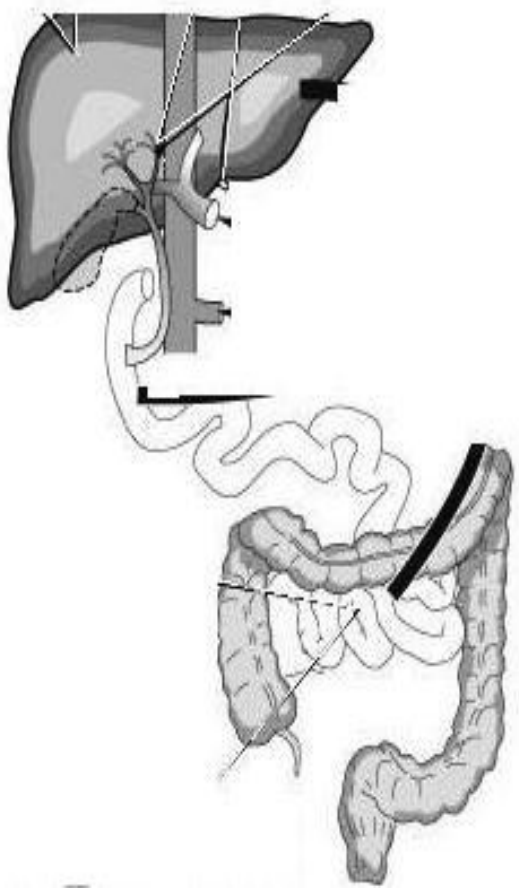


Réunion de Consensus sur la Maladie de Cröhn

# Situations particulières
# Quelle attitude adopter
# Complications hépato-biliaires

Pr Nabil DEBZI

Alger les 25 et 26 septembre 2013

Auditorium de l'Institut Pasteur d'Algérie  Dely Ibrahim

# Manifestations hépato-biliaires associées au MICI

La prévalence des anomalies hépato - biliaires

au cours de MICI est élevée : anomalies des tests hépatiques 12-15% ,
PBH systématique : 50% d'anomalies

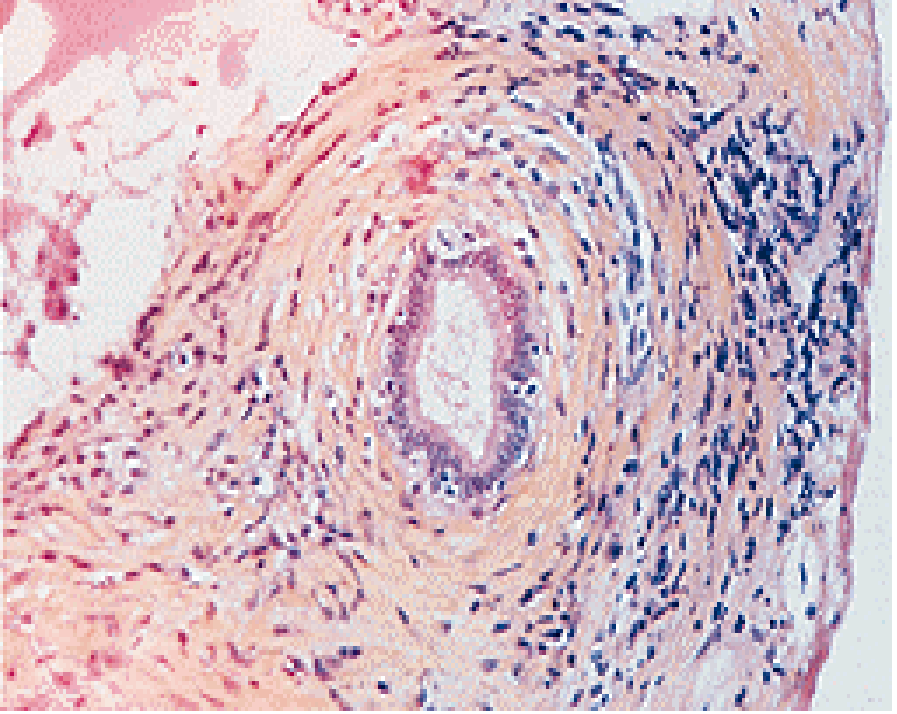
| | RCH | MC |
|---|---|---|
| Stéatose | ++ | + + |
| Effets indésirables des médicaments | + | + |
| Cholangite sclérosante primitive | ++ | + |
| Cholangiocarcinome | + | ± |
| Carcinome hépato-cellulaire | ± | - |
| Hépatite chronique active | + | - |
| Cirrhose | + | + |
| CBP | ± | - |
| Granulomes | - | + |
| Amylose | - | + |
| Lithiase biliaire | + | ++ |
| Abcès hépatiques | - | + |

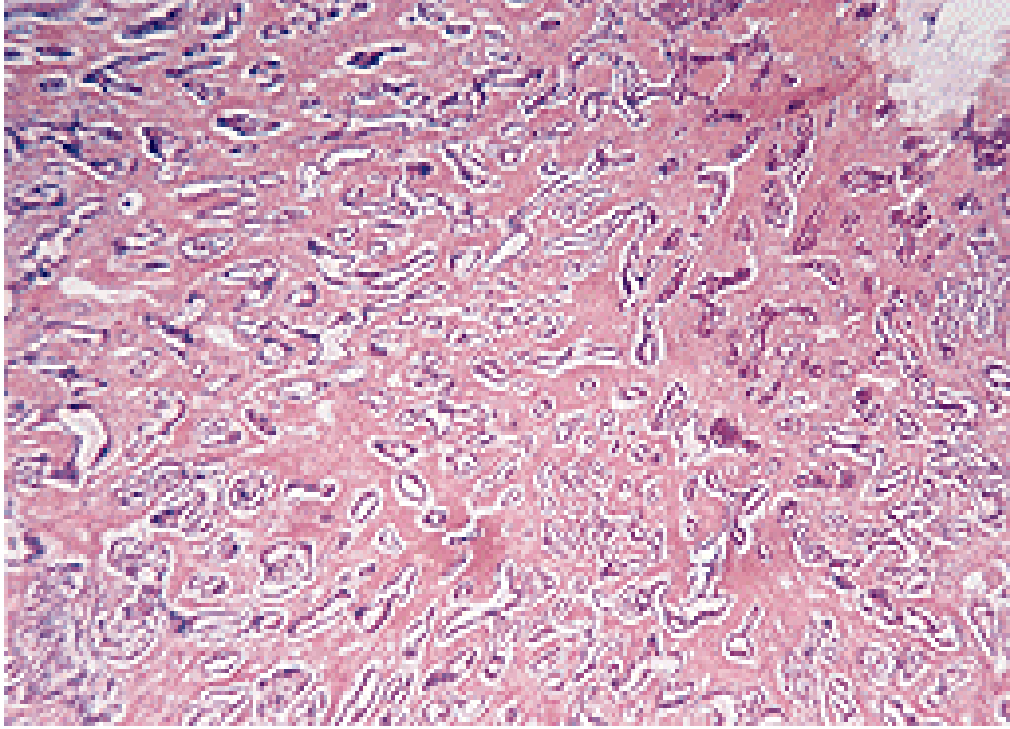
++ fréquente , +démontrée ,± possible , - pas d'association rapportée

***X.Causse et coll.Hépato-Gastro. Vol. 4, n° 2, mars-avril 1997 : 119-26***

# CSP et MICI

- **Prévalence :**
  **RCH = 2.4-7.5% 1-6 cas / $10^5$**
  **sex ratio H/F= 2 , Age = 39 ans**
  **75 % des CSP ont une MICI = 87% RCH , 13% MC.**
- **Critères Dg**
  **- cholestase chronique:**
  ***symptomatique**
  ***asymptomatique**
  **- cholangite fibreuse et oblitérante**
  **- anomalies des voies VBIH et /ou EH**
  **- association à une MICI : pancolite**
  **dg = 2 critères ( au moins Rx ou histologique)**
- **Small duct PSC : CSP des « petits » canaux = péricholangite , prévalence < 5%**
  **Critères Dg : Cholestase chronique + histologie + Cholangiographie normale+MICI+Dg =**





**CSP**

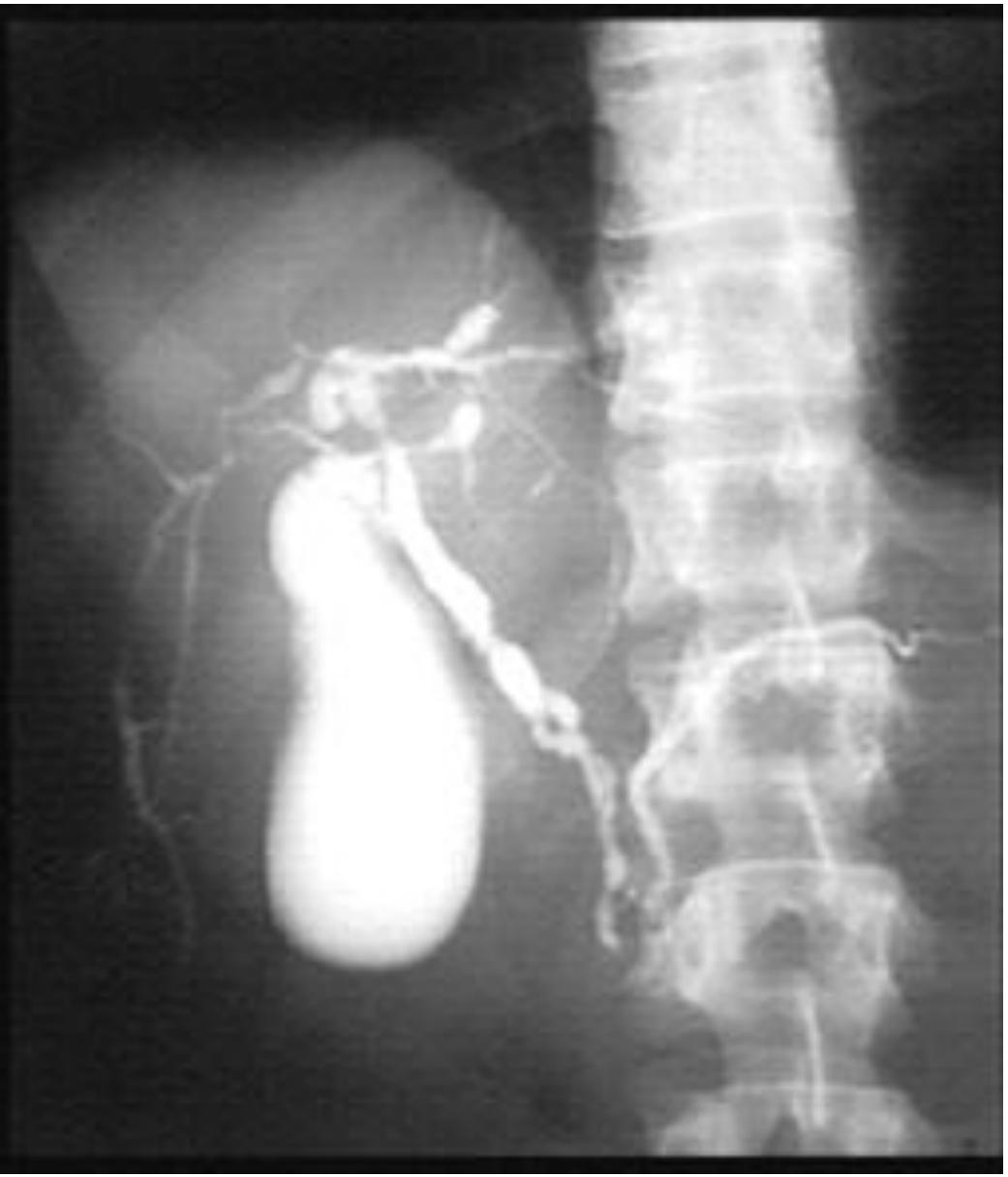
**Cholangiocarcinome**

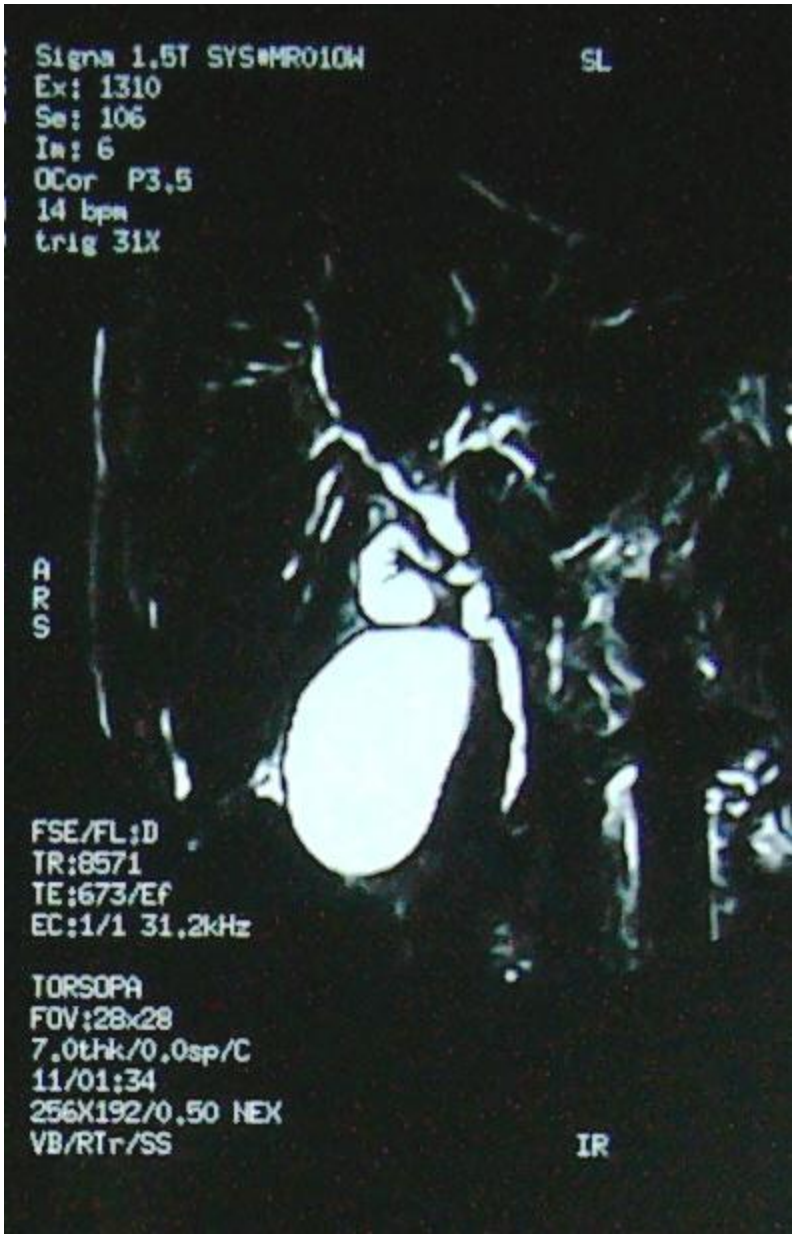
1 : lésions purement portales
2 : Périportales inflammation et fibrose débordent de l'espace porte
3 : fibrose extensive sans cirrhose
4 : Cirrhose avec nodules de régénération, et risque deCholangiocarcinome

**Recommendations**

1. A diagnosis of PSC is made in patients with biochemical markers of cholestasis not otherwise explained, when MRCP shows typical findings and causes of secondary sclerosing cholangitis are excluded (II-2/B1). A liver biopsy is not essential for the diagnosis of PSC in these patients, but allows activity and staging of the disease to be assessed.
2. A liver biopsy should be performed to diagnose small duct PSC if high-quality MRCP is normal, (III/C2). A liver biopsy may also be helpful in the presence of disproportionally elevated serum transaminases and/or serum IgG levels to identify additional or alternative processes (III/C1).
3. ERCP can be considered
   (i) If high-quality MRCP is uncertain (III/C2): the diagnosis of PSC is made in the case of typical ERCP findings.
   (ii) In patients with IBD with normal high-quality MRCP but high suspicion for PSC (III/C2).

Please cite this article in press as: EASL Clinical Practice Guidelines: Management of cholestatic liver diseases. J Hepatol (2009), doi:10.1016/j.jhep.2009.04.009




Signa 1.5T SYS#MR01GW
SL
Ex: 1310
Se: 106
Im: 6
OCor P3.5
14 bpm
trig 31X
A
R
S
FSE/FL:D
TR:8571
TE:673/Ef
EC:1/1 31.2kHz
TORSOPA
FOV:28x28
7.0thk/0.0sp/C
11/01:34
256X192/0.50 NEX
VB/RTr/SS
IR

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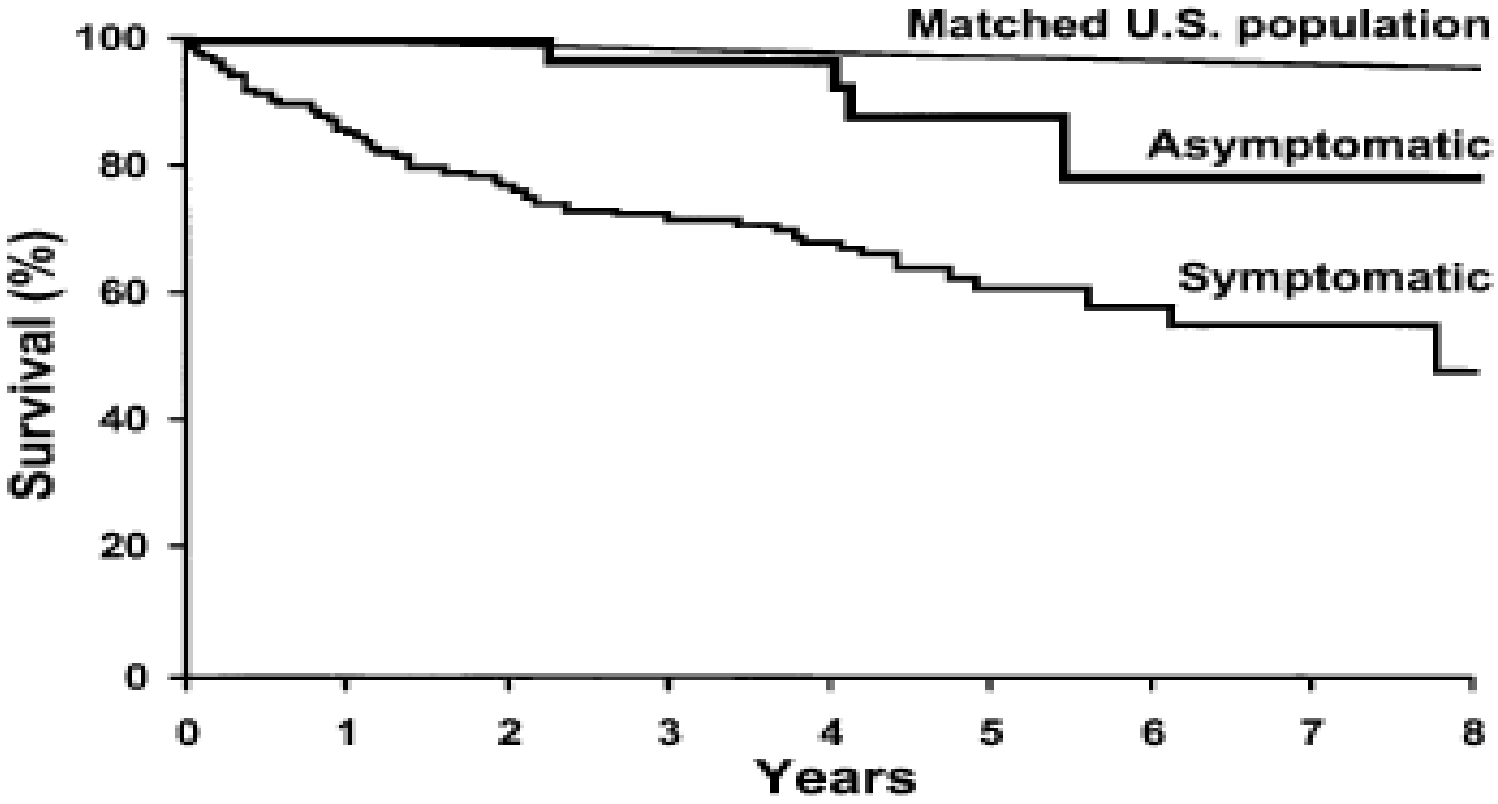



Wiesner RH, Grambsch PM, Dickson ER, Ludwig J, MacCarty RL, Hunter EB, et al. Primary sclerosing cholangitis: natural history, prognostic factors and survival analysis. Hepatology 1989;10:430–436.

# THE REVISED NATURAL HISTORY MODEL FOR PRIMARY SCLEROSING CHOLANGITIS

In the following model, survival probability of a patient with primary sclerosing cholangitis is estimated based on the following variables. Please enter data in the corresponding boxes.

| | | |
|---|---|---|
| How old is the patient? | 52 | (years) |
| What is the bilirubin? | 4.5 | (mg/dl) |
| What is the albumin? | 3.8 | (g/dl) |
| What is the AST? | 60 | (IU/l) |

Please choose one of the following for history of variceal bleeding.

- (•) No history
- ( ) Past history

Compute

**Risk score:** 1.3570

**Estimated Probability of Survival (%)**

| Time 0 | Year 1 | Year 2 | Year 3 | Year 4 |
|---|---|---|---|---|
| **100** | 95 | 89 | 82 | 77 |

Reset

# Cancers et CSP

- **Prévalence CholangioKc : 10-30%**
- ***Prévalence des Kc hépatobiliaires : CholangioKc , Kc VB , CHC = 13.3%**
  **Risque Kc pancréas X 14 ,**
  **Kc du colon X 10 / population générale**
- **Cancer colorectal**

| Suivi | CSP + RCH | RCH |
|---|---|---|
| 10 ans | 9% | 2% |
| 20 ans | 31% | 5% |
| 25 ans | 50% | 10 - 25% |

* Bergquist A, Ekbom A, Olsson R, Kornfeldt D, Loof L, Danielsson A, et al. Hepatic and extrahepatic malignancies in primary sclerosing cholangitis. J Hepatol 2002;36:321–327.

# Cholangiocarcinome et CSP

- **Localisation : intra, extrahépatique ou vésiculaire**
- **Prévalence : 15 %**
  **(le cancer révèle la CSP dans 1/3 des cas)**
- **Incidence annuelle : 1,5 %**
- **Facteurs de risque**
  - **Sévérité de la CSP**
  - **Antécédent de dysplasie ou de cancer colorectal**
- **Survie à 3 et 5 ans après la greffe < 30 %**
- **Problème du Dg précoce+++**

Tableau 3. Propositions de surveillance des CSP

- Tous les 6 mois :
  - examen clinique,
  - tests hépatiques simples (bilirubine, enzymes, électrophorèse des protides, NFS plaquettes, TP),
  - marqueurs tumoraux (CA 19-9) (?) ;
- Tous les ans :
  - imagerie du foie et des voies biliaires (échographie « experte » ou mieux IRM hépatique et biliaire),
  - coloscopie avec chromoendoscopie et biopsies systématiques (si MICI associée),
  - élastométrie (?);
- Tous les 4 ans :
  - ostéodensitométrie,
  - dosage sérique des vitamines liposolubles.

Post'U (2009) 1-12

O. Chazouillères (✉)

# Les manifestations hépatobiliaires au cours des MICI

# CSP et AUDC

**Placebo-controlled trials of UDCA in PSC[a]**

| Authors, year | No. of patients | Biochemical response | Histological response | Mayo Risk Score or survival | Dose (mean duration) |
|---|---|---|---|---|---|
| Beuers et al., 1992 | 14 | Yes | Yes | No improvement | 13–15 mg/kg/day (1 year) |
| Lo et al., 1992 | 18 | Trend | No | NA | 10 mg/kg/day (2 years) |
| Van Thiel et al., 1992 | 48 | Yes | NA | NA | 600 mg/day (18 months) |
| Stiehl et al., 1994 | 20 | Yes | Yes | NA | 750 mg/day (1 year) |
| De Maria et al., 1996 | 59 | No | No | NA | 600 mg/day (2 years) |
| Lindor, 1997 | 105 | Yes | No | No improvement | 13–15 mg/kg/day (2.2 years) |
| Van Hoogstraten et al., 1998 | 48 | Yes | Trend | No improvement | 10 mg/kg/day (2 years) |

[a] NA, not available.

a multicentre study using high doses of 28–30 mg/kg/d of UDCA in 150 PSC patients over 5 years has been aborted because of an enhanced risk in the UDCA treatment group to reach primary endpoints such as liver transplantation or development of varices in more advanced disease while biochemical features improved in the whole UDCA group

Lindor KD, Enders FB, Schmoll JA, Hoskin TL, Jorgensen RA, Petz JL, et al. Randomized, double-blind controlled trial of high-dose ursodeoxycholic acid for primary sclerosing cholangitis. Hepatology 2008;48:378A.

## Recommendations

1. The available data base shows that UDCA (15–20 mg/d) improves serum liver tests and surrogate markers of prognosis (I/B1), but does not reveal a proven benefit on survival (III/C2). The limited data base does not yet allow a specific recommendation for the general use of UDCA in PSC.
2. Currently there is suggestive but limited evidence for the use of UDCA for chemoprevention of colorectal cancer in PSC (II-2/C2). UDCA may be particularly considered in high-risk groups such as those with a strong family history of colorectal cancer, previous colorectal neoplasia or longstanding extensive colitis (III/C2).
3. Corticosteroids and other immunosuppressants are not indicated for treatment of PSC in adults unless there is evidence of an overlap syndrome (III/C2).

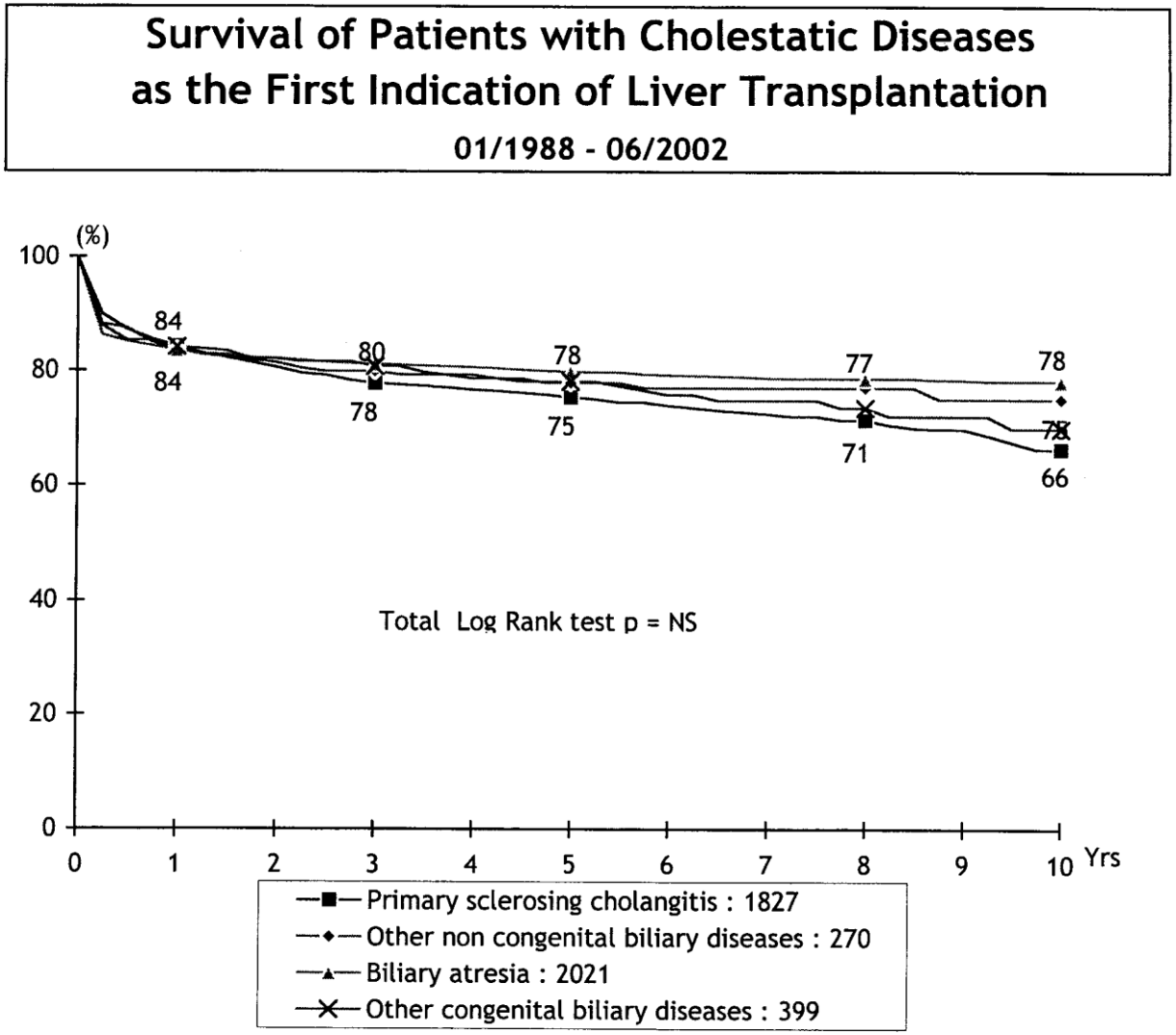
Please cite this article in press as: EASL Clinical Practice Guidelines: Management of cholestatic liver diseases. J Hepatol (2009), doi:10.1016/j.jhep.2009.04.009

# Traitement Endoscopique ?

⇒ dilatation au ballonnet (+/- prothèse biliaire temporaire) si sténose unique ou nettement prédominante au niveau du hile ou de la VBP

4. Dominant bile duct strictures with significant cholestasis should be treated with biliary dilatation (II-2/B1). Biliary stent insertion should be reserved for cases where stricture dilatation and biliary drainage are unsatisfactory (III/C2). Prophylactic antibiotic coverage is recommended in this setting (III/C1).

Please cite this article in press as: EASL Clinical Practice Guidelines: Management of cholestatic liver diseases. J Hepatol (2009), doi:10.1016/j.jhep.2009.04.009




**Récidive de la maladie initiale : 8-20%**

**Effet de la transplantation et des immunosuppresseurs**

Aggravation de la RCH (rechute, cortico-dépendance)

Survenue fréquente de dysplasie sévère : 15% à 5 ans

d'adéno-carcinome, de lymphome gastro-intestinal : 1.25% par an

# Indications de la TH

- Bilirubinémie > 100 umol/l
- Angiocholites récidivantes : mal contrôlées par les ATB , par le drainage endoscopique ,Rx , ou CRG , impossibilité de drainage
- IHC
- Complications de l'HTP
- Mayo score > 4
- MELD Score n'est pas adapté

# LES MEDICAMENTS

- Thiopurines
  Hyperplasie nodulaire régénérative
  -Atteinte non fibrosante du foie pouvant induire une HTP symptomatique
  -Thrombopénie
  -PBH dg difficile
  -Délai d'apparition 48 mois (R.Cumulé 1.25% 10 ans
  -Facteurs de risque : homme , sténose , grêle court
  devant une cytolyse et cholestase précoce = régression spontanée ; si – diminuer AZA n si – Switch 6MP
- Dérivés du 5 ASA : H. Cytolytique ou Cholestatique  voir hypersensibilité
- MTX : durée > 2ans poso>1500 mg , discuter PBH ou fibroscan > 8.7 Kpa
- Anti TNF = hépatoxicité Rare  Hépatite auto-immune ; interférence , VHB VHC  , Traitement corticoïde

*Clin Gastroenterol Hepatol. 2013 May;11(5):558-564.*
***Liver injury from tumor necrosis factor-α antagonists: analysis of thirty-four cases.***
*Ghabril M, Bonkovsky HL, Kum C, Davern T, Hayashi PH, Kleiner DE, Serrano J, Rochon J, Fontana RJ, Bonacini M; US Drug-Induced Liver Injury Network.*

# Autres

- Hépatite granulomateuse++  1% des MC
- Lithiase Biliaire
- Amylose secondaire

# Quelle Attitude Adopter

- Démarche pragmatique = diagnostic différentiel = anomalies liées à la MC et sans lien avec MC

1-sérologie virale B et C dés le diagnostic
2-Hépatite aigue : Virologie –CMV -EBV –VZV-Herpès , BAI , les médicaments
3-Cholestase: CSP , les médicaments , l'hépatite granulomateuse
4-Cytolyse et cholestase d'apparition secondaire CSP-médicaments-HNR (Thrombopénie+++)