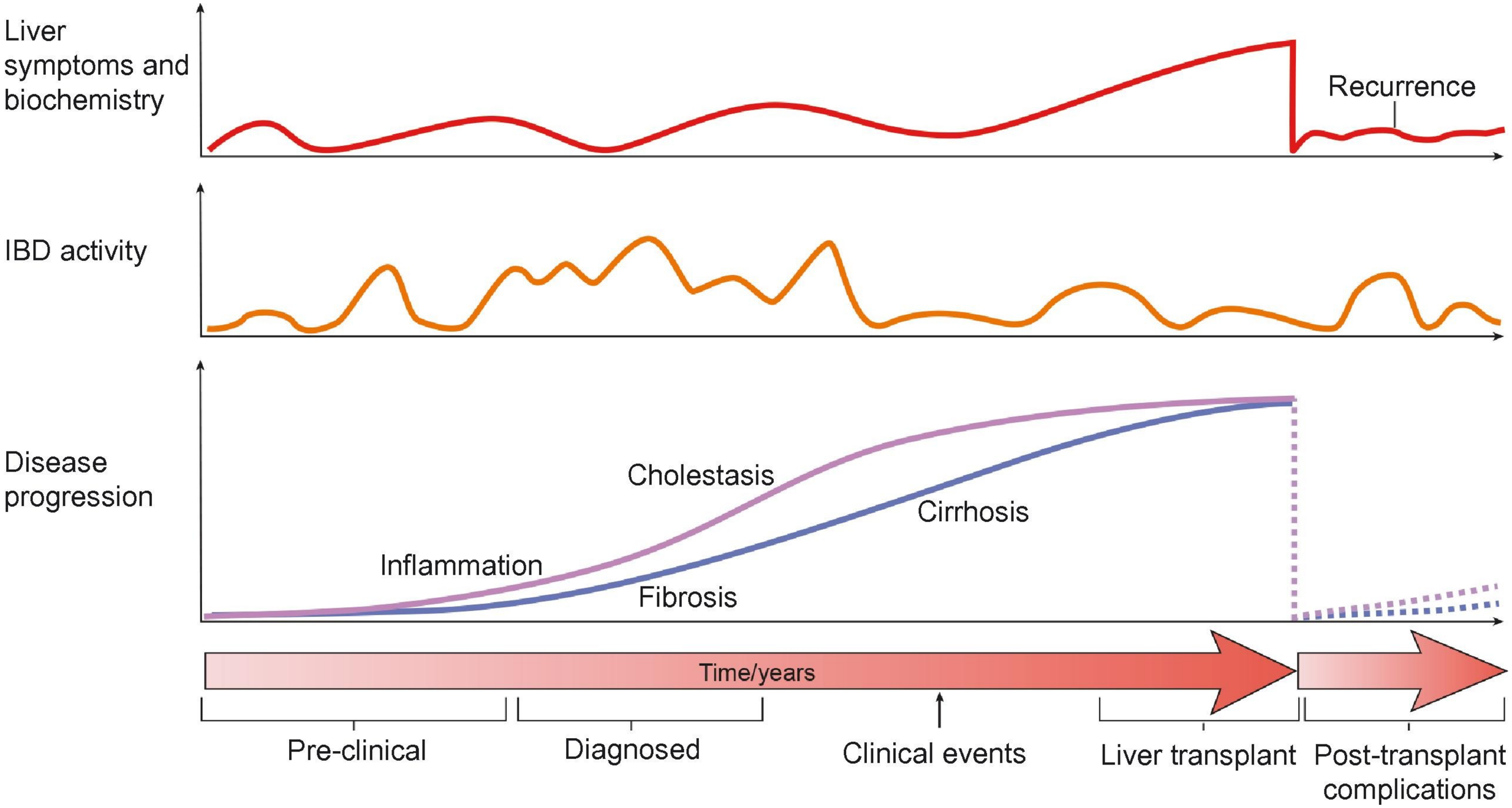




Clinical Gastroenterology and Hepatology 2023;21:2065–2075

Recent Advances in the Management of Primary Sclerosing Cholangitis

David N. Assis[1] and Christopher L. Bowlus[2]


Liver symptoms and biochemistry
Recurrence
IBD activity
Disease progression
Cholestasis
Cirrhosis
Inflammation
Fibrosis
Time/years
Pre-clinical
Diagnosed
Clinical events
Liver transplant
Post-transplant complications

Journal of *Clinical Medicine*

MDPI

Review

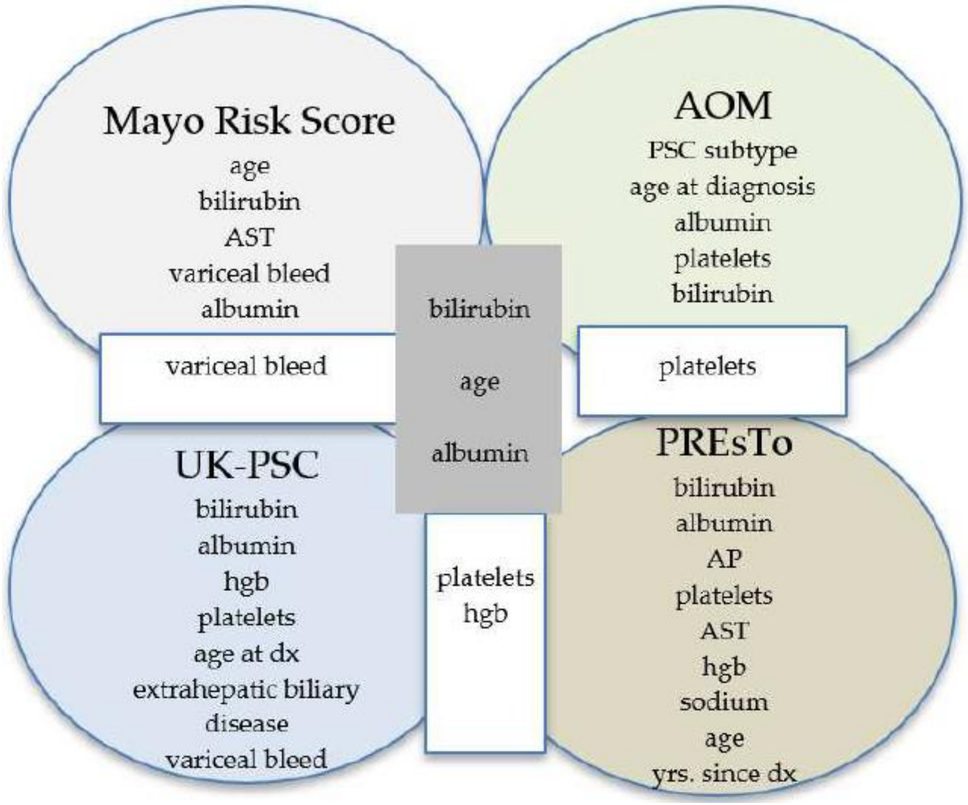
Systematic Review of Prognostic Models Compared to the Mayo Risk Score for Primary Sclerosing Cholangitis

Paul A. Schmeltzer and Mark W. Russo *

The more risk indices, the less we know about disease progression!

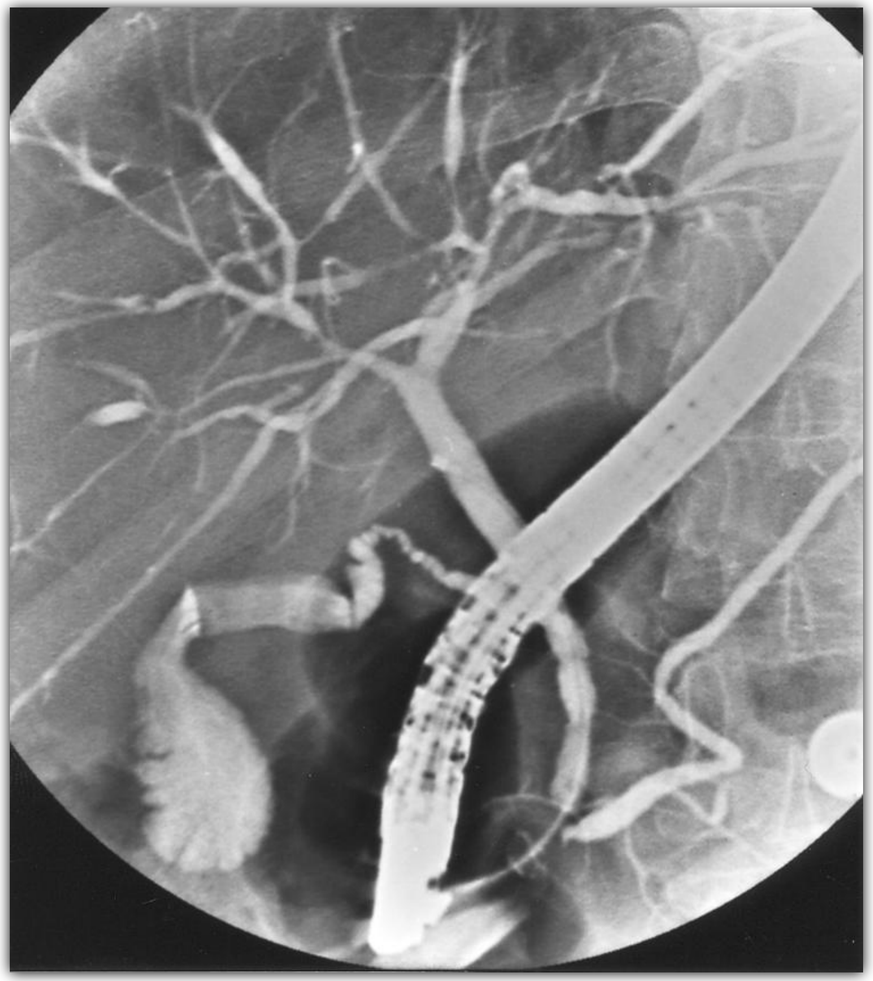
	Models			
	Amsterdam-Oxford 2017[230]	**UK-PSC 2019[231]**	**PREsTO 2020[232]**	**SCOPE 2020[162]**
Variables	Age Bilirubin Albumin AST ALP Platelets PSC subtype (large-duct or small-duct)	Age Bilirubin Albumin ALP Platelets Presence of extrahepatic biliary disease History of variceal hemorrhage	Age Bilirubin Albumin AST ALP Platelets Hemoglobin Sodium Years since PSC diagnosis	Bilirubin Albumin Platelets GGT Cholangiography (large-duct or small-duct involvement)
Endpoint	LT or liver-related death by 15 years	Short term: death or LT by 2 years Long term: death or LT by 10 years	Hepatic decompensation (ascites, variceal hemorrhage, encephalopathy) by 5 years	Portal hypertensive complications, biliary complications, CCA, listing for LT, or death from liver disease by 5 years
Risk thresholds[a]	Lower risk: < 1.58 Higher risk: ≥ 1.58	Lower risk: < 1.46 Higher risk: ≥ 1.46	Lower risk: < 20% Higher risk: ≥ 20%	Lower risk: 0–5 Higher risk: 6–11
Website	https://sorted.co/psc-calculator/	http://www.uk-psc.com/resources/the-uk-psc-risk-scores/	rtools.mayo.edu/PRESTO_calculator/	Scopeindex.net

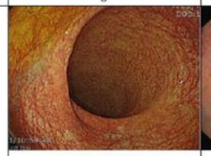
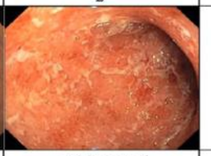
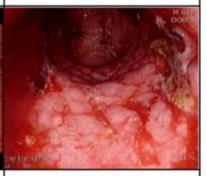
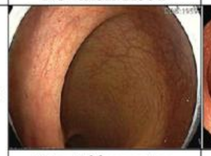
[a]Lower-risk group cutoffs were selected to identify patients with approximately 10% or less risk of transplant or death within 5 years. Cutoffs were not reported for the PREsTO model; however, approximately twice as many patients developed decompensation as were transplanted in follow-up, making a 20% risk of decompensation a reasonable approximation of a 10% risk of transplant or death.



Characteristic cholangiography of PSC

Wide spectrum of disease!



Score	0	1	2	3
Vascular pattern				
	Normal	Patchy obliteration	Obliterated	
Bleeding				
	No visible blood	Mucosal	Luminal mild	Luminal moderate
Erosion and ulcers				
	No visible erosion	Erosions	Superficial ulcer	Deep ulcer

We focus on the bile ducts, don’t forget the colon or stomach or gall bladder!

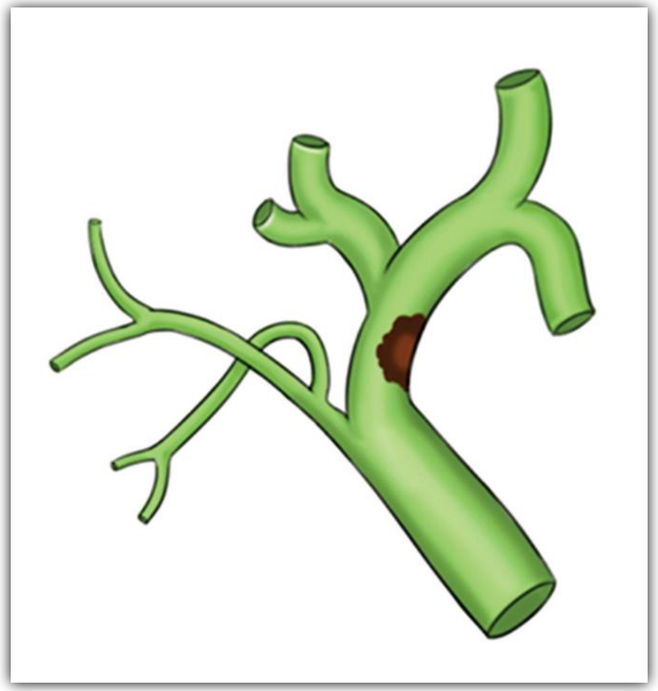
ERCP directed Choledochoscopy

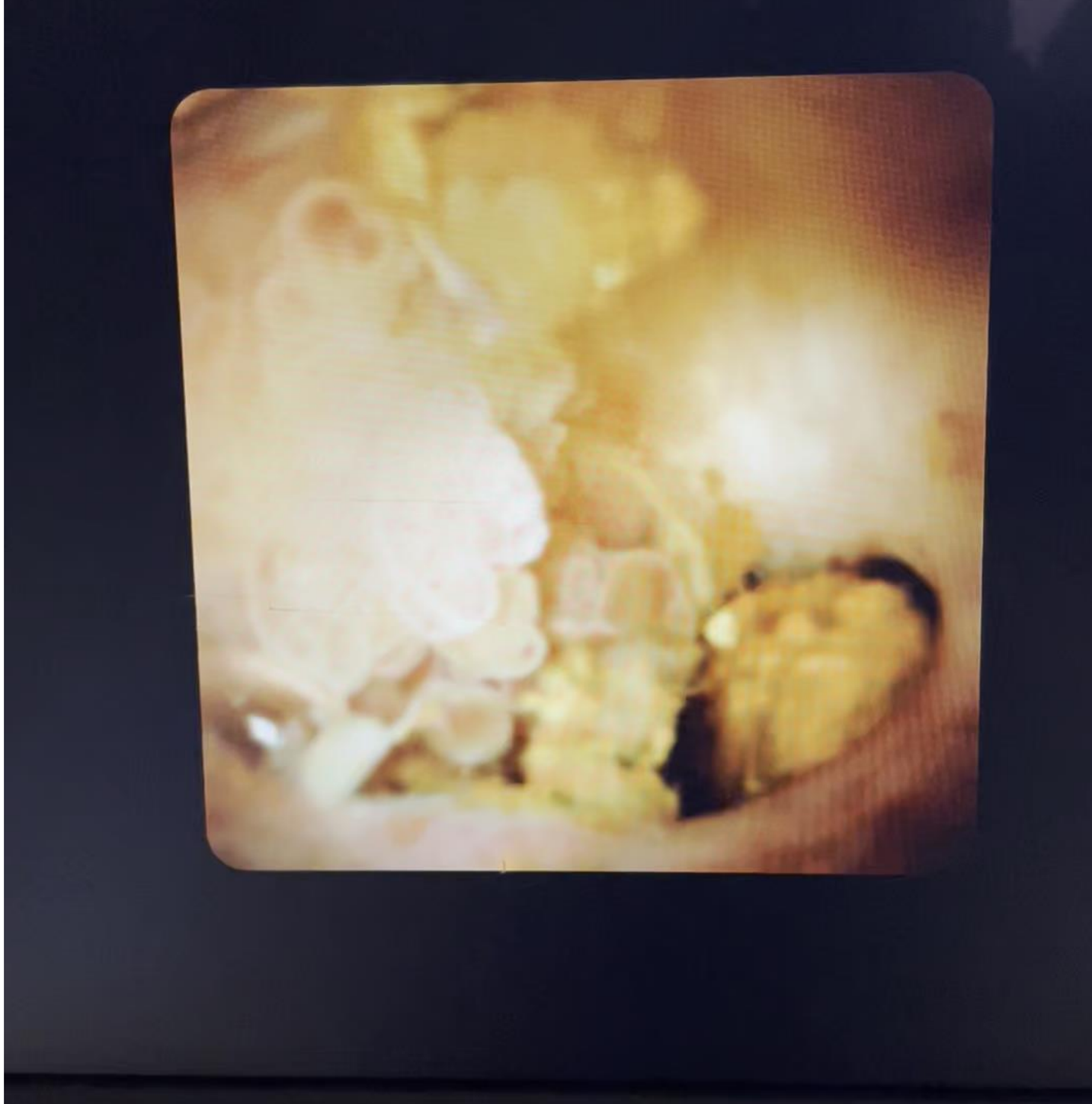
Video better than standard flouroscopy!

- Identify and sample areas of epithelial concern
- Direct drainage
- Allow for best quality sampling - brush / FISH / punch biopsies
- Allows for bile aspiration for Calprotectin and IL8 (indicator of disease severity)
- Endoscopic ultrasound helps uncover worrisome strictures
- Newer additions -

29 year old female

Biopsy proven PSC - preserved liver synthetic function but found this IPNB
High grade
Fast track to tx





Techniques to aid yield at ERCP

Know which duct and where the suspicious lesion is!

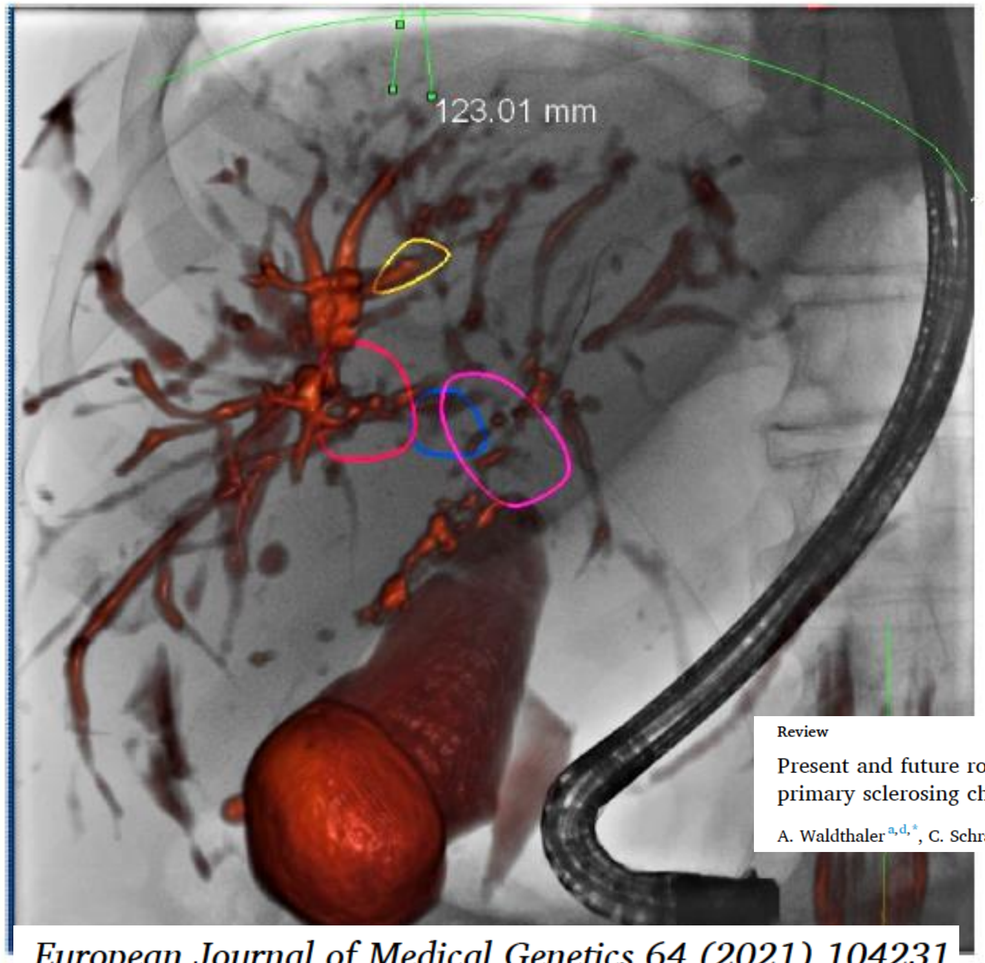


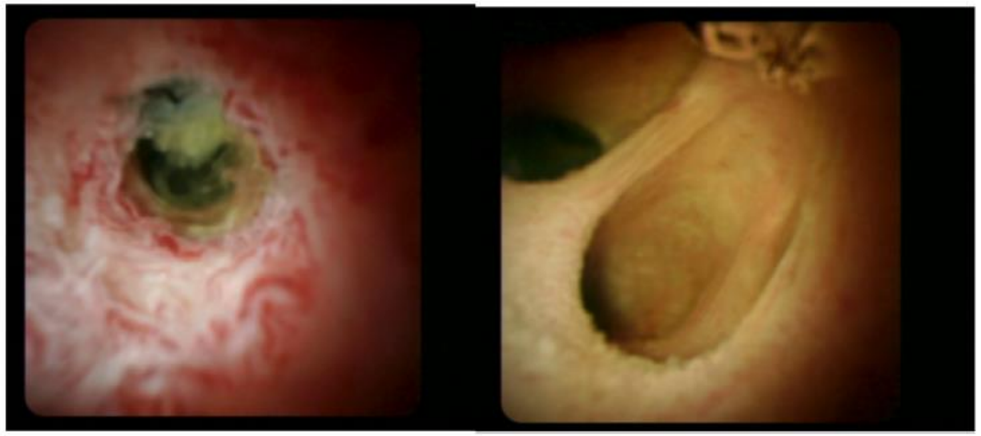
Fig. 1. Image fusion of fluoroscopy and MRI data. Before the ERCP, several spots in the biliary tree have been identified, in which brush sampling is desired. Those have been marked colour coded. For the fusion process, the spinal cord and the liver dome have been marked in appropriate MRI sequences. Finally, all sequences except for the MRCP are subtracted and the 3-dimensional image is aligned via fluoroscopy in 2 planes to the anesthetized patient. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Review

Present and future role of endoscopic retrograde cholangiography in primary sclerosing cholangitis

A. Waldthaler [a,d,*], C. Schramm [c,d], A. Bergquist [b,d]

European Journal of Medical Genetics 64 (2021) 104231



ORIGINAL ARTICLE

Clinical outcomes and reintervention after endoscopic retrograde cholangiopancreatography in primary sclerosing cholangitis in absence of cholangitis

Indian Journal of Gastroenterology (September–October 2024) 43(5):1021–1029

Ryosuke Horio[1] · Jun Kato[1] · Takashi Taida[1] · Yuki Ohta[1] · Keiko Saito[1] · Yuhei Oyama[1] · Hayato Nakazawa[1] · Yukiyo Mamiya[1] · Chihiro Goto[1] · Satsuki Takahashi[1] · Mayu Ouchi[1] · Akane Kurosugi[1] · Michiko Sonoda[1] · Motoyasu Kan[1] · Tatsuya Kaneko[1] · Hiroki Nagashima[1] · Naoki Akizue[1] · Koji Takahashi[1] · Kenichiro Okimoto[1] · Hiroshi Ohyama[1] · Tomoaki Matsumura[1] · Izumi Ohno[1] · Naoya Kato[1]

Clinical outcomes and reintervention after endoscopic retrograde cholangiopancreatography in primary sclerosing cholangitis in absence of cholangitis

Patients

99 patients with PSC

29 excluded

70 without cholangitis

within 3 years of PSC diagnosis

21 in the non-ERCP group

49 in the ERCP-performed group

Outcomes

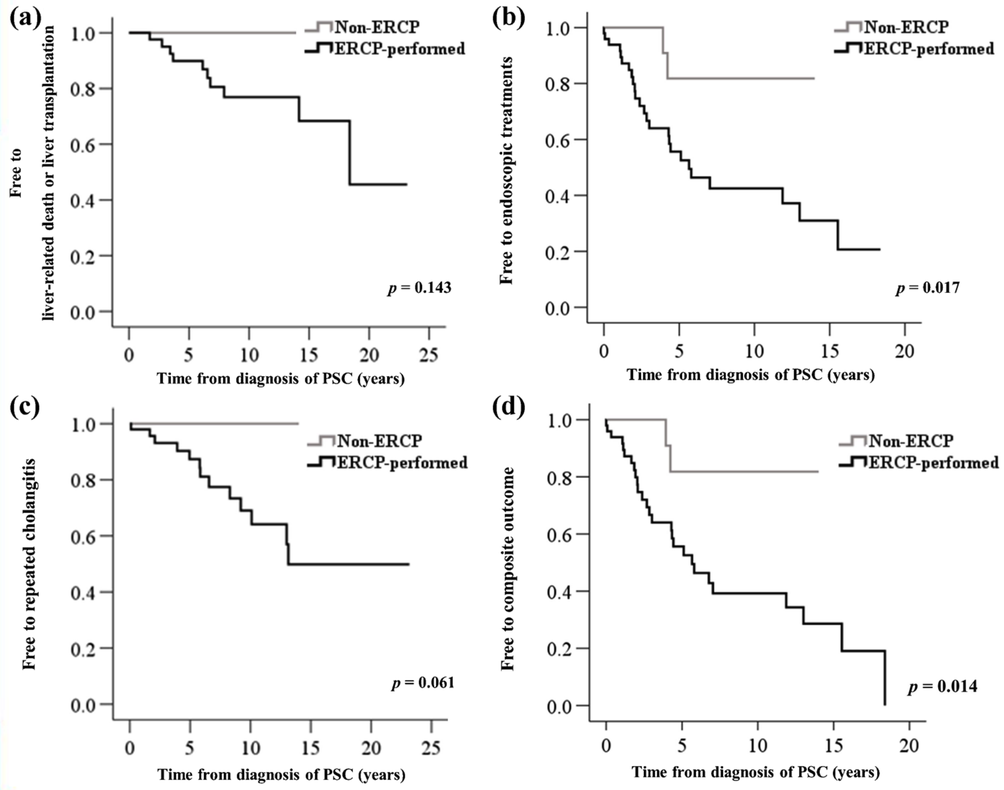
- liver-related death or liver transplantation
- endoscopic treatment requirement
- repeated cholangitis
- composite outcome

Results

Non-ERCP group was less likely to achieve the three outcomes and the composite outcome, showing statistical significance (endoscopic treatment requirement; $p = 0.017$ and composite outcome; $p = 0.014$).

Conclusion: ERCP in patients with PSC in the absence of cholangitis is likely to require further endoscopic treatment and may be associated with poor prognosis.

Horio et al.



British Society of Gastroenterology and UK-PSC guidelines for the diagnosis and management of primary sclerosing cholangitis

Recommendation 11: We recommend that non-invasive investigations such as MRCP, dynamic liver MRI and/or contrast CT should be performed in patients who have new or changing symptoms or evolving abnormalities in laboratory investigations (*strength of recommendation: STRONG; quality of evidence: MODERATE*).

Recommendation 12: We recommend that patients with PSC should ordinarily not undergo ERCP until there has been expert multidisciplinary assessment to justify endoscopic intervention (*strength of recommendation: STRONG; quality of evidence: MODERATE*).

Recommendation 13: We recommend that in patients undergoing ERCP for dominant strictures, pathological sampling of suspicious strictures is mandatory (*strength of recommendation: STRONG; quality of evidence: STRONG*).

Recommendation 14: We recommend that in patients undergoing ERCP for dominant strictures, biliary dilatation is preferred to the insertion of biliary stents (*strength of recommendation: STRONG; quality of evidence: MODERATE*).

Chapman MH, *et al. Gut* 2019;**68**:1356–1378. doi:10.1136/gutjnl-2018-317993

Clinical Practice Guidelines

Role of endoscopy in primary sclerosing cholangitis: European Society of Gastrointestinal Endoscopy (ESGE) and European Association for the Study of the Liver (EASL) Clinical Guideline☆

European Society of Gastrointestinal Endoscopy, European Association for the Study of the Liver*

Main recommendations

1. ESGE/EASL recommend that, as the primary diagnostic modality for PSC, magnetic resonance cholangiography (MRC) should be preferred over endoscopic retrograde cholangiopancreatography (ERCP).
Moderate quality evidence, strong recommendation.

2. ESGE/EASL suggest that ERCP can be considered if MRC plus liver biopsy is equivocal or contraindicated in patients with persisting clinical suspicion of PSC. The risks of ERCP have to be weighed against the potential benefit with regard to surveillance and treatment recommendations.
Low quality evidence, weak recommendation.

6. ESGE/EASL suggest that, in patients with an established diagnosis of PSC, MRC should be considered before therapeutic ERCP.
Weak recommendation, low quality evidence.

7. ESGE/EASL suggest performing endoscopic treatment with concomitant ductal sampling (brush cytology, endobiliary biopsies) of suspected significant strictures identified at MRC in PSC patients who present with symptoms likely to improve following endoscopic treatment.
Strong recommendation, low quality evidence.

9. ESGE/EASL recommend weighing the anticipated benefits of biliary papillotomy/sphincterotomy against its risks on a case-by-case basis. Strong recommendation, moderate quality evidence. Biliary papillotomy/sphincterotomy should be considered especially after difficult cannulation.
Strong recommendation, low quality evidence.

Biliary papillotomy/sphincterotomy should be considered especially after difficult cannulation.
Strong recommendation, low quality evidence.

16. ESGE/EASL suggest routine administration of prophylactic antibiotics before ERCP in patients with PSC.
Strong recommendation, low quality evidence.

17. EASL/ESGE recommend that cholangiocarcinoma (CCA) should be suspected in any patient with worsening cholestasis, weight loss, raised serum CA19-9, and/or new or progressive dominant stricture, particularly with an associated enhancing mass lesion.
Strong recommendation, moderate quality evidence.

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PRACTICE GUIDANCE

AASLD practice guidance on primary sclerosing cholangitis and cholangiocarcinoma

Christopher L. Bowlus[1] | **Lionel Arrivé**[2] | **Annika Bergquist**[3] | **Mark Deneau**[4] | **Lisa Forman**[5] | **Sumera I. Ilyas**[6] | **Keri E. Lunsford**[7] | **Mercedes Martinez**[8] | **Gonzalo Sapisochin**[9] | **Rachna Shroff**[10] | **James H. Tabibian**[11] | **David N. Assis**[12]

Guidance statements

1. In patients with suspected PSC, a 3D MRI/MRCP with T1w and T2w axial images and contrast enhancement should be obtained to evaluate for cholangiographic features of PSC, including intrahepatic and/or extrahepatic strictures alternating with normal or slightly dilated segments.
2. In patients with suspected PSC and a normal, high-quality MRI/MRCP, liver biopsy should be considered to rule out small-duct PSC. Patients with an equivocal MRI/MRCP should be referred to an experienced center for consideration of a repeat high-quality MRI/MRCP or liver biopsy. A repeat MRI/MRCP may be considered in 1 year if the diagnosis remains unclear.
3. ERCP should be avoided for the diagnosis of PSC.
4. In all patients with possible PSC, serum IgG4 levels should be measured to exclude IgG4-sclerosing cholangitis.
5. A liver biopsy should not be performed in patients with typical cholangiographic findings on MRI/MRCP, except when there is concern for AIH overlap.
6. Ileocolonoscopy with biopsies should be performed in patients with a new diagnosis of PSC and no previous diagnosis of IBD. In patients without IBD, subsequent ileocolonoscopy should be considered at 5-year intervals or whenever symptoms suggestive of IBD occur.

Guidance statements

23. ERCP may be indicated for the evaluation of relevant strictures as well as new-onset or worsening pruritus, unexplained weight loss, worsening serum liver test abnormalities, rising serum CA 19-9, recurrent bacterial cholangitis, or progressive bile duct dilation. MRI/MRCP should be considered prior to ERCP to clarify the need for biliary intervention and guide the technical approach.
24. Antimicrobial prophylaxis should be administered during the periprocedure period in patients with PSC undergoing ERCP.
25. The choice between biliary balloon dilation with and without stenting should be left to the endoscopist's discretion. In cases where a plastic biliary stent is placed, the stent should generally be removed within 4 weeks following placement.

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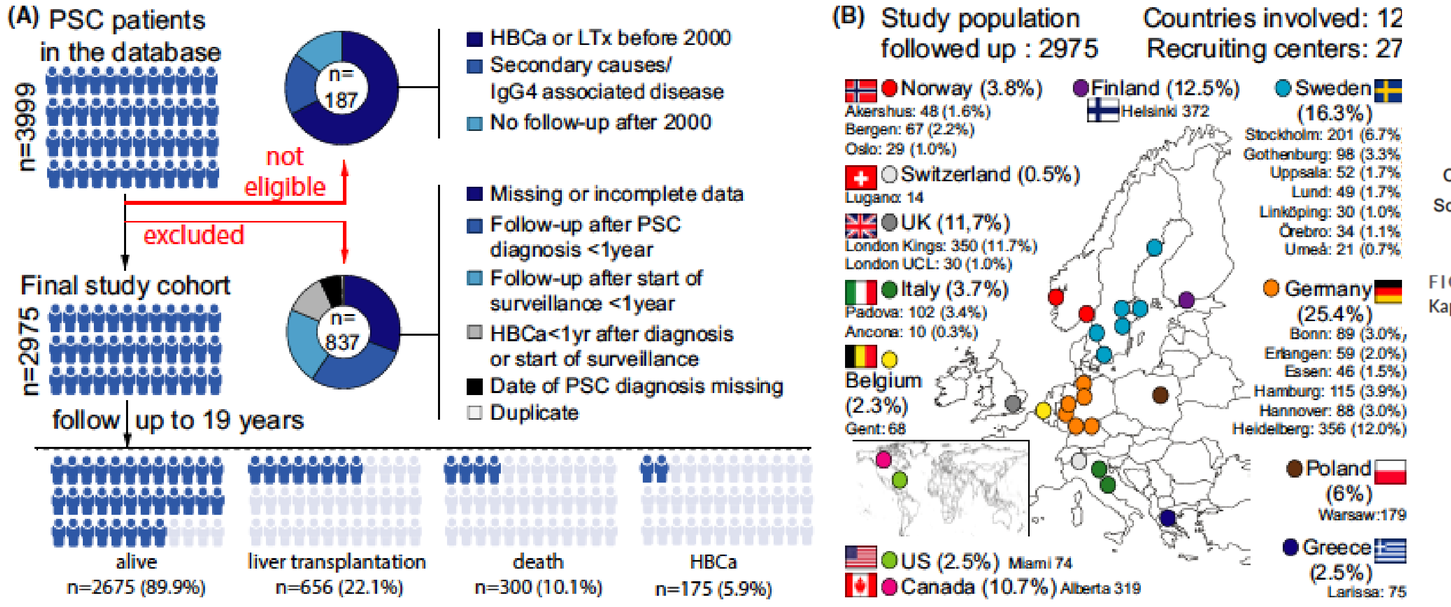
DOI: 10.1111/liv.15286

Liver INTERNATIONAL WILEY

Impact on follow-up strategies in patients with primary sclerosing cholangitis



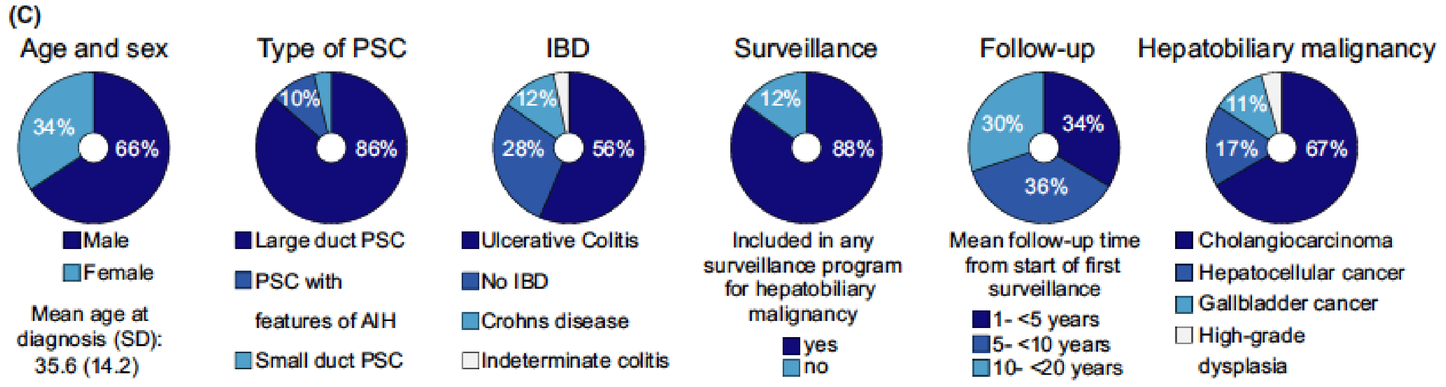
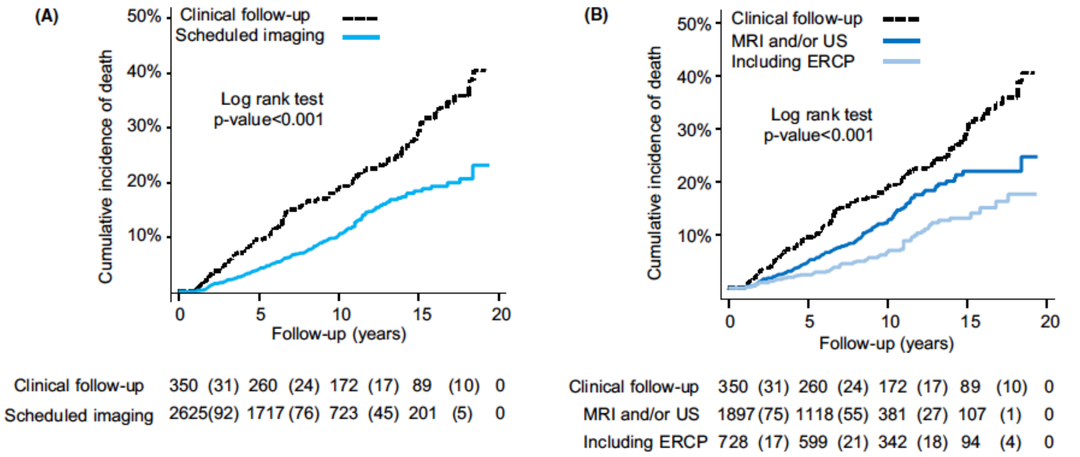


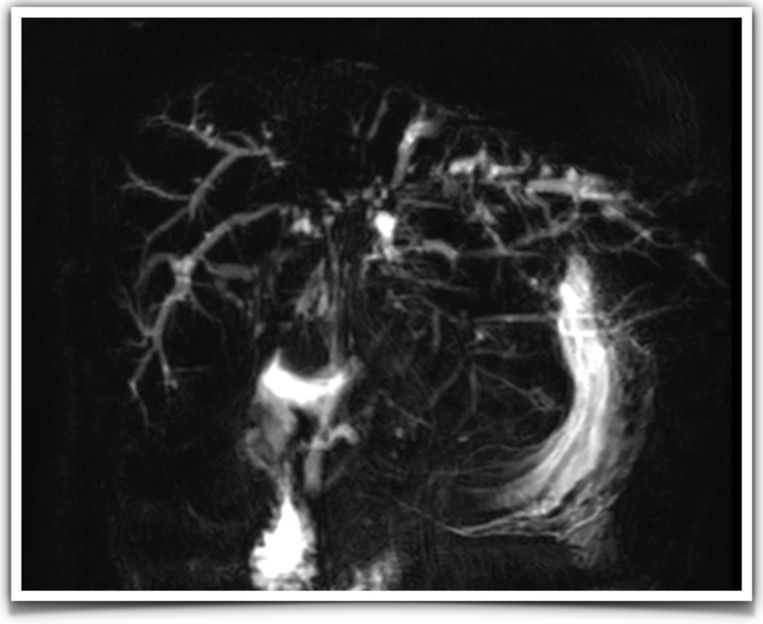
FIGURE 1 (A) Comprehensive description of the selection of the 2975 PSC patients included in the study. (B) Participating centres in the study. (C) Clinical characteristics and outcomes for all patients



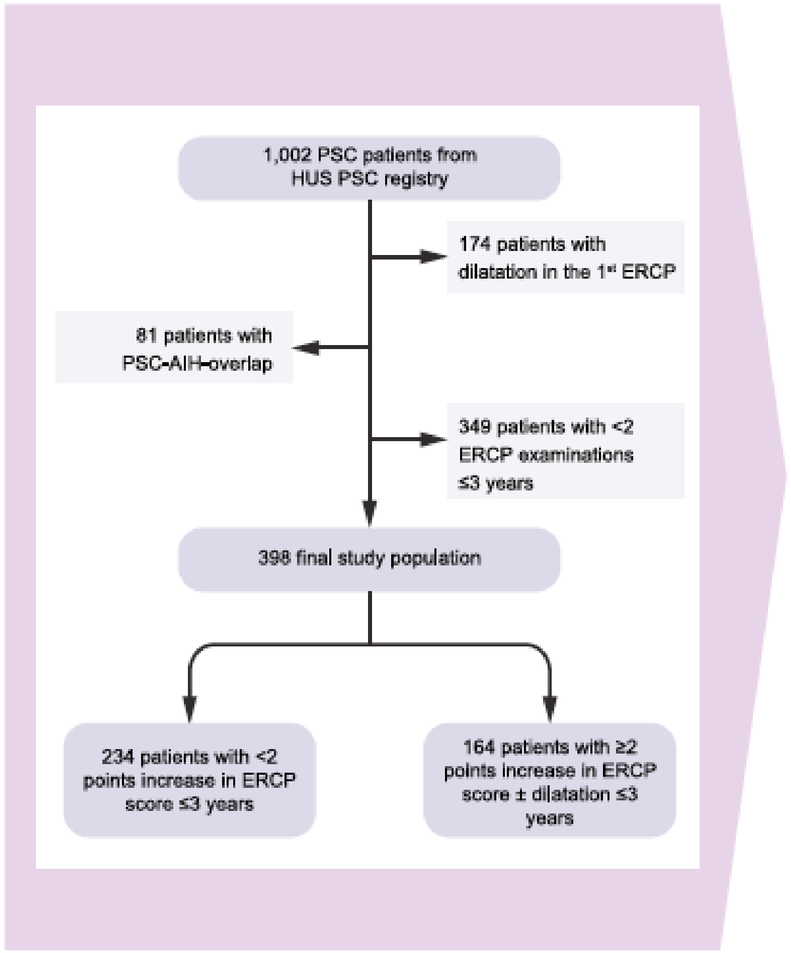
Clinical follow-up	350	(31)	260	(24)	172	(17)	89	(10)	0
Scheduled imaging	2625	(92)	1717	(76)	723	(45)	201	(5)	0

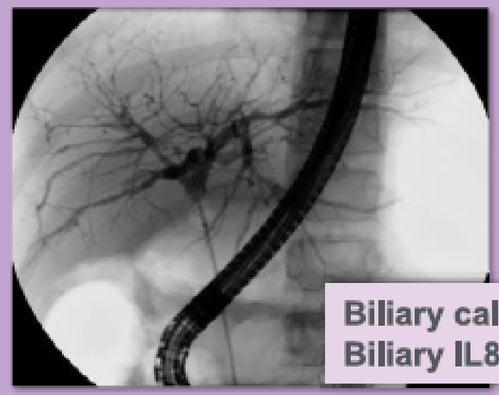
Clinical follow-up	350	(31)	260	(24)	172	(17)	89	(10)	0
MRI and/or US	1897	(75)	1118	(55)	381	(27)	107	(1)	0
Including ERCP	728	(17)	599	(21)	342	(18)	94	(4)	0

FIGURE 2 (A) Kaplan–Meier curves displaying the cumulative incidence of death for scheduled imaging versus clinical follow-up. (B) Kaplan–Meier curves displaying the cumulative incidence of death by type of follow-up

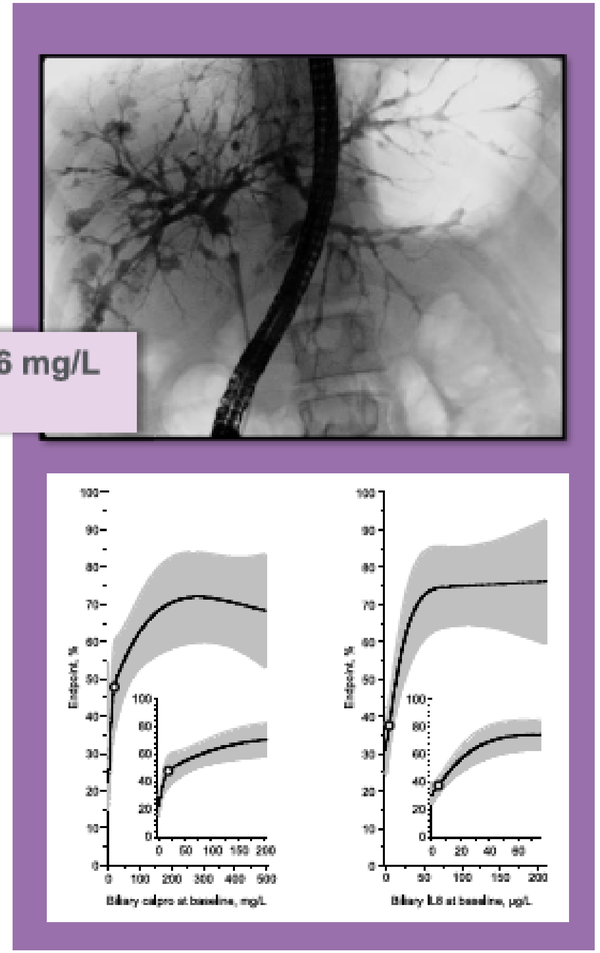


The most sensitive markers for bile duct disease progression were calprotectin and interleukin 8 in bile.





Biliary calprotectin >18.6 mg/L
Biliary IL8 >4.5 µg/L



- **164 (41%) patients with bile duct disease progression (≥2 point increase in ERC score and/or need for dilatation ≤3 years)**
- **Biliary calprotectin (AUC = 0.76) and IL8 (AUC = 0.76) were the only variables demonstrating a meaningful predictive value**
- **Limited predictive value of P-ALP**

In our unit, all patients with suspected PSC undergo ERCP to confirm the diagnosis due to the low sensitivity of MRCP for detecting early intrahepatic changes and even advanced extrahepatic lesions.[5] In addition, we use ERCP with BC and bile samples for evaluation of need for endoscopic therapy, individual risk stratification for progression and for exclusion of biliary neoplasia.

Research article

JHEP|Reports

Surrogate markers of bile duct disease progression in primary sclerosing cholangitis – A prospective study with repeated ERCP examinations

Martti Färkkilä[1,4*], Fredrik Åberg[2], Henrik Alfthan[3], Kalle Jokelainen[4], Lauri Puustinen[4], Hannu Kautiainen[5], Andrea Tenca[4]

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Conclusion

Interesting evolution tied with ERCP!

- Role of ERCP is limited to specific indications for therapy and surveillance
- Diagnostics are better and based on non-invasive markers and imaging
- Tumour risk is real and should be actively managed (Not wait and see!)
- Newer endoscopic techniques aid in tumour identification
- Data is heterogeneous and definitions are confusing
- MDT including Transplant Hepatology and Surgery key for best outcomes…

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Endoscopy Interest Group Meeting

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