

MÁSTER EN HEPATOLOGÍA

UAM
Universidad Autónoma
de Madrid

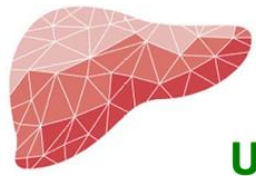
 Universidad
de Alcalá

Asignatura: enfermedad hepática autoinmune.

“Papel de la endoscopia en la colangitis esclerosante primaria”

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Madrid, España



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El papel de la **endoscopia** en la **colangitis** **esclerosante** **primaria**



Hospital Universitario
Puerta de Hierro
Majadahonda

Mariano González-Haba Ruiz
Servicio de Gastroenterología

endoscopia colangitis esclerosante primaria

Introduccion

Diagnostico CEP

Tratamiento estenosis

Diagnostico CCA

Cribado CCA

Otras aplicaciones

colangitis esclerosante primaria (CEP)

**Estenosis biliares multifocales con
enfermedad hepática progresiva**

Asociado a EII

Alto riesgo de colangiocarcinoma

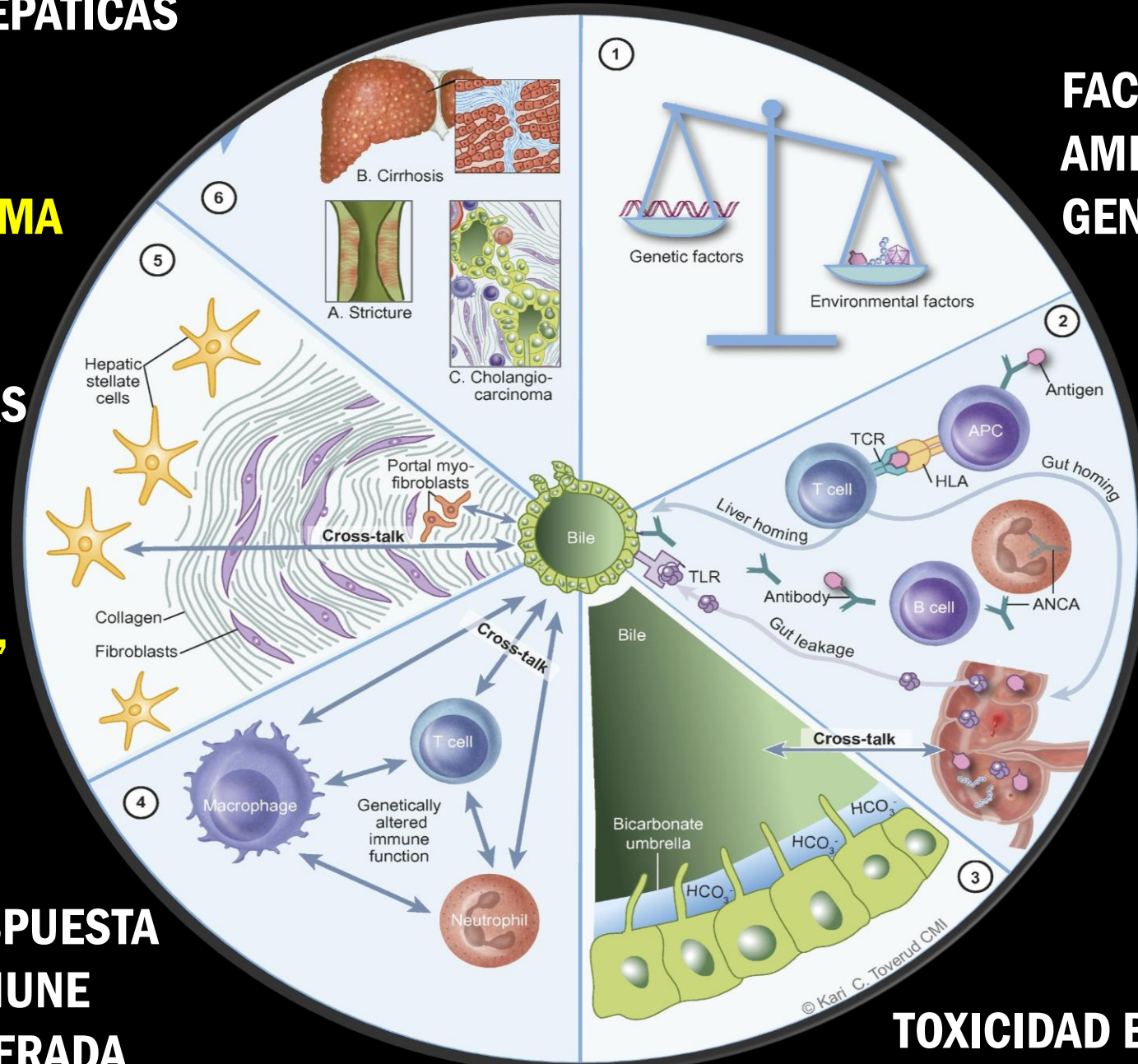
Trasplante hepático . Recurrencia

COMPLICACIONES HEPATICAS

CIRROSIS
ESTENOSIS
COLANGIOCARCINOMA

CELULAS ESTRELLADAS
&
MIOFIBROBLASTOS
vs COLANGIOCITOS
"CAPAS DE CEBOLLA"

RESPUESTA
INMUNE
ALTERADA



FACTORES
AMBIENTALES >>
GENETICOS

RELACION
INTESTINO
VIA BILIAR / HIGADO

TOXICIDAD BILIS

endoscopia
colangitis
esclerosante
primaria

introducción

Diagnostico CEP

Tratamiento complicaciones

Diagnostico CCA

Cribado CCA

Otras aplicaciones

CPRE DIAGNOSTICO

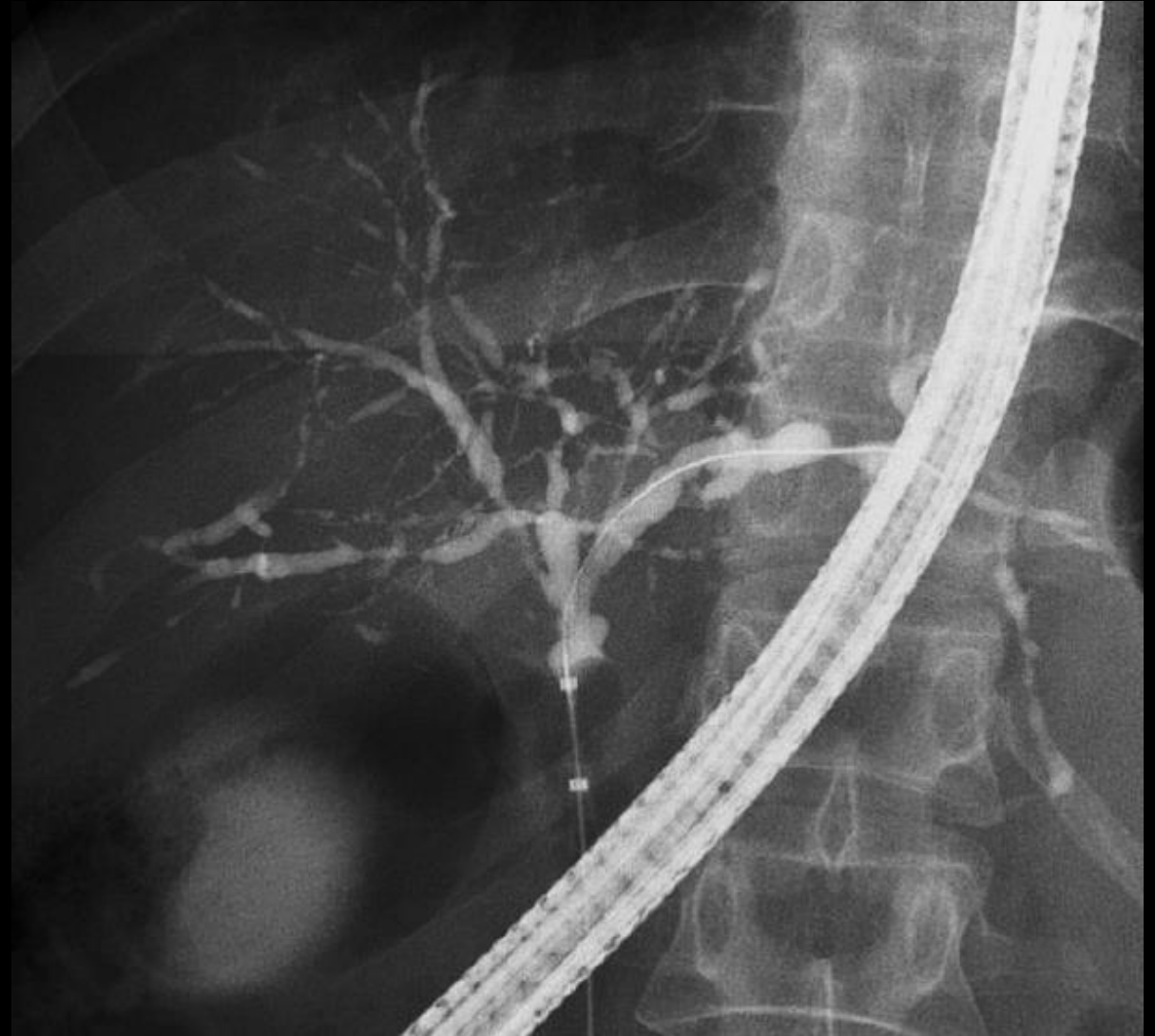
Estenosis multifocales

Beaded

Dilataciones leves

Divertículos

Imagen en árbol podado



CPRE DIAGNOSTICO

Estenosis multifocales

Beaded

Dilataciones leves

Divertículos

Imagen en árbol podado



CPRE - COMPLICACIONES

Tasa de complicaciones 1-18%

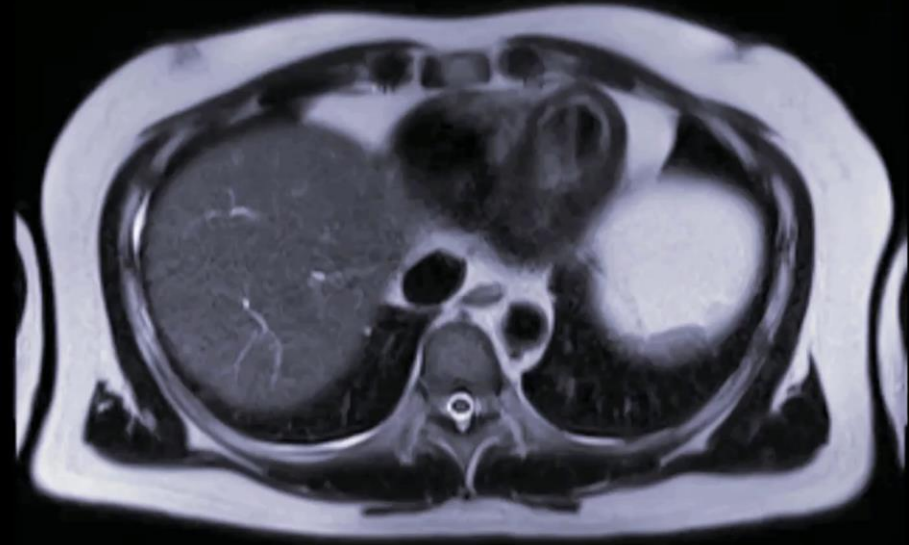
Colangitis: 0,25-8% - Abs profilácticos

**Pancreatitis
Canulación difícil**

Centros de referencia



MR - MRCP



Parameter	Estimate
Sensitivity	0.86 (0.80, 0.90)
Specificity	0.94 (0.86, 0.98)
Positive LR	15.3 (6.2, 38.1)
Negative LR	0.15 (0.11, 0.21)
Diagnostic score	5 (4, 6)
DOR	101 (38, 268)



MR - MRCP

Dilatación VBIH (77%)

Captacion parietal (67%)

Estenosis VBEH (50%)

Engrosamiento (50%)

Diverticulos redes



**NO
PATOGNOMONICO**

Classification of secondary sclerosing cholangitis and conditions that may mimic primary sclerosing cholangitis on cholangiography

Mechanical/toxic	Cholelithiasis/choledocholithiasis
	Surgical bile duct trauma
	Intra-arterial chemotherapy
	Drug-induced sclerosing cholangitis
Ischemic	Vascular trauma
	Hepatic allograft arterial insufficiency
	Paroxysmal nocturnal hemoglobinuria
Other pancreaticobiliary disease	Cystic fibrosis
	Sclerosing cholangitis of critical illness
	<i>ABCB4</i> -associated cholangiopathy
	Chronic pancreatitis
Systemic inflammatory diseases	IgG4-associated systemic disease
	Hypereosinophilic syndrome
	Sarcoidosis
	Graft-versus-host disease

Infection	Bacterial/parasitic cholangitis
	Recurrent pyogenic cholangitis
Immunodeficiency-related (infections)	Congenital immunodeficiency
	Acquired immunodeficiency (e.g. HIV)
	Combined immunodeficiencies
	Angioimmunoblastic lymphadenopathy
Potentially mimicking on cholangiography	Langerhans cell histiocytosis
	Systemic mastocytosis
	Caroli's disease
	Congenital hepatic fibrosis
	Hodgkin's disease
	Cholangitis glandularis proliferans
	Neoplastic/metastatic disease
	Amyloidosis
	Hepatic allograft rejection

MR VENTAJAS

Inocuidad

Valoracion parenquima

Coste efectiva

Avances tecnologicos

Guiar CPRE y complejidad

MR LIMITACIONES

Menor sensibilidad para cambios sutiles en CEP precoz (VBIH)

Precision limitada para CES y CCA

Imposibilidad para tomar muestras

Ausencia de técnica estandarizada

Recommendations on the Use of
Magnetic Resonance Imaging in PSC-A
Position Statement From the
International PSC Study Group

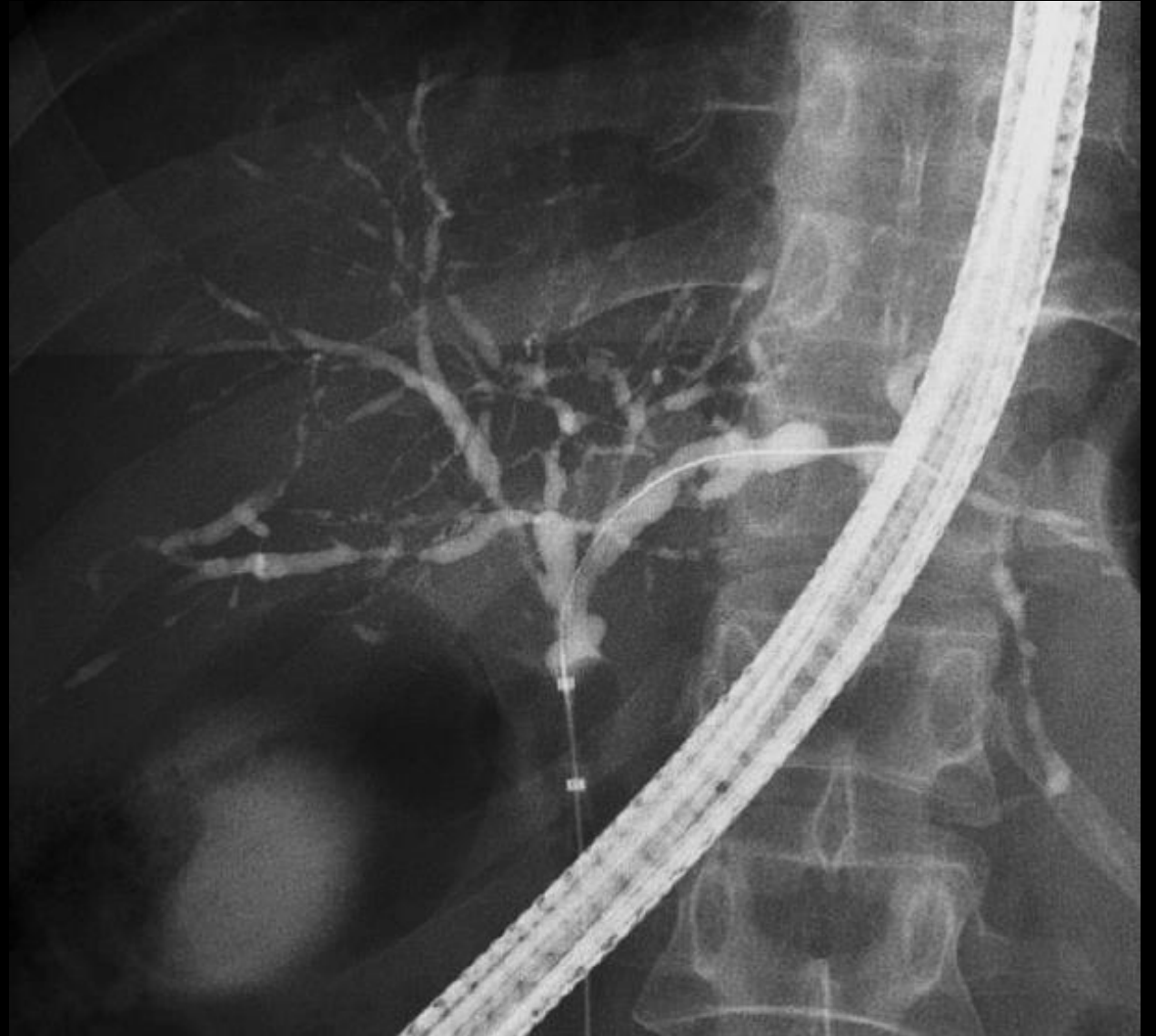
Tipo de colangitis esclerosante	Diagnostico
Colangitis esclerosante primaria “clásica”	Colestasis analítica o sintomática MRI CPRE
CEP pequeño conducto	MRI-CPRE normal Biopsia hepática EII confirmada
CEP asociada a IgG4	IgG4 sérica igG4 biopsia
CEP asociada a HAI	ANA, anti-SMA, anti-LKM, anti-SLA/LP, IgG, Biopsia hepática
CEP + colangiocarcinoma	MRI/CT, EUS, CPRE, tissue sampling for cyto- and histopathology

CPRE diagnostico

NO indicado

CEP pequeño conducto alta
sospecha y MR normal

Contraindicacion MR



CPRE

Complejidad técnica

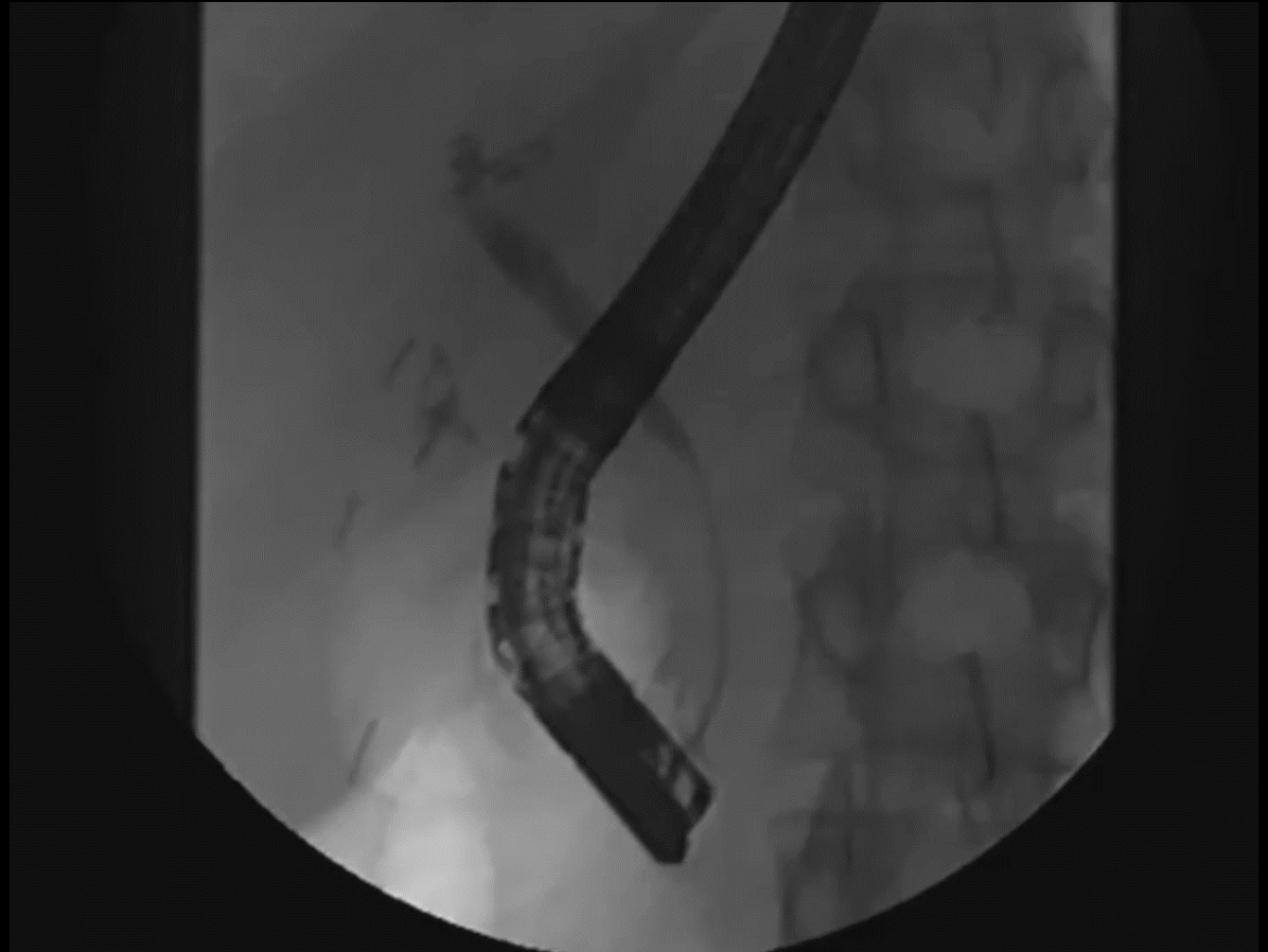
Complicaciones

Centros de referencia (THO)

Colangiograma oclusión

Imágenes tempranas

Antibióticos



CEP diagnostico **OBJETIVOS**

Detección temprana

Determinación estadio, actividad y pronóstico,

Evaluación de respuesta a tratamiento

Definición clínicamente significativa de estenosis dominante

Detección precoz de colangiocarcinoma (CCA)

endoscopia
colangitis
esclerosante
primaria

introducción

Diagnostico CEP

Tratamiento **complicaciones**

Diagnostico CCA

Cribado CCA

Otras complicaciones

CPRE en CEP establecida

Sintomas

(ictericia, colangitis, prurito)

Empeoramiento PFH

**Estenosis dominante
(nueva o progresion de
preexistente en MR-MRCP)**



ESTENOSIS DOMINANTE

ED **45-58%** pacientes con PSC

Estenosis dominante \neq
colangiocarcinoma

5 % ED albergan CCA

Impacto en **supervivencia**

Indistinguibles de
estenosis **benignas**

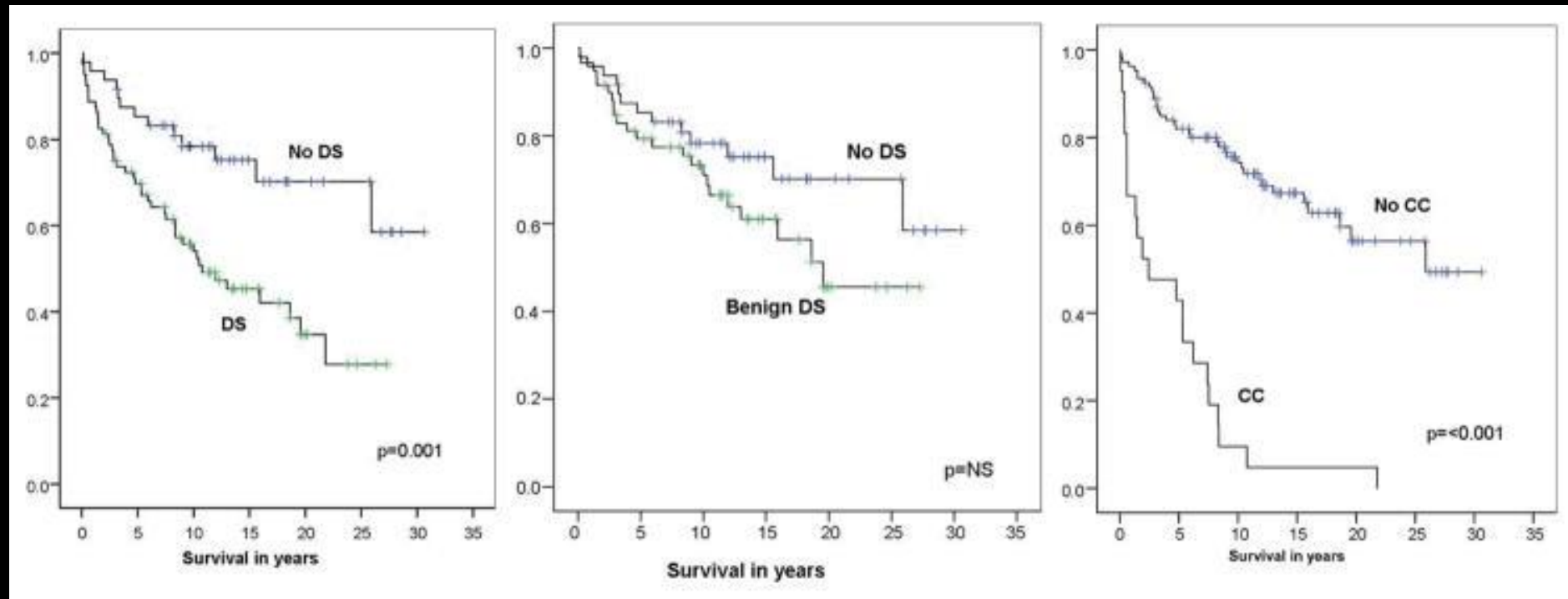
CPRE

Estenosis diametro
 ≤ 1.5 mm en
hepatocolodoco

≤ 1.0 mm en hepaticos a $<$
2cm confluencia

ESTENOSIS DOMINANTE

“...the mean survival of patients with DS was significantly worse than those without DS (13.7 vs. 23 years)..”



Tratamiento endoscópico - **dilatación**

30 -60 segundos

**4-6mm
(diámetro máximo)**

**2-3 sesiones
(perdida muesca)**



Tratamiento endoscópico - **stent**

7-10 Fr (1-2)

1-2 semanas

**Riesgo de oclusion y
colangitis ascendente**

ID paciente:
Nمبر paciente:

Sexo: Edad:
FDN:
09/02/2021
14:46:40

D.F:25
■■■/---
0/6
Eh:A1 Cm:1

Grabando. ■



Tratamiento endoscópico

Stents + dilatación

First author, Year [ref.]	Study design	Patients, n	Intervention	Outcomes	Results
1. Dilatation ± stenting					
Gotthardt, 2010 [42] (Extension of Stiehl 2002 study [33])	Prospective	96 (ALP > 2 × ULN)	Balloon dilation (8 mm in CBD, 6–8 mm for IHBD), plus stent in 5 patients with severe cholestasis and bacterial cholangitis	Short-term improvement in cholestasis Liver transplantation-free survival Complications	<ul style="list-style-type: none"> At 2 weeks, mean bilirubin level significantly decreased (by 56%) Improvement in symptoms and liver transplantation-free survival Comparison with Mayo model not reported (5-year and 10-year liver transplantation-free survival, 81% and 52%) Overall complication rate, 3.8%
Gluck, 2008 [35]	Retrospective	84 Symptomatic patients	Balloon dilation and stenting (70% and 51% of patients, respectively)	Liver transplantation-free survival	<ul style="list-style-type: none"> Higher proportion of patients alive with no liver transplantation at 3 and 4 years than predicted using Mayo model ($P < 0.05$); at 1 and 2 years survival similar to Mayo prediction Adverse events in 21 therapeutic ERCPs (7.2% of 291 procedures, 25% of patients)
Stiehl, 2002 [33]	Prospective	52 (ALP > 2 × ULN)	Balloon dilation (8 mm in CBD, 6–8 mm for IHBD), plus stent in 5 patients with severe cholestasis and bacterial cholangitis	Bilirubin and liver enzymes 2 weeks after dilation Symptoms Liver transplantation-free survival	<ul style="list-style-type: none"> At 2 weeks, significant decrease in liver enzymes and bilirubin Improvement of jaundice in 24/24 and of pruritus in 12/13 patients Longer liver transplantation-free survival than predicted using 1992 Mayo model ($P < 0.0001$)
Baluyut, 2001 [44]	Retrospective	56 with symptoms 7 without symptoms	Balloon dilation (4–12 mm, n = 61) Once per year, with stent if no significant radiological improvement following dilation (n = 33)	Liver transplantation-free survival Complication rate	<ul style="list-style-type: none"> Longer liver transplantation-free survival than predicted using 1999 Mayo model ($P = 0.027$) 12% complications
2. Stenting					
Ponsioen, 1999 [36]	Retrospective	32 Symptomatic patients with successful stenting for dominant stricture	1-week stenting (10-Fr stent) with no balloon dilation	2-month symptomatic and biochemical improvement, Actuarial curve of re-intervention-free patients	<ul style="list-style-type: none"> Improvement of symptoms in 83% Significant decrease in bilirubin (44% had increased conjugated bilirubin at baseline) and cholestasis enzymes Re-intervention-free patients (actuarial): 60% at 3 years
van Milligen de Wit, 1996 [45]	Retrospective	25 With symptoms or progression of serum tests for cholestasis	Stenting for a median of 3 months (plus 8-mm dilation in 3 patients)	Change in symptoms and biochemical tests within 6 months following stent insertion Adverse events	<ul style="list-style-type: none"> Improvement of symptoms in 76% Significant decrease in bilirubin (52% had increased bilirubin at baseline) and serum tests for cholestasis 32 episodes of cholangitis/jaundice related to stent clogging

Mejoría **PFH y síntomas**

Mayor **supervivencia libre de TH**

Mayor **supervivencia libre de TH (Mayo92)**

Mejoría **PFH y síntomas**

Mayor **supervivencia libre de TH (Mayo92)**

Mayor **supervivencia libre de TH (Mayo99)**

Mejoría **PFH y síntomas**

60% libre reintervención

Stents

ESGE/EASL guidelines. Endoscopy 2017

Stents vs dilatación

Table 1. The Incidence of Intervention-Related Complications

Procedure-Related Complication	Balloon Group (n)	PTC Group (n)	ERCP Group (n)
Cholangitis	1	10	2
Pancreatitis	0	1	2
Biliary duct perforation	2	3	2
Bleeding	2	3	1
Sepsis	1	2	0
Choledochoduodenal fistula	0	2	0
Biliary leak	0	1	0
Tube site infection	0	1	0
Total	6	23*	7†

ORIGINAL CONTRIBUTION: PDF ONLY

Balloon Dilatation Compared To Stenting of Dominant Strictures in Primary Sclerosing Cholangitis

Kaya
Am J Gastroenterol.
2001

No Superiority of Stents vs Balloon Dilatation for Dominant Strictures in Patients With Primary Sclerosing Cholangitis

Table 3. Procedure-Related SAEs

Procedure	Balloon dilatation n = 30 ^a	Short-term stenting n = 33 ^a	OR (95% CI)	P value
All cause, n (%)	2 (6.7)	15 (45.4)	11.7 (2.4–57.2)	.001
Cholangitis/cholecystitis, n (%)	1 (3.3)	4 (12)	4.0 (0.42–38.0)	.36
Post-ERCP pancreatitis, n (%)	1 (3.3)	8 (24)	9.3 (1.1–79.4)	.03
Postprocedural pain, n (%)	0	2 (4.5)	n.a.	—
Ascites	0	1 (3)	n.a.	—

Ponsioen.
Gastroenterology
2018

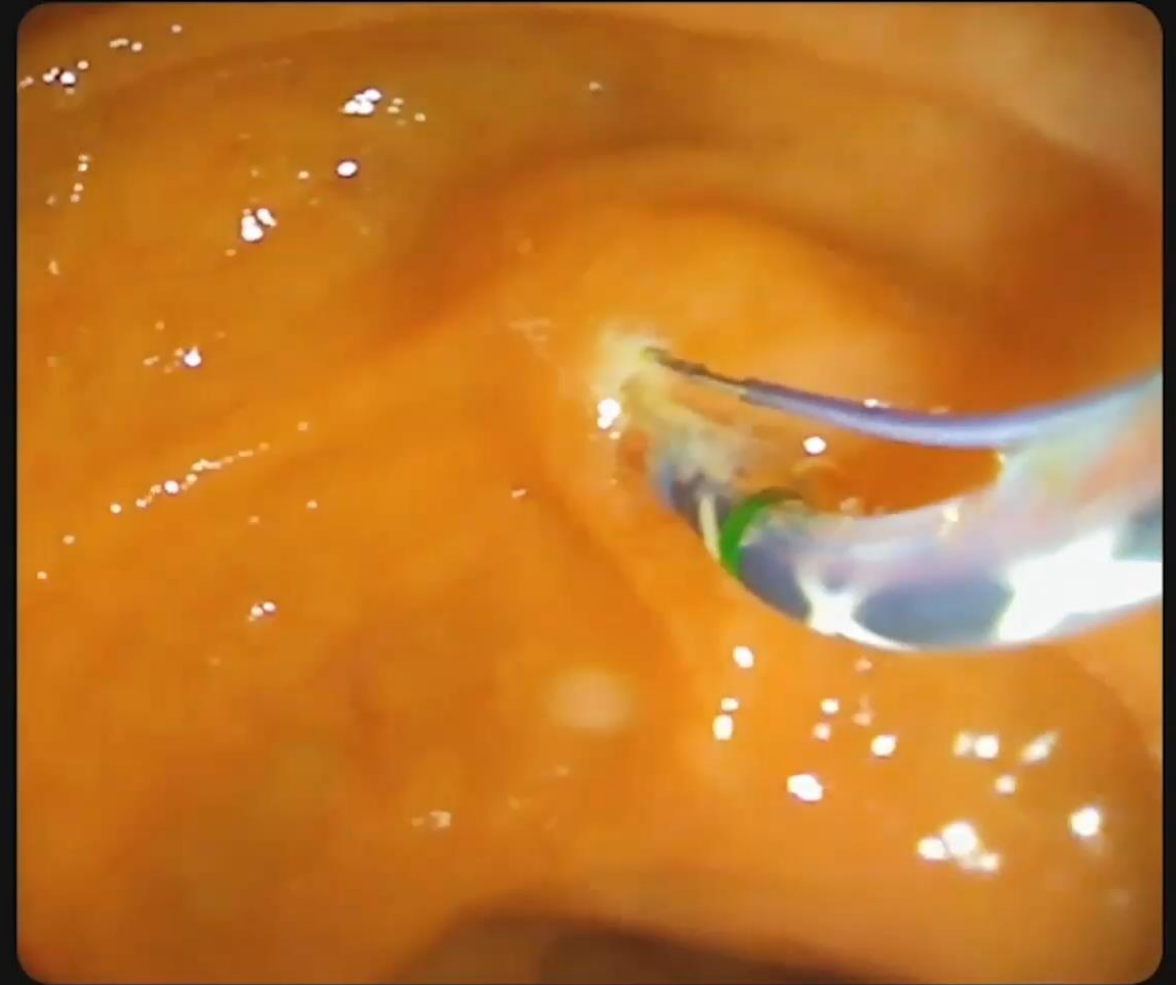
Esfinterotomía biliar

Incierto

Colangitis ascendente

Múltiples CPRE – EVITAR PEP

Canulación difícil



Tratamiento endoscópico

Conclusiones

Beneficio vs riesgo

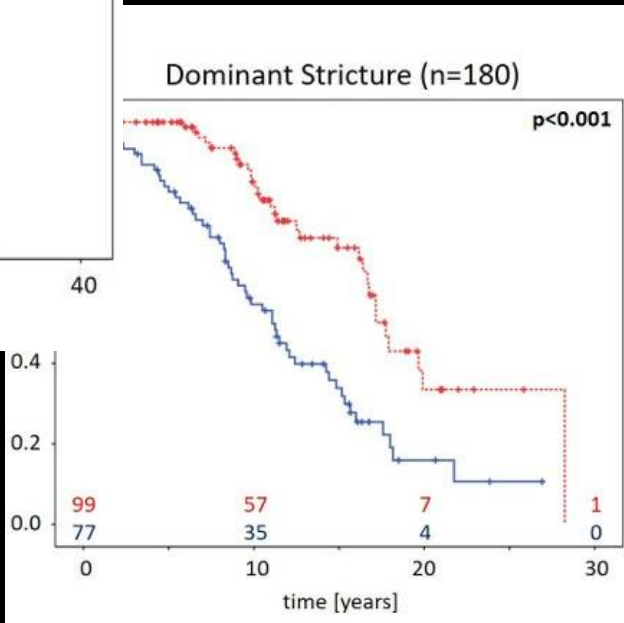
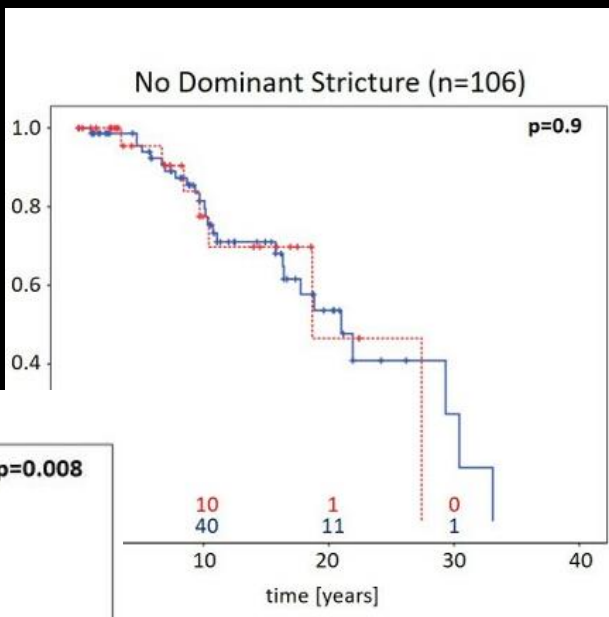
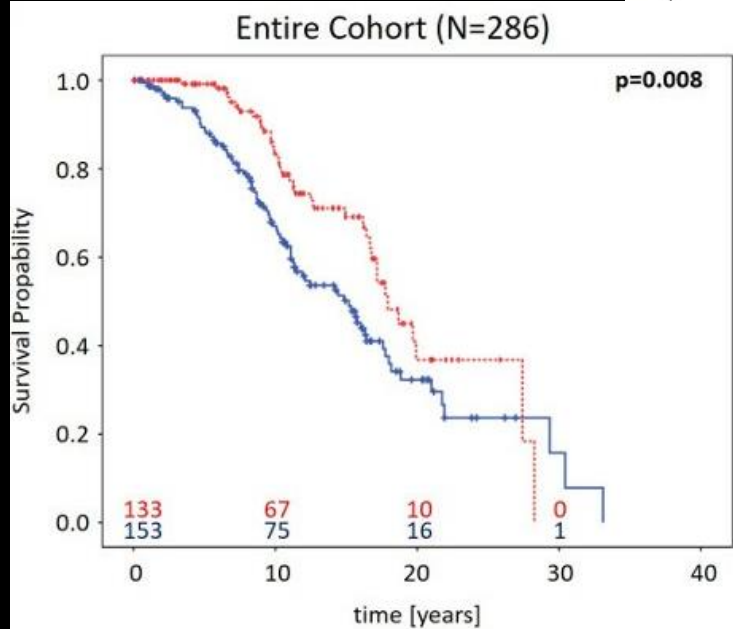
¿**Qué esperamos** que mejore?

El tratamiento es efectivo

S libre TH 81% -94%, vs 65% - 78% modelo predictivo Mayo

Dilatación tratamiento de elección

n=286
133 scheduled ERCP
153 on-demand ERCP
9.9 years



Tratamiento endoscópico programado

Transplantation-free survival
(51% vs 29.3%; $p<0.001$)

Transplantation-free survival time
(median: 17.9 vs 15.2 years; $p=0.008$).

Only in patients with initial (17.1%) or later (45.5%) **diagnosis of a DS** (17.8 vs 11.1 years)

IBD ($p=0.03$), DS ($p=0.006$), higher Mayo RS ($p=0.02$) and non-adherence to endoscopy ($p=0.005$)

CEP & colangiocarcinoma (CCA)

endoscopia
colangitis
esclerosante
primaria

introducción

Diagnostico CEP

Tratamiento complicaciones

Diagnostico **CCA**

Cribado CCA

Otras complicaciones

CEP & colangiocarcinoma (CCA)

CCA 10%-20% CEP
(x400 población gral)

Principal causa de mortalidad
(S<20% 3a)

0.5%-2.0% anual

6.2% - 26.3% CEP con ED
-> CCA (6-10 años)

30% primer año de diagnostico

CEP & CCA

¿Cuándo sospechar?

Empeoramiento colestasis

Perdida de peso

Elevacion Ca 19.9

Estenosis dominante nueva / progresiva

Lesion visible



Ca 19-9

Baja sensibilidad per se (<10%)

Ag Lewis -> 6-22% **no expresan** (Le^{a-b-})

FUT2, FUT3

>129 CCA avanzado

Combinación con otras pruebas

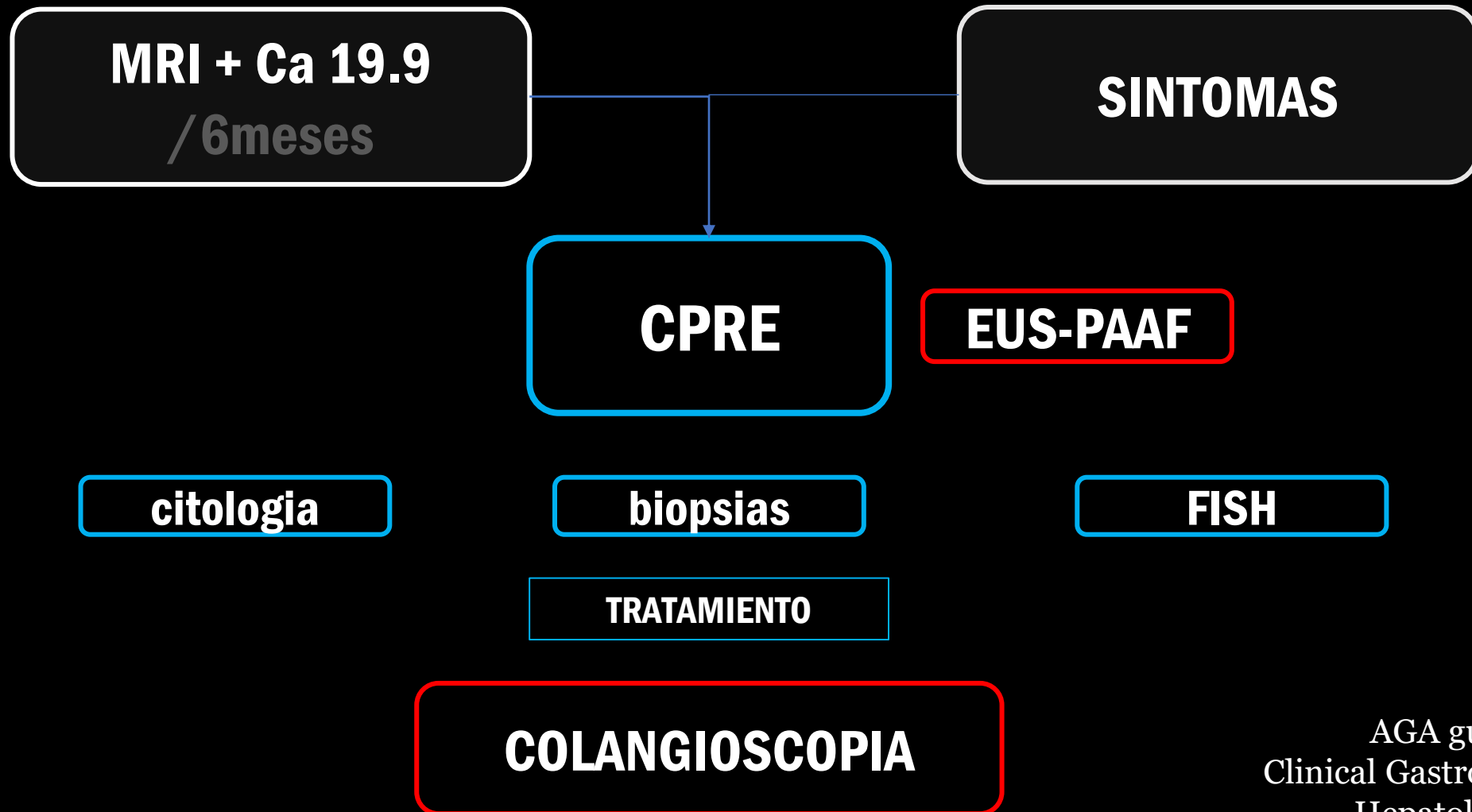


Surveillance Modalities

Folseraas and Boberg. Clin Liv Dis 20 (2016) 79-98

Modality	Sensitivity %	Specificity %	Accuracy %
Ultrasound	57	94	90
MRI	63	79	76
MRCP	78	76	76
CT	75	80	79
ERCP	91	66	69
MRI/MRCP	89	75	76
CA 19-9 \geq 20IU/mL	78	67	68
CA 19-9 \geq 130IU/mL	13	100	90
CA 19-9 + ultrasound	91	62	65
CA 19-9 + MRI/MRCP	100	38	47
CA 19-9 +CT	100	38	47
CA 19-9 + ERCP	100	43	49
Biliary Brush Cytology	43	97	NA
FISH	51	93	NA

CEP & colangiocarcinoma (CCA)

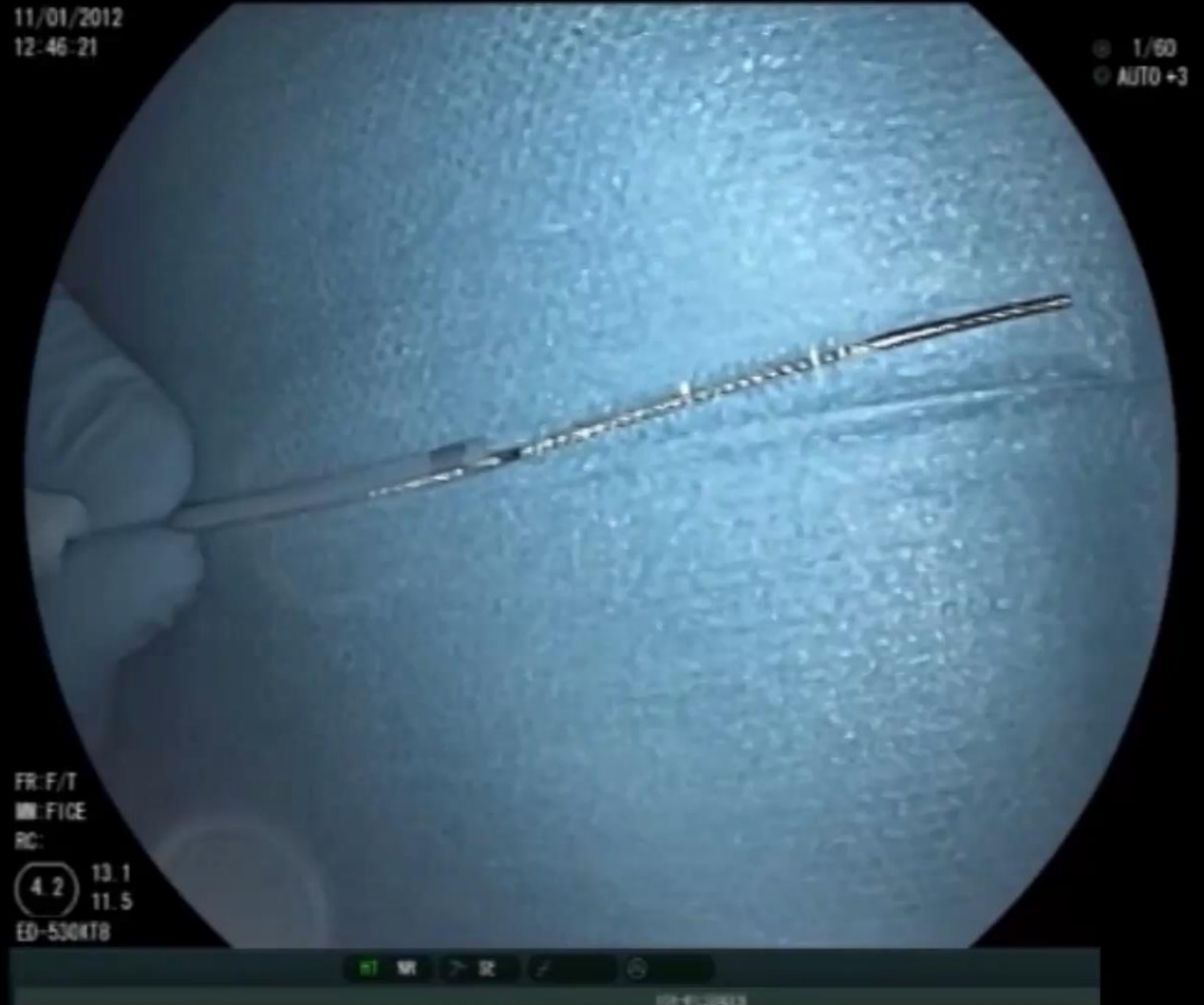


Cepillado biliar

**Sensibilidad 43% (35%–52%),
Especificidad 97% (95%–98%)**

PPV 78.2% (63.6%–86.7%)

NPV 87.2% (85.4%–89.1%)

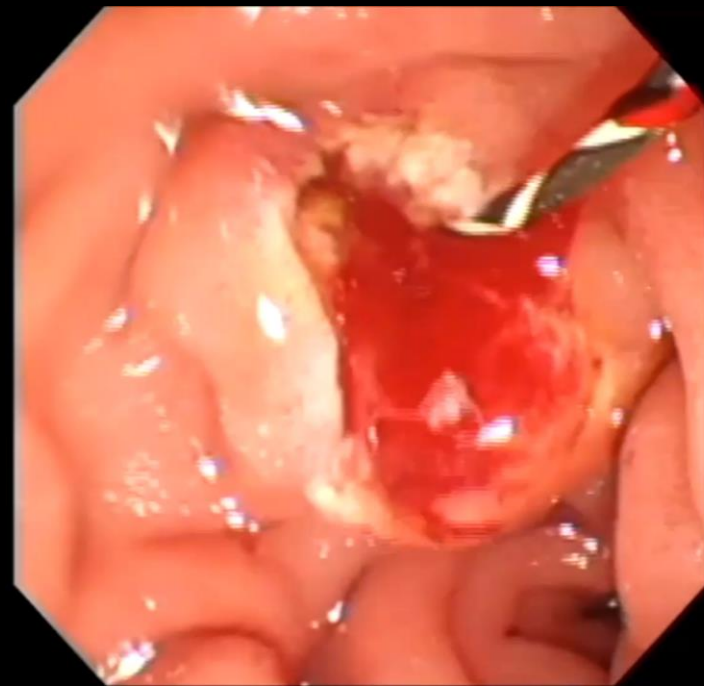


Biopsia transpapilar

Cepillado + biopsia

Sensibilidad 47%-86%

Especificidad 97% -100%



Lower the elevator when pushing the forceps out of the endoscope channel.

Fluorescence in situ hybridization **FISH**

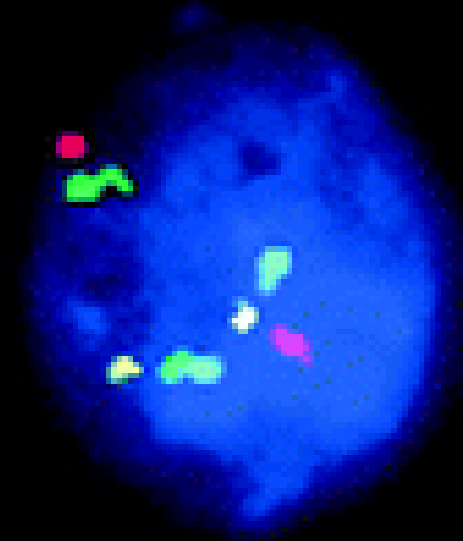
Numero anormal de cromosomas
Aneuploidia

Positivo / negativo
(disomia, trisomía, polisomia)

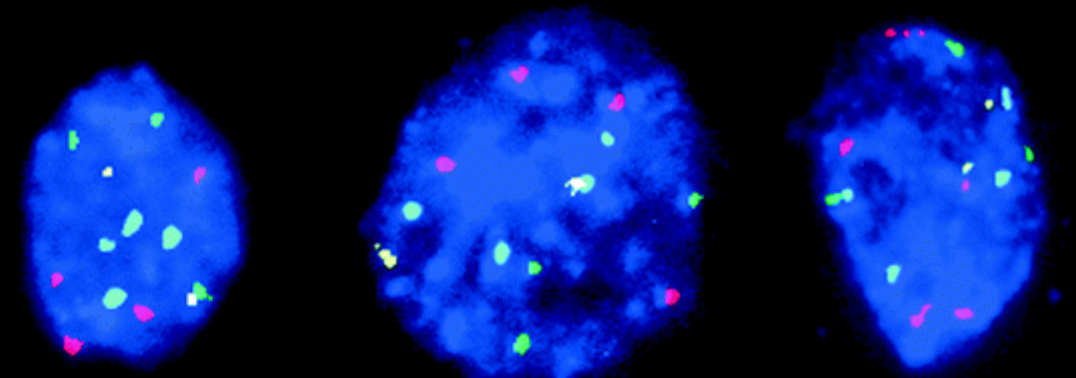
Varias polisomias en ED – CCA

Citología + bx + FISH Sens >>70%

NORMAL



POLISOMIAS



COLANGIOSCOPIA



COLANGIOSCOPIA

Boston
Scientific

Estenosis biliares indeterminadas

vasos dilatados y tortuosos


mucosa nodular neovascularización

friabilidad

características papilares



Subhash . Gastroenterol Hepatol (N Y) 2021

Ext 

COLANGIOSCOPIA

ESTENOSIS BILIARES INDETERMINADAS

CLASIFICACIONES

ROBLES MEDRANDA

MALIGNO

- Patrón plano tipo 1
- Patrón polipoide tipo 2
- Patrón ulcerado tipo 3
- Patrón de panal tipo 4

BENIGNO

- Tipo 1 patrón vellosa
- Patrón polipoide tipo 2
- Patrón inflamatorio tipo 3 N

Patrón irregular / ulcerado/ infiltrante /fibroso
Vascularización irregular +/- "araña"
Ulceraciones

Robles-Medranda, Endoscopy 2018

MONACO

- (1) Estenosis 75%
- (2) Lesion 55%
- (3) Patron mucoso 55%
- (4) Proyecciones papilares 45%
- (5) Ulceracion 42.5%
- (6) Vascularizacion 10%,
- (7) cicatrices 40%
- (8) Patron criptico prominente 10%

Sethi, J Clin Gastroenterol. 2022

COLANGIOSCOPIA

MENDOZA

Vasos tortuosos y dilatados

Nodularidad irregular

Lesiones intraductales sobreelevadas

Superficie irregular +/- ulceraciones

Friabilidad

All DSOC videos were recorded using the Spyglass DS (Boston Scientific, Marlborough, Mass, USA) from adult patients evaluated for indeterminate biliary strictures between January 2016 and May 2018 (Table 2). None of these cases had any history of primary sclerosing cholangitis. A final diagnosis of malignancy was obtained from histopathology results and confirmed on follow-up.

ESTENOSIS BILIARES INDETERMINADAS

CLASIFICACIONES



COLANGIOSCOPIA

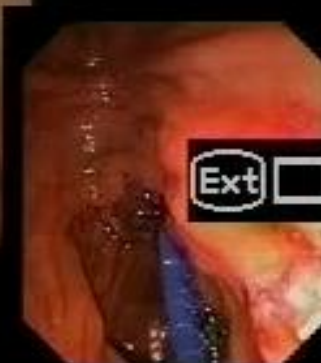
DIAGNOSTICO VISUAL

S/ E \approx 80%

BIOPSIAS DIRIGIDAS

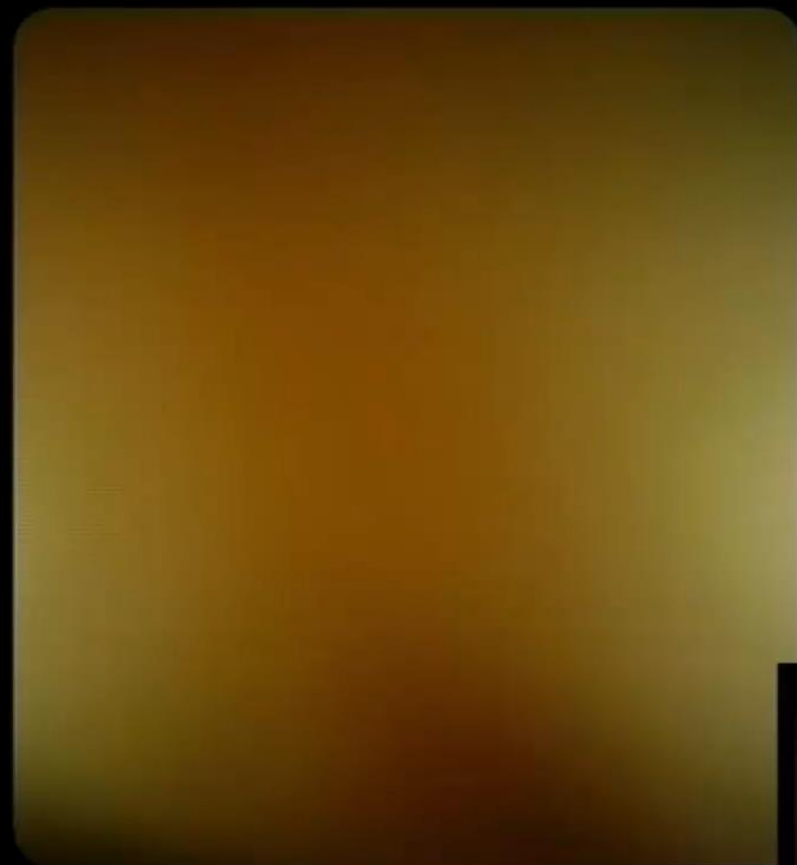
S = 66-86%

E= 94-100%



COLANGIOSCOPIA PSC

Boston
Scientific



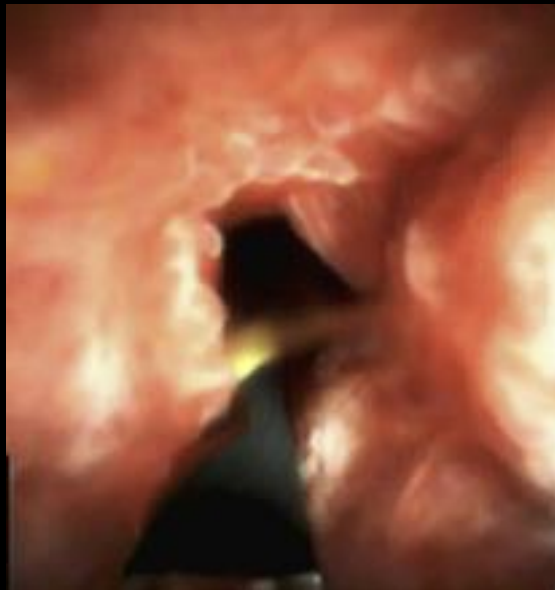
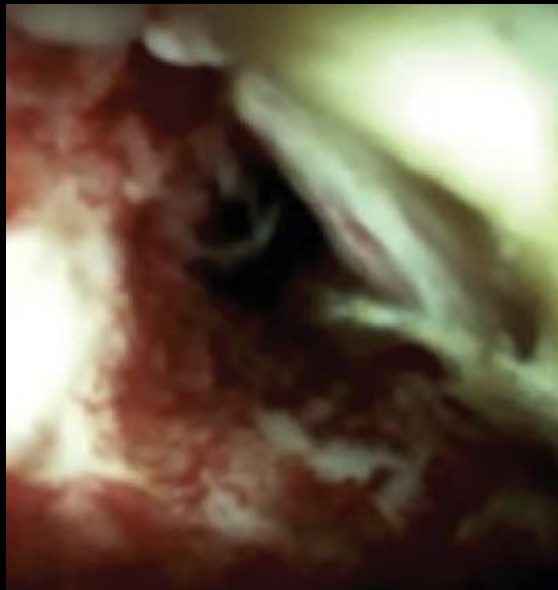
Boston
Scientific



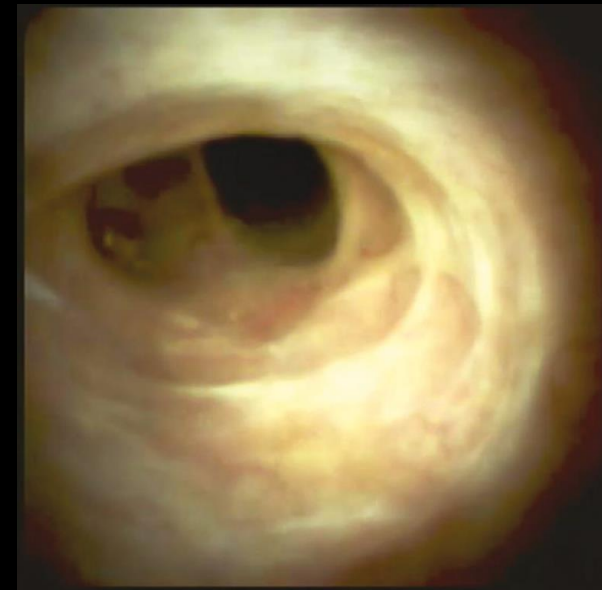
Phenotypic Stratification of Dominant Bile Duct Strictures in Primary Sclerosing Cholangitis—the **Edmonton Classification**

Sandha, Journal of the Canadian Association of Gastroenterology, 2018

PATRON INFLAMMATORIO



PATRON NODULAR



PATRON FIBRO-ESTENOSTICO

COLANGIOSCOPIA PSC

Boston
Scientific



Comparative Study > Dig Dis Sci. 2020 May;65(5):1471-1478. doi: 10.1007/s10620-019-05866-2.

Epub 2019 Sep 30.

Cholangioscopy Biopsies Improve Detection of Cholangiocarcinoma When Combined with Cytology and FISH, but Not in Patients with PSC

Karan Kaura ¹, Tarek Sawas ¹, Fateh Bazerbachi ¹, Andrew C Storm ¹, John A Martin ¹, Gregory J Gores ¹, Barham K Abu Dayyeh ¹, Mark D Topazian ¹, Michael J Levy ¹, Bret T Petersen ¹, Vinay Chandrasekhara ²

N=92 (36PSC), 41 CCA

Citologia = **S 44.77%**

Citologia + FISH = **S 56.8%** (p=0.12)

Citologia + FISH + biopsia Colangioscopia = **S 71.4%** (p = 0.03)

Citologia + FISH + biopsia transpapilar = **64.5%** (p = 0.01).

NO EN PSC

endoscopia
colangitis
esclerosante
primaria

introducción

Diagnostico CEP

Tratamiento complicaciones

Diagnostico CCA

Cribado CCA

Otras aplicaciones

ECOENDOSCOPIA y CEP

Diagnostico CEP- Cambios precoces
Biopsia hepatica

Diagnostico **CCA** (83-100%)

EUS FNA Estenosis biliares **distales**
(81% vs. 59% ERCP)

Adenopatías

Masa visible



ECOENDOSCOPIA Y CEP

CCA hilar

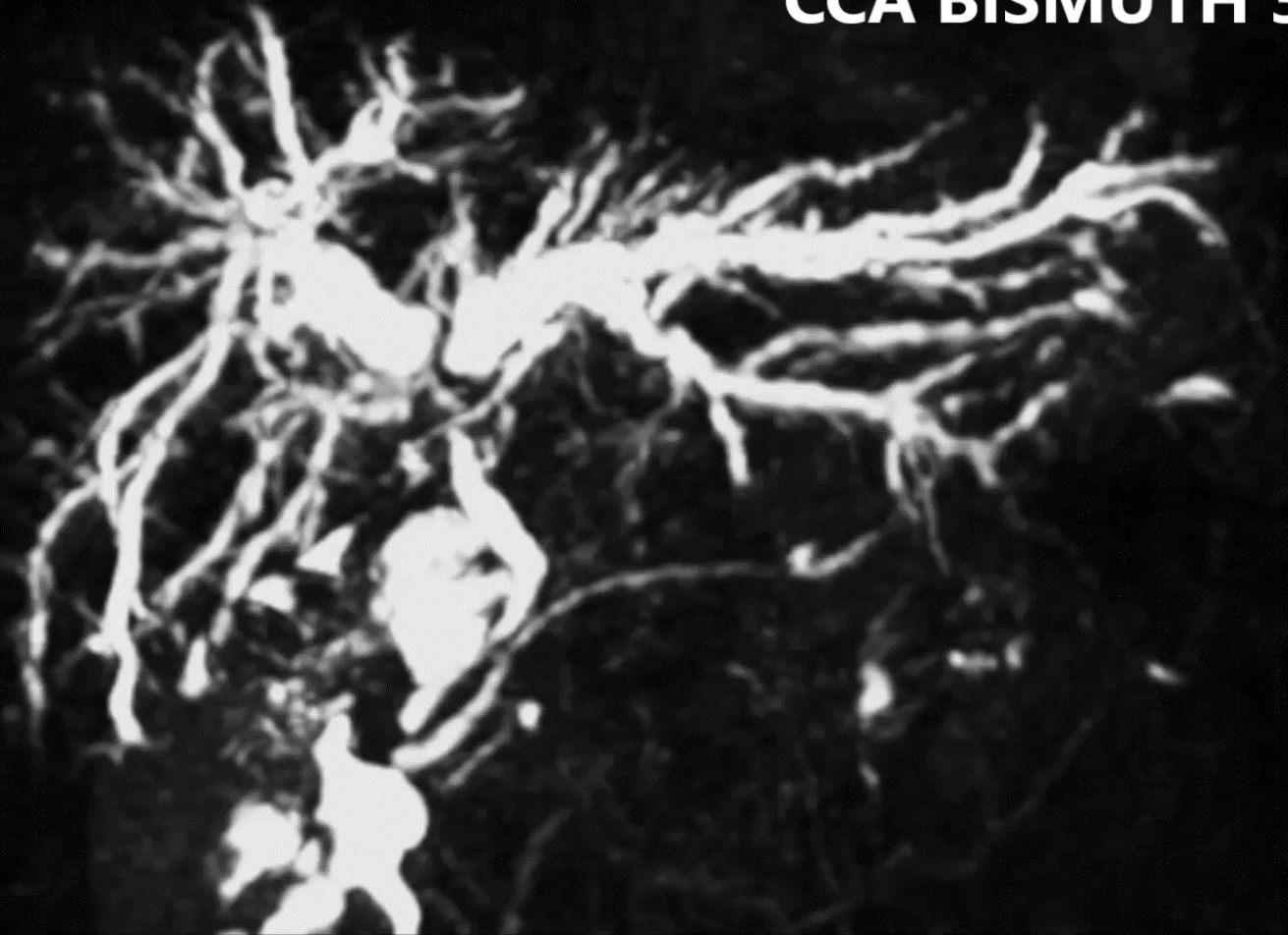
Biopsia lesión

Adenopatías (estadiaje N)

> Riesgo de diseminación <

Criterio exclusión protocolo
Mayo Trasplante hepático

CCA BISMUTH 3B



ORIGINAL

EUS-FNA is effective for lymph node staging in patients with cholangiocarcinoma

Thomas Malikowski, Michael J. Levy, Ferga C. Gleeson, Andrew C. Storm, Eric J. Vargas Valls, Mark D. Topazian, Barham K. Abu Dayyeh, Prasad G. Iyer, Elizabeth Rajan, Gregory J. Gores ... See all authors

First published: 20 December 2019 | <https://doi.org/10.1002/hep.31077>

157 patients

24 (15%) iCCA

124 (79%) pCCA

9 (6%) dCCA

51

CEP

Identificación LN vs CT / MRI
(86% vs 47%; p<0.001)

PAAF 133 (98.5%)

EUS FNA 27/31 (87.1%)

pacs con LN+

EUS preoperatorio CCA
Neoadyuvancia (eCCA)
Protocolo TH (pCCA)
Adenopatías no LR

ENDOMICROSCOPIA OPTICA CONFOCAL (CLE)

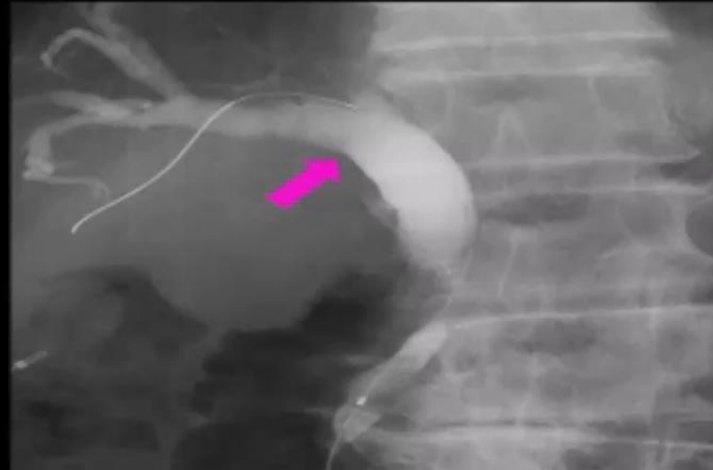
Miami¹ & Paris² criteria

CLE en CEP³

59 pts (11 CCA)

Conf histológica vs 1 año

S 85.7% - E 73.1%



Ausencia muestras

Variabilidad interobservador

Baja especificidad

Normal bile duct

Tanisaka, VideoGIE 2020

¹ Wallace GIE 2011

²Caillol Dig Dis Sci. 2013

Han, Gastrointest Endosc. 2021

ECOGRAFIAINTRADUCTAL (iDUS)

Technical Equipment & Characteristics

Length [mm]	1920
Max. Diameter [mm]	max. 2,6
Frequency [MHz]	12/15/20/30



RADIOFRECUENCIA INTRADUCTAL (iDUS)

**E térmica – necrosis
superficial**

Cateter 8FR

**Aumento permeabilidad
protesis NO EN supervivencia**

Salvo un RCT

Wang, Endoscopy. 2018

**Endoscopic radiofrequency ablation
for palliative treatment of hilar
cholangiocarcinoma**

Pedro Pereira, Ana Luísa Santos*, Rui Morais, Filipe Vilas-Boas, Eduardo Rodrigues-Pinto, Guilherme Macedo*

Gastroenterology Department, Centro Hospitalar Universitário de São João, Porto, Portugal

Pereira, VideoGIE 2021

El papel de la
endoscopia
en la colangitis
esclerosante
primaria

TAKE HOME MESSAGES

CPRE

tratamiento **complicaciones**
diagnostico **CCA**

Sintomas o estenosis dominante en MR

Riesgos vs beneficios

Dilatacion >>stent

Antibioterapia

CCA

Diagnostico multimodal

Cepillado + bx + FISH + SOC

Papel de la **EUS** en CCA



GRACIAS