



PSC Forum 8

Thursday, 14 November 2024
San Diego, CA

PSC Forum Acute Cholangitis Working Group Update

Clinical Definition of Acute Cholangitis

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Div. of Gastroenterology & Hepatology
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Clinical Definition of Acute Cholangitis

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Faculty Disclosure

I herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments, and anything else which could potentially be viewed as a conflict of interest:

Advisor

Abbvie, Albireo, Agomab, Boehringer Ingelheim, Chemomab, Falk, Gilead, Genfit, Hightide, Intercept, Ipsen, Janssen, Mirum, Novartis, Pliant, Rectify

Grants / research support

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Speakers bureau

Albireo, Falk Foundation, Gilead, Intercept, Ipsen, Madrigal

Travel grants

AbbVie, Falk Foundation, Gilead, Intercept, Janssen

Property rights

Co-inventor (service invention) for patents on medical use of *norUDCA* (filed by the Medical Universities of Graz and Vienna)

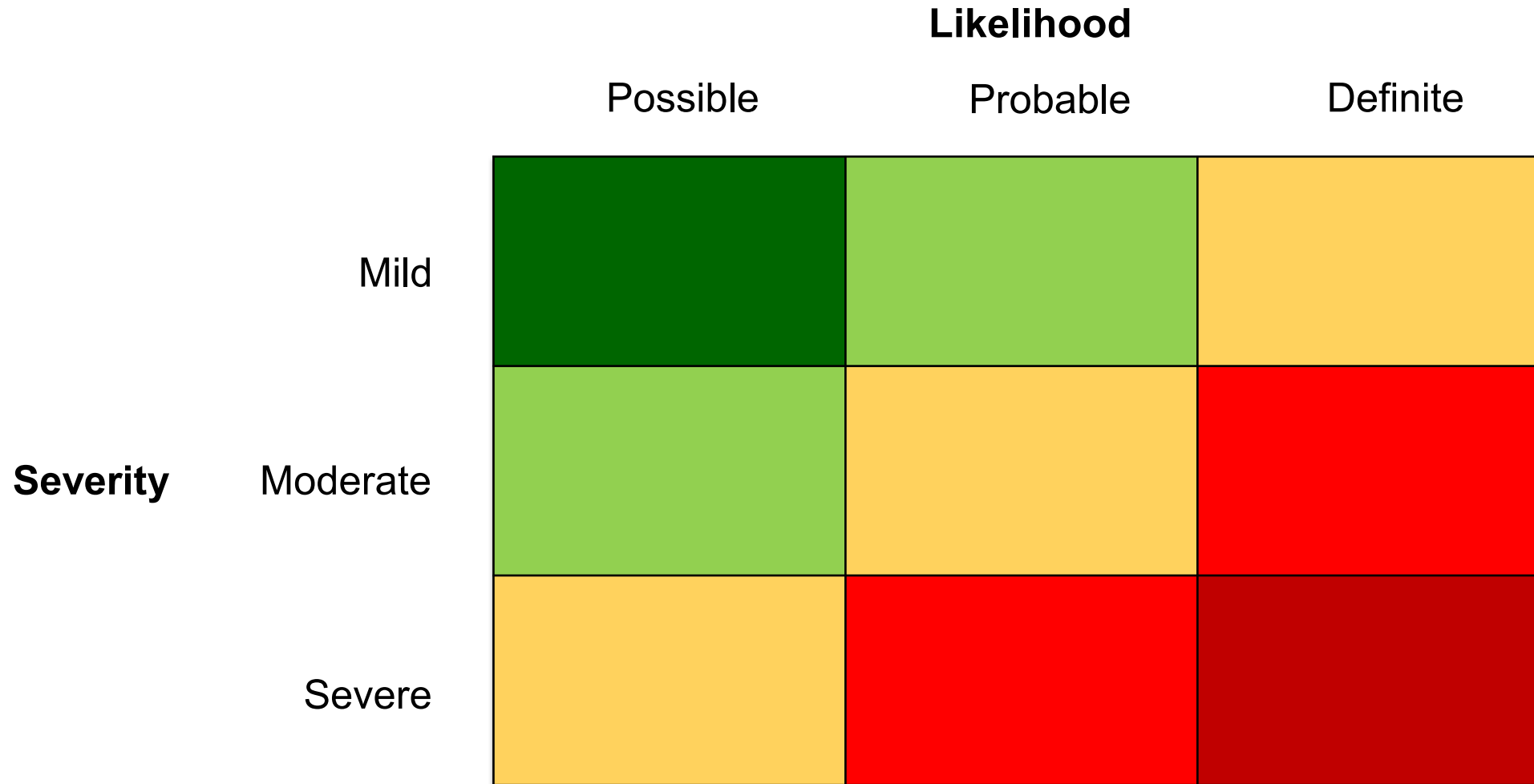


Aims of the Acute Cholangitis working group

- Clear definition and grading system for acute cholangitis in PSC
- Establish acute cholangitis as a recognized endpoint in clinical trials
- Understand the impact of acute cholangitis on patient outcomes



Heatmap of acute cholangitis



Defining the severity of acute cholangitis

GRADE	Definition
Mild	Oral antibiotics
Moderate	iv antibiotics (more than 1 day)
Severe	Invasive procedures: endoscopic, radiologic, or surgical intervention Life threatening consequences; hypotension; ICU admission Death

Suggestions for use of Common Terminology Criteria for Adverse Events (CTCAE) grades

GRADE	Definition
2	Oral antibiotics
3	IV antibiotics; endoscopic, radiologic, or surgical intervention
4	Life threatening consequences; hypotension; ICU admission
5	Death



Defining the likelihood of acute cholangitis

- Criteria / domains -

Domain
Symptoms (& Signs) (emphasis on new or worsening!)
Inflammation (in the absence of other source)
Infection
Cholestasis
Imaging (US, CT, MRI) Could be integrated in above (cholestasis, inflammation, infection)



Domain	Major/strong
Symptoms (& Signs) (emphasis on new or worsening!)	RUQ pain
	Pruritus (new onset or worsening)
	New / increasing jaundice
Inflammation (in the absence of other source)	Fever T > 38°C and/or shivering
	Leukocytosis > 12,000/ μ l
	CRP > 10 mg/L
	PCT > 2.0 ng/mL
Infection	Pus on ERCP
	Positive bile culture
	Positive blood culture (in absence of other source)
Cholestasis	ALP > 75% increase from baseline
	Total bilirubin > 75% increase
Imaging (US, CT, MRI) Could be integrated in above (cholestasis, inflammation, infection)	New or worsening biliary dilations, strictures, sludge/stones
	Enhancement (arterial + DWI / MRI)
	Biliary abscess



Domain	Major/strong	Minor/weak
Symptoms (& Signs) (emphasis on new or worsening!)	RUQ pain	Abdominal discomfort/pain Pain in unusual locations (e.g. back/shoulder pain)
	Pruritus (new onset or worsening)	New onset fatigue (or worsening)
	New / increasing jaundice	Change in stool colour Change in urine colour
Inflammation (in the absence of other source)	Fever T > 38°C and/or shivering	
	Leukocytosis > 12,000/ μ l	
	CRP > 10 mg/L	
	PCT > 2.0 ng/mL	
Infection	Pus on ERCP	
	Positive bile culture	
	Positive blood culture (in absence of other source)	
Cholestasis	ALP > 75% increase from baseline	AST and/or ALT > 75% increase
	Total bilirubin > 75% increase	GGT > 75% increase from baseline
Imaging (US, CT, MRI) Could be integrated in above (cholestasis, inflammation, infection)	New or worsening biliary dilations, strictures, sludge/stones	
	Enhancement (arterial + DWI / MRI)	Bile duct wall thickening
	Biliary abscess	



Defining the likelihood of acute cholangitis

Possible Acute Cholangitis

1 Symptom + 1 Inflammation

1 Symptom + 1 Cholestasis

Probable Acute Cholangitis

1 Symptom + 1 Inflammation + 1 Cholestasis (or Imaging feature)

Definite Acute Cholangitis

1 Symptom + 1 Inflammation + 1 Infection

OR

1 Symptom + 2 Inflammation + 1 Cholestasis (or 1 + 1 + 2)

N.B.: Pus on ERCP (suppurative cholangitis) and/or biliary abscess allows a definite diagnosis as single criterium

Minor criteria could “count as half” or qualify only for possible cholangitis?



Defining the likelihood of acute cholangitis

Possible Acute Cholangitis: **meeting 2 criteria**

1 Symptom + 1 Inflammation

1 Symptom + 1 Cholestasis

Probable Acute Cholangitis: **3 criteria**

1 Symptom + 1 Inflammation + 1 Cholestasis (or Imaging feature)

Definite Acute Cholangitis: **4 criteria (or 3 including infection)**

1 Symptom + 1 Inflammation + 1 Infection

OR

1 Symptom + 2 Inflammation + 1 Cholestasis (or 1 + 1 + 2)

N.B.: **Pus on ERCP** (suppurative cholangitis) and/or **biliary abscess** allows a definite diagnosis as **single criterium**

Minor criteria could “count as half” or qualify only for possible cholangitis?



GUIDELINE

Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos)

Table 2 TG18/TG13 diagnostic criteria for acute cholangitis [4]

- A. Systemic inflammation
 - A-1. Fever and/or shaking chills
 - A-2. Laboratory data: evidence of inflammatory response
- B. Cholestasis
 - B-1. Jaundice
 - B-2. Laboratory data: abnormal liver function tests
- C. Imaging
 - C-1. Biliary dilatation
 - C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)

Suspected diagnosis: one item in A + one item in either B or C

Definite diagnosis: one item in A, one item in B and one item in C

Thresholds:

A-1	Fever		BT >38°C
A-2	Evidence of inflammatory response	WBC count (×1,000/μL) CRP (mg/dL)	<4 or >10 ≥1
B-1	Jaundice		T-Bil ≥2 (mg/dL)
B-2	Abnormal liver function tests	ALP (IU) γGTP (IU) AST (IU) ALT (IU)	>1.5 × STD ^a >1.5 × STD ^a >1.5 × STD ^a >1.5 × STD ^a



Wannhoff criteria of superimposed bacterial cholangitis

Single criterion: Suppurative cholangitis on ERC

Main criteria (≥ 1): Body temperature $> 38.0^{\circ}\text{C}$

Leukocyte count $> 12/\text{nL}$ or CRP $> 75.0 \text{ mg/L}$

Minor criteria (≥ 2): Clinical signs of acute cholangitis (e.g., right upper abdominal pain)

Positive bile culture

Increase in the level of ALP or total bilirubin above two times the upper limit of normal

No other focus of infection

Single criterion
OR
1 Main + 2 Minor





Article

Cholangitis Definition and Treatment after Kasai Hepatoportoenterostomy for Biliary Atresia: A Delphi Process and International Expert Panel

Ana M. Calinescu ^{1,*}, Omid Madadi-Sanjani ^{2,†}, Cara Mack ³, Richard A. Schreiber ⁴, Riccardo Superina ⁵, Deirdre Kelly ^{6,†}, Claus Petersen ^{2,†} and Barbara E. Wildhaber ^{1,†}

A. Clinical elements

- Fever and/or shivering
- Stool color change
- New/increasing jaundice
- Abdominal discomfort*

B. Laboratory and imaging elements

- Inflammatory response (WBC and/or CRP and/or PCT)
- Increased/increasing transaminases
- Increased/increasing GGT and/or bilirubin
- Bile lakes

*Definition for abdominal discomfort: vomiting, poor feeding, irritability

Suspected Cholangitis**:

- **Definition:** one item in A + one item in B
- **Treatment:** 10 – 14 days

Confirmed Cholangitis**:

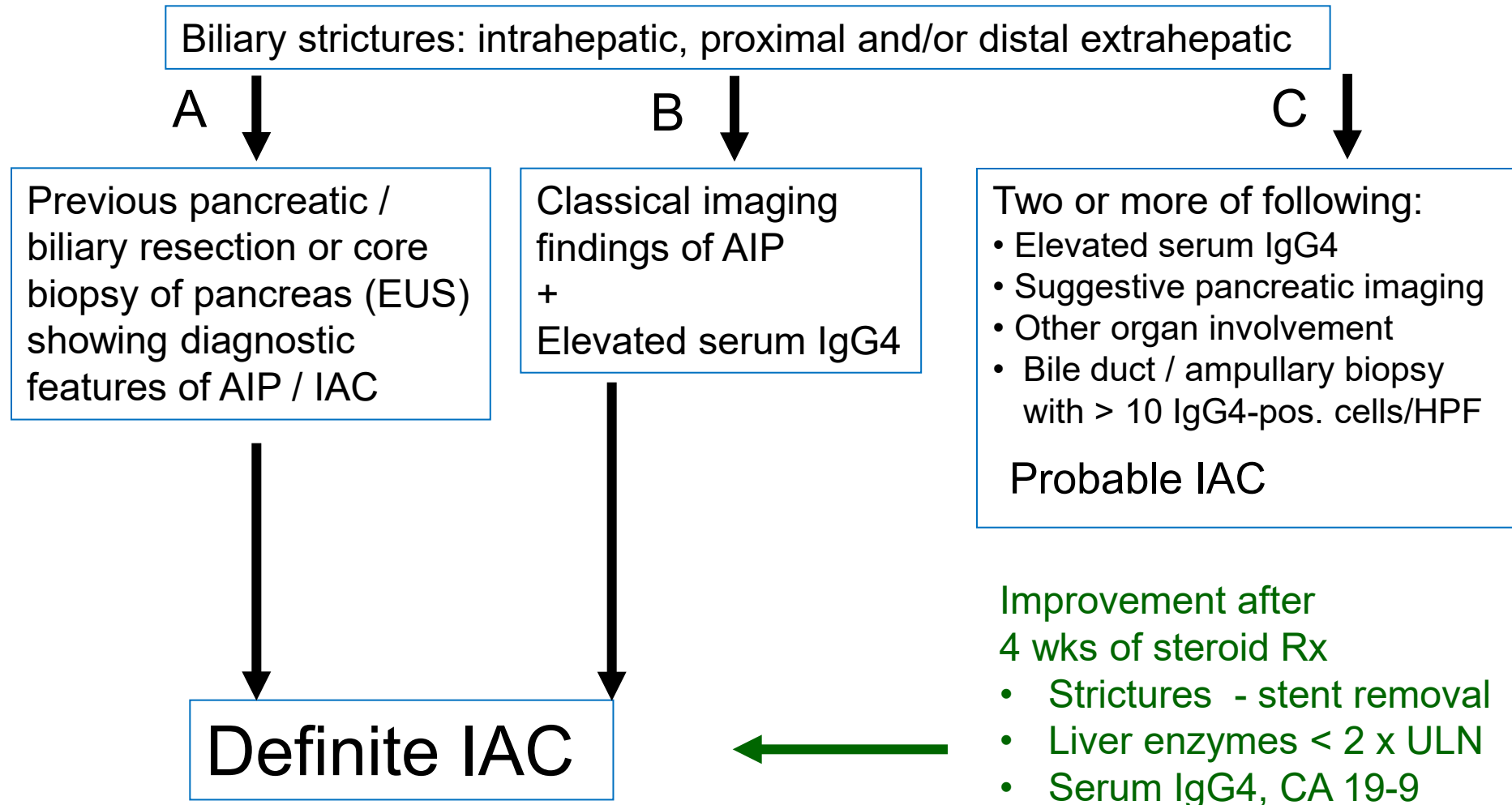
- **Definition:** two items in A + two items in B
- or
- “suspected cholangitis” + positive blood culture
- **Treatment:** 14 – 21 days

Peroral **prophylaxis** of cholangitis: 6 – 12 months

**Cholangitis within 1st year after Kasai



Diagnosis of IgG4-related Cholangitis - HISORt Criteria -



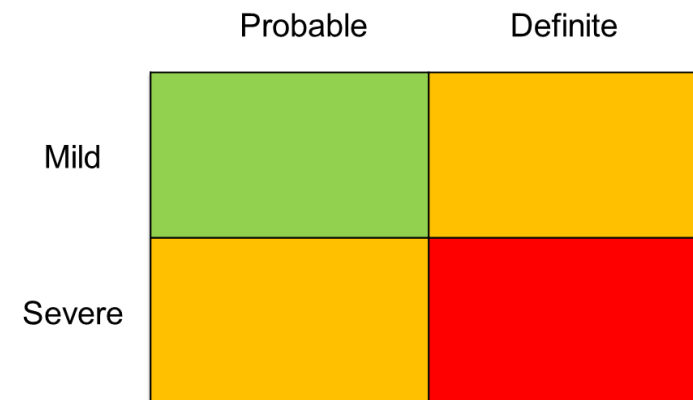
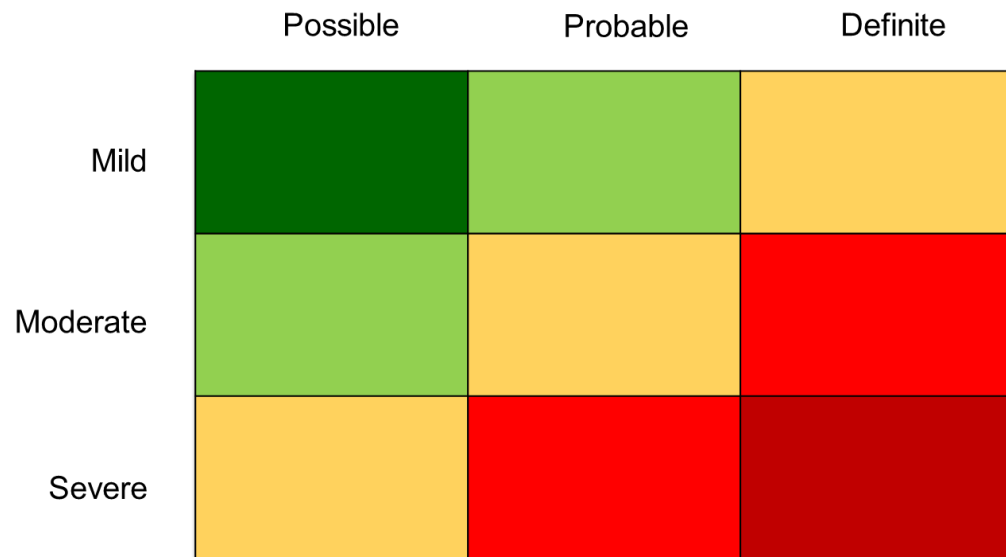
Ghazale et al., *Gastroenterology* 2008;134:706

EASL Clinical Practice Guidelines *J Hepatol* 2009; 51: 237-67

UEG Guidelines - Loehr et al., *United European Gastroenterology Journal* 2020; 8: 637-666



Heatmap of acute cholangitis - hypothetical trial



Heatmap of acute cholangitis - hypothetical trial

14 cases PBO vs 9 cases XYZ

PBO

	Probable	Definite
Mild	4	2
Severe	2	6

XYZ

	Probable	Definite
Mild	5	1
Severe	1	2





**Thank you for
your attention!**
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Wannhoff criteria of superimposed bacterial cholangitis

- If the SINGLE criterion was met, no further requirements had to be fulfilled for the diagnosis of cholangitis
- In all other cases:
 - presence of at least ONE of the MAIN criteria, indicating inflammation
 - AND at least TWO MINOR criteria were mandatory for the diagnosis of cholangitis
- Minor criteria were chosen to differentiate between cholangitis-induced increase in inflammation markers and increase due to other causes

