MRCP in Primary Sclerosing Cholangitis in Children with Inflammatory Bowel Disease: A Retrospective Study

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Disclosures

- None


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[Insert funny comment about the biliary ducts]

Primary Sclerosing Cholangitis (PSC)

- Progressive autoimmune disease affecting the hepatobiliary system
- Advanced fibrosis leading to end-stage liver disease; liver transplantation
- Associated with inflammatory bowel disease (IBD), ulcerative colitis (UC)
- No effective medical therapy
- Evaluation by liver biopsy, biochemical markers, imaging

Imaging of PSC

- ERCP
- MRCP

Imaging of PSC

- ERCP
  - Modified Majoie criteria, validated by Ponsioen et al
- MRCP
  - Modified Majoie classification applied to MRCPs by Ferrara et al.
  - Reliability?
  - Validity?
  - Prognostication?

Objective

- To determine the inter-rater reliability, construct validity, and prognostic utility of the modified Majoie ERCP classification applied to MRCP in a pediatric PSC cohort.

Methods

- Design and Setting
- Patient Population

Methods

- Design and Setting
  - Single-center retrospective cohort study
- Patient Population
  - Children with PSC underwent MRCP: 2008-2016
  - Liver biopsy-proven PSC
  - Control group for comparative purposes

Methods

- Data Collection and Definitions

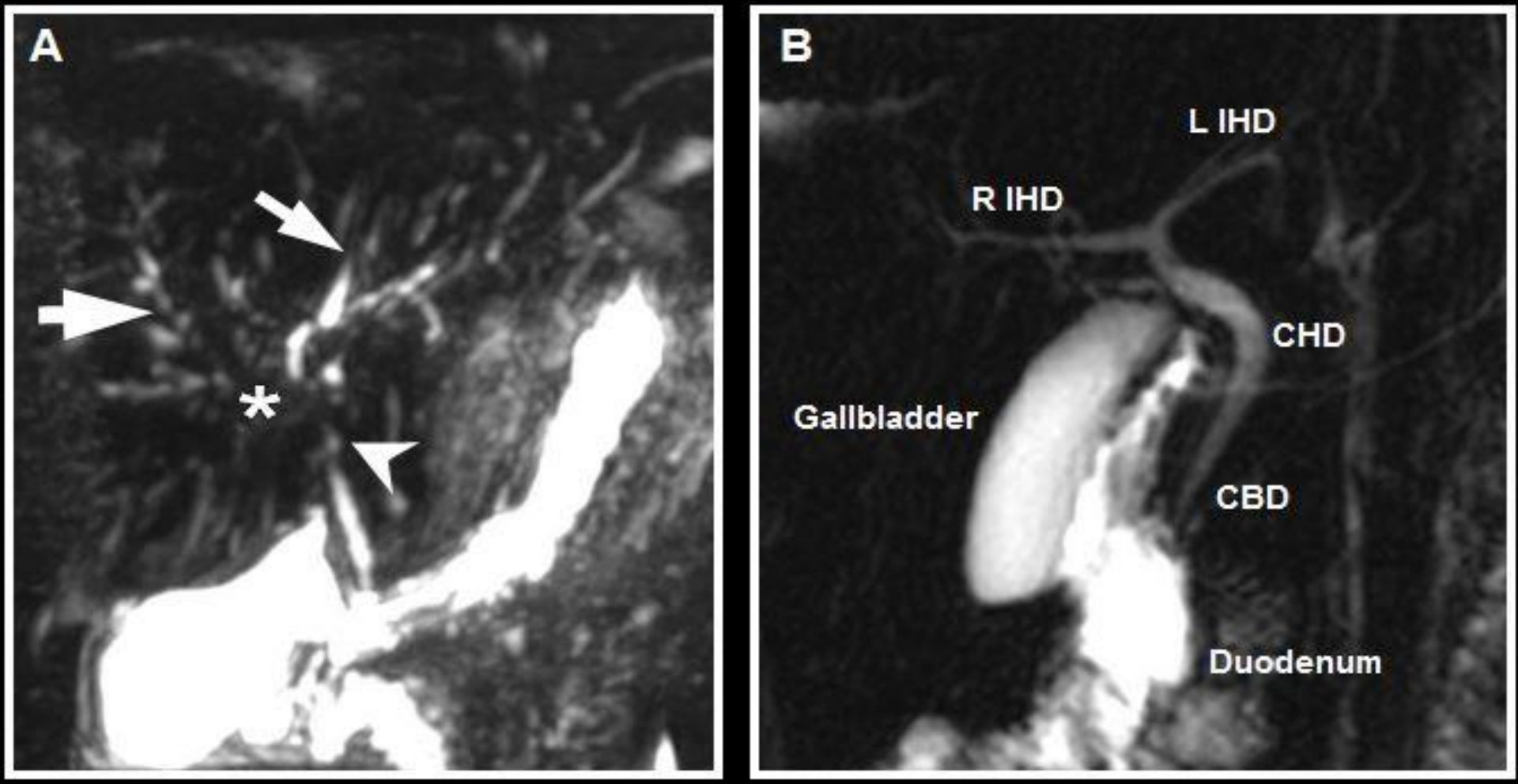
Methods

- Data Collection and Definitions

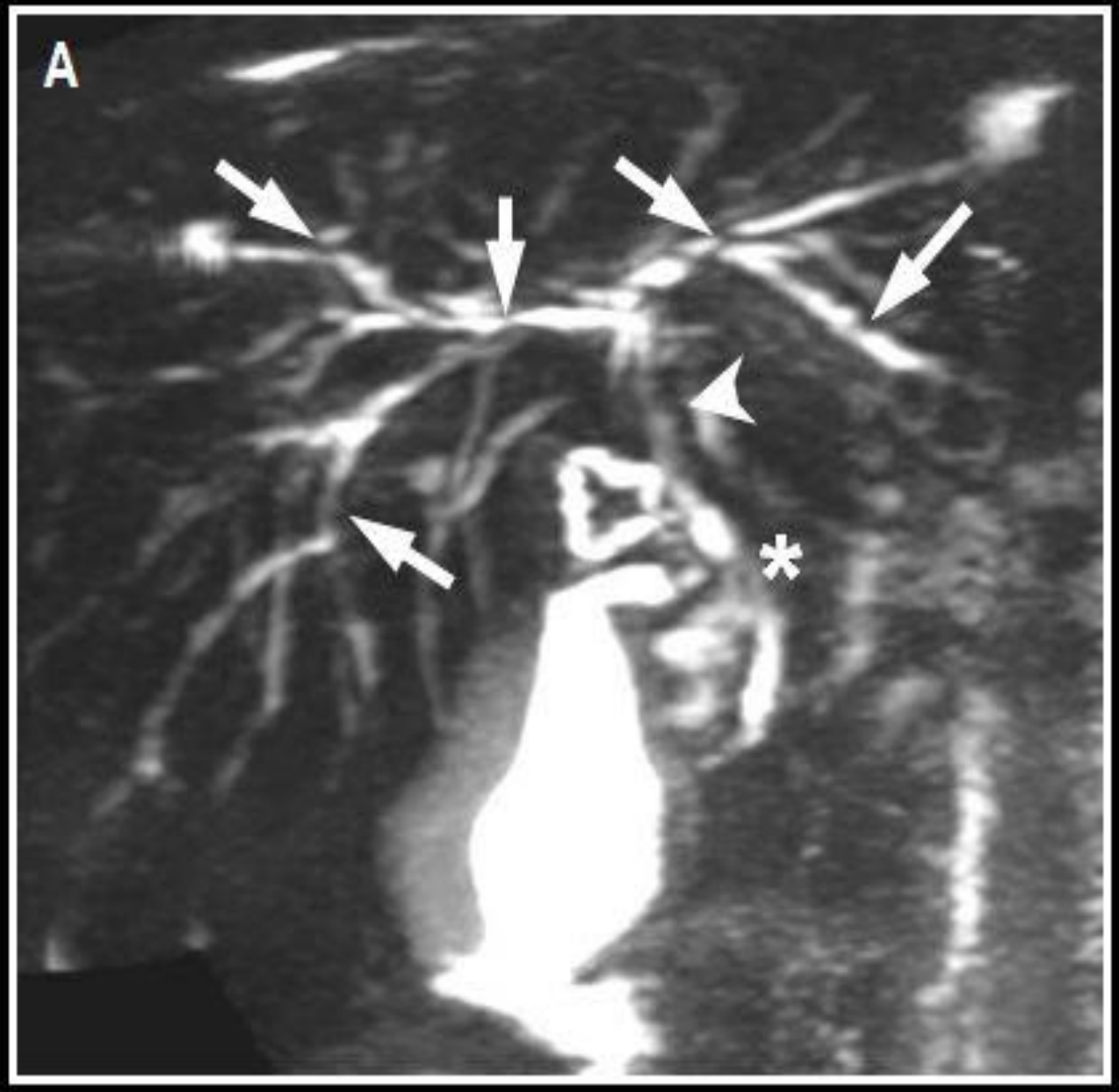
Modified Majoie classification
(As Applied to MRCP by Ferrara et al.)

Classification	Cholangiographic Findings
Intrahepatic (IHD)	
o	No visible abnormalities
I	Multiple Stricture, normal calibre of bile ducts or minimal dilatation
II	Multiple strictures, saccular dilatations, decreased arborisation
III	Closed stenosis to carrefour with obstruction or lack of visualization of one of the main hepatic ducts.
Extrahepatic (EHD)	
o	No visible abnormalities
I	Slight irregularities of duct contour, no stricture
II	Segmental Stricture
III	Stricture of almost entire length of duct
IV	Extremely irregular margin, diverticulum-like outpouching

- scored each of the intrahepatic segments; extrahepatic (CBD, CHD)



(A) 11-year old female with ulcerative colitis and non-specific intrahepatic biliary duct dilatation seen on ultrasound. Severe pruning of the left IHD (thin Arrow), Grade III, and lack of visualization of the right main IHD (asterisk), Grade III. Also, multiple strictures/saccular dilatations of the right IHD (thick Arrow), Grade II. Stricture of the CHD, Grade III (arrowhead). **(B)** 4-year old female with suspected pancreatic pseudocyst on ultrasound, no known history of PSC or IBD (control patient) – normal MRCP.



(A) 17-year old female with ulcerative colitis and PSC. Multiple strictures/saccular dilatations of all IHD (arrows), Grade II. Stricture of CHD, Grade III (arrowhead) and segmental stricture of the proximal CBD (asterisk).

Methods

- Data Collection and Definitions
  - Two blinded pediatric radiology fellows
  - Discrepancies resolved by a third blinded radiologist
  - Clinical data correlation provided by pediatric gastroenterologist

Methods

- **MRCP Imaging Technique**

Methods

- **MRCP Imaging Technique**
  - coronal 3 dimensional (3D) heavy T2-weighted turbo spin echo (TSE) MRCP
  - axial balanced steady-state free precession (bSSFP)
  - radial coronal single-shot T2 sequences
  - thin axial single-shot T2 weighted sequences
  - thin coronal single-shot T2 weighted sequences
  - axial T2-weighted TSE sequence with fat suppression
  - axial 3D T1-weighted gradient echo imaging without fat suppression,

Approximately 20-30 minutes

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Methods

- **MRCP Imaging Technique**
  - **coronal 3 dimensional (3D) heavy T2-weighted turbo spin echo (TSE) MRCP**
    - qualitatively grading bile ducts abnormalities
  - **axial balanced steady-state free precession (bSSFP)**
    - define their segmental anatomy
  - ~~radial coronal single-shot T2 sequences~~
  - ~~thin axial single-shot T2 weighted sequences~~
  - ~~thin coronal single-shot T2 weighted sequences~~
  - ~~axial T2-weighted TSE sequence with fat suppression~~
  - ~~axial 3D T1-weighted gradient echo imaging without fat suppression,~~

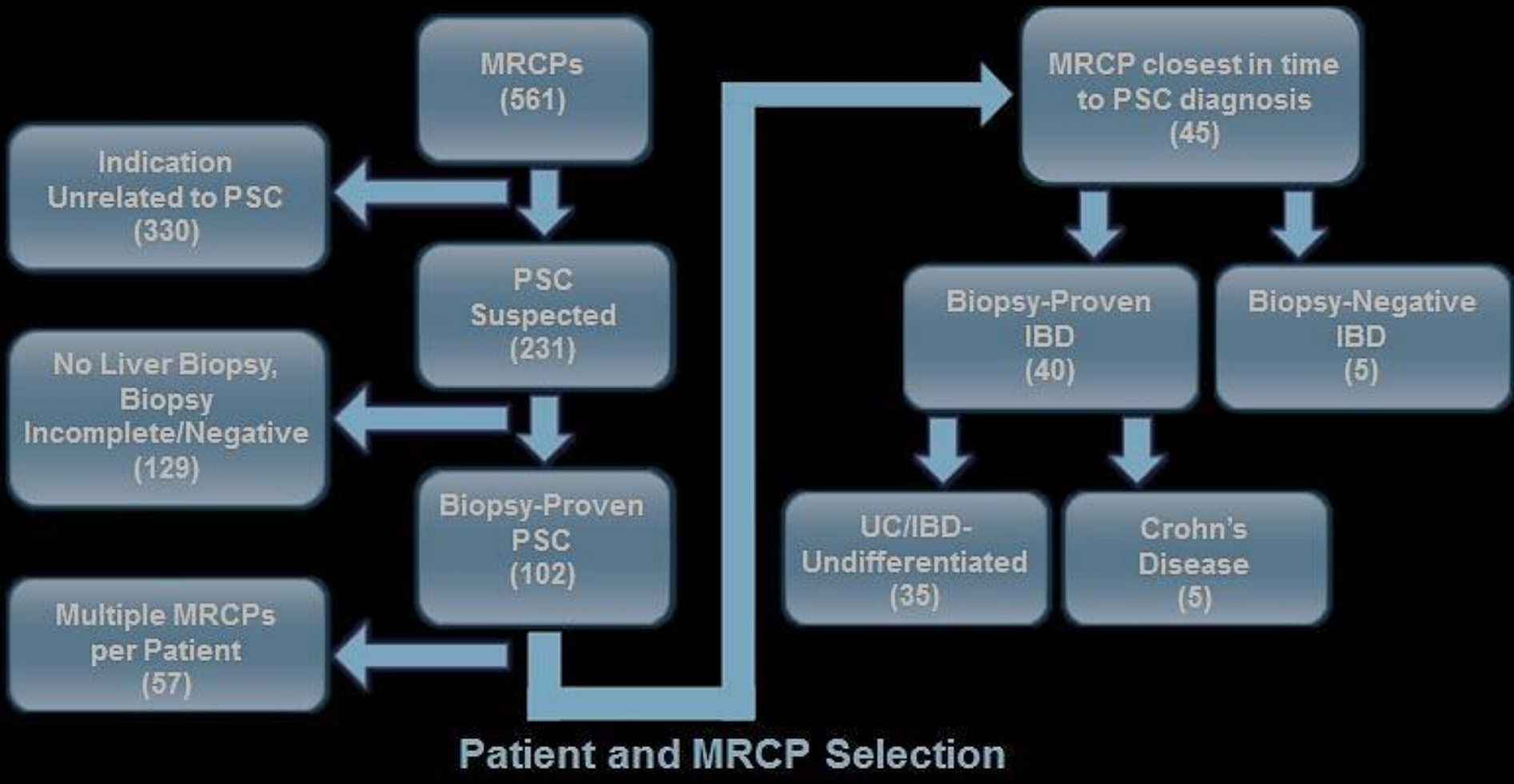
Approximately <10 minutes

Methods

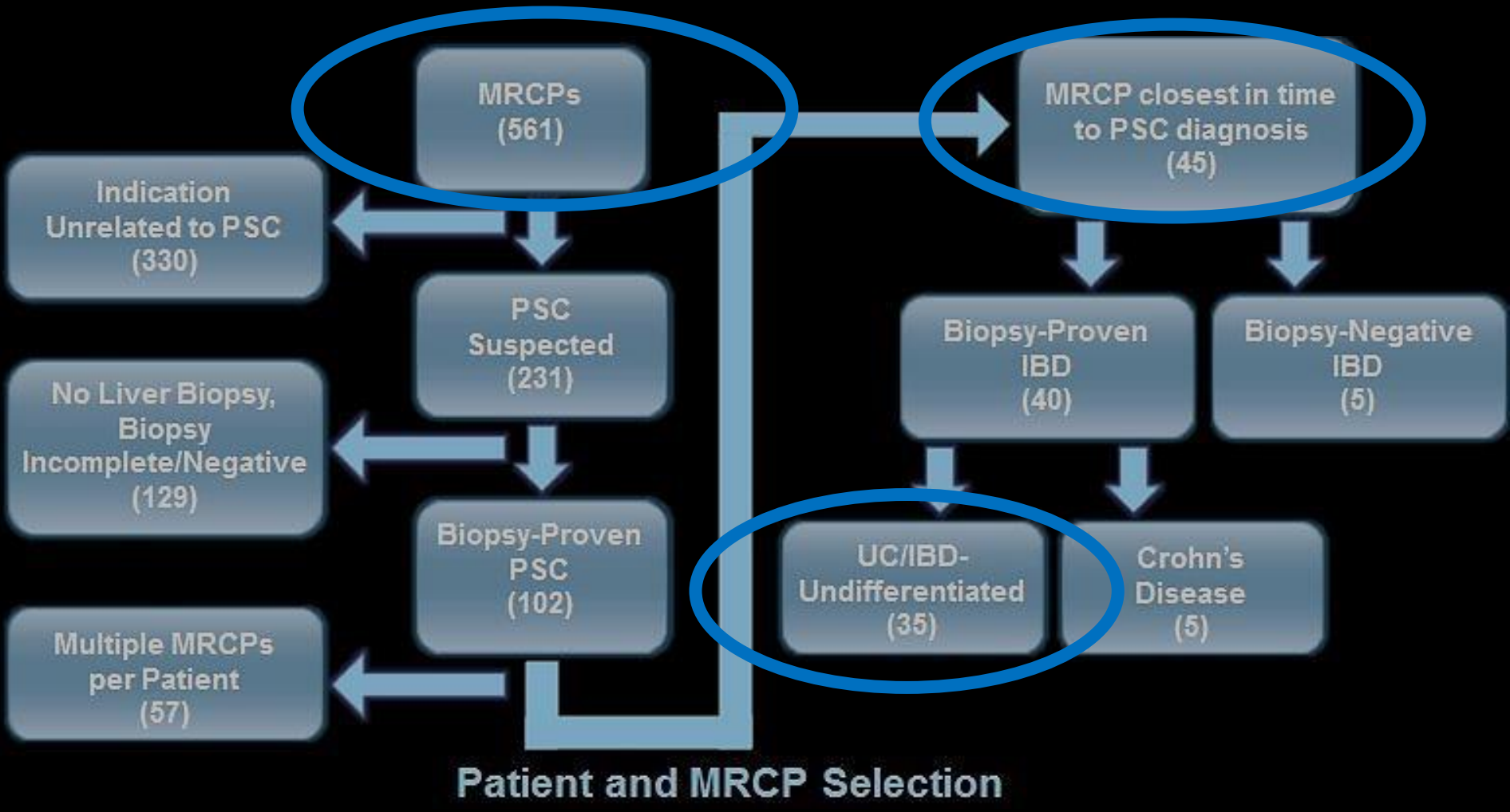
- Statistical Methods
  - Inter-rater **reliability** (Kappa, Intra-class correlation coefficients)
  - Construct **validity** (Spearman correlations)
  - Ability to **prognosticate** time to PSC-related complications

RESULTS

Results


MRCPs
(561)
Indication Unrelated to PSC
(330)
PSC Suspected
(231)
No Liver Biopsy, Biopsy Incomplete/Negative
(129)
Biopsy-Proven PSC
(102)
Multiple MRCPs per Patient
(57)
MRCP closest in time to PSC diagnosis
(45)
Biopsy-Proven IBD
(40)
Biopsy-Negative IBD
(5)
UC/IBD-Undifferentiated
(35)
Crohn's Disease
(5)
Patient and MRCP Selection

Results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Results

N (%) or median (IQR)	All PSC Patients (N=45)
Male	30 (67%)
Age at diagnosis (y)	
PSC	13.6 (10.3-15.2)
IBD	13.5 (10.1-15.5)
PSC follow-up duration (y)	3.4 (2.4-4.4)
Ulcerative Colitis (UC)/IBD-U	35 (78%)
Crohn's disease	5 (11%)
No IBD	5 (11%)
ASC	12 (27%)
Biochemistry at diagnosis	
ALT (U/L)	166 (73-359)
AST (U/L)	130 (51-383)
ALP (U/L)	398 (248-684)
GGT (U/L)	241 (122-484)
GGT x upper limit of normal	4.2 (2.5-9.4)
Bile acids (µmol/L)	21.6 (13.5-39.4)
Clinical outcomes	
Portal hypertension	15 (33%)
Ascites	5 (11%)
Esophageal varices	8 (18%)
Variceal bleed	4 (9%)
Cholangiocarcinoma	1 (2%)
Liver transplant	5 (11%)
PSC-related complication	10 (22%)

Results

IHD		EHD		Sum IHD + EHD	
0	4 (9%)	0	17 (40%)	0	4 (9%)
1	20 (44%)	1	12 (28%)	1	7 (16%)
2	17 (38%)	2	9 (21%)	2	15 (33%)
3	4 (9%)	3	5 (12%)	3	9 (20%)
		4	0 (0%)	4	5 (11%)
				5	3 (7%)
				6	2 (4%)
				7	0 (0%)
Average IHD	1 (1-1.6)	**Average EHD**	0.5 (0-1.5)	**Sum average IHD + EHD**	1.9 (1-2.5)

Hepatic changes	
Periportal edema	11 (24%)
None	26 (58%)

*More patients with IBD had IHD and EHD scores ≥2 than those without IBD.**
*Scores ≥2 were observed in 42% of left lobes, 33% of right lobes**
*(*not statistically significant)*

Results

Inter-rater reliability

Measure	Weighted Kappa (95% CI)	Intra-class Correlation Coefficient (95% CI)
IHD	0.81 (0.68-0.95)	-
EHD	0.79 (0.63-0.94)	-
Sum IHD + EHD	0.78 (0.64-0.91)	-
Average IHD score	-	0.81 (0.69-0.89)
Average EHD score	-	0.82 (0.69-0.90)
Sum average IHD + EHD	-	0.79 (0.66-0.88)

Results

Validity Assessment and Predictive Ability

Measure	C-statistic for PSC Complication (standard error)	C-statistic for Liver Transplant (standard error)
IHD	0.76 (0.12)	0.71 (0.10)
EHD	0.79 (0.16)	0.90 (0.04)
Sum IHD + EHD	0.87 (0.10)	0.95 (0.04)
Average IHD score	0.81 (0.08)	0.75 (0.10)
Average EHD score	0.75 (0.16)	0.78 (0.14)
Sum average IHD + EHD	0.82 (0.05)	0.81 (0.18)

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Sum average IHD + EHD	0.82 (0.05)	0.81 (0.18)

•Sum MRCP score incorporating worst intrahepatic and extrahepatic involvement outperforms individual intrahepatic and extrahepatic scores, as well as scores averaged across the multiple hepatic segments and ducts

Conclusions

- Modified Majoie classification is a **reliable** and **valid** tool for grading severity of PSC in MRCP of pediatric patients, including good ability to **prognosticate** progression to clinically relevant outcomes
  - Limited MRCP protocol using only two sequences

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- **Worse** area of disease i.e. severity, rather than the average involvement - or disease burden - across the liver, plays a bigger role in driving disease progression

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- In addition to use in research, this encourages application in routine reporting as a **standardized tool** to facilitate **consistent communication** of pediatric PSC severity amongst radiologists and clinicians

Thank You

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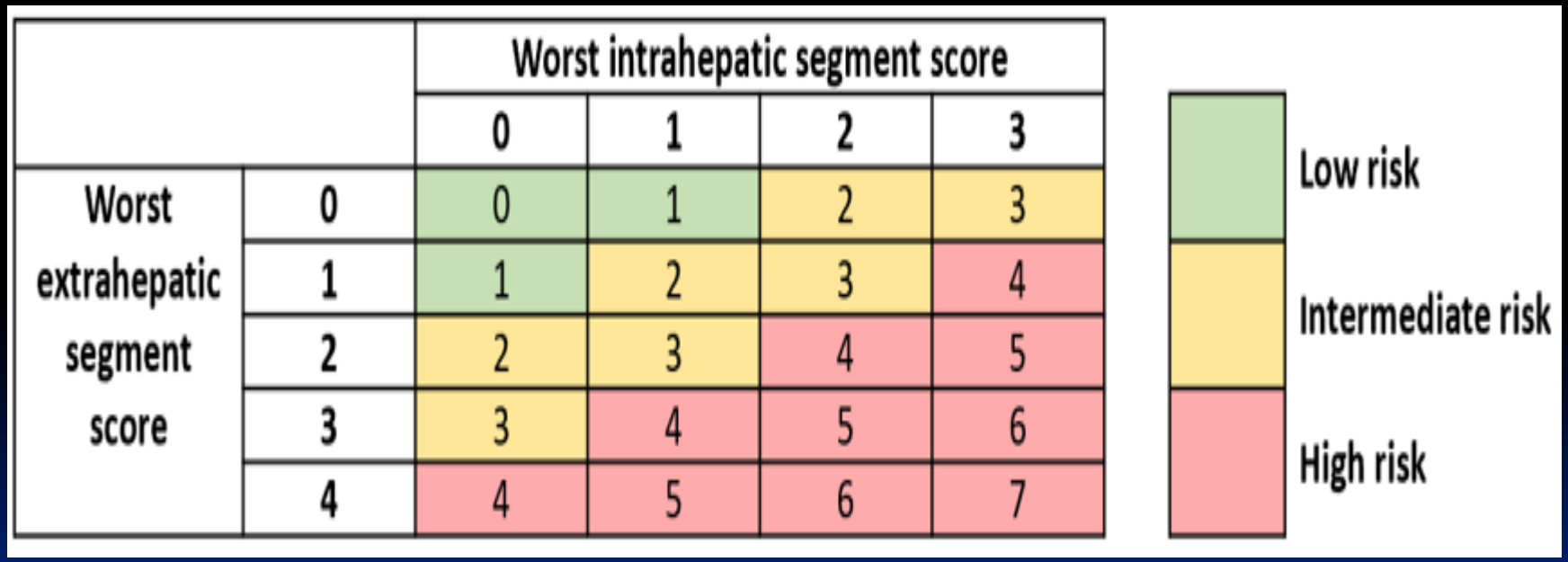
EXTRA SLIDES



		Worst intrahepatic segment score			
		0	1	2	3
Worst extrahepatic segment score	0	0	1	2	3
	1	1	2	3	4
	2	2	3	4	5
	3	3	4	5	6
	4	4	5	6	7

Low risk

Intermediate risk

High risk

EXTRA SLIDES

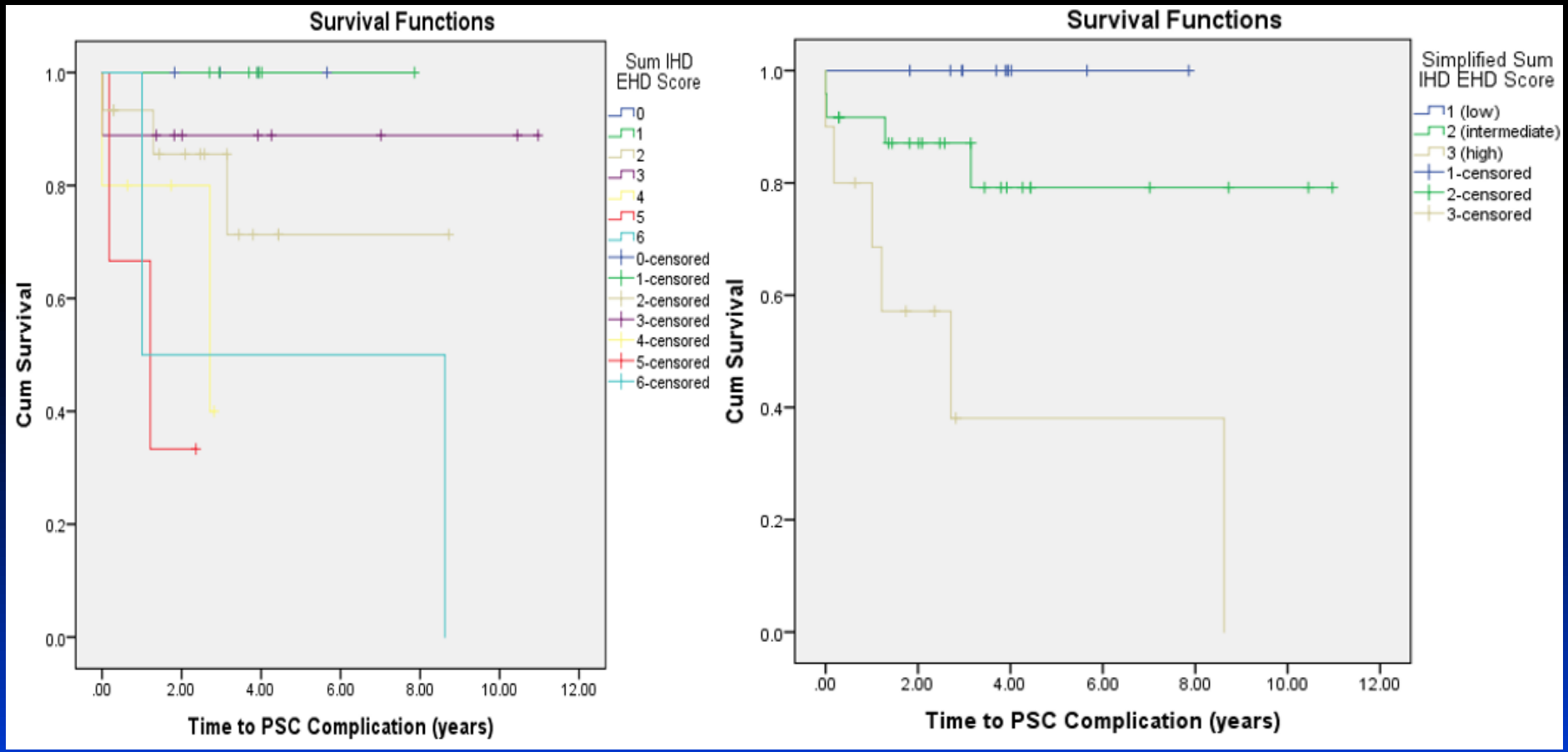


FIGURE 4: Kaplan-Meier curve for time to PSC-related complication by category of (A) sum IHD and EHD score (overall log-rank p=0.001); and (B) simplified sum (overall log-rank p=0.018).

EXTRA SLIDES

Statistical Analysis:

- The traditional intrahepatic duct (IHD) and extrahepatic duct (EHD) scores, as well as sum and averaged variations, were examined. MRCPs in patients without PSC served as controls.
- Inter-rater reliability was determined using weighted kappa statistics and intra-class correlation coefficients and the ability of the various scores to discriminate progression to PSC-related complications was examined using Uno c-statistics.
- The association between the best performing score and time to PSC complications was investigated with univariate and multivariable Cox proportional hazards regression.