Prise en charge chirurgicale du Cholangiocarcinomes

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@Eric_Vibert

Links of interest in my lab of Digital Innovation for OR

bopA
bloc opératoire augmenté

Institut Mines-Télécom
université PARIS-SACLAY
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS
INRIA
CNAM

Startups

LETTRIA
Xperteye
TOYS FILMS
aneo the other solution
LYNX
MOON SURGICAL
caresyntax
OPEN MIND NEUROTECHNOLOGIES

Mecenes

FONDATION Mines-Télécom
FONDATION DE L'AP-HP
relyens
orange
Boston Scientific Foundation
FUJIFILM
Arthrex
GETINGE
Medtronic
Johnson & Johnson MEDTECH
THALES

Disclosure – Co Founder of Startup

Twinical

Digital Twins for better outcomes in oncologic liver surgery

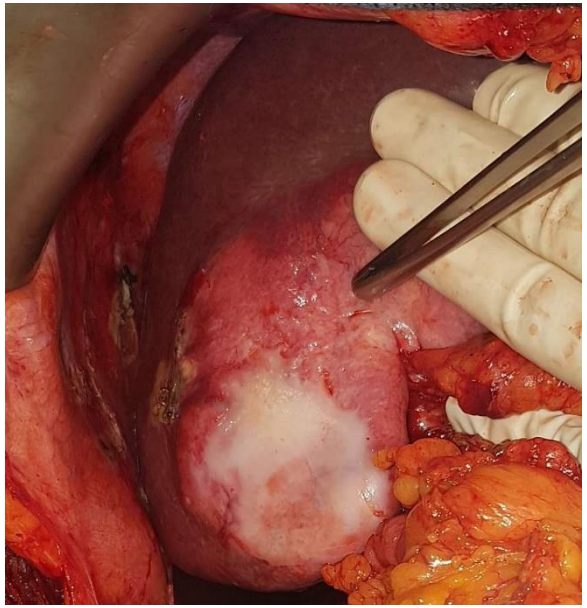
Augment vision. Reduce errors. Save lives.

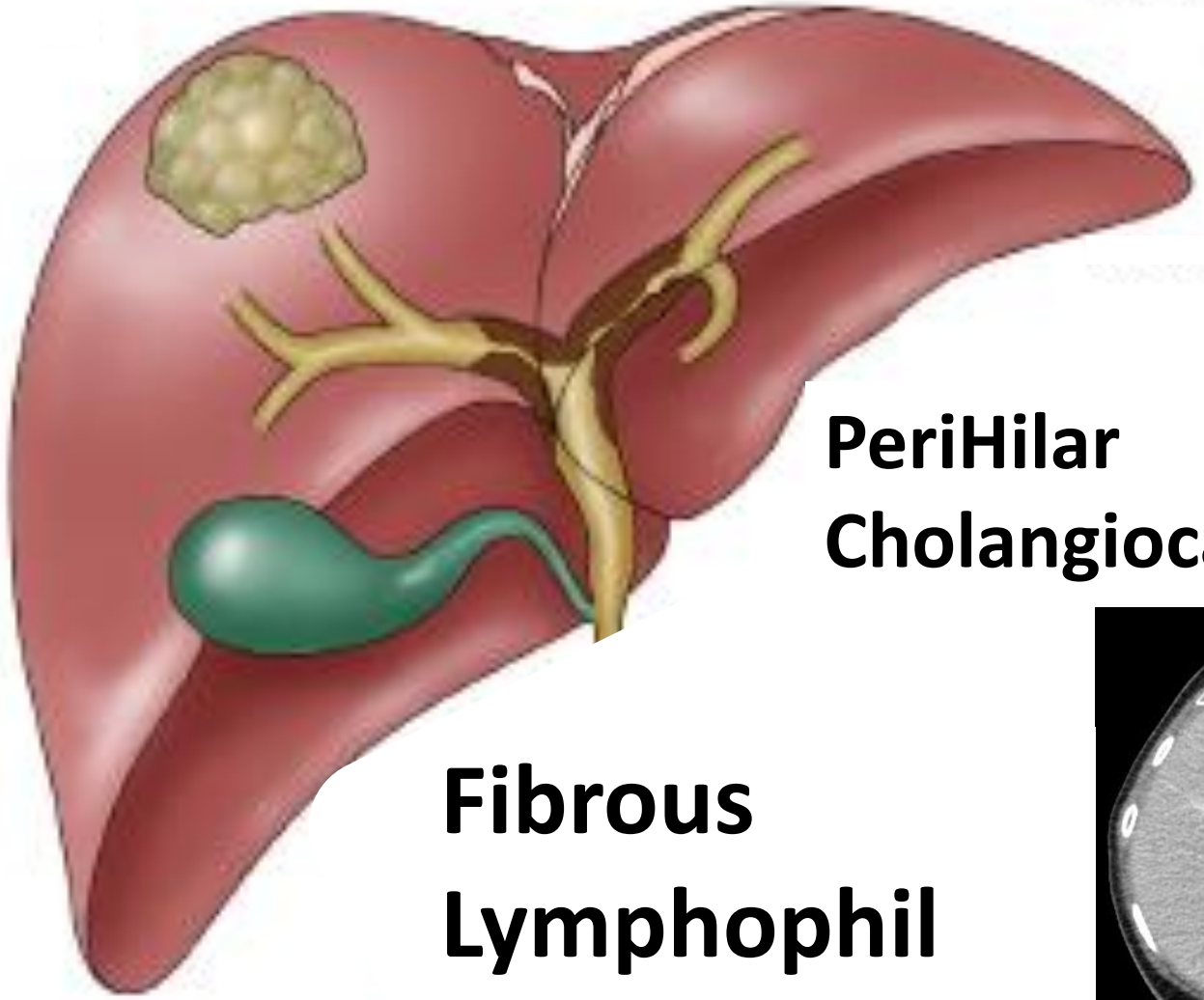
Mario Aricò, CEO
Ph.D. in Surgical Robotics
BFC19 INSEAD graduate

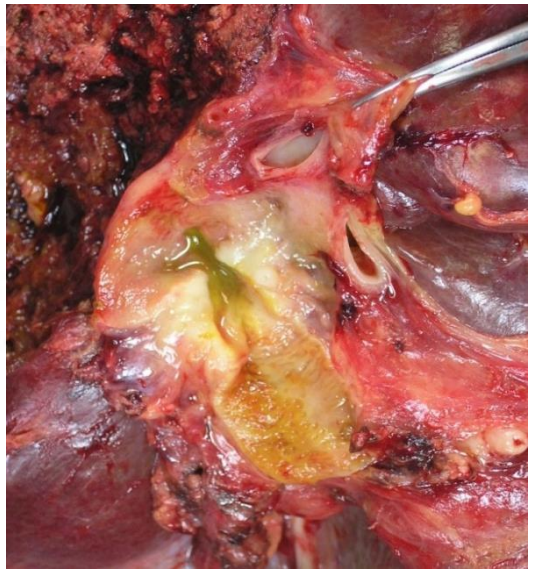
Stéphane Cotin, CSO
Research Scientist
Head of MIMESIS @INRIA

Eric Vibert, CMO
HPB Surgeon @ AP-HP
France2030 Ambassador

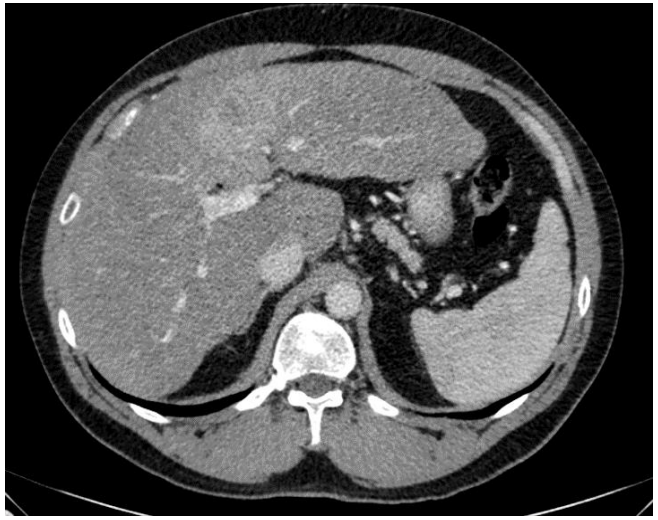
IntraHepatic Cholangiocarcinoma

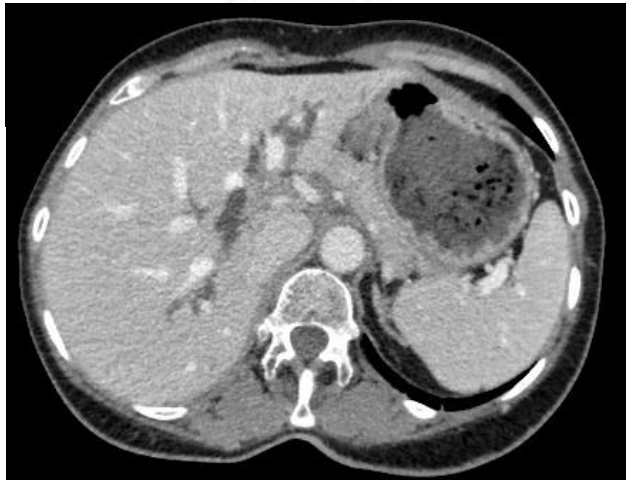






PeriHilar Cholangiocarcinoma



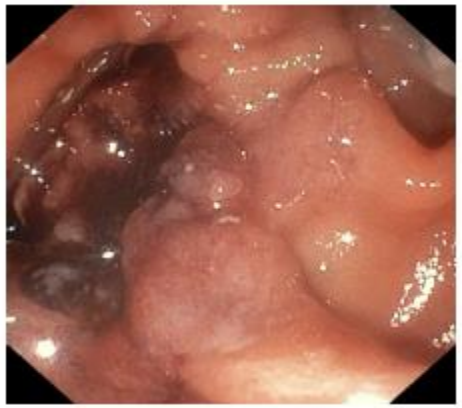


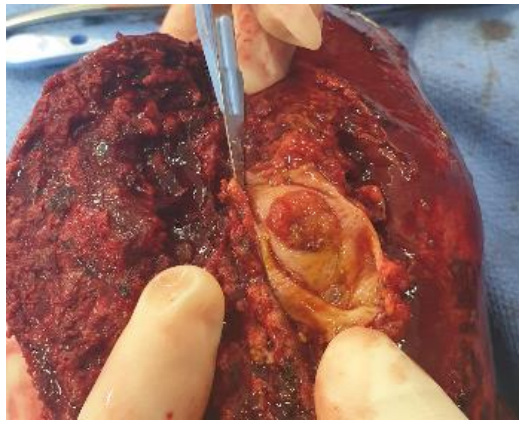
Fibrous
Lymphophil
Limits unclear

Intra Ductal Papillary Neoplasm of the Bile Duct - IPNB

Papillomatoses,
Tumeurs Intra-Canalaire et Mucineuses des Voies Biliaires,
Tumeurs Mucineuses des Voies Biliaires

7-10% des cholangiocarcinomes





Introduction

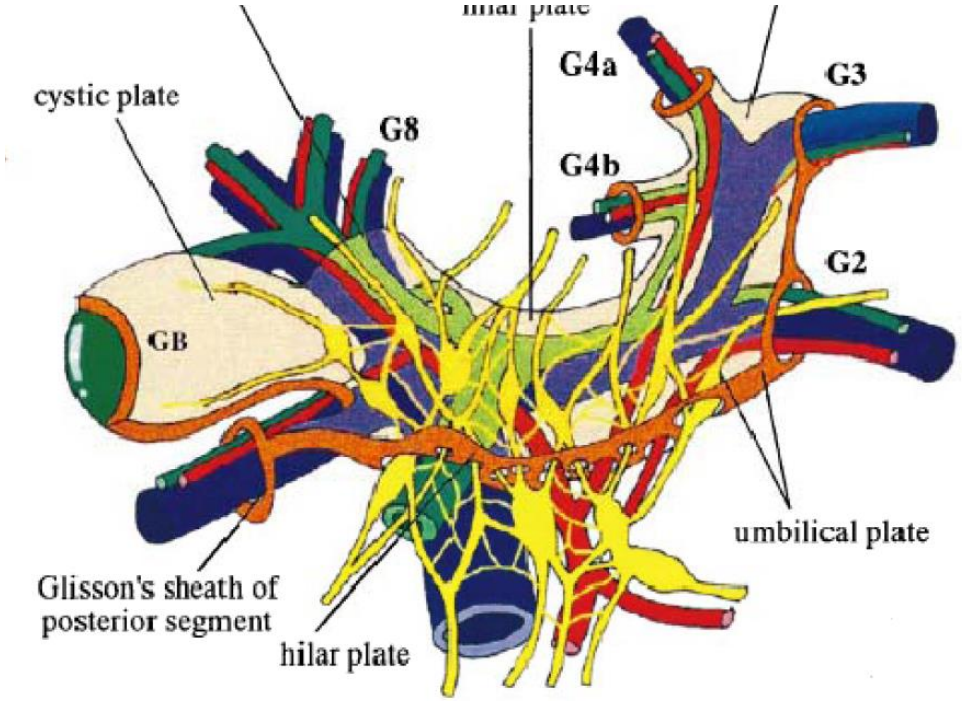
The intraductal papillary neoplasm of the bile duct (IPNB) is characterized by dilated intrahepatic bile ducts filled with papillary or villous neoplastic biliary epithelium [1–3]. Before the term IPNB was widely accepted, this entity was called by various names such as biliary papillomatosis, biliary intraductal papillary mucinous neoplasm, and mucin-producing bile duct tumor [4–6]. Although IPNB is basically a non-invasive lesion, quite often it accompanies adenocarcinoma [2]. In addition, IPNB tends to spread superficially along the bile duct mucosa [7,8].

Hyo Jung Park, *AJR, 2018*

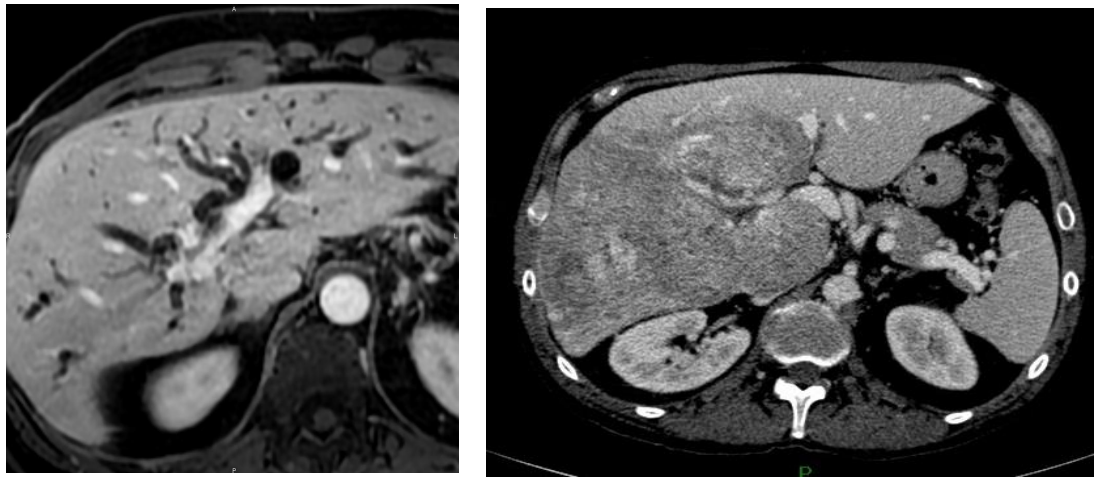
Gordons-Week et al. *Ann Surg 2016*

Jung et al. *J Hepatol 2012*

Les 2 grandes spécificités du Cholangiocarcinome

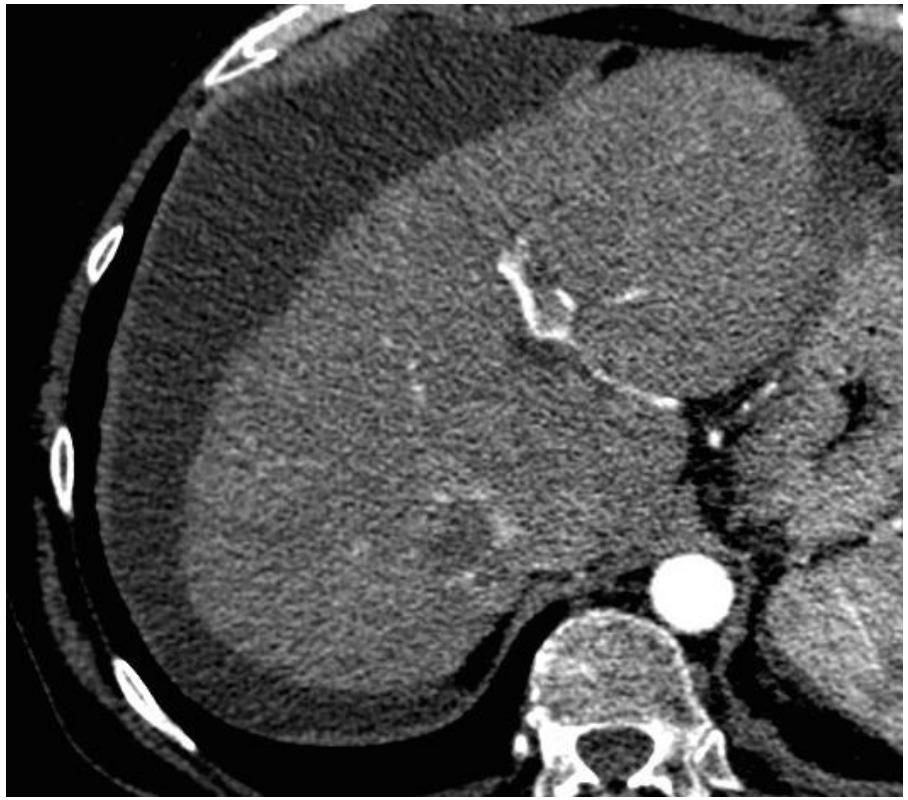


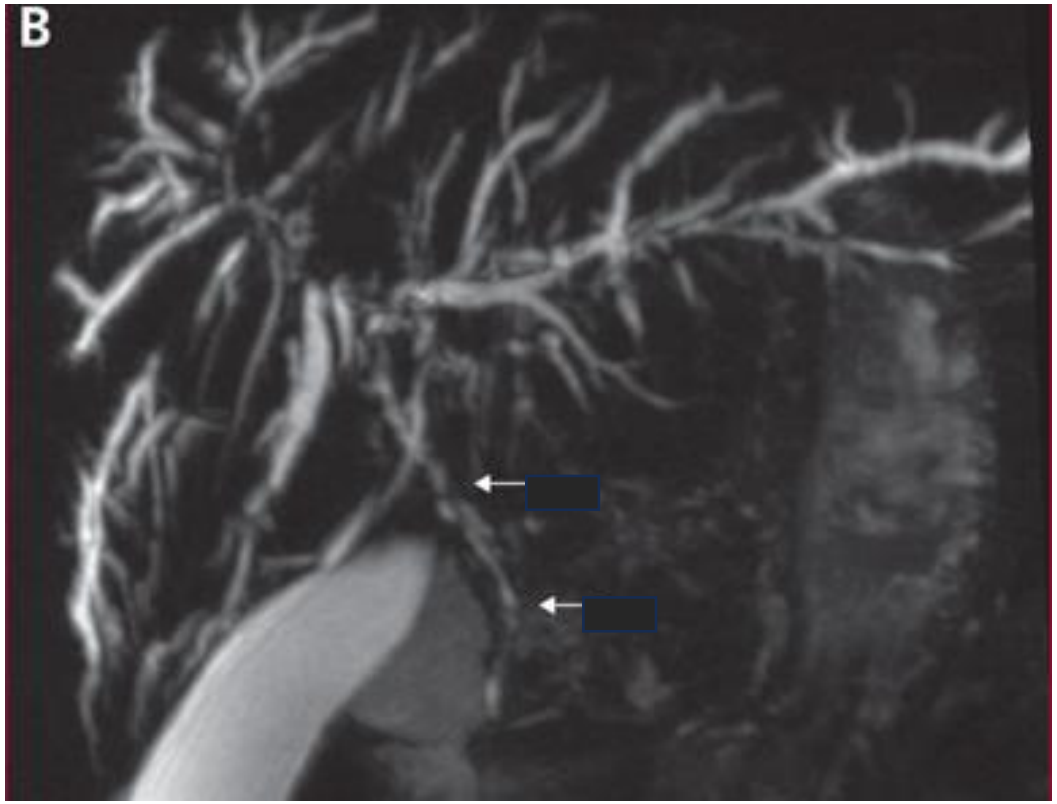
Lymph Node Invasion



Vascular Infiltration

Hepatopathie ou Cholangiopathie ?





Facteurs de Risque des Cholangiocarcinomes

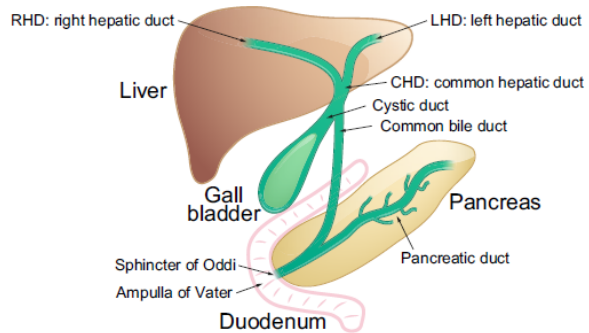
Intra Hépatique	Péri - Hilaire
35% d'Hépatopathie associée	**20% de Cholangiopathie associée**
Hepatopathie Virale B et C Hépatopathie Alcoolique Hemochromatose Maladie de Wilson Syndrome Métabolique Diabète	Cholangite Sclérosante Primitive Maladie de Caroli et/ou Kystique des VB Anomalie de la jonction bilio-pancréatique Infection Parasitaire en Asie Sud-Est Clonorchisis Sinensis et Opisthorchis Viverrini Incidence la plus élevé du monde en Thailande : 100 / 100 000 Hab

Tyson et al. Hepatology 2011 Sripa et al. PLoS Medecine 2011 Palmer et al. J Hepatol 2014

Risk factors for intrahepatic and extrahepatic cholangiocarcinoma: A systematic review and meta-analysis

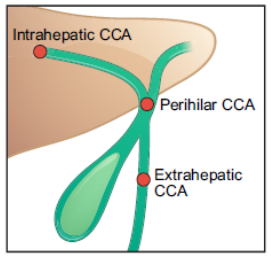
Oliver Clements[1], Joseph Eliahoo[2], Jin Un Kim[1], Simon D. Taylor-Robinson[1], Shahid A. Khan[1,*]

[1]*Division of Digestive Diseases; Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom;*
[2]*Statistical Advisory Service, Imperial College London, London, United Kingdom*



Intrahepatic CCA risk factors:

- Choledochal cysts (OR 26.71)
- Choledocholithiasis (OR 10.08)
- Cirrhosis (OR 15.32)
- Cholelithiasis (OR 3.38)
- HBV (OR 4.57)
- HCV (OR 4.28)
- Alcohol (OR 3.15)
- Cholecystocholithiasis (OR 1.75)
- IBD (OR 2.68)
- T2DM (OR 1.73)
- Smoking (OR 1.25)



Extrahepatic CCA risk factors:

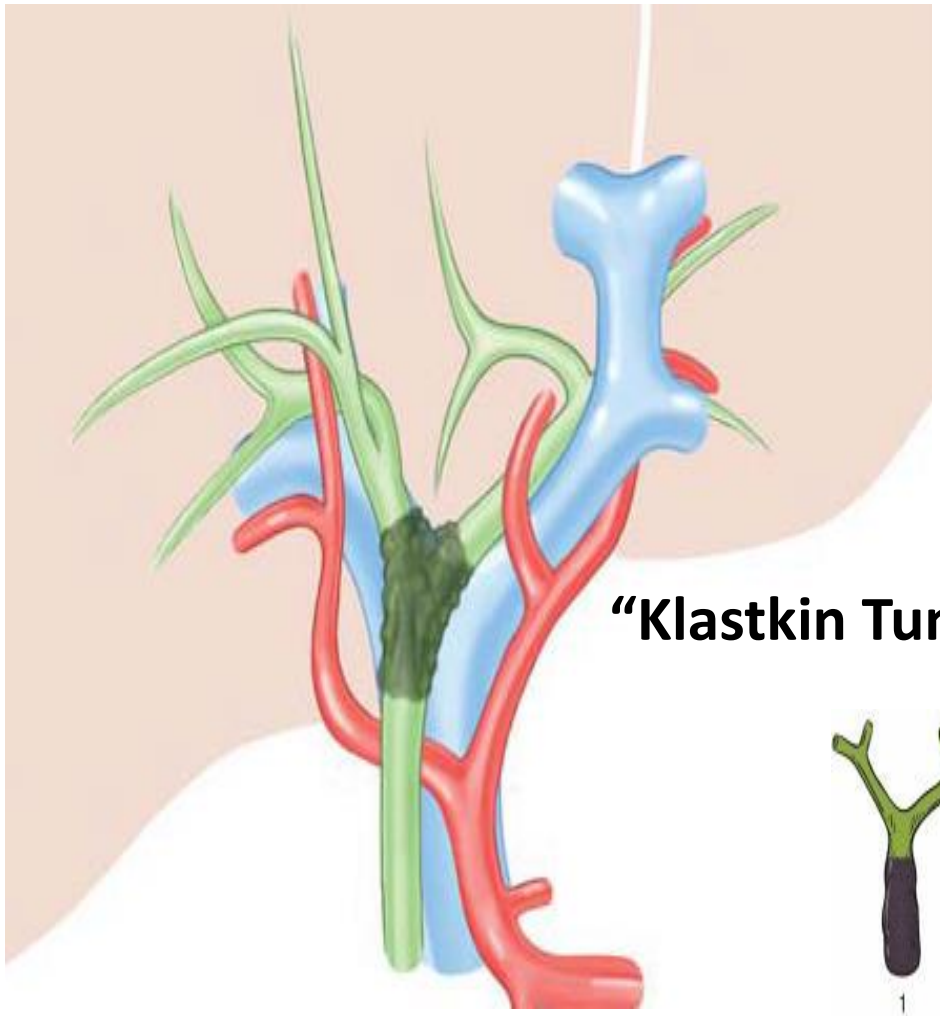
- Choledochal cysts (OR 34.94)
- Choledocholithiasis (OR 18.58)
- Cirrhosis (OR 3.82)
- Cholelithiasis (OR 5.92)
- HBV (OR 2.11)
- Alcohol (OR 1.75)
- Cholecystocholithiasis (OR 2.95)
- IBD (OR 2.37)
- T2DM (OR 1.50)
- Smoking (OR 1.69)

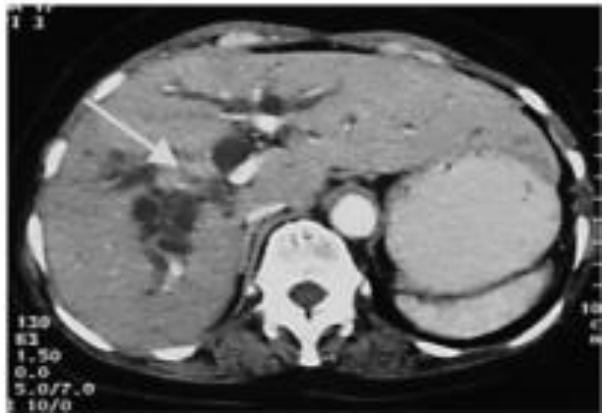
Highlights

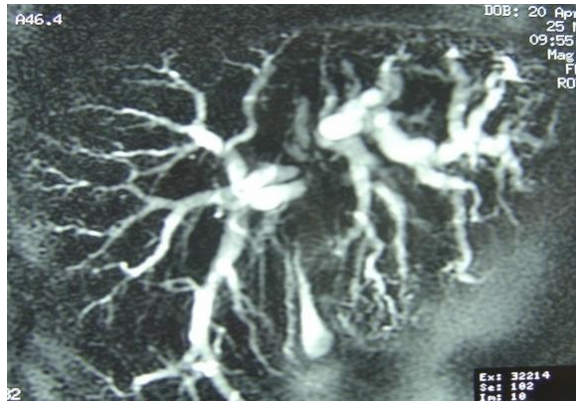
- Choledochal cysts were found to be most strongly associated with both iCCA and eCCA.
- Cirrhosis was a significant CCA risk, with a stronger association with iCCA than eCCA.
- Choledocholithiasis had a stronger association with eCCA than iCCA.
- In Eastern countries, cirrhosis and HBV conferred a greater risk of iCCA than in Western countries.
- Rising global incidence of iCCA may be linked to increases in T2DM, cirrhosis, alcoholic liver disease and cholelithiasis.

Journal of Hepatology **2020** vol. 72 | 95–103

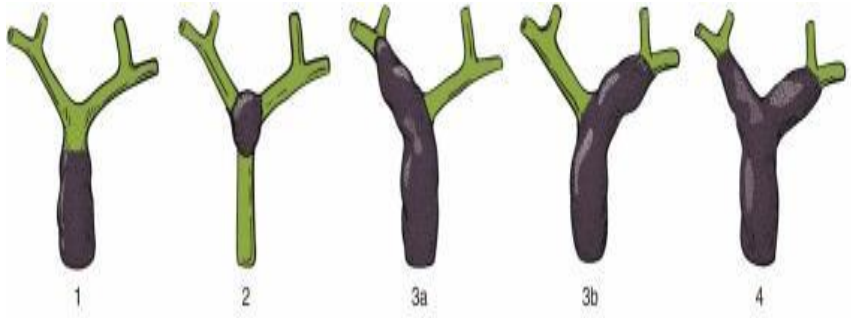
Cholangiocarcinome Péri-Hilaire et non pas Hilaire

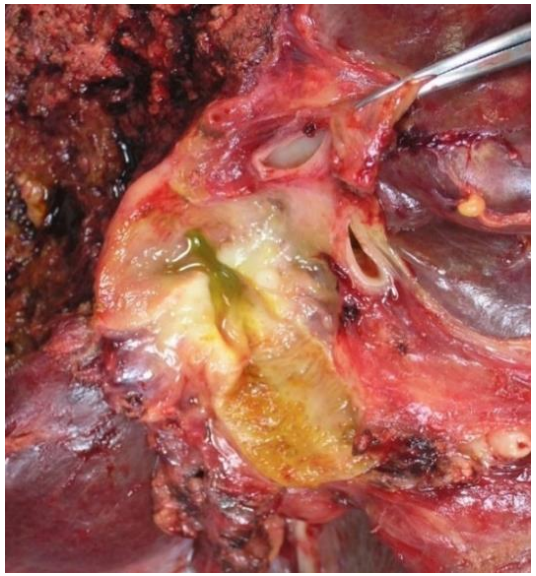






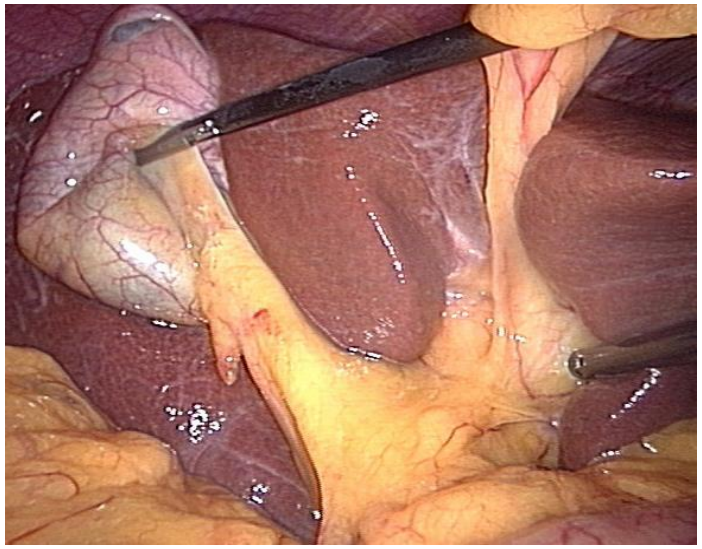
Bismuth Classification
“Klastkin Tumor” or “Hilar Cholangiocarcinoma”



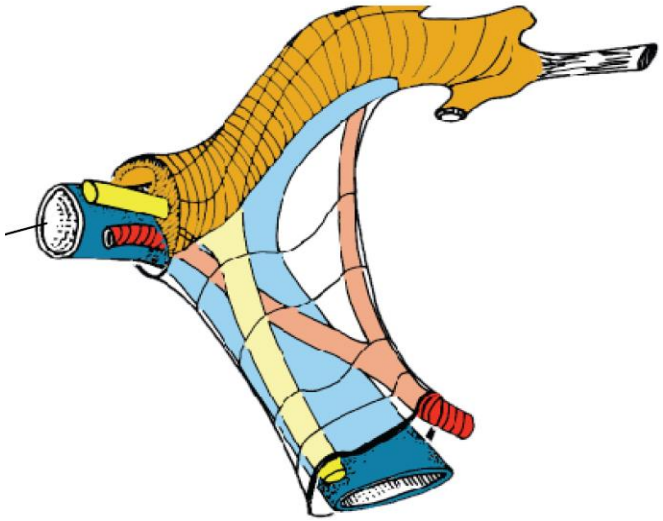


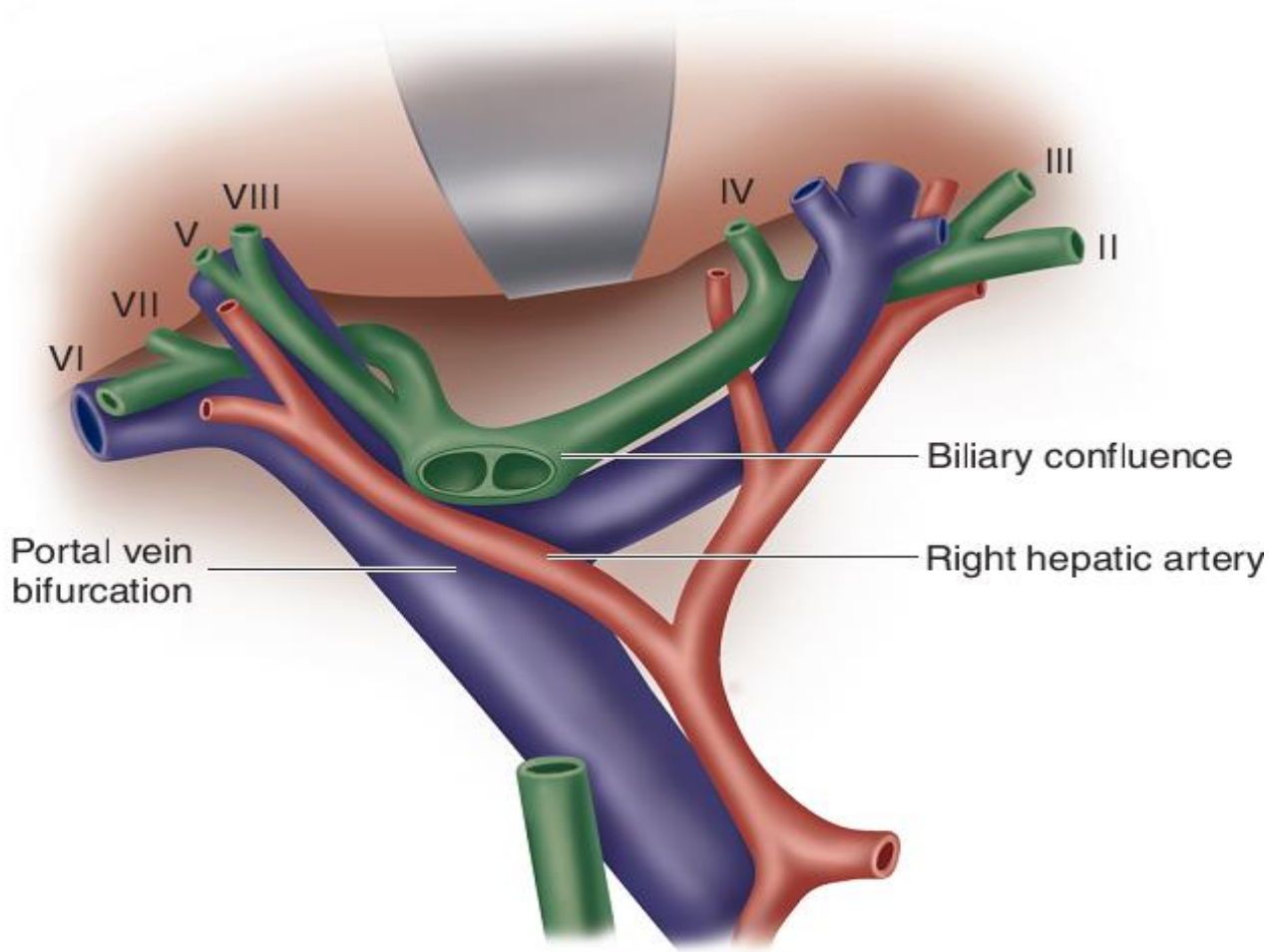
Bismuth, Corlette et al. Surg Gyn Obs 1975

Anatomie du hile hépatique



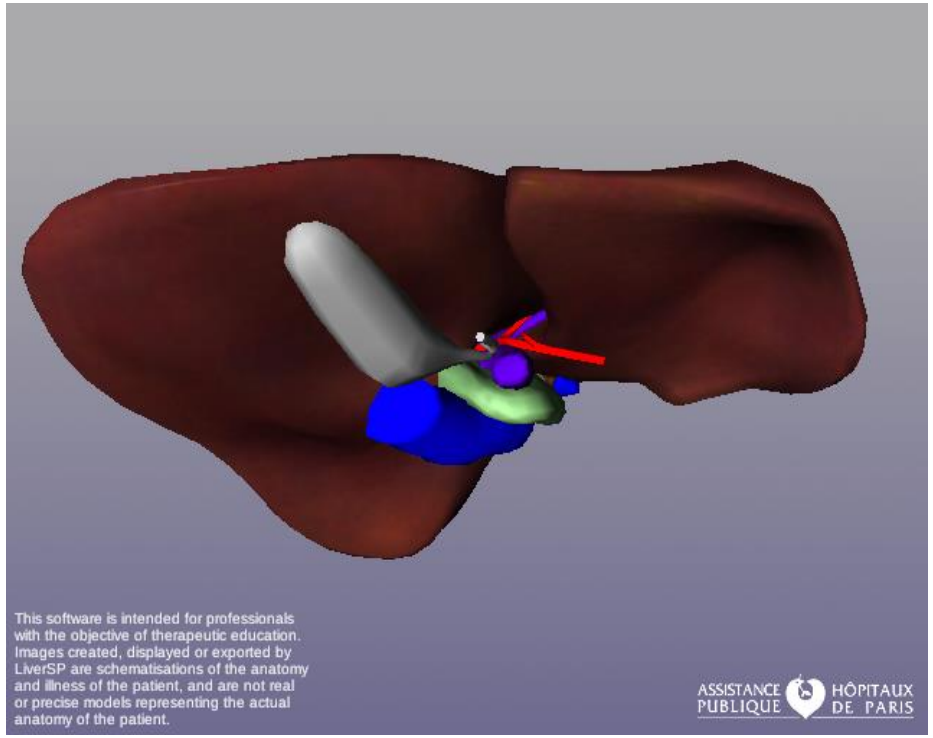
Plaque Hilaire

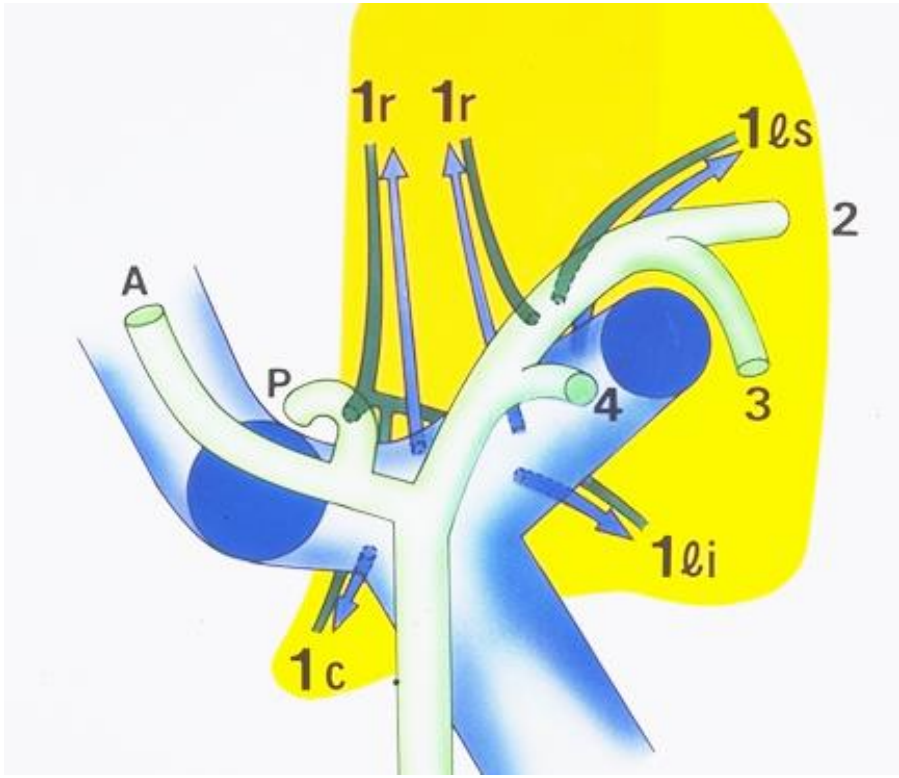




La convergence biliaire est inclue dans la plaque hilaire

Derrière le hile et devant la veine cave : le Segment 1 du foie



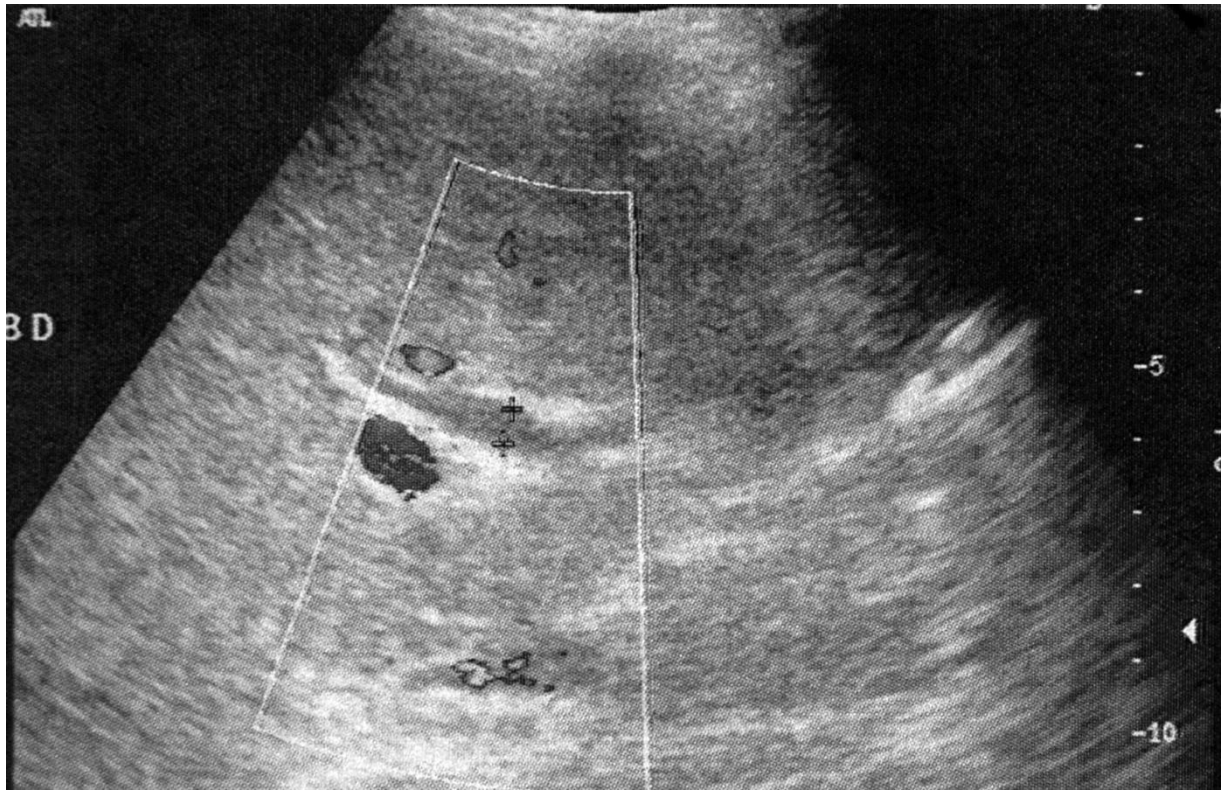


Les canaux biliaires du Segment 1 se jettent dans la convergence biliaire

Mode de Présentation

- Ictère nu avec une vésicule non distendue
- Plus rarement une cholestase isolée
- Deux problèmes initiaux
  - Eliminer une autre diagnostic de sténose hilaire
  - Evaluer la stratégie thérapeutique avant d'envisager le traitement de l'ictère et donc la mise en place d'une prothèse…

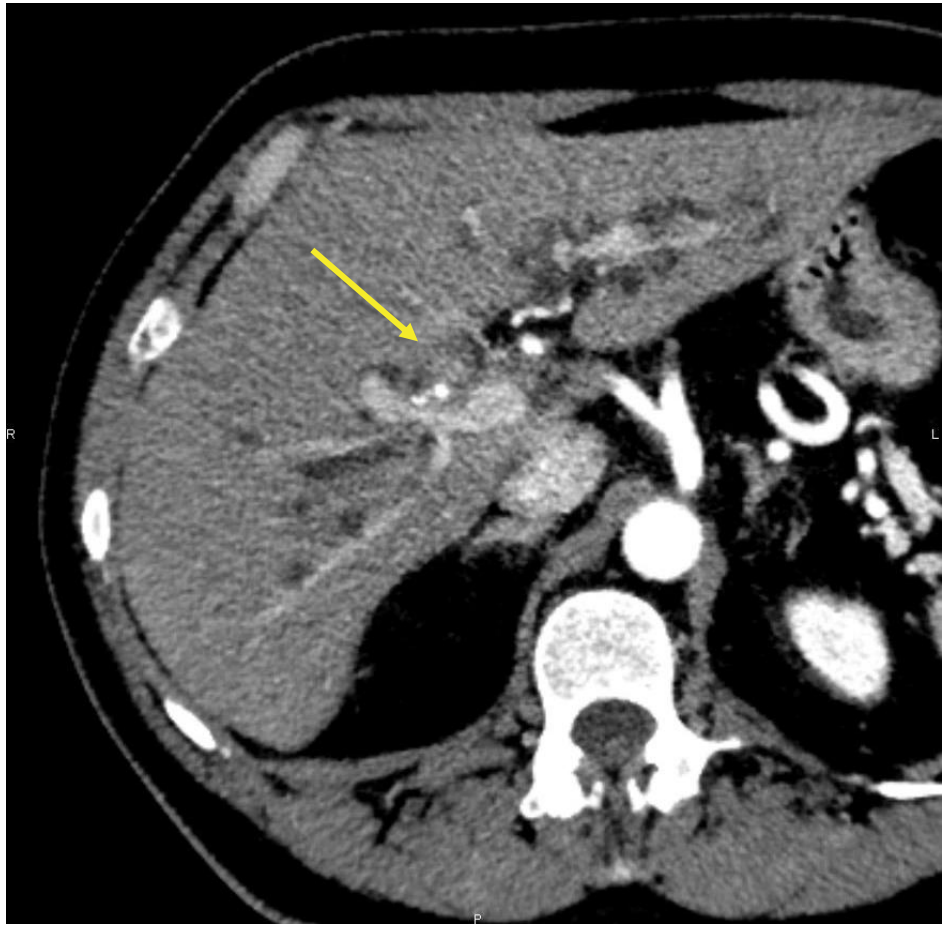
L’échographie hépatique



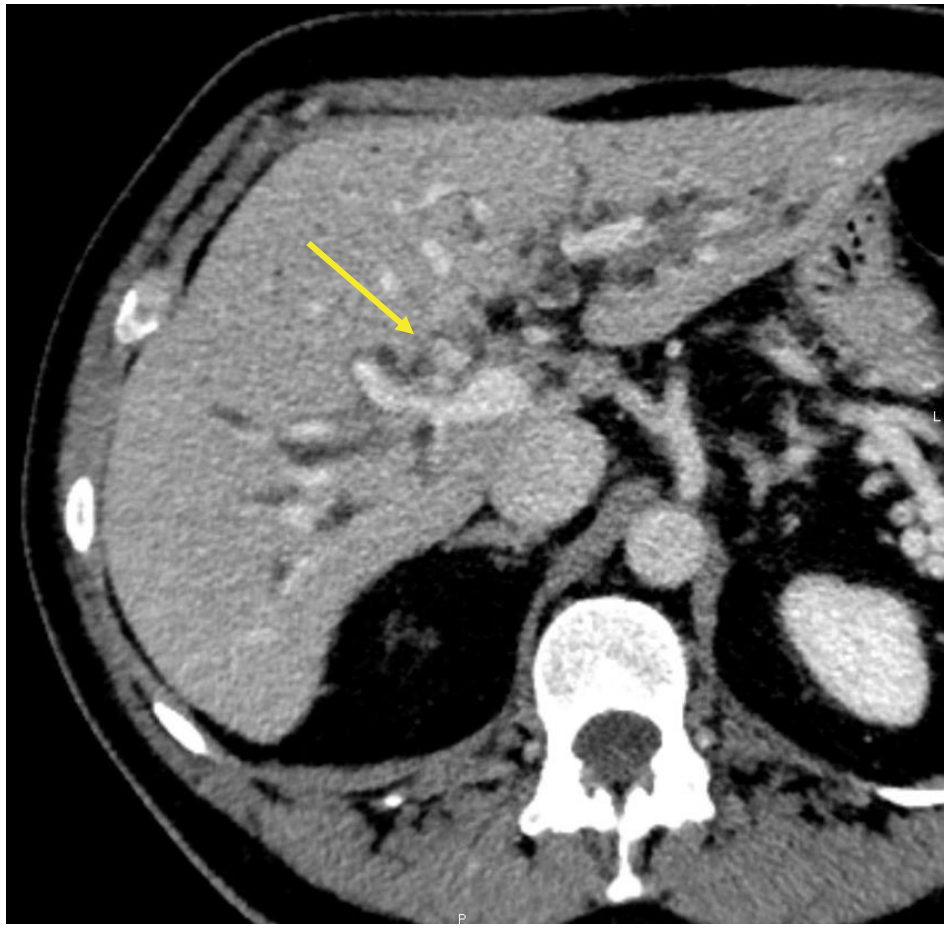
Dilatation isolée des VBIH

Vésicule Biliaire non distendue

Scanner Abdominal injecté

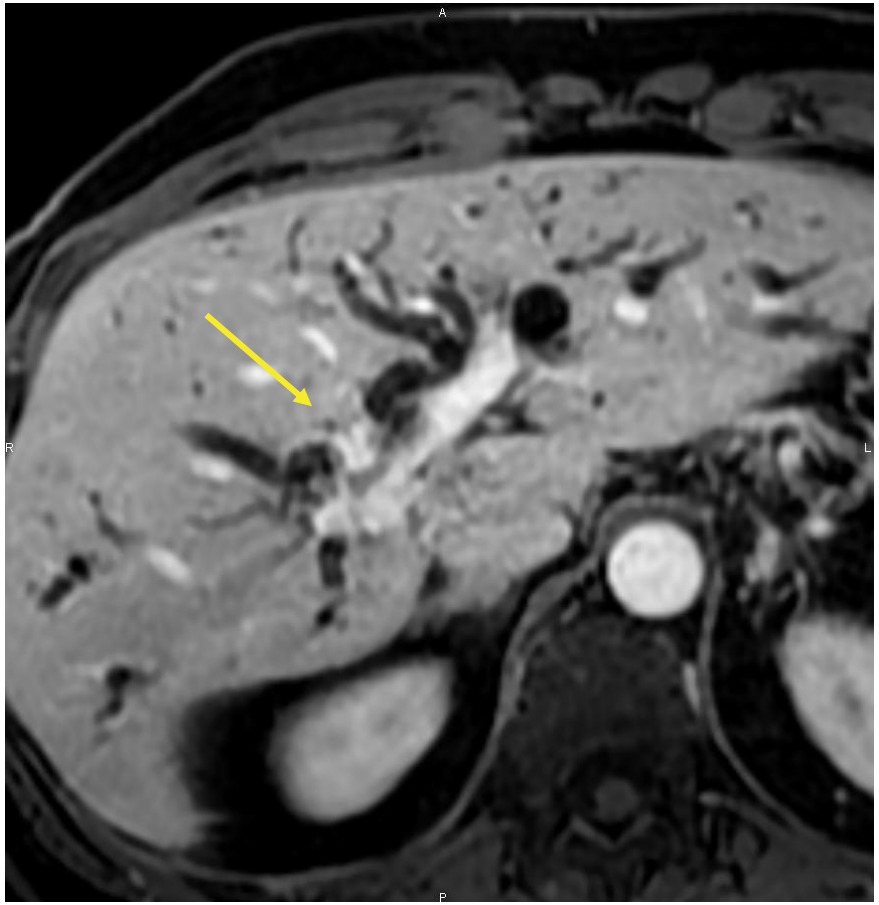


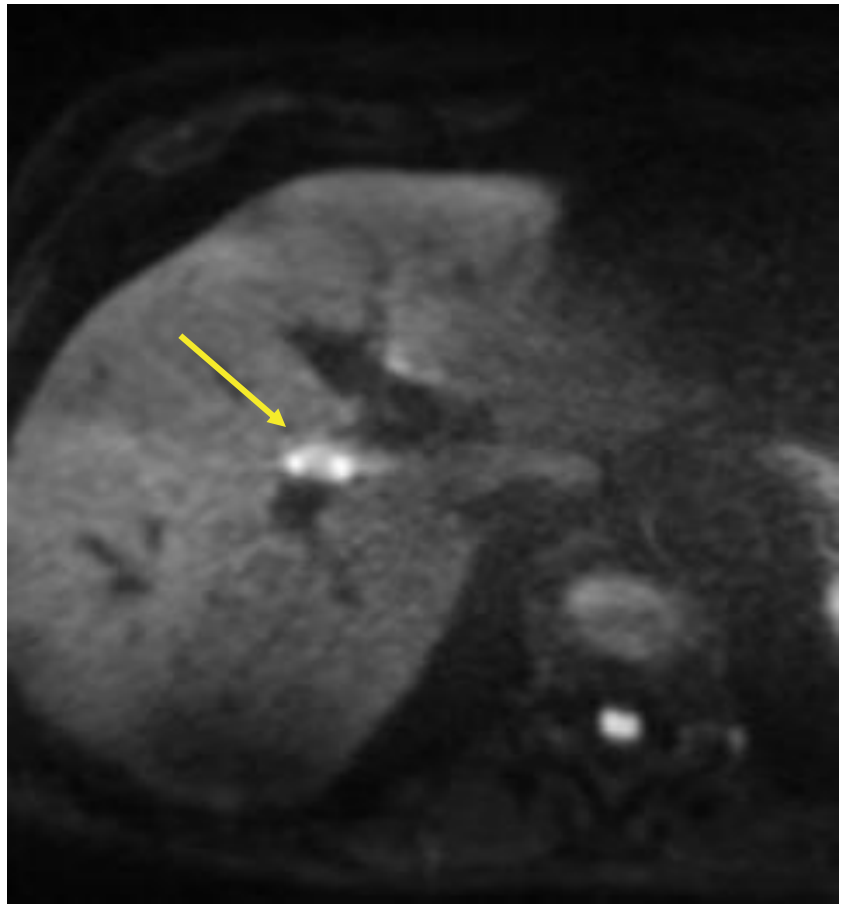
Petit syndrome de masse visible



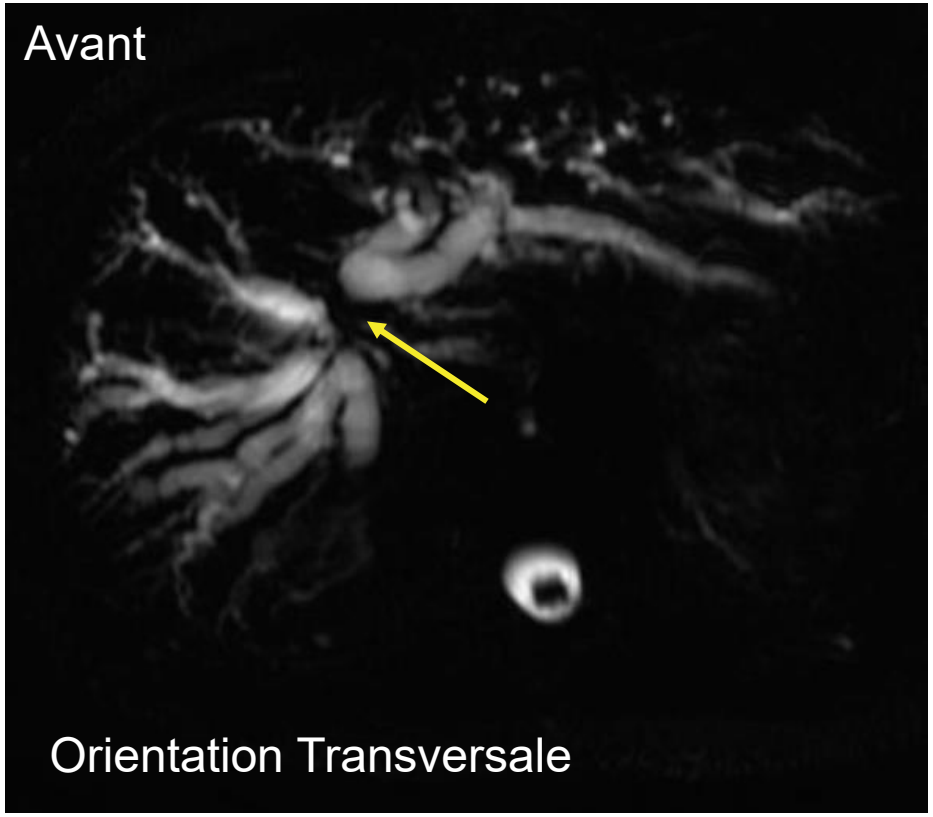
Persistance du réhaussement au temps portal

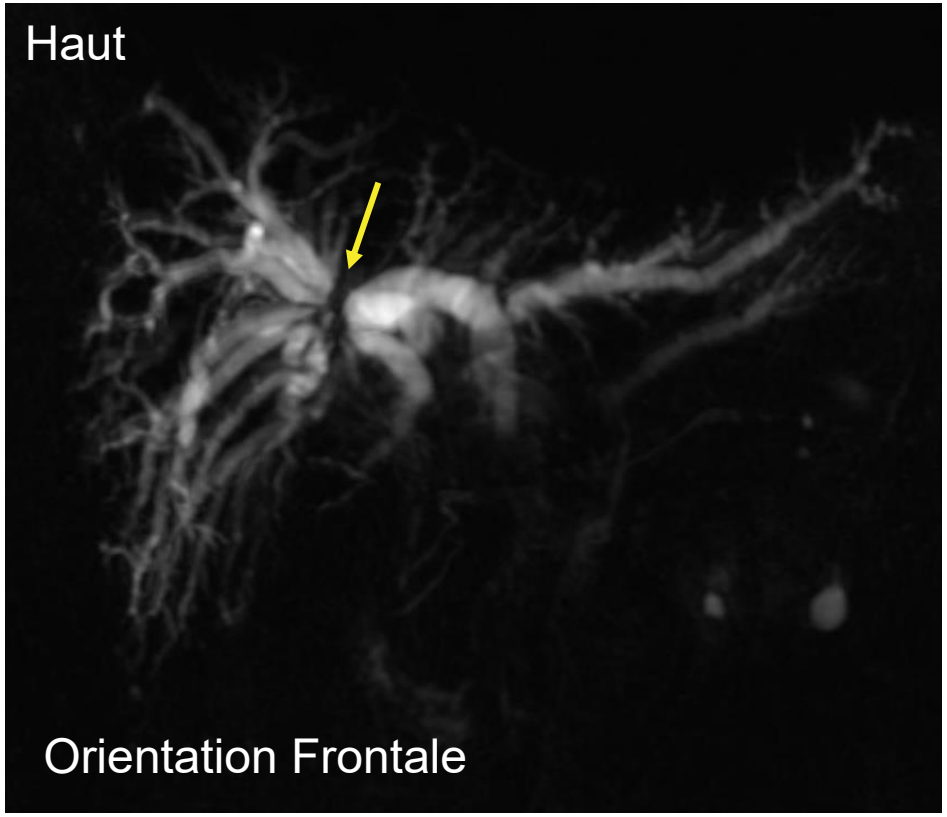
IRM avec séquences de diffusion



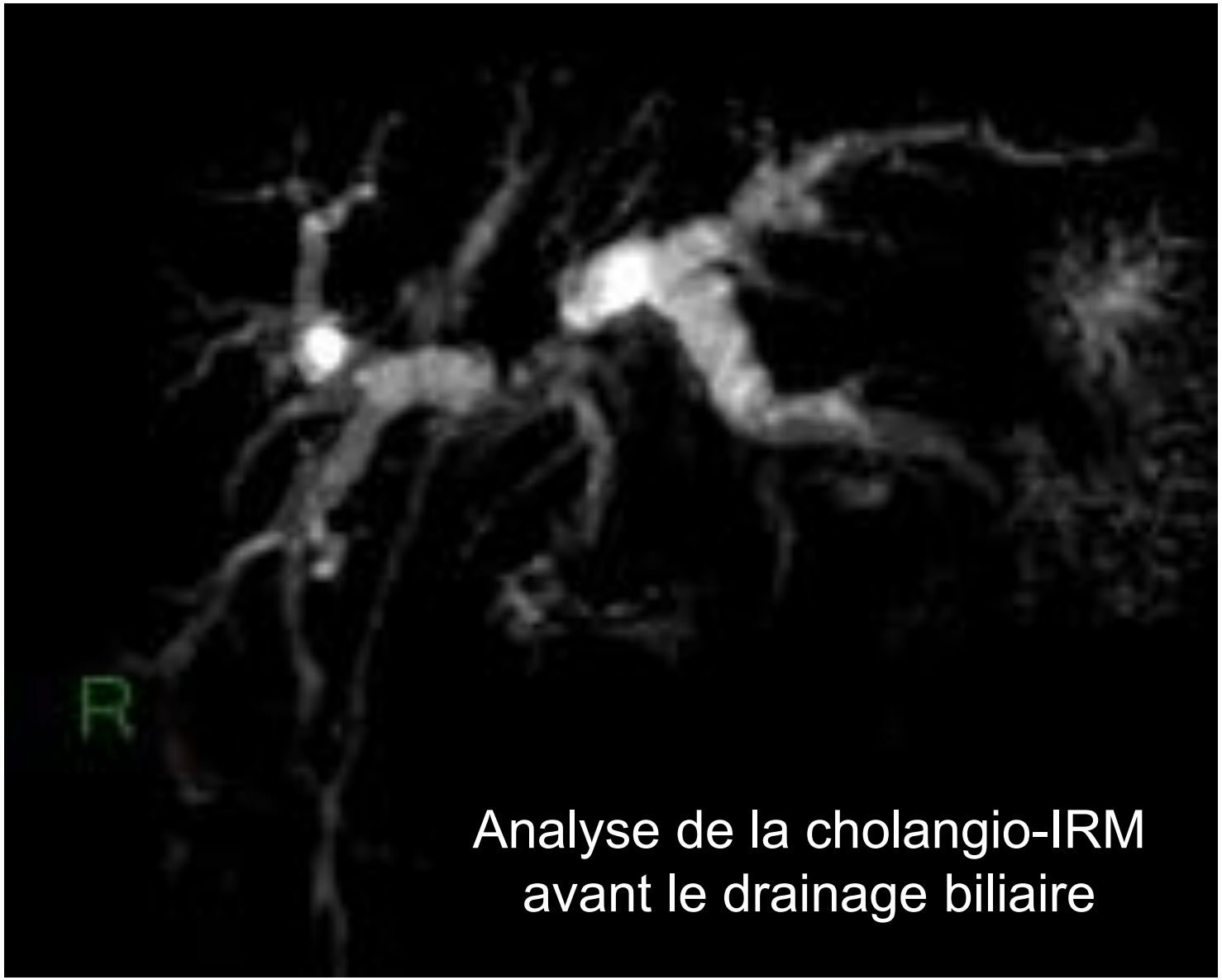


La cholangio-IRM





Vide de signal à la confluence des voies biliaires droites et gauches dilatées



Analyse de la cholangio-IRM
avant le drainage biliaire

Les diagnostics différentiels des cholangiocarcinomes hilaires

Bénin

Sténose Inflammatoire à IgG4

Cholangite Sclérosante Primitive

Sténose Post-traumatique ou Ischémique des VB

Compression Biliaire due à un cavernome portal

Syndrome de Mirizzi

Buc et al. HPB 2008

Malin

Cholangiocarcinome intra-hép. étendu au hile

Cancer de la vésicule biliaire étendu au hile

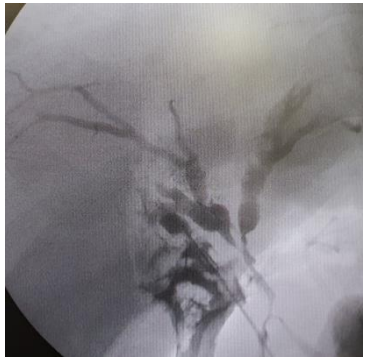
Pédiculite Néoplasique d'un cancer du sein

Pédiculite Néoplasique d'un cancer estomac

Hadjis et al. Br J Surg 1985

Benign hilar bile duct strictures resected as perihilar cholangiocarcinoma

S. Otsuka[1,2], T. Ebata[1], Y. Yokoyama[1], T. Igami[1], T. Mizuno[1], J. Yamaguchi[1], S. Onoe[1], N. Watanabe[1], Y. Shimoyama[2] and M. Nagino[1]



2001 – 2016 / Nagoya / Retrospective analysis of Prospective data

707 pts operated for Hilar Chol → 22 Benin Sténosis (3.1%)

Table 1 Patient characteristics and surgical outcomes

	Malignant (n = 685)	Benign (n = 22)	P‡
Age (years)*	68 (30–89)	67 (34–80)	0·566§
Sex ratio (M : F)	444 : 241	14 : 8	1·000
Jaundice (total bilirubin > 2·0 mg/dl)	441 (64·4)	12 (55)	0·366
CEA (ng/ml)*	2·3 (0·3–174)	2·7 (0·9–7·6)	0·613§
CA19-9 (units/ml)*	84 (1–52 831)	16 (2–510)	0·002§
ICG-R15 (%)*	9·2 (1·0–31·1)	10·9 (4·0–20·9)	0·517§
Bismuth classification			0·785
I	53 (7·7)	1 (5)	
II	65 (9·5)	1 (5)	
III	263 (38·4)	11 (50)	
IV	304 (44·4)	9 (41)	
Duration of operation (min)*	600 (344–1150)	544 (332–759)	0·043§
Blood loss (ml)*	1328 (46–11 115)	1133 (376–3022)	0·313§
Duration of postoperative hospital stay (days)*	30 (6–218)	20 (12–66)	0·002§
90-day mortality	13 (1·9)	0 (0)	1·000

Table 2 Diagnostic accuracy of preoperative histological assessment

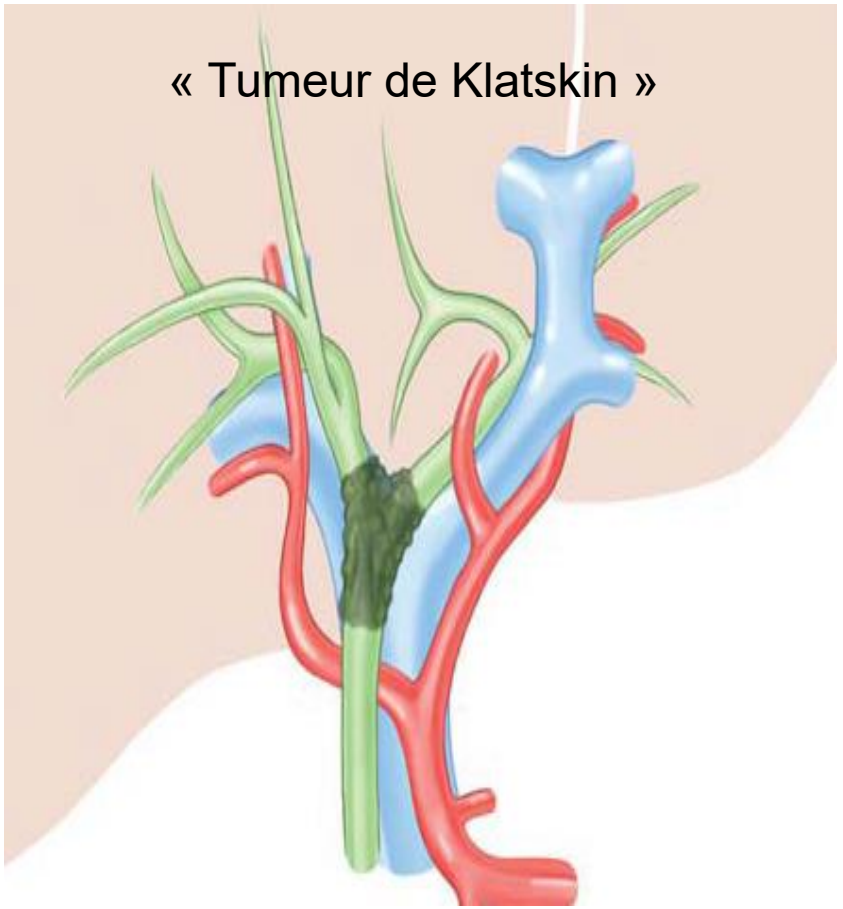
	n	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Bile duct biopsy	382	63	100	100	9	65
Aspiration cytology	483	44	89	99	6	46
Biopsy and/or cytology						
2001–2004	55	40	–	100	0	40
2005–2008	167	60	71	98	7	61
2009–2012	181	66	100	100	11	67
2013–2016	197	66	100	100	9	67
Overall	600	62	90	99	8	63

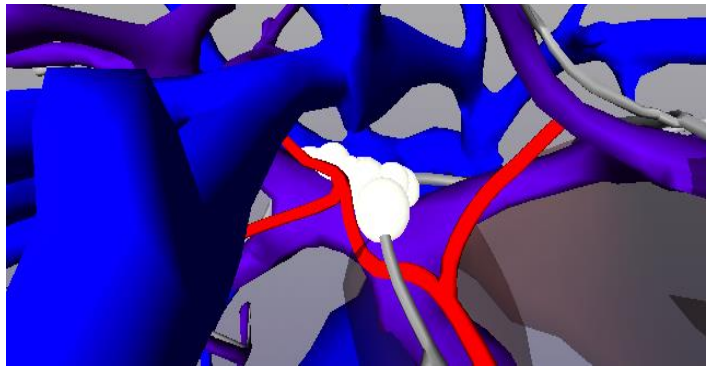
PPV, positive predictive value; NPV, negative predictive value.

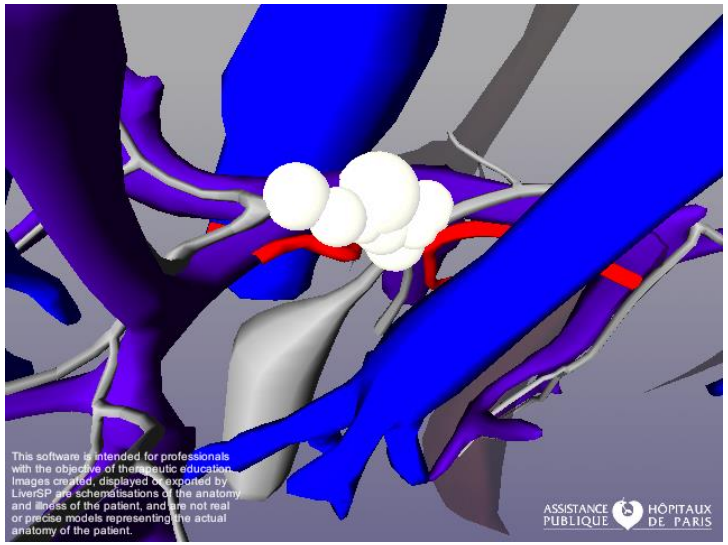
BJS 2019; **106**: 1504–1511

107 / 707 (16%) : Pas de Masse TDM / Biopsie Neg / CA19.9 Nle → 11.5 % Benin… Seulement

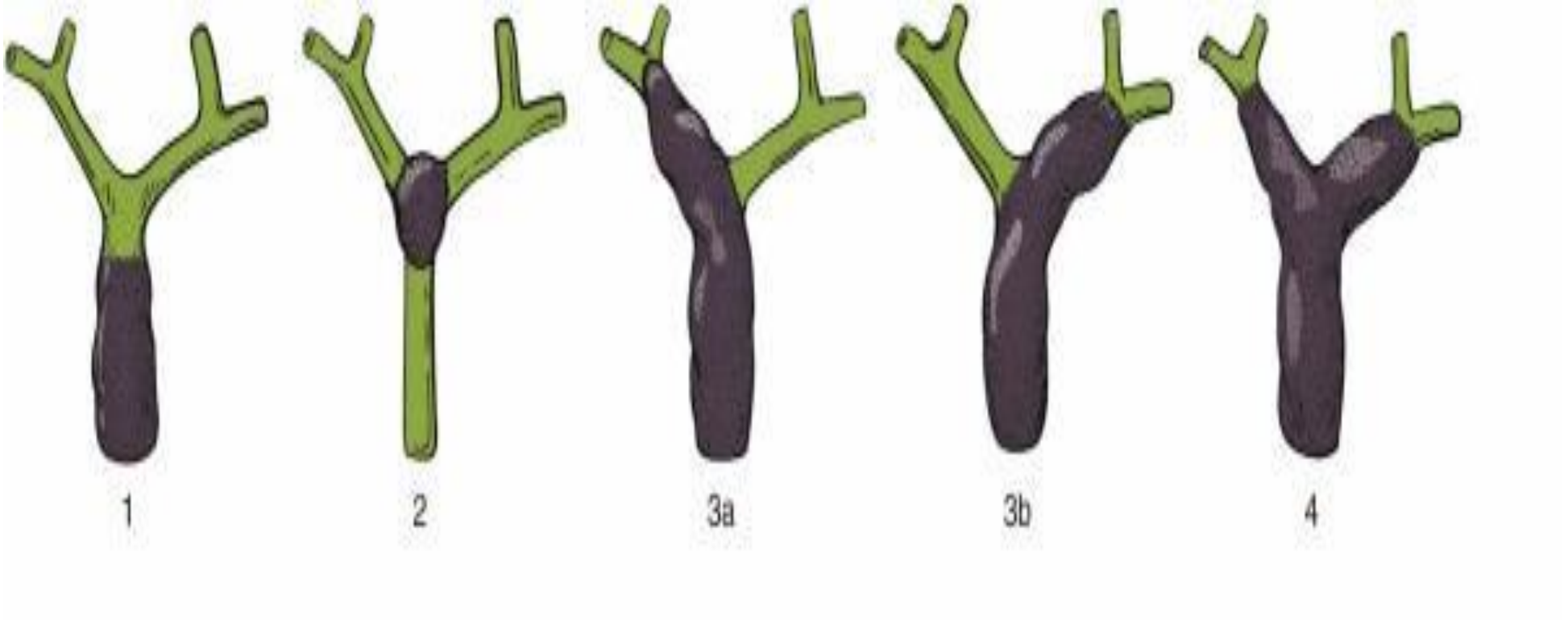
Intérêts et limites de la classification des cholangiocarcinomes hilaires





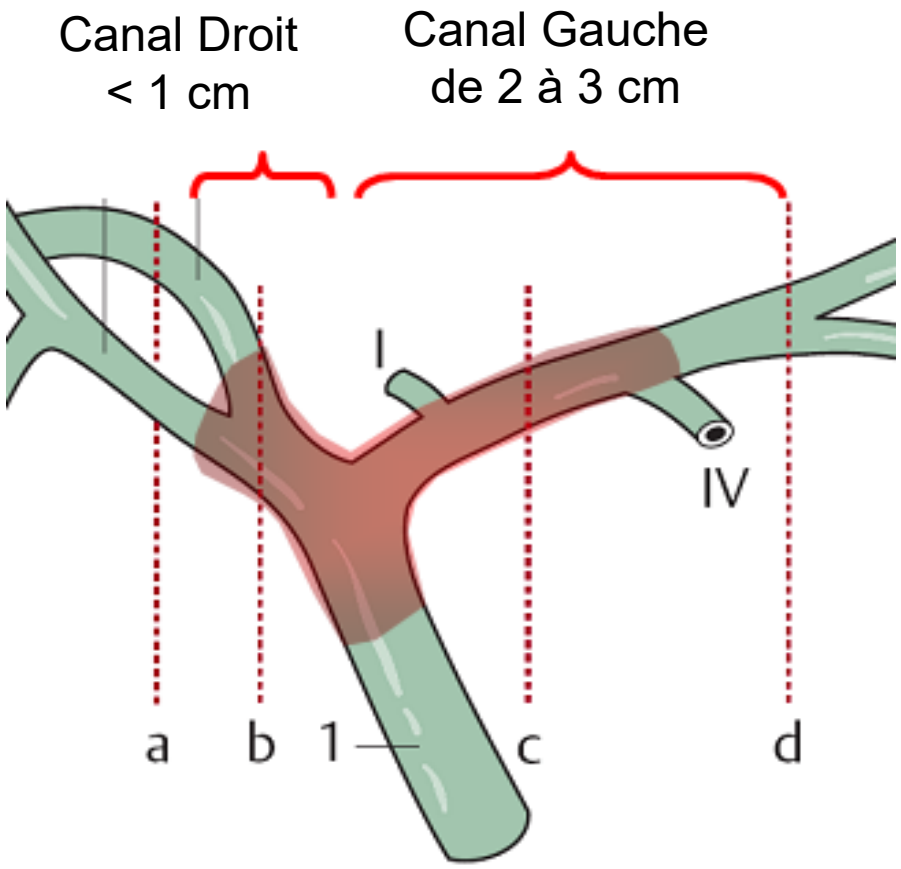


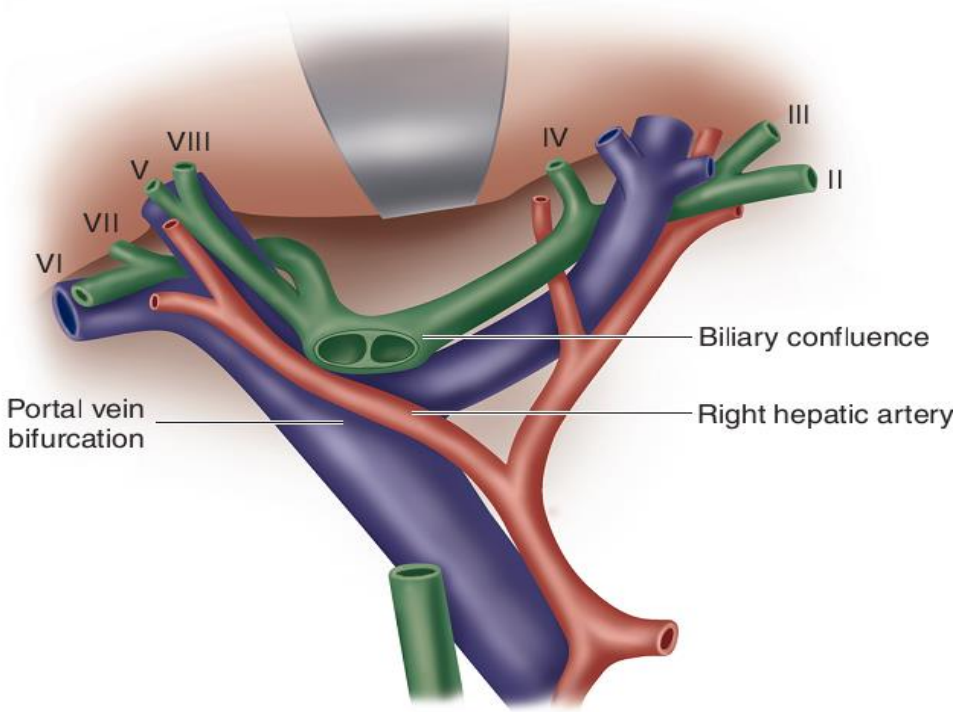
La classification de Bismuth et Corlette



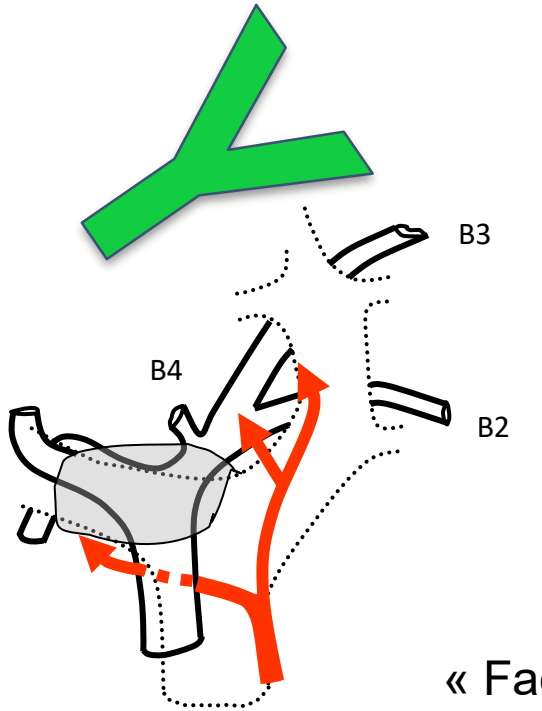
Bismuth, Corlette et al. Surg Gyn Obs 1975

La marge biliaire et péri-biliaire



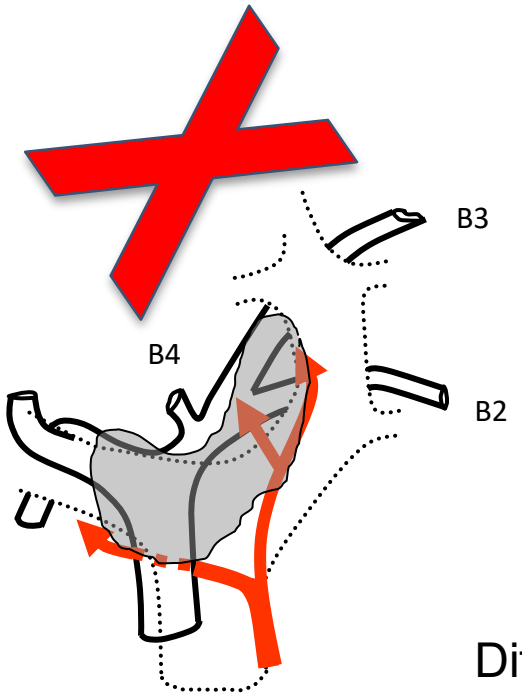


L’union des canaux du lobe gauche ?



« Facile »….

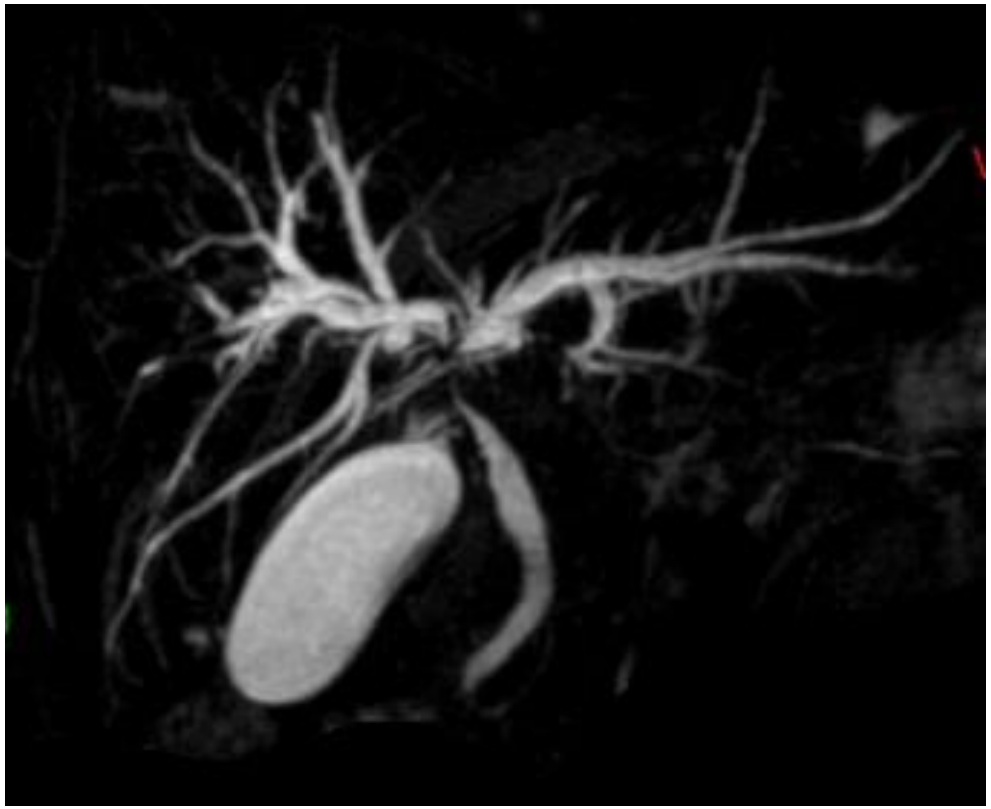
Hépatectomie D élargie au S1 + S4
Reconstructions Artérielle peu fréquentes
Artère hépatique gauche jamais infiltrée

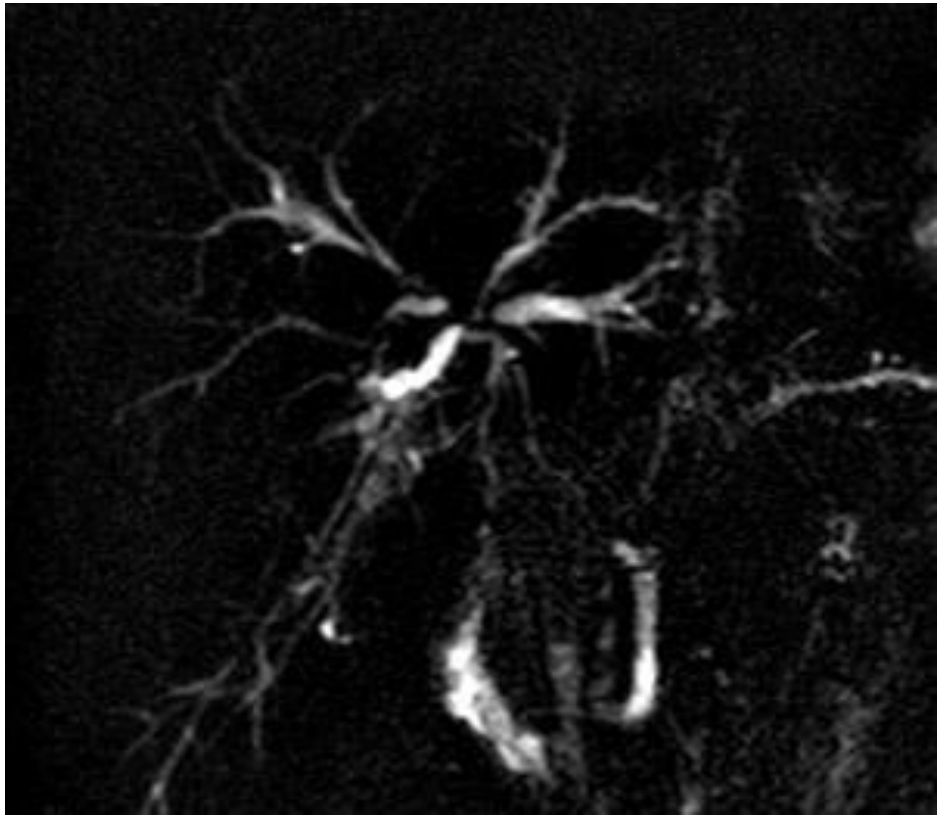


Difficile….

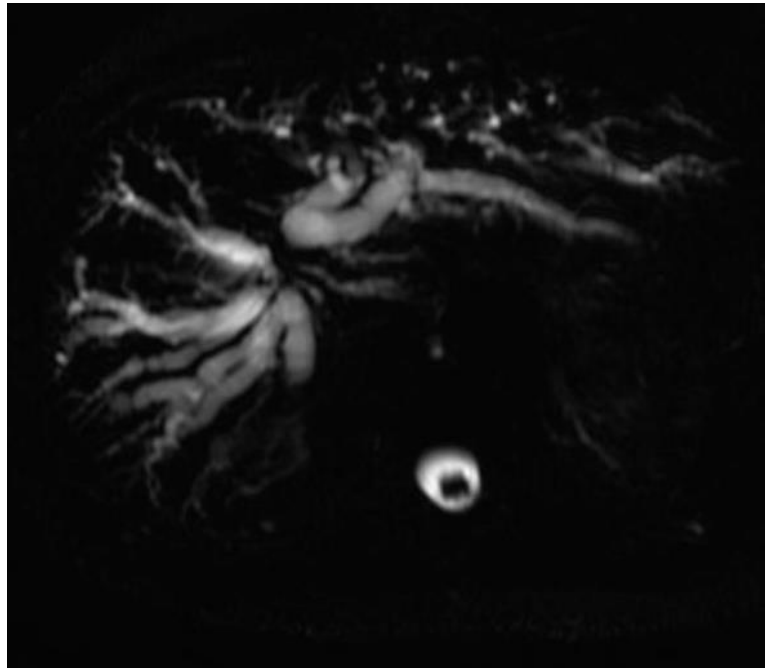
Hépatectomie G élargie au S5 et S8
Reconstructions Artérielles fréquentes
Artère droite rapidement infiltrée

Boudjema et al. J Gastrointest Surg 2013

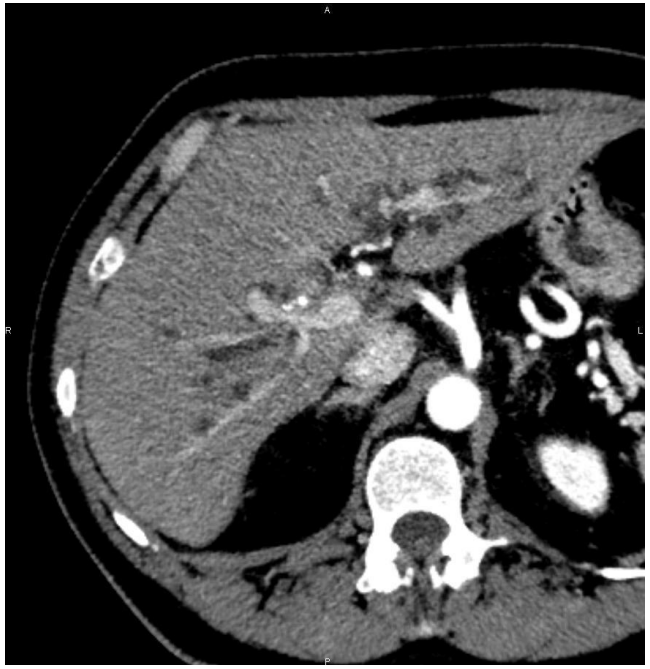




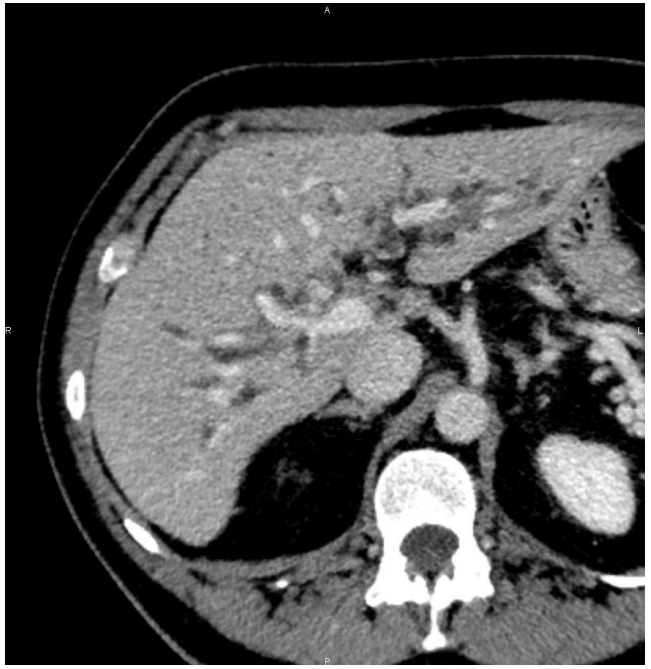
Le bilan d’extension locale du cholangiocarcinome hilaire



Extension Biliaire ?



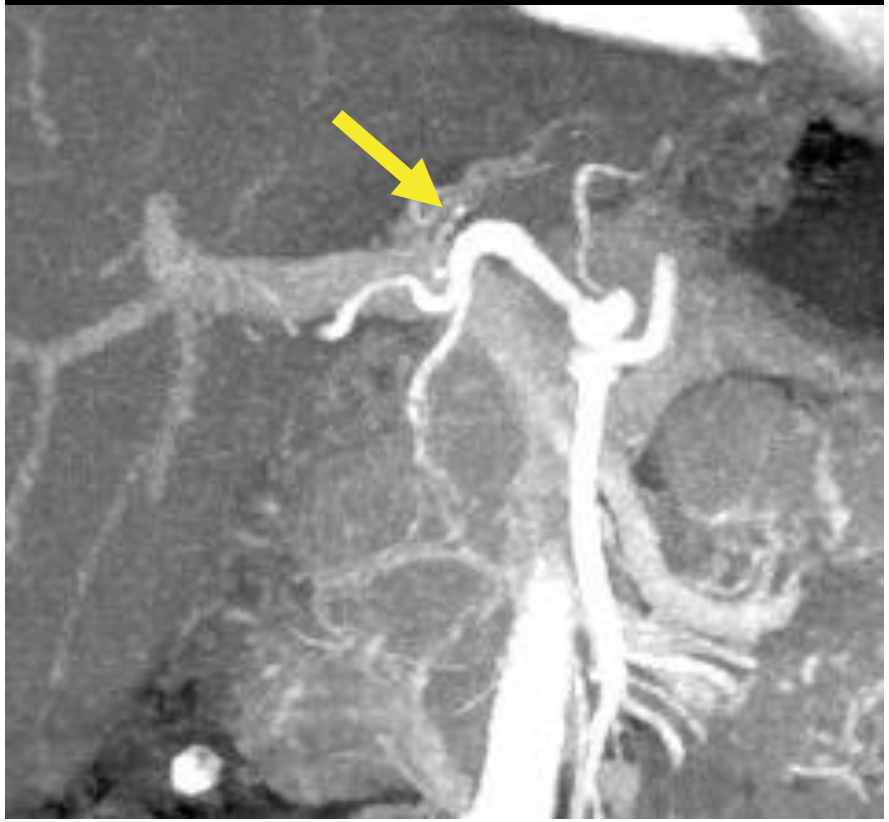
Extension Artérielle ?



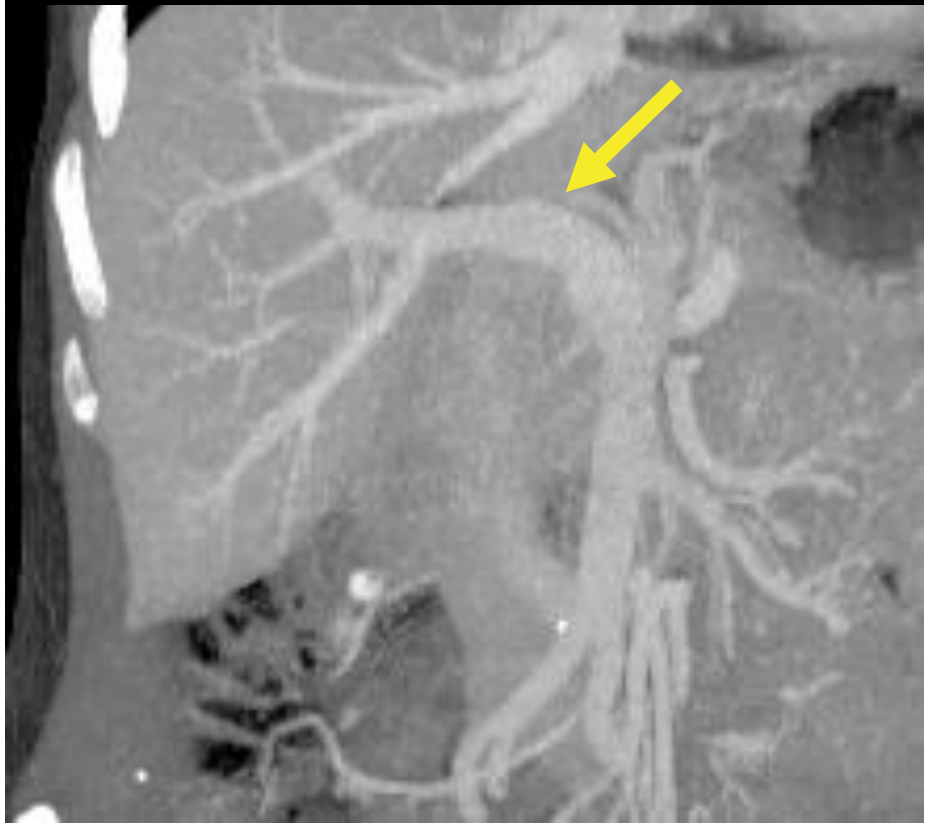
Extension Portale ?

Reconstruction vasculaire

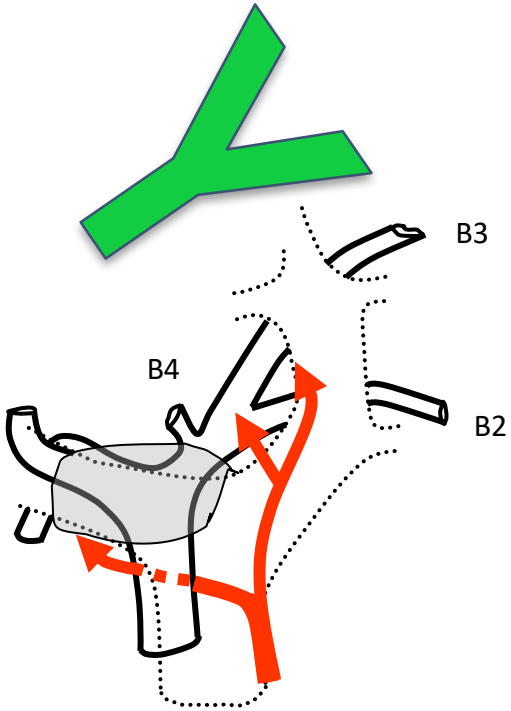
Envahissement de la branche gauche de l'artère hépatique

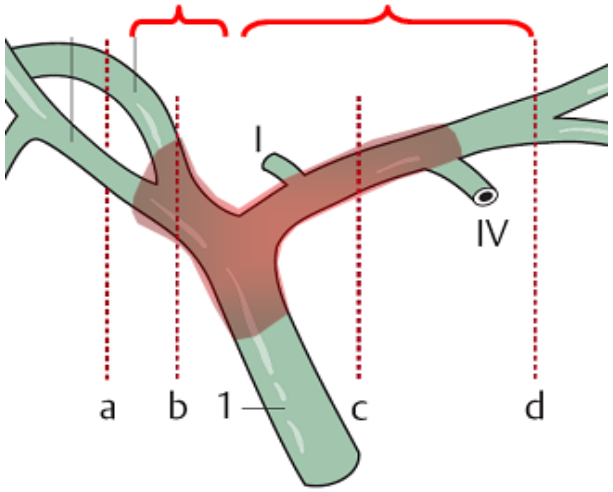


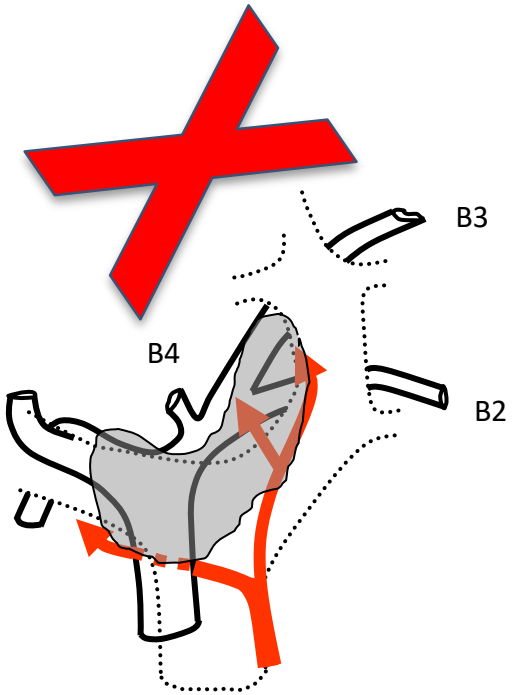
Envahissement et non visibilité de la branche gauche de la veine porte

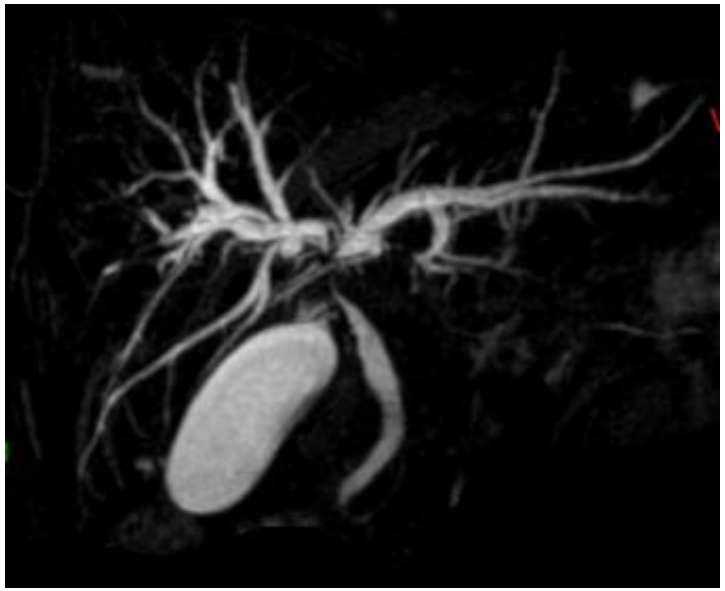


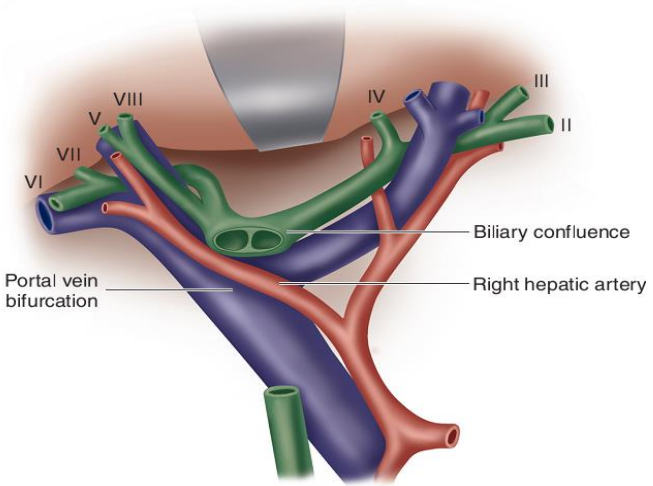
Left Bile Duct is longer

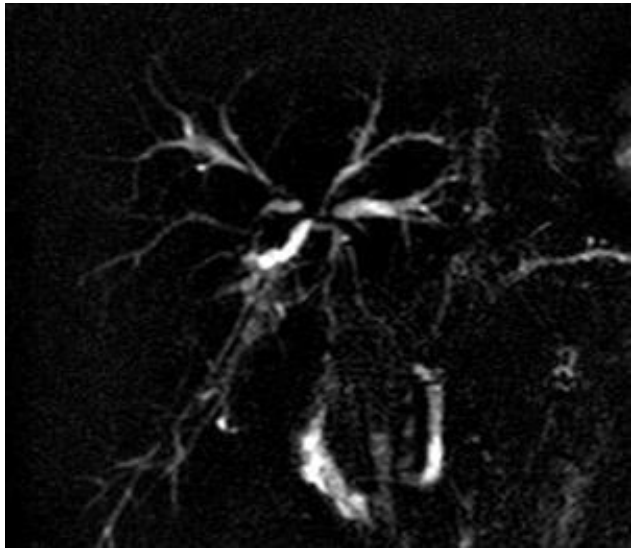




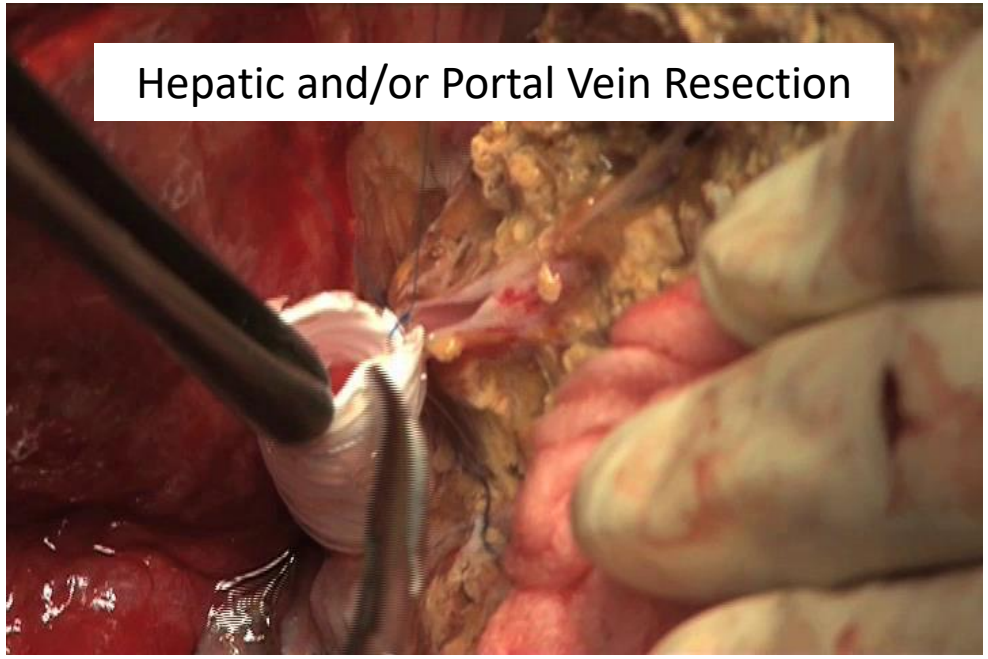


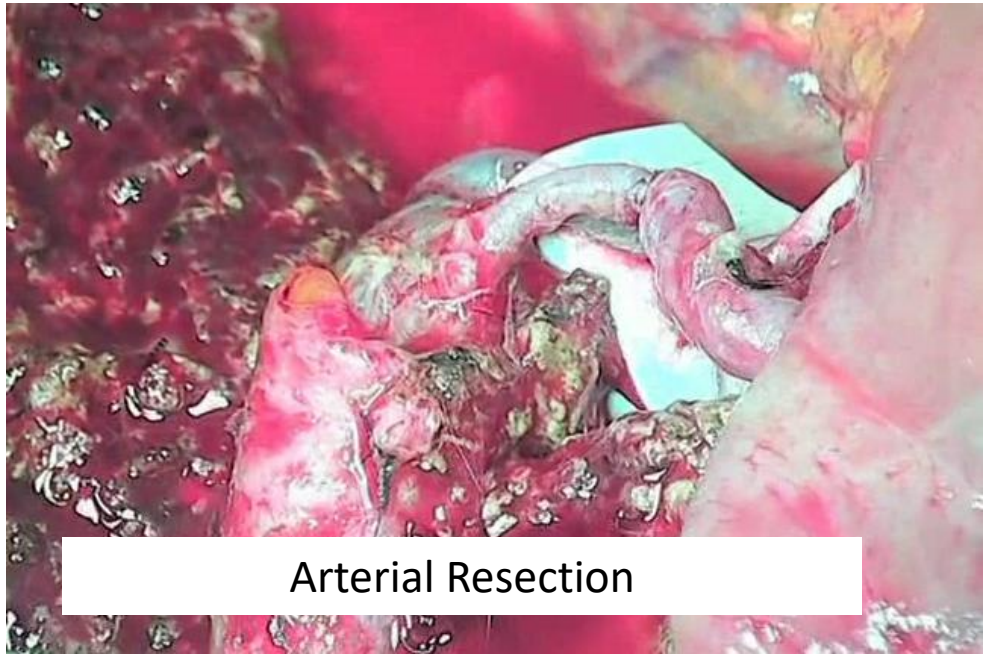




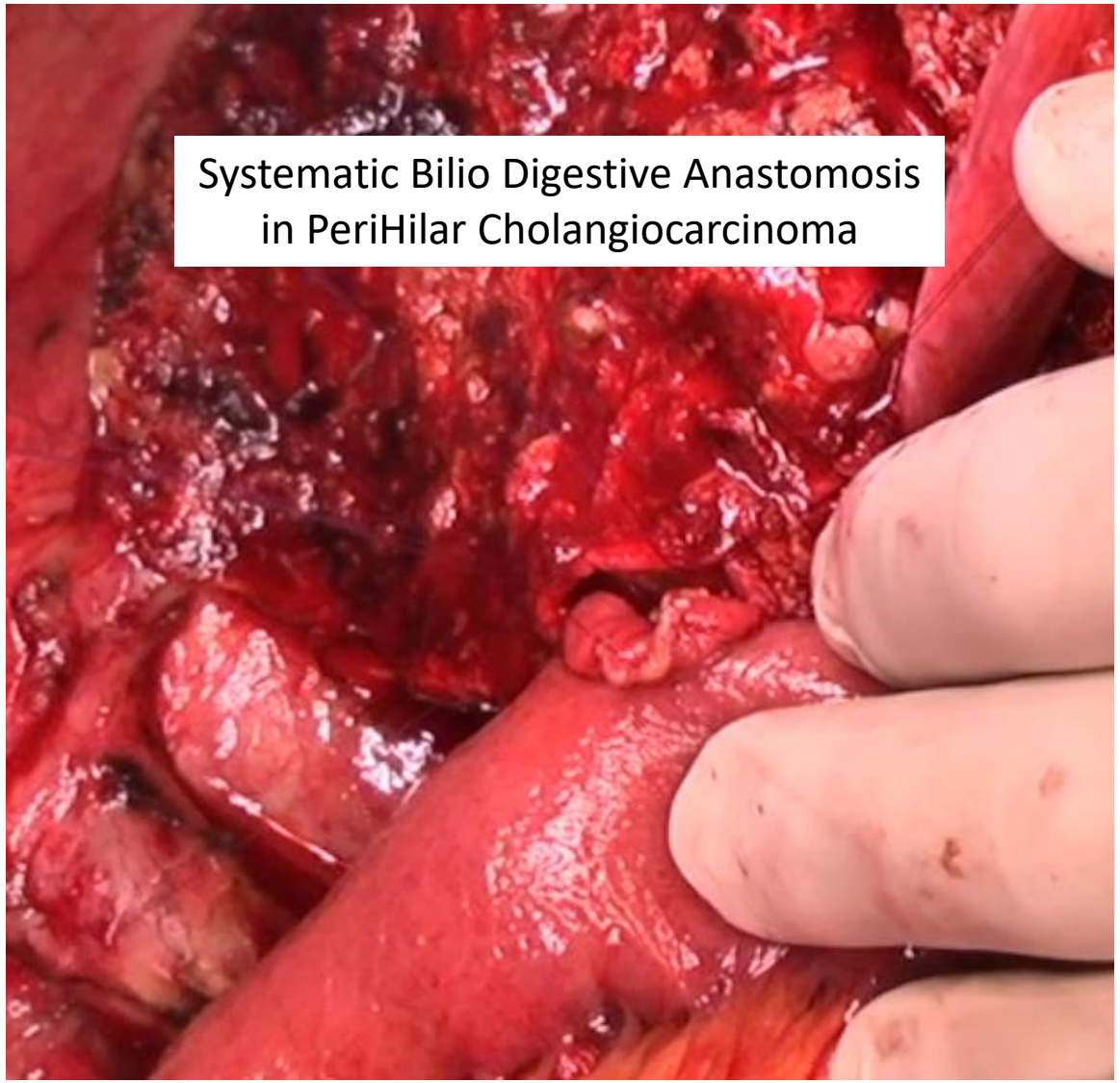


Boudjema et al. J Gastrointest Surg 2013

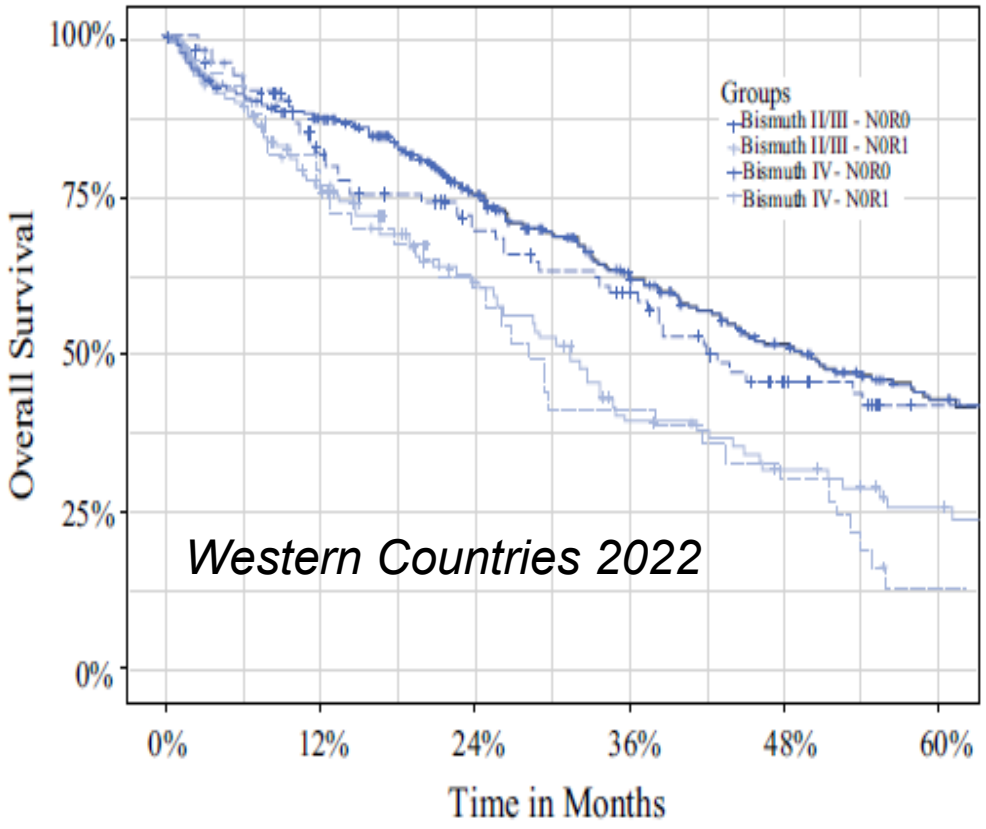


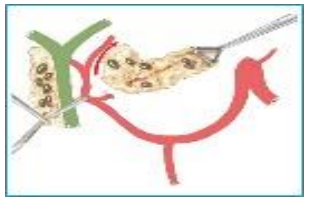


After a Drop Out of 30% before surgery



Aim : R0 in N0 patient → 45-50% 5-years OS

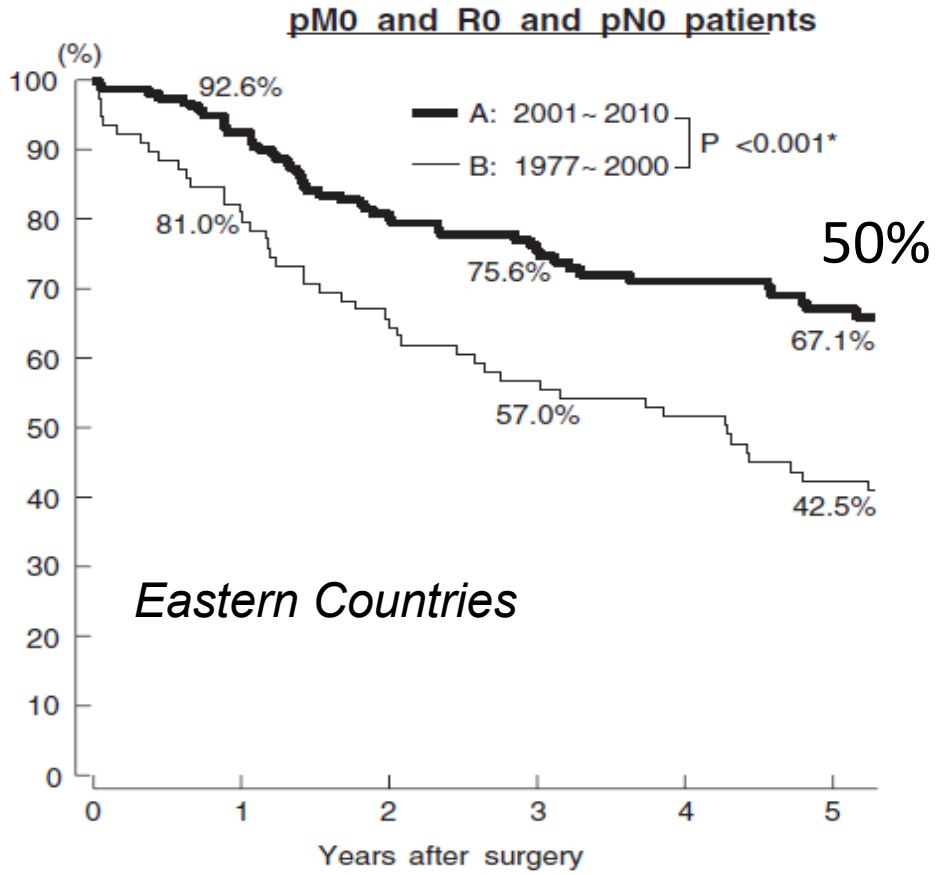




43% R0-N0

26% R1-N0

13% R1-N1



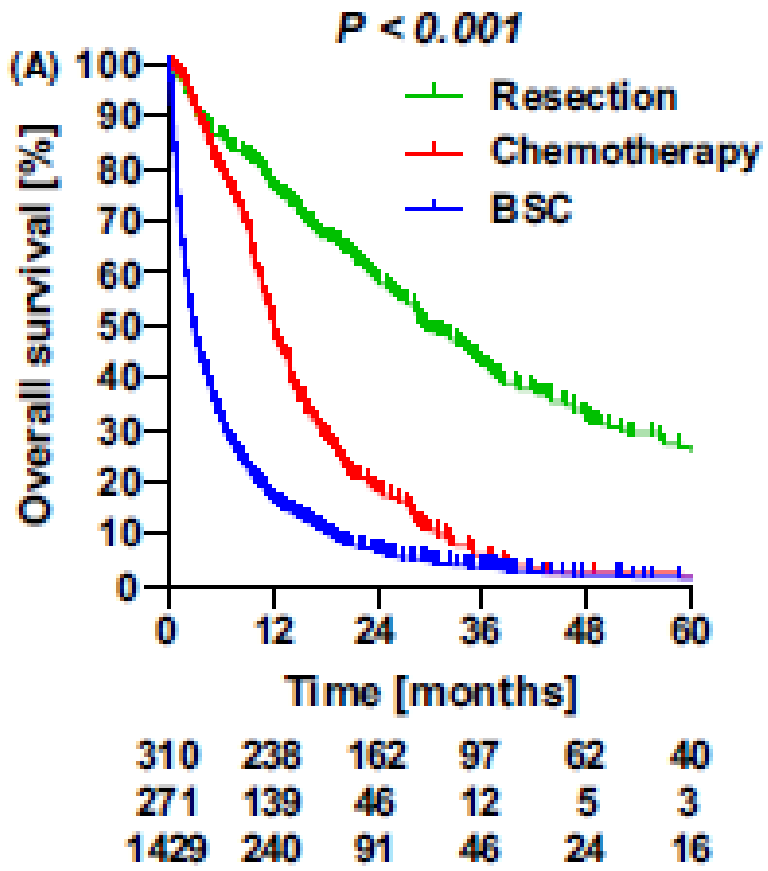
Ruzzenente et al. Ann Surg Oncol 2022

Zang et al. Ann Surg 2020

Nagino et al. Ann Surg 2013

Nationwide treatment and outcomes of perihilar cholangiocarcinoma

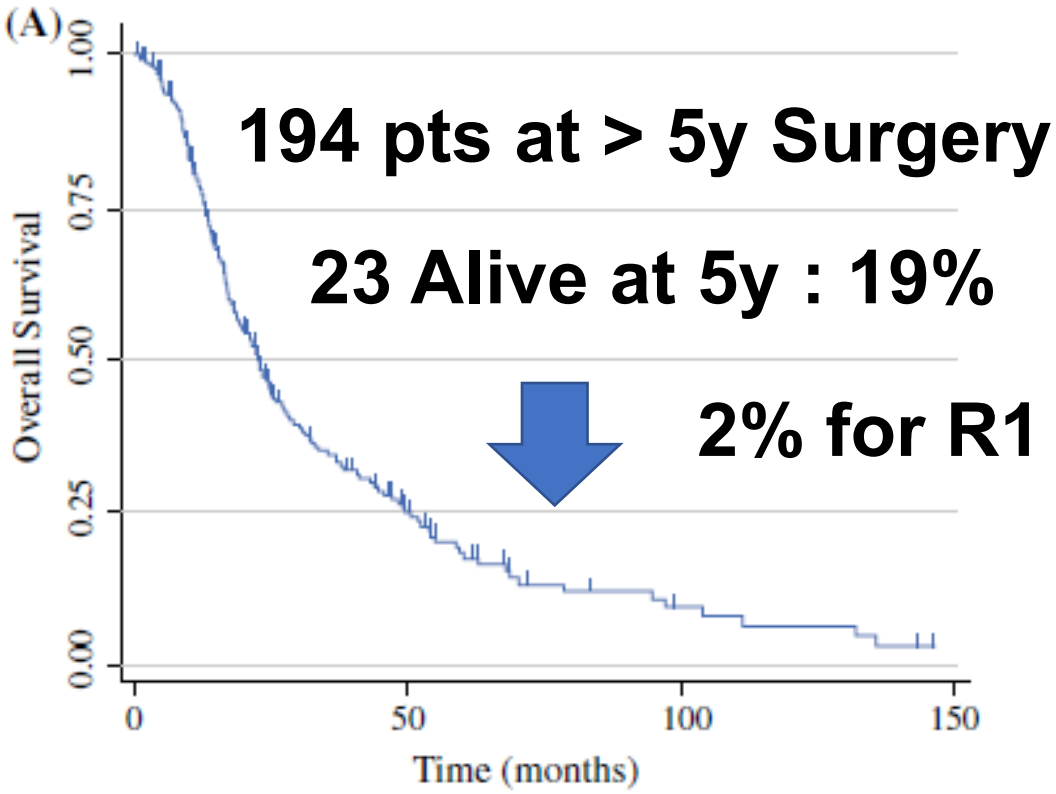
Anne-Marleen van Keulen[1,2] | Stijn Franssen[1] | Lydia G. van der Geest[3] | Marieke T. de Boer[4] | Minneke Coenraad[3] | Lydi M. J. W. van Driel[6] | Joris I. Erdmann[7] | Nadia Haj Mohammad[8] | Lara Heij[9,10,11] | Heinz-Josef Klümpen[12] | Eric Tjwa[13] | Liselot Valkenburg-van Iersel[14] | Joanne Verheij[15] | Bas Groot Koerkamp[1] | Pim B. Olthof[1,7] | the Dutch Hepatocellular & Cholangiocarcinoma Group (DHCG)



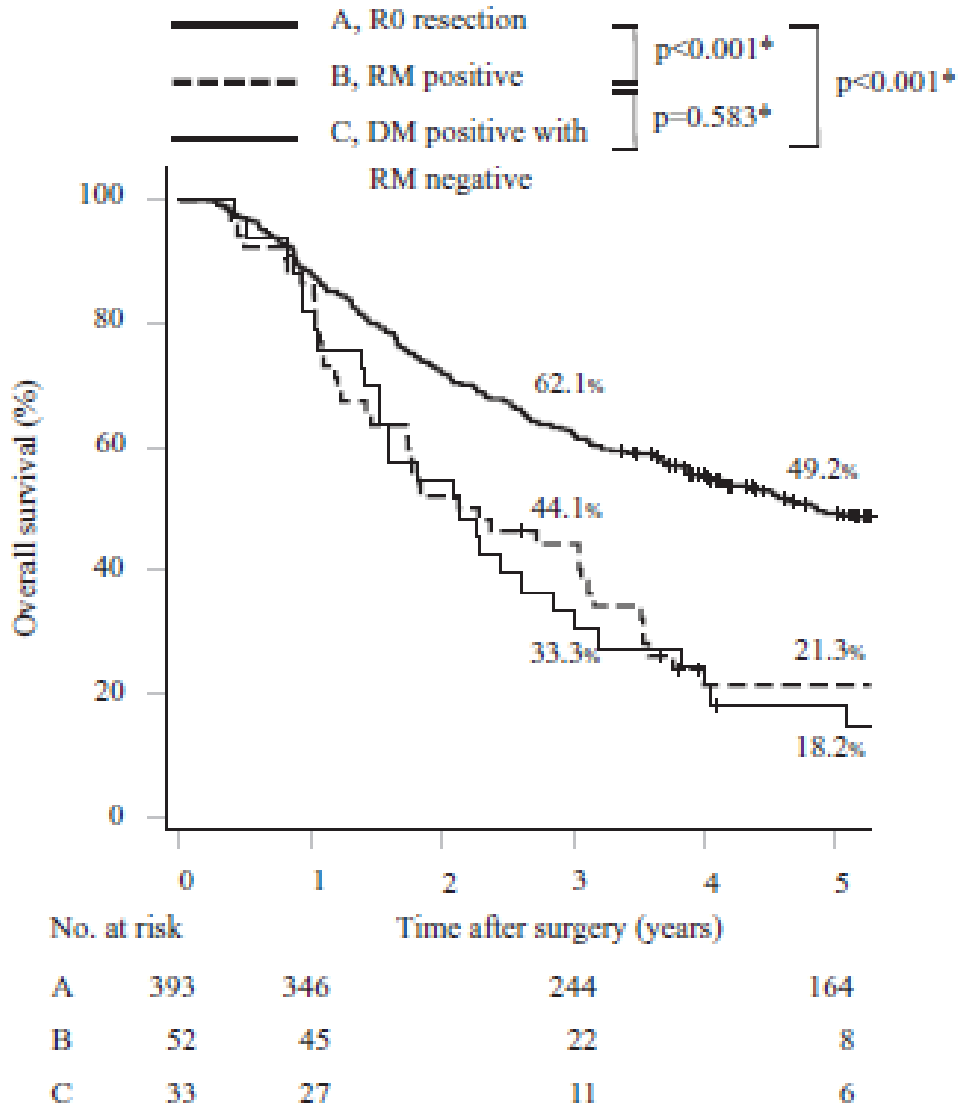
Liver International 2020

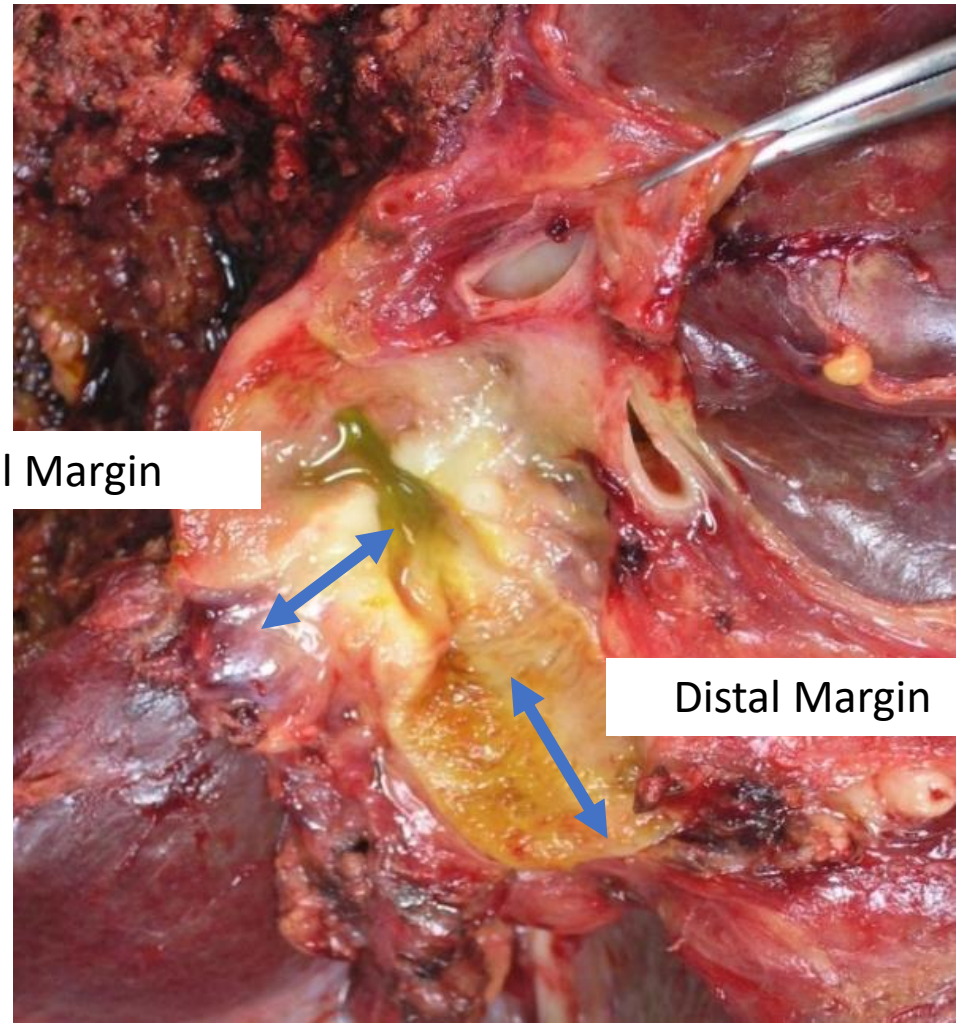
Actual 5-Year Survivors After Surgical Resection of Hilar Cholangiocarcinoma

Thuy B. Tran, MD[1], Cecilia G. Ethun, MD[2], Timothy M. Pawlik, MD, MPH, PhD[3,4], Carl Schmidt, MD[4], Eliza W. Beal, MD[4], Ryan C. Fields, MD[5], Bradley Krasnick, MD[5], Sharon M. Weber, MD[6], Ahmed Salem, MD[6], Robert C. G. Martin, MD[7], Charles R. Scoggins, MD[7], Perry Shen, MD[8], Harveshp D. Mogal, MD[8], Kamran Idrees, MD[9], Chelsea A. Isom, MD[9], Ioannis Hatzaras, MD[10], Rivfka Shenoy, MD[10], Shishir K. Maithel, MD[2], and George A. Poultsides, MD, MS, FACS[1]



Ann Surg Oncol 2019

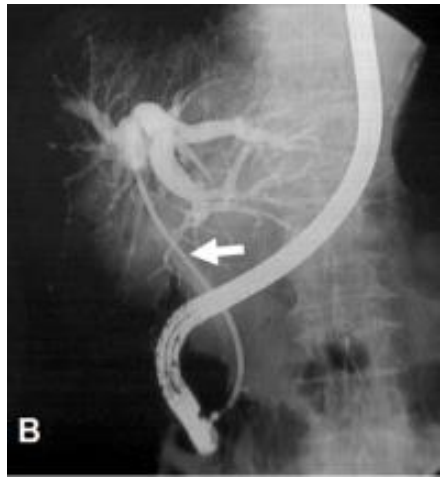


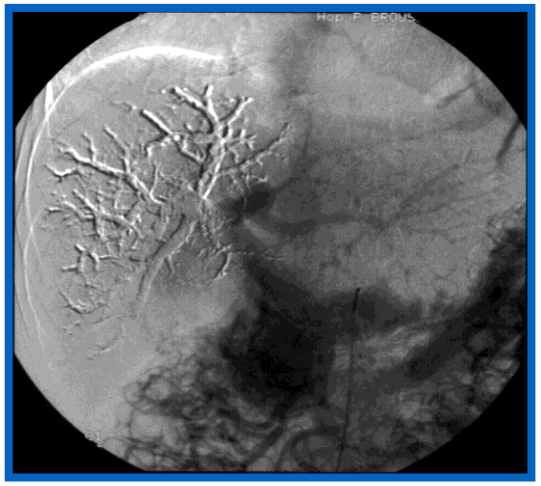


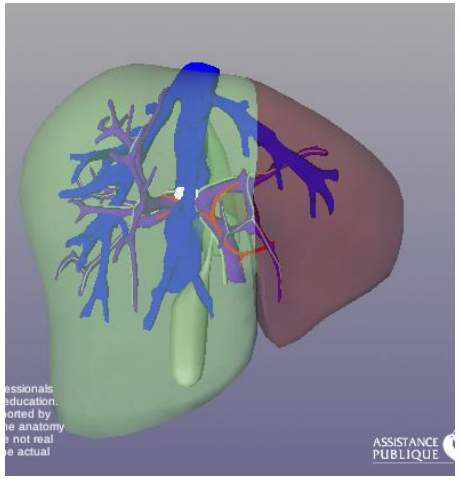
Shinohara et al. Ann Surg 2021

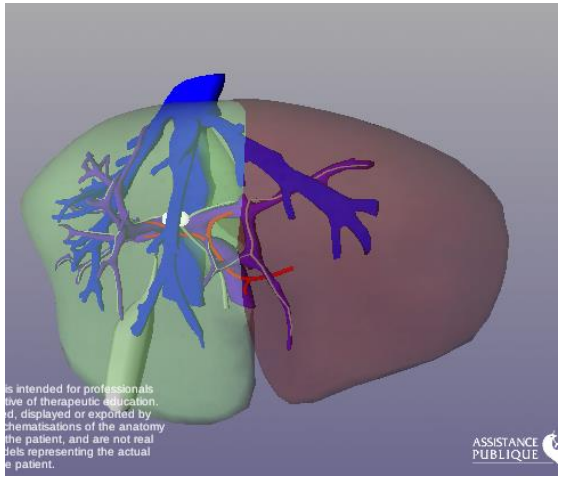
Endoscopic Biliary Drainage and Portal Vein Embolization

3 to 6 weeks









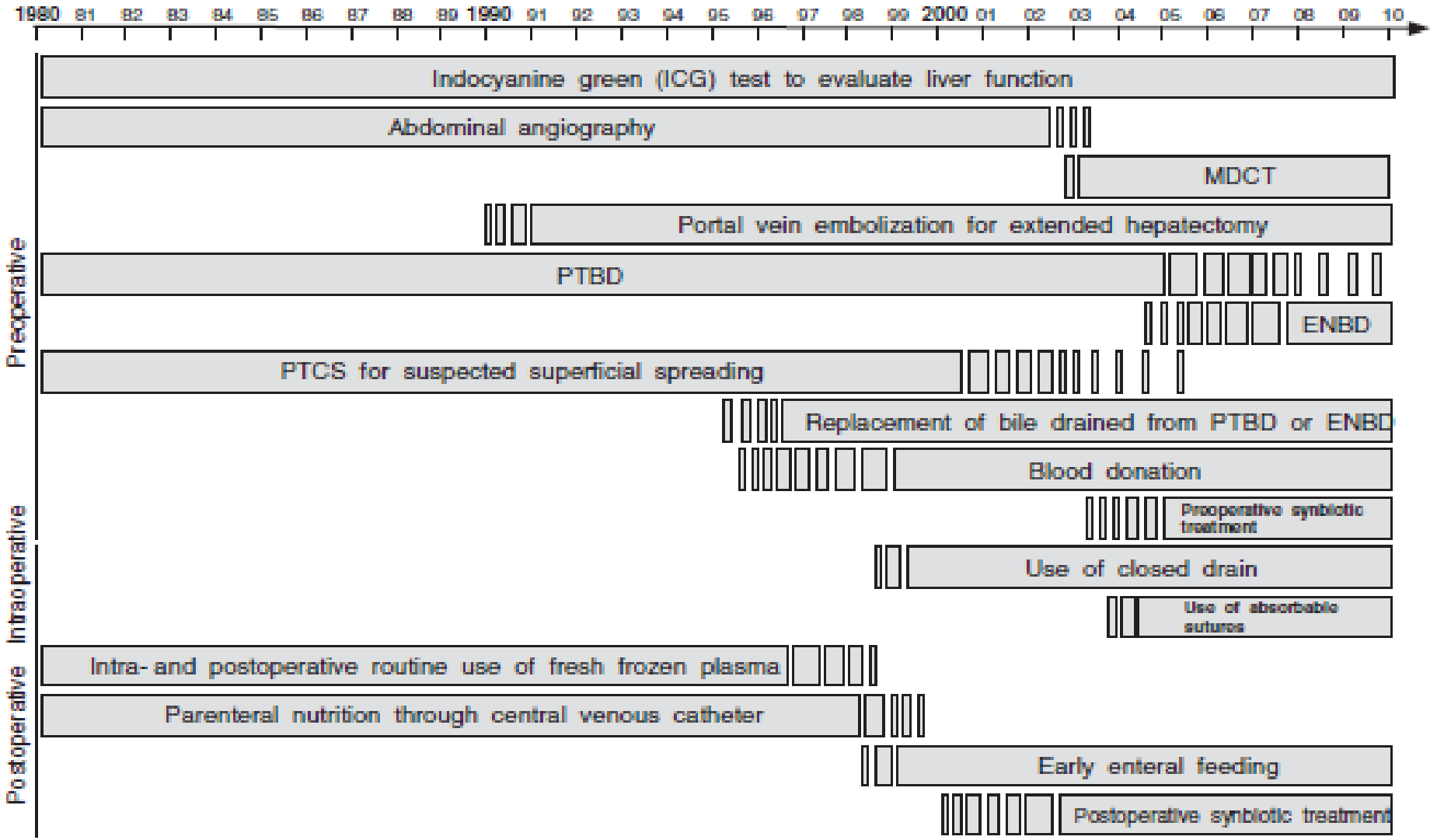
Endoscopic Biliary Drainage
Portal Vein Emb or Venous Deprivation

Volume >> 0.5% of body weight (1% if possible)

Coelen, Lancet Gastroenterology 2018

Kobayashi, Surgery 2020

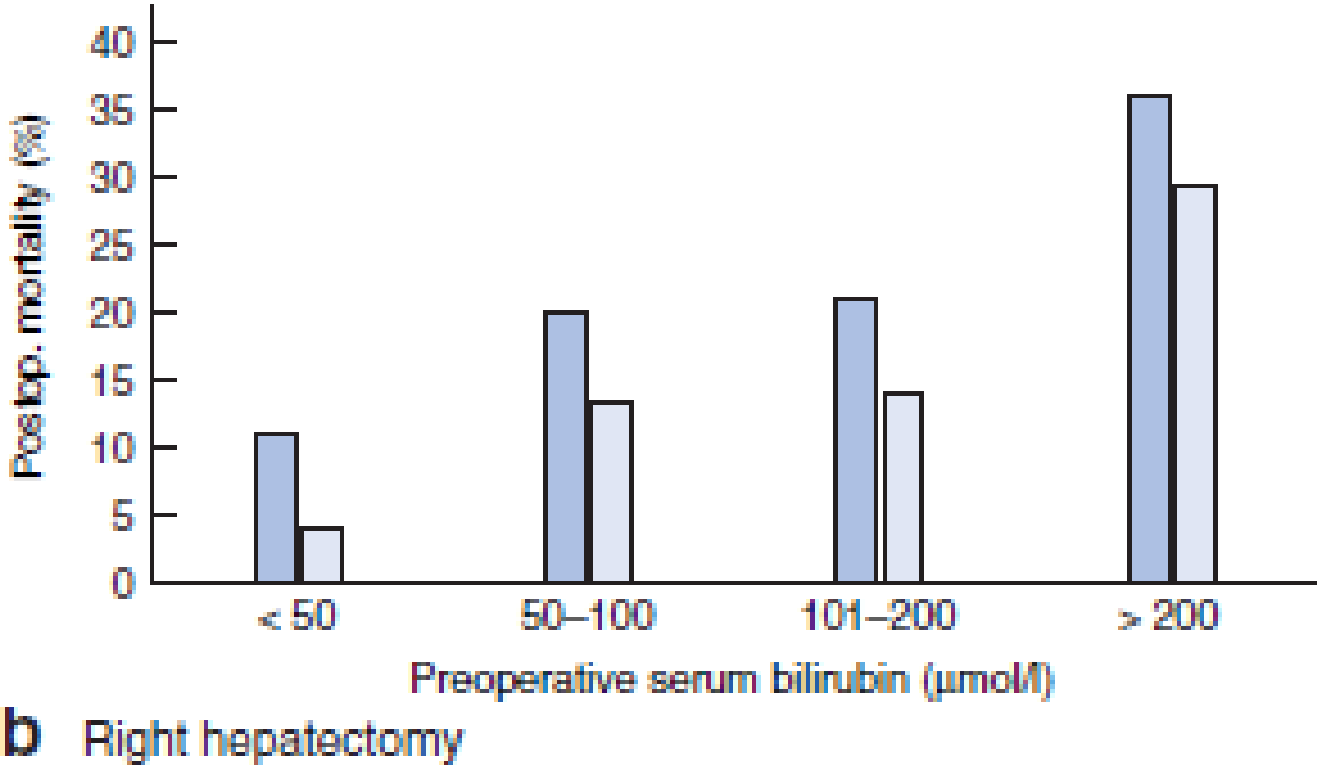
11% Mortalité po. 9,5% Mortalité 3% Mortalité 1,4% Mortalité



Nagino et al. Ann Surg 2013

Drainage Biliaire avant Hépatectomie

Pas hépatectomie si Bilirubine > 50 µmol/L



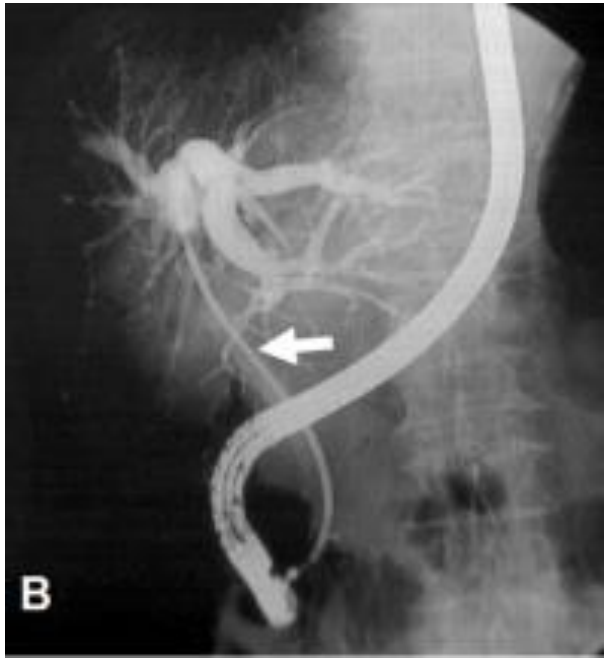
Pas de drainage avant hépatectomie gauche
si le volume de foie restant est suffisant…

Farges et al. Br J Surg 2009

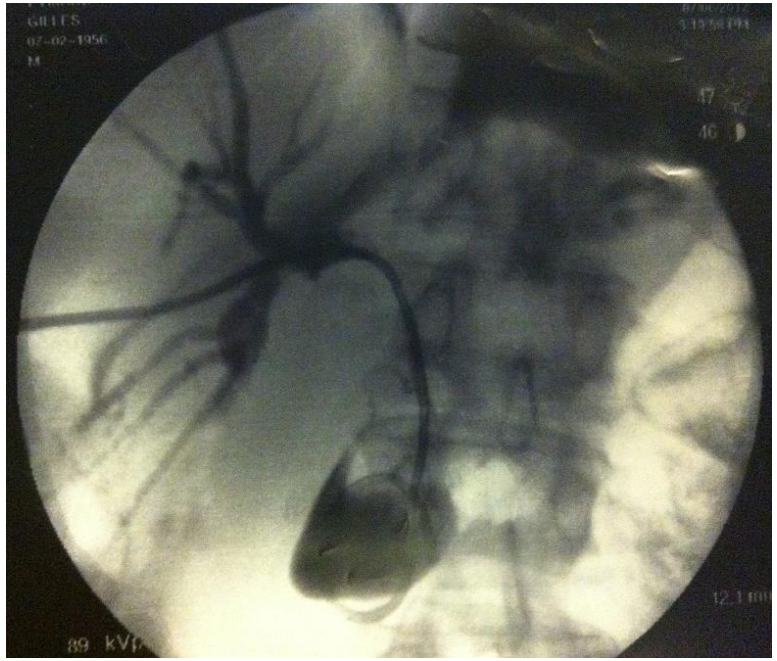
Drainage biliaire endoscopique plutôt que percutané du foie qui reste

23 récidives locales chez 455 pts drainés par voie percutanée

→ 5.3% en particulier pour drainage > 2 mois



>



Takahashi et al. Br J Surg 2009

Endoscopic versus percutaneous biliary drainage in patients with resectable perihilar cholangiocarcinoma: a multicentre, randomised controlled trial

Robert J S Coelen*, Eva Roos*, Jimmie K Wiggers, Marc G Besselink, Carlijn I Buis, Olivier R C Busch, Cornelis H C Dejong, Otto M van Delden, Casper H J van Eijck, Paul Fockens, Dirk J Gouma, Bas Groot Koerkamp, Michiel W de Haan, Jeanin E van Hooft, Jan N M IJzermans, G Matthijs Kater, Jan J Koornstra, Krijn P van Lienden, Adriaan Moelker, Steven W M Olde Damink, Jan-Werner Poley, Robert J Porte, Rogier J de Ridder, Joanne Verheij, Victor van Woerden, Erik A J Rauws, Marcel G W Dijkgraaf, Thomas M van Gulik†

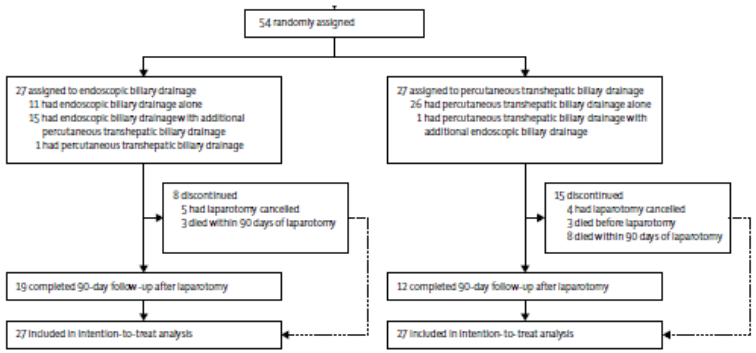
Added value of this study

In this multicentre, randomised controlled trial, we randomly assigned 54 patients with jaundice because of perihilar cholangiocarcinoma to undergo either endoscopic or percutaneous transhepatic biliary drainage before a major liver resection. The trial was prematurely closed because of higher mortality in the percutaneous transhepatic biliary drainage group. To our knowledge, this is the first prospective trial in an unselected group of patients with potentially resectable perihilar cholangiocarcinoma. Despite early termination, the trial provides insight into this complex disease.

	Endoscopic biliary drainage (n=27)	Percutaneous transhepatic biliary drainage (n=27)	p value
Death	0	3 (11%)	0·24
Number of complications	..	..	0·88†
0	9 (33%)	10 (37%)	..
1	11 (41%)	8 (30%)	..
≥2	7 (26%)	9 (33%)	..

Data are n (%). *Relative risk 0·94, 95% CI 0·64–1·40; absolute risk difference 3·7%. †Jonckheere-Terpstra test.

Table 3: Severe complications between randomisation and surgery



	Endoscopic biliary drainage (n=22)	Percutaneous transhepatic biliary drainage (n=20)	p value
Any complications	12 (55%)	13 (65%)	0·49*
Cholangitis	6 (27%)	3 (15%)	0·46
Intra-abdominal abscess	4 (18%)	2 (10%)	0·67
Wound infection	1 (5%)	1 (5%)	1·00
Pneumonia	0	1 (5%)	0·48
Haemorrhage	1 (5%)	2 (10%)	0·60
Portal vein thrombosis	0	1 (5%)	0·48
Biliary leakage	4 (18%)	2 (10%)	0·67
Liver failure	2 (9%)	5 (25%)	0·23
Relaparotomy	3 (14%)	5 (25%)	0·45
Death within 90 days			
With or without resection	3 (14%)	8 (40%)	0·08†
After resection	2 (17%; n=12)	5 (45%; n=11)	0·19

Data are n (%), or n (%; n). *Relative risk 1·19, 95% CI 0·73–1·96; absolute risk difference 10·4%. †Relative risk 2·93, 95% CI 0·91–9·55; absolute risk difference 26·4%.

Lancet Gastroenterology 2018

Liver Surgery for PHCK : 13% of 3-Month Mortality

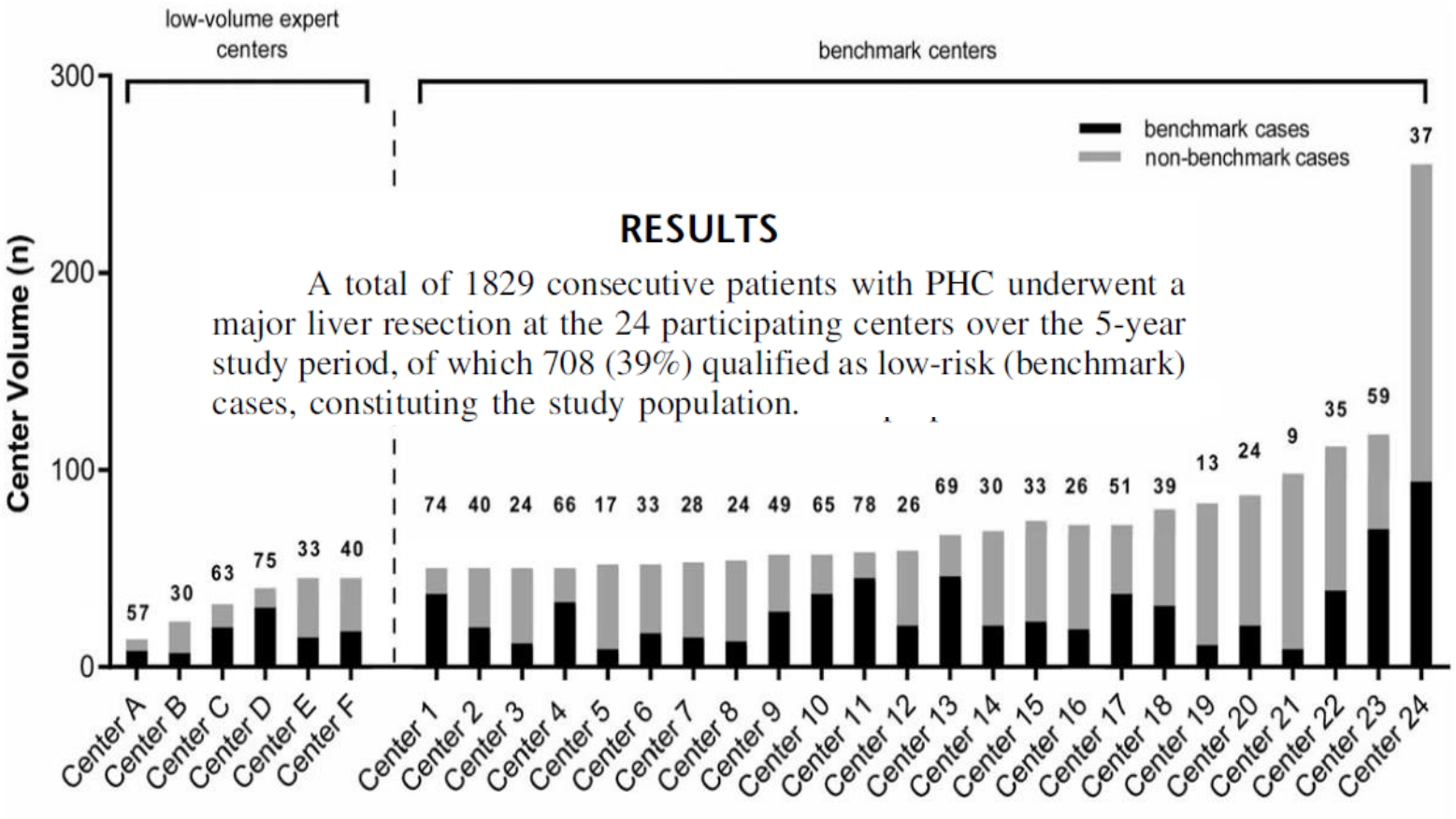
TABLE 1. Inclusion and Exclusion Criteria for the Low-Risk Cohort Treated in High-Volume Centers

Inclusion criteria
- Age ≥18 y
- Resectable perihilar cholangiocarcinoma
- Major hepatectomy (right or left-sided hepatectomy)

Surgical exclusion criteria
- Central liver resections
- Distant or intrahepatic metastases (based on final pathology)
- Vascular invasion with need of vascular resection (HA or PV). (routine-PV-resection as part of standard PHC surgery are included)
- Liver transplantation
- PHC with distal extension with need for pancreaticoduodenectomy

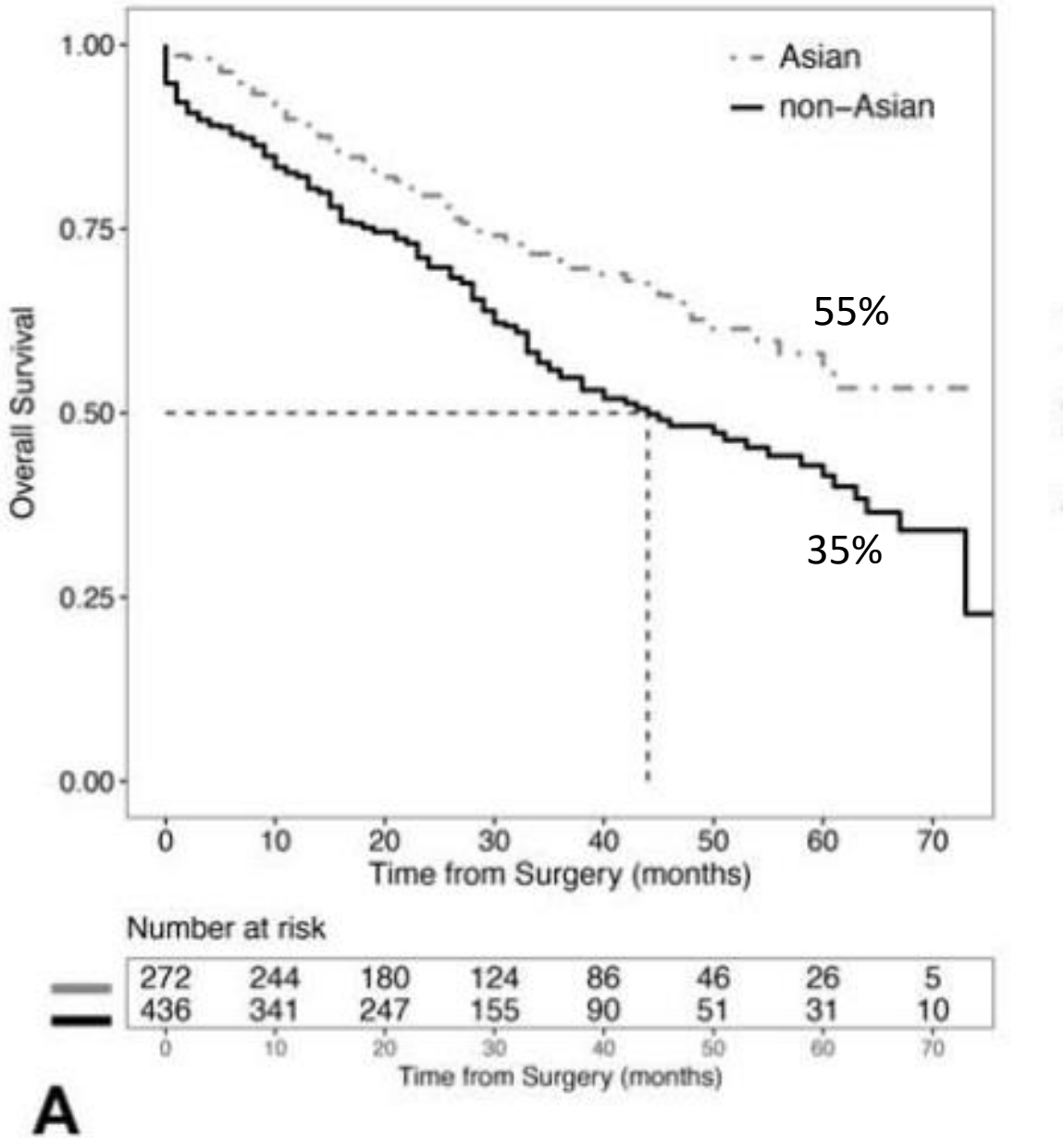
Medical exclusion criteria
- American Society of Anesthesiologists (ASA) classification ≥3
- Body mass index ≥35 kg/m^2
- *Cardiac disease defined as:*
  - Congestive heart failure onset or exacerbation in 30 days before surgery
  - History of angina pectoris within 1 mo before surgery
  - Myocardial infarct within 6 mo before surgery
  - History of percutaneous coronary intervention or cardiac surgery.
  - Atrial fibrillation
- Chronic renal failure MDRD ≥ Stage 3: GFR<60 mL/min/1.73 m^2 or serum creatinine >1.8 mg/dL or 160 mmol/L
- Chronic obstructive pulmonary disease with FEV1<80%
- *Use of anticoagulants:*
  - Non-vitamin K antagonist oral anticoagulants (NOACs)
  - Vitamin K antagonist
  - Clopidogrel
- Diabetes mellitus ≥2 oral antidiabetic drugs or insulin

FEV, forced expiratory volume; GFR, glomerular filtration rate; HA, hepatic artery, MDRD, modification of diet in renal disease; PV, portal vein, PHC, perihilar cholangiocarcinoma.



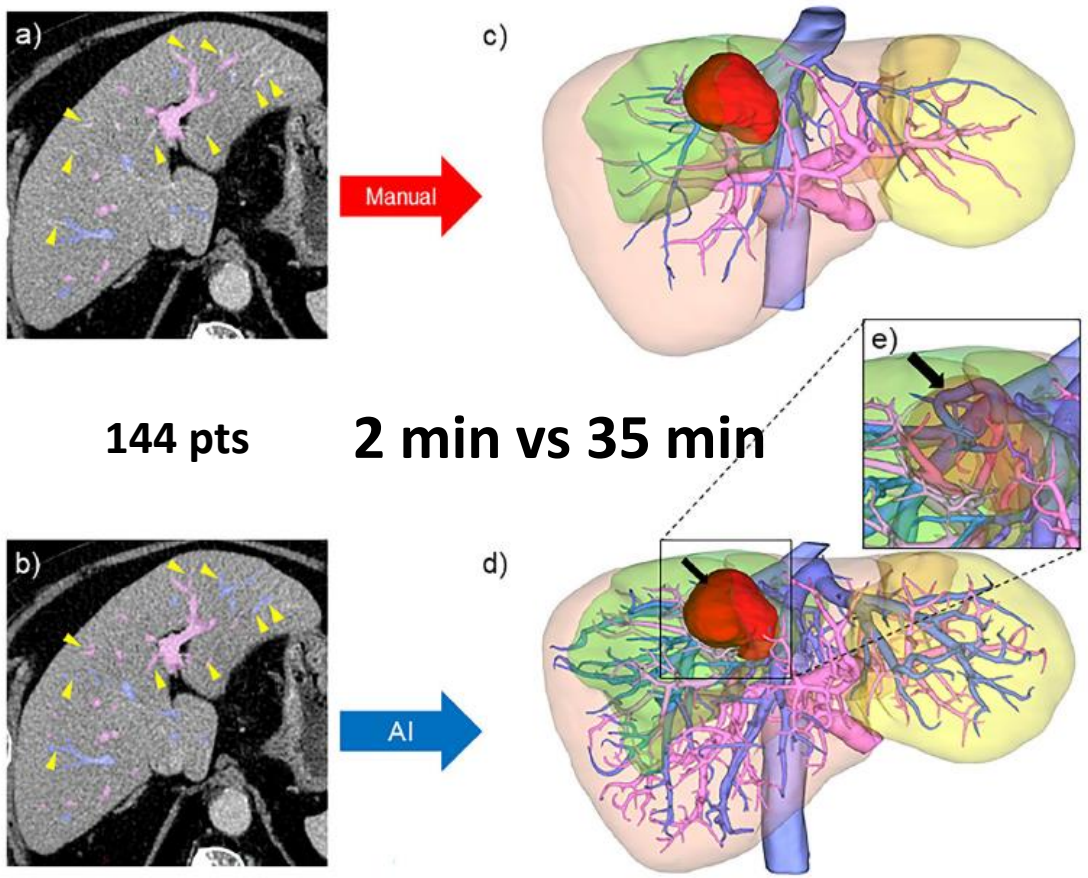
Perihilar Cholangiocarcinoma – Novel Benchmark Values for Surgical and Oncological Outcomes From 24 Expert Centers. Mueller et al. Ann Surg 2021

	Benchmark 75th Percentile	
Operation time	≤8 h	
Blood loss	≤1100 mL	
Intensive care unit stay	≤2 days	
Hospital stay	≤19 days	
Postoperative morbidity at 3 mo		
Any complication	≤87%	
Clavien-Dindo Grade ≥ 3a	≤70%	
CCI	≤30.5	
1-year hospital readmission rate	≤31%	
Liver failure – all severities	≤35%	
Grade A	≤5%	
Grade B	≤16%	
Grade C	≤10%	
Bile leak (surface/anastomosis)	≤47%	
Re-Laparotomy rate (30d)	≤19%	
Postoperative mortality		
In-hospital mortality	≤8%	
Right-sided hepatectomy	≤11.0%	
Left-sided hepatectomy	≤2.1%	
3-month mortality	≤13%	
Oncological outcomes		
	R0	**R1**
Positive resection margin rate	≥56.7%	≤43%
Right-sided hepatectomy	≥60.6%	≤39.4%
Left-sided hepatectomy	≥52.3%	≤47.7%
Total number of lymph nodes resected	≥4	



Automated Three-Dimensional Liver Reconstruction with Artificial Intelligence for Virtual Hepatectomy

Takeshi Takamoto[1] · Daisuke Ban[1] · Satoshi Nara[1] · Takahiro Mizui[1] · Daisuke Nagashima[1] · Minoru Esaki[1] · Kazuaki Shimada[1]



144 pts

2 min vs 35 min

J Gastro Intestinal Surgery 2022

A meta-analysis of the three-dimensional reconstruction visualization technology for hepatectomy

Yu Liu, Qing Wang, Bo Du, XuZhi Wang, Qian Xue, WeiFeng Gao*

Department of Hepatobiliary Surgery, People's Hospital of Leshan, Sichuan Leshan, 614000, China

12 Retrospectives studies that evaluated some intraoperatives and postoperatives data with or without preoperative virtual hepatectomy : 2053 Patients

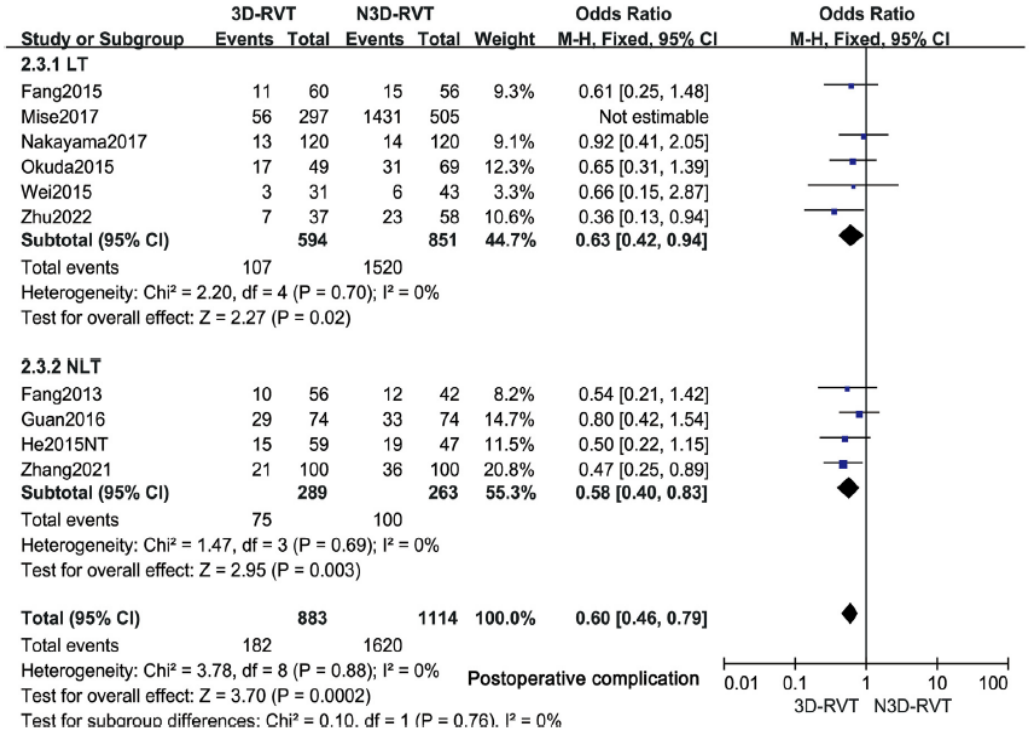


Fig. 7. Forest plot of overall postoperative complications in combined and subgroup analysis.

Asian Journal of Surgery 2023

Less Post Operatives Complications with 3D…

A meta-analysis of the three-dimensional reconstruction visualization technology for hepatectomy

Yu Liu, Qing Wang, Bo Du, XuZhi Wang, Qian Xue, WeiFeng Gao*

Department of Hepatobiliary Surgery, People's Hospital of Leshan, Sichuan Leshan, 614000, China

12 Retrospectives studies that evaluated some intraoperatives and postoperatives data with or without preoperative virtual hepatectomy : 2053 Patients

Studies	Year	Country	Disease types	Age(years)[a]	3D reconstruction system	Sample Size			NOS
						Total	3D-RVT	N3D-RVT	
Fang et al	2013	China	NLT	50.6 ± 11.5/53.5 ± 12.6	MI-3DVS[b]	98	56	42	8
Wei et al	2015	China	LT	50 ± 10.6/48 ± 10.0	3D Plus Body Visible System, Yorktal Medical, ShenZhen, China	74	31	43	7
Fang et al	2015	China	LT	47.5 ± 13.8/46.5 ± 13.3	MI-3DVS[b]	116	60	56	8
He et al	2015	China	NLT	41.4 ± 13.1/42.5 ± 13.2	IQQA Liver, EDDA Technology, Princeton, NJ, United States	106	59	47	6
Okuda et al	2015	Japan	LT	64 ± 11/66 ± 9	IAP[c]	118	49	69	7
Su et al	2016	China	LT	NA	Hisense CAS system	26	16	10	6
Guan et al	2016	China	NLT	52.9 ± 11.6/53.3 ± 11.9	MI-3DVS[b]	148	74	74	7
Mise et al	2017	Japan	LT	68 (22–85)/68 (19–88)	Surgical Planning Software	802	297	505	7
Nakayama et al	2017	Japan	LT	67 (17–81)/65 (22–80)	Synapse Vincent, FUJIFILM Medical Co., Ltd., Tokyo, Japan	240	120	120	7
Yang et al	2018	China	LT	NA	Transparent VeroClear™ and RGD720	30	15	15	6
Zhang et al	2021	China	NLT	NA	NA	200	100	100	6
Zhu et al	2022	China	LT	57.6 ± 9.2/60.2 ± 9.2	TM-MIS 1.0, Tuomeng Science and Technology Ltd, Heilongjiang, China	95	37	58	7

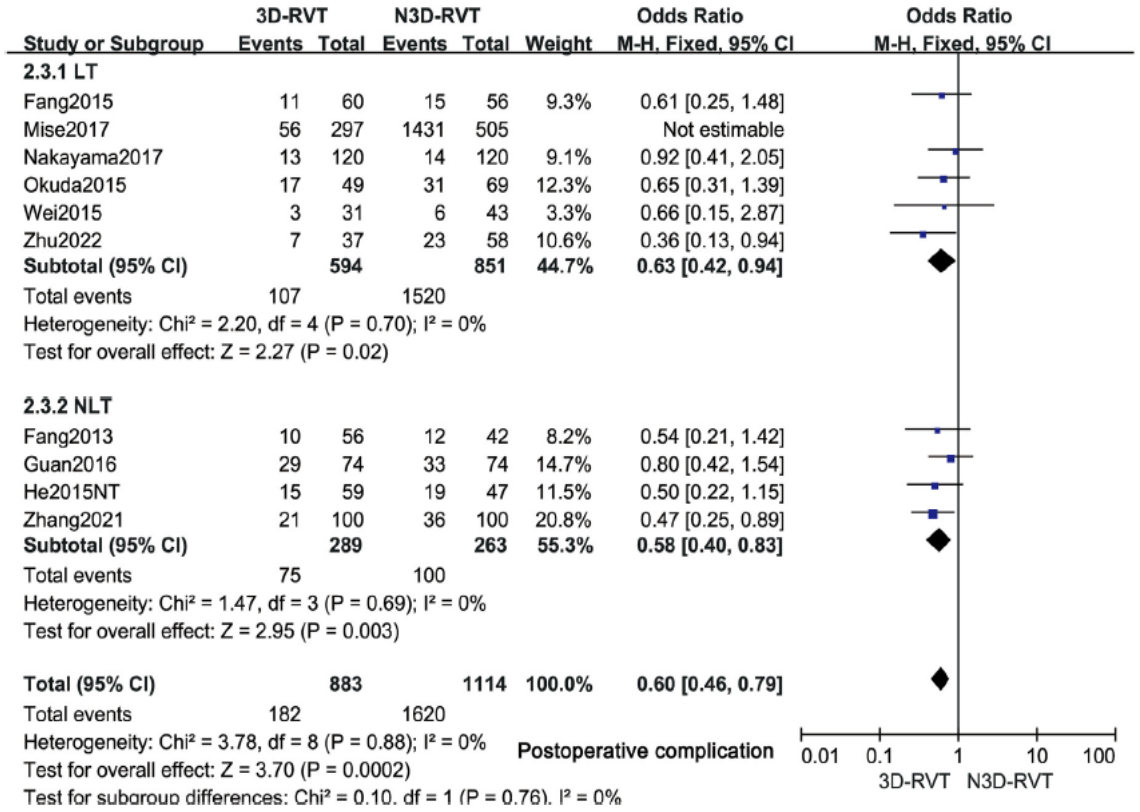
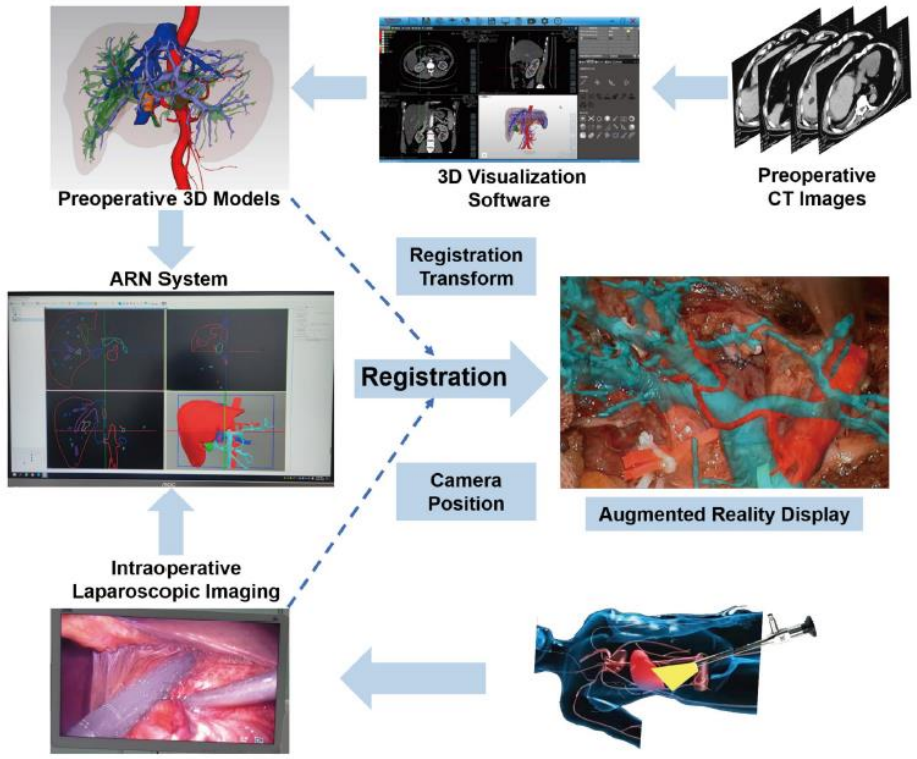


Fig. 7. Forest plot of overall postoperative complications in combined and subgroup analysis.

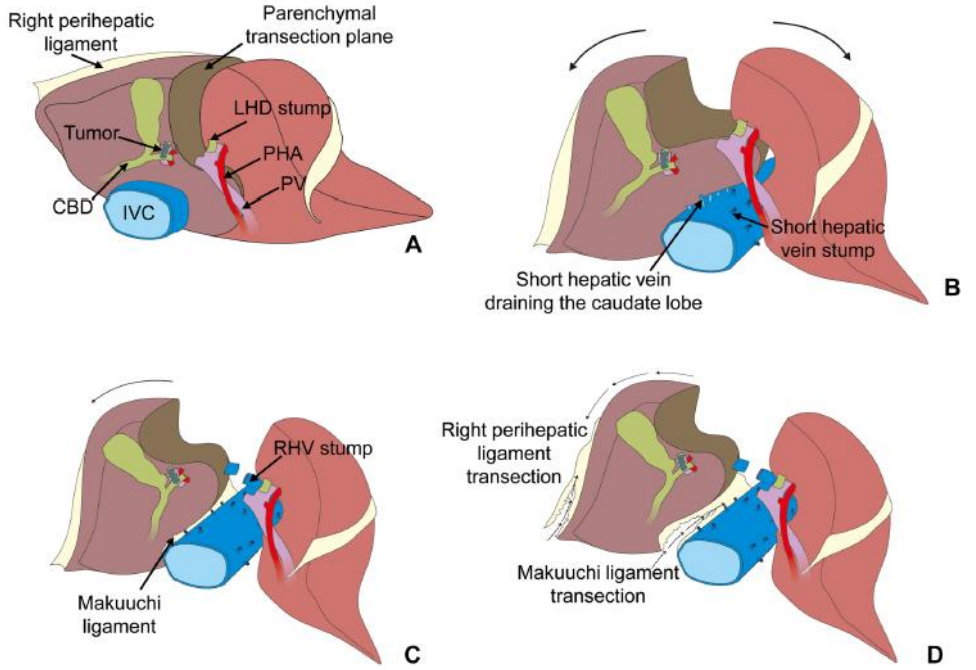
Hepatectomy for Cancer or Intra Hepatic Lithiasis

Asian Journal of Surgery 2023

Augmented Reality For Difficult Laparoscopic Surgery



Caudo-Cranial Approach with less liver mobilisation

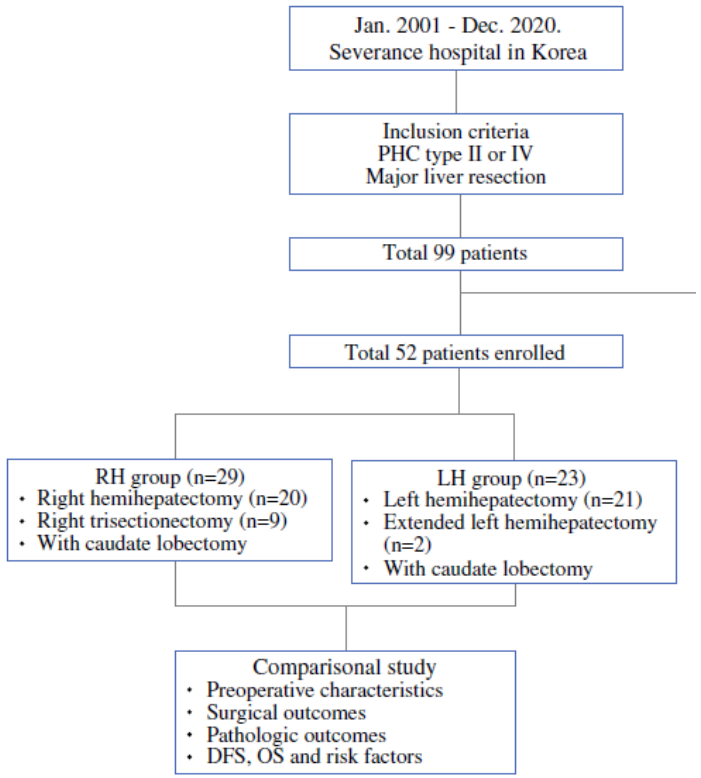


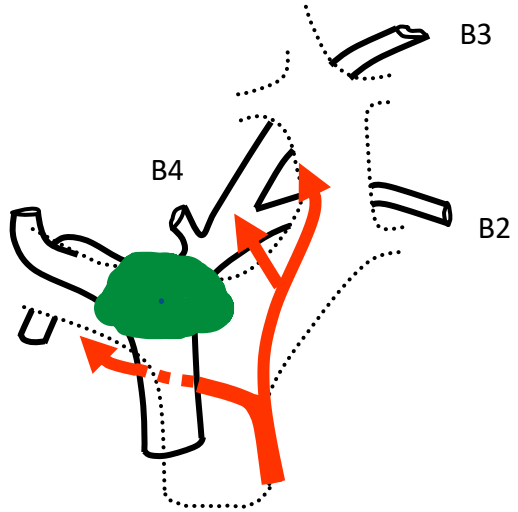
Results Right hemi-hepatectomy plus total caudate lobectomy was successfully performed in all 11 enrolled patients. Among the 11 patients, the mean operation time was 454.5 ± 25.0 min and the mean estimated blood loss was 209.1 ± 56.1 ml. Negative surgical margins were achieved in all patients. The postoperative course of all the patients was uneventful, and the mean length of postoperative hospital stay was 10.5 ± 1.2 days.

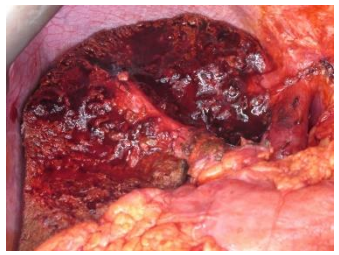
Conclusion Laparoscopic right hemi-hepatectomy plus total caudate lobectomy via the anterior approach may be feasible and safe for pCCA with the assistance of augmented reality navigation.

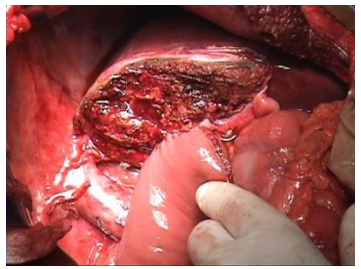
Wang et al. Surg Endoscopy 2023

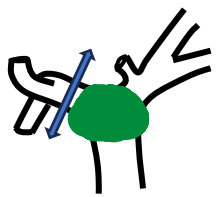
Left Hepatectomy : Upfront and less dangerous

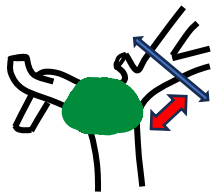












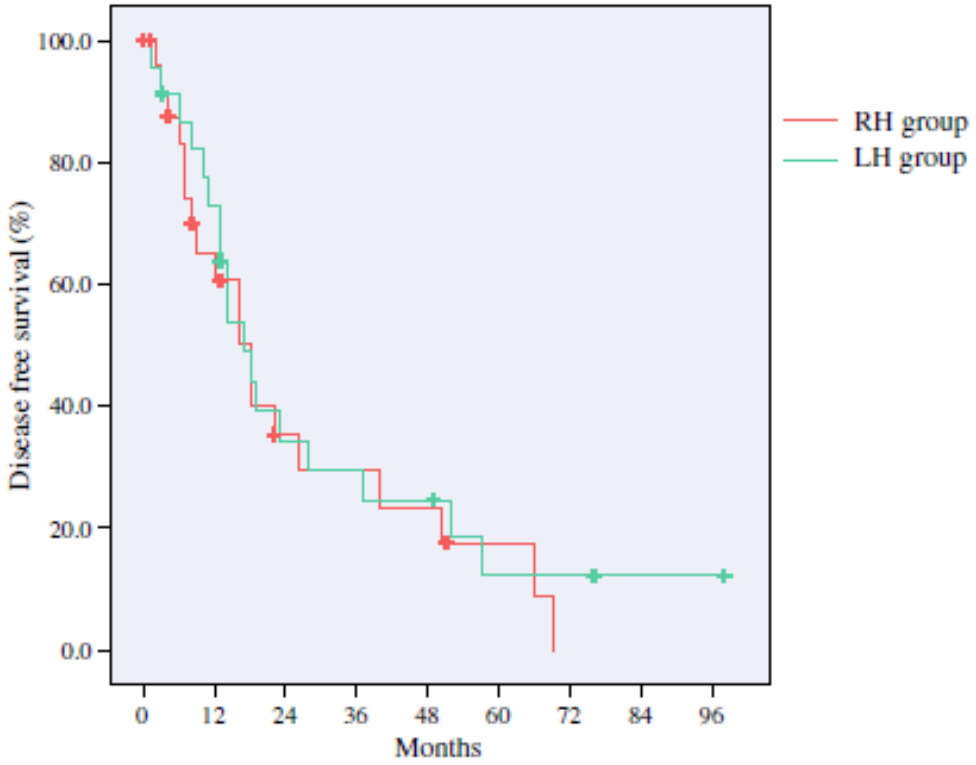
	RH group (n = 29)	LH group (n = 23)	p value
A.			
Age	61.0 ± 9.3	63.6 ± 11.7	0.373
Male sex	23 (79.3%)	17 (73.9%)	0.646
Bismuth type			
II	16 (55.2%)	11 (47.8%)	0.598
IV	13 (44.8%)	12 (52.2%)	
Preoperative PVE	14 (48.3%)	0 (0.0%)	< 0.001*
Duration from Dx to surgery (days)	31.0 ± 16.2	18.8 ± 13.4	0.006
B.			
*Name of operation**			
Right hemihepatectomy	20 (69.0%)		
Right trisectionectomy	9 (31.0%)		
Left hemihepatectomy		21 (91.3%)	
Extended left hepatectomy		2 (8.7%)	
Operation time (min)	470.3 ± 133.0	520.9 ± 160.6	0.220
Intraoperative bleeding (ml)	1271.7 ± 1665.0	1330.0 ± 1296.9	0.891
Transfusion	11 (37.9%)	11 (47.8%)	0.473
Postoperative mortality	4 (13.8%)	0 (0.0%)	0.120
Hospital stay (days)	22.3 ± 10.8	17.0 ± 10.8	0.086
Overall complications	18 (62.1%)	9 (39.1%)	0.110
Severe complications (Grade III over)	11 (37.9%)	6 (26.1%)	0.366
Postoperative liver failure ≥ Grade B	16 (55.2%)	5 (21.7%)	0.015*
Bile leakage	2 (6.9%)	2 (8.7%)	1.000

PVE portal vein embolization; *Dx* diagnosis

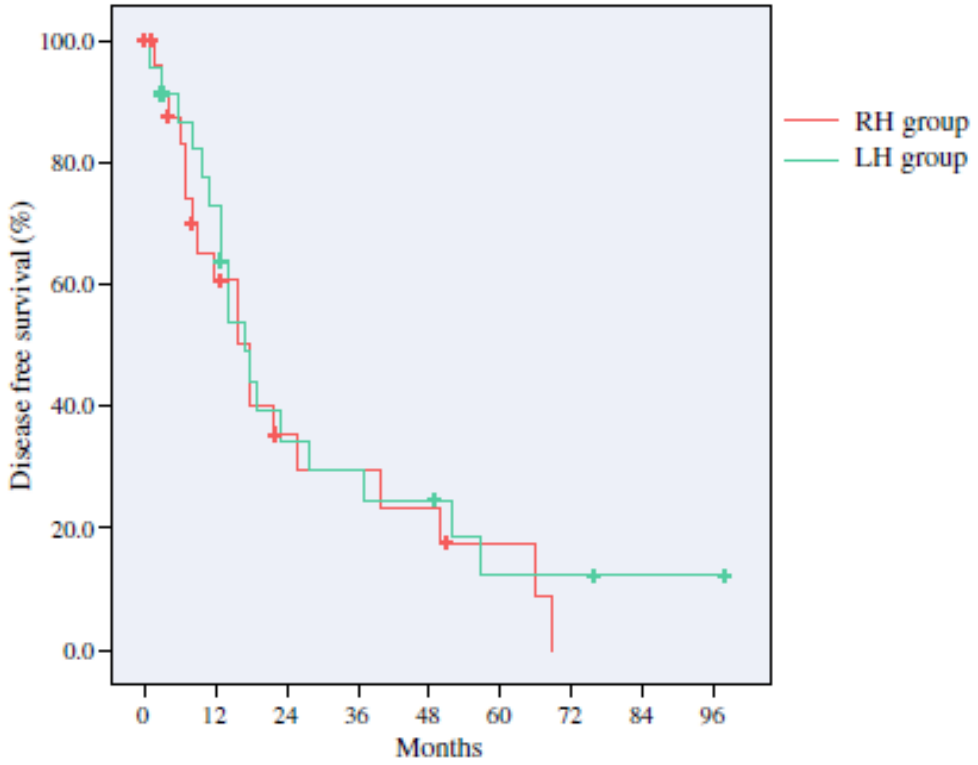
*All lobectomies included caudate lobectomy

Hong et al. Ann Surg Oncol 2023

Same Results but probably better in « Intent to Treat » in patients planed for left hepatectomy

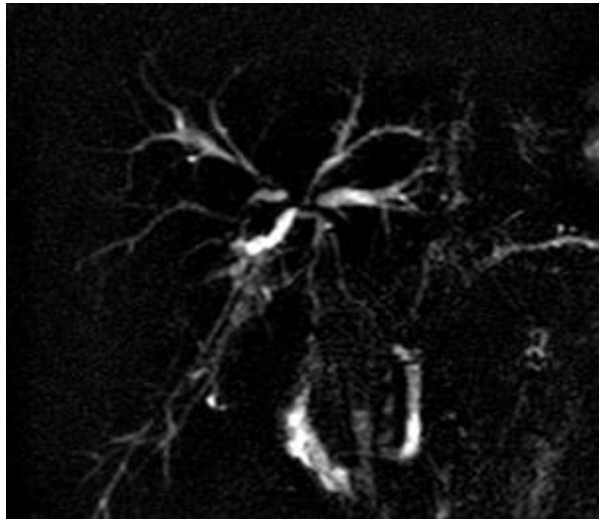


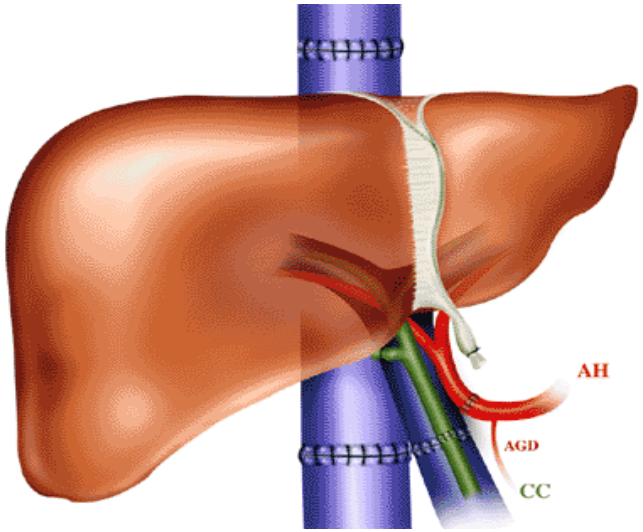
DFS	1 Year	3 Year	5Year	Median	P-value
Right (n=29)	60.7%	29.5%	17.7%	18.0±3.2 (11.8-24.2)	0.620
Left (n=23)	73.0%	29.5%	12.3%	17.0±2.8 (11.6-22.4)	

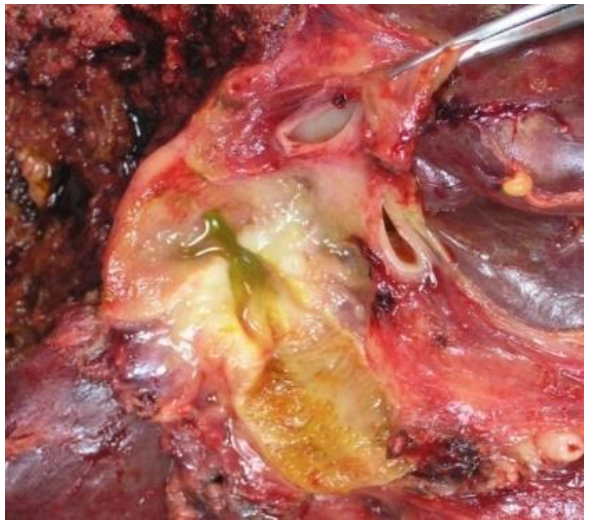


OS	1 Year	3 Year	5Year	Median	P-value
Right (n=29)	71.0%	32.4%	13.5%	26.0±6.0 (14.2-37.8)	0.487
Left (n=23)	86.4%	33.6%	19.2%	25.0±4.0 (17.2-32.8)	

Transplantation for Peri hilar Cholangiocarcinoma





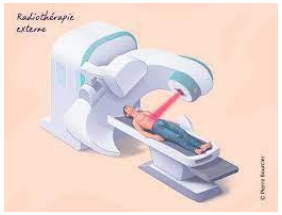


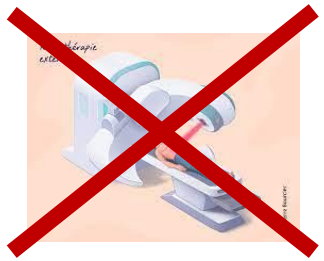
Liver Transplantation (LT) is recommended for non resectable peri hilar cholangiocarcinoma and/or developed on sclerosing cholangitis.
This assumption is based on results of Mayo Clinic protocol

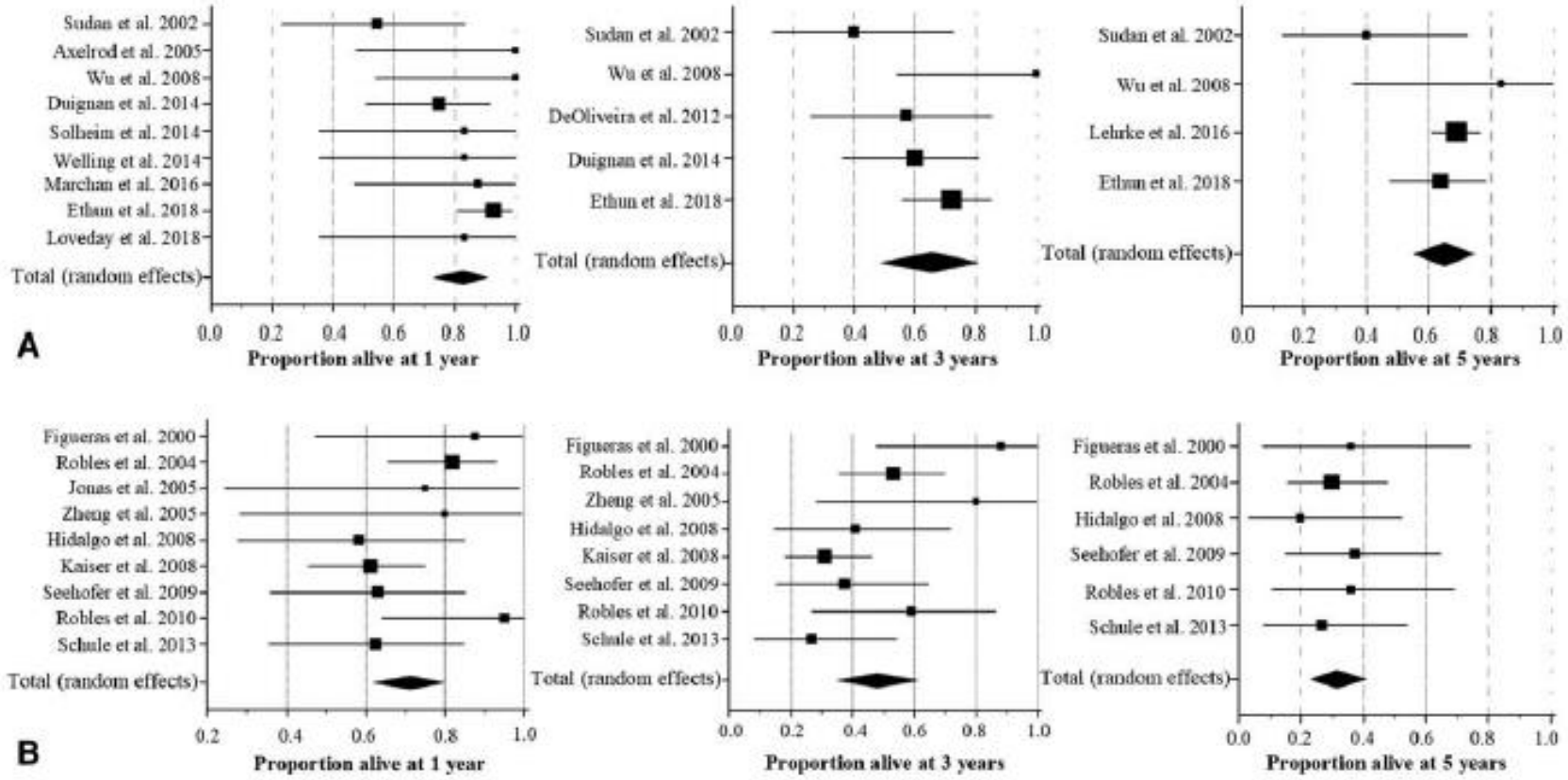
Bridgewater. ILCA guidelines. J Hepatol 2014

Twenty Studies including 428 patients transplanted for unresectable perihilar cholangiocarcinoma

Neo Adj RT







65%

32%

Cambridge, Ann Surg, Feb 2021

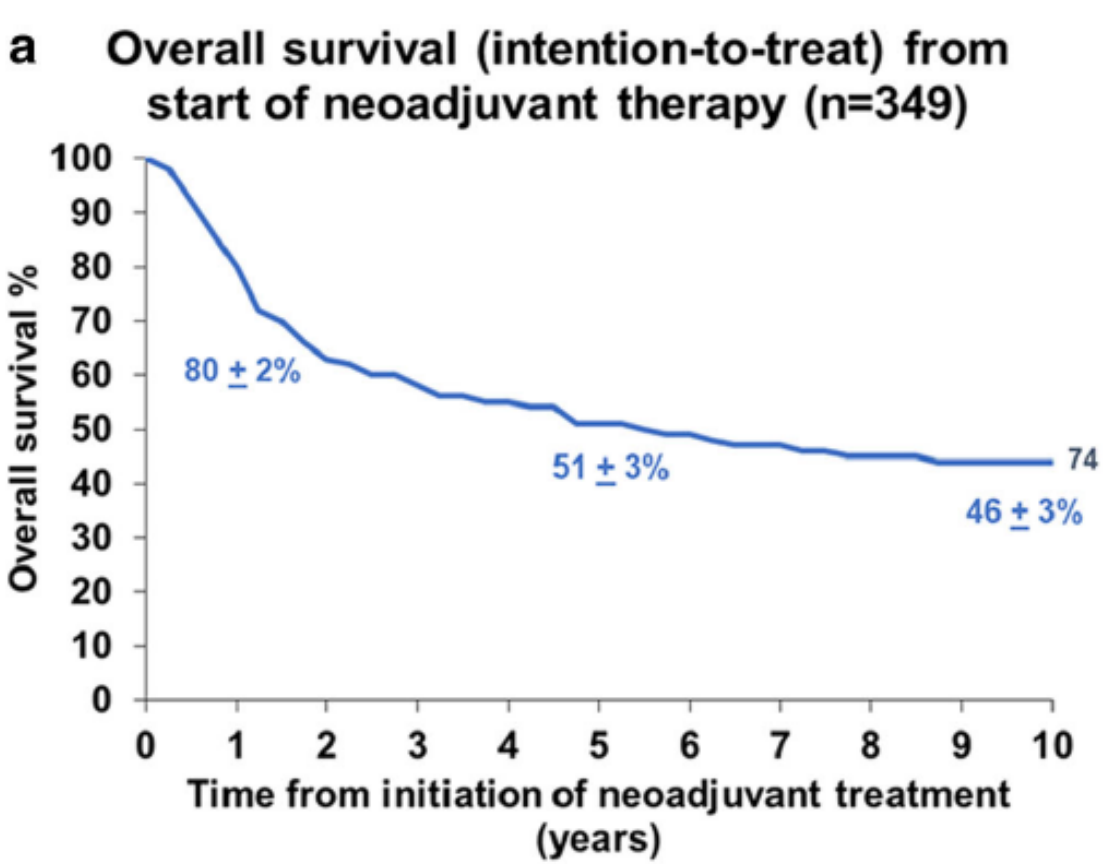
Pooled Recurrence after 3 years : 24% vs 52%

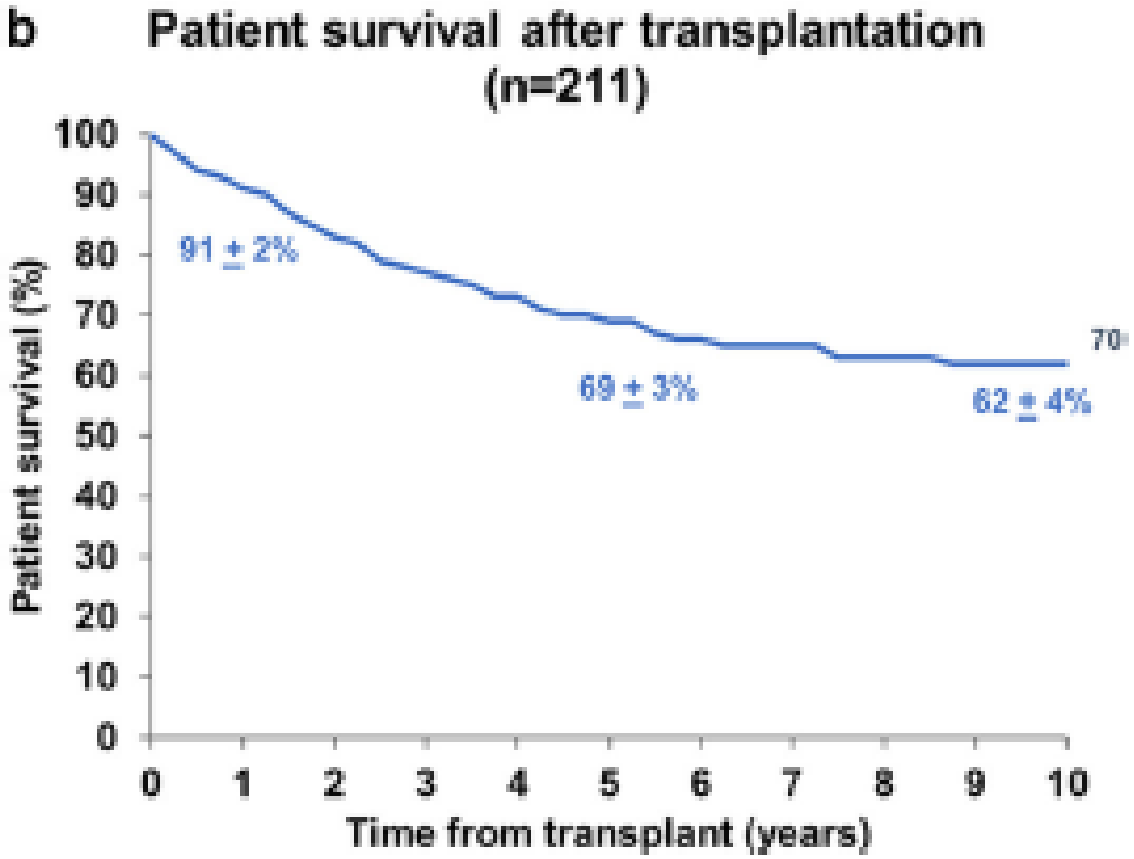
Listing is not transplant…

The #1 hospital in the nation.

You Know Where to Go.

MAYO CLINIC





Tan et al, J Gastro Surgery Feb 2020

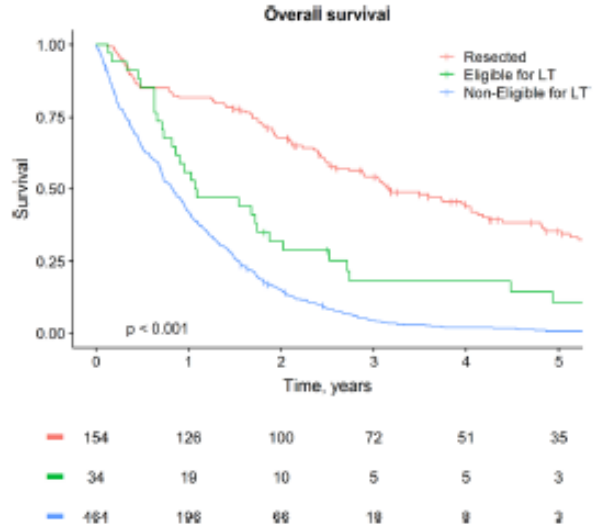
732 Patients… 34 (5%) Eligible with Mayo Criteria

TABLE 1 Eligibility criteria. Mayo protocol for liver transplantation for pCCA. Patients should fulfill all criteria

Inclusion criteria	
1	Perihilar cholangiocarcinoma
2	Malignant appearing stricture on cholangiography; pathological confirmation; CA 19-9 > 100 U/ml; mass on imaging; polysomy on FISH
3	Unresectability or PSC diagnosis
4	Medical suitability for transplant
5	Completion of neoadjuvant chemotherapy
Exclusion criteria	
1	Intrahepatic/extrahepatic/lymph node metastases on imaging, or at staging laparoscopy/exploratory laparotomy
2	Prior malignancy < 5 years
3	Tumor > 3 cm anterior–posterior
4	Prior abdominal radiotherapy/resection of cholangiocarcinoma
5	Uncontrolled infection
Age criterion	
1	Age < 70 years

CA 19-9 cancer antigen 19-9, *FISH* fluorescent in situ hybridization, *PSC* primary sclerosing cholangitis

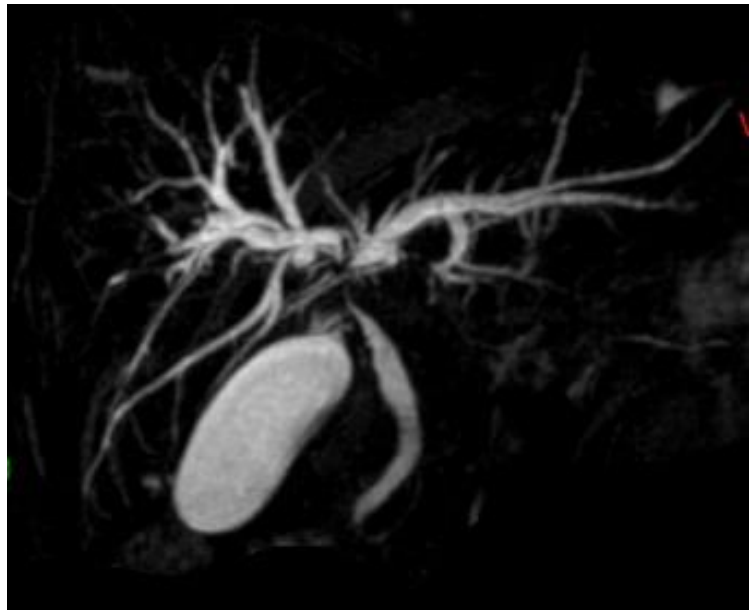
Netherland Patients from 2002 to 2014

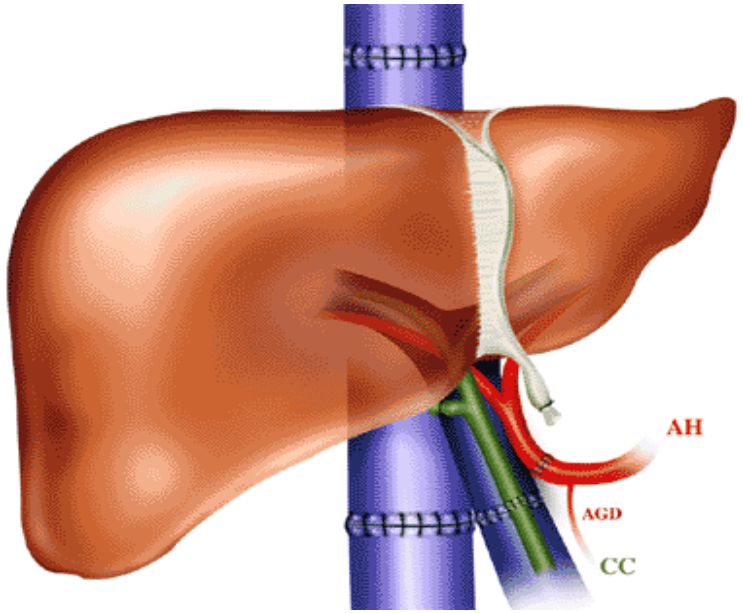


Liver Transplant for pCCA start in 2011 : 11 patients listed … 2 patients transplanted in 2014

Vugts et al, Ann Surg Oncol 2020

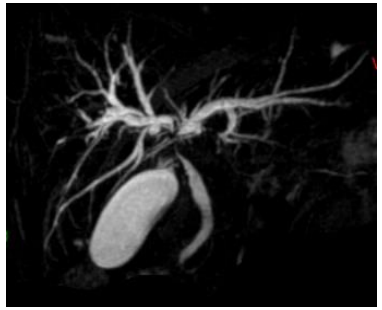
Mayo Clinic Protocol in resectable patient ?

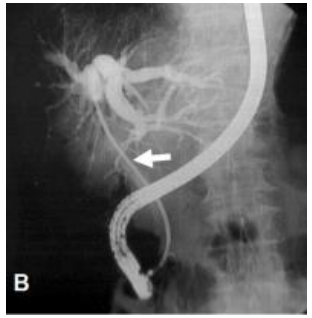




Perihilar Cholangiocarcinoma < 3 cm and without transhepatic biliary drainage

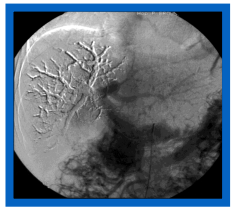
TRANSPHIL Study : Surgery Vs Mayo Clinic



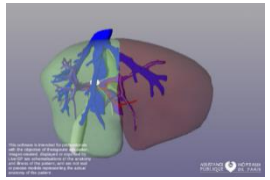


Radiological : Resectable Peri Hilar CK / < 3 cm
No pathological liver including PSC
Exhaustive Exploration (including Laparoscopy)
To exclude Intra- ou Extra Metastatic Disease

RANDOMIZATION 1:1



PVE



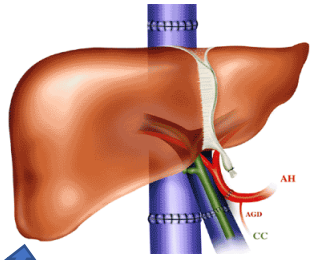
Hepatectomy

6 Weeks

Capecitabine
Ext RT (50 grays)

Laparotomy
Lymph Node ?

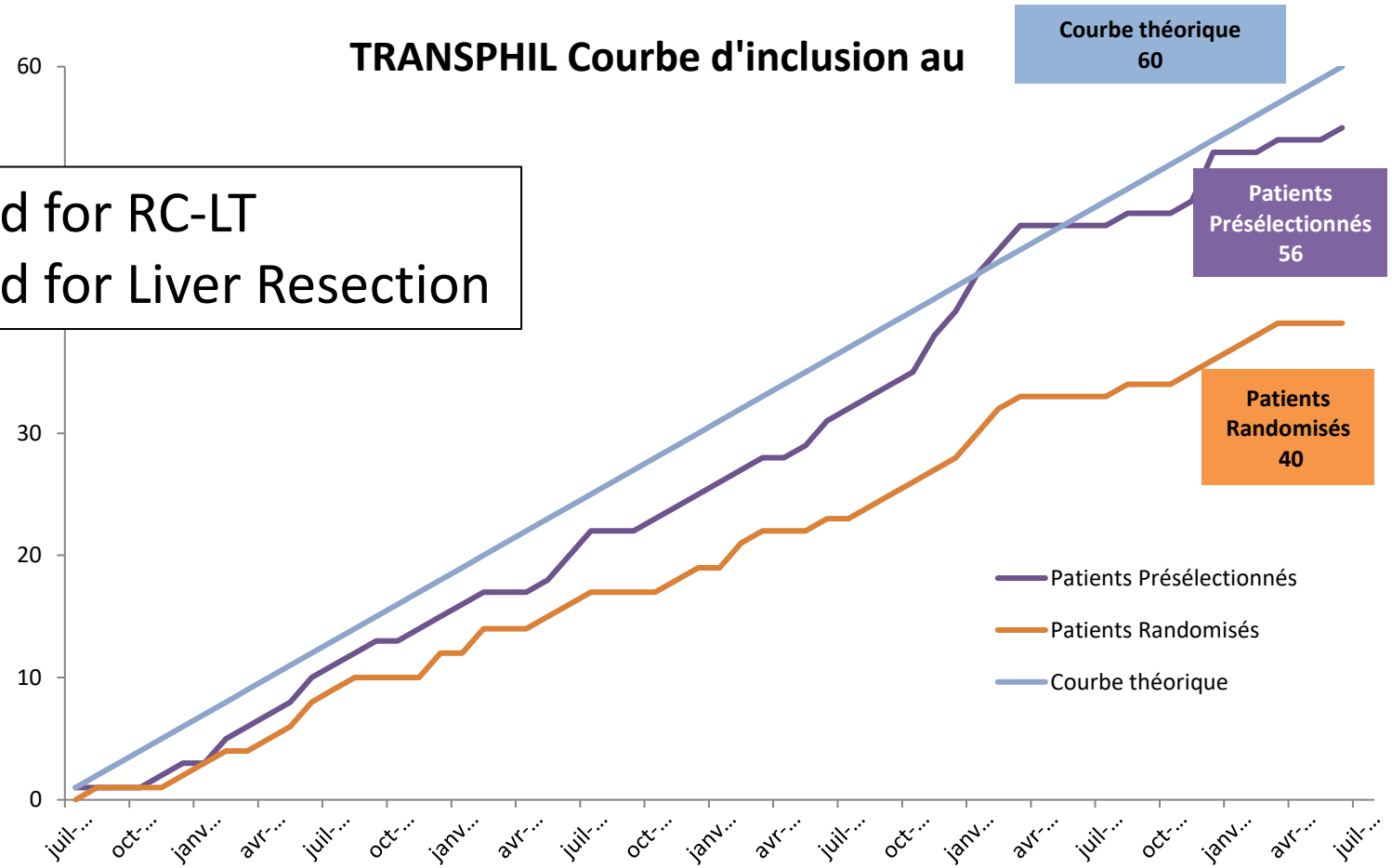
1-2 Weeks



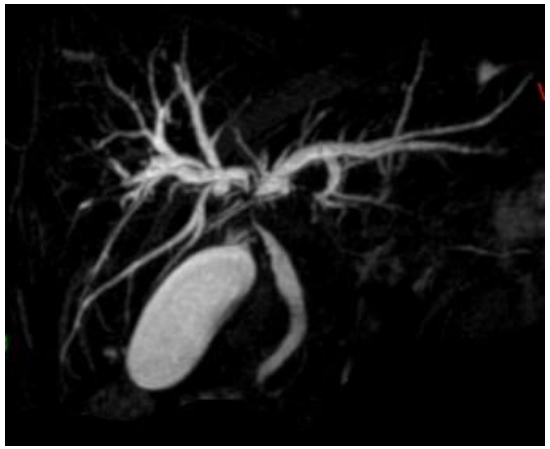
TRANSPHIL Study : Inclusion Curve (Mai 2021)

Aim : 60 patients to have 54 randomized (27 pts x 2)

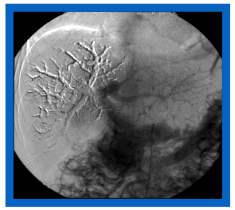
20 pts Randomized for RC-LT
20 pts Randomized for Liver Resection



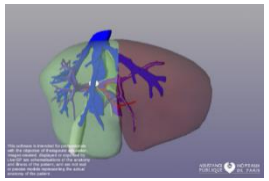
RANDOMIZATION 1:1



N=20



PVE



Hepatectomy

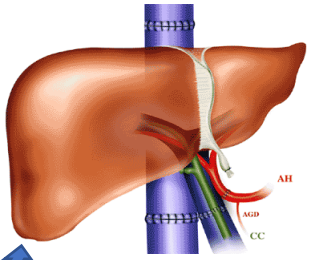
N=19

N=20

6 Weeks

Capecitabine
Ext RT (50 grays)

Laparotomy
Lymph Node ?



1-2 Weeks

N=9

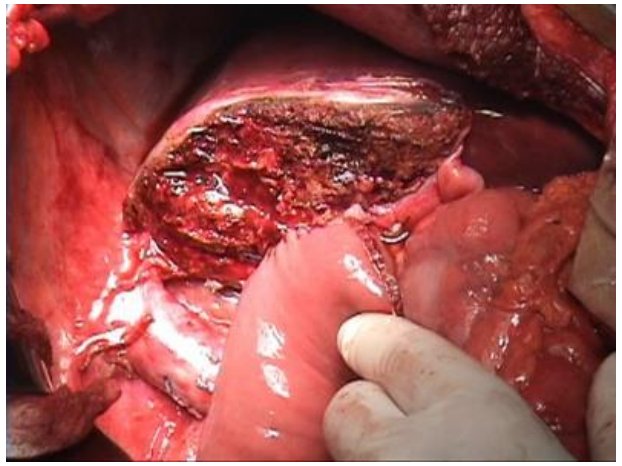
Safety Board : Stop the Study… Too Much Drop Out in Liver Transplant Arm
Data of Survival in 2022… But it will Impossible to conclude about the impact of LT…
Multicentric study : No Centralisation of the cases ? Failure of Endoscopic drainage only ?

Phase I study of neoadjuvant S-1 plus cisplatin with concurrent radiation for biliary tract cancer (Tokyo Study Group for Biliary Cancer: TOSBIC02)

Yuta Abe[1] | Osamu Itano[1,2] | Yusuke Takemura[1] | Takuya Minagawa[2] | Hidenori Ojima[3] | Masahiro Shinoda[1,4] | Minoru Kitago[1] | Hideaki Obara[1] | Naoyuki Shigematsu[5] | Yuko Kitagawa[1]

12 Malades Résécables

9 Malades Opérés dont 7 R0



5 fistules Biliaire et 1 mort par rupture artérielle

ARRET DE L'ETUDE et PAS DE PHASE II

Aim: Neoadjuvant chemoradiotherapy may improve survival in patients with advanced cholangiocarcinoma. This Phase I study aimed to determine the recommended dose of neoadjuvant chemoradiotherapy and decide whether to move to a Phase II study.

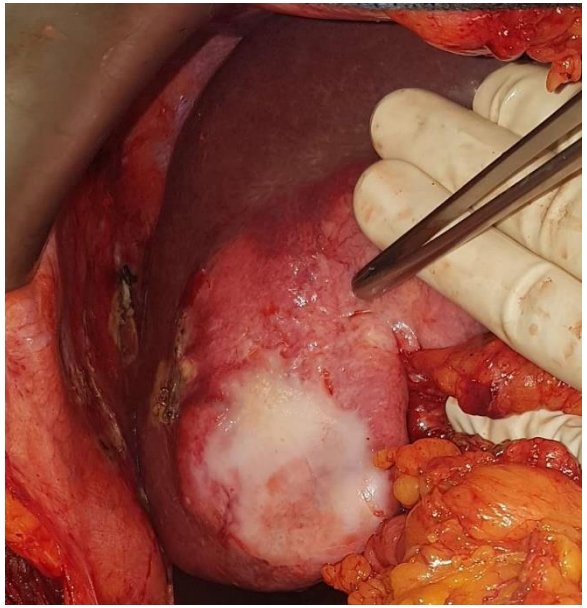
Methods: Patients diagnosed with resectable stage II–IVa cholangiocarcinoma were administered cisplatin (40 [level 0], 50 [level 1 as starting dose], or 60 [level 2] mg/m^2), 80 mg/m^2 of S-1, and 50.4 Gy of external beam radiation. The recommended dose was defined as a dose one-step lower than the maximum-tolerated dose, which was defined when dose-limiting toxicity was observed in three or more of the six patients.

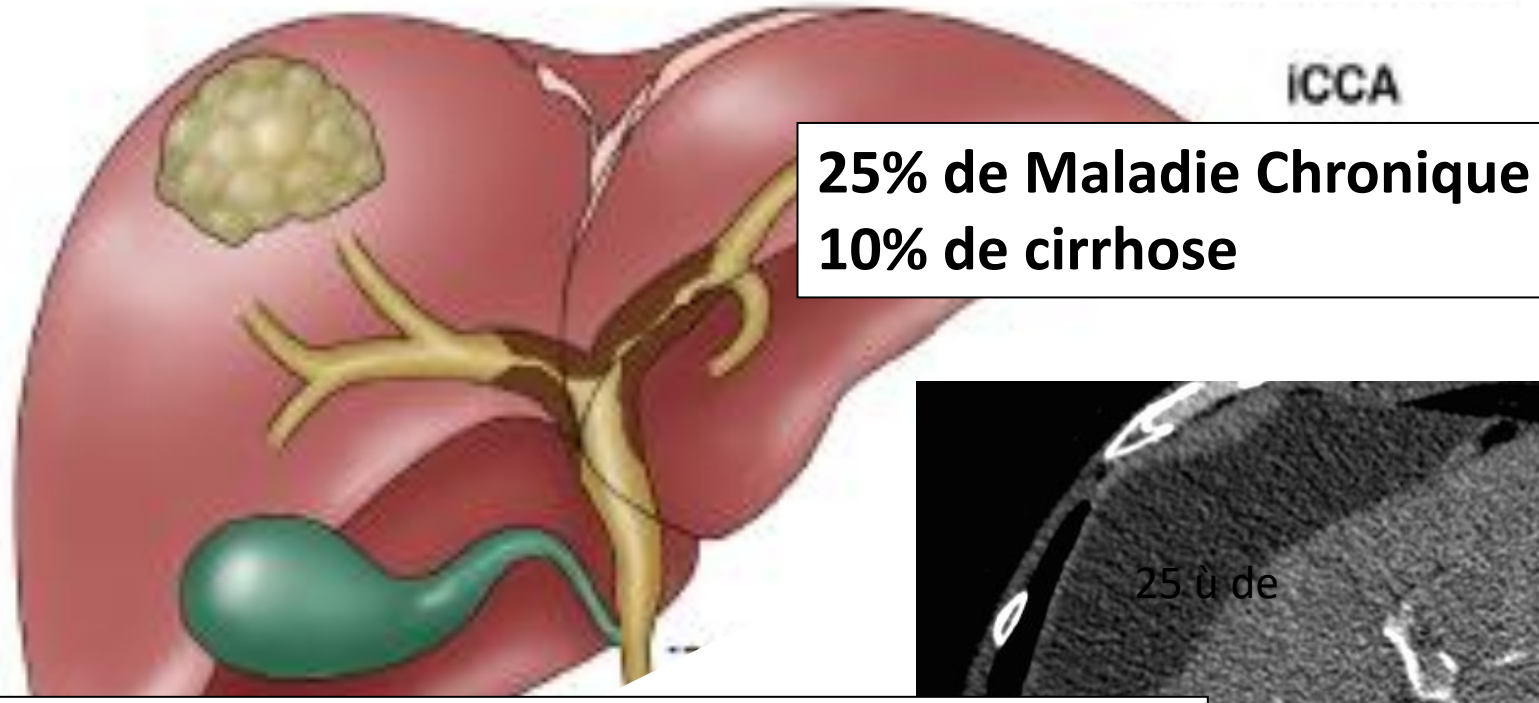
Results: Twelve patients were eligible from November 2012 to May 2016. Ten patients had perihilar cholangiocarcinoma and two patients had distal cholangiocarcinoma. Dose-limiting toxicity was observed in one of the first six patients at level 1 and two of the next six patients at level 2; thus, the maximum-tolerated dose was not determined even at level 2 and the recommended dose was determined as level 2. Four patients had partial response, four patients had stable disease, and two patients had progression of disease because of liver metastases. Finally, nine patients underwent radical surgery and seven cases achieved R0 resection. However, five cases suffered biliary leakage and one suffered intrahospital death due to rupture of the hepatic artery.

Conclusion: We determined the recommended dose of neoadjuvant chemoradiotherapy for resectable cholangiocarcinoma. However, we terminated the trial due to a high incidence of morbidity and unexpected mortality.

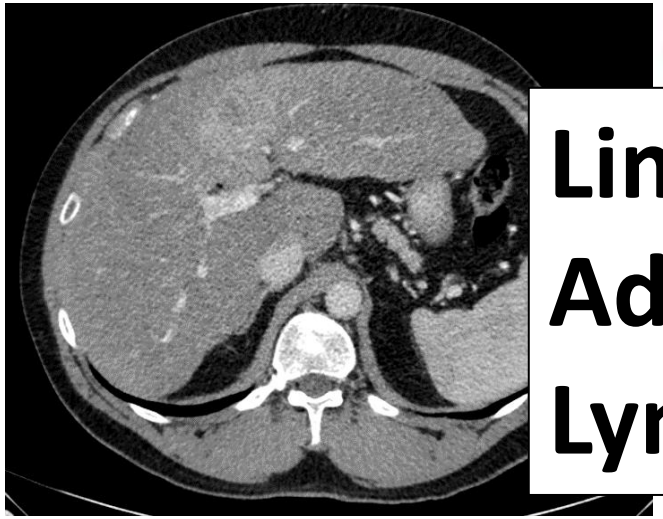
Annal of GastroIntestinal Surgery 2023

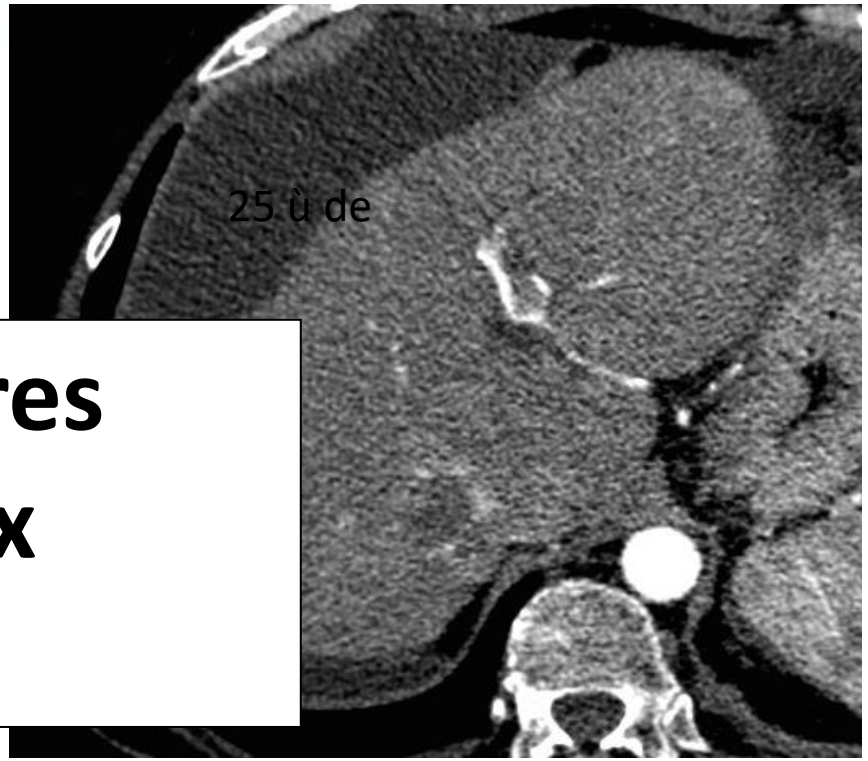
Cholangiocarcinome Intra Hépatique





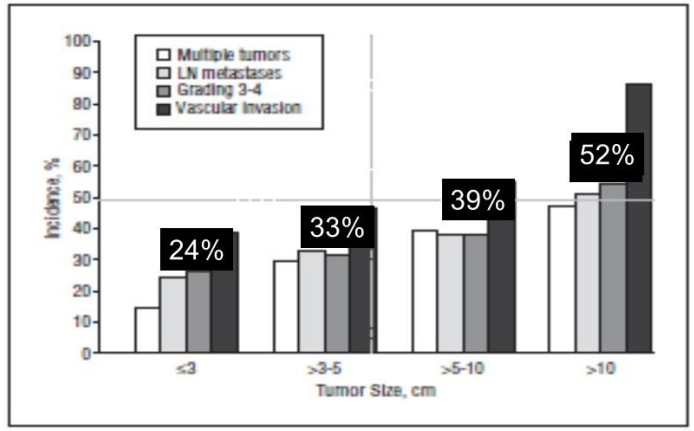
25% de Maladie Chronique du foie
10% de cirrhose





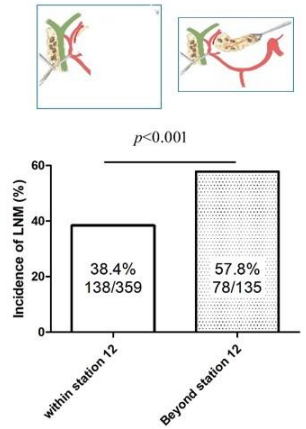
Limites jamais très claires
Adhérente au Vaisseaux
Lymphophile

Lymph Node Invasion with Tumoral Mass Diameter

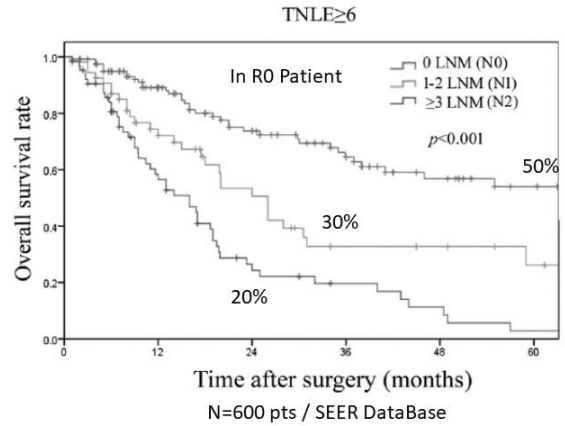


Ribeiro et al. Arch Surg 2012

Lymphadenectomy must include 6 lymph nodes



Farges et al. Ann Surg 2011

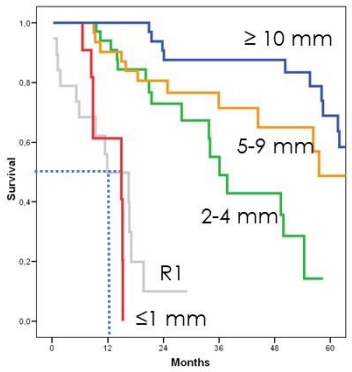


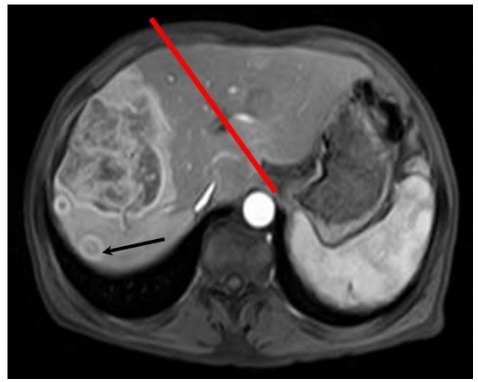
N=600 pts / SEER DataBase

Zang et al. Ann Surg 2021

Importance of margin in Cholangiocarcinoma

134 patients N0

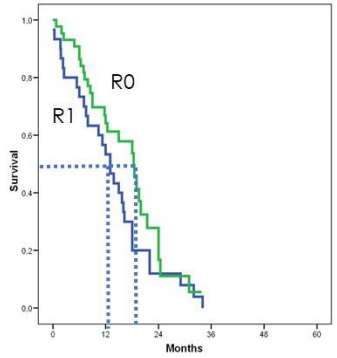




Farges et al. Ann Surg 2011

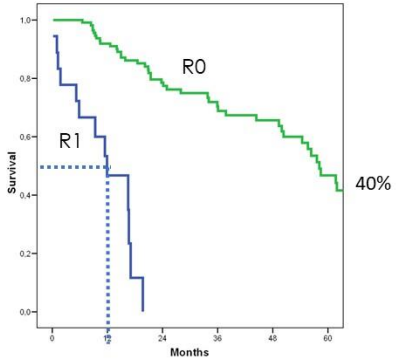
No impact of margin in N+ with upfront surgery

N+



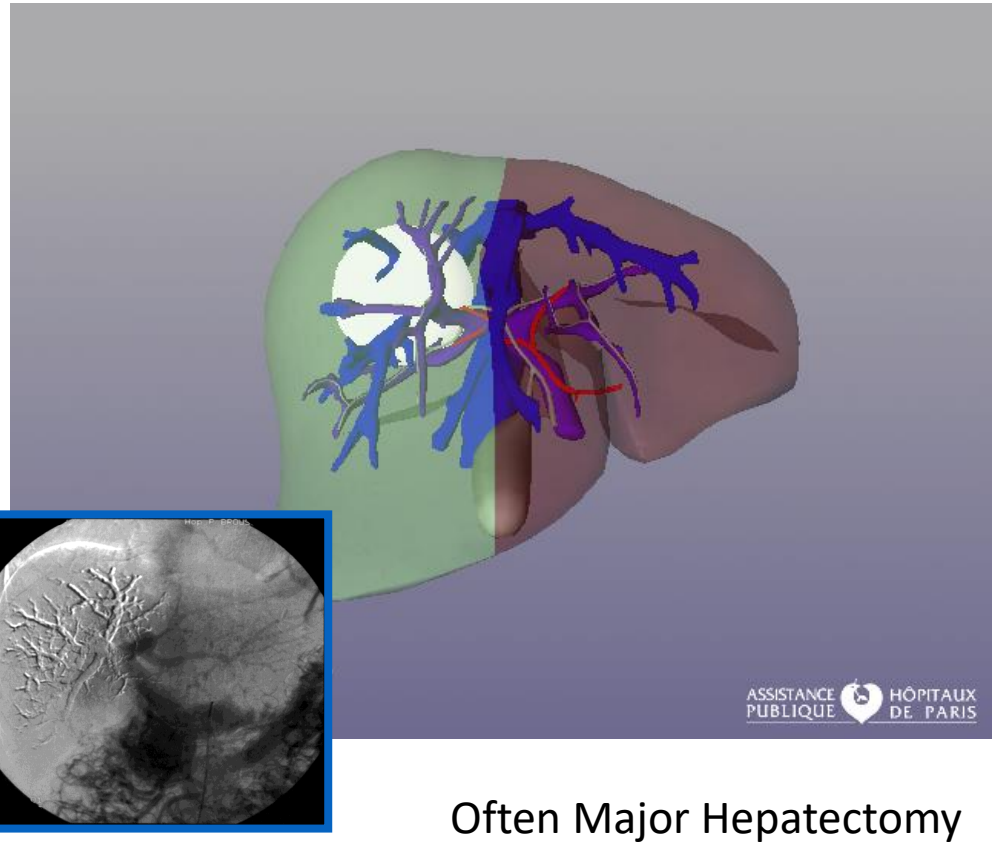
Farges et al. Ann Surg 2011

N0

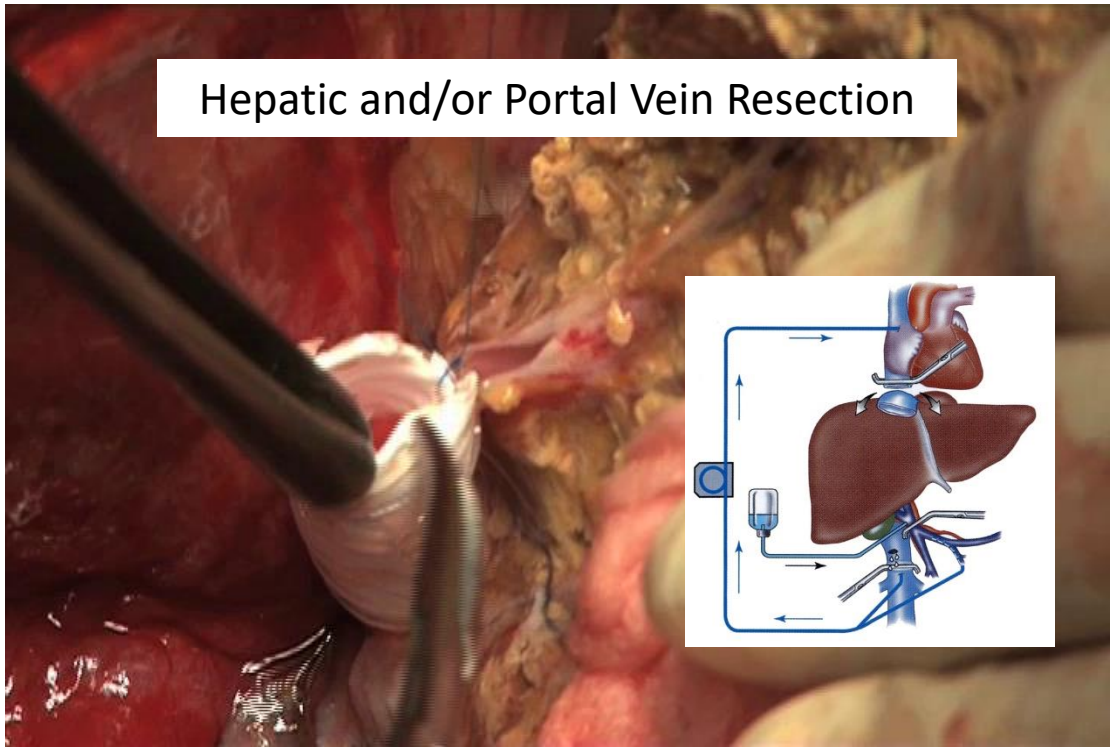


Nagino et al. Ann Surg 2013

Liver is the only curative treatment of intra hepatic Cholangiocarcinoma but…

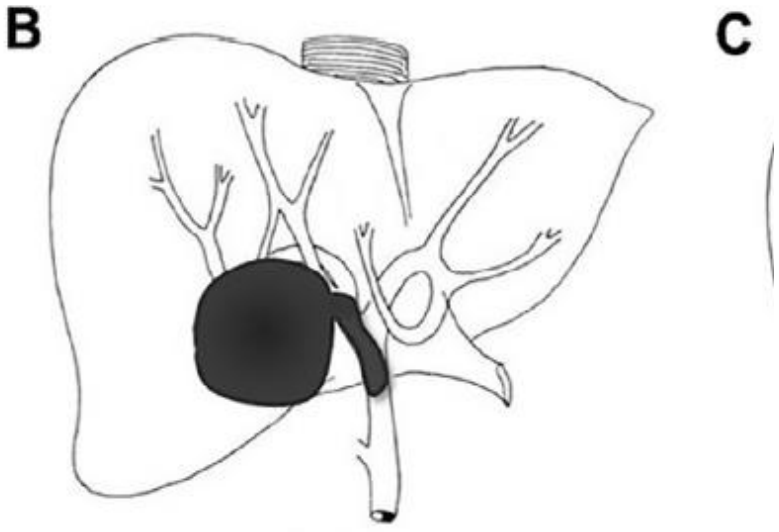


Often Major Hepatectomy
Drop Out 25% after Portal Vein Embolisation



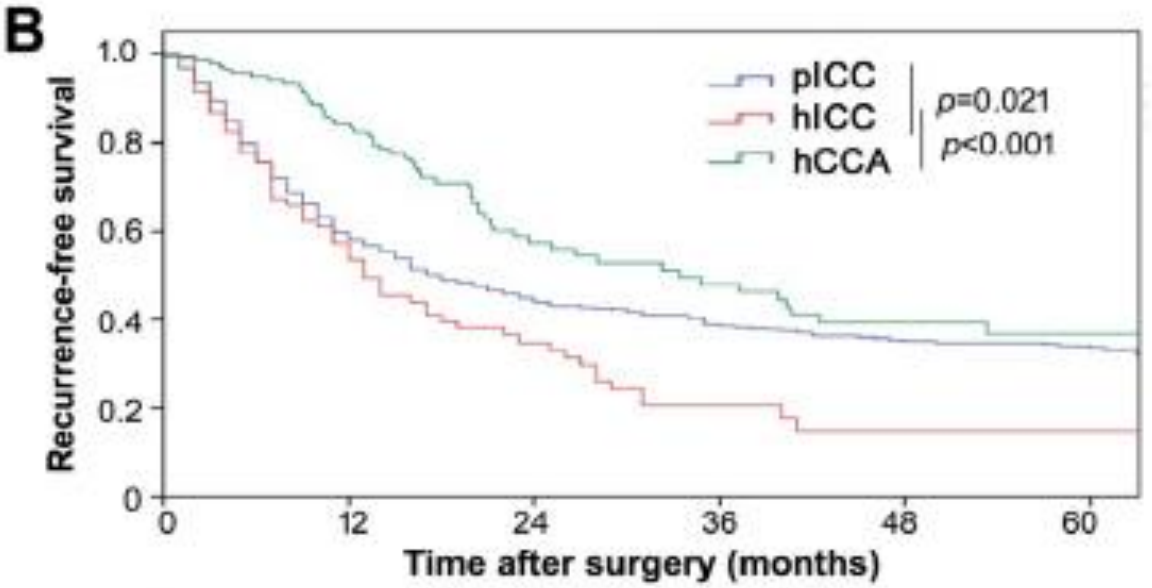
Peri-Operative Mortality 8% to 10%
Surgery must be performed in HPB Surgeon that do LT

Intra Hepatic Cholangiocarcinoma with Hilar Involvement… Still More Difficult… Because often R1 like PeriHilar CKI



Mass-froming ICC with hilar involvement (hICC)

10% of CKI

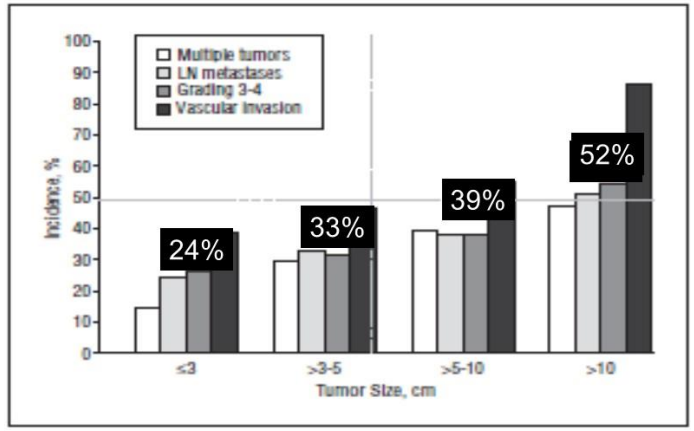


Patient No. at risk

pICC	912	447	264	176	118	83
hICC	101	44	22	9	4	4
hCCA	159	92	39	29	20	13

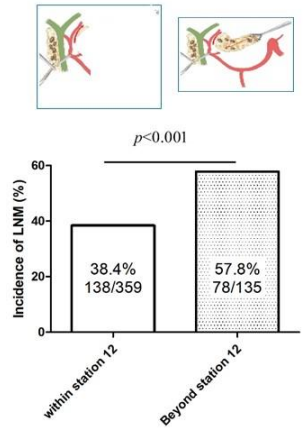
Surg

Lymph Node Invasion with Tumoral Mass Diameter

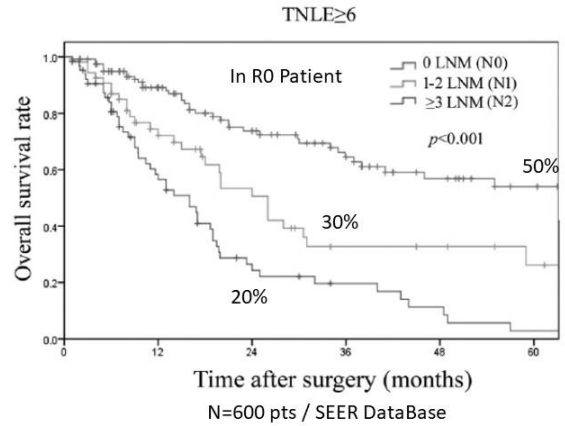


Ribeiro et al. Arch Surg 2012

Lymphadenectomy must include 6 lymph nodes



Farges et al. Ann Surg 2011

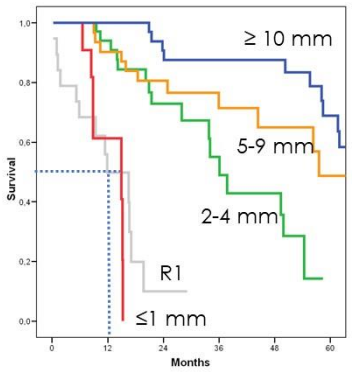


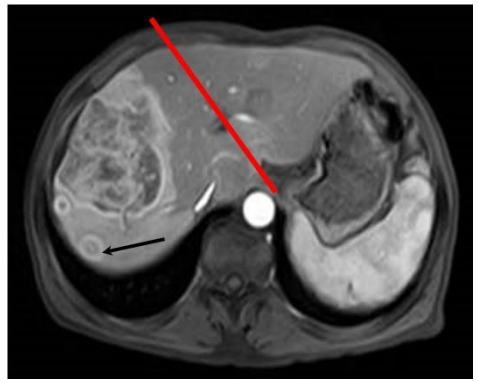
N=600 pts / SEER DataBase

Zang et al. Ann Surg 2021

Importance of margin in Cholangiocarcinoma

134 patients N0





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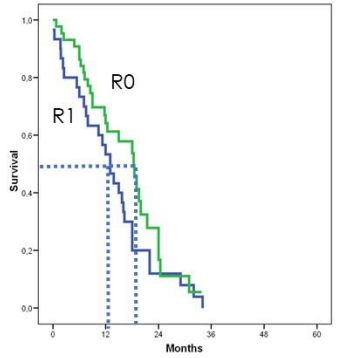
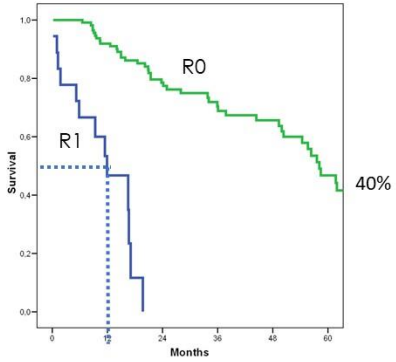
No impact of margin in N+ with upfront surgery

N+



Farges et al. Ann Surg 2011

N0

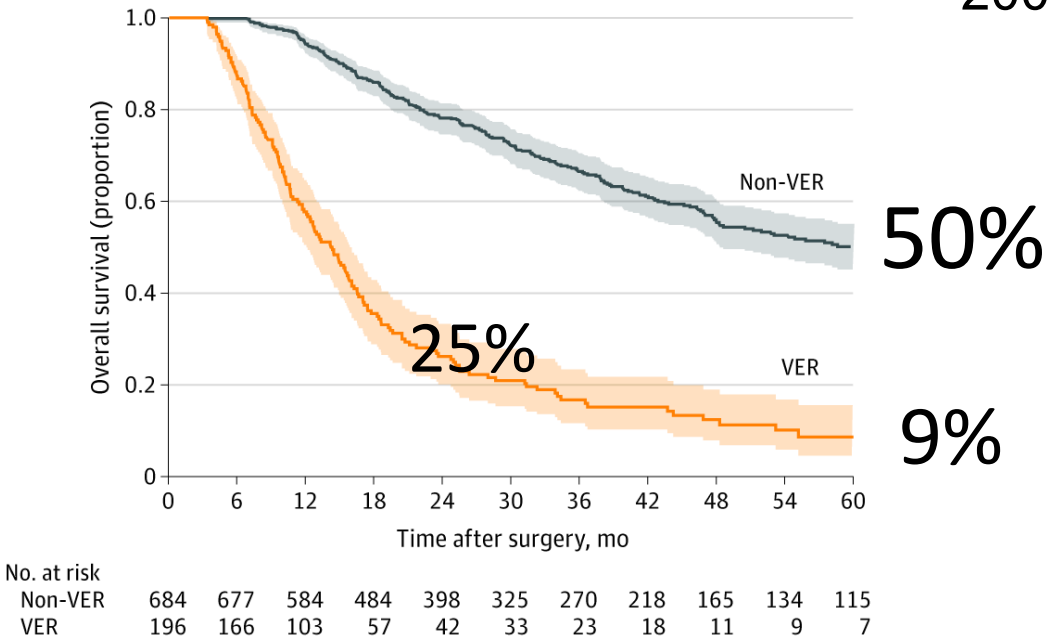


Nagino et al. Ann Surg 2013

JAMA Surgery | Original Investigation

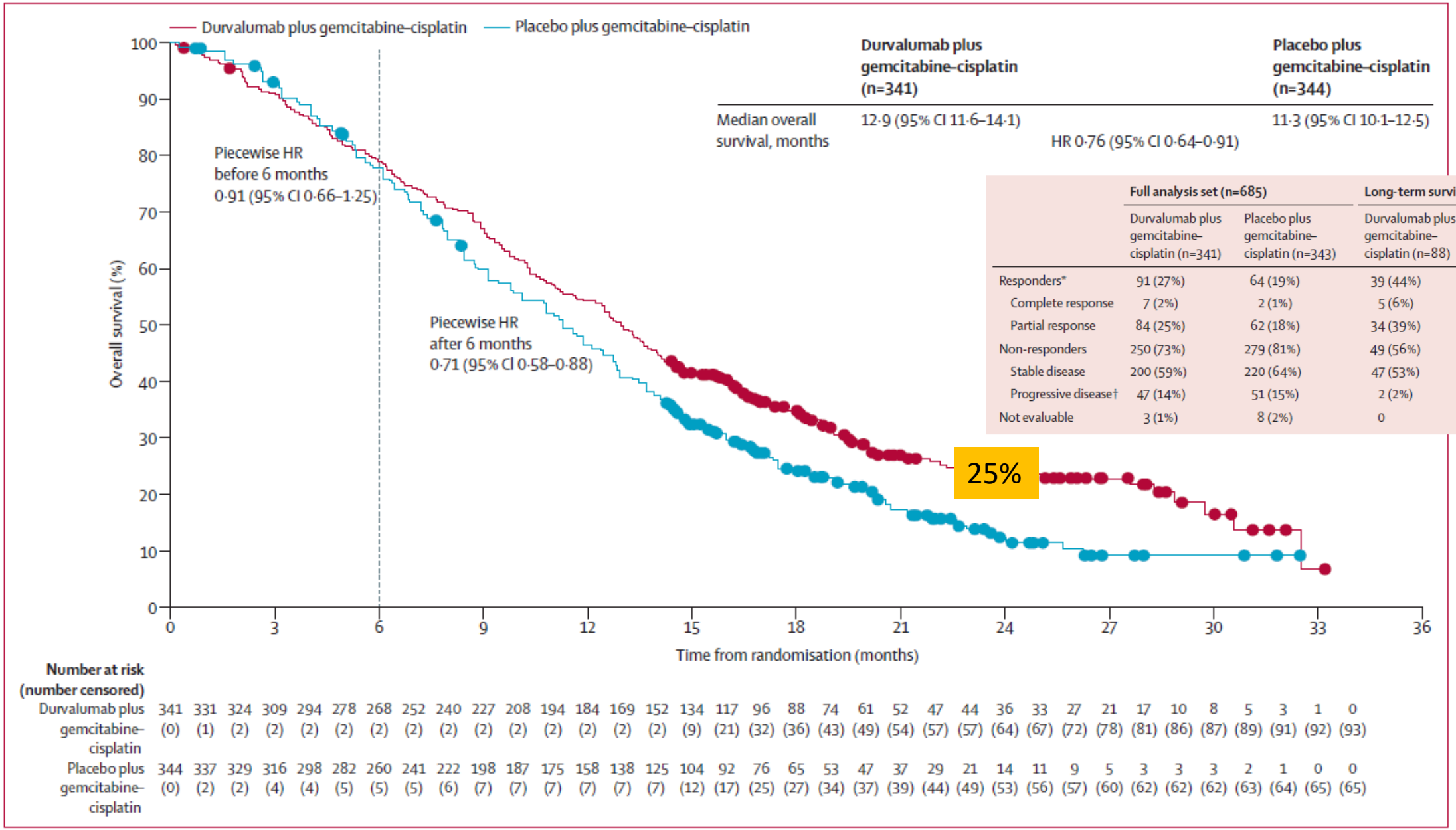
Very Early Recurrence After Liver Resection for Intrahepatic Cholangiocarcinoma Considering Alternative Treatment Approaches

Diamantis I. Tsilimigras, MD; Kota Sahara, MD; Lu Wu, MD; Dimitrios Moris, MD; Fabio Bagante, MD; Alfredo Guglielmi, MD; Luca Aldrighetti, MD; Matthew Weiss, MD; Todd W. Bauer, MD; Sorin Alexandrescu, MD; George A. Poultsides, MD; Shishir K. Maithel, MD; Hugo P. Marques, MD; Guillaume Martel, MD; Carlo Pulitano, MD; Feng Shen, MD; Olivier Soubrane, MD; B. Groot Koerkamp, MD; Amika Moro, MD; Kazunari Sasaki, MD; Federico Aucejo, MD; Xu-Feng Zhang, MD; Ryusei Matsuyama, MD, PhD; Itaru Endo, MD, PhD; Timothy M. Pawlik, MD, MPH, PhD



2000-2016 : 880 pts operated for ICC / Multicentric Database

196 (22%) pts with Very early recurrence (≤ 6 months)



	Durvalumab plus gemcitabine–cisplatin (n=341)		Placebo plus gemcitabine–cisplatin (n=344)
Median overall survival, months	12·9 (95% CI 11·6–14·1)	HR 0·76 (95% CI 0·64–0·91)	11·3 (95% CI 10·1–12·5)

	Full analysis set (n=685)		Long-term survivors (n=153)	
	Durvalumab plus gemcitabine–cisplatin (n=341)	Placebo plus gemcitabine–cisplatin (n=343)	Durvalumab plus gemcitabine–cisplatin (n=88)	Placebo plus gemcitabine–cisplatin (n=65)
Responders*	91 (27%)	64 (19%)	39 (44%)	22 (34%)
Complete response	7 (2%)	2 (1%)	5 (6%)	2 (3%)
Partial response	84 (25%)	62 (18%)	34 (39%)	20 (31%)
Non-responders	250 (73%)	279 (81%)	49 (56%)	43 (66%)
Stable disease	200 (59%)	220 (64%)	47 (53%)	41 (63%)
Progressive disease†	47 (14%)	51 (15%)	2 (2%)	2 (3%)
Not evaluable	3 (1%)	8 (2%)	0	0

Number at risk (number censored)

Durvalumab plus gemcitabine–cisplatin	341 (0)	331 (1)	324 (2)	309 (2)	294 (2)	278 (2)	268 (2)	252 (2)	240 (2)	227 (2)	208 (2)	194 (2)	184 (2)	169 (2)	152 (2)	134 (9)	117 (21)	96 (32)	88 (36)	74 (43)	61 (49)	52 (54)	47 (57)	44 (57)	36 (64)	33 (67)	27 (72)	21 (78)	17 (81)	10 (86)	8 (87)	5 (89)	3 (91)	1 (92)	0 (93)
Placebo plus gemcitabine–cisplatin	344 (0)	337 (2)	329 (2)	316 (4)	298 (4)	282 (5)	260 (5)	241 (5)	222 (6)	198 (7)	187 (7)	175 (7)	158 (7)	138 (7)	125 (7)	104 (12)	92 (17)	76 (25)	65 (27)	53 (34)	47 (37)	37 (39)	29 (44)	21 (49)	14 (53)	11 (56)	9 (57)	5 (60)	3 (62)	3 (62)	3 (62)	2 (63)	1 (64)	0 (65)	0 (65)

Oh et al. Lancet Gastro Hepatol 2024

Trois Groupes de CKI pour la récidive précoce

(A) MENU | Pre-op | Post-op | References

Age (Range: 18-90)
40

Race
Non-white

Cirrhosis
Yes

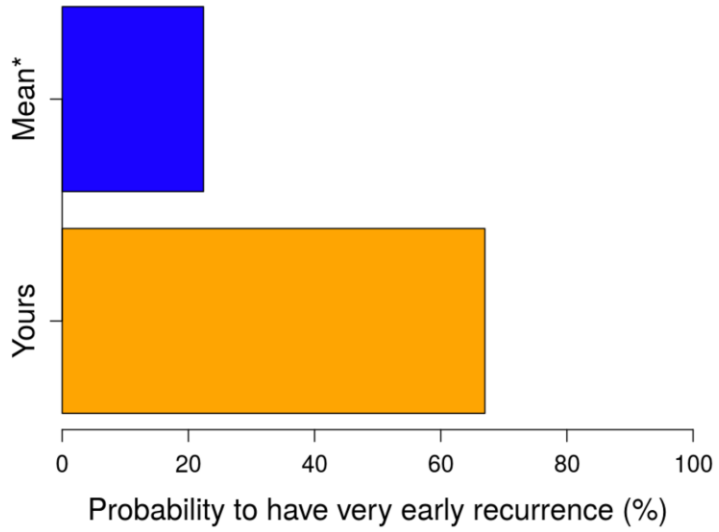
Tumor size (cm)
8

Number of lesions
1

LNM on imaging
Suspicious or Positive

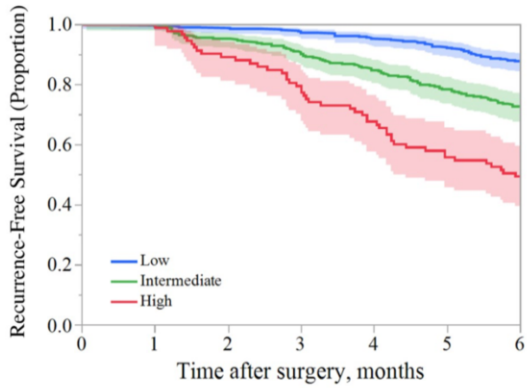
Probability of very early recurrence: 67 %

Risk group: High



*The mean of probability to have very early recurrence in the model is 22.4%

Reference



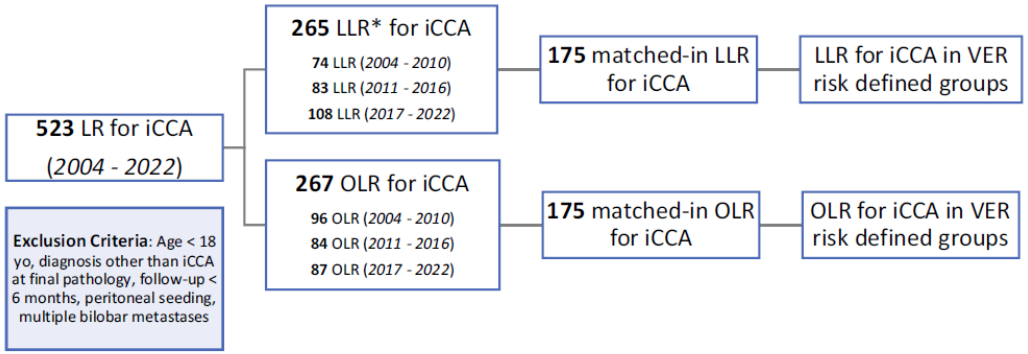
	Median RFS (months)	6 month RFS	12 month RFS
Low	21.8	87.7%	67.3%
Intermediate	12.9	72.3%	51.2%
High	5.9	49.5%	30.7%

*Tsilimigras DI, et al. *JAMA Surgery* 2020

https://k-sahara.shinyapps.io/Veryearly-recurrence/

Coelioscopie ou Laparotomie ?

4% des malades avaient eu un traitement néo-adjuvant



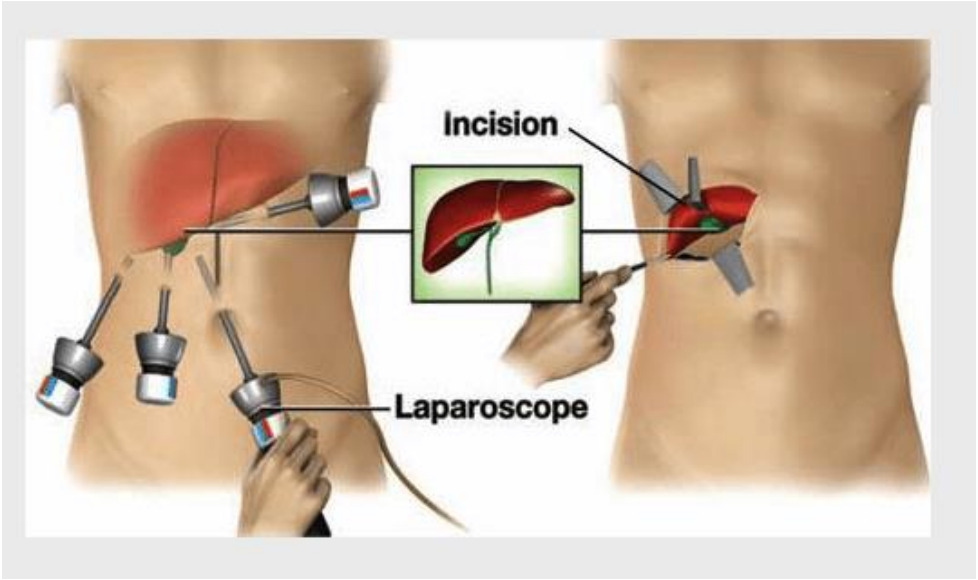


TABLE 1 Demographic, clinical, and pathological characteristics before and after PSM

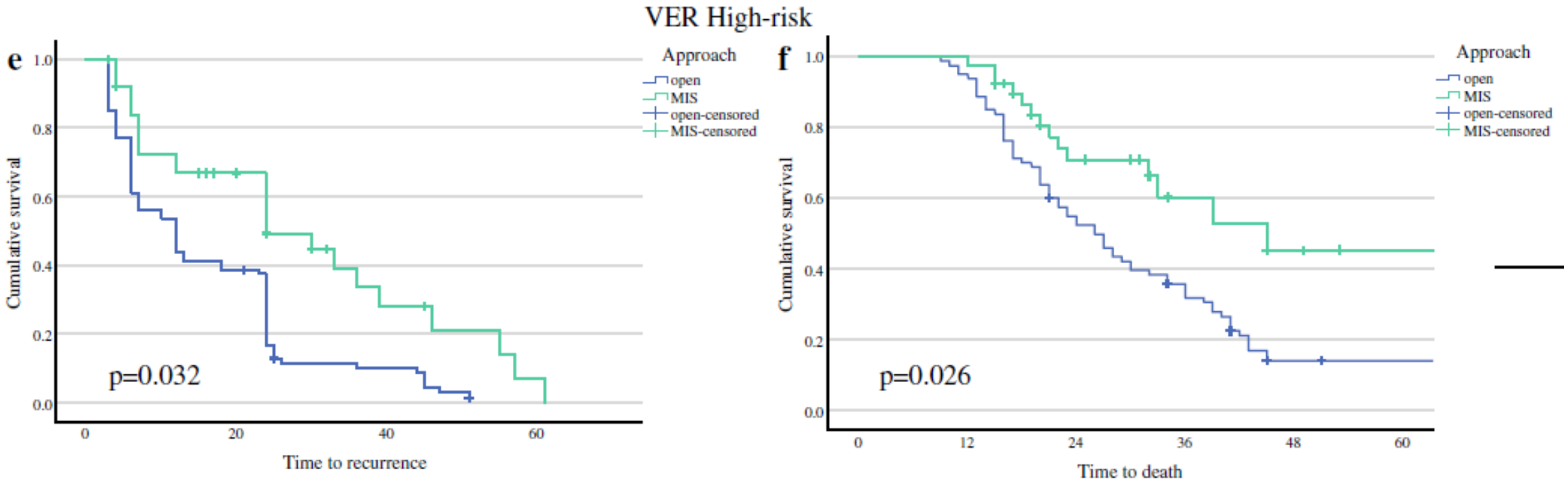
		Before PSM		*p* value	After PSM (1:1)		*p* value
		LLR group (*n* = 265)	OLR group (*n* = 267)		LLR group (*n* = 175)	OLR group (*n* = 175)	
Age (years, mean ± SD)		58 ± 5	67 ± 4	0.001	61 ± 4	62 ± 7	0.123
Male sex, *n* (%)		169 (63.8)	153 (57.3)	0.150	106 (60.6)	100 (57.1)	0.518
ASA score, *n* (%)				< 0.001			0.860
	1	55 (20.8)	48 (18.0)		39 (22.3)	36 (20.6)	
	2	158 (59.6)	126 (47.2)		92 (52.6)	97 (55.4)	
	3	52 (19.6)	93 (34.8)		44 (25.1)	42 (24)	
BMI		23.8 ± 3.4	24.1 ± 2.9	0.483	24.6 ± 2.6	24.9 ± 1.8	0.547
Underlying liver disease, *n* (%)				< 0.001			0.143
	None	194 (73.2)	149 (55.8)		123 (70.3)	133 (76)	
	Steatosis/mild impairment	43 (16.2)	83 (31.1)		29 (16.6)	27 (15.3)	
	Cirrhosis	28 (10.6)	35 (13.1)		23 (13.1)	15 (8.7)	
CEA (ng/mL)		23 ± 9	37 ± 12	0.06	22 ± 21	35 ± 19	0.08
CA 19.9 (U/mL)		91 ± 24	203 ± 48	0.002	89 ± 76	93 ± 64	0.177
Size (cm)		4.5 ± 3.1	5.9 ± 1.5	0.018	5.3 ± 2.3	5.8 ± 1.2	0.904
Positive nodal status at imaging, *n* (%)		57 (21.5)	74 (27.7)	0.119	33 (18.9)	37 (21.1)	0.590
Tumor number, *n* (%)				0.03			0.936
	Single	184 (69.4)	160 (59.9)		126 (72)	123 (70)	
	Single with satellites	45 (17.0)	49 (18.4)		26 (14.9)	28 (16)	
	Multiple	36 (13.6)	58 (21.7)		23 (13.1)	24 (13.7)	
Preoperative CT, *n* (%)				0.862			0.791
	Yes	12 (4.5)	13 (4.9)		6 (3.4)	8 (4.6)	
	No	253 (95.5)	254 (95.1)		169 (96.6)	167 (95.4)	
VER low risk, *n* (%)		41 (15.5)	25 (9.4)	0.045	19 (10.9)	16 (9.1)	0.718
VER intermediate risk, *n* (%)		138 (52.1)	159 (59.5)	0.082	99 (56.6)	97 (55.4)	0.823
VER high risk, *n* (%)		86 (32.4)	83 (31.1)	0.740	57 (32.6)	62 (35.4)	

*Percentage refers to number of patients undergoing lymphadenectomy; *PSM* propensity score matching

119 Malades avec un CKI à Haut Risque de Récidives Précoces

F. Ratti. Ann Surg Oncol 2024

La coelioscopie donne de meilleurs résultat que la chirurgie ouverte dans les cholangiocarcinomes agressifs



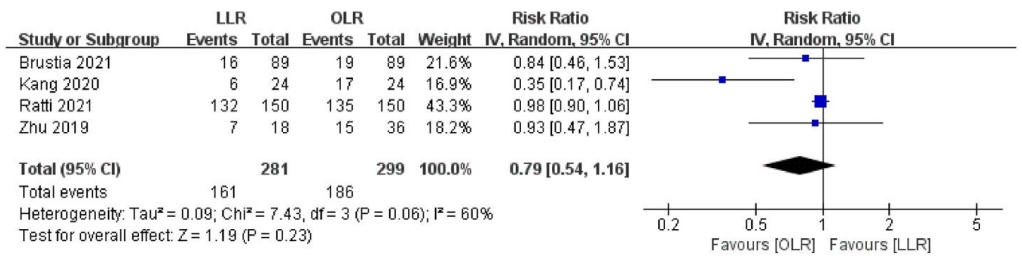
Moins de Complications, Durée d'Hospitalisation plus courte après coelioscopie donc…

Début de la chimiothérapie ajduvante par capecitabine dans les tumeurs agressives : 82% Coelio vs 71% Laparo, p=0.03

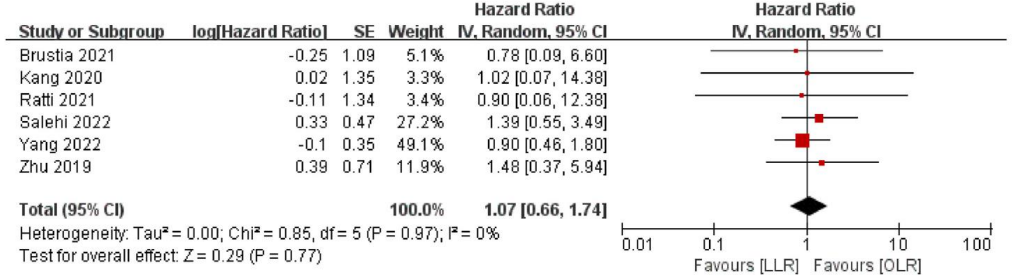
Confirme une meta-analyse sur coelio et CKI Moins de Morbidité et d'Hospitalisation

First author, year of publication	Country	Study design	Variables matched	No. of patients	LH	OH	Quality Score
Brustia 2021	France	Retrospective study	Age; Difficulty classification; Year of surgery; Number of lesions; Tumor size	178	89	89	8
Kang 2020	Korea	Retrospective study	Age; Gender; Tumor number; Tumor location; Extent of hepatectomy	48	24	24	8
Ratti 2021	Italy	Retrospective study	Age; ASA grade; Chronic liver disease; Ca 199 serum level; Tumor size; Tumor number; Tumor stage	300	150	150	8
Salehi 2022	USA	Retrospective study	Age; Gender; Resection extent; Year of diagnosis; Tumor size; Lymphatic invasion; Insurance status	230	115	115	7
Yang 2022	China	Retrospective study	Age; Gender; BMI, Smoking and drinking status; Tumor size, Tumor number, Tumor stage, Tumor differentiation, Lymphatic invasion; HBV infection; Hepatolithiasis; Diabetes; Liver cirrhosis, Previous abdominal surgery; Liver function; Resection extent; Charlson comorbidity index score; Anatomical resection	244	122	122	8
Zhu 2019	China	Retrospective study	Age; Tumor size; Tumor number; Tumor location; Tumor stage; Microvascular invasion; ASA grade; Underlying liver cirrhosis; Liver function; Resection extent	54	18	36	8

Moins de ganglions en coelioscopie



Pas de différence de survie à 3 ans



Li et al. European J. Surg Oncol 2024

Neoadjuvant chemotherapy: Clinical trials

Table 3. Selected clinical trials of neoadjuvant and adjuvant therapy in ICC

Trial identifier	Regimen/intervention	Estimated enrollment	Study type	Primary outcome	Country	Setting
NCT04506281	Toripalimab (PD-1 antibody) + GEMOX + lenvatinib vs. observation	128	Phase 2, RCT	EFS	China	Neoadjuvant
NCT04523402	GEMOX vs. observation	100	Phase 2, RCT	EFS	China	Neoadjuvant
NCT04546828	Gemcitabine + cisplatin + nab-paclitaxel	34	Phase 2, single arm	Increased rate of R0 resection	Korea	Neoadjuvant
NCT04669496	Toripalimab (PD-1 antibody) + GEMOX + lenvatinib vs. observation	178	Phase 2–3, RCT	EFS	China	Neoadjuvant
NCT04989218	Gemcitabine + cisplatin + durvalumab (PD-L1 antibody) + tremelimumab (CTLA4 antibody)	20	Phase 1–2, single arm	ORR	USA	Neoadjuvant
NCT03579771	Gemcitabine + cisplatin + nab-paclitaxel	34	Phase 2, single arm	Completion of all therapy rate, AE	USA	Neoadjuvant

*Tsilimigras DI, et al. *Ann Surg Oncol* 2020

Is it safe to administer neoadjuvant chemotherapy to patients undergoing hepatectomy for intrahepatic cholangiocarcinoma? ACS-NSQIP propensity-matched analysis

Woo Jin Choi[1,2], Tommy Ivanics[2,3,4], Marco P.A.W. Claasen[2,5], Steven Gallinger[1,2], Bettina Hansen[6] & Gonzalo Sapisochin[1,2]

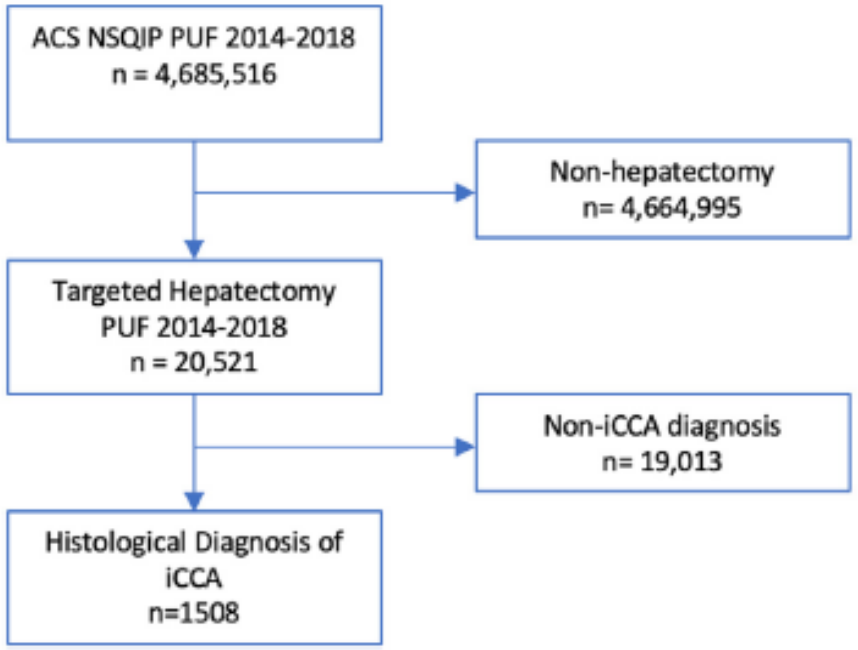
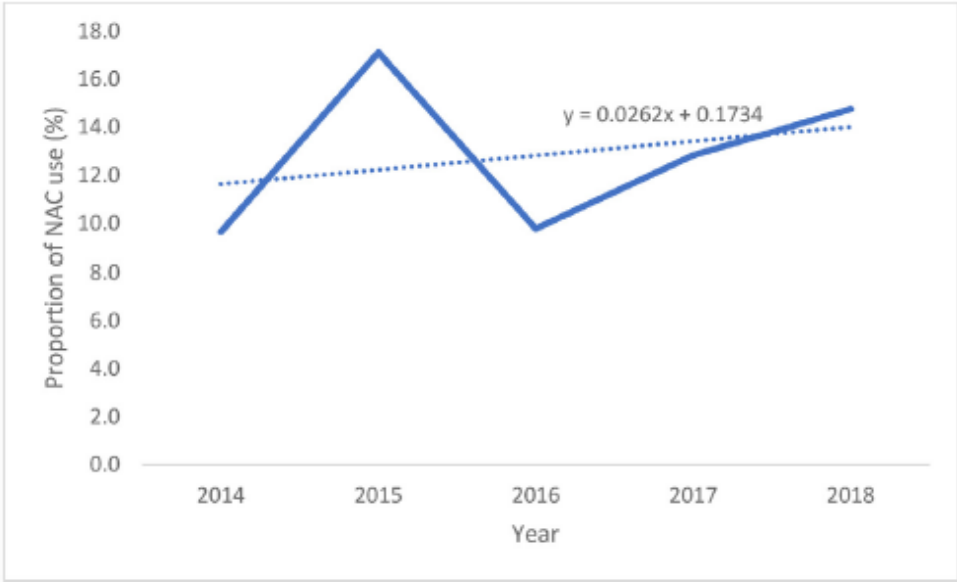


Figure 1 Flow Diagram for cohort selection from American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database with Participant Use Data Files (PUF)

Globaly strategies using chemotherapy first increased



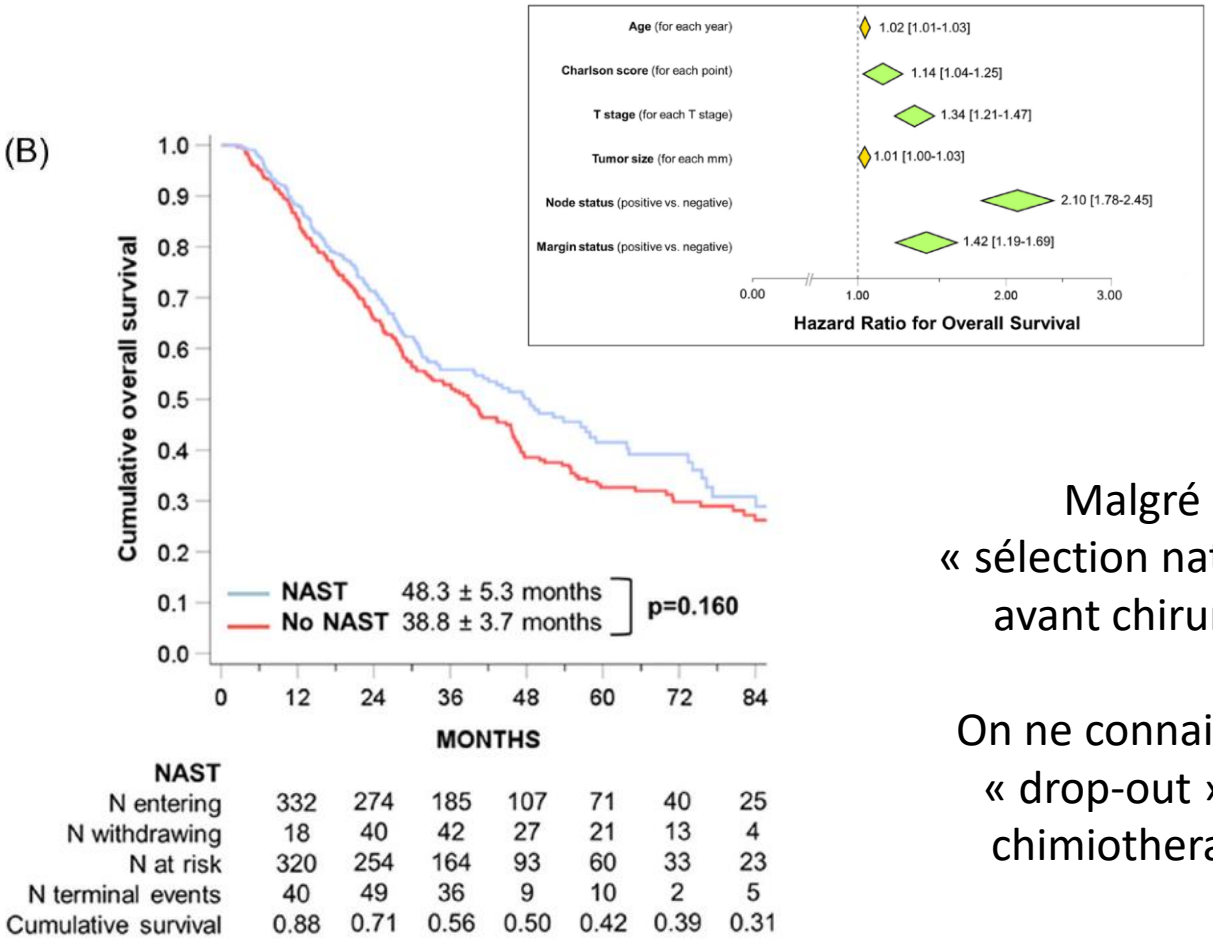
More Difficult Intra Operatively
No Impact of Post-Operative Course
No Impact of Lenght of Hospitalisation

Choi et al. *HPB Journal 2022*

Neoadjuvant therapy reduces node positivity but does not confer survival benefit versus up-front resection for resectable intrahepatic cholangiocarcinoma: A propensity-matched analysis

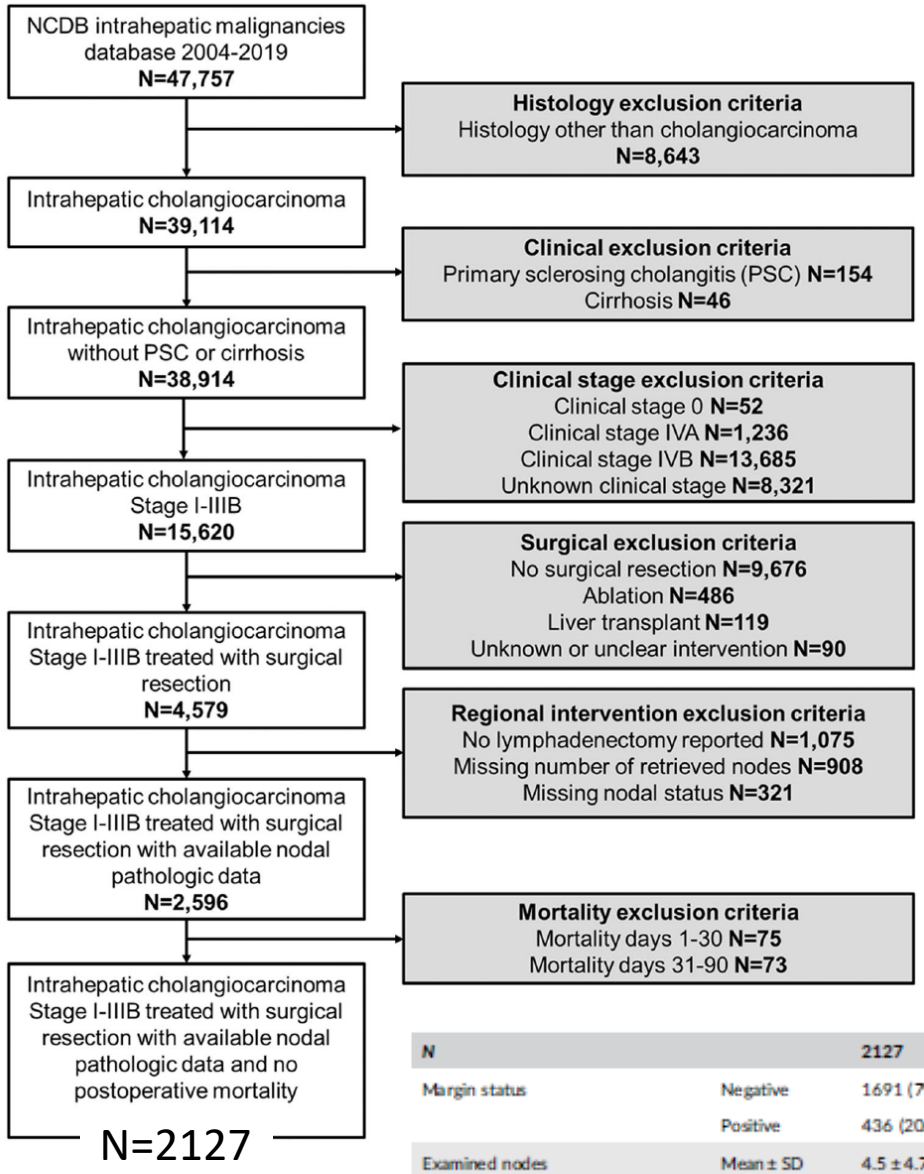
J Surg Oncol. 2024;130:453–461.

Chase J. Wehrle MD[1] | Jenny Chang MD[1] | Kimberly Woo MD[1] |



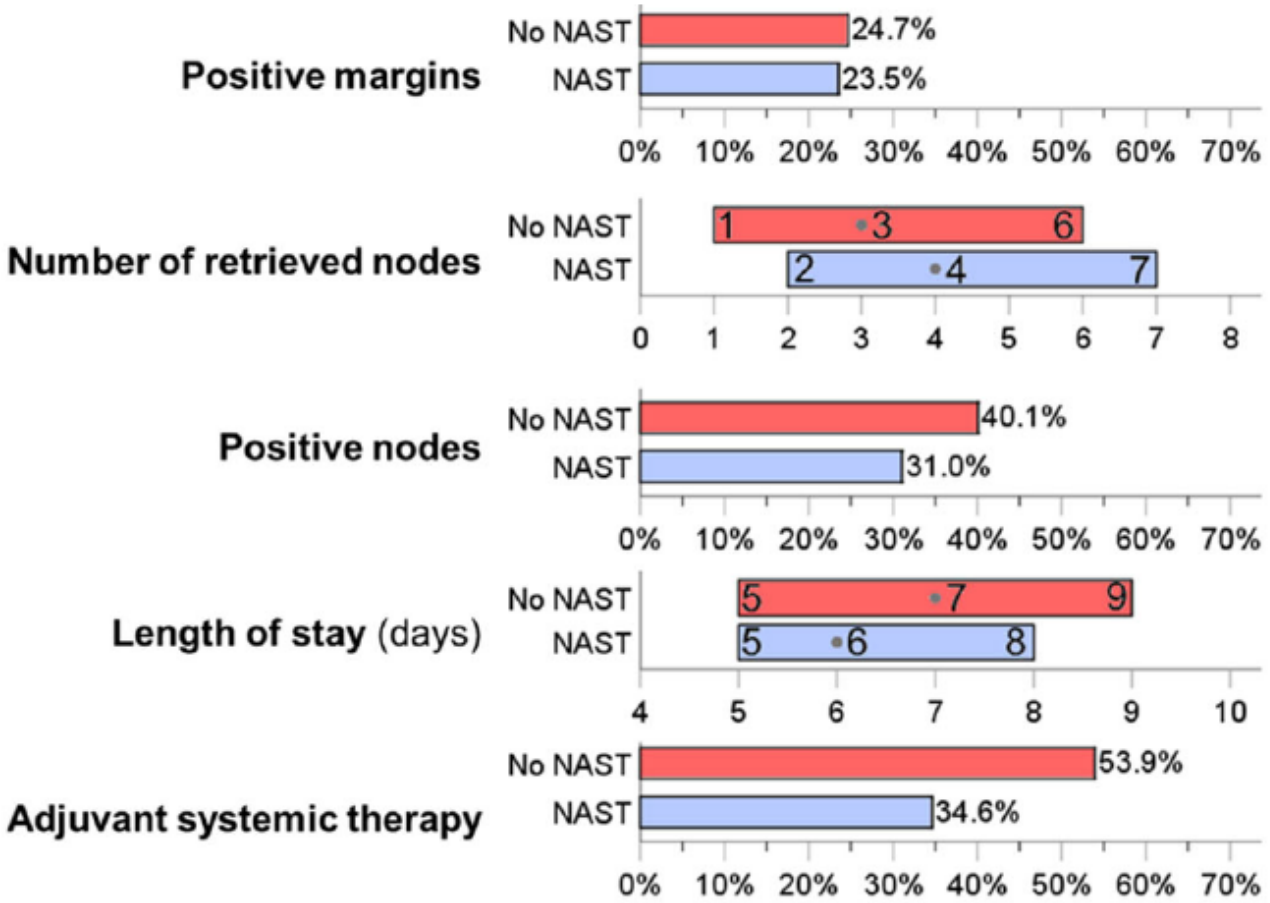
Malgré la « sélection naturelle » avant chirurgie ?

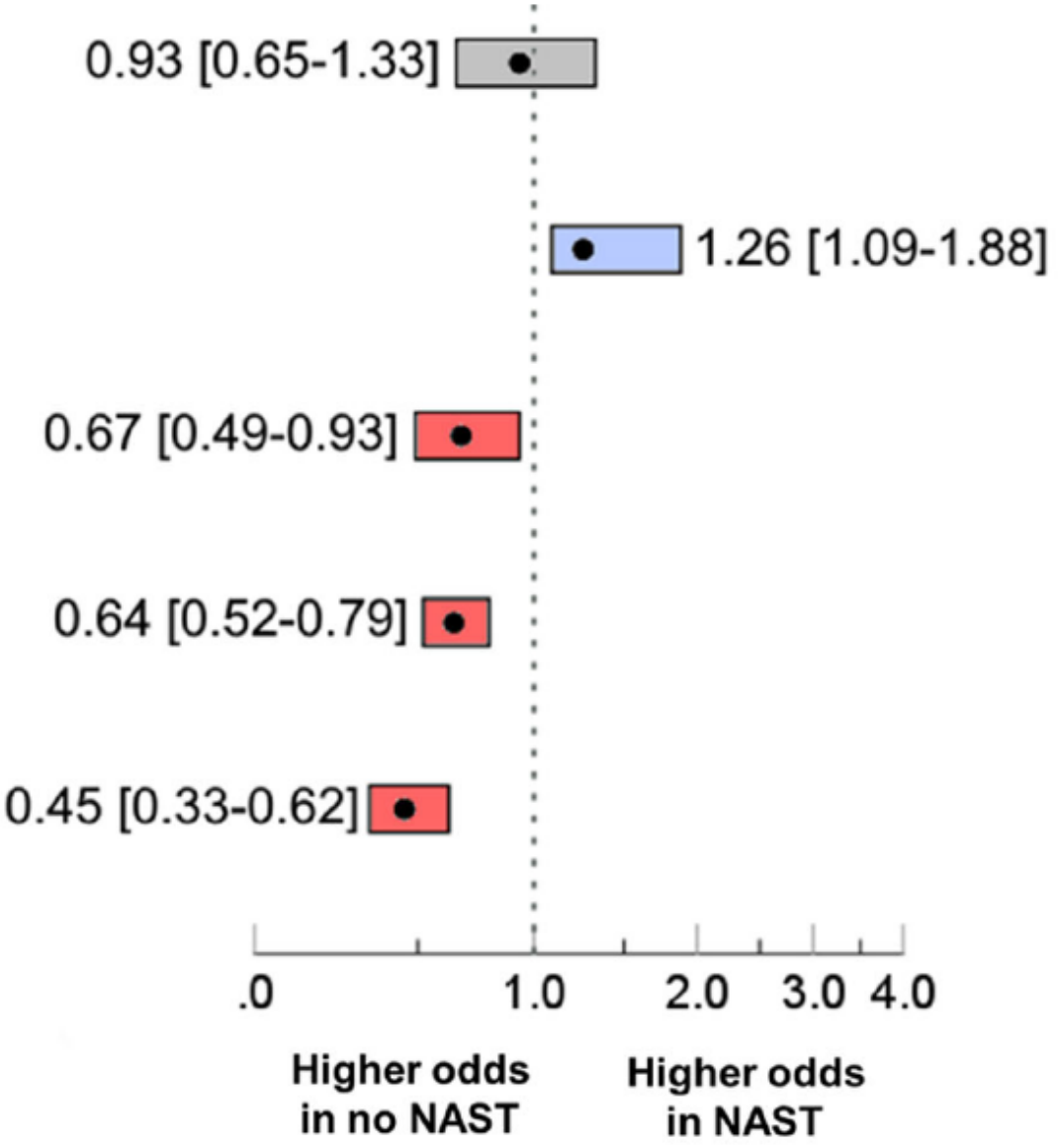
On ne connait pas le « drop-out » sous chimiotherapie…



N		2127
Margin status	Negative	1691 (79.5%)
	Positive	436 (20.5%)
Examined nodes	Mean ± SD	4.5 ± 4.7
	Median	3

Diam Tum 6.5 cm
N preop (CT/PET) 17%
Traitement Neo Adj : 20% dont 3% (CT+RT)

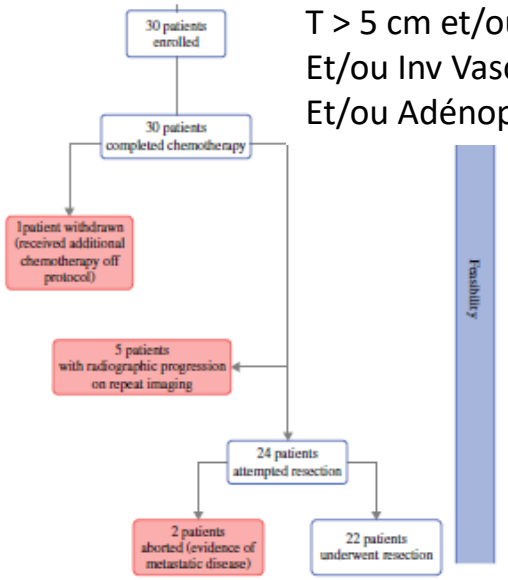




Meilleur Curage, Moins de Ganglions
Suites Opératoires plus longues
Moins de Chimiothérapie post-op

NEO-GAP: A Single-Arm, Phase II Feasibility Trial of Neoadjuvant Gemcitabine, Cisplatin, and Nab-Paclitaxel for Resectable, High-Risk Intrahepatic Cholangiocarcinoma

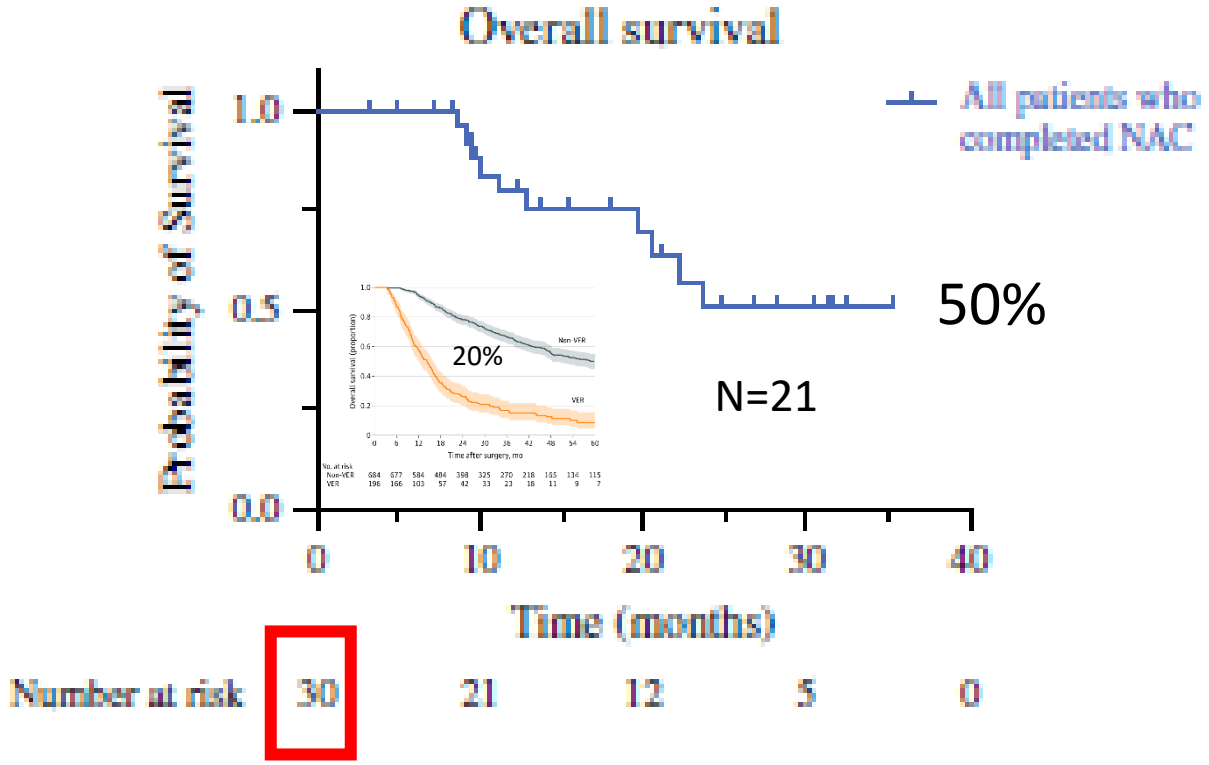
Shishir K. Maithel, MD, FACS, FSSO[1], Jessica M. Keilson, MD, MS[1], Hop S. Tran Cao, MD[2], Manali Rupji, MS[3], Amit Mahipal, MBBS[4], Bruce S. Lin, MD[5], Milind M. Javle, MD[6], Sean P. Cleary, MD[7], Mehmet Akce, MD[8], Jeffrey M. Switchenko, PhD[3,9], and Flavio G. Rocha, MD[10]

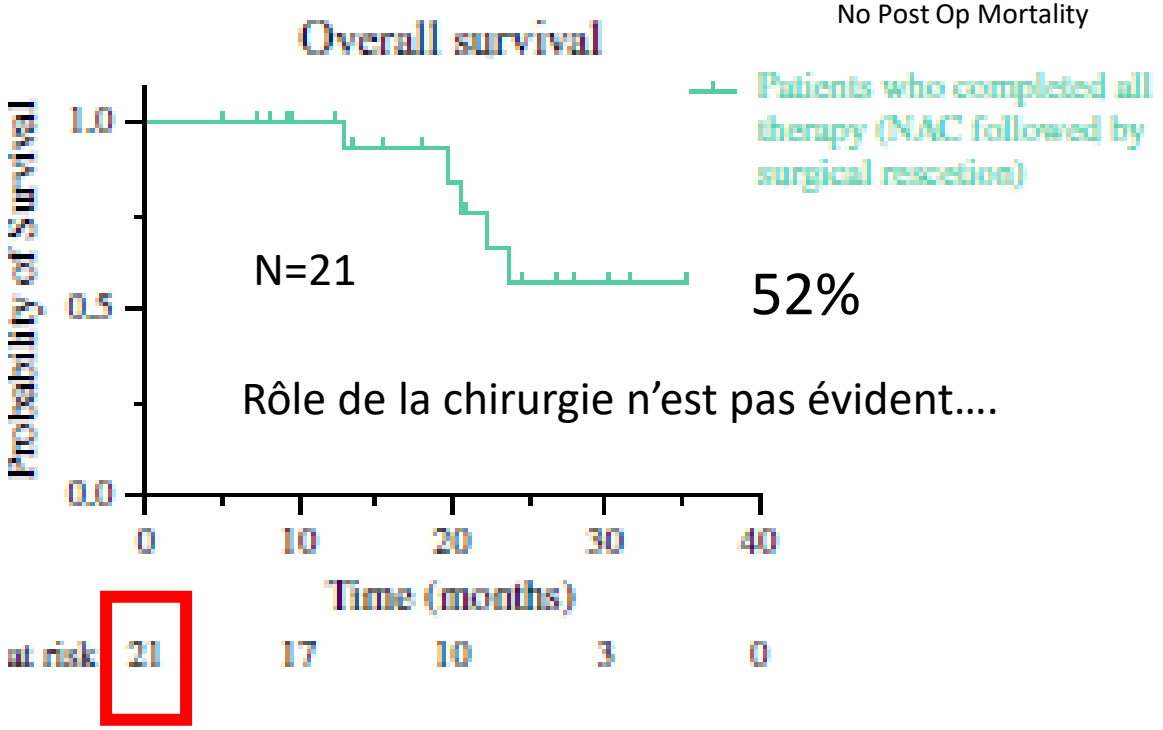


T > 5 cm et/ou N > 1
Et/ou Inv Vasculaire
Et/ou Adénopathie

No Post Op Mortality

A





Ann Surg Oncol 2023

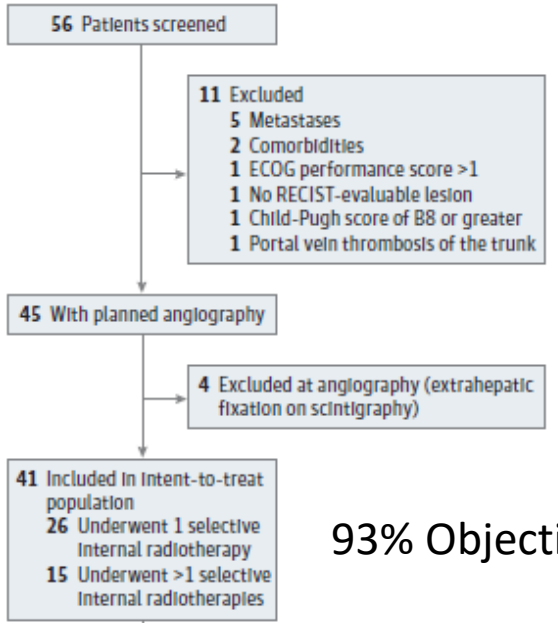
JAMA Oncology | Original Investigation

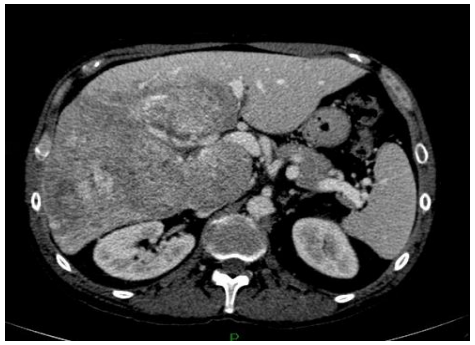
Radioembolization Plus Chemotherapy for First-line Treatment of Locally Advanced Intrahepatic Cholangiocarcinoma
A Phase 2 Clinical Trial

Julien Edeline, MD, PhD; Yann Touchefeu, MD; Boris Guiu, MD, PhD; Olivier Farge, MD, PhD; David Tougeron, MD, PhD; Isabelle Baumgaertner, MD; Ahmet Ayav, MD, PhD; Boris Campillo-Gimenez, MD, PhD; Luc Beuzit, MD; Marc Pracht, MD; Astrid Lièvre, MD, PhD; Samuel Le Sourd, MD; Karim Boudjema, MD, PhD; Yan Rolland, MD; Eveline Boucher, MD, PhD; Etienne Garin, MD, PhD

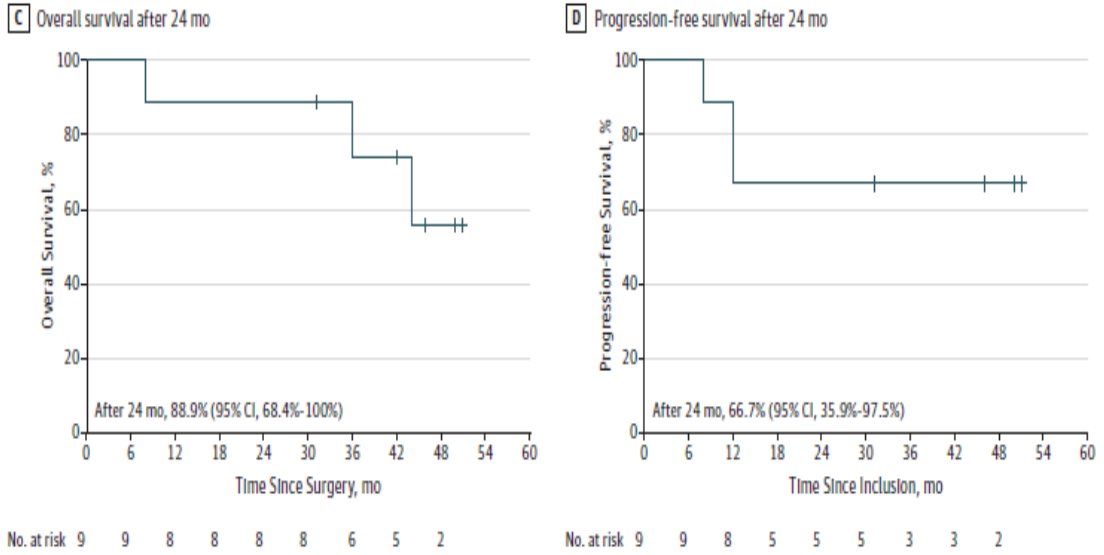
9/40 (22%) of Downstaging for SURGERY

OS Median : 46 months
89% of 2 years Overall Surival





93% Objective Response (mRECIST)



A and B, Overall (A) and progression-free (B) survival in all patients in the intent-to-treat population. C and D, Overall (C) and relapse-free (D) survival among the 9 patients who underwent resection starting on the date of surgery.

Outcomes

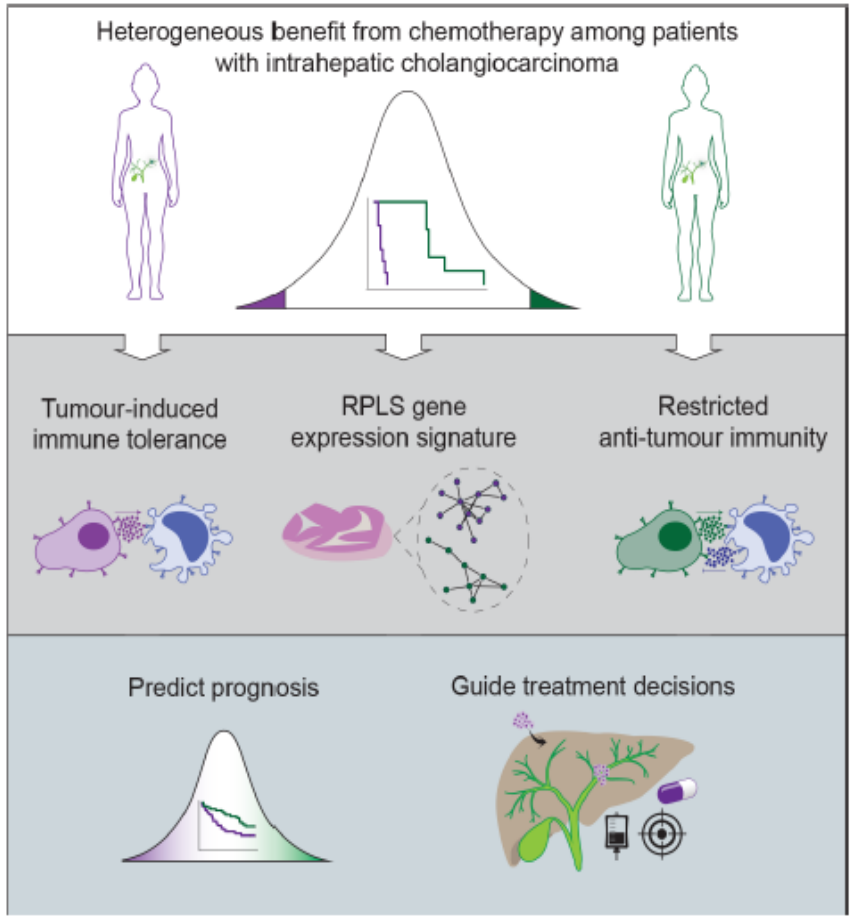
After a median follow-up of 36 months (95% CI, 26-51 months; range, 1-56 months), 40 patients were evaluable for response

JAMA Oncology Published online October 31, 2019

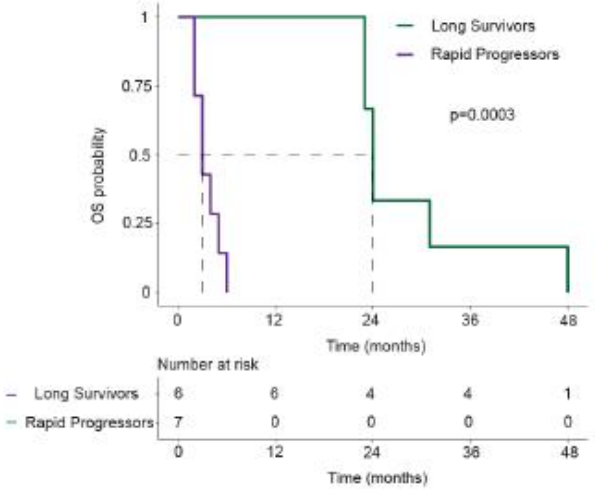
Molecular portraits of patients with intrahepatic cholangiocarcinoma who diverge as rapid progressors or long survivors on chemotherapy

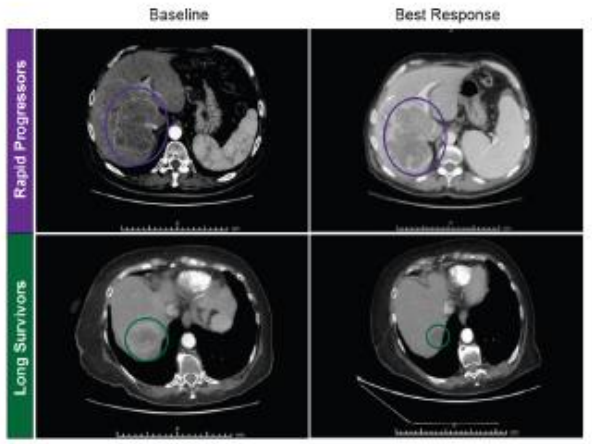
Colm J O'Rourke,[1] Massimiliano Salati,[2,3] Colin Rae,[4] Guido Carpino ,[5] Holly Leslie,[4] Antonio Pea,[4] Maria G Prete,[4] Luca R Bonetti,[6] Francesco Amato,[4] Robert Montal[7]

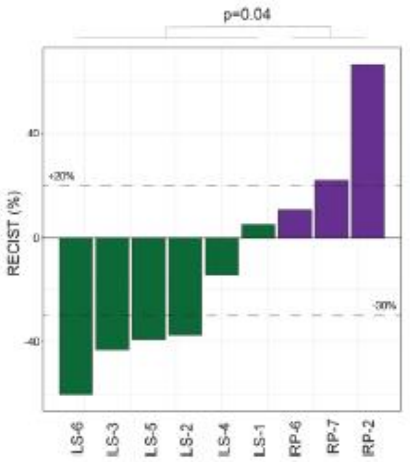
Identifier les malades chez qui tout est possible…



Design We identified a cohort of advanced iCCA patients with comparable baseline characteristics who diverged as extreme outliers on chemotherapy (survival <6 m in rapid progressors, RP; survival >23 m in long survivors, LS). Diagnostic biopsies were characterised by digital pathology, then subjected to whole-transcriptome profiling of bulk and geospatially macrodissected tissue regions. Spatial transcriptomics of tumour-infiltrating myeloid cells was performed using targeted digital spatial profiling (GeoMx). Transcriptome signatures were evaluated in multiple cohorts of resected cancers.



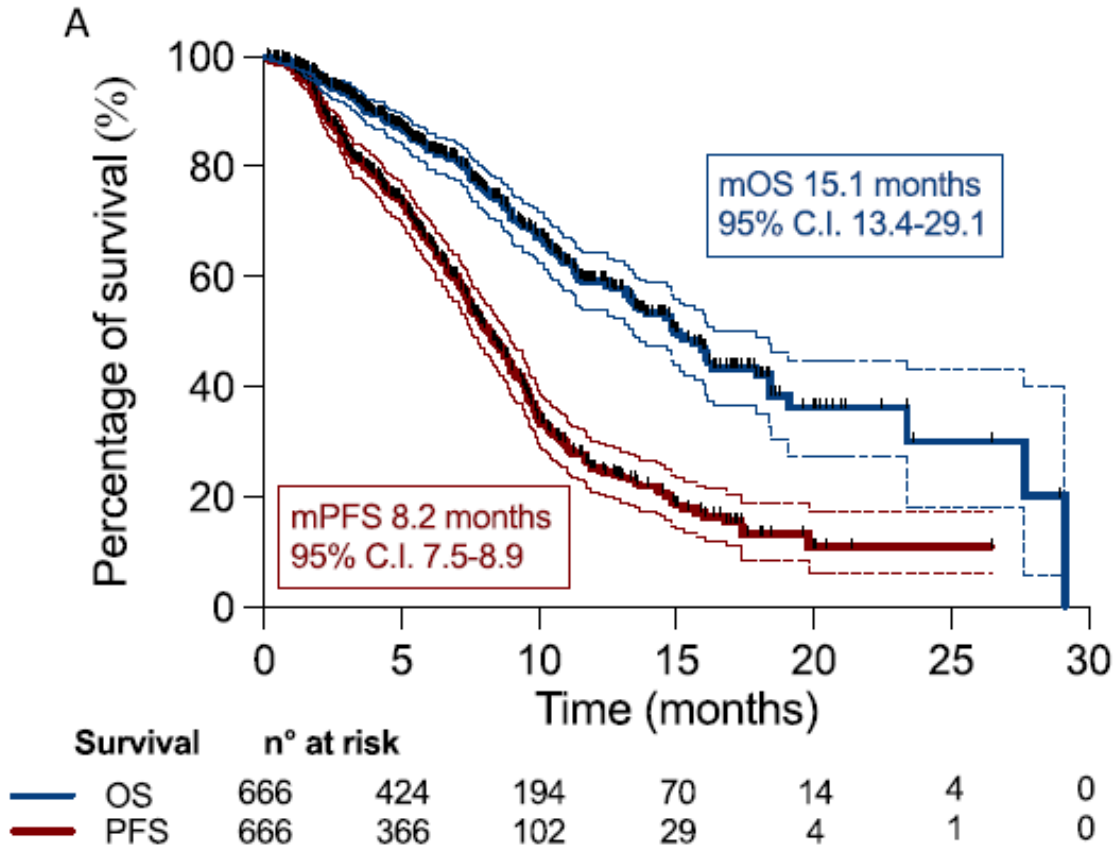




O'Rourke CJ, *et al*. *Gut* 2024;**73**:496–508.

Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer: A large real-life worldwide population

Margherita Rimini [a,1], Lorenzo Fornaro [b,*,1], Mario Domenico Rizzato [c], Lorenzo Antonuzzo [d,e], Federico Rossari [a], Tomoyuki Satake [f], Hanne Vandeputte [g], Caterina Vivaldi [b,h], Et al.



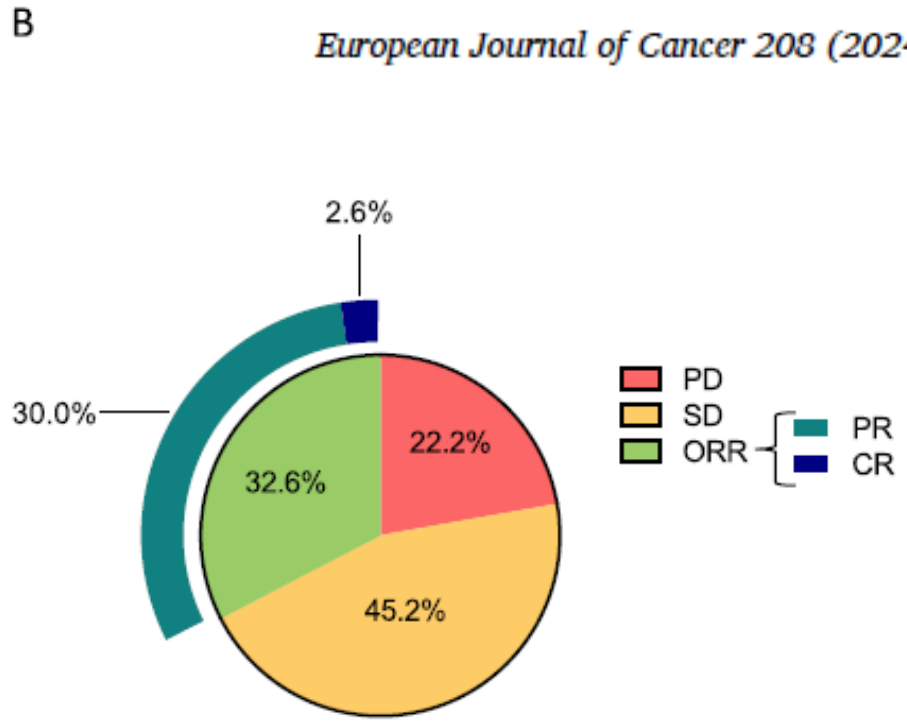


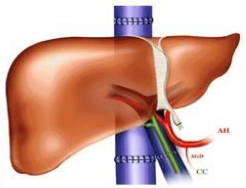
Fig. 1. A: Kaplan Meier curves for OS and PFS; B: Graphical representation of response to treatment in the cisplatin, gemcitabine, durvalumab cohort.

Analysis of Liver Resection Versus Liver Transplantation on Outcome of Small Intrahepatic Cholangiocarcinoma and Combined Hepatocellular-Cholangiocarcinoma in the Setting of Cirrhosis

Eleonora De Martin,[1,2] Michael Rayar,[3,4] Nicolas Golse,[1,2*] Margot Dupeux,[5,6*] Maximiliano Gelli,[7] Viviane Gnemmi,[8] Marc Antoine Allard,[1,2] Daniel Cherqui,[1,2] Antonio Sa Cunha,[1,2] Rene Adam,[1,2] Audrey Colly,[1,2] Teresa Maria Antonini,[1,2] Catherine Guettier,[5,6] Didier Samuel,[1,2] Karim Boudjema,[3,4] Emmanuel Boleslawski,[9] and Eric Vibert[1,2]

2002 – 2014 : 60 cirrhotic patients (F4) with iCCA or HCA on the specimen

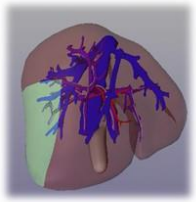
Hôpitaux universitaires Paris-Sud
Assistance Publique Hôpitaux de Paris



N=38

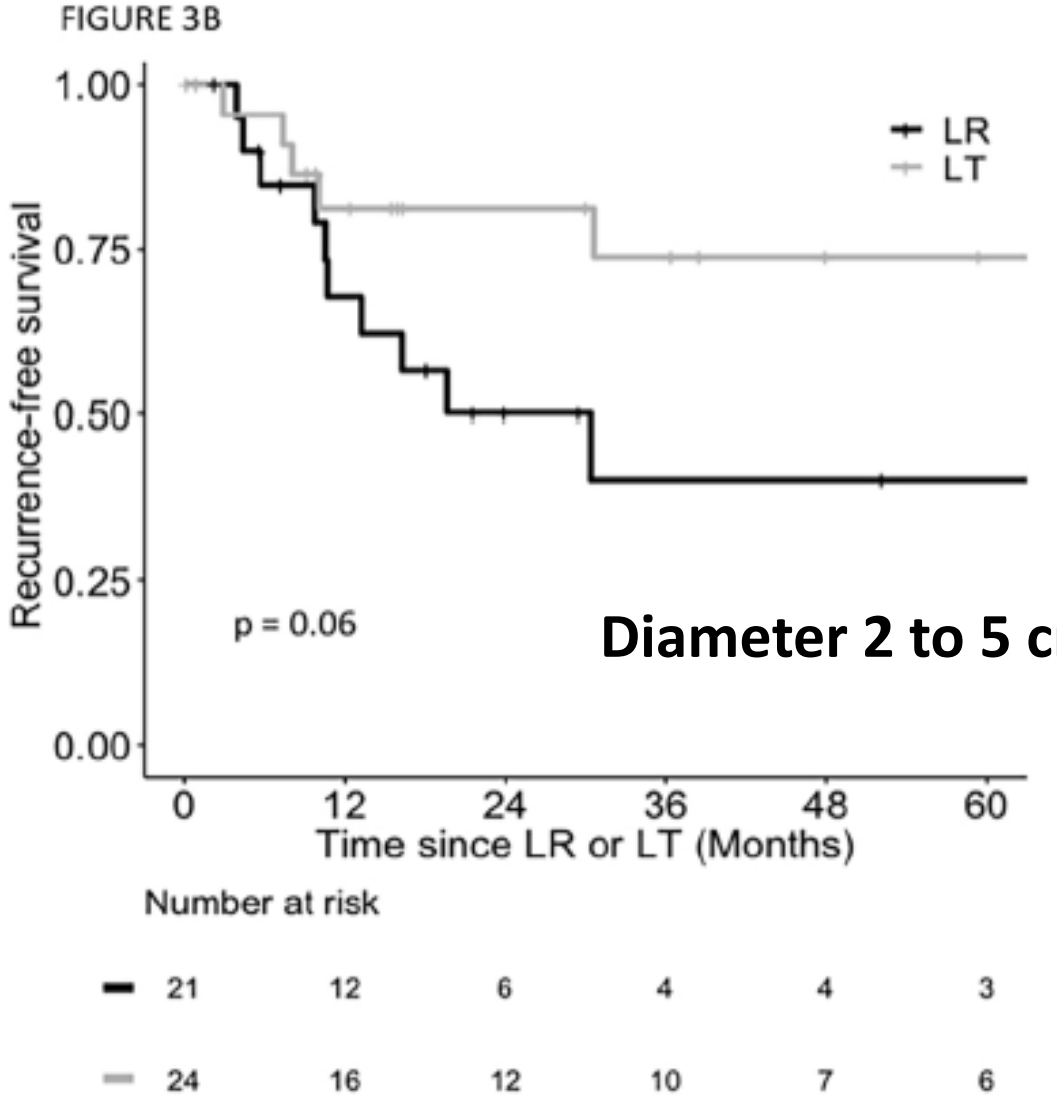
Centre Hospitalier Régional Universitaire de Lille

CHU Rennes



N=22

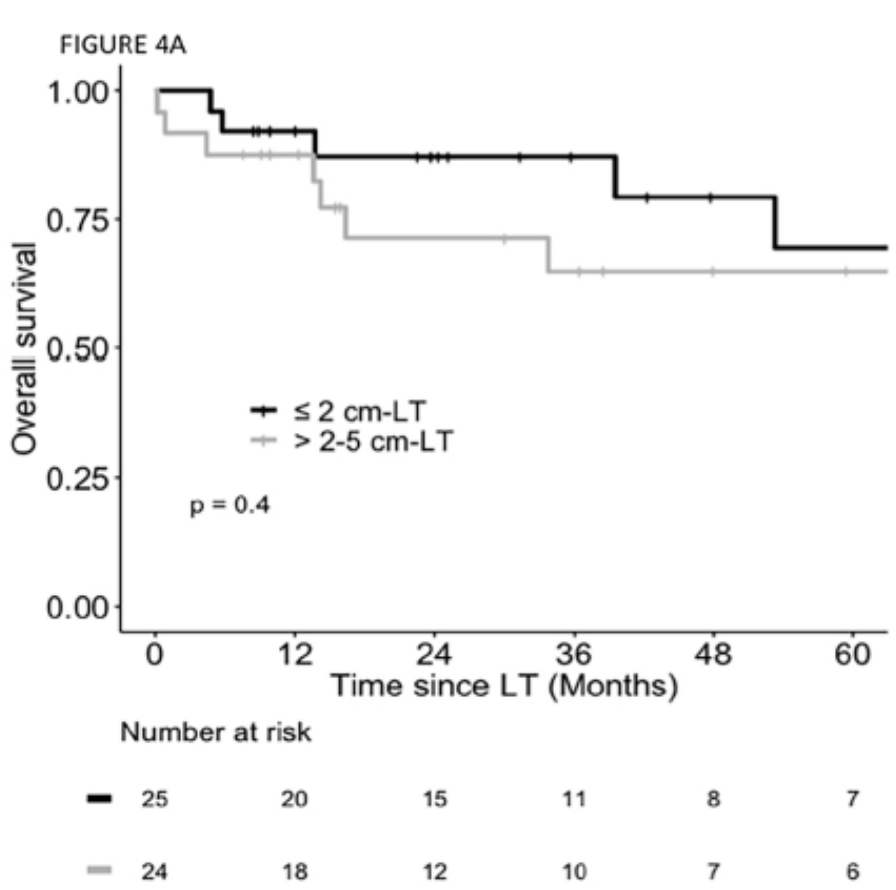
Unique ou Multiple Tumor < 5 cm

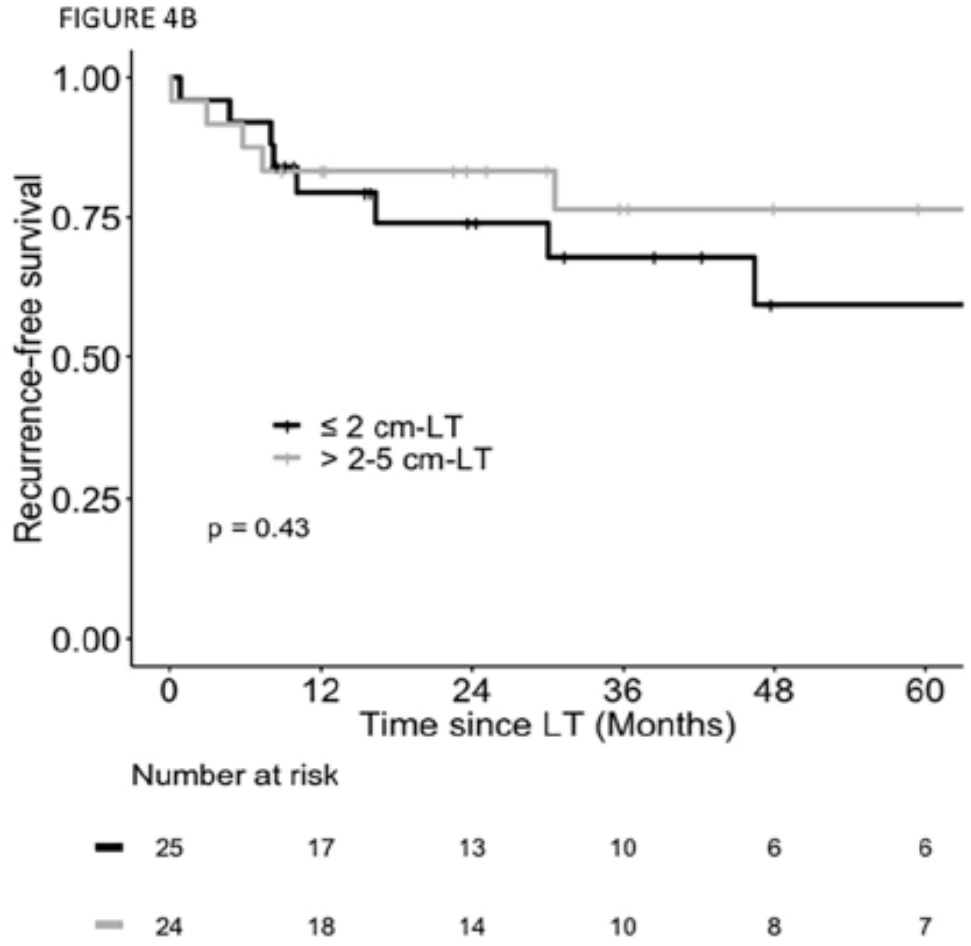


Diameter 2 to 5 cm

Liver Transpl, Nov 2020

No difference according to diameter in Liver Transplant





Intrahepatic cholangiocarcinoma
Tumour characteristics
- Biopsy-proven cholangiocarcinoma
- Intrahepatic rather than periductal location
- Not amenable to surgical therapy
- No evidence of extrahepatic disease

Diagnostic criteria
- Triple-phase CT of the chest, abdomen, and pelvis
- MRI bone scan
- FDG-PET scan if serum cancer antigen 19-9 elevated
- Endoscopic ultrasound-guided biopsy of enlarged nodes

↓

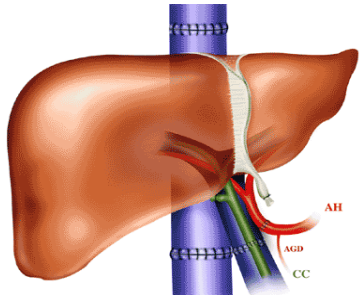
Neoadjuvant chemotherapy
- First-line platinum-based therapy and gemcitabine
- Second-line chemotherapy for progression or intolerance
- Addition of targeted biologics on case-by-case basis

↓

Disease stability for at least 6 months on given regimen
- Repeat imaging every 3 months
- Stable or regressing disease
- No extrahepatic disease

↓

Liver transplantation
- Post-transplant adjuvant therapy for 4–6 months depending on explant pathology



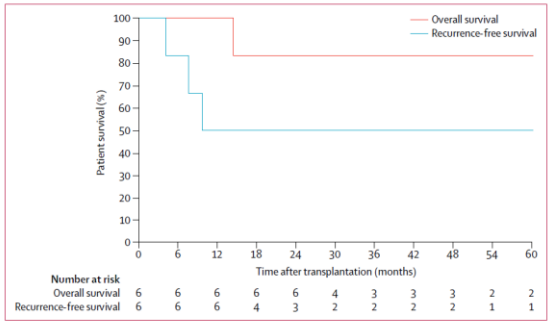
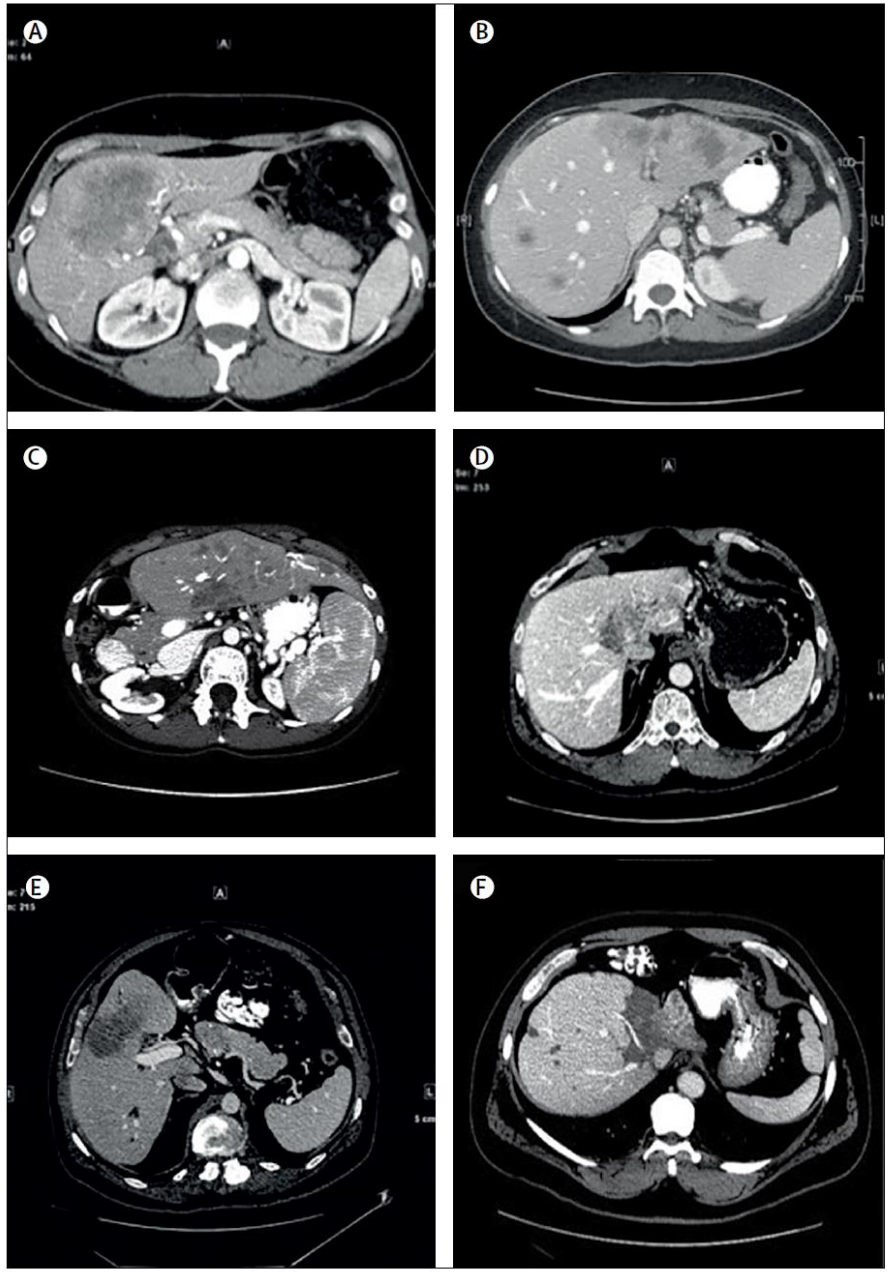


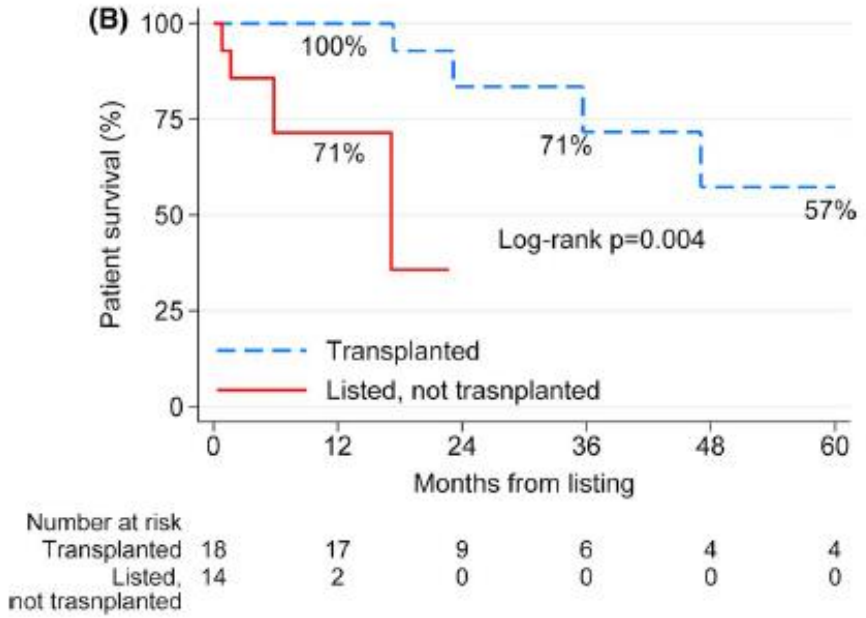
Figure 3: Cumulative overall and recurrence-free survival after liver transplantation for intrahepatic cholangiocarcinoma



Lancet Hepato Gastro 2018

Survival following liver transplantation for locally advanced, unresectable intrahepatic cholangiocarcinoma

Robert R. McMillan[1] | Milind Javle[2] | Sudha Kodali[3] | Ashish Saharia[1] | Constance Mobley[1] | Kirk Heyne[4] | Mark J. Hobeika[1] | Keri E. Lunsford[5] | David W. Victor III[3] | Akshay Shetty[3] | Robert S. McFadden[3] | Maen Abdelrahim[4] | Ahmed Kaseb[2] | Mukul Divatia[6] | Nam Yu[7] | Joy Nolte Fong[1] | Linda W. Moore[1] | Duc T. Nguyen[6] | Edward A. Graviss[6] | A. Osama Gaber[1] | Jean-Nicolas Vauthey[8] | R. Mark Ghobrial[1]



Le meilleur moyen d'être R0…

Am J Transplant. 2022;22:823–832.

En Conclusion…

La survie est dans la marge si la biologie tumorale à respecter les ganglions

Hépatectomies complexes avec une planification 3D et une préparation (drainage biliaire, embolisation portale, déprivation veineuse) qui fait cependant prendre le risque d'une progression de la maladie…

Les questions auxquelles on doit répondre

- Hépatectomie gauche plutôt qu'une hépatectomie droite demain ou jamais …
- Transplantation dans les cholangiocarcinomes intra-hépatiques ?
- Traitements néo-adjuvants chez les patients « résécables » avec des CKI ?