Pitfalls στη Χειρουργική Θεραπεία του Χολαγγειοκαρκινώματος

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Cholangiocarcinoma

EPIDEMIOLOGY

Relatively uncommon malignancy
More common outside the United States, particularly in South America and Eastern/Central Europe

Less common than gallbladder cancer

Incidence per 100,000 in U.S.: 1.0 in females
1.5 in males

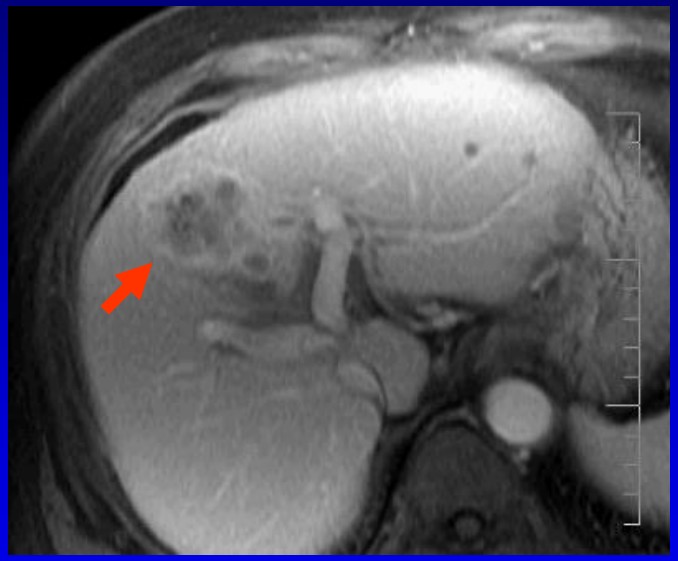
Increasing incidence with age
70% of cases in over 65 years

Hilar location most common

Cholangiocarcinoma

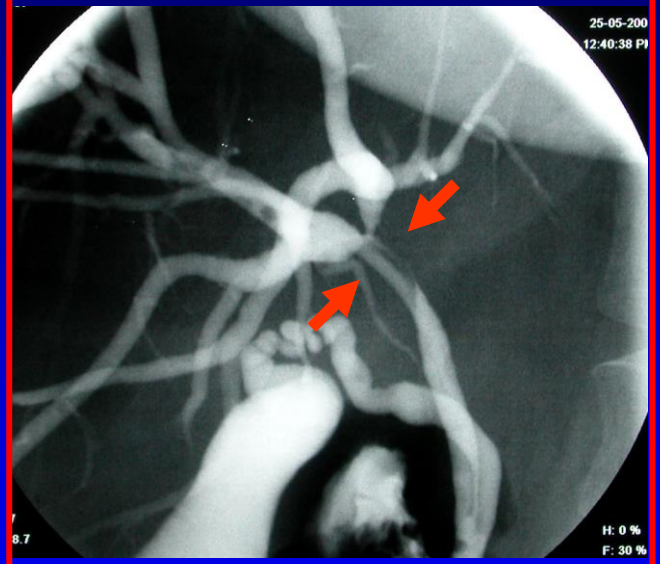
Location

Peripheral



- 7-20%
- Intrahepatic mass
- Cirrhosis uncommon
- Etiology unknown

Hilar



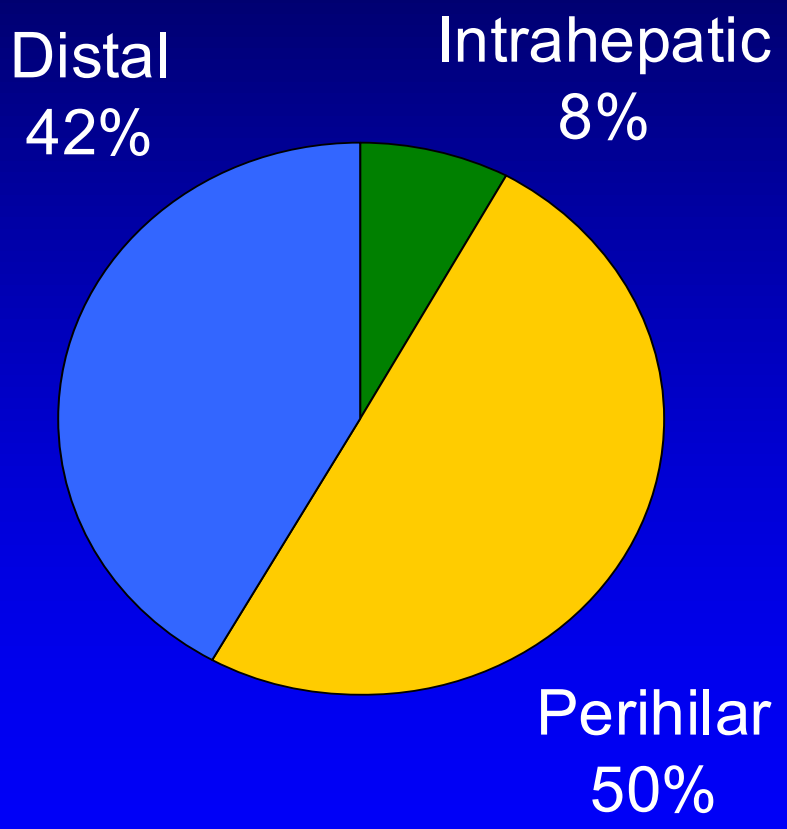
- 40-60%
- Biliary confluence
- Most common

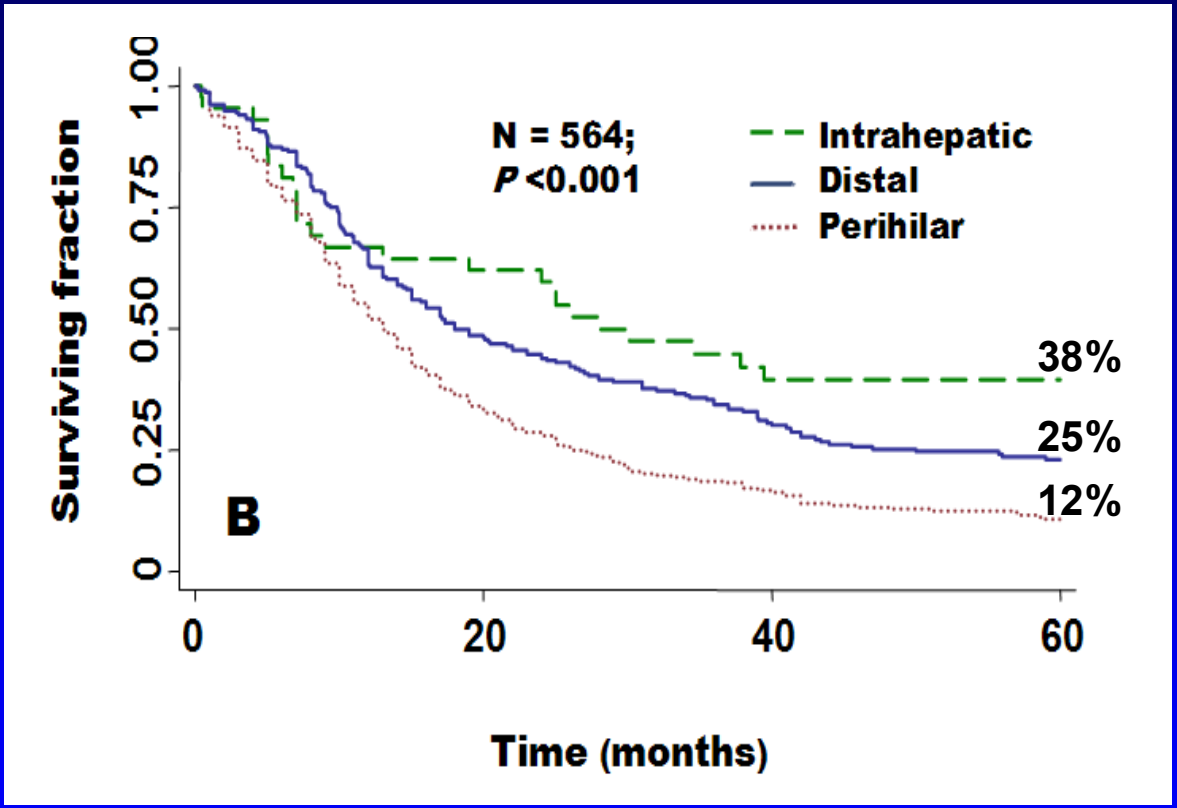
Distal

- 20-30%
- 10-15% of peripancreatic tumors

Cholangiocarcinoma

Johns Hopkins Experience (1973-2004)

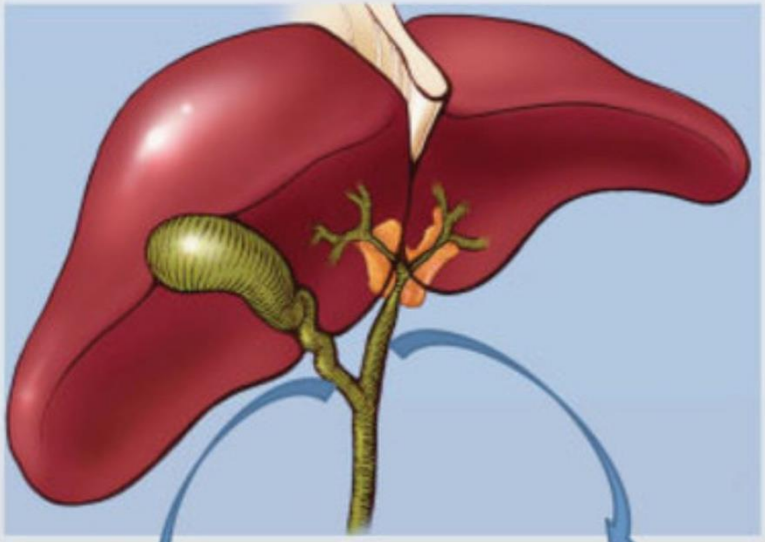




PeriHilar Cholangiocarcinoma

Peripheral circulation

- Tumor markers (e.g. CA 19-9)
- Circulating tumor cells
- Differentially methylated regions in cell-free DNA



Assays on bile duct brushings

- Conventional cytology
- Fluorescence in situ hybridization
- Next-generation sequencing

Molecular diagnostics on bile

- Extracellular vesicles
- MicroRNAs in extracellular vesicles
- Proteomics
- Mutational profiling of cell-free DNA

PeriHilar Cholangiocarcinoma

Treatment

- Complete resection is the only effective therapy.
- Outcomes after R0 resection:
  - 5-year overall survival of 25-40%
  - DFS of 15-25%
- Few patients are resectable.
- R1/2 resections are not uncommon.

Questions to Ask When Considering Surgery?

1. Is complete (R0) resection possible?

2. Can it be done with enough remaining liver, adequate blood supply and good biliary drainage?
    - Extent of disease
    - Vascular involvement
    - Lobar atrophy
    - Metastatic disease
    - Underlying liver disease
    - Other comorbidities

Perihilar Cholangiocarcinoma

CRITERIA OF UNRESECTABILITY

Patient-Related Factors

- Medical contraindication to major abdominal surgery
- Cirrhosis or insufficient remnant hepatic volume

Metastatic Disease

- N2 lymphadenopathy
- Distant metastases

Perihilar Cholangiocarcinoma

CRITERIA OF UNRESECTABILITY

Local Tumor-Related Factors

- Tumor extension to secondary biliary radicles bilaterally
- Encasement or occlusion of the main portal vein proximal to its bifurcation
- Unilateral tumor extension to secondary bile ducts with contralateral vascular encasement or occlusion
- Atrophy of one hepatic lobe with contralateral portal vein encasement or secondary biliary extension

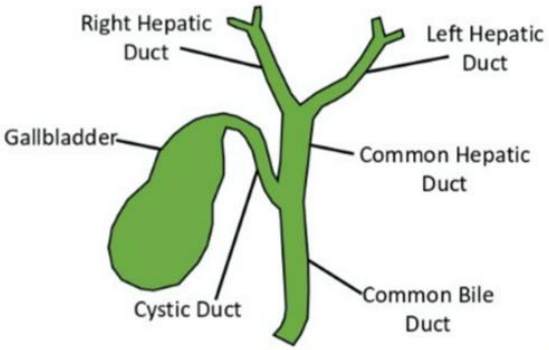
Aggressive Surgical Treatment

- True resectability is defined at surgery
- Pre-operative evaluation of resectability is often difficult
- No histologic confirmation is usually needed
- Liver Resection – Biliary Resection-Reconstruction
- Vascular Resection
- Surgical exploration!!!

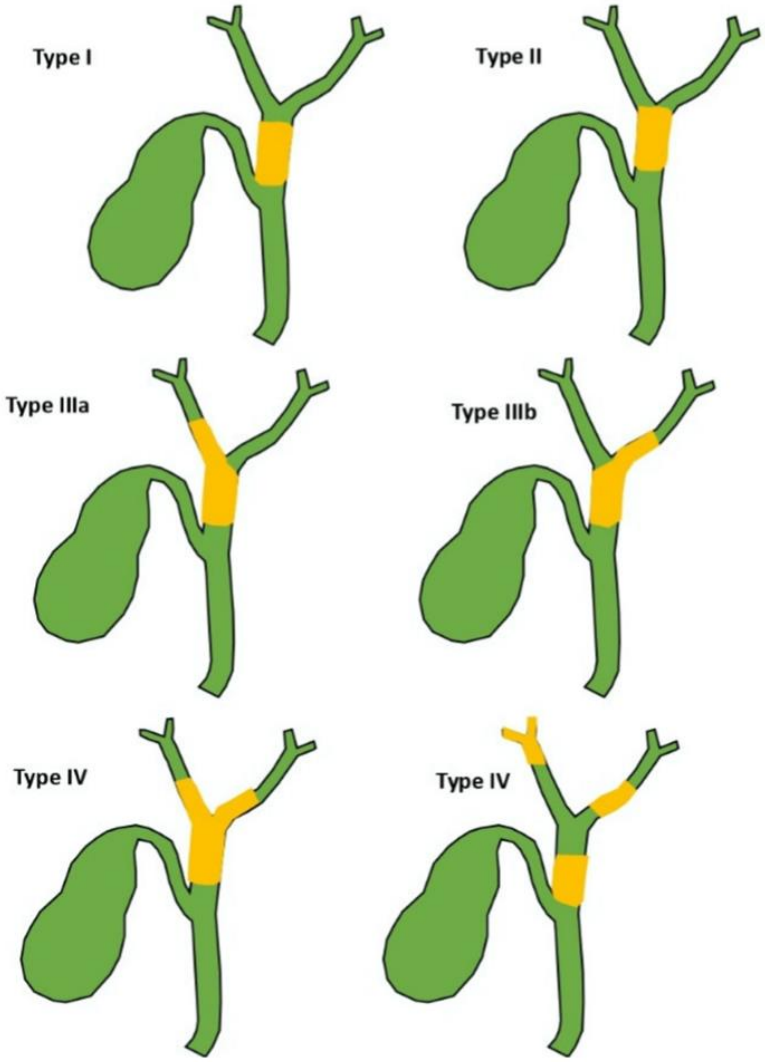
Sue CW, et al. Ann Surg 1996

Neuhaus O, et al. J Hepatobiliary Pancrat Surg 2000

Bismuth-Corlette Classification of Biliary Extent of Hilar Cholangiocarcinoma



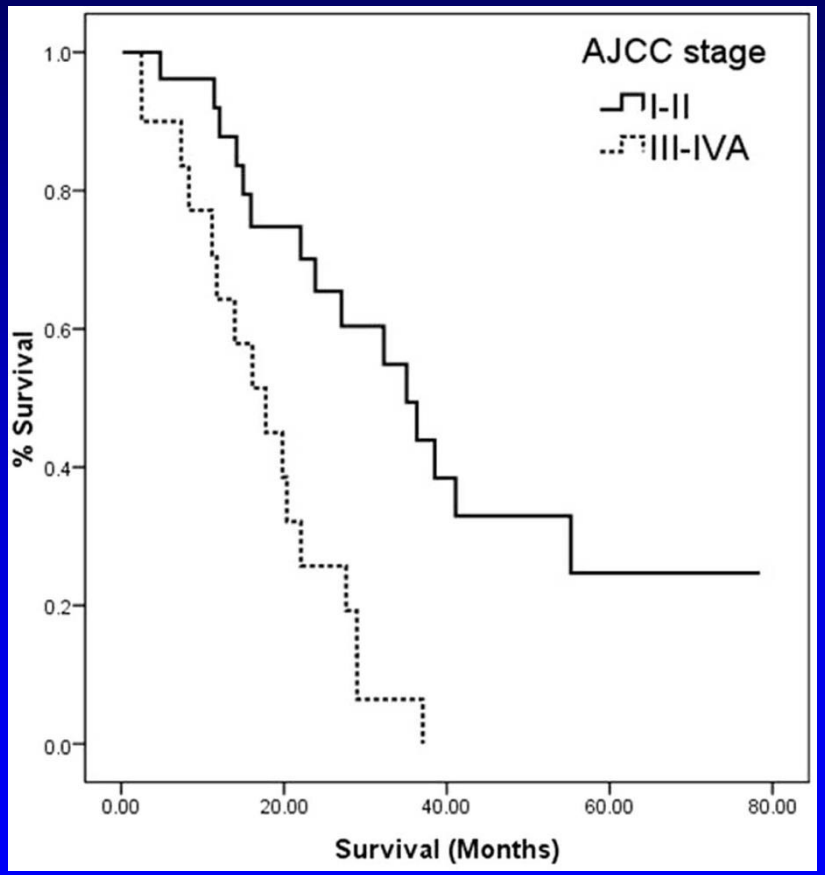
Bismuth-Corlette Classification Perihilar Cholangiocarcinoma	
Type I	Tumor below the confluence of the left and right hepatic ducts
Type II	Tumor reaching the confluence of the left and right hepatic ducts
Type IIIa	Tumor involving the confluence and right hepatic duct
Type IIIb	Tumor involving the confluence and left hepatic duct
Type IV	Tumor involves the confluence and both the left and right hepatic ducts
Type IV	Multicentric tumors



TNM Classification 7th Ed

Table 2 Perihilar bile duct tumors (American Joint Commission on Cancer Staging 7th edition)

T1	Tumor confined to bile duct histologically
T2a	Tumor beyond the wall of bile duct into adjacent fat
T2b	Tumor beyond the wall of bile duct into liver parenchyma
T3	Tumor invades ipsilateral portal vein (R or L) or hepatic artery (R or L)
T4	Tumor invades (1) Main portal vein or its branches bilaterally (or) (2) Common hepatic artery (or) (3) The second-order biliary radicals bilaterally (4) Unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement
Node	
Nx	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis (including nodes along the cystic duct, common bile duct, hepatic artery, and portal vein)
N2	Metastasis to periaortic, pericaval, superior mesenteric artery, and/or celiac artery lymph nodes
Metastasis	
M0	No distant metastasis
M1	Distant metastasis
Tumor stage AJCC staging 6th edition	
0	Tis, N0, M0
I	T1, N0, M0
II	T2a-b, N0, M0
IIIa	T3, N0, M0
IIIb	T1 or T2 T3, N1, M0
IVa	T4, N0 N1, M0
IVb	Any T, N2, M0 Any T, any N, M1



American Joint Committee on Cancer. AJCC cancer staging manual. 7th ed. Springer, 2011

Evaluation of the New American Joint Committee on Cancer Staging Manual 8th Edition for Perihilar Cholangiocarcinoma

pCCA 8th TNM Classification

Table 1 American Joint Committee on Cancer (AJCC) staging system by tumor–node–metastasis (TNM) stage on imaging

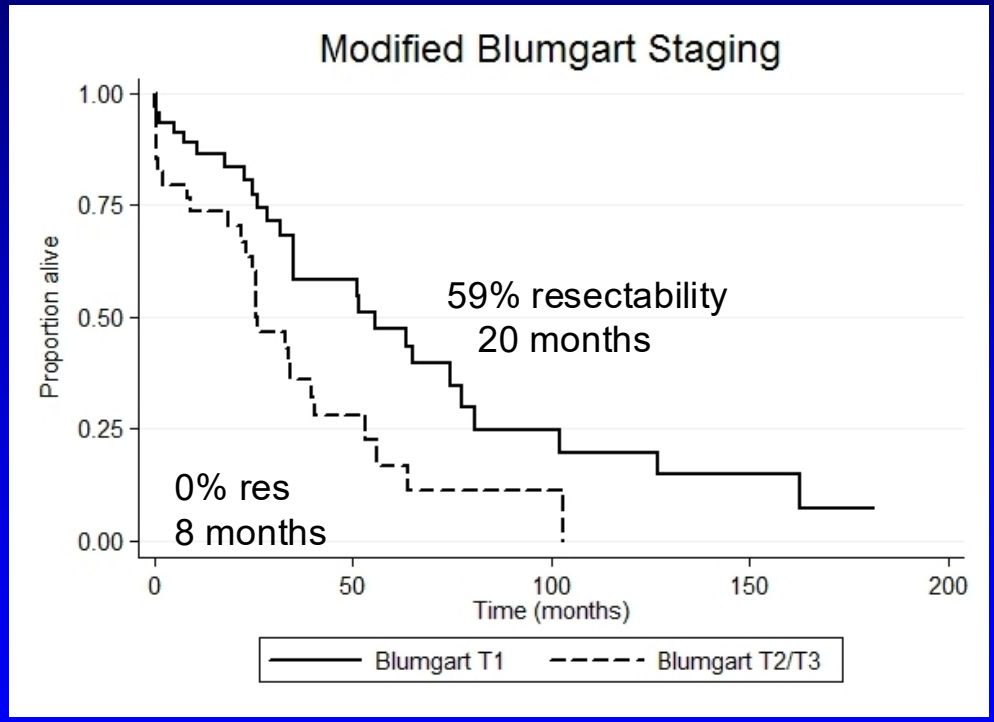
Stage	AJCC, 7th edition	AJCC, 8th edition
Tumor (T) stage		
T1	Tumor confined to the bile duct, with extension up to the muscle layer or fibrous tissue	
T2a	Tumor invades beyond the wall of the bile duct to surrounding adipose tissue	
T2b	Tumor invades adjacent hepatic parenchyma	
T3	Tumor invades unilateral branches of the PV or HA	
T4	Tumor invades main PV or its branches bilaterally, or the common hepatic artery, second-order bile ducts bilaterally, unilateral second-order bile ducts with contralateral portal vein or hepatic artery involvement	Tumor invades main PV or its branches bilaterally, or the common hepatic artery, or unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement.
Node (N) stage		
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	Regional lymph node metastasis: hilar (along CBD, cystic duct, HA, or PV)	One to three positive lymph nodes typically involving the hilar, cystic duct, common bile duct, hepatic artery, posterior pancreatoduodenal, and portal vein lymph nodes
N2	Metastasis to periaortic, pericaval, SMA, or coeliac lymph nodes	Four or more positive lymph nodes from the sites described for N1
Metastasis (M) stage		
M0	No distant metastasis	No distant metastasis
M1	Distant metastasis	Distant metastasis (includes lymph node metastasis distant to the hepatoduodenal ligament)

J Gastrointest Surg (2020) 24:1612–1618

MSKCC Classification of HCC

Summary of the T classification of the AJCC (seventh edition) and MSKCC staging systems

	AJCC	MSKCC
T1	Confined to the bile duct	Involves biliary confluence; ± unilateral extension to second-order biliary radicals
T2	Invades beyond the wall of the bile duct to adjacent adipose (a) or hepatic parenchyma (b)	T1 ± ipsilateral PV involvement ± ipsilateral hepatic lobar atrophy
T3	Invades unilateral branches of PV or HA	Involves biliary confluence with bilateral extension to second-order radicles; or unilateral extension to second-order radicles with contralateral PV involvement or contralateral lobar atrophy; or main or bilateral PV involvement
T4	Invades main PV or its branches bilaterally; or CHA; or second-order biliary radicles bilaterally; or unilateral second-order biliary radicles with contralateral PV or HA	—

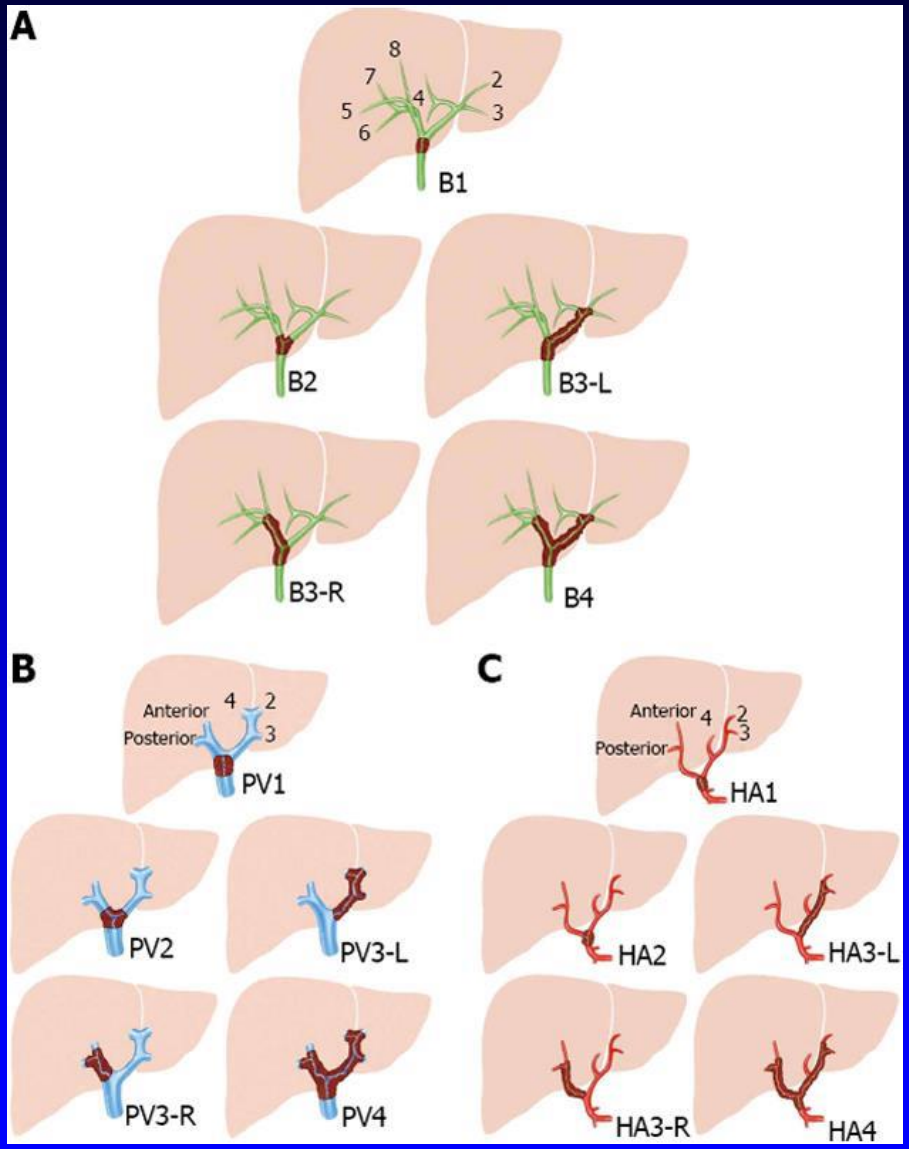


Jarnagin WR, et al. Ann Surg 2001

Table 3 Consensus classification (European Hepato-Pancreato-Biliary Association)

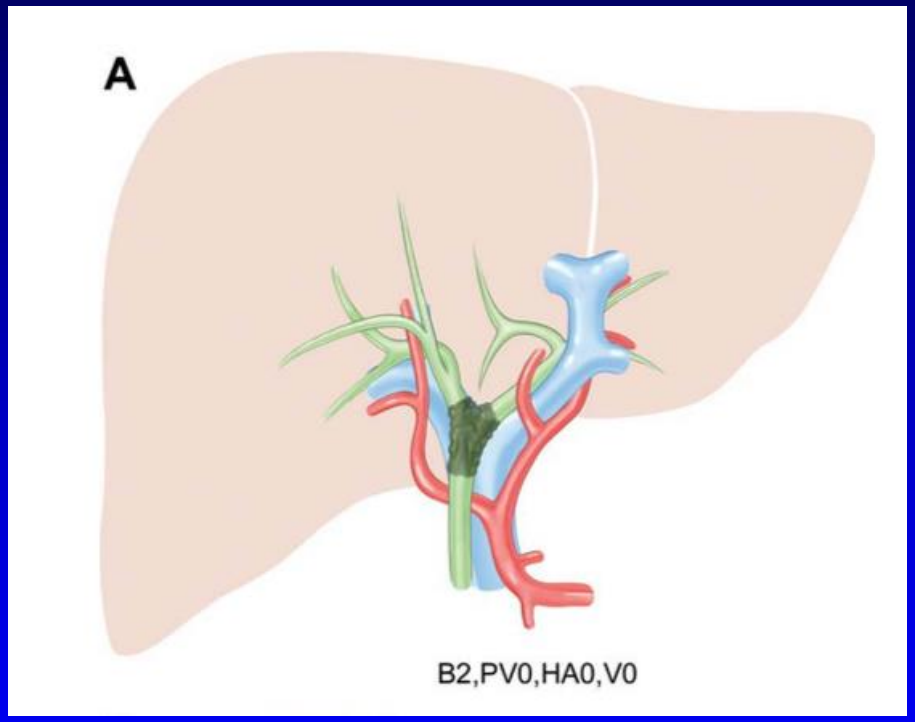
Label	Side location	Description
Bile duct (B)		
B1		Common bile duct
B2		Hepatic duct confluence
B3	R	Right hepatic duct
B3	L	Left hepatic duct
B4		Right and left hepatic duct
Tumor size (T)		
T1		< 1 cm
T2		1-3 cm
T3		⩾ 3 cm
Tumor form (F)		
Sclerosing		Sclerosing (or periductal)
Mass		Mass-forming (or nodular)
Mixed		Sclerosing and mass-forming
Polypoid		Polypoid (or intraductal)
Involvement (> 180°) of the portal vein (PV)		
PV0		No portal involvement
PV1		Main portal vein
PV2		Portal vein bifurcation
PV3	R	Right portal vein
PV3	L	Left portal vein
PV4		Right and left portal veins
Involvement (> 180°) of the hepatic artery (HA)		
HA0		No portal involvement
HA1		Proper hepatic artery
HA2		Hepatic artery bifurcation
HA3	R	Right hepatic artery
HA3	L	Left hepatic artery
HA4		Right and left hepatic artery
Liver remnant volume (V)		
V0		No information on the volume needed (liver resection not foreseen)
V%	Indicate segments	Percentage of the total volume of a putative remnant liver after resection
Underlying liver disease (D)		Fibrosis
		Nonalcoholic steatohepatitis
		Primary sclerosing cholangitis
Lymph nodes (N)		
N0		No lymph node involvement
N1		Hilar and/or hepatic artery lymph node involvement
N2		Periaortic lymph node involvement
Metastases (M)		
M0		No distant metastases
M1		Distant metastases (including liver and peritoneal metastases)

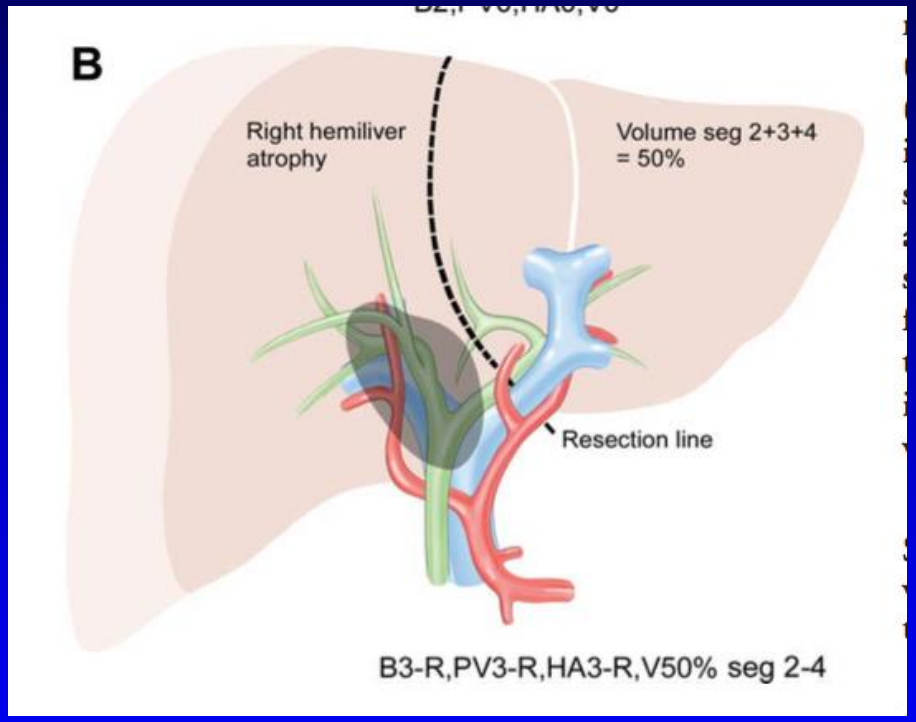
EHPBA Consensus Classification



Toouli J, et al. Oxford: HPB, 2008

EHPBA Classification



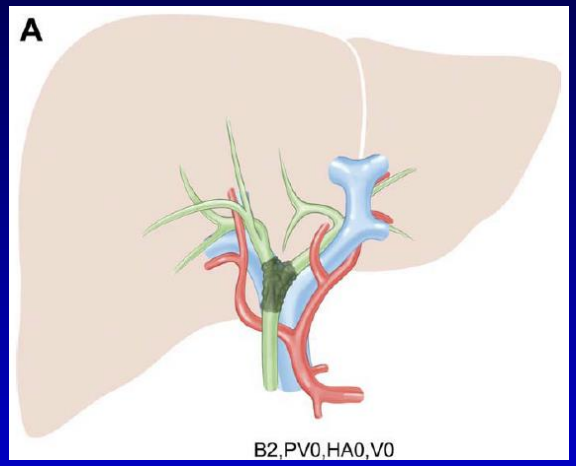


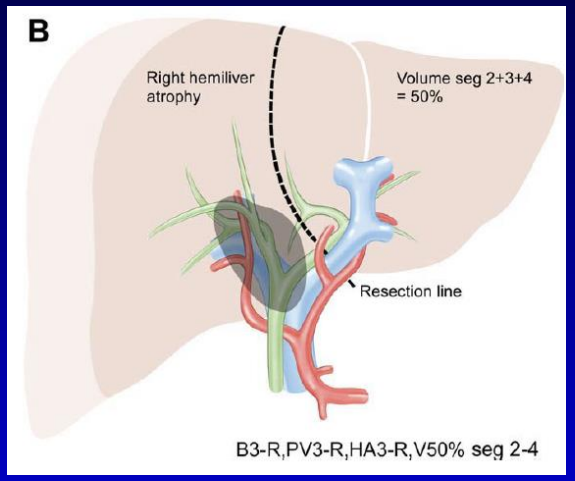
2.5 cm tumor involving the bile duct confluence

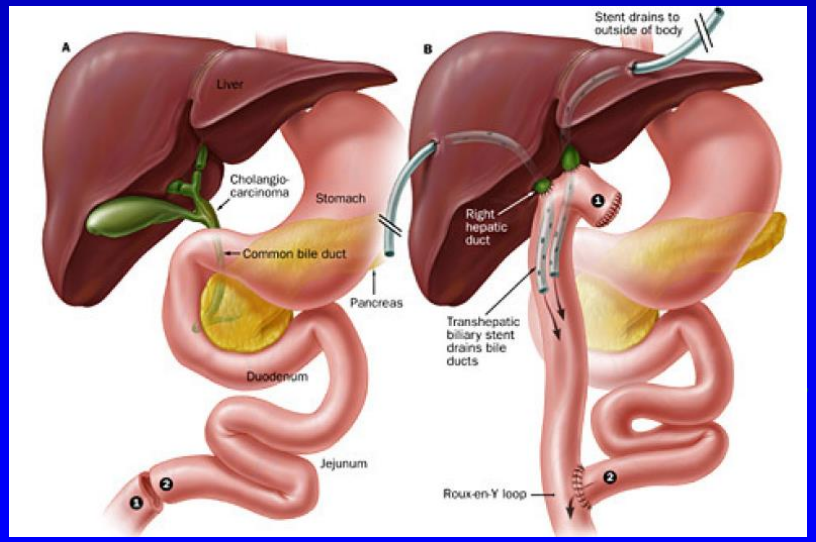
a larger tumor involving the right biliary system, hepatic artery, and portal vein that is associated with right hemiliver atrophy

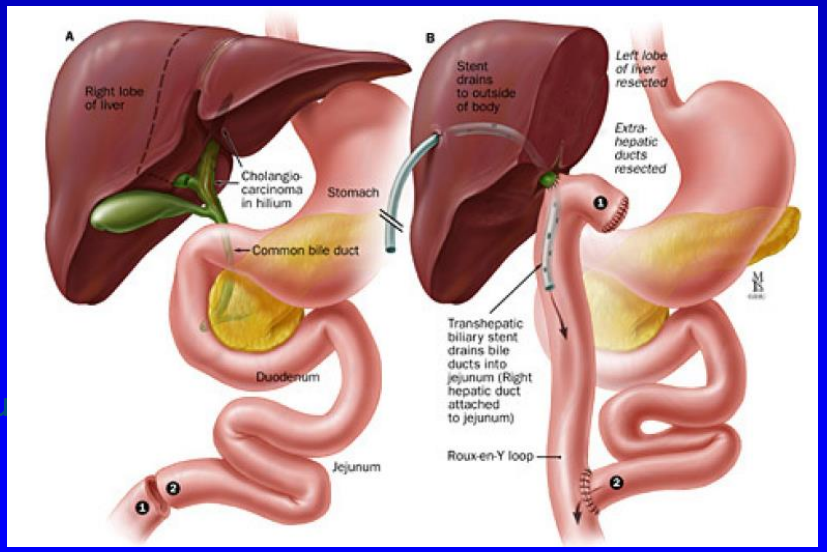
New Staging System and a Registry for Perihilar Cholangiocarcinoma

pCCA – Surgical Classification - Extended









HEPATOLOGY, April 2011

Classification Systems

Table 2 Comparison of different classification systems.

Classification systems	Basis of classification	Advantage	Disadvantage
Bismuth–Corlette Classification System	Tumor location and the extent of ductal infiltration	1. One of the first anatomical classification systems to describe proximal involvement of tumor into the bile ducts	1. Absence of parameters such as vascular encasement, lymph node metastases and hepatic atrophy 2. Limited to predict resectability and survival
Memorial Sloan-Kettering Cancer Center Staging System	In addition to bile duct involvement, portal vein involvement and lobar atrophy, tumor location and extent of bile duct involvement were taken into account as well	1. The resectability can be determined 2. Predict prognosis	1. Could not reflect pathological factors such as LN metastasis and distant metastasis
Tumor-Node-Metastasis Staging System	The scope of the primary tumor, lymph node metastasis and distant metastasis.	1. Mainly used postoperatively as a prognostic tool	1. Results are usually obtained after surgery, so as a preoperative evaluation of resectability is of little significance 2. The T-classification criteria did not stratify patients with regard to prognosis (an improved T-stage was in version 8)
New staging system proposed by International Cholangiocarcinoma Group	The size and the extent of the tumor, the involvement of the hepatic artery, portal vein and lymph nodes, distant metastases, and the volume of the putative remnant liver after resection.	1. Making a more accurate judgment on the resectability of PHC, surgical selection and prognosis	1. A large number of clinical data and studies are needed to verify the effectiveness of this new staging system

Perihilar Cholangiocarcinoma

Goal of Resection:
Complete Tumor Excision with Negative Margins

Recommended

ESTABLISHED:

- Excision of supraduodenal bile duct
- Cholecystectomy
- Restore bilioenteric continuity

LESS CONTROVERSIAL:

- Routine hepatectomy/caudate
- Portal lymphadenectomy
- Selected major vascular reconstruction

MORE CONTROVERSIAL:

- Routine PV resection (Neuhaus)
- Arterial resections

Perihilar Cholangiocarcinoma

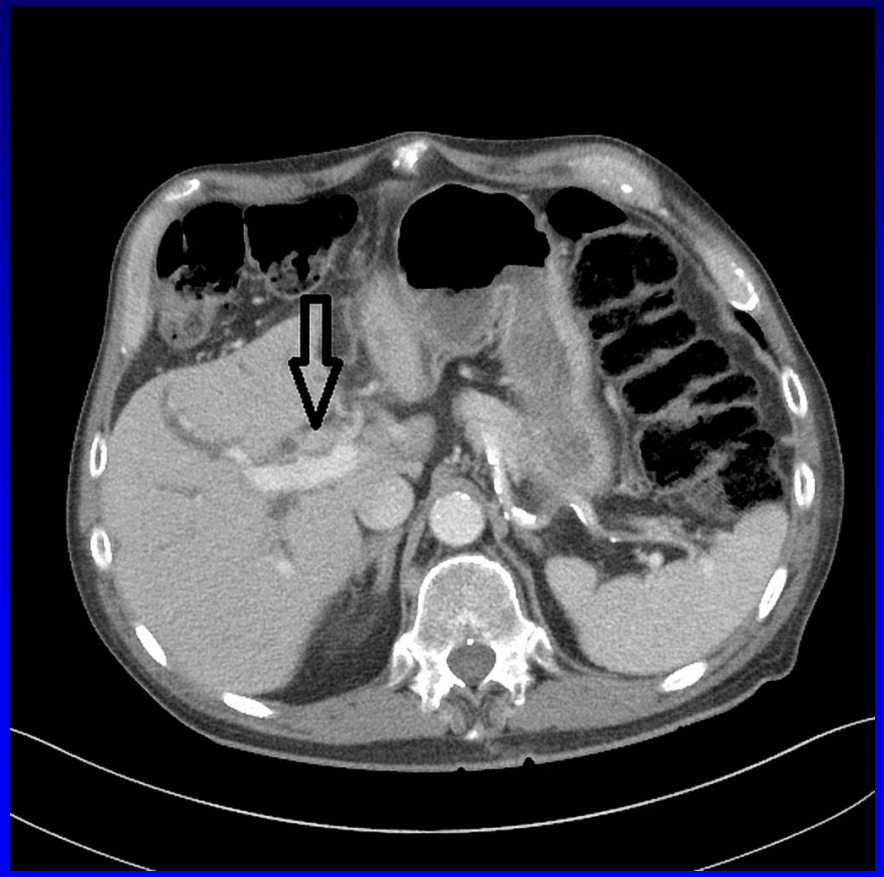
PREOPERATIVE EVALUATION

1. Cholangiography
   - Assessment of extent of biliary ductal involvement
   - ERCP vs MRCP vs PTC
2. Cross-sectional imaging
   - Soft tissue extent, lobar atrophy, vascular involvement, remnant volume, metastases
   - CT vs MRI

Controversies:

- Role of preoperative stenting
- FDG-PET
- Staging laparoscopy

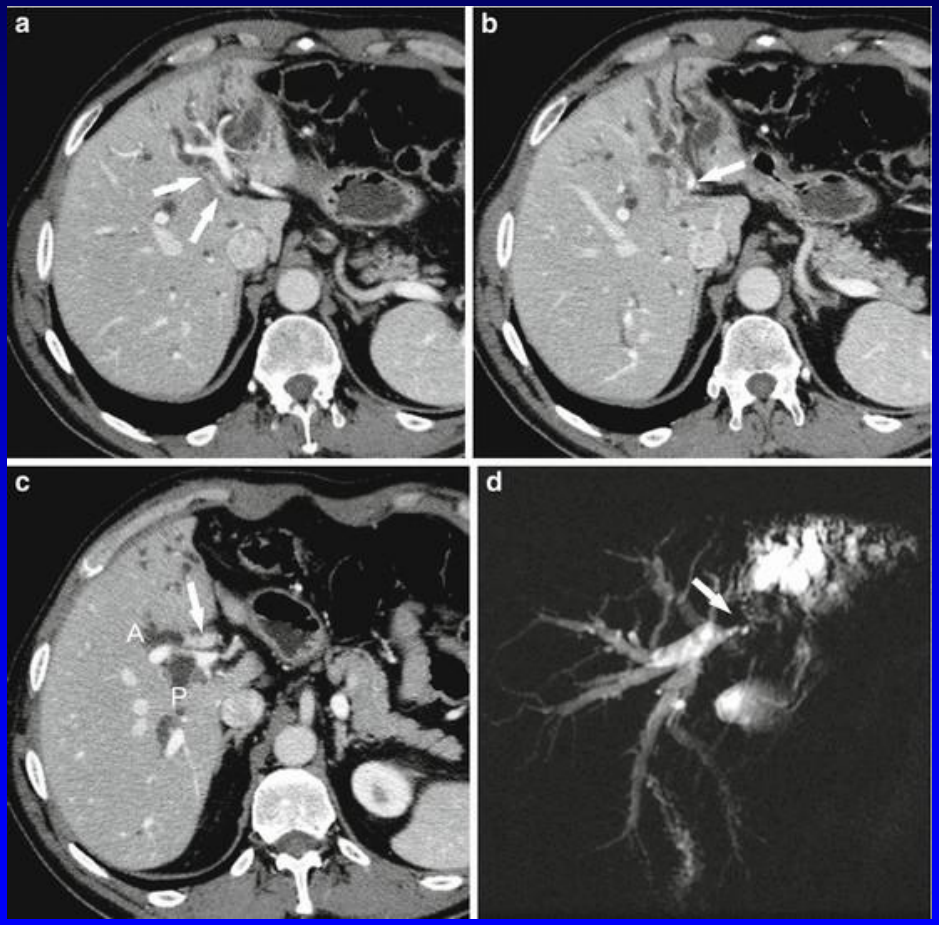
Triple-phase Liver CT scan



”…High quality helical multi-slice MDCT scan with I.V. contrast and appropriately time scans remains the best single test to identify and stage HCC…”

AHPBA/SSAT/SSO/ASCO Consensus Conference on the Multidisciplinary Management of Bile Duct Cancer 2014

Triple-phase Liver CT scan



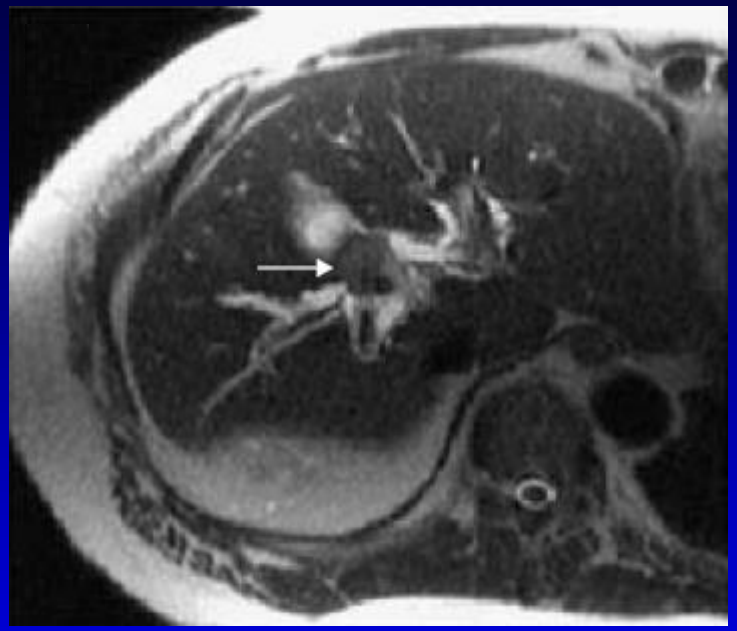
- PV invasion
  - sensitivity 96.3%
  - specificity 92.6%
  - accuracy 94%
- HA invasion >90%
- Bile Duct extension 96%
- Resectability 60-90%

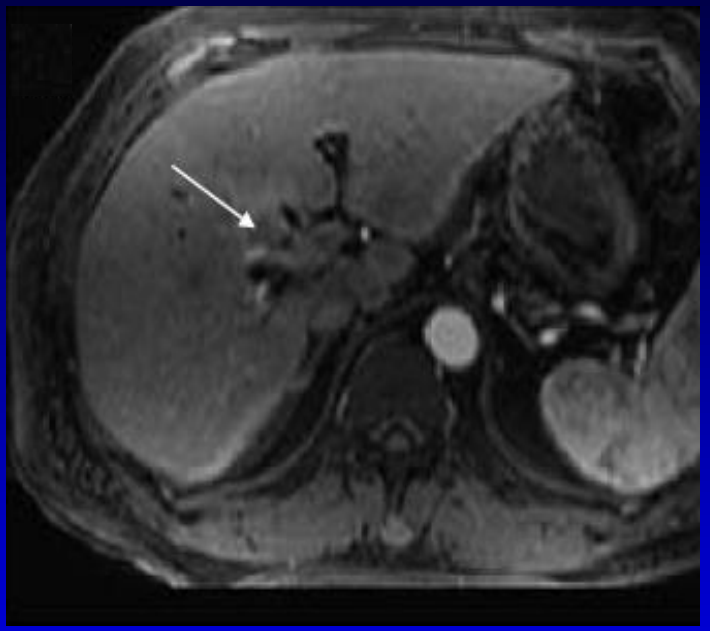
- RHA in Left-sided tumors!!!

- Best before biliary drainage and stents

Nagino M. J Gastroenterol 2012

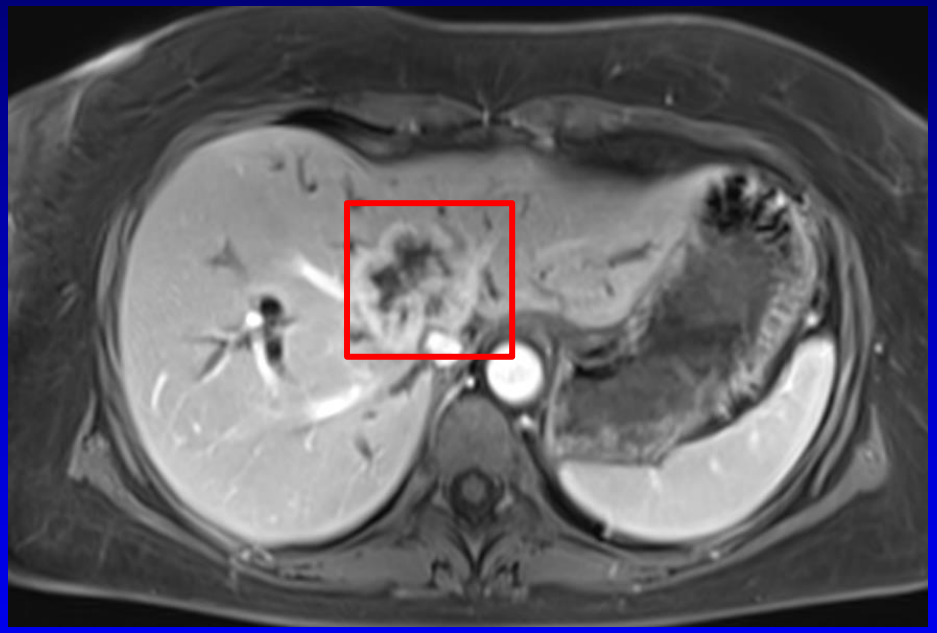
Non-Invasive Imaging: MRI/MRCP

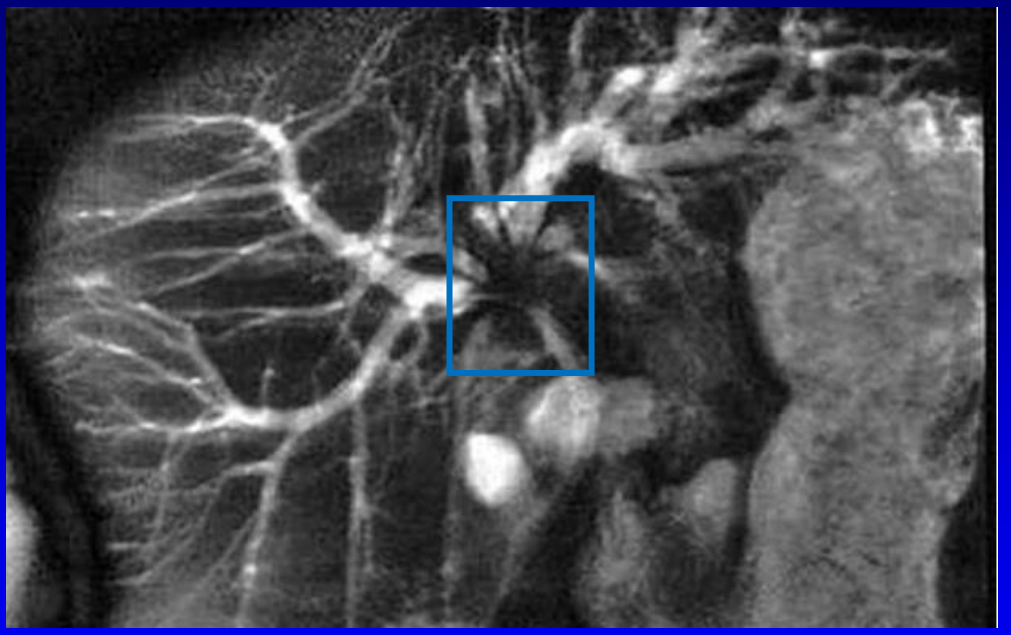




- High quality images of the biliary tree - as good as cholangioscopy for assessing biliary tumor extent*.
- Provides additional data regarding metastases, vascular involvement, lobar atrophy.
- Predicts overall resectability in 80% of cases

pCCA – Different Types of Hilar Invasion





Perihilar Cholangiocarcinoma

Role of FDG-PET

	GC	Nodular CC (Mass 1 cm)	Infiltrating CC (No mass)	Total CC
Total patients	14	22	14	36
True positive	7	17	2	19
False negative	2	3	9	12
True negative	4	1	3	4
False positive	1	1	0	1
Sensitivity	78% (7/9)	85% (17/20)	18% (2/11)	61% (19/31)
Specificity	80% (4/5)	50% (1/2)	100% (3/3)	80% (4/5)
PPV	88% (7/8)	94% (17/18)	100% (2/2)	95% (19/20)
NPV	67% (4/6)	25% (1/4)	25% (3/12)	25% (4/16)

- Not useful for infiltrating cholangiocarcinoma
- Extensive desmoplastic reaction – poor vascularity
- False negatives due to low volume metastases
- False positives due to stents or recent cholecystectomy

Pathological Confirmation is NOT required before Surgical Resection in Suspected pHCC!!!

- ERCP
  brush cytology<50%
- PTC
- Per oral cholangioscopy (Spyglass)
- Intraductal US: op dependent
- EUS – FNAB: LNs<30%
- Tumor seeding
- FISH analysis!!!

Consider benign causes:

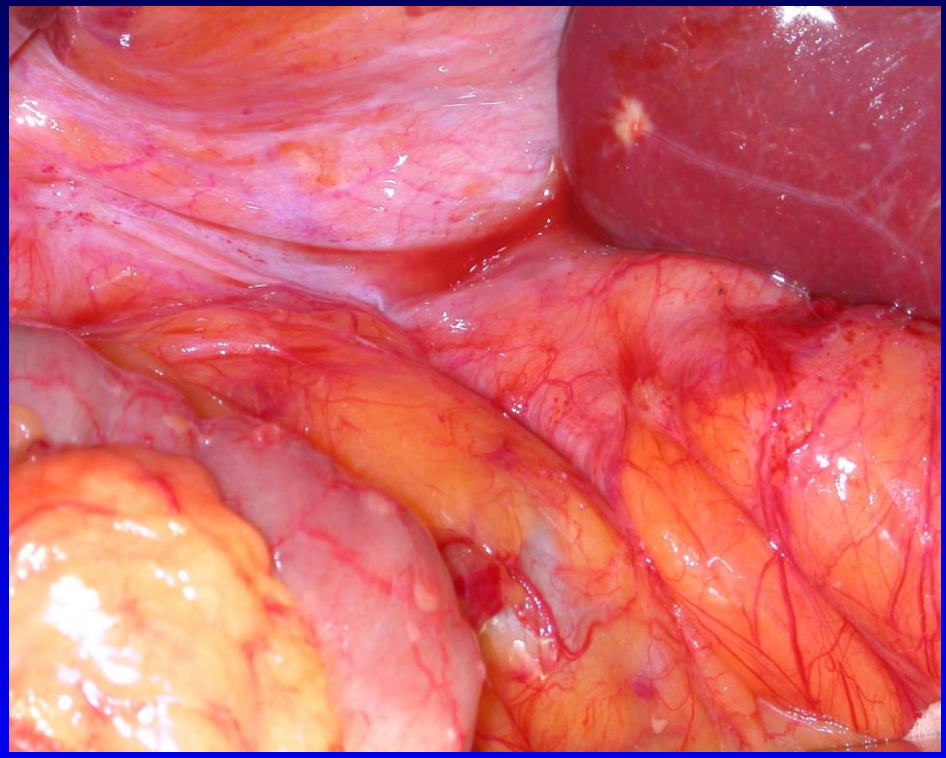
-IgG4 cholangiopathy
-Mirrizi's syndrome
-PSC
-Previous biliary surgery

Forsmark CE, et al. HPB 2015 AHPBA/SSAT/SSO/ASCO Consensus Conference on the Multidisciplinary Management of Bile Duct Cancer

Staging Laparoscopy

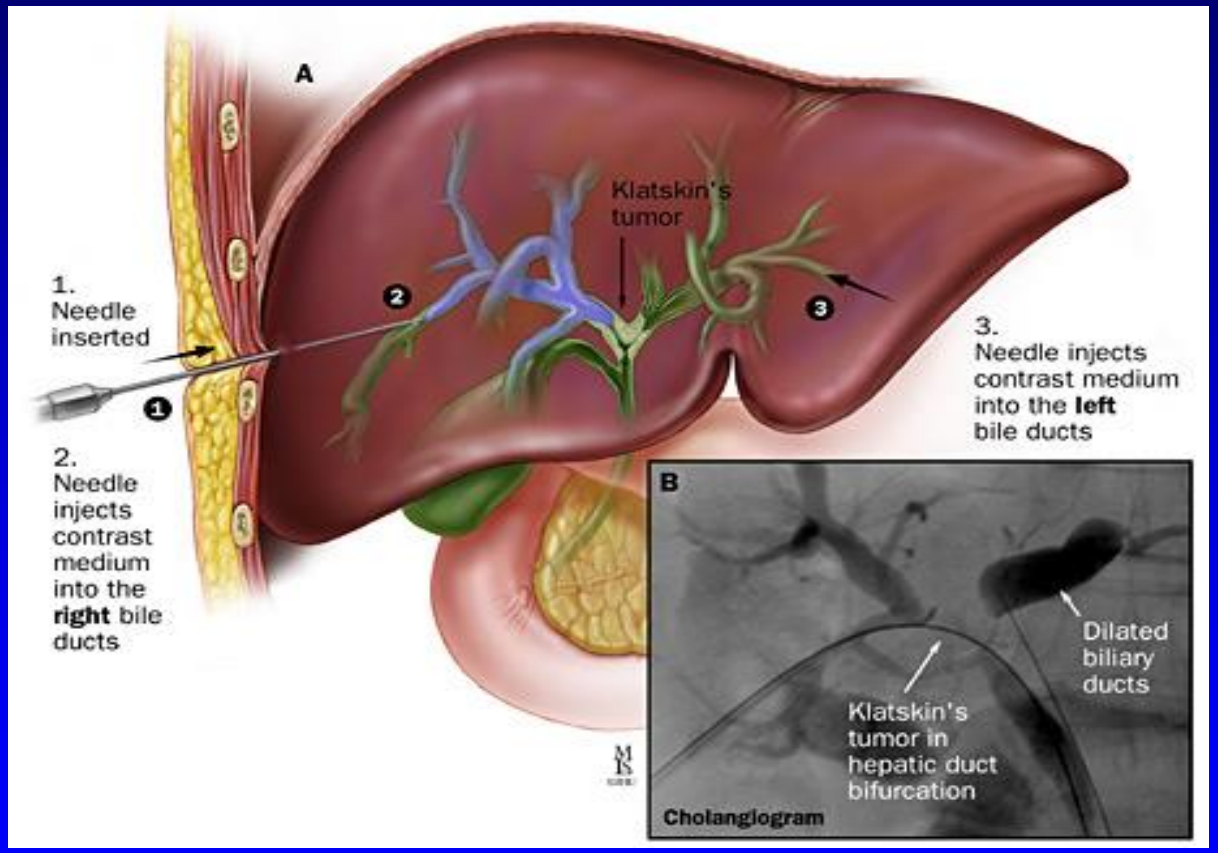
Study	No. of patients	Yield (%)	Accuracy (%)
Tilleman[a]	110	41	72
Connor	84	24	53
Goere	20	25	45
Ruys	175	14	32
Barlow	100	45	71

- Most useful to detect liver and/or peritoneal metastasis
- In locally advanced tumors T2/T3
- Increased levels of CA19.9> 1000
- Combined with LapUS
- Fewer nontherapeutic laparotomies
- Shorter LOS



Ruys AT, et al. Ann Surg Oncol 2011
Barlow AD, et al. Langenbeck's Arch Surg 2013

Biliary Stents for the Management of HCC



Preoperative Biliary Drainage
Pros

Treatment

- **Pre-operative biliary drainage**
  - Cholestasis, liver dysfunction, biliary cirrhosis develop rapidly with un-relieved obstruction.
    - Hyperbilirubinemia impairs liver regeneration
  - Liver dysfunction increases post-operative mortality and morbidity
    - Reduces resistance to systemic infection
  - S.Bili > 10 mg% - Pre-operative biliary drainage to bring down to 2.5-3.0 mg%

Roger et al. Surg Clin N Am 2008; 1409-28

Treatment

- **Pre-operative biliary drainage**
  - Cholestasis, liver dysfunction, biliary cirrhosis develop rapidly with un-relieved obstruction.
  - Liver dysfunction increases post-operative mortality and morbidity
  - S.Bili > 10 mg% - Pre-operative biliary drainage to bring down to 2.5-3.0 mg%
    - Jaundice predisposes to mortality 36%vs16% morbidity 50%vs15% after hepatectomy

Roger et al. Surg Clin N Am 2008

Preoperative Biliary Drainage
Cons

Preoperative Biliary Drainage Before Resection for Hilar Cholangiocarcinoma: Whether or Not? A Systematic Review

- **Pre-operative biliary drainage**
  - Cholestasis, liver dysfunction, biliary cirrhosis develop rapidly with un-relieved obstruction.
  - Liver dysfunction increases post-operative mortality and morbidity
  - S.Bili > 10 mg% - Pre-operative biliary drainage to bring down to 2.5-3.0 mg%

Roger et al. Surg Clin N Am 2008; 1409-28

- PTBD only when:

1. Cholangitis
2. Renal dysfunction
3. Possible vascular invasion on the side of the FLR
4. PVE

Liu F, et al. Dig Sci 2011
Cherqui D, et al Arch Surg 2000

Preoperative Biliary Drainage

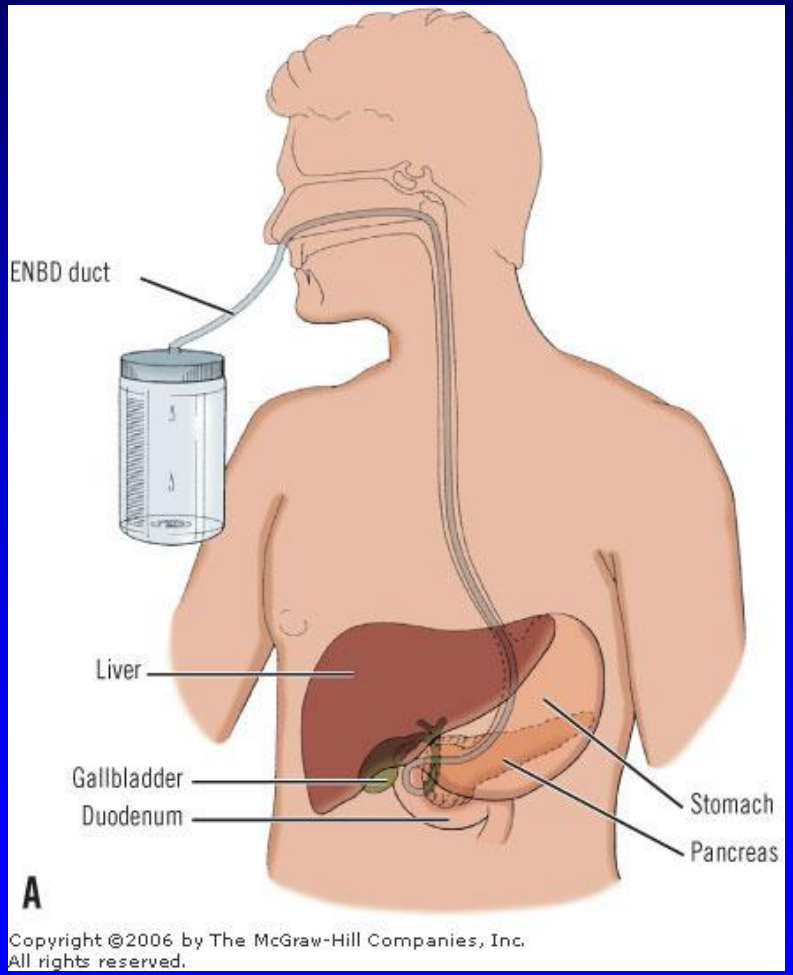
	HCCA by Bismuth classification, n[a]
EBD	I – 48
	II – 87
	III – 139
	IV – 106
PTBD	I – 9
	II – 41
	III – 77
	IV – 62

Table 3 Post-procedure complications and post-operative results by type of PBD[a]

	EBD, total (%)	PTBD, total (%)	Studies explicitly reported in, n
Post-procedure complications			
Cholangitis	153/557 (27)	51/380 (13)	6 (EBD); 7 (PTBD)
Pancreatitis	51/562 (9)	3/42 (7)	7 (EBD); 1 (PTBD)
Catheter dislocation/dislodgment	21/90 (23)	7/156 (4)	1 (EBD); 3 (PTBD)
Haemobilia/Bleeding	1/87 (1)	14/277 (5)	1 (EBD); 6 (PTBD)
Portal vein injury and/or thrombosis	–	15/248 (6)	3 (PTBD)
Retroperitoneal or duodenal perforation	4/257 (2)	–	3 (EBD)
Cancer seeding (tract)	–	10/248 (4)[b]	3 (PTBD)
Failure to proceed to surgery	27/164 (16)	9/72 (13)	1 (EBD); 2 (PTBD)[e]
Others			
Biliary perforation/intra-peritoneal bile leak or peritonitis	2	1	2 (EBD); 1 (PTBD)
External bile leak	–	6	1 (PTBD)
AV shunt formation	–	2	1 (PTBD)
Post-operative results			
Mortality[c]	6/281 (2)	23/416 (6)	
Morbidity[c]			
Hepatic failure	22/194 (11)	56/432 (13)	
Sepsis/abscess/cholangitis	17/120 (14)	44/262 (17)	
Bile leak	NR	21/166 (13)	
Anastomotic leak	NR	25/205 (12)	
Survival, %[d]			
1-year, median (range)	91 (89–92)	73 (67–90)	2 (EBD); 6 (PTBD)
5-year, median (range)	46 (41–51)	30 (11–60)	2 (EBD); 5 (PTBD)

Kennedy TJ, et al. HPB(Oxford) 2009
Hameed A, et al HPB 2016

Endoscopic Naso-Biliary Drainage



- Multiple PTBDs
  - Hemorrhage 15%
  - Sepsis 10%
  - Biliary injury 9%
  - Seeding meta 5%
- EBDs
  - Dislocation-Recurrent cholangitis 60%
- ENBD Unilateral in Future Remnant Lobe

Kawakamy H, et al. J Gastroenterol 2011
Kawashima H, et al. Ann Surg 2012
Takahashi Y, et al. Br J Surg 2012

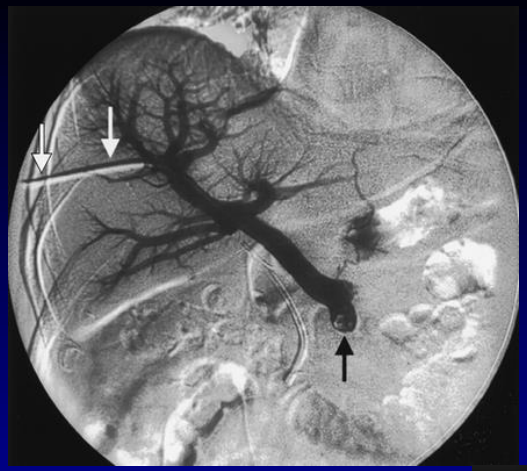
Preoperative Biliary Drainage

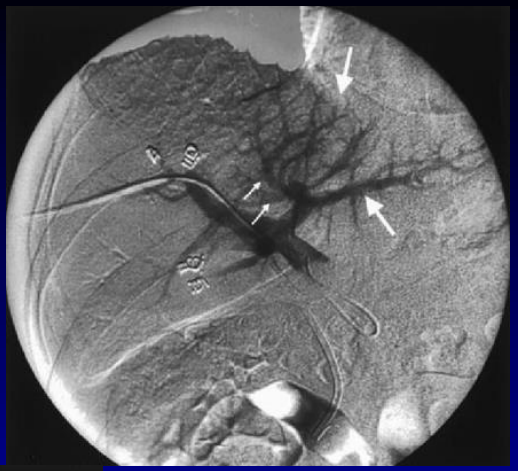
- EBD and PTBD are equally effective
- Unilateral drainage of the FLR
- Single and temporary PBD
- Drainage of contralateral liver only when persistent jaundice/ sepsis
- PBD always when PVE is performed
- PBD when FLR <30 - 40%
- PBD when vascular reconstruction is anticipated

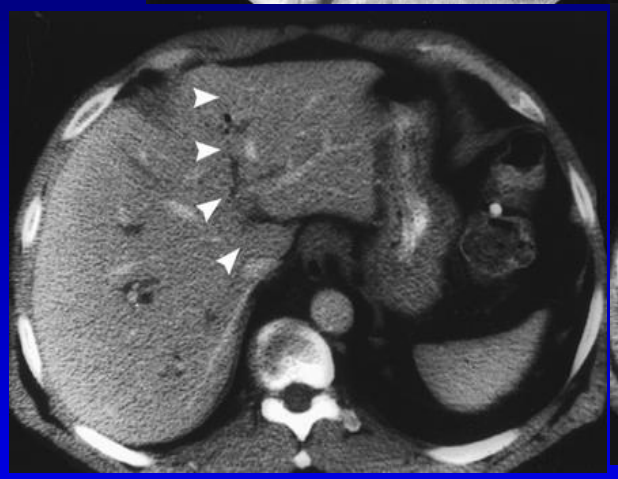
PTBD should be THE STANDARD OF CARE!!!

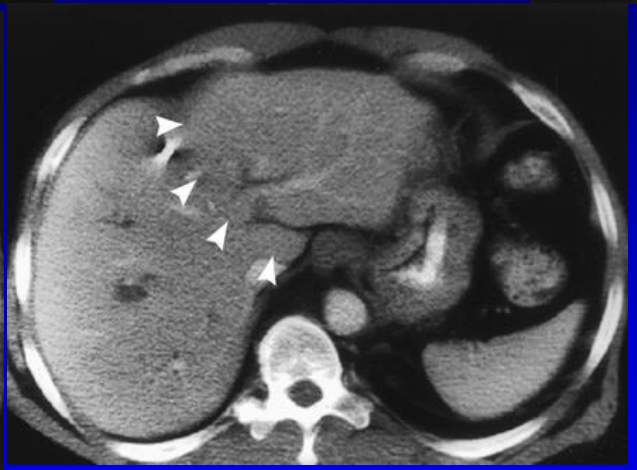
Hameed A, et al HPB 2016

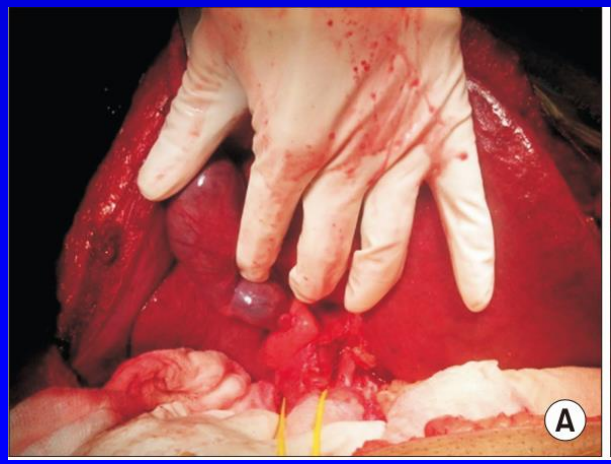
PVE

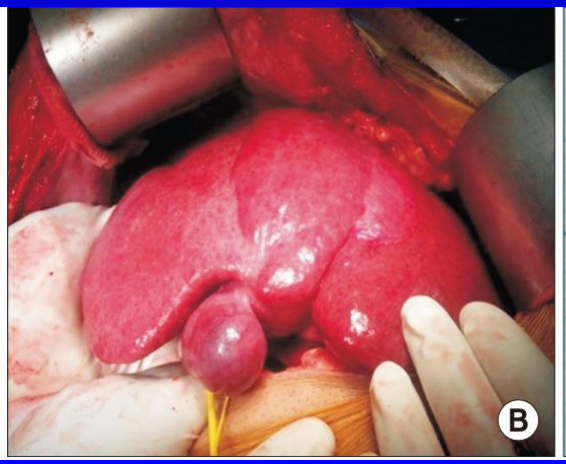


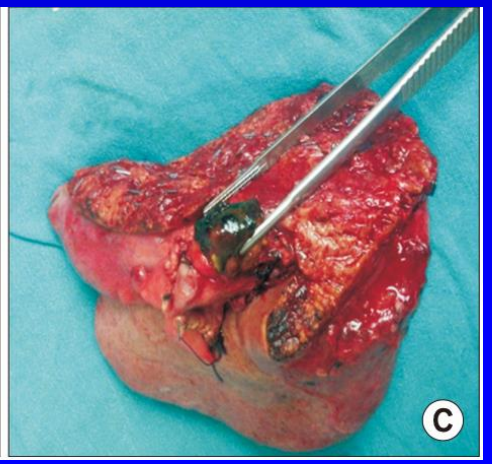






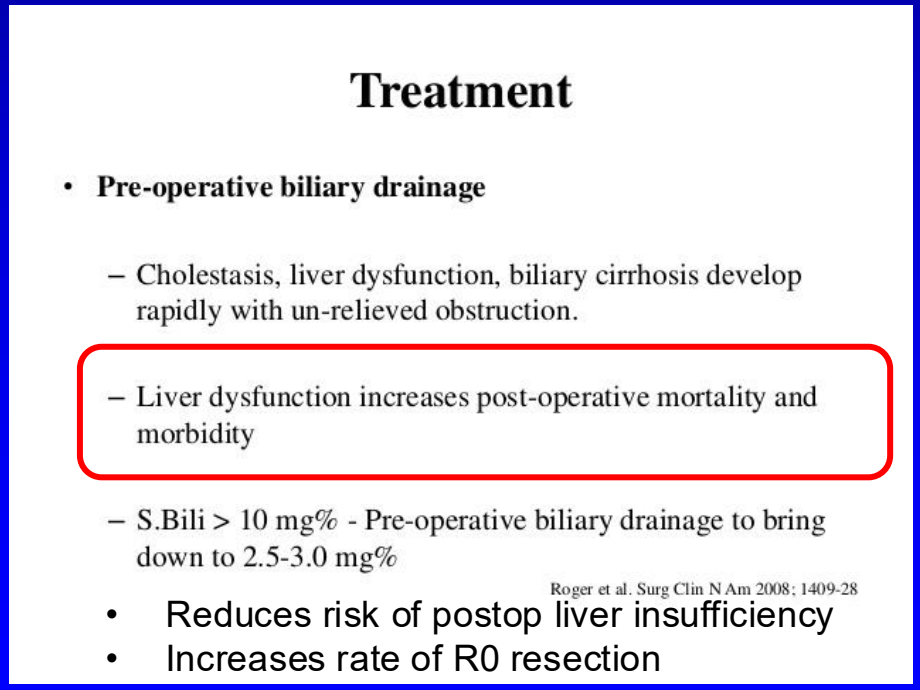






PVE

	Pts with HCC	Negative Resection Margins	5year Survival
PVE	51	75%	40%
Non-PVE	18	45% p<0.0178	6% p<0.0001



Treatment

- **Pre-operative biliary drainage**
  - Cholestasis, liver dysfunction, biliary cirrhosis develop rapidly with un-relieved obstruction.
  - Liver dysfunction increases post-operative mortality and morbidity
  - S.Bili > 10 mg% - Pre-operative biliary drainage to bring down to 2.5-3.0 mg%

Roger et al. Surg Clin N Am 2008; 1409-28

- Reduces risk of postop liver insufficiency
- Increases rate of R0 resection

- No RCTs
- When FLR: 25-30%
- In cirrhotic livers
- Before any major hepatectomy
- Always with PTBD

Van Gulik, et al. Dig Surg 2011
Hemming AW, et al. Ann Surg 2005

PVE

Preoperative Portal Vein Embolization for Major Liver Resection

- **Pre-operative biliary drainage**
  - Cholestasis, liver dysfunction, biliary cirrhosis develop rapidly with un-relieved obstruction.
  - Liver dysfunction increases post-operative mortality and morbidity
  - S.Bili > 10 mg% - Pre-operative biliary drainage to bring down to 2.5-3.0 mg%

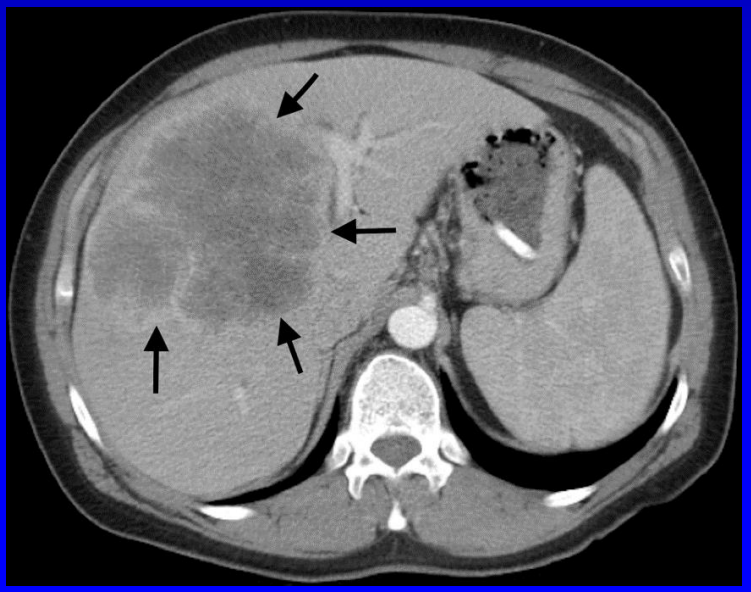
Roger et al. Surg Clin N Am 2008; 1409-28

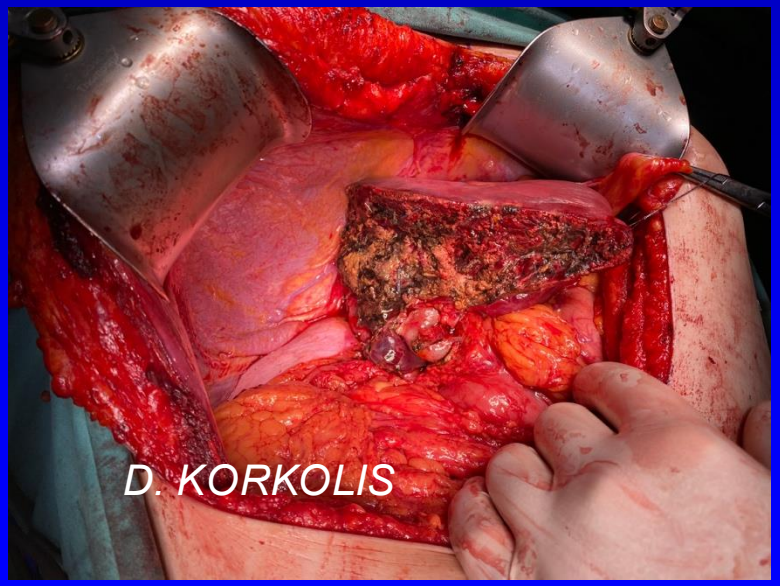
PVE Disadvantages:

- Waiting time for FLR to hypertrophy
- Preoperative difficulty in deciding whether a Right or Left Hemihepatectomy is necessary in centrally placed HCC

Abulkhir A, et al. Ann Surg 2008

Liver Venous Deprivation – PVE+HVE



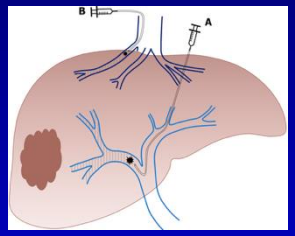


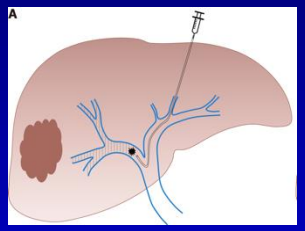
FLR Augmentation

OXFORD

BJS, 2021, 1–9
DOI: 10.1093/bjs/znaa149
Original Article

Preoperative portal vein or portal and hepatic vein embolization: DRAGON collaborative group analysis



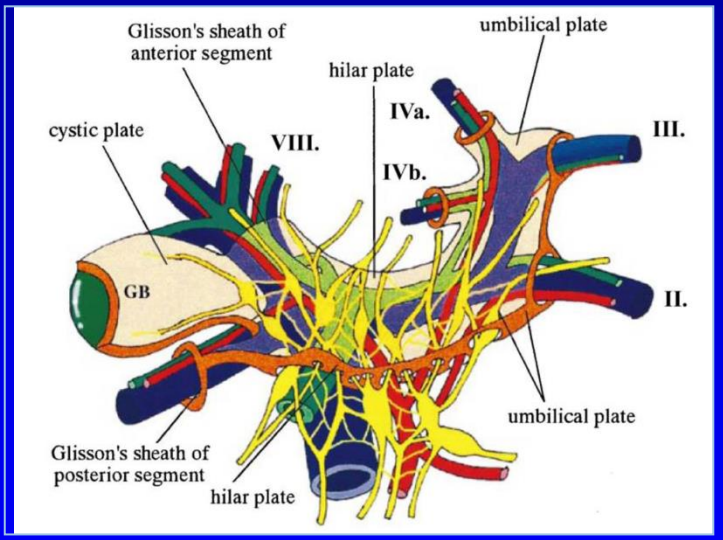


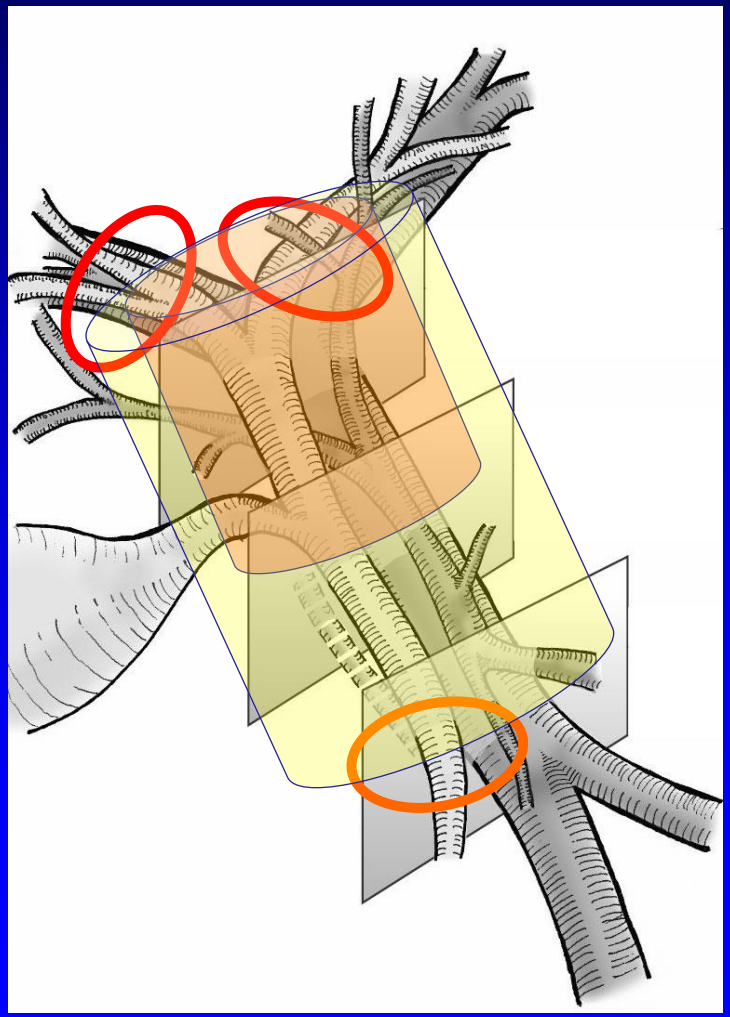
	LVD	PVE	
Liver volume after intervention			
Time from intervention to first volumetry (days)*	17 (13–32)	24 (19–37)	0.009‡
FLR (ml)*	470 (381.9–598.4)	442 (342–562.5)	0.227‡
sFLR (%)*	31 (24–39)	28 (21–37)	0.102‡
LBWR (ml/kg bodyweight)*	0.66 (0.52–0.85)	0.6 (0.45–0.77)	0.105‡
FLR increase (ml/day)*	7 (5–18)	6 (2–9)	0.002‡
%Hypertrophy*	59 (45–79)	48 (24–69)	0.020‡
%Hypertrophy/week*	21 (11–33)	13 (6–20)	< 0.001‡
Degree of hypertropy (%)*	10 (8–14)	9 (5–13)	0.017‡
Kinetic growth rate (sFLR/week)*	3.5 (2.2–7.1)	2.5 (1.1–3.8)	< 0.001‡
Kinetic growth rate ≥ 2.0 (sFLR/week)	30 (77)	92 (57.5)	0.026

World J Hepatol 2021 November 27; 13(11): 1629-1641

Surgical Treatment

Στόχος χειρουργείου = Ριζική εκτομή με αρνητικά όρια (R0 resection)





3+1 διαστάσεις

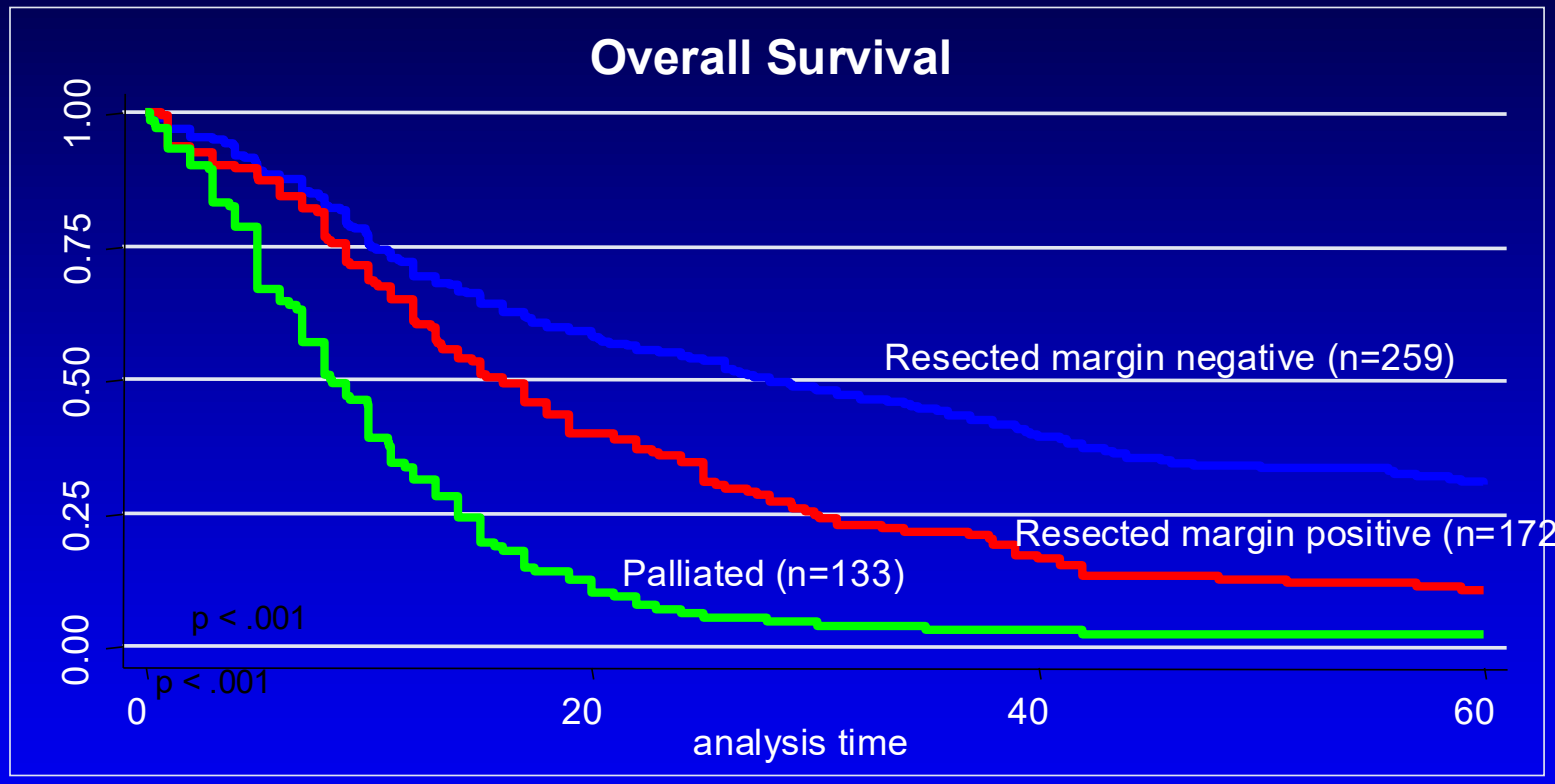
Tumor-free Resection

Difficult to achieve a wide/long resectional margin with curative intent.

1. HCC is located in the liver hilum surrounded by vital structures
2. Vertical and longitudinal spread up to 2 cm
3. Cannot predict exact length and width of microscopic Tu extension
4. IntraOp frozen-section examination of margins is inaccurate in 10-15% of pts

Endo I , et al. Ann Surg Oncol 2008
Xiang S, et al Int J Colorectal Dis 2015
Okazaki Y, et al. Hepatogastroenterology 2002

Cholangiocarcinoma: Johns Hopkins Series



	Resected Margin neg (n = 259)	Resected Margin pos (n = 172)	Palliated (n = 133)
5-year Survival	30 %	10 %	2 %
Median Survival	28 mo	16 mo	8 mo

Tumor-free Resection

West

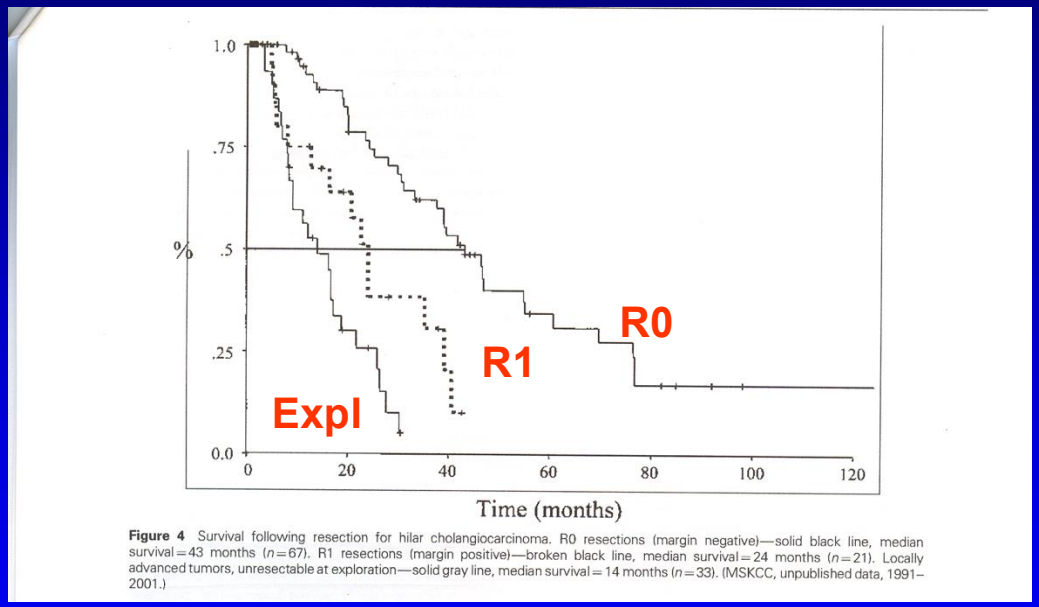
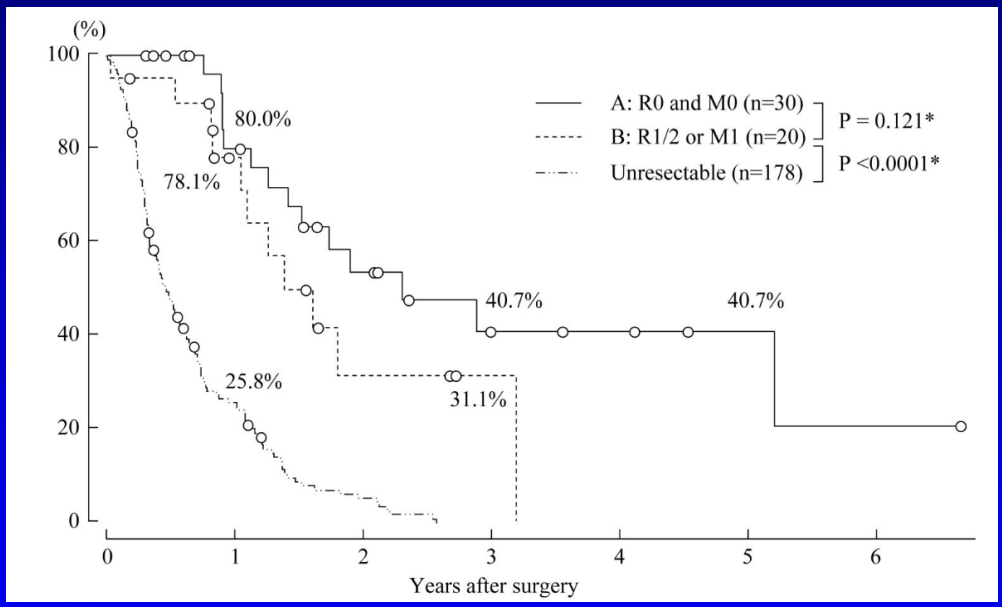


Figure 4 Survival following resection for hilar cholangiocarcinoma. R0 resections (margin negative)—solid black line, median survival = 43 months ($n = 67$). R1 resections (margin positive)—broken black line, median survival = 24 months ($n = 21$). Locally advanced tumors, unresectable at exploration—solid gray line, median survival = 14 months ($n = 33$). (MSKCC, unpublished data, 1991–2001.)

East

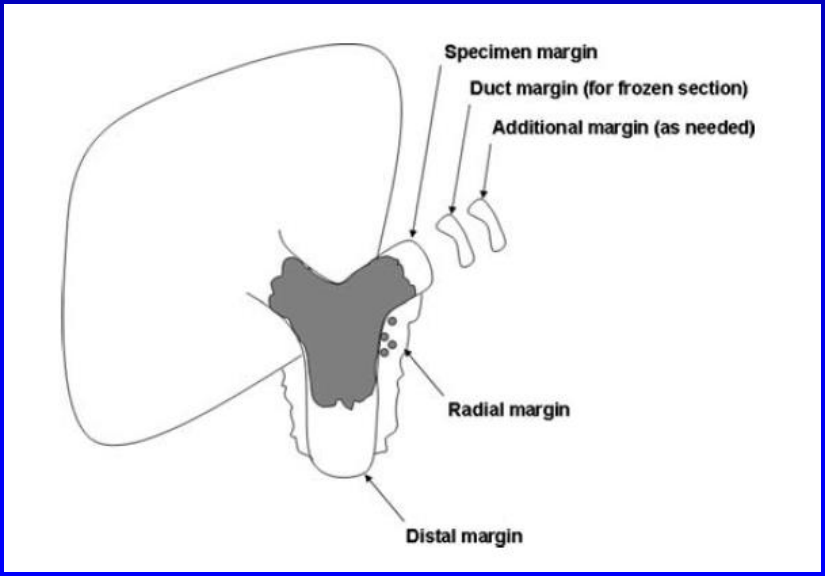


R0 resection: median survival 43 mo
R1 resection: 24 mo
Exploration: 14 mo

Nagino M, et al. Ann Surg 2010
Jarnagin M, et al. Ann Surg 2004

Tumor-free Resection

- Ταχεία Βιοψία ορίου εκτομής κατά την αφαίρεση του παρασκευάσματος
- Αν R(+) πρέπει να γίνει πιο ευρεία εκτομή για να επιτευχθεί R0
- Διεύρυνση ορίων = επισφαλής αναστόμωση = αυξημένη νοσηρότητα/θνητότητα



Clinical Significance of Intraoperative Bile Duct Margin Assessment for Hilar Cholangiocarcinoma

101 patients 1992-2005

Frozen section analysis of the proximal bile duct margin is misleading in 9% of patients

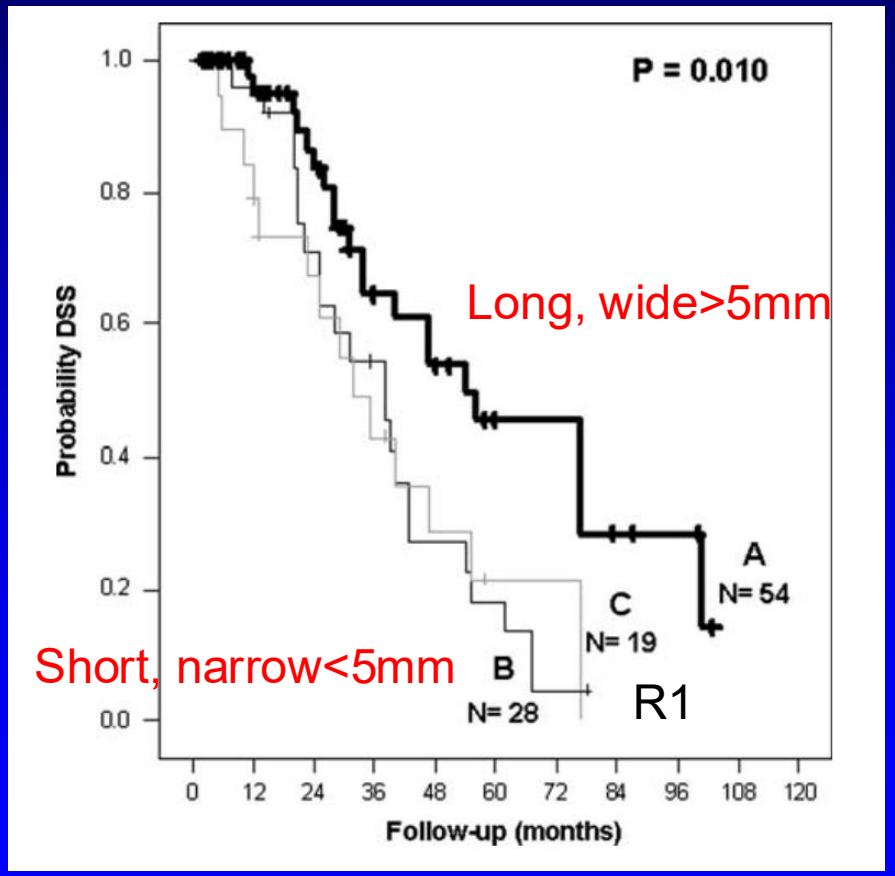
Hemming et al, Ann Surg 2005
Kawasaki et al, Ann Surg 2003
Endo et al, Ann Surg Oncol 2008

Tumor-free Resection

1. Secondary R0 resection margin after additional resection have an equivalent survival to those with a primary R0 resection

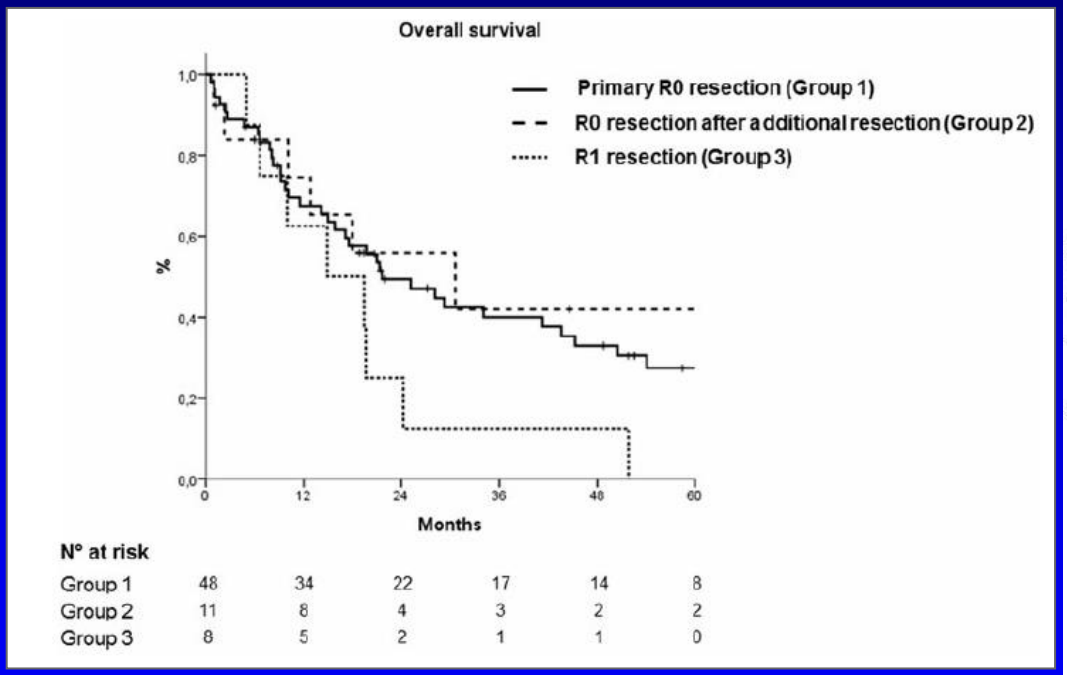
2. Increased incidence of biliary fistula, vascular injury, pseudoaneurysm

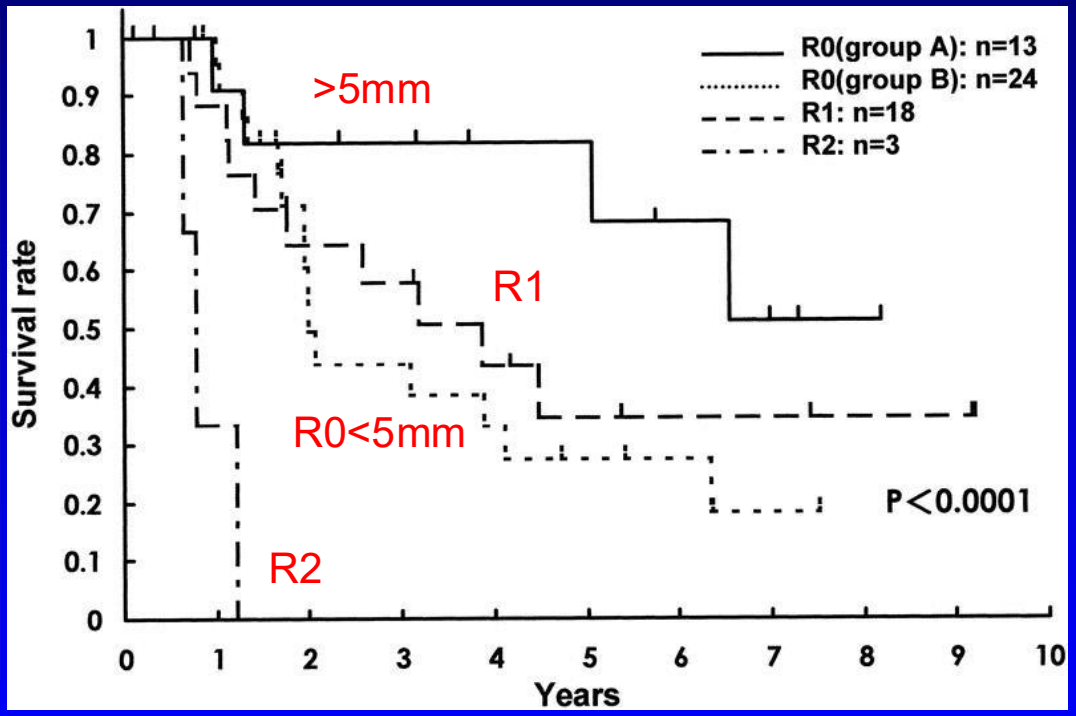
3. Dysplasia at the margin NOT associated with worse prognosis!!!



Endo I, et al. Ann Surg Oncol 2008

Tumor-free Resection





Ribero D, et al. Ann Surg 2011

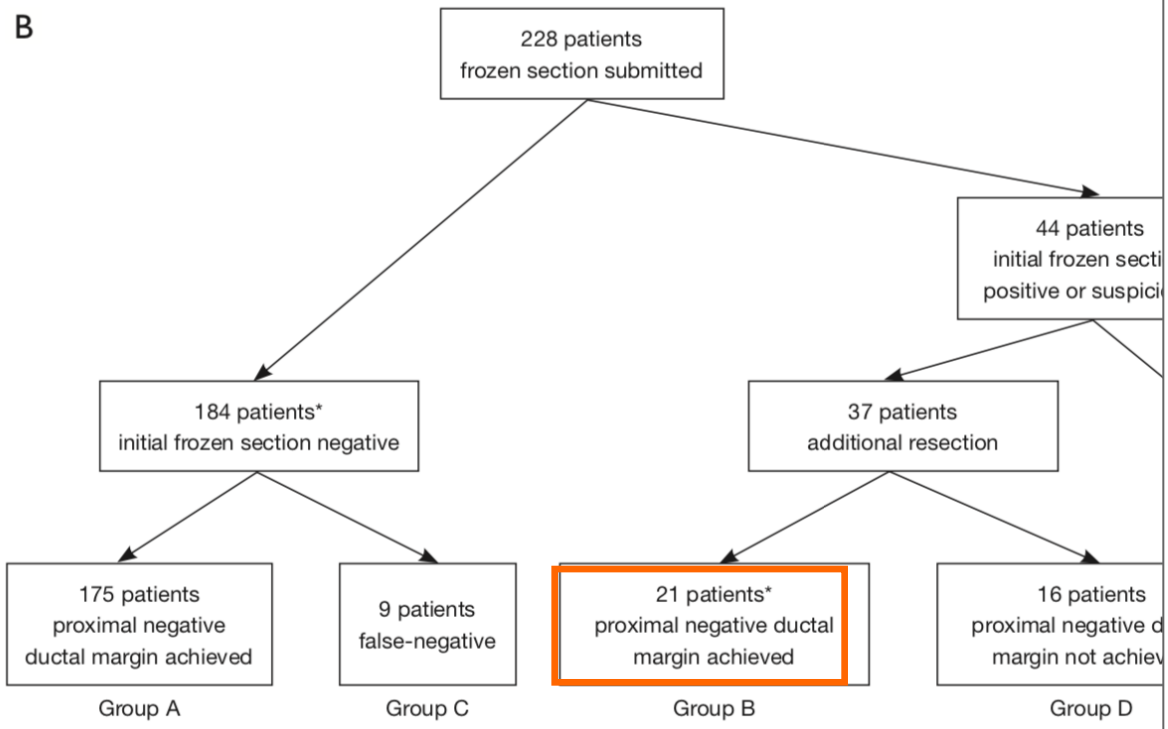
Tumor-free Resection

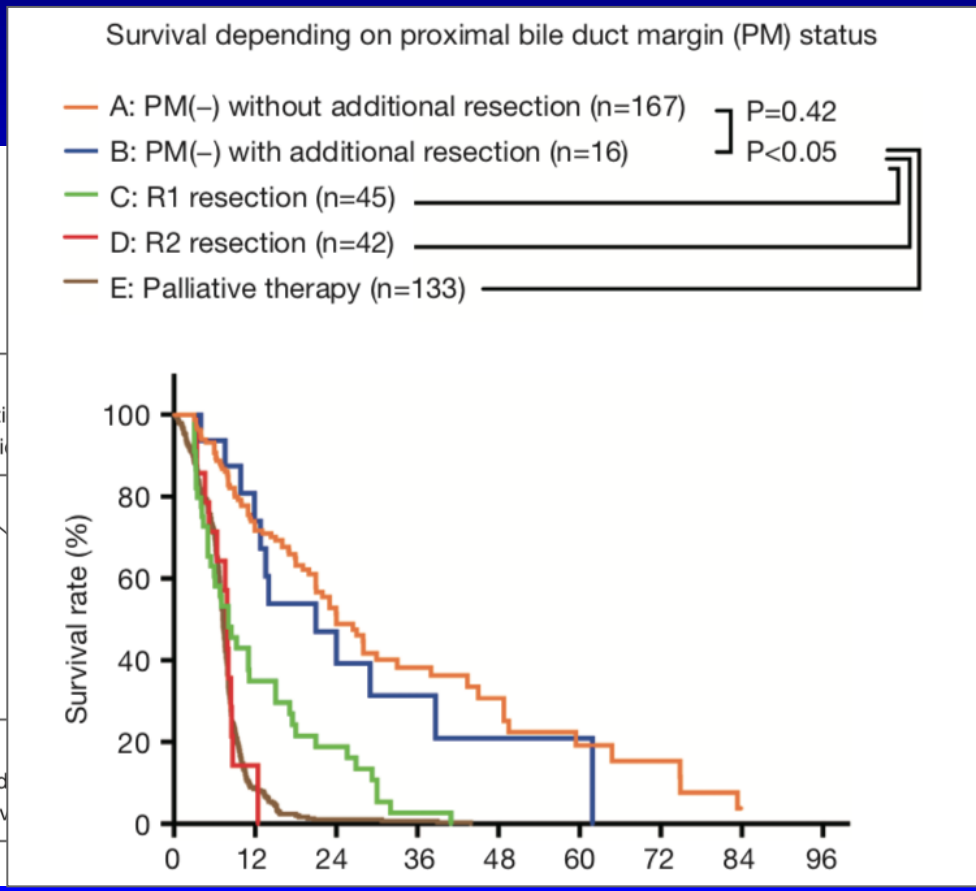
Effectiveness of additional resection of the invasive cancer-positive proximal bile duct margin in cases of hilar cholangiocarcinoma

Wen-Jie Ma[1#], Zhen-Ru Wu[2#], Anuj Shrestha[1,3], Qin Yang[1], Hai-Jie Hu[1], Jun-Ke Wang[1], Fei Liu[1], Rong-Xing Zhou[1], Quan-Sheng Li[1], Fu-Yu Li[1]

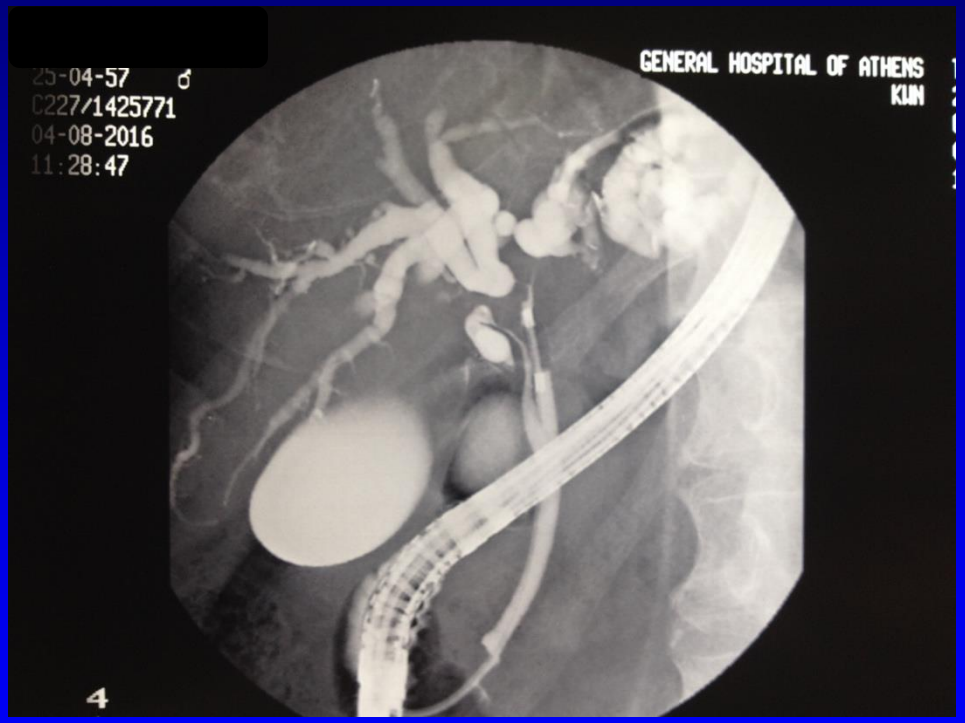
2000-2017, 228 patients resected hCCA

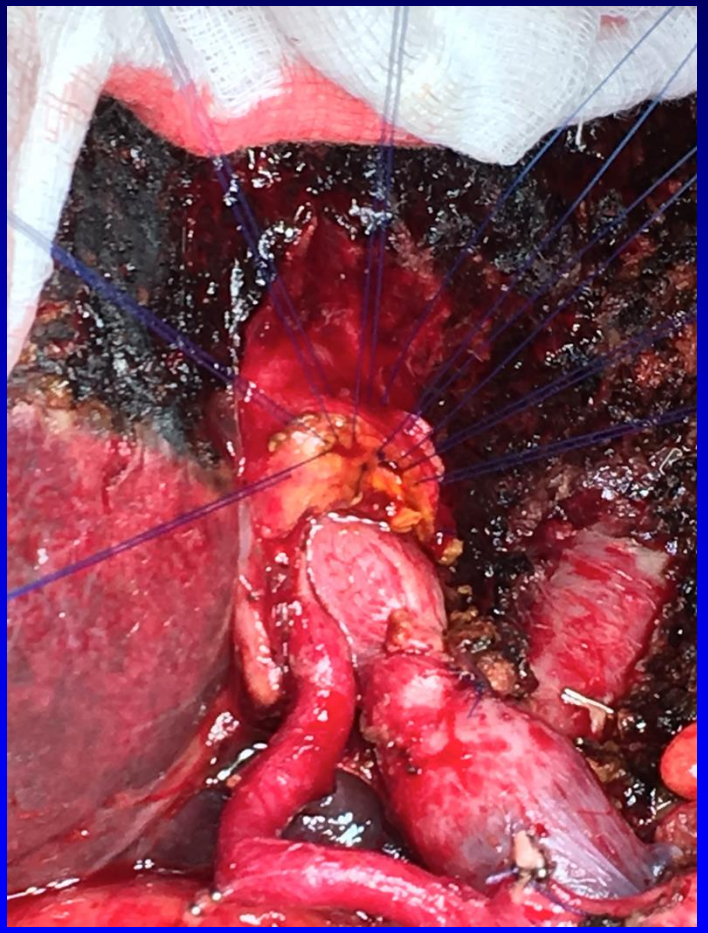
HepatoBiliary Surg Nutr 2018;7(4):251-269



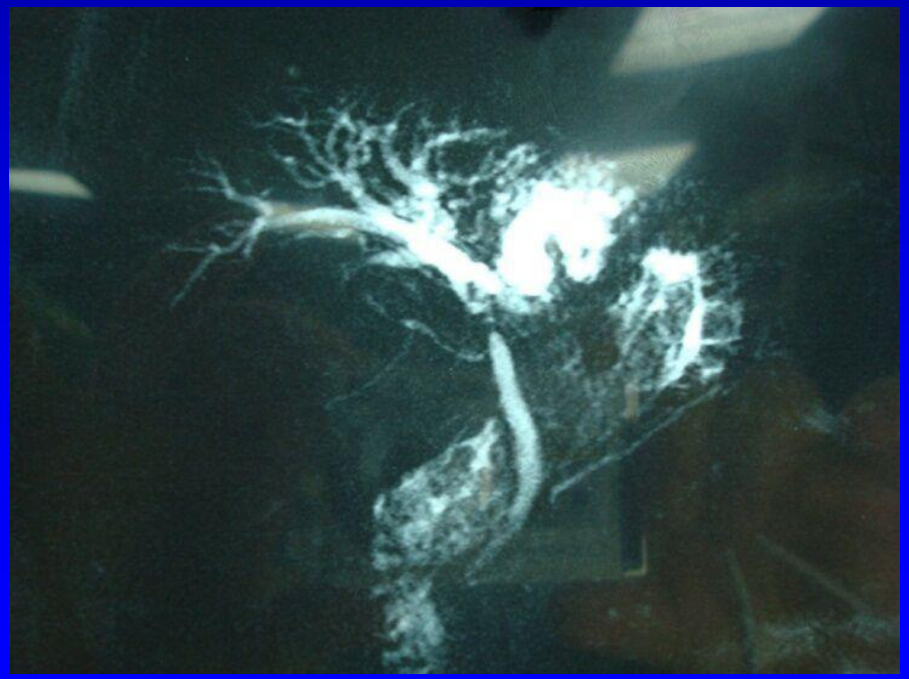


Tumor-free Resection

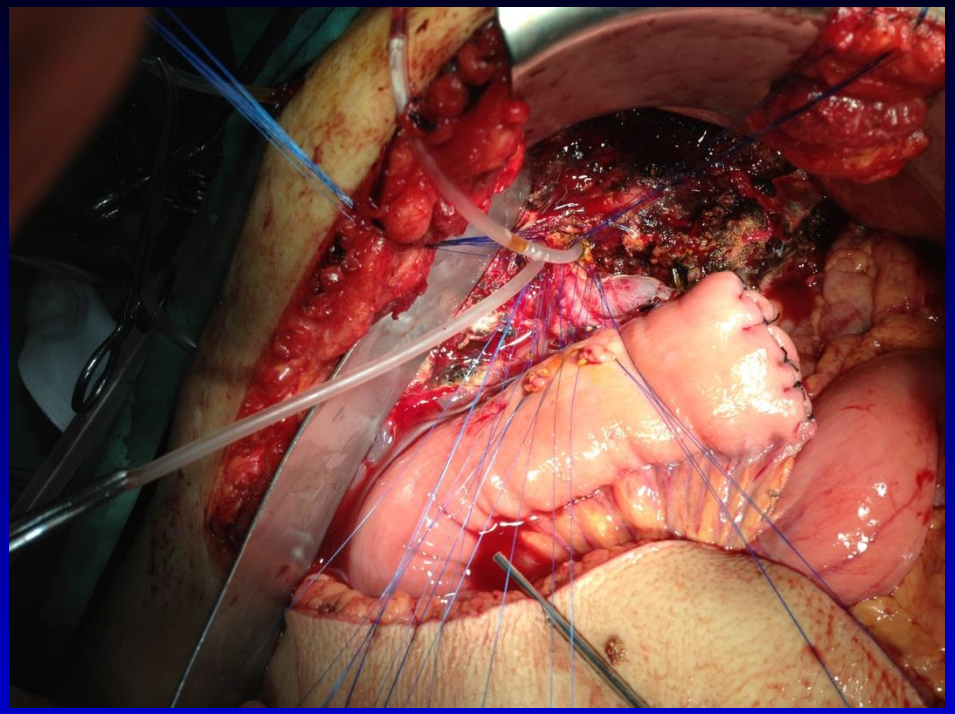


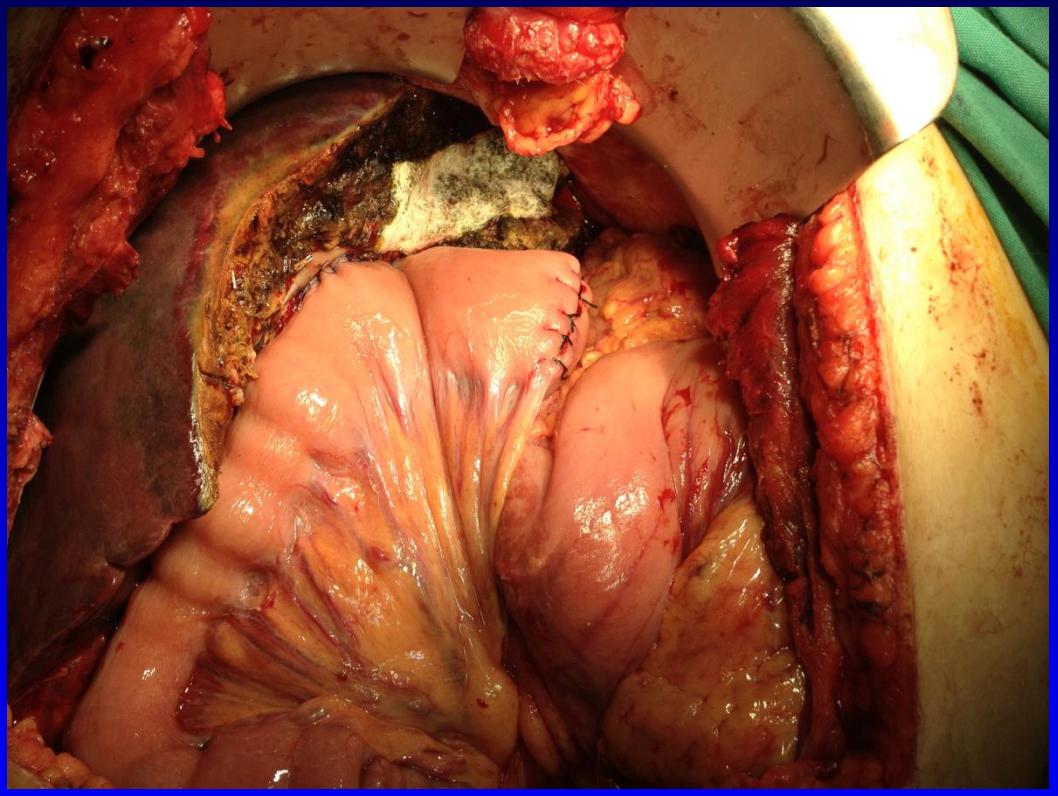


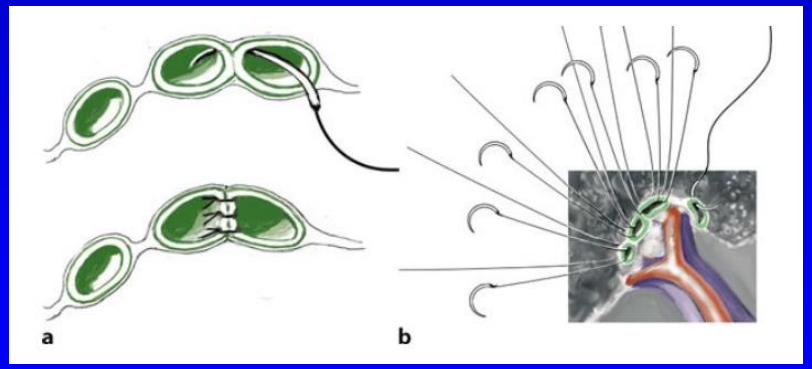
by Dimitris P. Korkolis, MD, PhD



by Dimitris P. Korkolis, MD, PhD

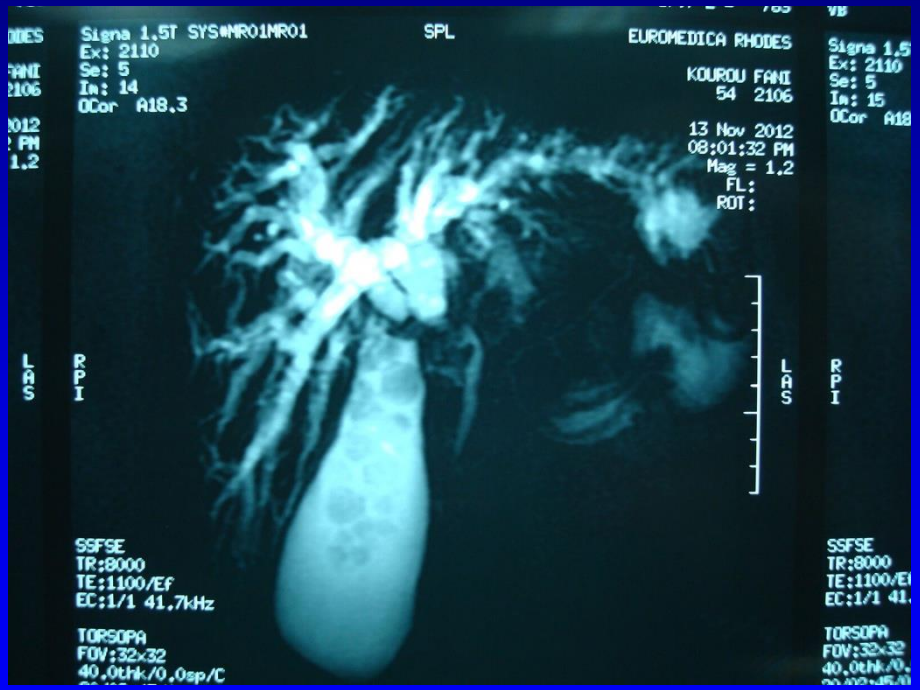


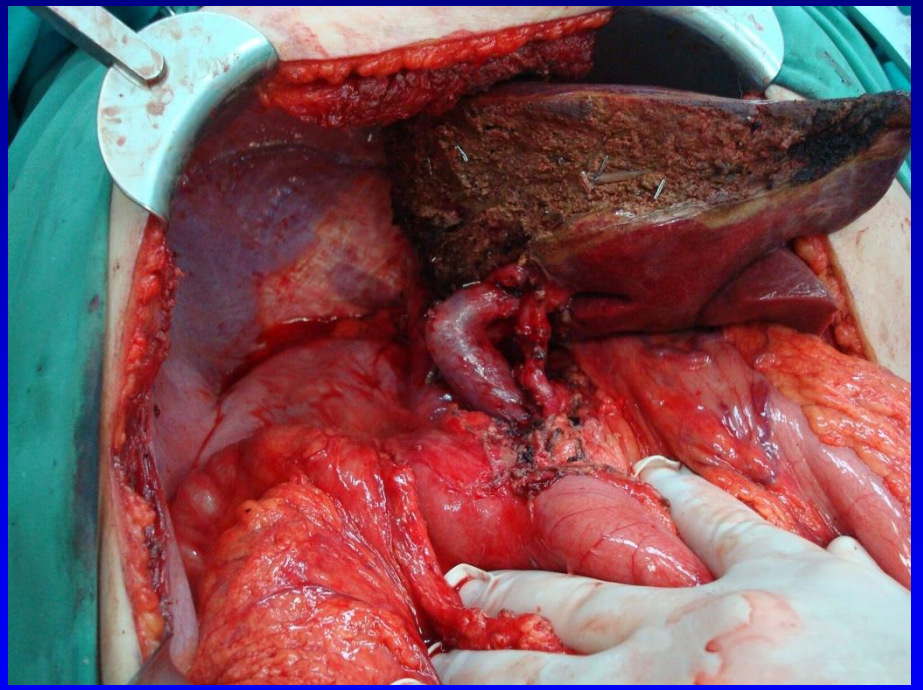




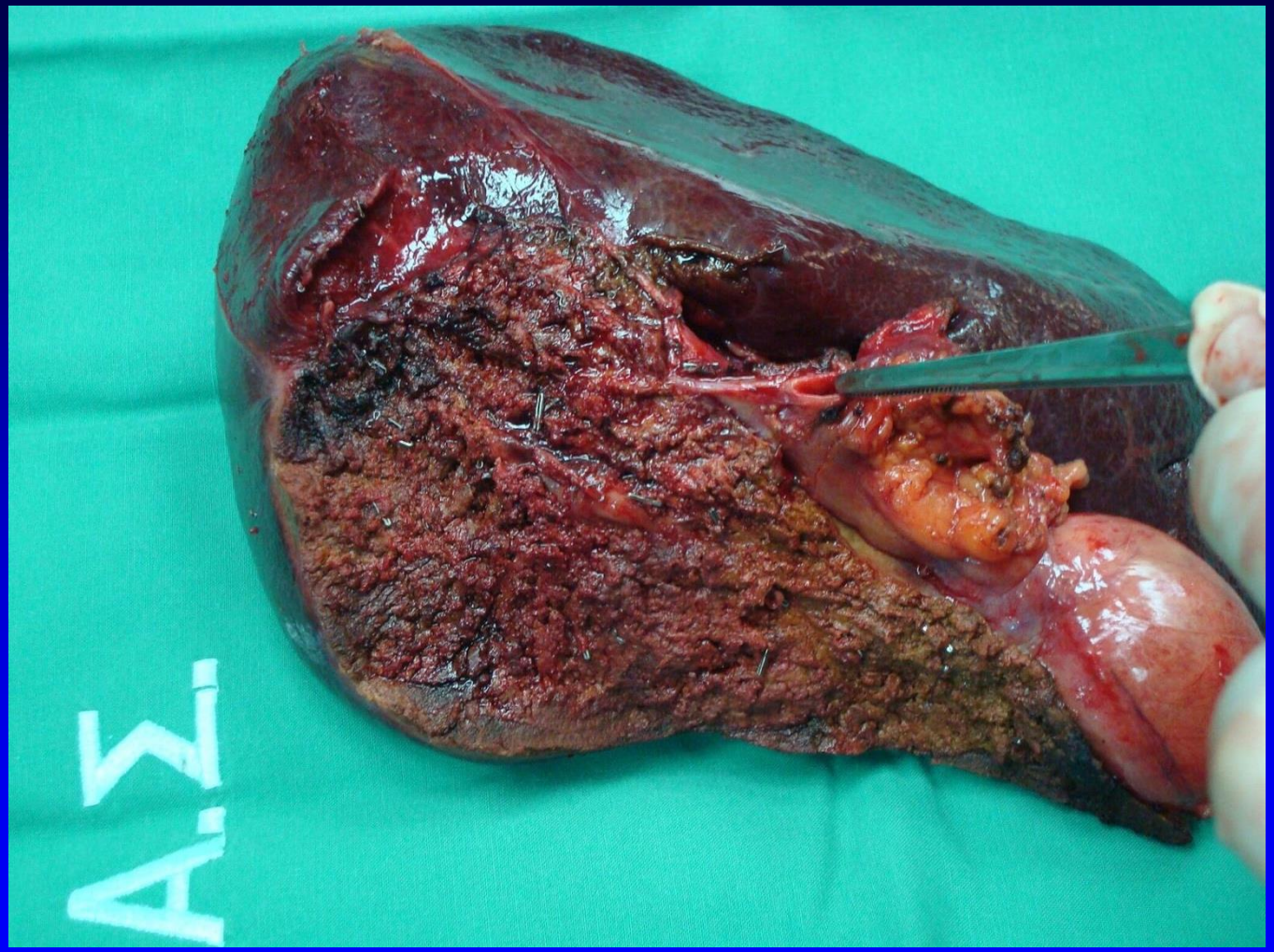
by Dimitris P. Korkolis, MD, PhD

Resection Margins





by Dimitris P. Korkolis, MD, PhD



by Dimitris P. Korkolis, MD, PhD

Hepatic Resection

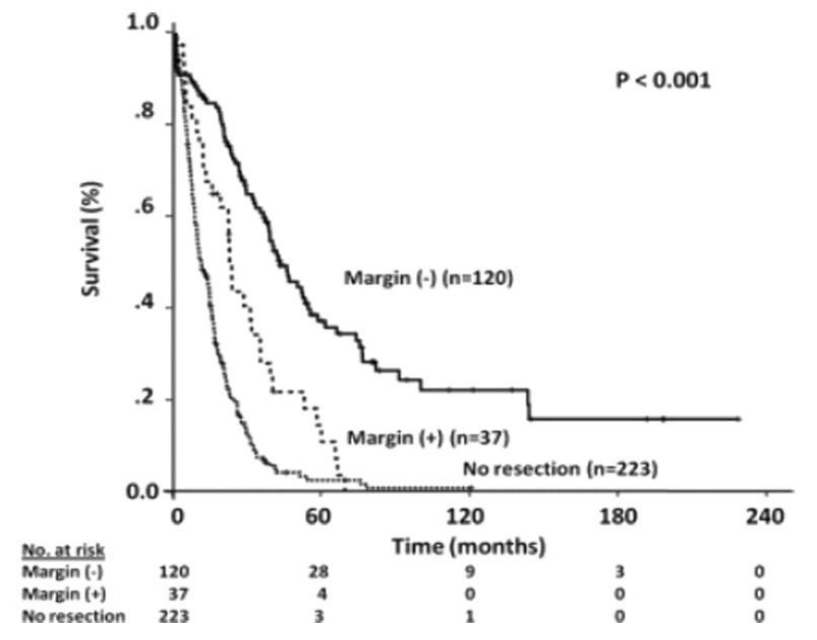
Authors	Published year	Time period		Resections	R0 (%)	PH (%)	Mortality (%)	Morbidity (%)	5-year survival (%)
Gerhards et al.	2000	1983	–1987	42	5	36	19	66	NA
		1988	–1992	45	13	9	20	73	NA
		1993	–1997	25	32	52	12	52	NA
Kawarada et al.	2002	1976	–1993	62	55	65	2	31	20
		1994	–2000	25	88	100	4	20	50
Dinant et al.	2006	1988	–1993	45	13	9	20	73	22
		1993	–1998	25	32	52	12	52	35
		1998	–2003	29	59	72	10	68	59
Gulik et al.	2010	1988	–1993	45	13	9	NA	NA	20
		1993	–1998	25	32	52	NA	NA	
		1998	–2003	29	59	72	10	68	33
Nagino et al.	2012	1977	–1990	72	75	92	11	76	23
		1991	–2000	116		93	10	80	
		2001	–2005	168	78	98	3	52	38
		2006	–2010	218		99	1	43	
Furusawa et al.	2014	1990	–2000	70	70	99	1.4	85.7	33
		2001	–2012	74	78	100	0	61	35

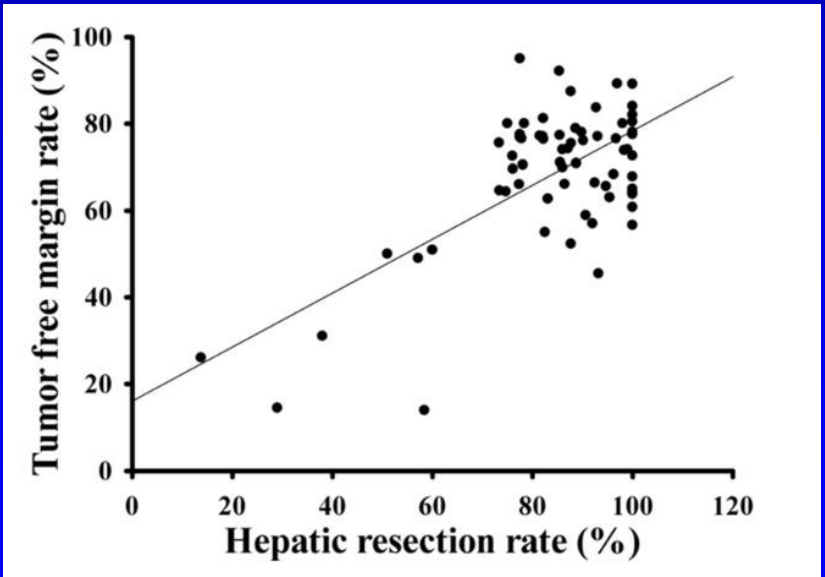
Concomitant Liver Resection

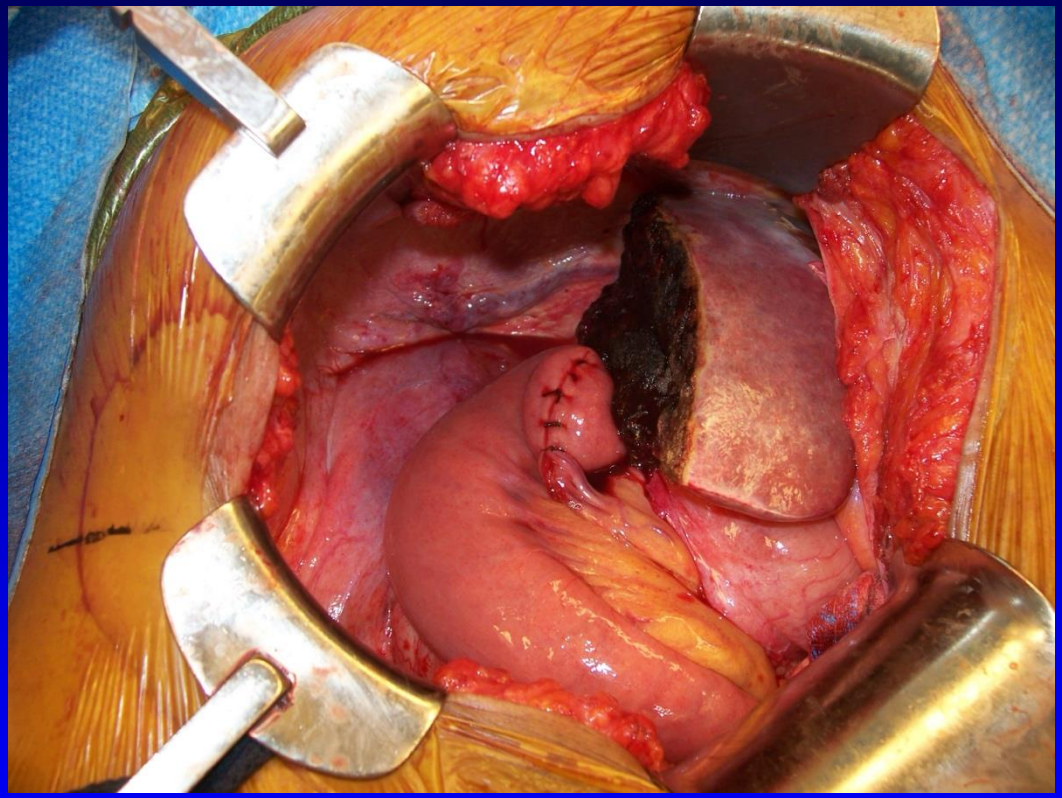
Study	Year	Total Number	Liver resections	R0 resections		30-day mortality		5-Year survival	
				Liver resection (%)	Bile duct resection only (%)	Liver resection (%)	Bile duct resection only (%)	Liver resection (%)	Bile duct resection only (%)
Capussotti	2002	36	32	91	75	NR	NR	39.5	0
Ito	2008	38	20	85	39	0[a]	0[a]	50	0
Lee	2010	302	268	76.5	26.4	1.7	0	35.5	17.5
Song	2012	230	177	86.4	49	NR	NR	45	18
Nuzzo	2012	440	376	79.2	65.6	NR	NR	26.6	0
De Jong	2012	355	224	66.5	54.3	6.7	1.2	22	10
Matsuo	2012	157	129	83.7	42.9	8.5	3.6	37.5	8
Lim	2013	52	26	100	27	0	0	87.4*	76.1*

Nuzzo G, et al. Arch Surg 2012
Capussoti L, et al. J Am Coll Surg 2002
Van Gulik TM, et al. Dig Surg 2012

Hepatic Resection







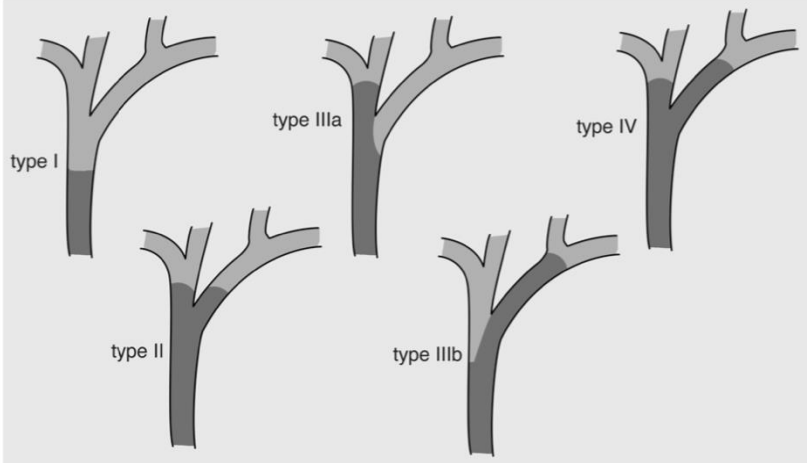
De Jong MC, et al. Arch Surg 2011
Matsuo K, et al. J Am Coll Surg 2012

Guidelines for the diagnosis and treatment of cholangiocarcinoma: an update

Shahid A Khan,[1] Brian R Davidson,[2] Robert D Goldin,[3] Nigel Heaton,[4] John Karani,[4] Stephen P Pereira,[5] William M C Rosenberg,[5] Paul Tait,[6] Simon D Taylor-Robinson,[1] Andrew V Thillainayagam,[1] Howard C Thomas,[1] Harpreet Wasan[7]

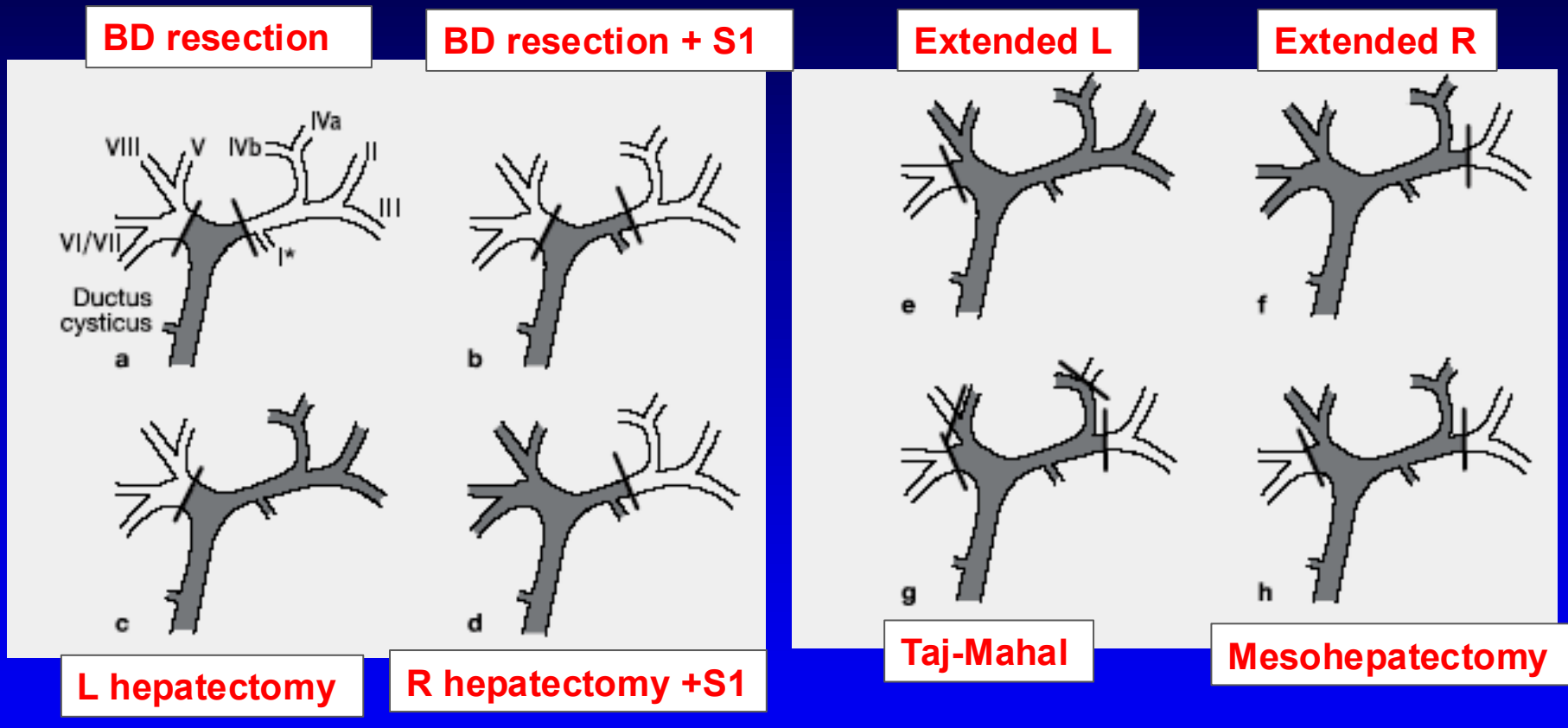
Recommendations

- For perihilar CC, the Bismuth classification is a guide to the extent of surgery required (aim is tumour-free margin of >5 mm). Surgical treatment is principally as follows (Grade B):
  - For types I and II: en bloc resection of the extrahepatic bile ducts and gall bladder, regional lymphadenectomy and Roux-en-Y hepaticojejunostomy.
  - For type III: as above plus right or left hepatectomy.
  - For type IV: not usually resectable but extended right or left hepatectomy may be feasible, dependent on biliary anatomy.
- Segment 1 of the liver may preferentially harbour metastatic disease from hilar CC and removal should be considered with stages II–IV.



Gut 2012;**61**:1657–1669.

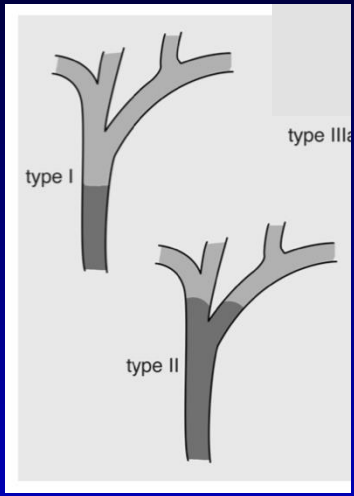
Types of Resection for pHCC



- Segment 1 of the liver may preferentially harbour metastatic disease from hilar CC and removal should be considered with stages II–IV.

Gut 2012;**61**:1657–1669.

Type I-II Bismuth Corlette



- BC I-II ευκολότερες εκτομές από BC III-IV
- Υψηλά ποσοστά υποτροπής ακόμα και μετά από R0 εκτομή

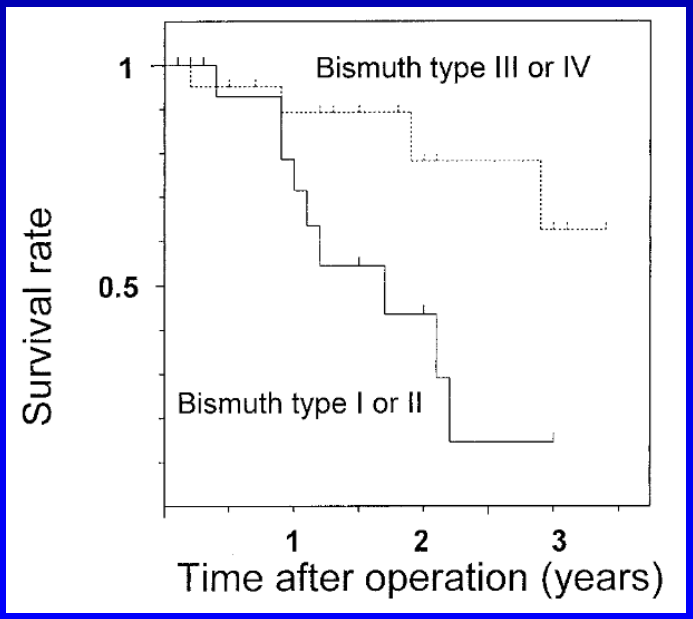
Forty Consecutive Resections of Hilar Cholangiocarcinoma With No Postoperative Mortality and No Positive Ductal Margins

Results of a Prospective Study

Satoshi Kondo, MD, Satoshi Hirano, MD,* Yoshiyasu Ambo, MD,* Eiichi Tanaka, MD,* Shunichi Okushiba, MD,* Toshiaki Morikawa, MD,* and Hiroyuki Katoh, MD**

19 patients I-II, 10 local resection, R0 95%

"To improve long-term results, additional strategies are proposed including right hepatectomy for Bismuth type I or II tumors"



Annals of Surgery • Volume 240, Number 1, July 2004

Is Hepatic Resection Necessary for type I and II HCC?

- Local Hilar Resection:
  - Bismuth type I-II
  - Tis – T2
  - Papillary tumor type

- Concomitant liver resections should be considered in all pts with type I-II HCC
  - higher curability
  - lower local recurrence rate
  - better OS
  - similar postop M&M

Lim GH, et al. World J Surg 2013
Chen XP, et al. Br J Surg 2009

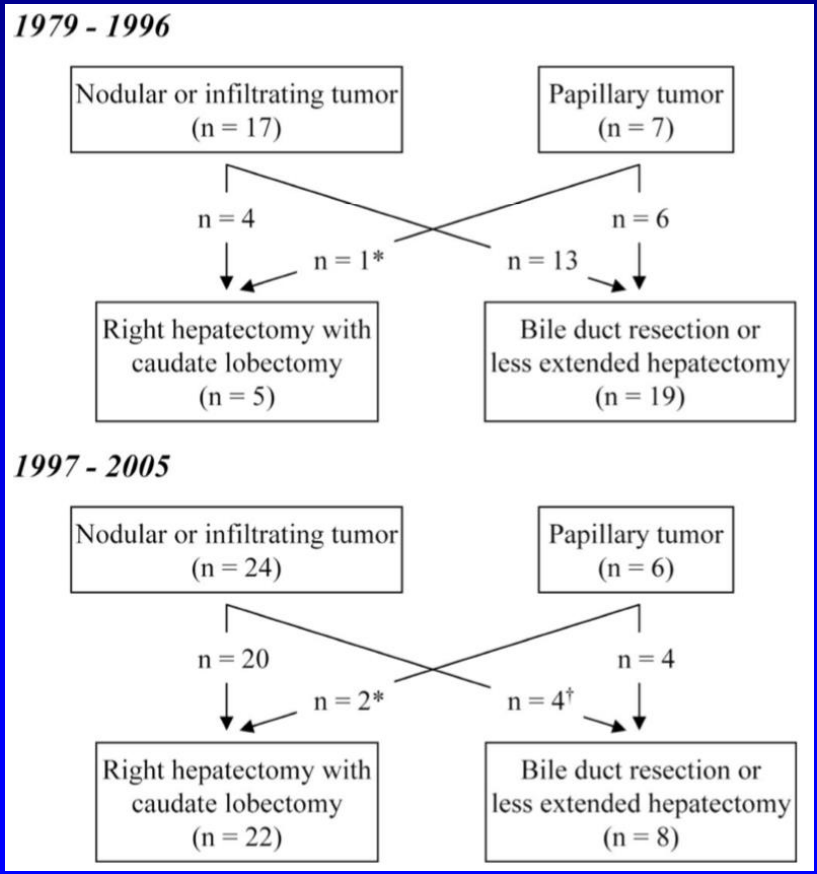
Type I-II Bismuth Corlette

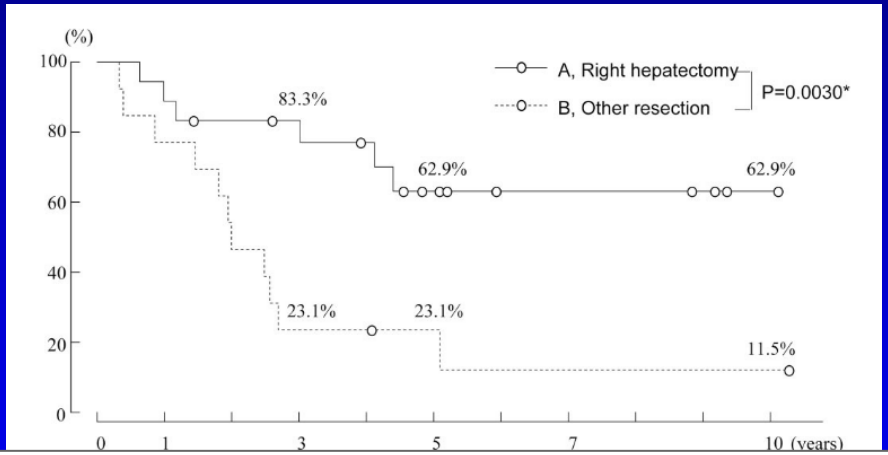
Surgical Approach to Bismuth Type I and II Hilar Cholangiocarcinomas

Audit of 54 Consecutive Cases

Takashi Ikeyama, MD, Masato Nagino, MD, Koji Oda, MD, Tomoki Ebata, MD, Hideki Nishio, MD, and Yuji Nimura, MD

1979-2004, 54 ασθενείς BC I-II

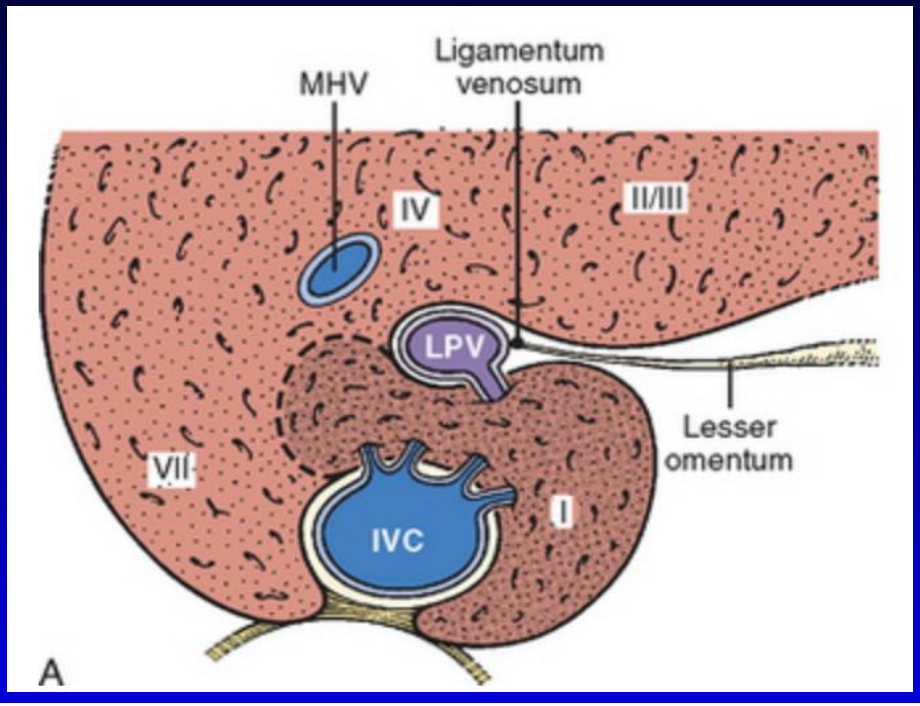




In conclusion, we recommend that the surgical approach to Bismuth type I and II hilar cholangiocarcinomas should be based on the tumor type seen on the preoperative cholangiogram. For nodular and infiltrating hilar cholangiocarcinomas, right hepatectomy offers the best long-term survival, whereas for papillary tumor, bile duct resection with or without limited hepatectomy is adequate unless extension of superficial cancer spreading is discovered preoperatively.

(*Ann Surg* 2007;246: 1052–1057)

Caudate Lobectomy



Hepatic Segmentectomy with Caudate Lobe Resection for Bile Duct Carcinoma of the Hepatic Hilus

Yuji Nimura, M.D., Naokazu Hayakawa, M.D., Junichi Kamiya, M.D., Satoshi Kondo, M.D., and Shigehiko Shionoya, M.D.

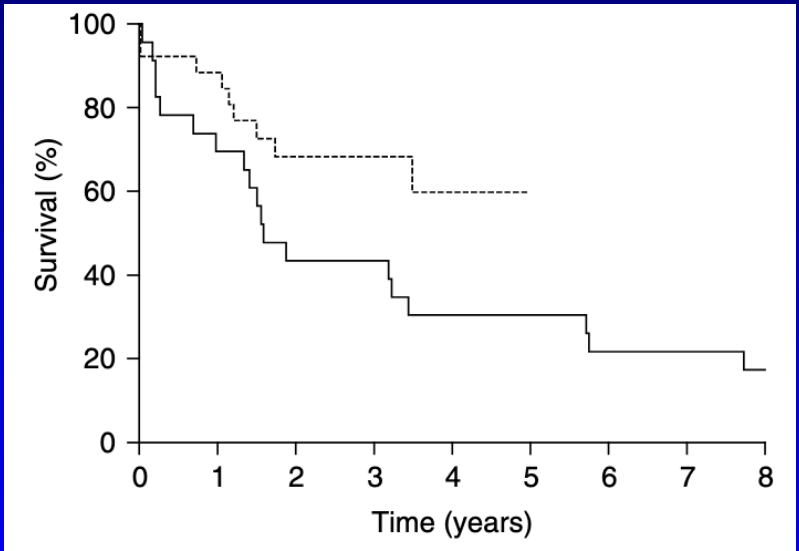
Microscopic tumor involvement in the caudate branches was confirmed in 44 of 45 patients who underwent caudate lobe resection.

Mizomoto et al. W J Surg 1988
Nimura et al. W J Surg 1990

Caudate Lobectomy

The importance of complete excision of the caudate lobe in resection of hilar cholangiocarcinoma

SANDER DINANT[1], MICHAEL F. GERHARDS[2], OLIVIER R. C. BUSCH[1], HUGO OBERTOP[1], DIRK J. GOUMA[1] & THOMAS M. VAN GULIK[1]



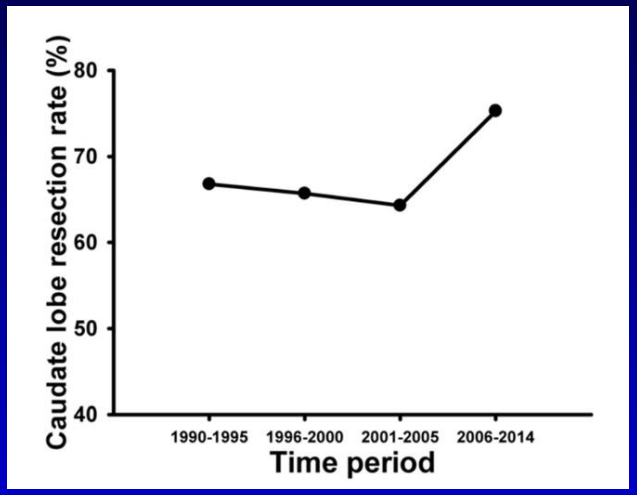
Concomitant complete excision of segment I for patients with hCCA did not lead to increased morbidity or mortality.

Segment I, which drains into the ductal bifurcation, where the cancer lies, has to be removed in any curative procedure.

Dinant et al. HPB (oxford) 2005
Valle et al. Ann Oncol 2016

Caudate Lobe Resection

- Nagoya University Medical Center, Japan
- 91 pts with HCC
- R0 resection in 86% with resection pf segment I
- Median Survival: 33 μήνες



Nimura Y, et al. J Hepatobiliary Pancreat Surg 1995

- 75 pts with HCC stage II-IV
- With caudate lobe resection: 5ετής επιβίωση=25%
- Without caudate lobe resection: 2ετής επιβίωση=0%

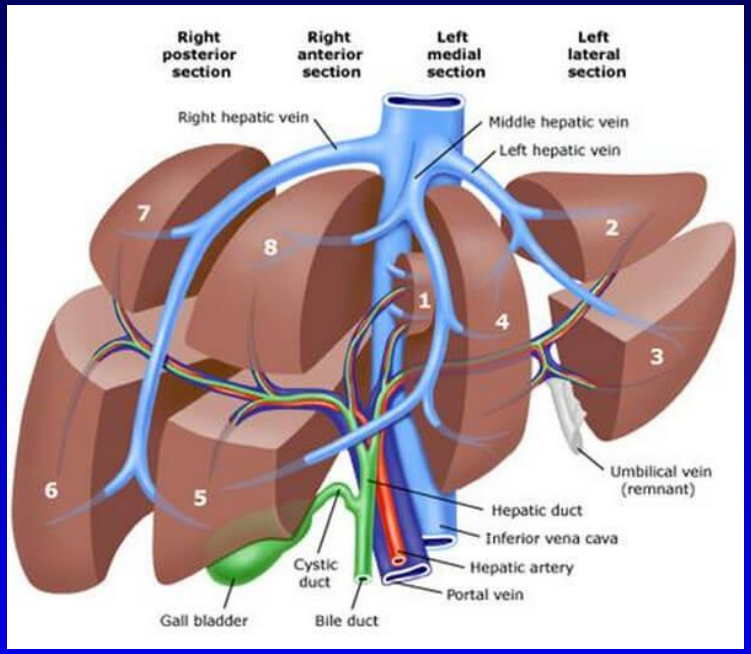
Gazzaniga GM, et al. J Hepatobiliary Pancreat Surg 2000

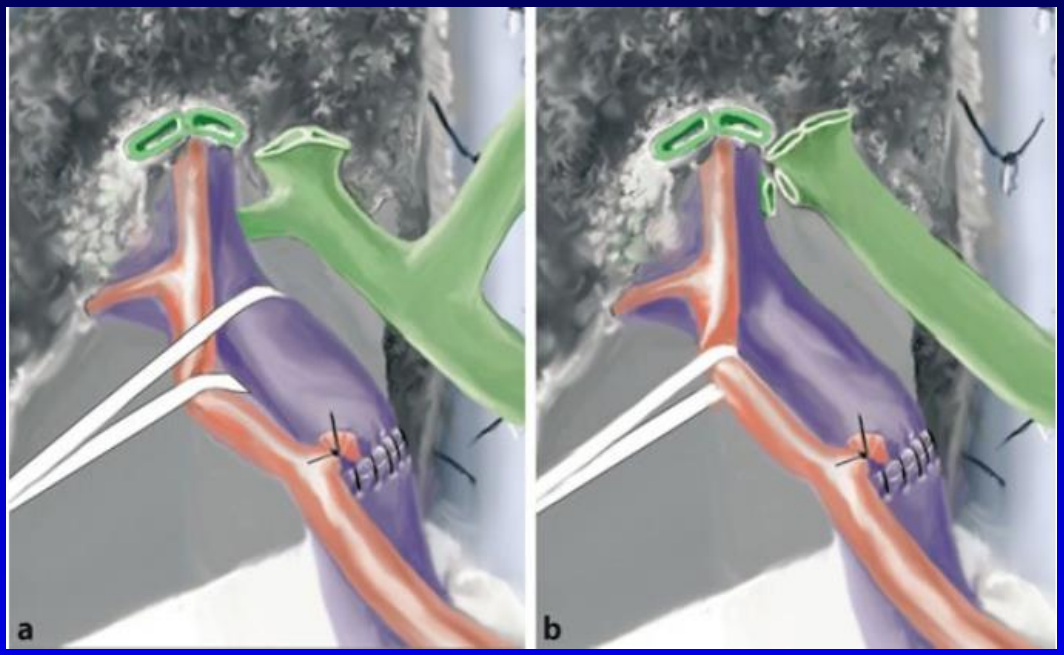
Caudate Lobe Resection

	N	Εκτομή	Εγχειρητικό Bypass	Stent	5ετής επιβίωση	10ετής επιβίωση	Εκτομή Κερκοφόρου Λοβού
Lahey Clinic USA	100	25	53	22	7%	0%	8%
Nagoya University Hospital Japan	155	122	10	23	16%	18%	89%

Dugan JM, et al. Ann Surg 2000

Caudate Lobe Resection



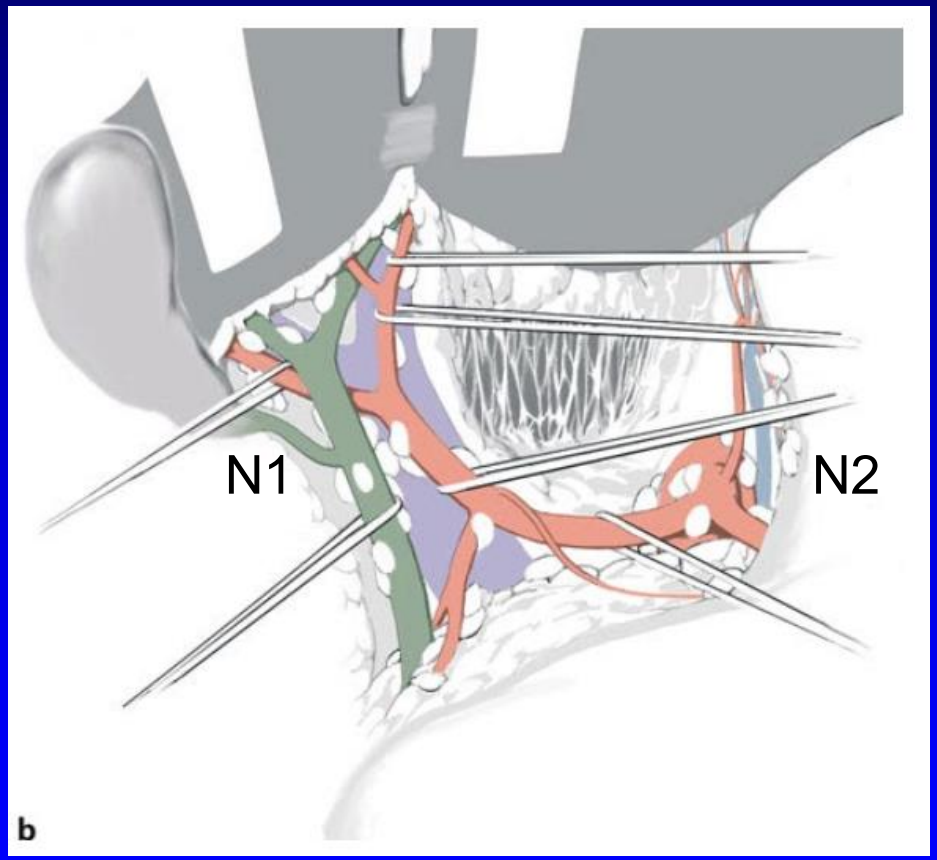


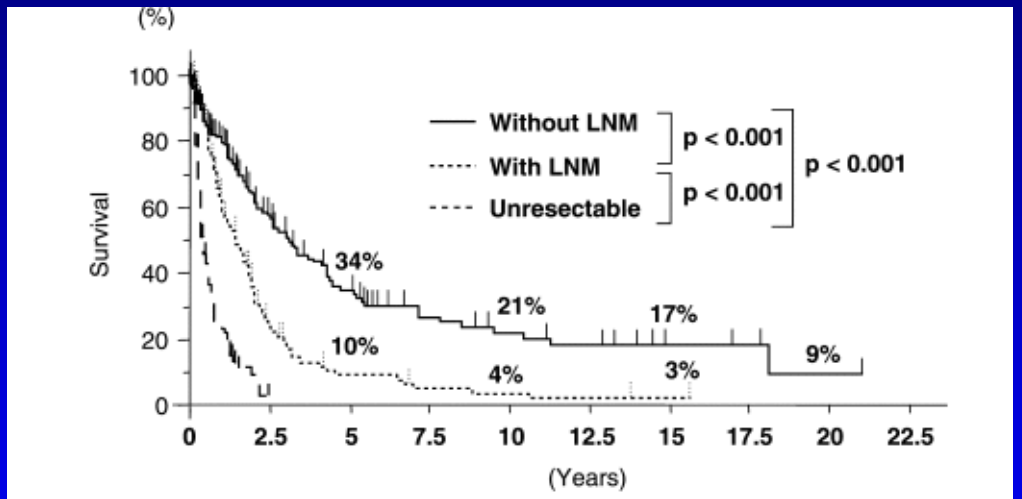
- Segment I involvement in 40-58%
- Biliary communications
- Frequent direct invasion

- Site of tumor recurrence
- Postop bile leak

Eur J Surg Oncol 2012
J Gastrointest Surg 2012

Lymphadenectomy in HCC

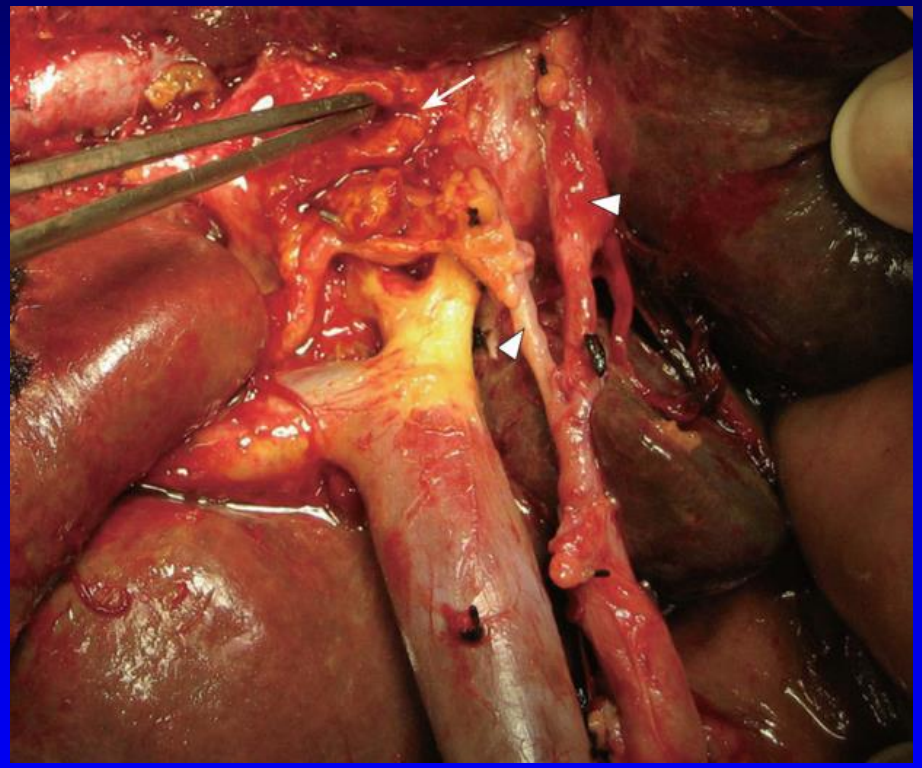




No. at risk					MST
Without LNM 152	31	12	4	1	3.0 Y
With LNM 149	8	3	1	-	1.5 Y
Unresectable 99	-				0.4 Y

DeOliveira ML, et al. Curr Opinion in Gastroenterol 2013

Lymphadenectomy in HCC



by Dimitris P. Korkolis, MD, PhD

Regional Lymphadenectomy

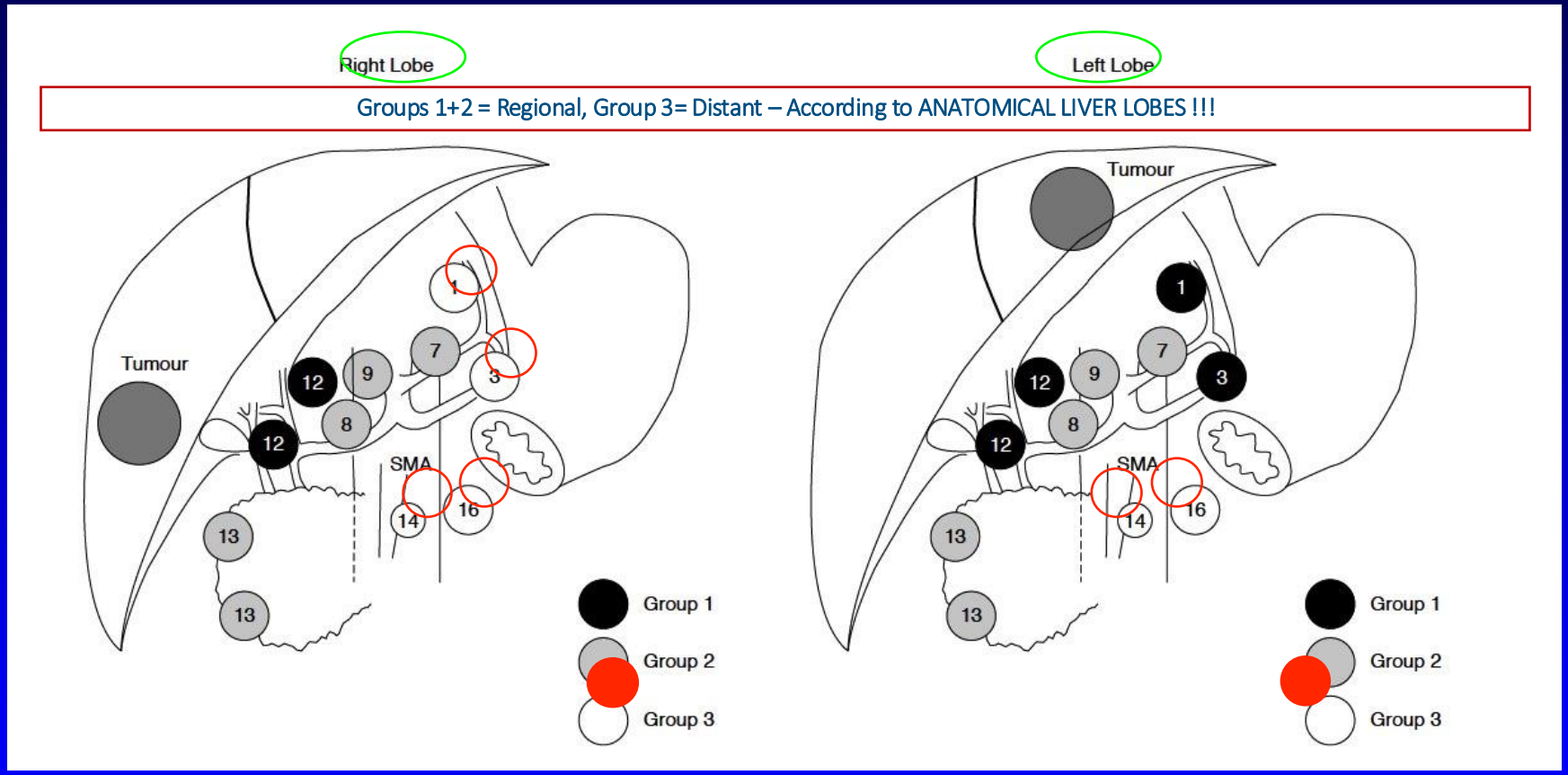
- Η λεμφαδενεκτομή έχει μικρή επιρροή στο αποτέλεσμα επιβίωσης
- Σημαντικές πληροφορίες για την σταδιοποίηση που μπορούν να επηρεάσουν την μετεγχειρητική διαχείριση η οποία με την σειρά της μπορεί να επηρεάσει την επιβίωση

NCCN

Lymphadenectomy of the porta hepatis (hilar cholangiocarcinoma) is considered standard part of curative resections

N	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One to three positive lymph nodes typically involving the hilar, cystic duct, common bile duct, hepatic artery, posterior pancreatoduodenal, and portal vein lymph nodes
N2	Four or more positive lymph nodes from the sites described for N1

Extend of LNs Resection for pCCA



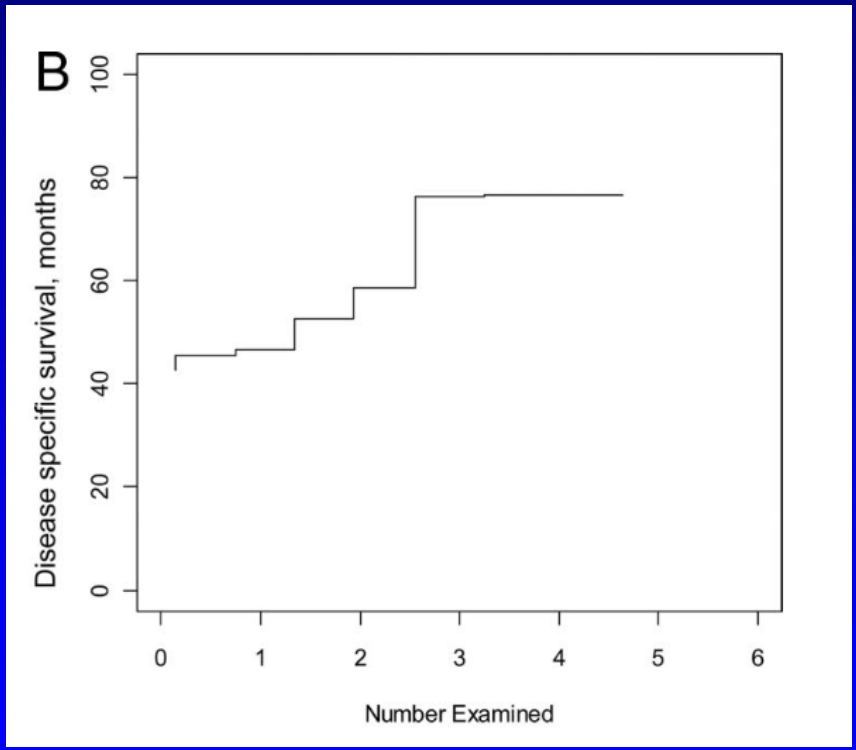
Minimum Harvest of *6* Lymph Nodes is Required

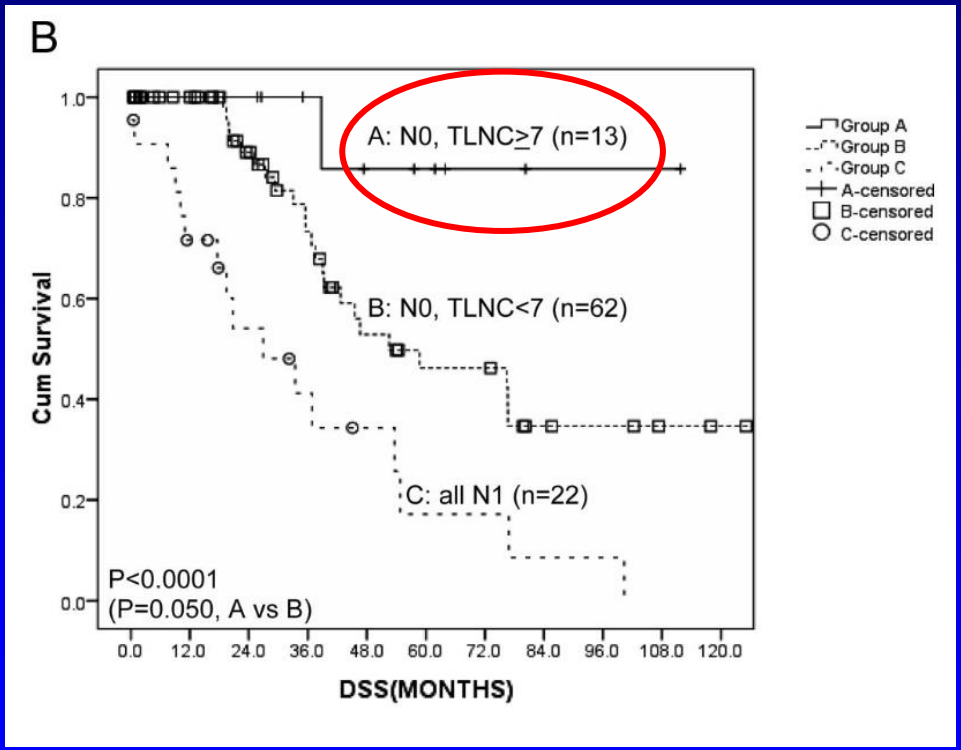
British Journal of Surgery 2001, **88**, 1463–1466

M. Shimada, Y. Yamashita, S. Aishima, K. Shirabe, K. Takenaka and K. Sugimachi

Adequate Lymph Node Assessment for Extrahepatic Bile Duct Adenocarcinoma

Kaori Ito, MD, Hiromichi Ito, MD,* Peter J. Allen, MD, FACS,* Mithat Gonen, PhD,† David Klimstra, MD,‡ Michael I. D'Angelica, MD, FACS,* Yuman Fong, MD, FACS,* Ronald P. DeMatteo, MD, FACS,* Murray F. Brennan, MD, FACS, FRCS,* Leslie H. Blumgart, MD, FACS, FRCS,* and William R. Jarnagin, MD, FACS**





Ito K, et al. Ann Surg 2010

Radical Lymphadenectomy

- Nodal invasion beyond the hepatoduodenal ligament, including para-aortic nodal metastases = dismal prognosis / 5-year 0%-12%
- Dissection beyond the hepatoduodenal ligament is not generally recommended
- Tumor positive lymph nodes along the common hepatic artery or celiac axis are usually considered a contraindication for resection.

Lymph Node Metastasis from Hilar Cholangiocarcinoma: Audit of 110 Patients Who Underwent Regional and Paraaortic Node Dissection

Yuichi Kitagawa, MD, Masato Nagino, MD, Junichi Kamiya, MD, Katsuhiko Uesaka, MD, Tsuyoshi Sano, MD, Hideo Yamamoto, MD, Naokazu Hayakawa, MD, and Yuji Nimura, MD

From the First Department of Surgery, Nagoya University School of Medicine, Nagoya, Japan

110 patients with HC who underwent both regional and para-aortic lymphadenectomy (median 24 LN)

Para-aortic LN+ = Long-term outcomes with M1

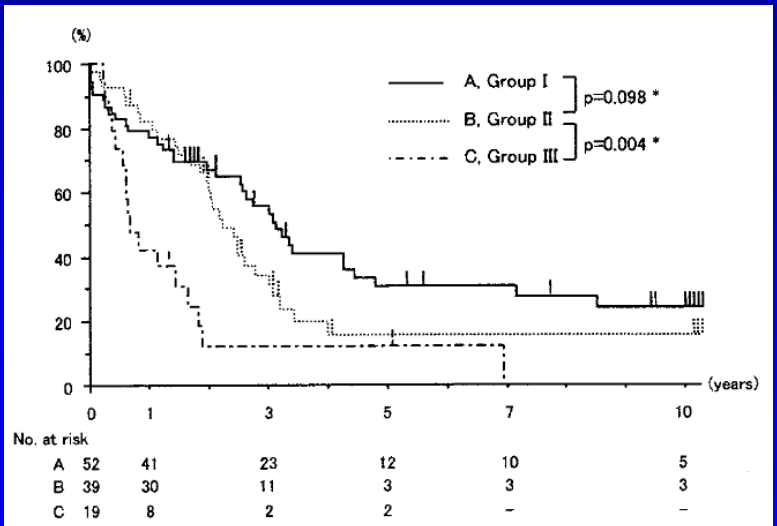
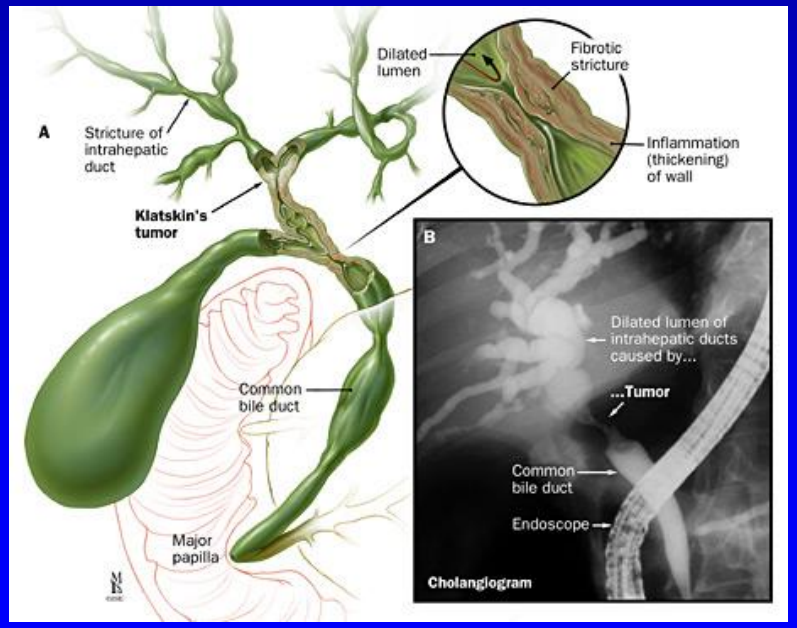
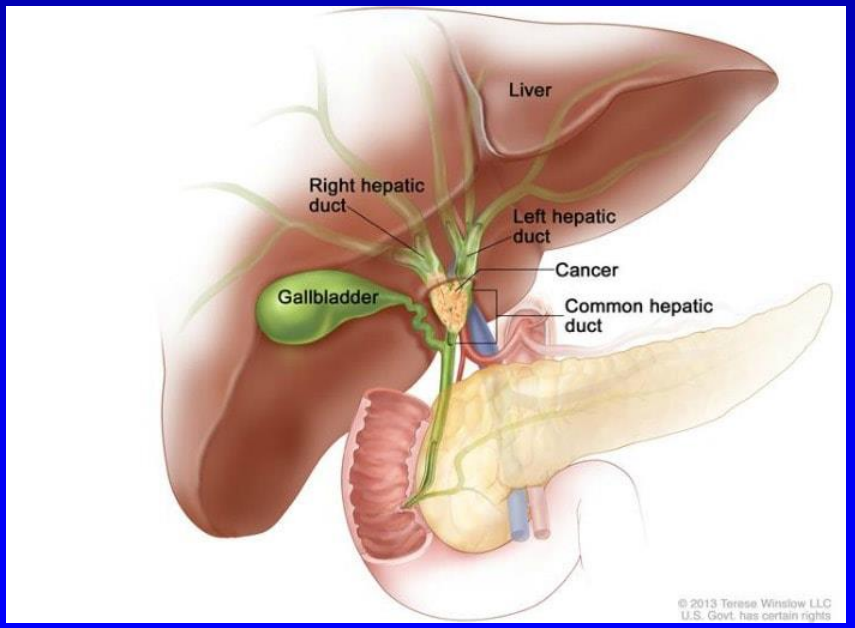


Figure 1. Survival according to nodal status in 110 patients with hilar cholangiocarcinoma who underwent resection with regional and paraaortic lymphadenectomy (all deaths included). Group 1, patients without lymph node metastasis; group 2, patients with regional lymph node metastasis; group 3, patients with paraaortic node metastasis. *, by log-rank test.

Left- or Right- Sided Hepatectomy?

- According to the predominant site of the lesion
- RH for type I-II-IIIA-IV LH for type IIIB-IV
- Extended Right Hemihepatectomy: The most radical for centrally located HCC





Anatomical Considerations in HCC

1.Extrahepatic part of left hepatic duct is longer

2.Hepatic duct confluence lies on the right side of the hepatic hilum

3.Bile duct confluence lies at the base of segment IV

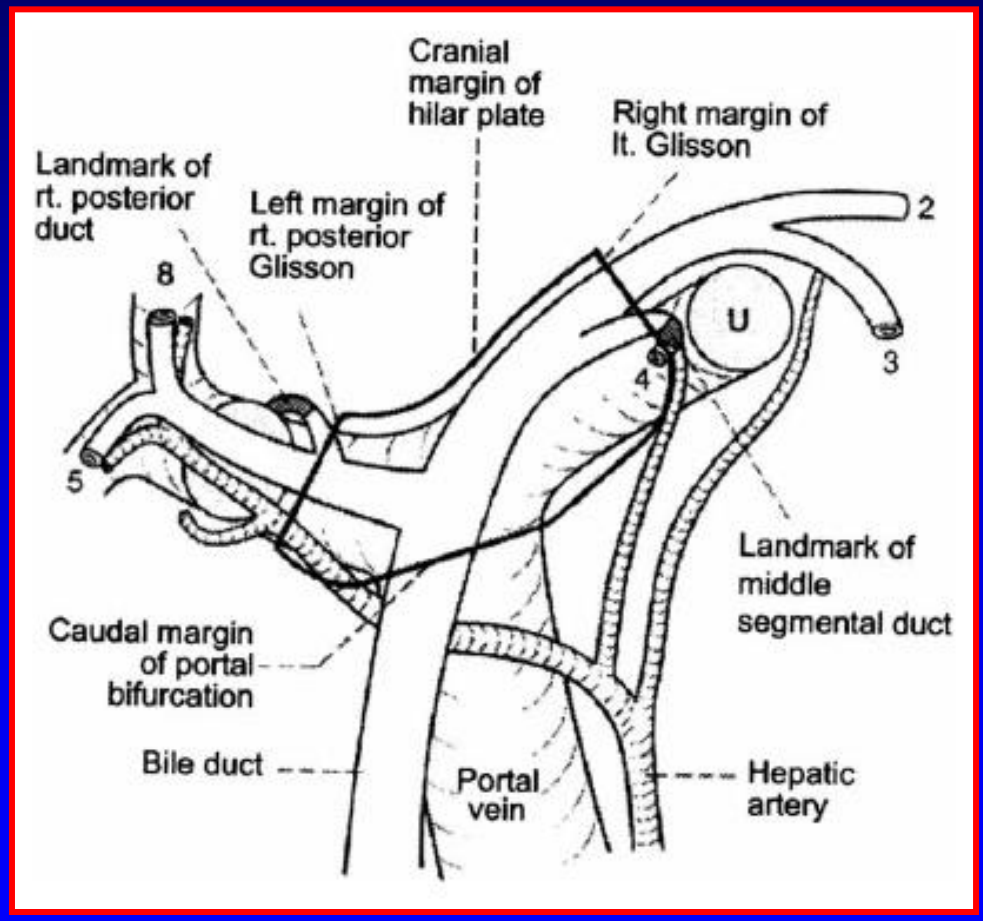
4.Right hepatic artery runs behind the CBD

5.Left portal vein is longer than the RPV

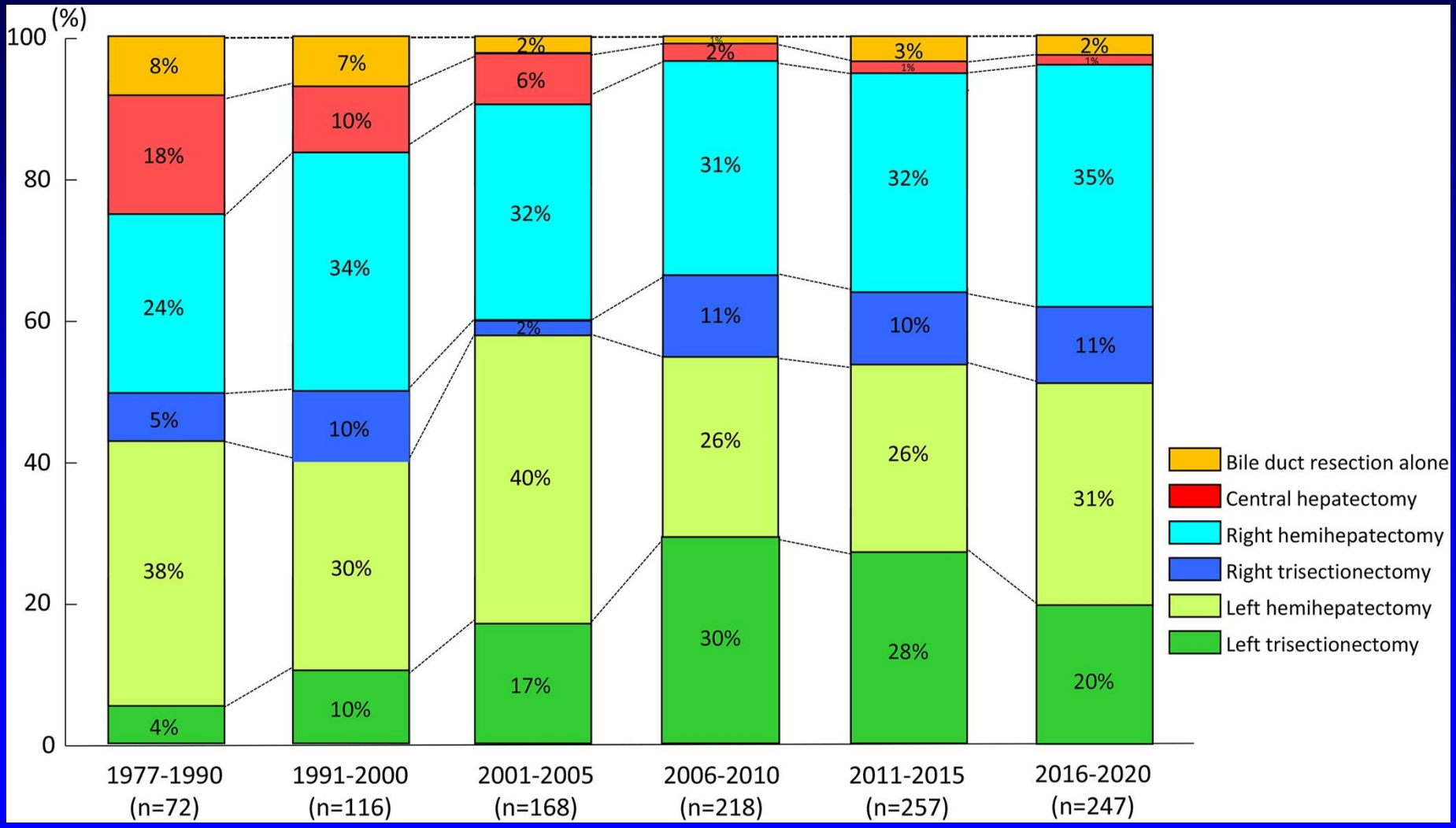
6.Anatomic variations jeopardize a left-sided hemihepatectomy

7.Enables en-block PV bifurcation (non-touch technique)

8.Enables en-block resection of ductal confluence and structures

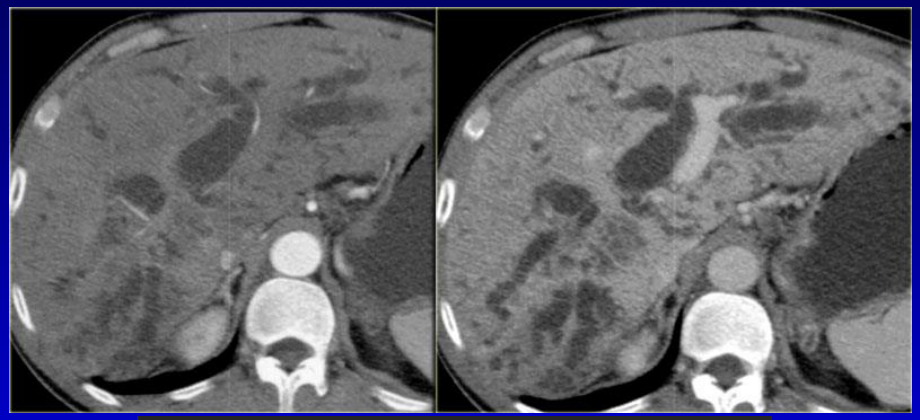


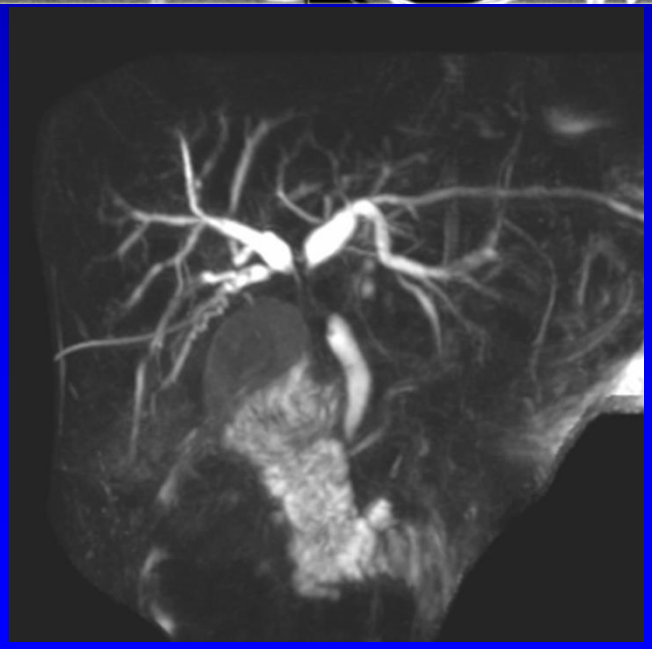
Left- or Right- Sided Hepatectomy?



Nagino, Liver 2023

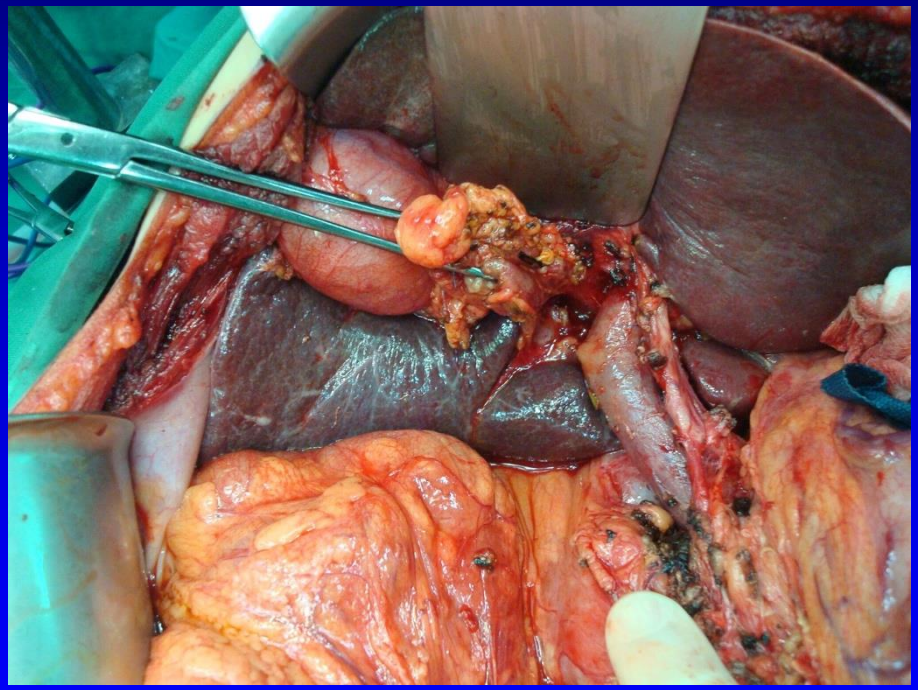
Type IIIA HCC

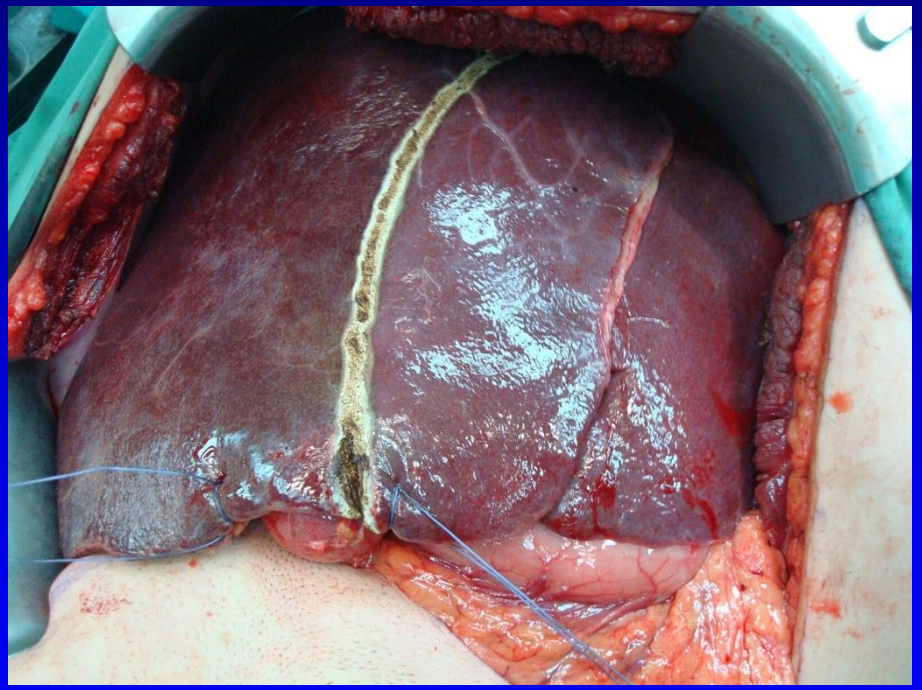




by Dimitris P. Korkolis, MD, PhD

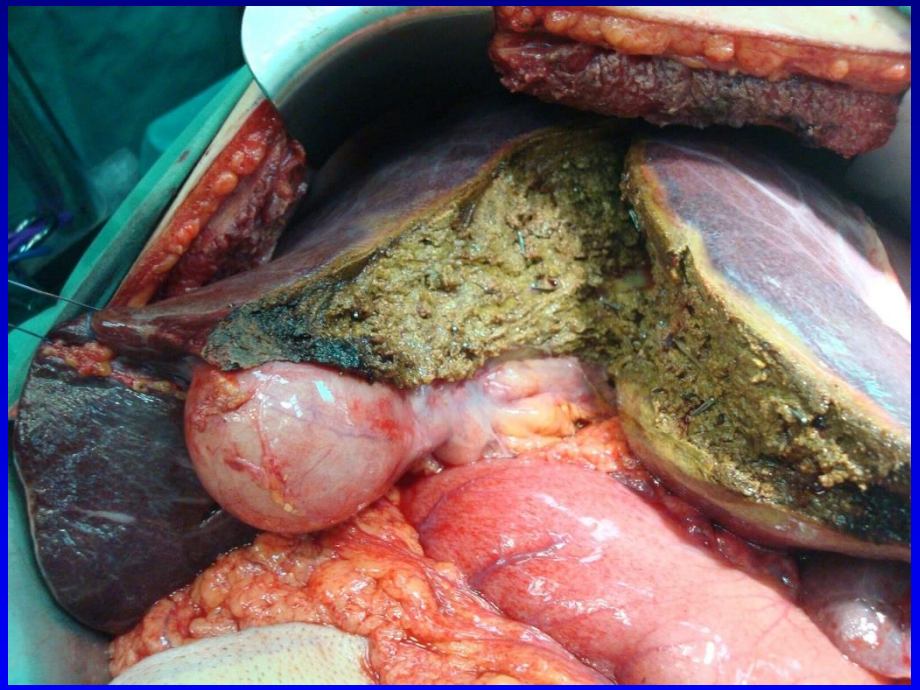
Type IIIA HCC





by Dimitris P. Korkolis, MD, PhD

Type IIIA HCC



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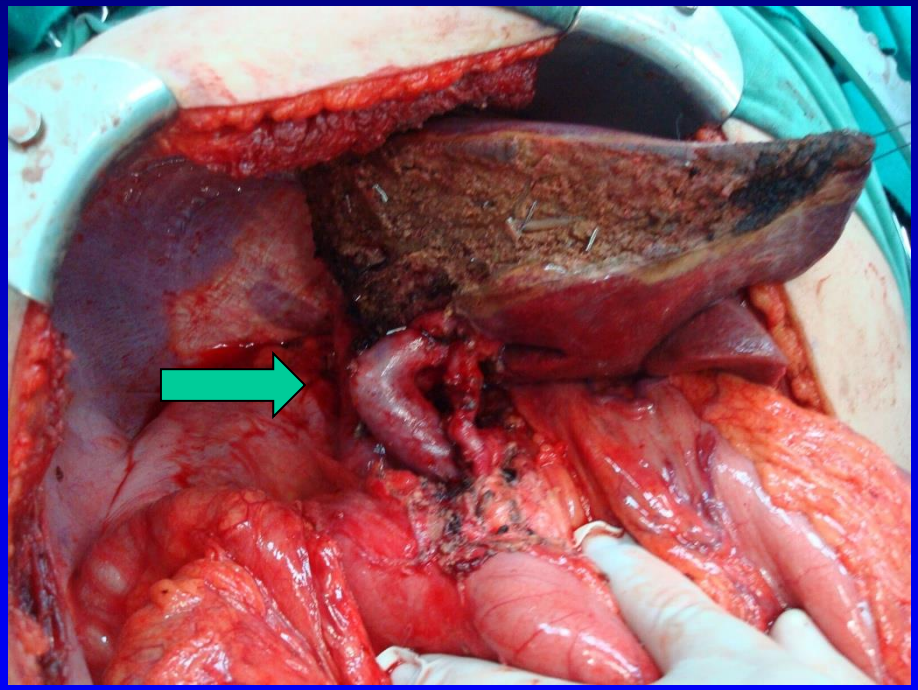
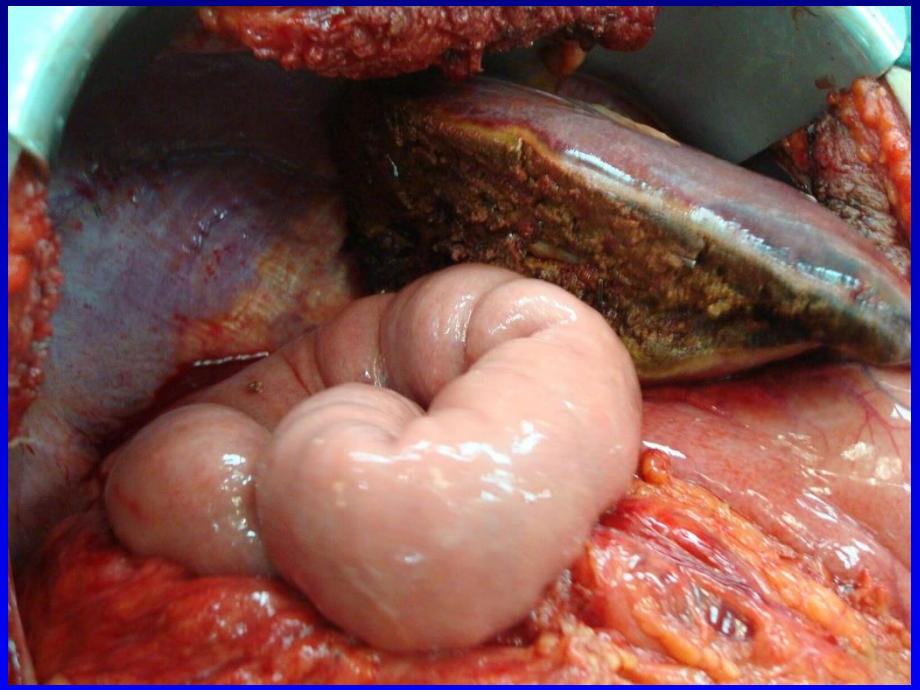
Type IIIA HCC





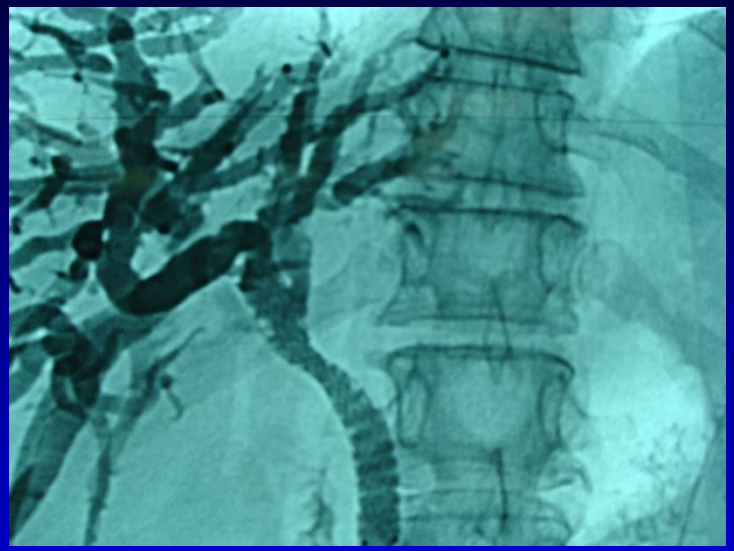
by Dimitris P. Korkolis, MD, PhD

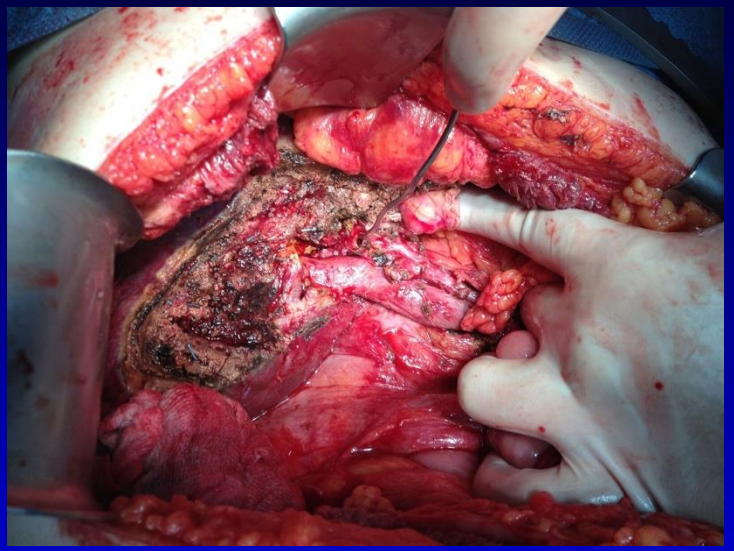
Minor Liver Resections

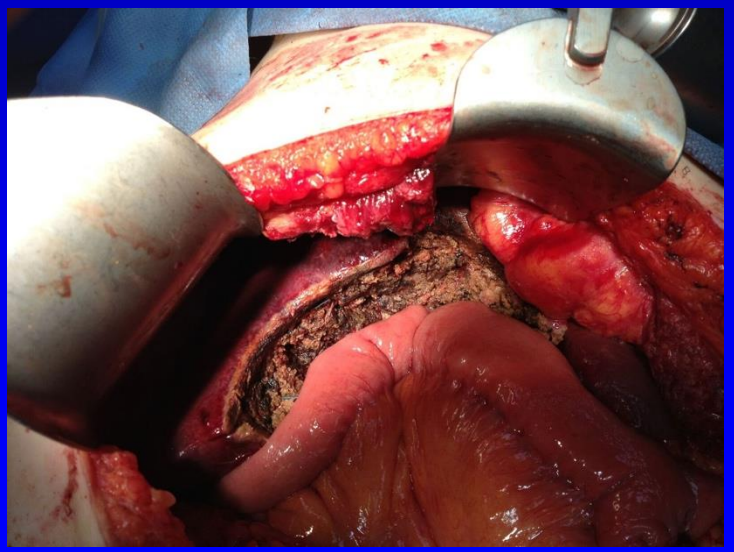
- In selected pts with limited disease extension
- When PVE is not available
- To avoid complications such as PV injury
- When concerns exist about liver hypertrophy
- In pts with insufficient residual liver function
- S4a + S5 + S1 minor hepatectomy (Taj-Mahal)
- May provide comparable results

Noji T, et al. J Gastrointest Surg 2014
Tsuchikawa T, et al. Exp Rev Gastroenterol Hepatol 2015

Taj - Mahal





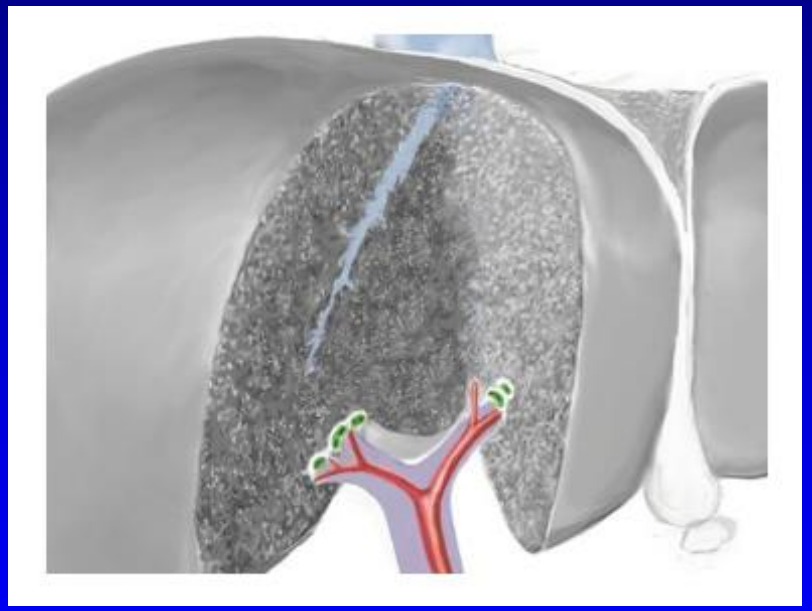


by Dimitris P. Korkolis, MD, PhD

Central Hepatectomy for HCC

Central Lobe resection 4,5,8 and 1 is technically difficult because:

- The operation involves two liver transection lines
- Need to preserve blood supply to the outer liver segments
- Many intrahepatic ductal openings may be left in the liver remnant requiring multiple anastomoses



Chen XP, et al. Br J Surg 2009

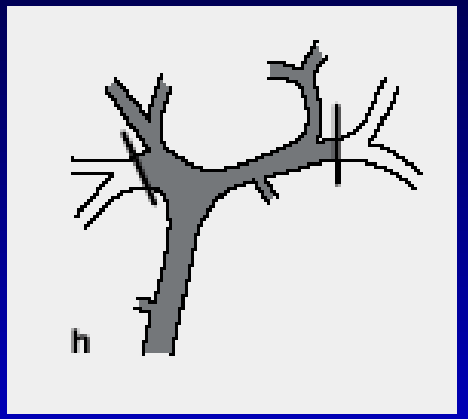
Central Hepatectomy

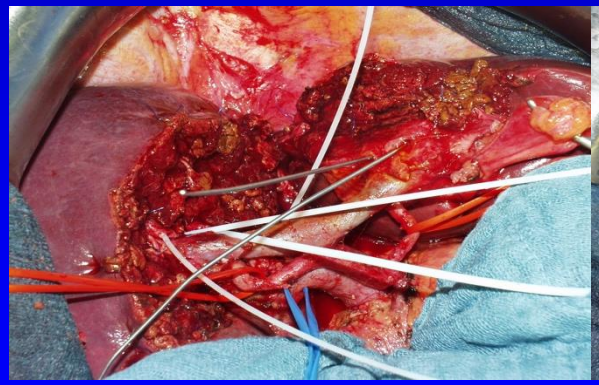
Απαιτητικός τύπος εκτομής

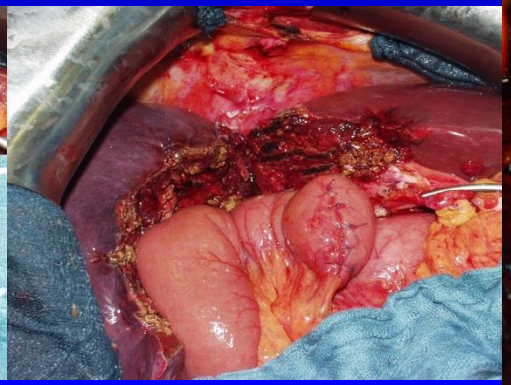
Parenchyma sparing (S1, S4, S5, S8)

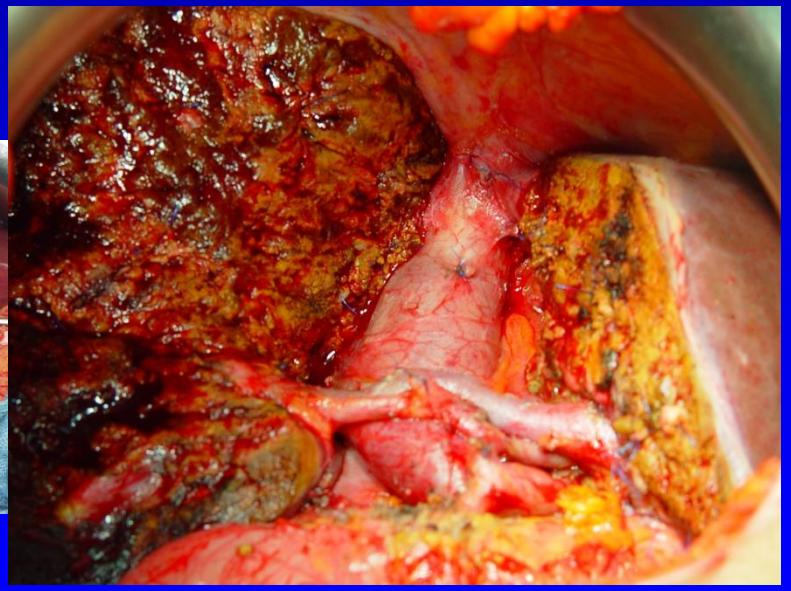
„open book“ με 2 επιφάνειες εκτομής

2-6 αναστομώσεις









Sotiropoulos GC et al. Am J Surg 2009

Perihilar Cholangiocarcinoma – Novel Benchmark Values for Surgical and Oncological Outcomes From 24 Expert Centers

1829 consecutive pCCA resections – 708 Benchmark (low-risk)

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.

Complications	
CCI®, median (IQR)	28.9 (16.4-42.4)
Any complication, n (%)	570 (80.5)
CCI® ≥ 26.2 (≥ Clavien-Dindo 3a), n (%)	411 (58.1)
In-hospital mortality, n (%)	33 (4.7)
Liver failure, n (%)	
Grade A	60 (8.5)
Grade B	83 (11.7)
Grade C	44 (6.2)
Bile leak, n (%)	237 (33.5)
Bile leak (anastomosis), n (%)	130 (18.4)
Bile leak (surface), n (%)	108 (15.3)
Portal vein thrombosis, n (%)	27 (3.8)
Hemorrhage, n (%)	60 (8.4)
Intraabdominal abscess, n (%)	135 (19.1)
Cholangitis, n (%)	91 (12.9)
Re-Laparotomy, n (%)	64 (9.0)
Blood transfusion, n (%)	146 (20.6)
Readmissions (3 months), n (%)	102 (14.4)

Mueller M et al. Ann Surg 2021

Evolution of Surgical Treatment for Perihilar Cholangiocarcinoma

A Single-Center 34-Year Review of 574 Consecutive Resections

Masato Nagino, MD, PhD, Tomoki Ebata, MD, PhD,* Yukihiro Yokoyama, MD, PhD,* Tsuyoshi Igami, MD, PhD,* Gen Sugawara, MD, PhD,* Yu Takahashi, MD, PhD,* and Yuji Nimura, MD, PhD†*

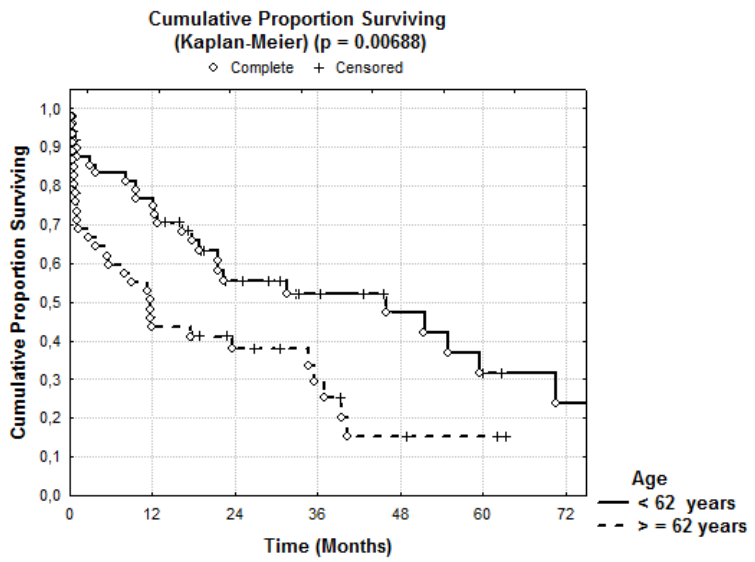
TABLE 6. Literature Review on Resection of Perihilar Cholangiocarcinoma (Single-Center Study, Published After 2000)

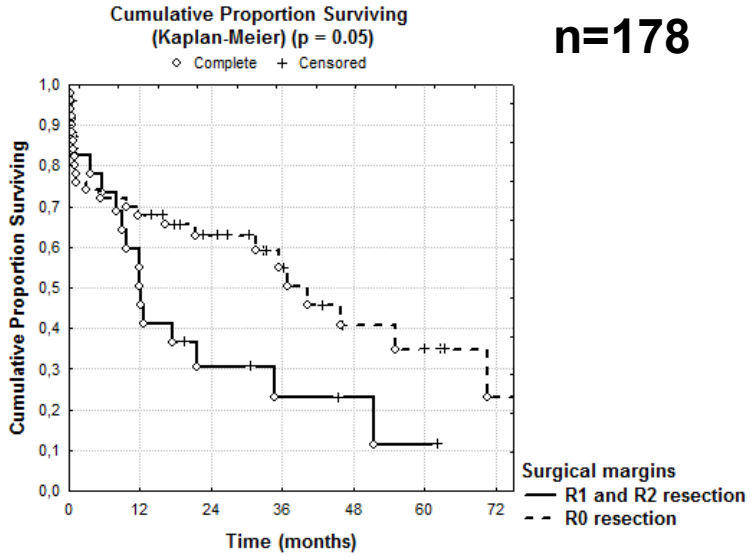
Reference	Period	Resected, N	Volume, resected /y	Surgical Procedure, %				Bismuth Type IV, %	pN1, %	R0 resection, %	Mortality, %	5-Year Survival, %	
				Hx	PV	HA	PD					All	R0
Jarnagin[5]	1991–2000	80	8.0	78	11	0	3	—	24	78	10.0	27	—
Capussotti[6]	1988–2001	36	2.6	89	14	3	0	0	39	89	2.8	27	29
Kawarada[7]	1976–2000	87	3.5	75	8	0	3	—	—	64	2.3‡	26	—
Seyama[8]	1989–2001	58	4.5	100	16	0	16	28	52	64	0	40	46
Kawasaki[9]	1990–2001	79	6.6	96	6	3	16	47	44	68	1.3	—	40
Kondo[10]	1999–2002	40	10.0	78	20	20	18	15	38	95	0	—	—
IJitsma[11]	1986–2001	42	2.6	100	17	9	0	—	38	64	11.9	22	—
Hemming[12]	1997–2004	53	6.6	98	43	6	8	5	21	80	9.4	35	45
Sano[13]	2000–2004	102	20.4	100	22	5	7	—	—	61	0	44	—
DeOliveira[14]	1973–2004	173	5.4	20	0	0	0	—	28 ?	19	5.4	10	30
Miyazaki[15]	1981–2004	161	6.7	88	25	6	4	—	48	63	6.8	—	36
Lee[16]	2001–2008	302	37.8	89	13	2	2	17	24	71	1.7	33	47
Gulik[17]	1988–2003	99	6.2	38	18	0	0	—	—	31	10	20,* 33†	—
Young[18]	1994–2008	83	5.5	93	39	10	2	—	57	46	7.2	20	33
Saxena[19]	1992–2009	42	2.3	100	26	0	0	2	29	64	2.4	24	—
Cannon[20]	1992–2010	59	3.1	83	—	—	—	—	15	63	5.1‡	<20	—
This study	1977–2000	188	7.8	93	31	3	12	41	50	75	10.1	23	30
	2001–2005	168	33.6	98	35	15	12				3.0		
	2006–2010	218	43.6	99	41	21	15	]48	]48	]78	1.4	]38	]45

Nagino, et al. Ann Surg 2013

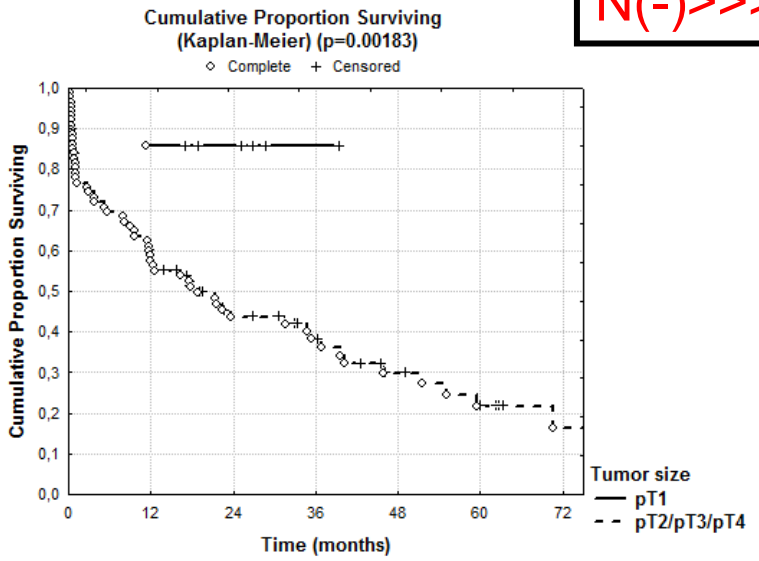
Πυλαίο χολαγγειοκαρκίνωμα (Klatskin)

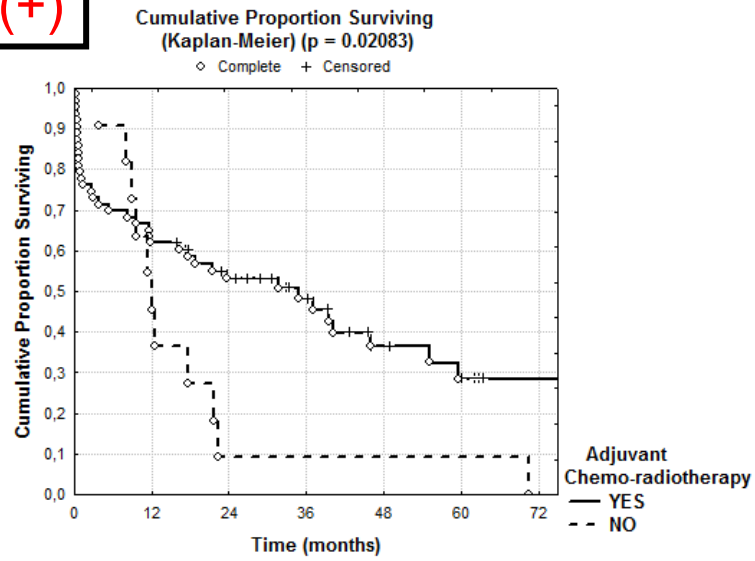
n=178





N(-)>>>N(+)





Vascular Resections

Resection and reconstruction of PV and/or HA may be necessary for complete resection, especially in patients with more advanced disease. This approach requires substantial experience and appropriate surgical support for such technical operations

Vascular resections at the hilum are possible but their invasion affects prognosis

In some cases with portal vein invasion, combined portal vein resection is useful because the prognosis of patients with PV resection is similar to that of patients without PV resection

Vascular Resections

- Indications:

    1. Intraoperative suspicion of gross invasion to vessels

    2. Tight adherence of tumor during vessel skeletonization

    3. Routine resection of PV in systematic radical surgery??

Dumitraskou T, et al. J Gastrointest Surg 2013
Young AL, et al. J Hepato-Biliary-Pancreat Sci 2010
De Jong, et al. Cancer 2012

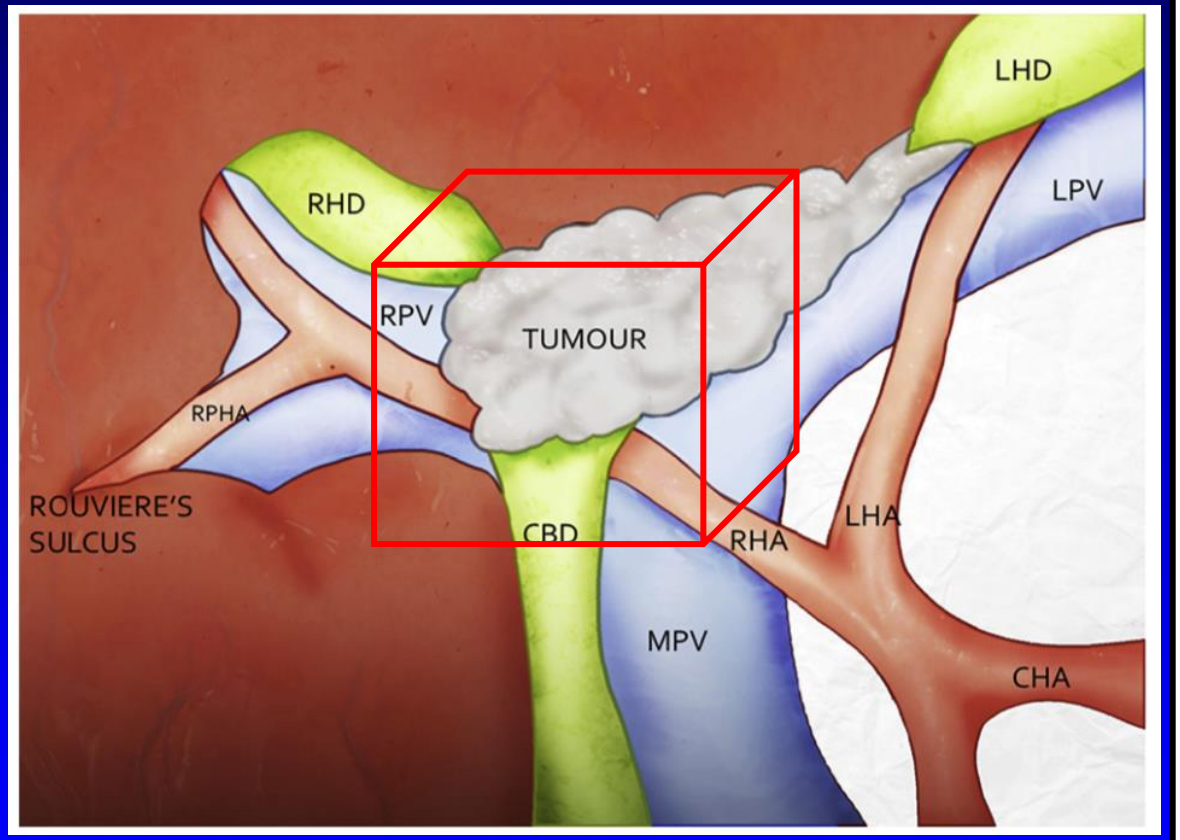
Vascular Resections

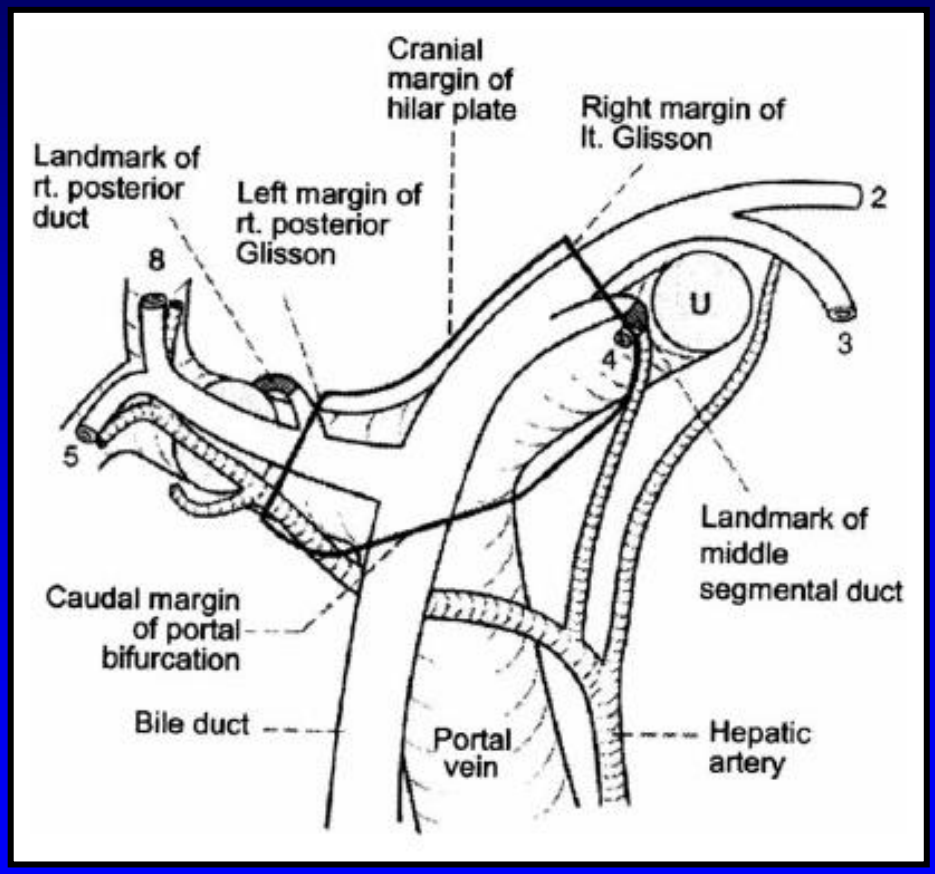
Study	Positive for invasion, *n* (%)	Portal vein resection, *n*
Song *et al*. 2009[25]	28 (54%)	51
Ebata *et al*. 2003[8]	36 (69%)	52
Nagino *et al*. 2010[19]	44 (80%)	50
Muñoz *et al*. 2002[7]	5 (50%)	10
Hemming 2011[20]	17 (40%)	42
Neuhaus *et al*. 1999[6]	5 (22%)	23
Miyazaki *et al*. 2007[27]	38 (88%)	44

- **Reported rates of actual tumor invasion into the resected PV varies significantly**
- **Difficult to determine the actual status of vascular involvement preoperatively or even intra-operatively**

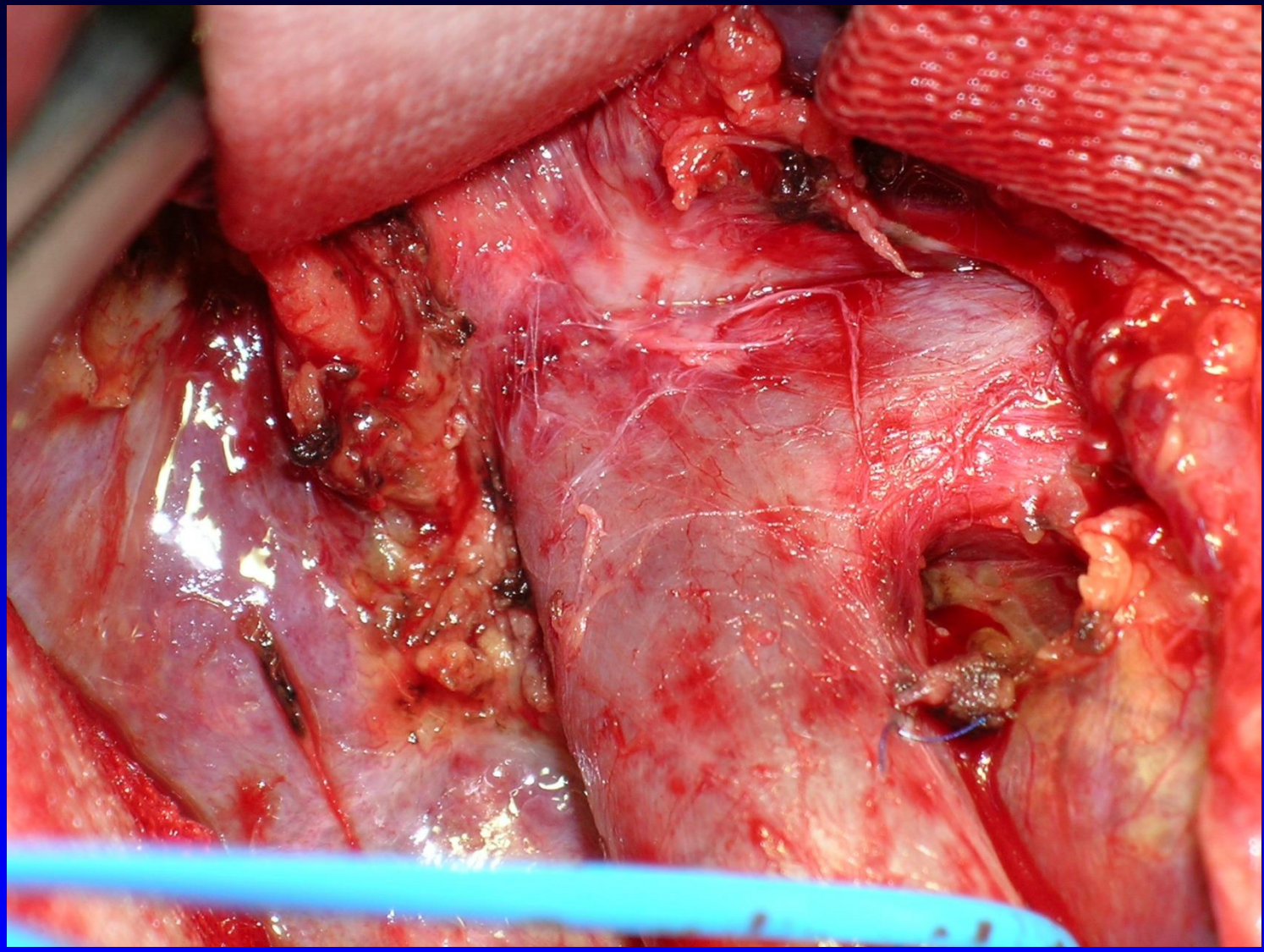
Ramia WJGIO 2013
Xiang et al. Int J Colorect Dis 2015
Abbas et al. HPB 2013

Anatomical - Vascular Considerations

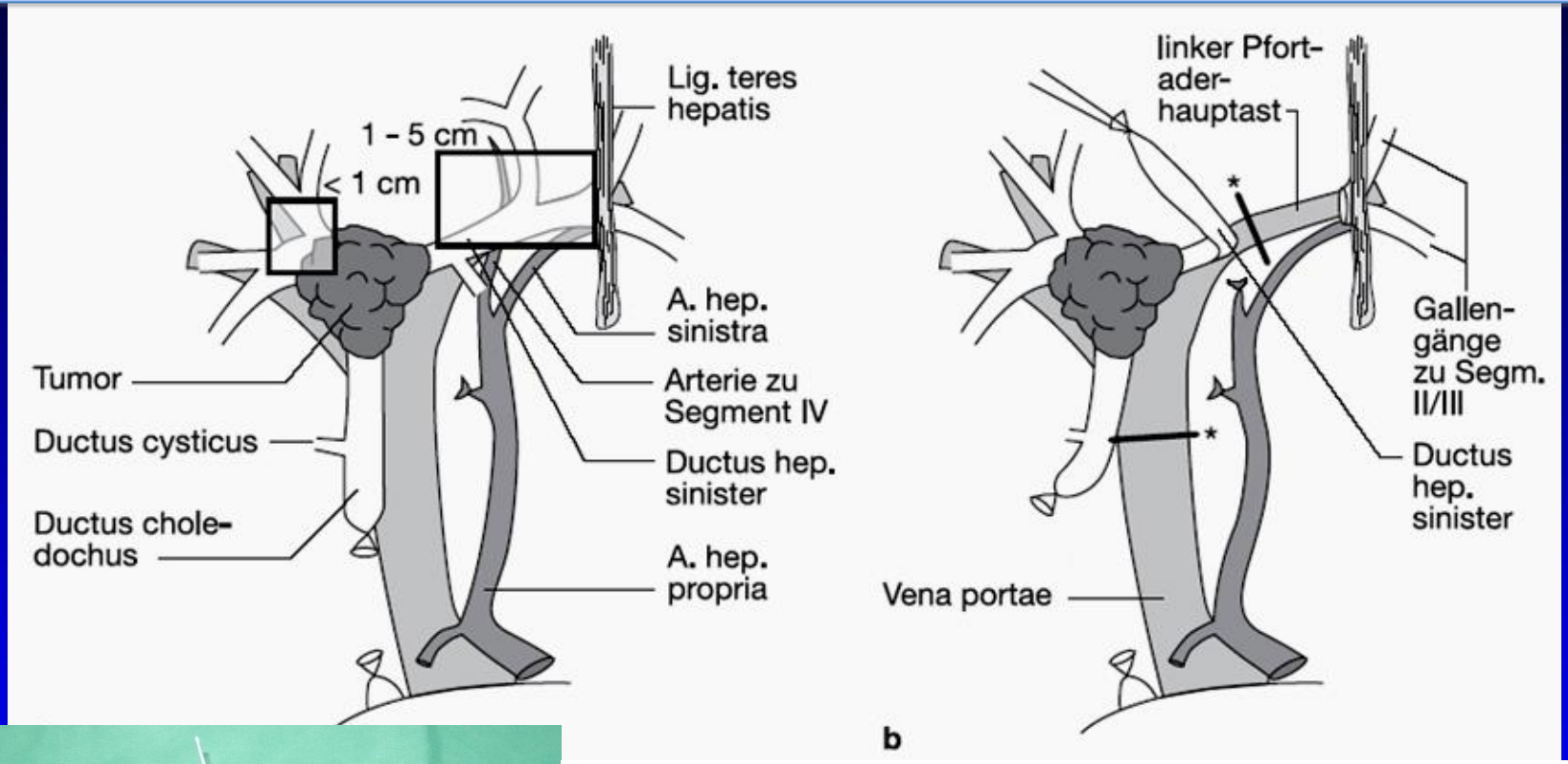


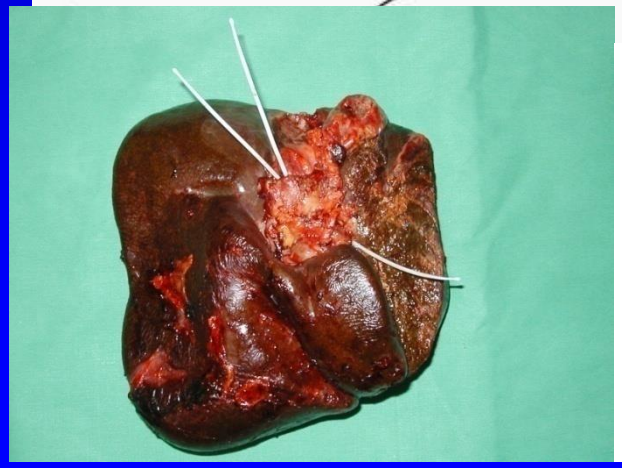


Neuhaus et al. Ann Surg Oncol 2012
Hogil et al. HPB (Oxford) 2016



Εκτεταμένη δεξιά ηπατεκτομή συνδυασμένη με μερική εκτομή πυλαίας φλέβας





- Παρέχει το δυνητικά ευρύτερο υγιές όριο εκτομής
- συμμορφώνεται καλύτερα με τους βασικούς κανόνες της ογκολογικής χειρουργικής
- Απαιτεί μεταμοσχευτική εμπειρία

Portal Vein Resection for HCC

Study	Year	No. of patients	Portal vein resection	Morbidity		Mortality		5-Year survival	
				With resection (%)	Without resection (%)	With resection (%)	Without resection (%)	With resection (%)	Without resection (%)
Ebata	2003	188	54	Nr	Nr	9.6	9.3	9.9	36.8
Miyazaki	2007	161	34	NR	NR	8.8	4.2	14	30
Hirano[a]	2008	64	43	28.5	57.1	4.8	4.8	NR	NR
Song	2009	259	51	Nr	Nr	9.8	NR	22.8	30.9
Young	2010	51	21	78	NR	8	NR	20	NR
Nagino	2010	50	50	54	NA	2	NA	30.3	NA
Igami	2010	293	111	NR	NR	NR	NR	23	51
Lee	2010	302	40	NR	NR	0	1.7	31.5	41.3
Hemming	2011	95	42	NR	NR	2	8	38	38
Nuzzo	2012	376	42	NR	NR	19	9	22.8	25.5
De Jong	2012	305	51	NR	NR	11.8	6.7	24	30
Tamoto	2013	49	36	58	76	2	7	59	51

Maddern GJ, et al. World J Surgery 2015

PORTAL VEIN RESECTION IN HCC

- Overall Mortality 6.8% (161 pts)
- Mortality:

PVR (+)	8.8%	
PVR (-)	4.2%	NS

- PVR (+) Poor prognostic factor
- Survival

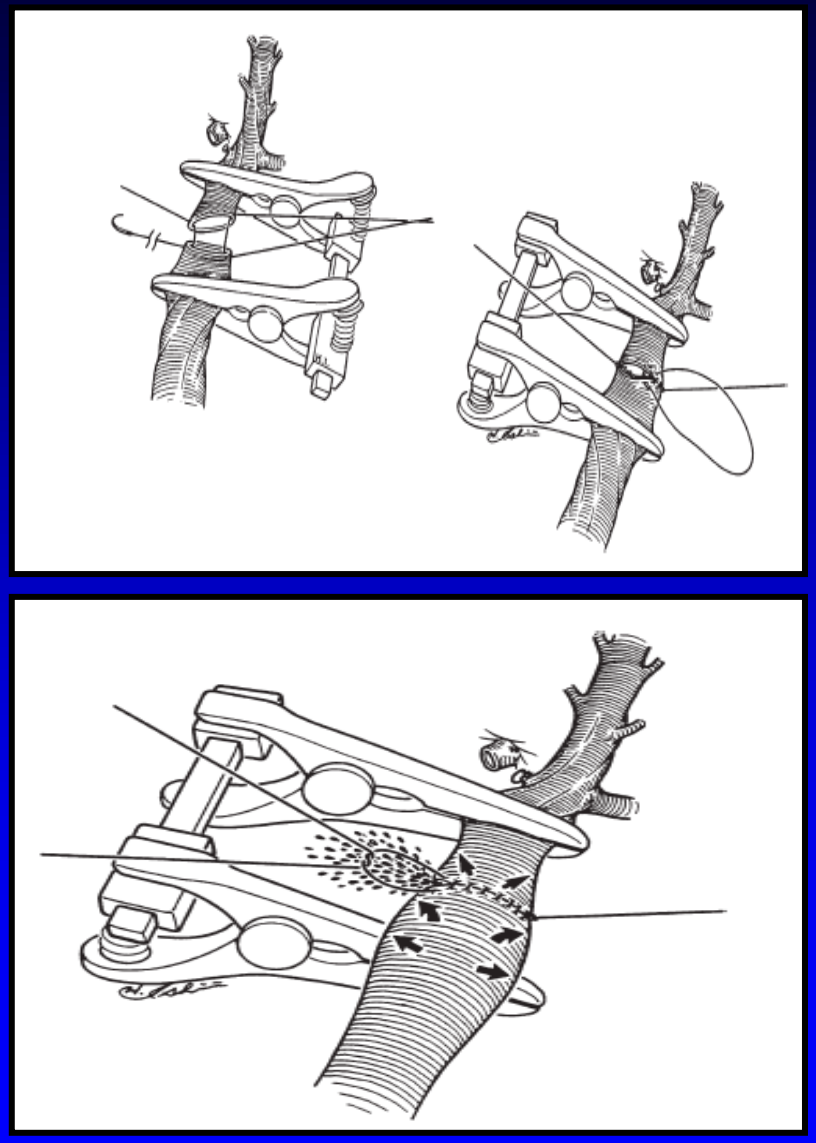
	1 yr	3 yr	5 yr
PVR (-)	63%	39%	30%
PVR (+)	42%	17%	14%
Unres	15%	0%	0%

$p<0.001$

Miyazaki M, et al. Surgery 2007

PORTAL VEIN RESECTION IN HCC

- Before or After Hepatectomy
- End-to-end Anastomosis
- Autologous Vein graft
- Continuous 6-0 Prolene
- No growth factors
- No prostaglandin E1
- No iv heparin

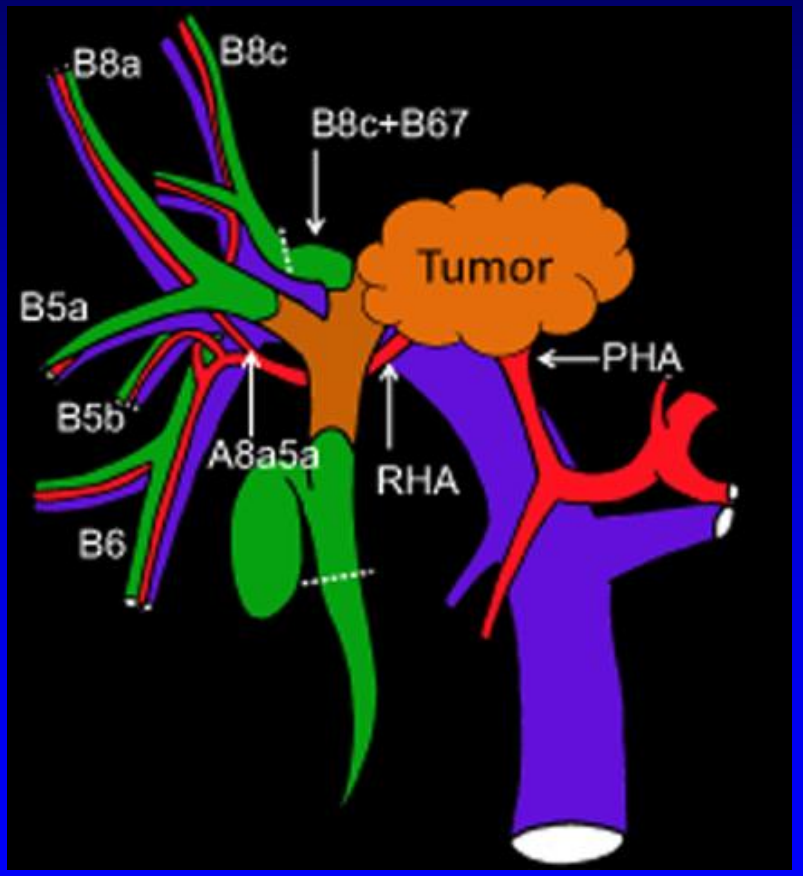


Nagino M, et al. Ann Surg 2012

HEPATIC ARTERY RESECTION IN HCC

- Mortality rates

Madariaga 1998: *55%*
Gerhards 2000: *56%*
Miyazaki 2007: *33%*
Nagino 2010: *5%*

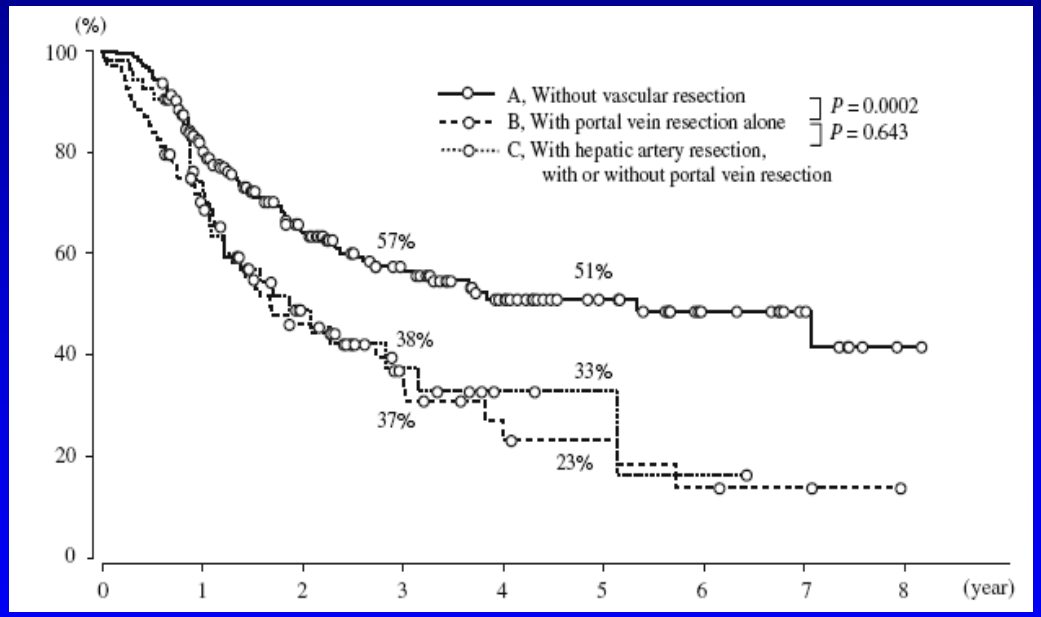


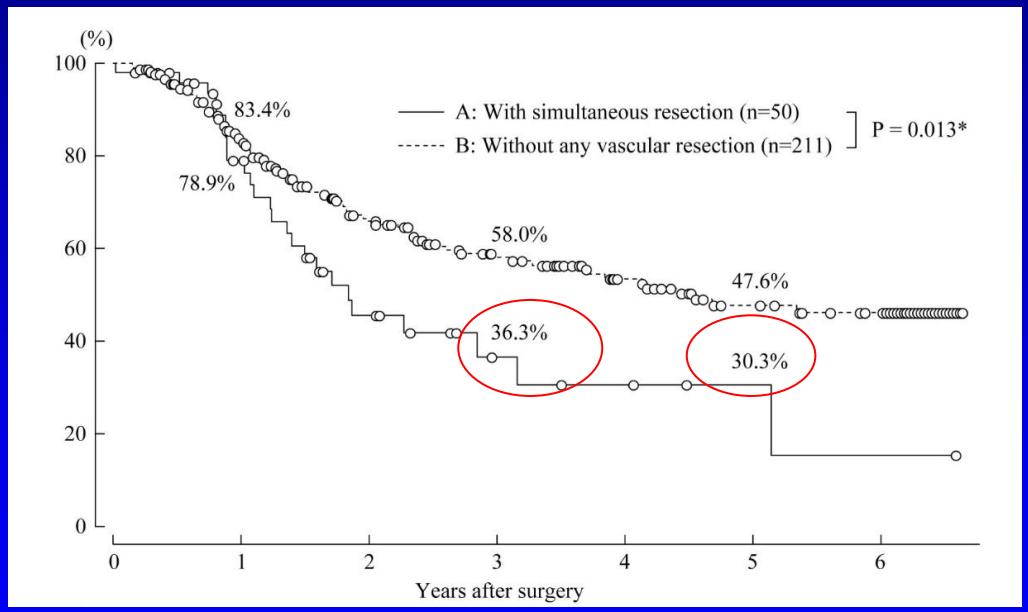
Nagino M, et al. Ann Surg 2010
Miyazaki M, et al. J Hepatobiliary Pancreat Surg 2007

Combined Vascular Resections

Hepatectomy With Simultaneous Resection of the Portal Vein and Hepatic Artery for Advanced Perihilar Cholangiocarcinoma

An Audit of 50 Consecutive Cases

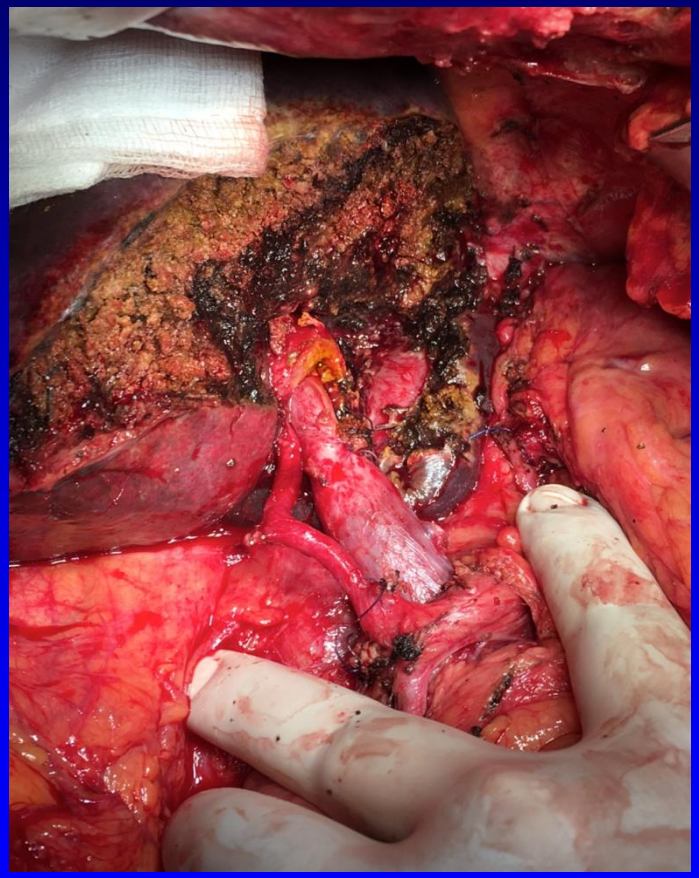


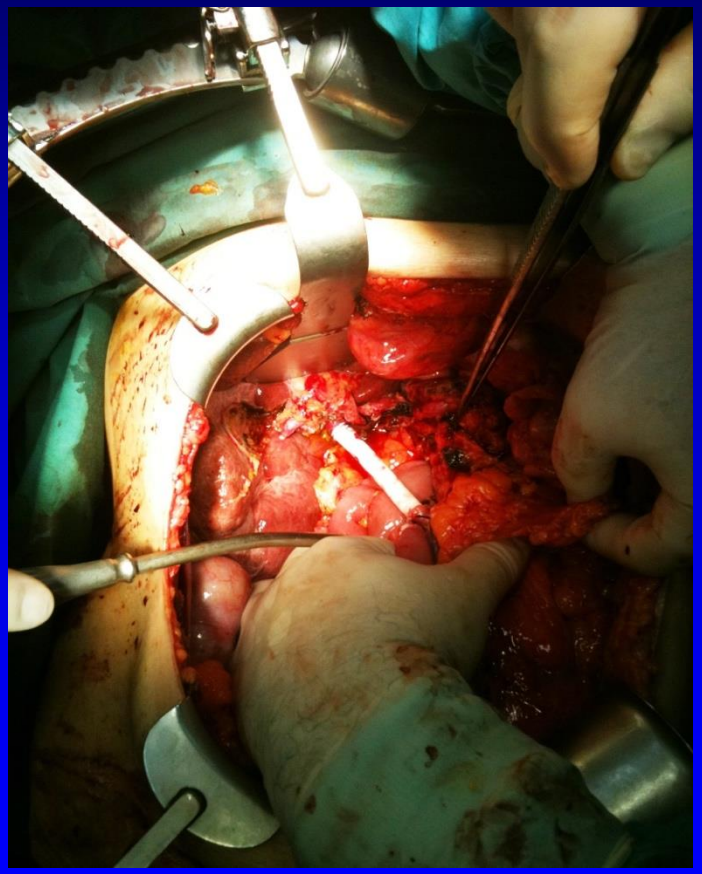


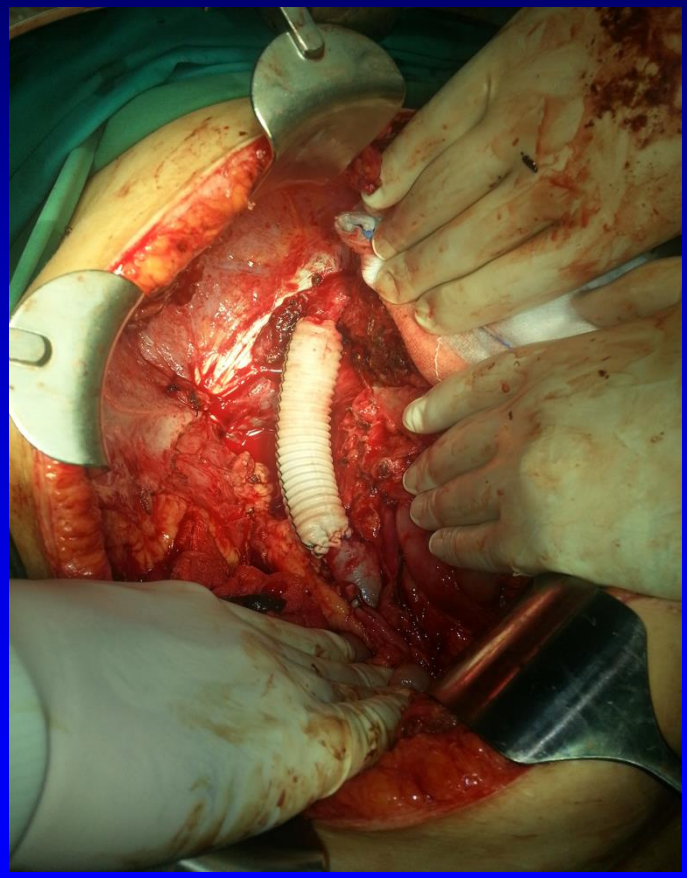
Igami T, et al. J Hepatobiliary Pancret Surg 2009

Nagino M, et al. Ann Surg 2010

PV – IVC Resection for the treatment of HCC







by Dimitris P. Korkolis, MD, PhD

"BERLIN'S CONCEPT"

- Strongest determinant of Survival: *Surgical Radicality!!!*
- R0 resection after Right trisectionectomy: 65% p<0.05
- R0 resection:

	1-yr	3-yr	5-yr survival:	
PV(-):	79%	40%	29%	
PV(+):	87%	70%	58%	p<0.001

- R0 resection:

	5-yr survival	
Right trisegm and PV(-):	52%	
Right trisegm and PV(+):	72%	p<0.05

- Mortality: 5 -15%!!!

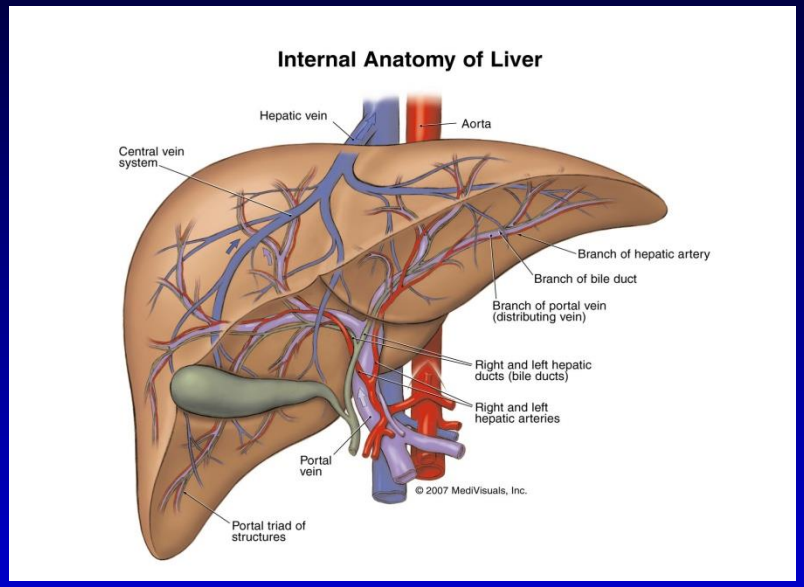
Peter Neuhaus, et al. Ann Surg 2008
Peter Neuhaus, et al. Langenbecks Arch Surg 2003

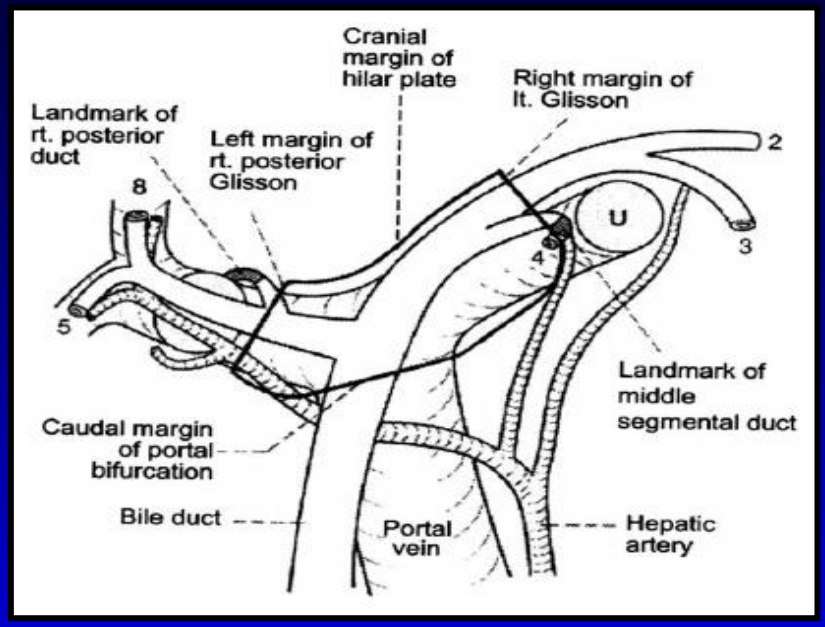
"NO – TOUCH TECHNIQUE"

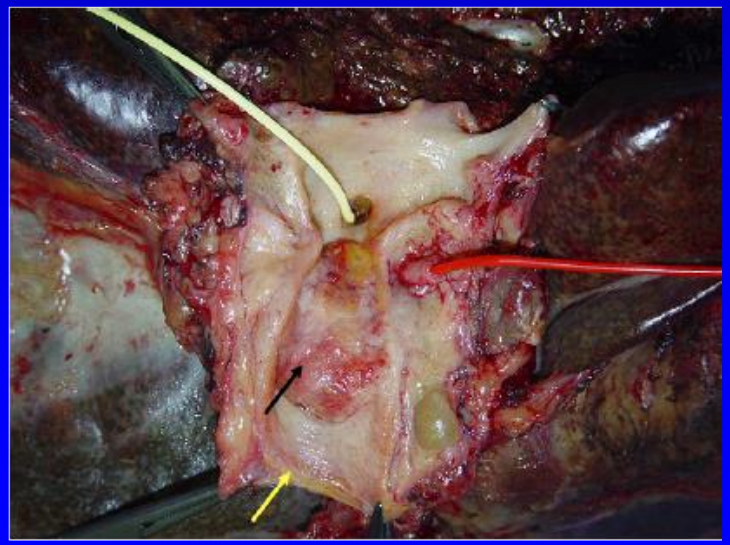
- Right Trisectionectomy with en-block portal vein and bile duct resection
- Wide negative resection margins> 2 cm
- No manipulation between the tumor, RHA and RPV
- No microscopic tumor dissemination
- Stable surgical anatomy of segments II - III
- Avoids vascular kinking after R Trisectionectomy and caudate lobectomy
- Prerequisites: PTC – PTBD of the remnant liver
  PVE

P. Neuhaus. HPB 2008

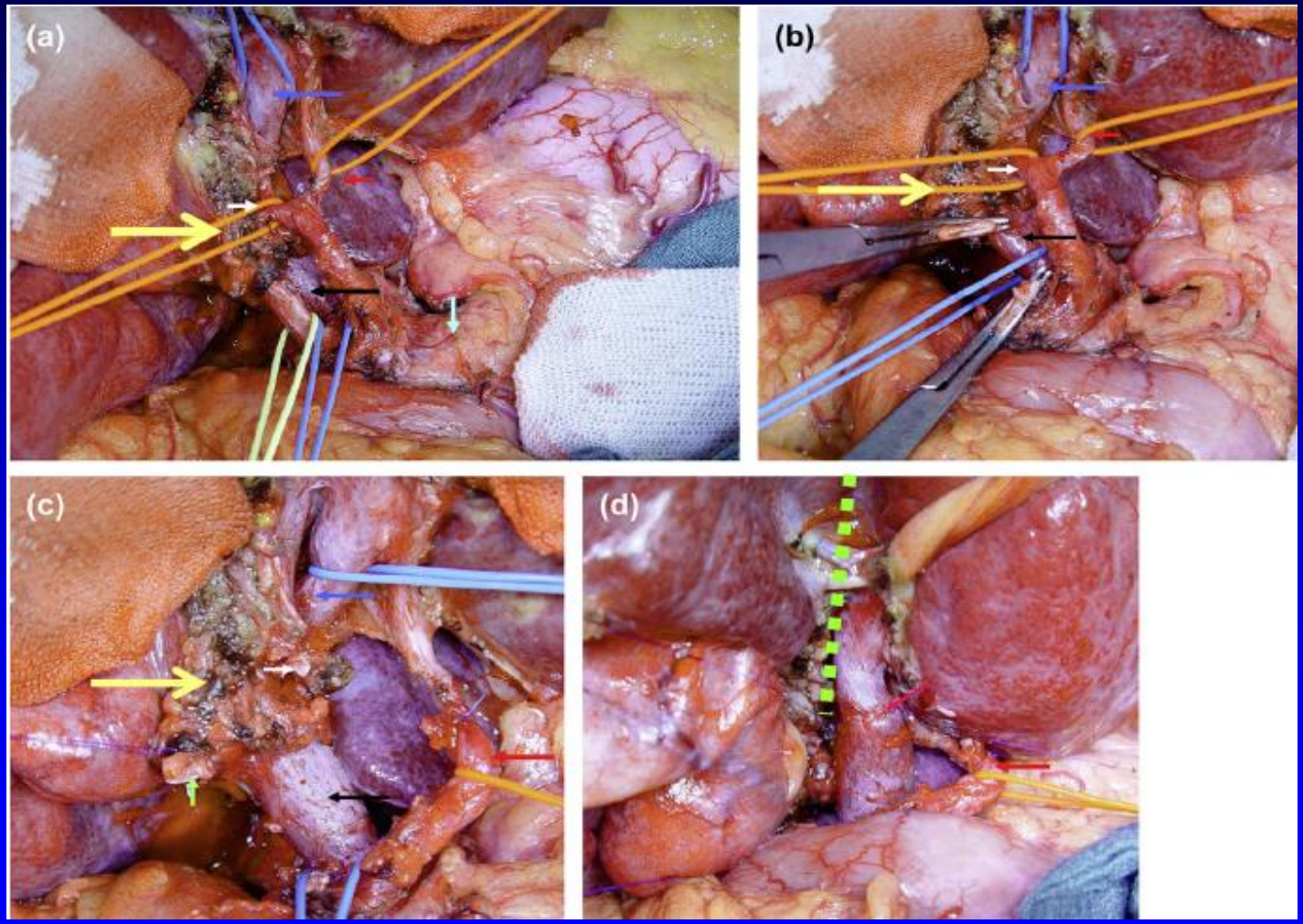
“NO – TOUCH TECHNIQUE”







“NO – TOUCH TECHNIQUE”



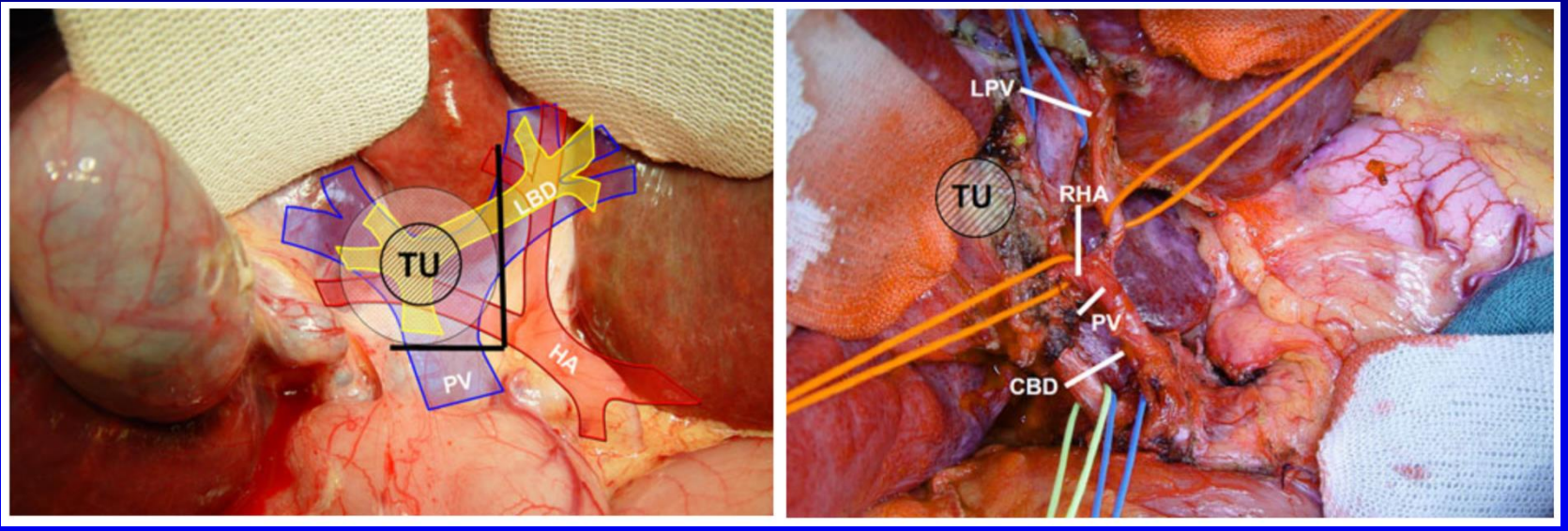
P. Neuhaus. HPB 2008

“NO – TOUCH TECHNIQUE”

Oncological Superiority of Hilar En Bloc Resection for the Treatment of Hilar Cholangiocarcinoma

Peter Neuhaus, MD[1], Armin Thelen, MD[1], Sven Jonas, MD[1], Gero Puhl, MD[1], Timm Denecke, MD[2], Wilfried Veltzke-Schlieker, MD[3], and Daniel Seehofer, MD[1]

1990-2004, 50 (R0) hilar en bloc resection vs 50 curative conventional major hepatectomy



1-, 3-, and 5-year OS en bloc resection vs conventional major hepatectomy 87%, 70%, and 58%, respectively, vs 79%, 40%, and 29%, respectively (P = 0.021)

Ann Surg Oncol (2012) 19:1602–1608

Routine PV resection for all patients?

J Hepatobiliary Pancreat Surg (2009) 16:502–507
DOI 10.1007/s00534-009-0093-7

ORIGINAL ARTICLE

No-touch resection of hilar malignancies with right hepatectomy and routine portal reconstruction

Satoshi Hirano · Satoshi Kondo · Eiichi Tanaka · Toshiaki Shichinohe · Takahiro Tsuchikawa · Kentaro Kato

	N-PVR ($n = 21$)	C-PVR ($n = 18$)	R-PVR ($n = 25$)	p
Operating time (min)[a]	695.0 (521–902)	676.5 (532–979)	695.0 (479–879)	0.791[b], 0.825[c]
Blood loss (ml)[a]	2130.0 (780–4815)	1532.5 (930–2929)	1840.0 (840–5970)	0.237[b], 0.237[c]
Blood transfusion (unit)[a]	0.0 (0–10)	0.0 (0–7)	0.0 (016)	0.137[b], 0.703[c]
Portal cross-clamp time (min)[a]	–	18.5 (12–29)	20.0 (15–56)	0.343
Portal thrombus formation	0	2	2	0.492[b], >0.999[c]
ASAT (units/l)[a] on 1st POD	480.0 (144–4545)	537.5 (152–1624)	483.0 (124–3680)	0.741[b], >0.999[c]
ALAT (units/L)[a] on 1st POD	382.0 (84–3400)	598.5 (107–1348)	413.0 (63–3080)	0.544[b], 0.658[c]
Maximum bilirubin level (mg/dl)[a]	5.5 (1.6–17.0)	4.2 (1.6–13.4)	3.4 (0.9–11.6)	0.028[b], 0.307[c]
Postoperative day of max. bilirubin[a]	3.0 (1–15)	2.0 (1–14)	1.0 (0–14)	0.069[b], 0.284[c]
Residual tumor status (R0/R1)	20/0	17/1	24/1	>0.999[b], >0.999[c]
Histologic portal vein invasion	2	11	8	0.086[b], 0.058[c]
UICC stage (I/II/III)	9/11/1	0/8/10	8/10/7	0.429[b], 0.020[c]

- No-touch resection of hilar malignancies with R hepatectomy and the routine use of portal reconstruction was feasible and safe.
- ***The oncologic impact of this technique merits further evaluation.***

Routine PV resection for all patients?

Systematic review and meta-analysis of the role of vascular resection in the treatment of hilar cholangiocarcinoma

Saleh Abbas & Charbel Sandroussi

Study	Vascular resection Events	Total	No vascular resection Events	Total	Weight	M–H random effects OR (95% CI)
Baton 2007	5	7	45	52	4.1%	0.39 (0.06-2.41)
Ebata 2003	47	52	67	108	8.2%	5.75 (2.12-15.64)
Hemming 2011	25	42	32	53	9.5%	0.97 (0.42-2.20)
Hidalgo 2008	13	17	12	27	6.0%	4.06 (1.05-15.73)
Igami 2010	86	111	92	187	12.0%	3.55 (2.09-6.03)
Klempnauer 1997	33	37	45	61	7.0%	2.93 (0.90-9.59)
Kondo 2004	1	14	4	26	2.9%	0.42 (0.04-4.20)
Miyazaki 2007	21	34	70	118	9.9%	1.11 (0.51-2.42)
Muñoz 2002	8	10	11	18	4.1%	2.55 (0.41-15.65)
Nagino 2010	35	50	111	211	10.9%	2.10 (1.08-4.08)
Neuhaus 2003	10	34	7	14	6.4%	0.42 (0.12-1.50)
Nimura 2000	41	43	72	99	5.4%	7.69 (1.74-34.00)
Shimada 2003	8	10	12	16	3.8%	1.33 (0.20-9.08)
Song 2009	42	51	153	208	9.9%	1.68 (0.77-3.67)
Total (95% CI)		**512**		**1198**	**100.0%**	**1.88 (1.22-2.90)**
Total events	375		733			

Heterogeneity: Tau² = 0.33; Chi² = 29.75, d.f. = 13 (P = 0.005); I^2 = 56%

Test for overall effect: Z = 2.87 (P = 0.004)

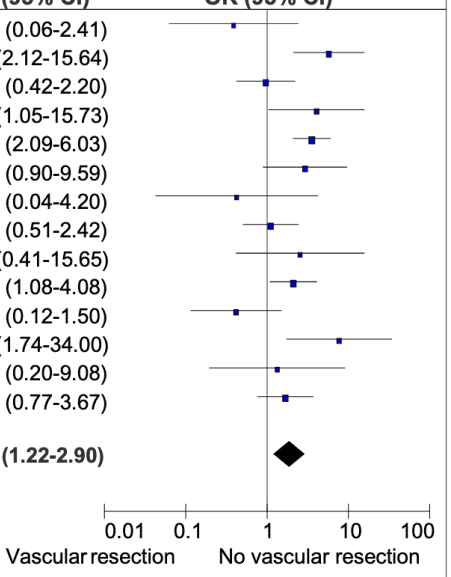
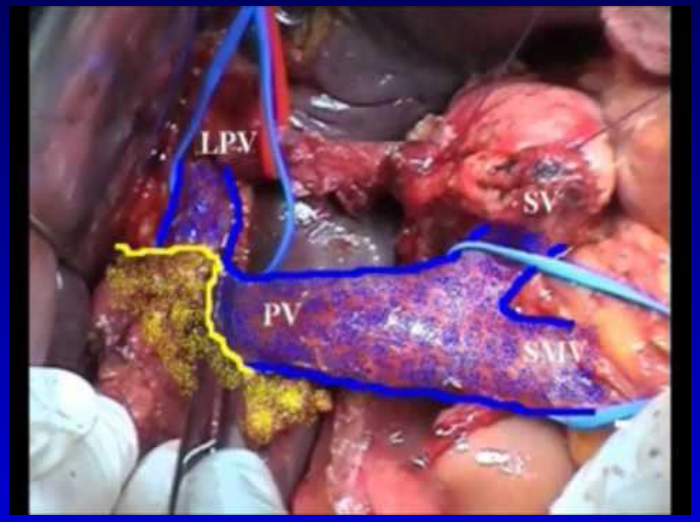


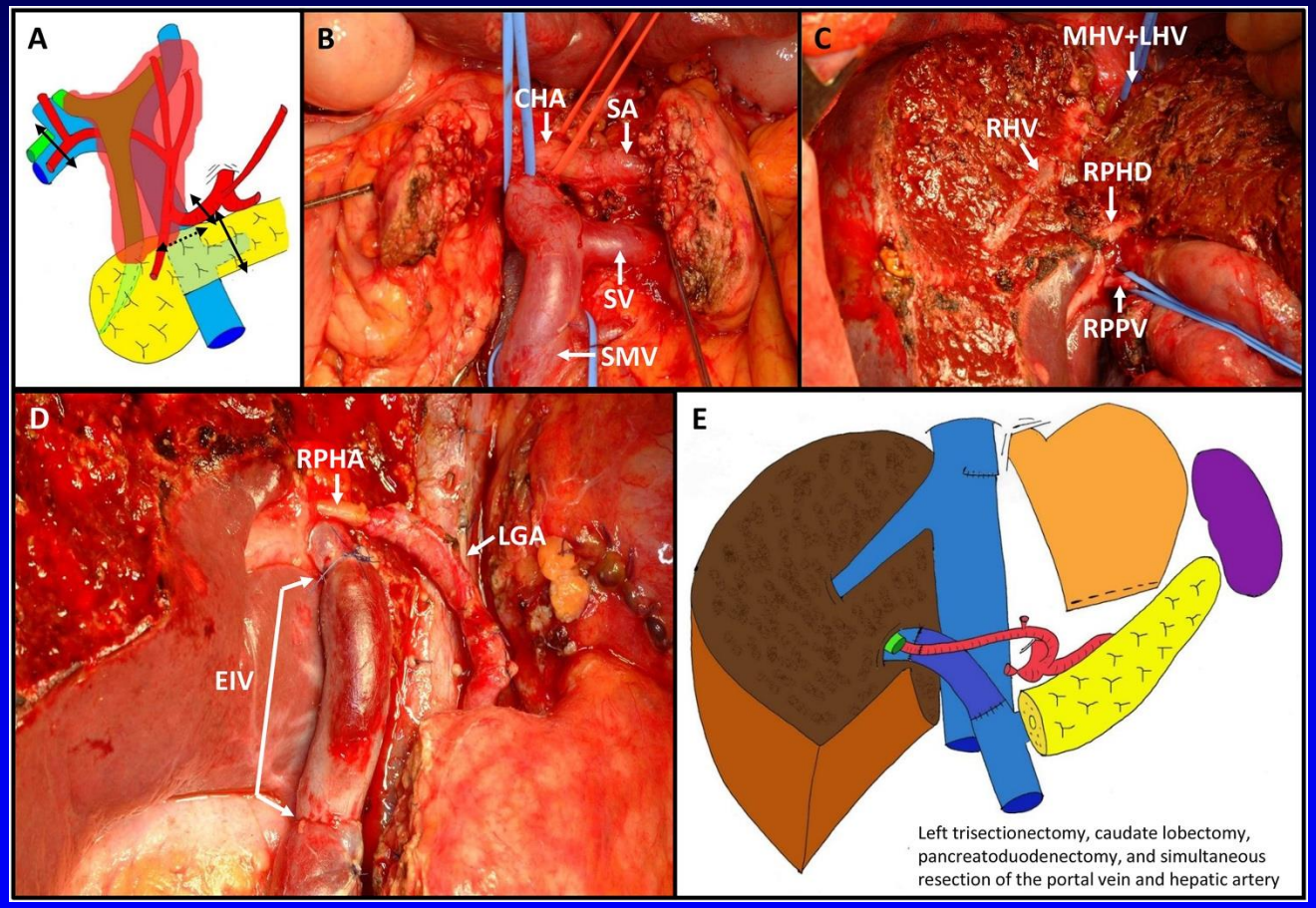
Figure 8 Five-year survival in patients with and without vascular resection. M–H, Mantel–Haenszel test; OR, odds ratio; 95% CI, 95% confidence interval

- **The validity of resection of the involved portal vein is well established and the procedure is likely to increase long-term survival.**
- **Routine resection, however, remains controversial and there is little possibility that randomized data will become available.**

HPB 2013, 15, 492–503

Hepato - Pancreatoduodenectomy





- Diffusely infiltrating tumors
- Downward superficial spreading
- Bulky nodal metastases
- Mortality <5%

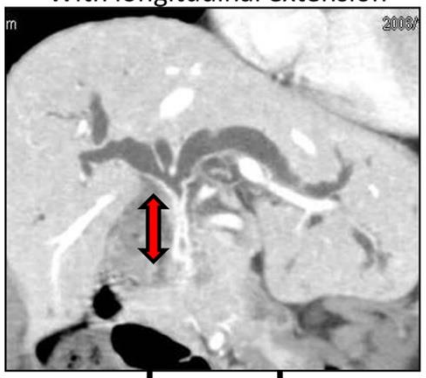
Nagino, Liver 2022

Extended Resections for pHCC

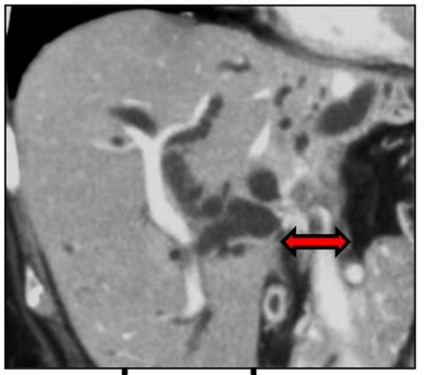
Standard resection for perihilar cholangiocarcinoma

Major hepatectomy (left or right hemihepatectomy, left or right trisectionectomy) with caudate lobectomy and extrahepatic bile duct resection

With longitudinal extension



With vertical extension



Extended resection

Standard resection with pancreatoduodenectomy (Hepatopancreatoduodenectomy)

Extended resection

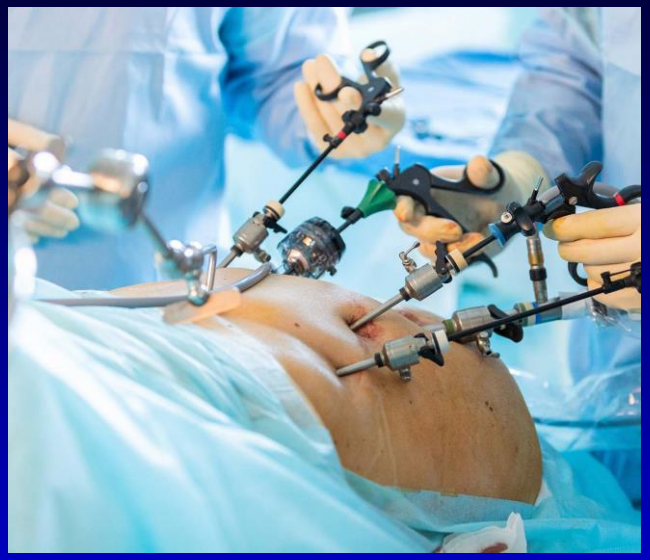
Standard resection with vascular (portal vein and/or hepatic artery) resection

Superextended resection

Hepatopancreatoduodenectomy with vascular (portal vein and/or hepatic artery) resection

MIS

- Small cohorts
- No RCTs
- Better short-term results eg. Blood loss
- Comparable R0 resections
- Equal survival
- Surgical Time – Cost Increased!!!
- Robotic Platform
- EndoWrist within the DaVinci Surgical System
- Increased Risk of Hepatic Artery Pseudoaneurysm!



Liver Transplantation

- Mayo Clinic CRT Protocol 1993

Indications

- Biopsy(+) or Highly Suspicious
- Mass lesion on imaging
- CA 19.9<100

Contraindications

- Lesion> 3cm
- N(+) or M(+) disease
- Attempted resection or transperitoneal Bx
- 5year history of malignancy

Post LT Survival

1yr	3yr	5yr
77%	55%	45%

Procedure	Morbidity (%)	Mortality (%)	5- year overall survival (%)
Major hepatectomy [94]	43–65	2–17	25–40
Portal vein resection [95]	34.3	2.9	37.7
Arterial and portal vein resection [96]	52	6.8	18
Caudate lobectomy [62]	36.3	4.51	10.6–33
Hepatopancreato-duodenectomy [97]	37–97.4	0–34.2	17.9–49.2
Liver transplantation [98]	20–50	4.8–25	36–75

Conclusions

- Treatment of HCC remains challenging
- Strategy of surgical resection has improved over years

- Some consensus have been reached:
    a. R0 margin achievement
    b. Combination of partial hepatectomy
    c. Routine caudate lobe resection
    d. PVE – Biliary Drainage
    e. Portal vein resection when involved by tumor
    f. Adequate Lymphadenectomy

- Controversial issues: “No – Touch” - Arterial res - MIS - LT
- RCTs