
# Ενδοηπατικό Χολαγγειοκαρκίνωμα

## Χειρουργική Αντιμετώπιση:

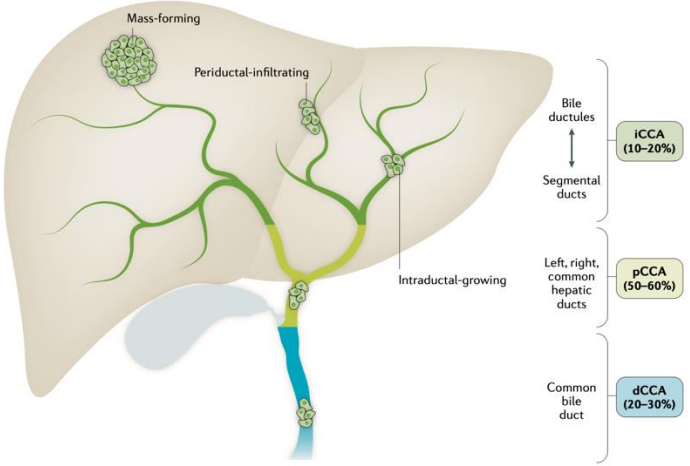
## Ενδείξεις, Αποτελέσματα, Πρόγνωση

Δημήτρης Π. Κορκολής

Δ/ντής Χειρουργικής Κλινικής

ΓΑΟΝΑ «Άγιος Σάββας»

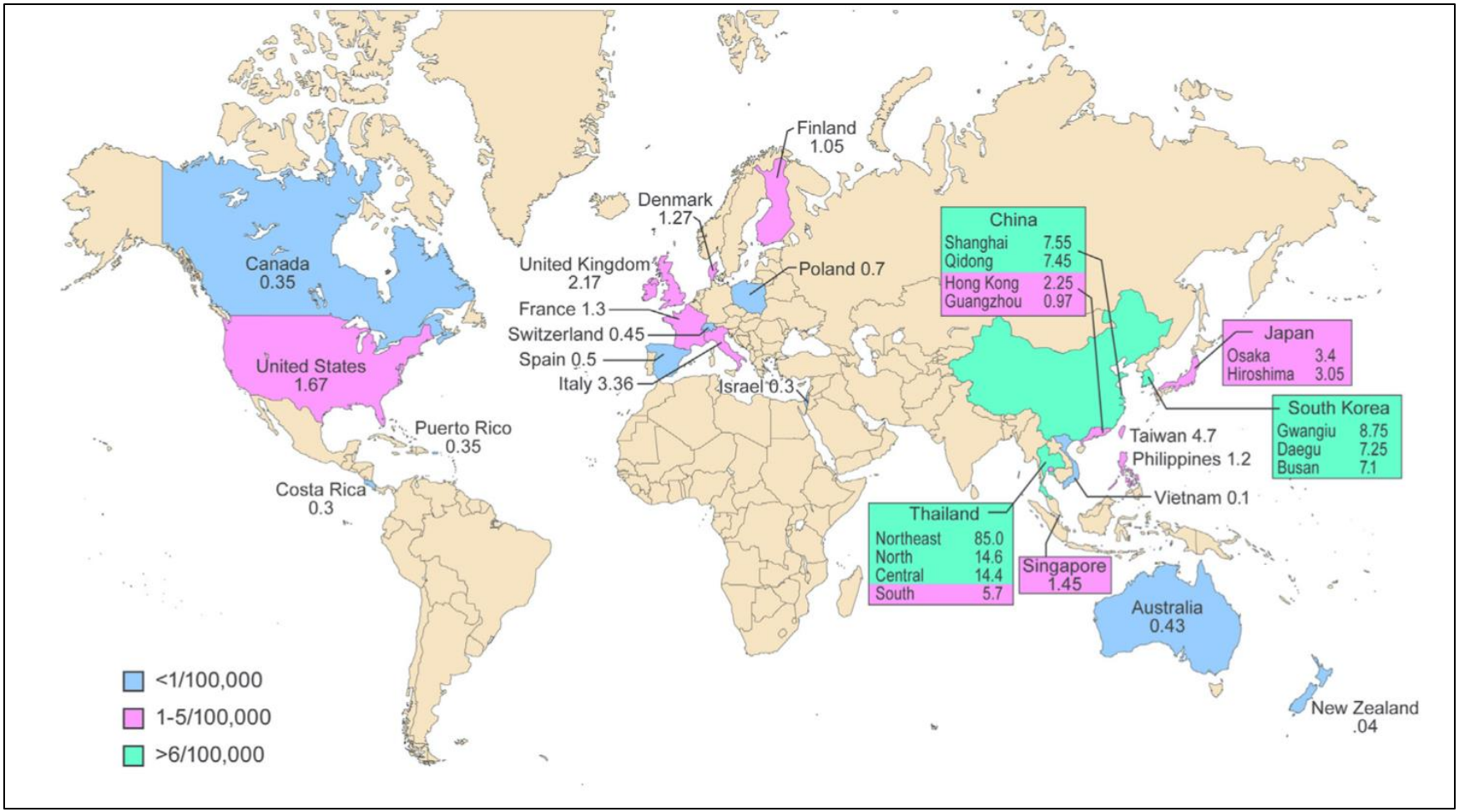
# Ενδοηπατικό Χολαγγειοκαρκίνωμα (ICC)



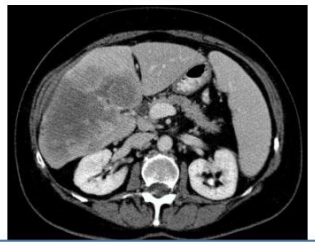

- 10% - 15% των όγκων του ήπατος
- 2ος συχνότερος μετά το ΗΚΚ
- Ενδοηπατικά χολαγγεία 2ας τάξεως
- Αύξηση της συχνότητας
- <u>Χειρουργική εξαίρεση: Η μόνη θεραπευτική επιλογή</u>
- 15 – 30% εξαιρέσιμοι κατά τη διάγνωση
- Πρώιμη υποτροπή – Φτωχή Πρόγνωση
- Μέση επιβίωση: 27 - 36 μήνες

*HPB 2015*

# Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma

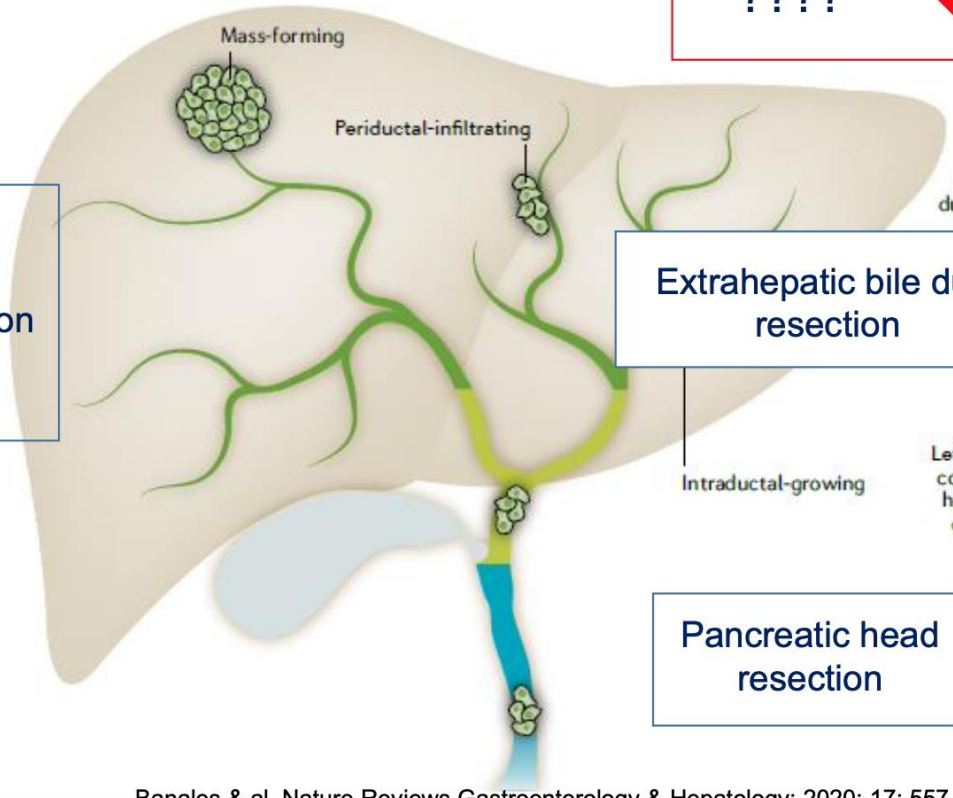


# Cholangiocarcinoma



Parenchymal resection

????




Extrahepatic bile duct resection

Pancreatic head resection

Banales & al. Nature Reviews Gastroenterology & Hepatology; 2020: 17: 557–588

# Characterization of intrahepatic cholangiocarcinoma after curative resection: outcome, prognostic factor, and recurrence

Kun-Ming Chan*, Chun-Yi Tsai, Chun-Nan Yeh, Ta-Sen Yeh, Wei-Chen Lee, Yi-Yin Jan* and Miin-Fu Chen

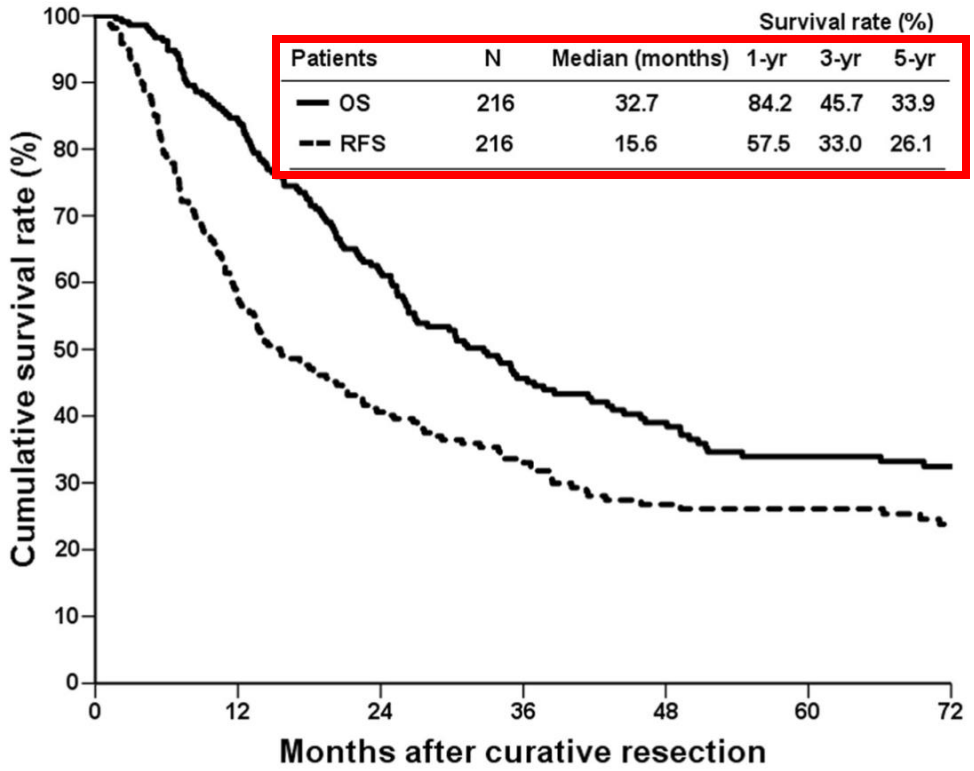
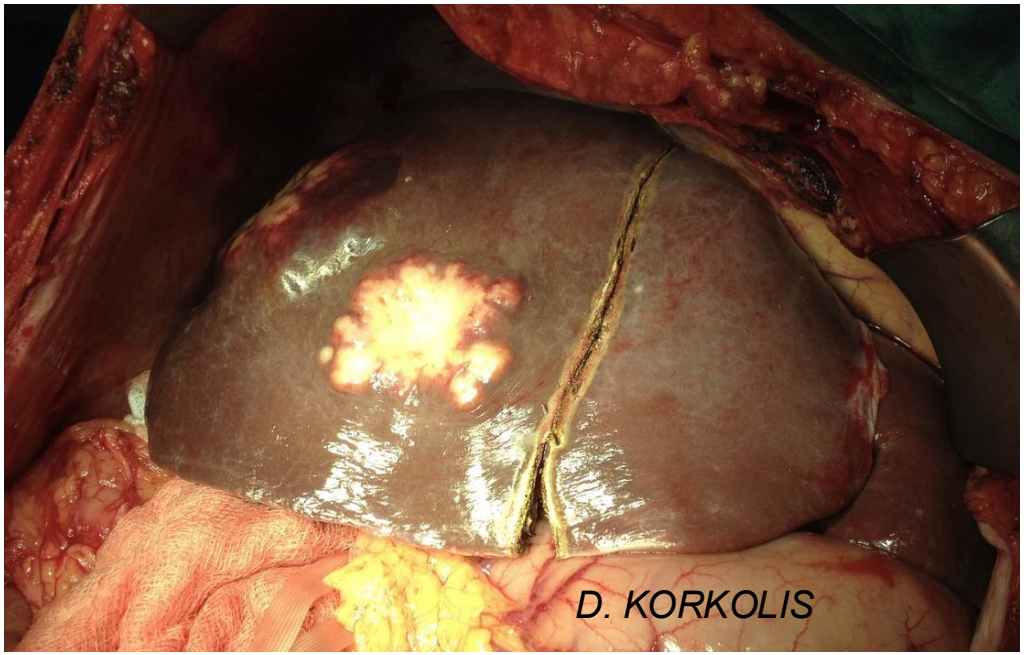



**Fig. 1** Kaplan-Meier cumulative survival curves of the patients who underwent curative resection for intrahepatic cholangiocarcinoma by recurrence-free survival (RFS) and overall survival (OS)

# Ενδοηπατικό Χολαγγειοκαρκίνωμα (ICC)

## Ενδείξεις Χειρουργικής Θεραπείας

- Τεχνικές
- Ογκολογικές



# Τεχνικές Ενδείξεις

- Δύο τουλάχιστο γειτονικά τμήματα (FLR)
- Εκτεταμένες Ηπατεκτομές (70%)
- Liver Volumetry!!!
- FLR >20%
- FLR<20%  PHI: 20%  Mortality: 15%
- Χρόνια ηπατοπάθεια-ίκτερος  FLR>30% + PTC/PTBD  Tbilir <10
- Κίρρωση  FLR>40%

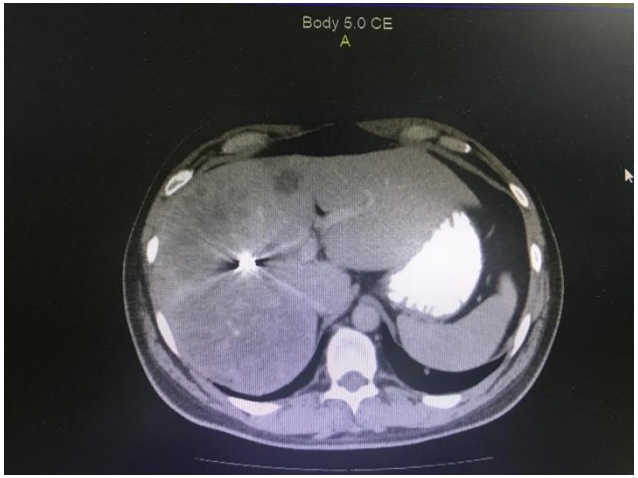
- Αγγεία 15% - Χολαγγεία 20%

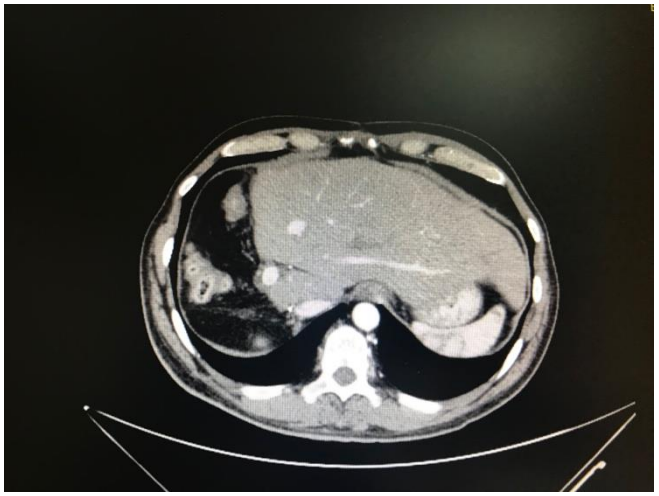
*Weber SM, et al. HPB(Oxford) 2015*

# Τεχνικές Ενδείξεις

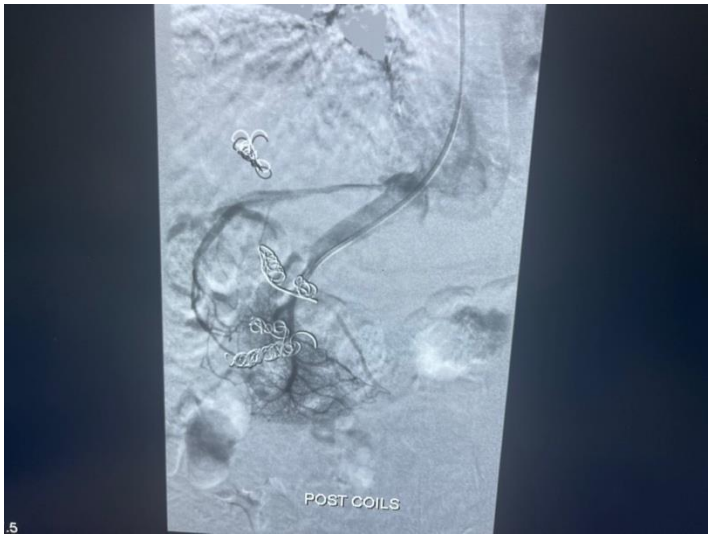
- 10%  R Lobe >75%
- 75%  LLS <20%
- PVE – ALPPS - LVD
- R Hepatectomy  PHI 10%
- R Ext Hepatectomy  PHI 75%  (no PVE)

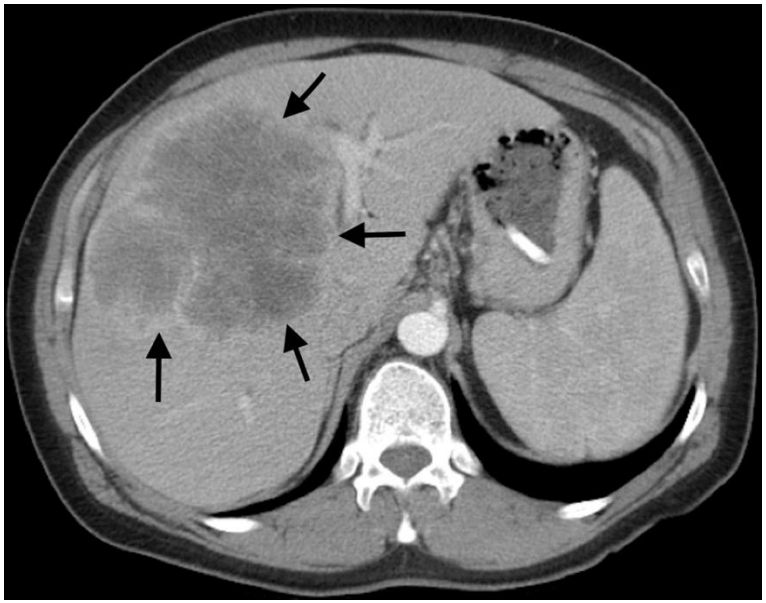
*Cieslak KP. Surgery 2017*

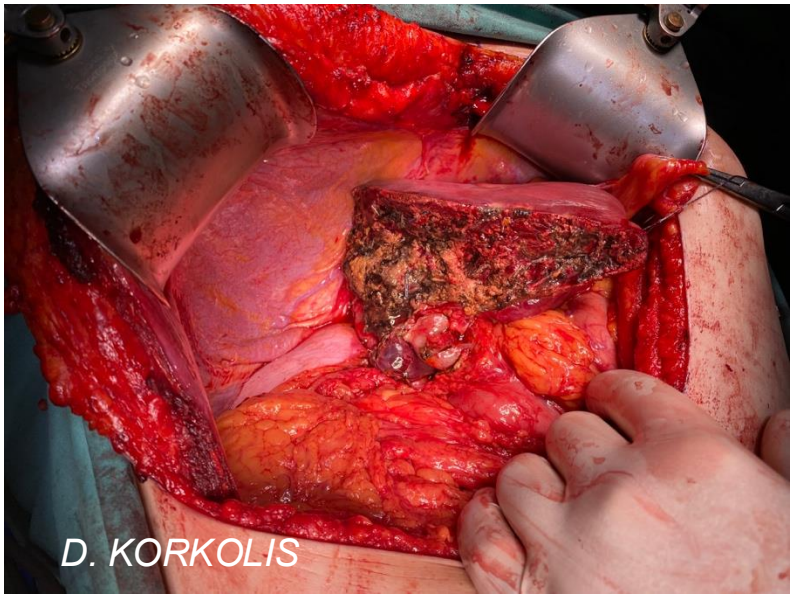



# Liver Venous Deprivation



# Αντενδείξεις

- Αμφοτερόπλευρη πολυεστιακή νόσος
- Περιτοναική Καρκινωμάτωση
- Απομακρυσμένες Μεταστάσεις
- N2 Λεμφαδενική νόσος (κοιλιακός άξονας, παραορτικοί)
- Βαριά υποκείμενη Ηπατοπάθεια (ίνωση, PSC, κίρρωση)
- FLR<20% και φτωχή ανταπόκριση σε PVE
- Σοβαρές συνοσηρότητες

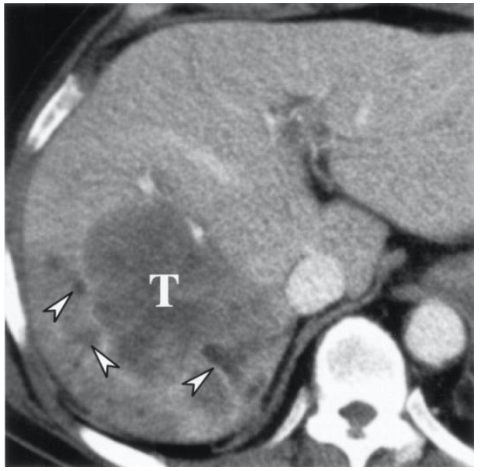
*Weber SM, et al. HPB (Oxford) 2015*
*Squires MH, et al. Expert Rev Gastroenterol Hepatol 2018*

# Ογκολογικές Ενδείξεις

- Δεν απαιτείται ΒΙΟΨΙΑ σε εξαιρέσιμο ICC!!!
- Κίνδυνος διασποράς - ↓↓↓ Διαγνωστική Ακρίβεια
- Σε τοπικά εκτεταμένο/ανεγχείρητο για ΧΜΘ
- US/CT/EUS guided FNA: Μεταστατικό αδενοCA???
- Διερεύνηση πρωτοπαθούς
- FNB: Απαραίτητη ανοσοιστοχημεία
- Διερεύνηση εξαιρεσιμότητας: CT/MRI scan προ PTC/BD
- PET scan: ασαφής ρόλος
- Staging Laparoscopy/Lap US: 30% μεταστατική νόσος!!!

# Ογκολογικές Ενδείξεις – Προγνωστικοί Παράγοντες

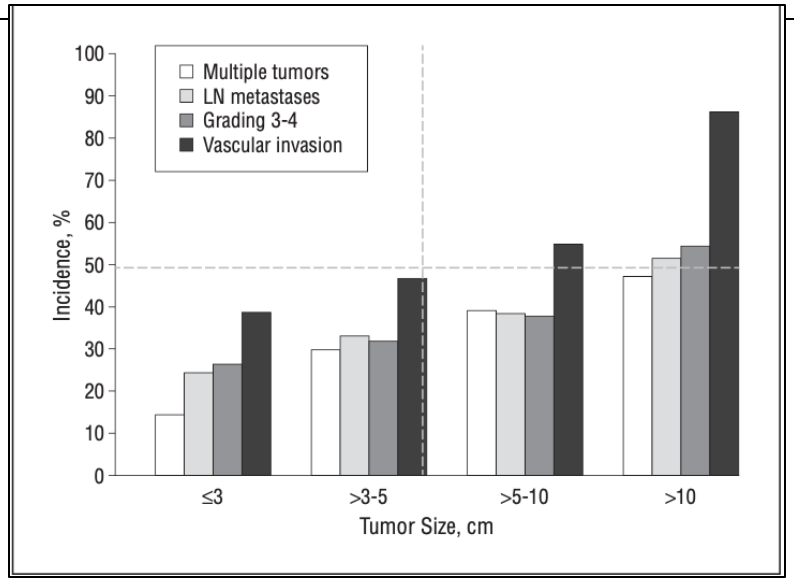
- Μέγεθος όγκου
- Πολυεστιακή νόσος
- Εκτεταμένες Ηπατεκτομές
- Σταδιοποίηση κατά AJCC
- Λεμφαδενεκτομή
- Χειρουργικά Όρια
- Αγγειακές Εκτομές
- MILS
- Αντιμετώπιση Υποτροπής
- Μεταμόσχευση

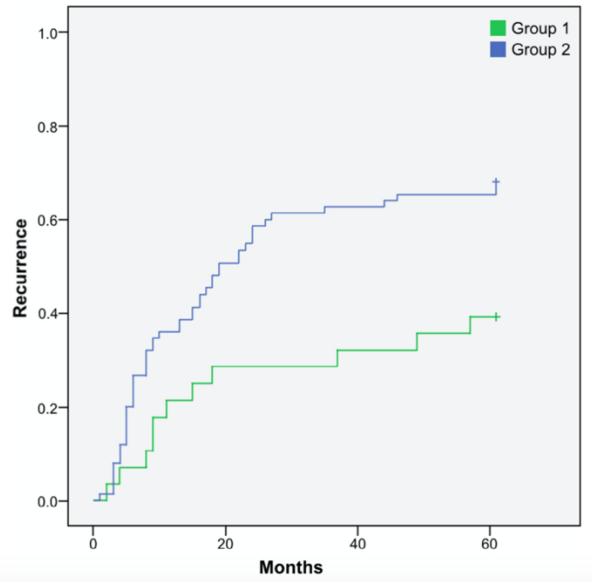


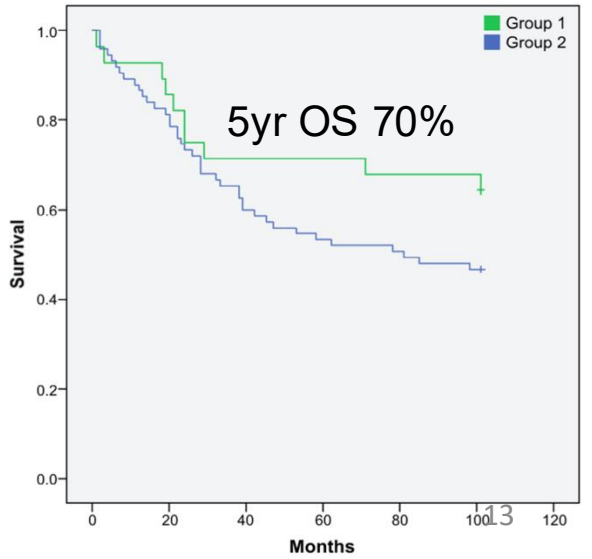

# Outcomes of resection for solitary ≤5 cm intrahepatic cholangiocarcinoma

*Tarchi P, te al. Surgery 2017*

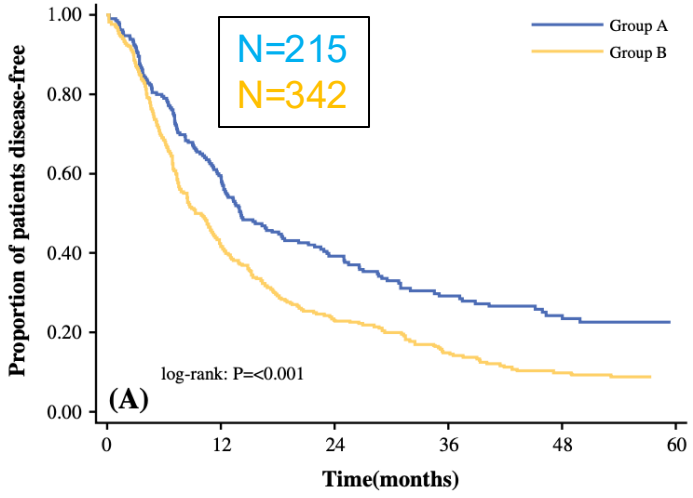
| Clinical variables | Group 2 (*n*, %) | Group 1 (*n*, %) | *P* value |
|---|---|---|---|
| Age, mean (SD), y | 61.26 (12) | 65.44 (8) | .030 |
| Male | 34 (39) | 17 (50) | .254 |
| Ethnicity (white) | 57 (65) | 20 (59) | .541 |
| Underlying liver disease (none versus other) | 17 (19) | 17 (50) | .001 |
| Cirrhosis | 2 (2) | 5 (15) | .019 |
| Extent of resection (major) | 77 (87) | 21 (62) | .001 |
| Transfusion (yes/no) | 25 (29) | 6 (19) | .308 |
| Histologic differentiation (poor, versus good and moderate) | 81 (96) | 31 (100) | .562 |
| Perineural invasion | 32 (37) | 6 (18) | .05 |
| Vascular invasion (none versus others) | 32 (37) | 6 (18) | .05 |
| Lymph node involvement | 26 (44) | 2 (25) | .05 |
| Satellite nodules | 28 (32) | 6 (18) | .05 |
| Operative margin positive (R1) | 18 (20) | 4 (12) | .263 |
| Adjuvant chemotherapy | 40 (48) | 4 (13) | .001 |

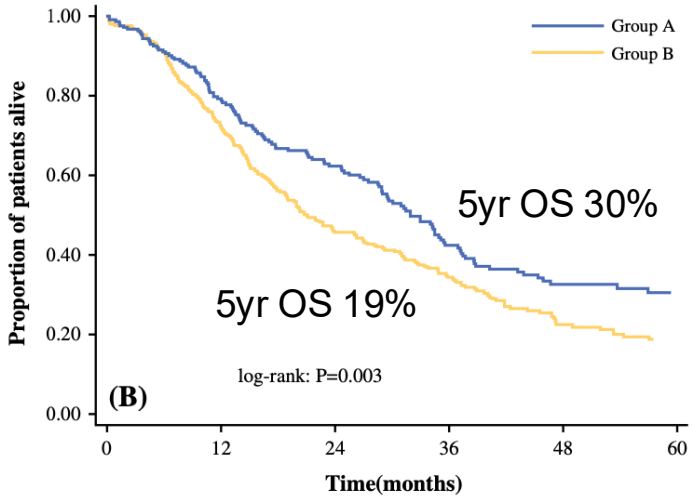


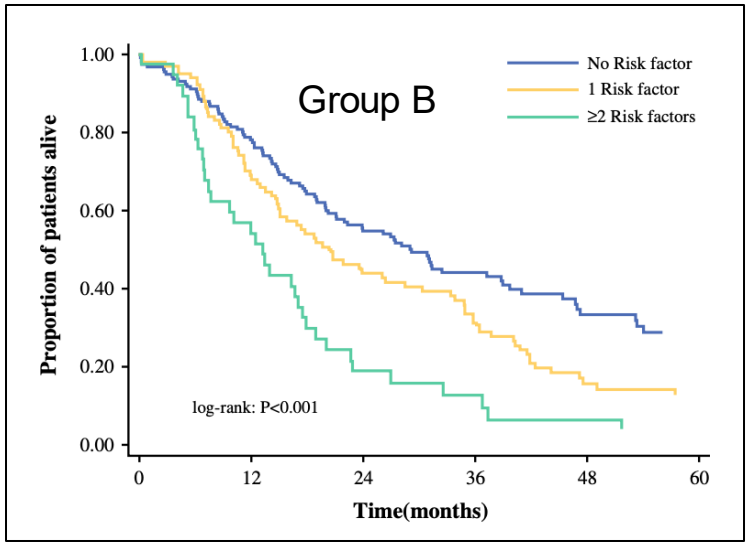



# Is Hepatic Resection for Large or Multifocal Intrahepatic Cholangiocarcinoma Justified? Results from a Multi-Institutional Collaboration



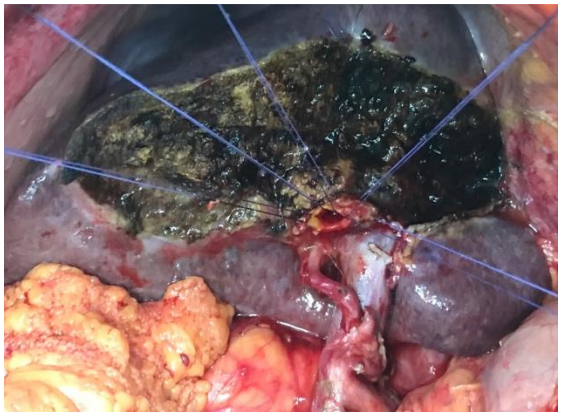



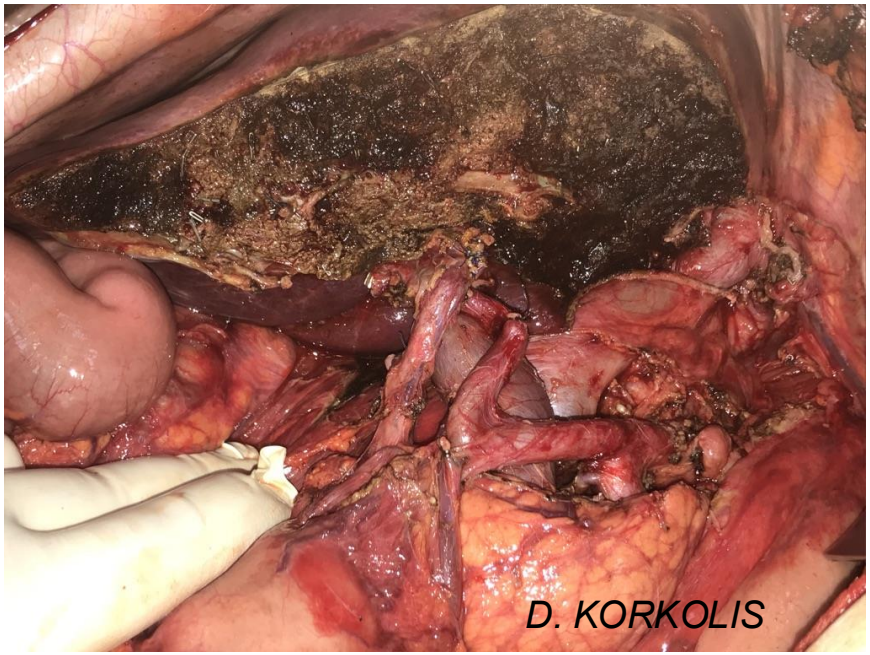

1. Pts with ICC tumors >7cm or multifocal >2 could safely undergo resection without increased morbimortality….

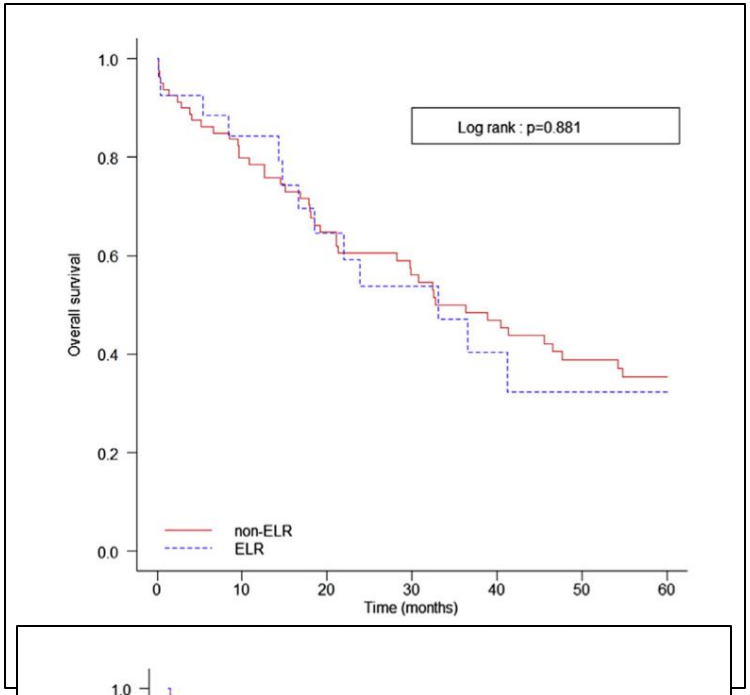
2. Slight inferiority of DFS and OS over pts with small, unifocal ICCs….

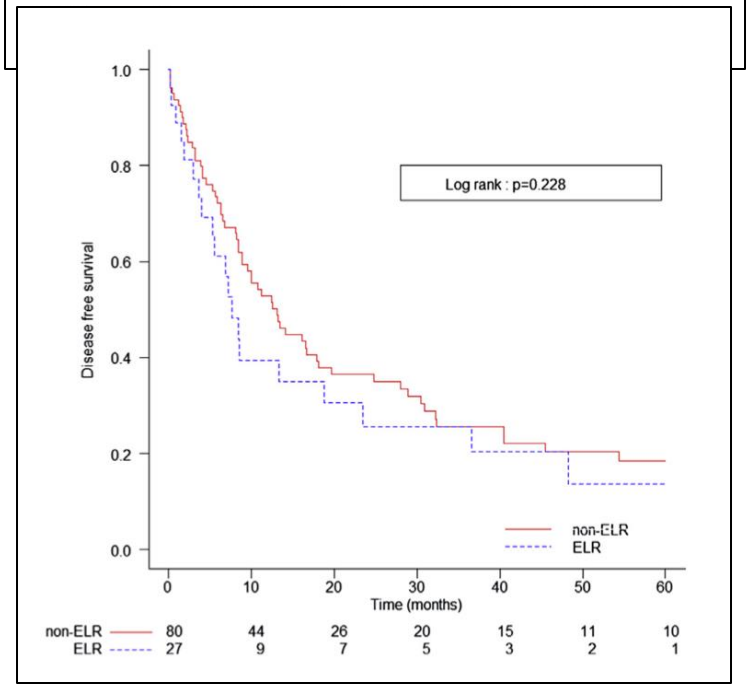
*Spolverato G, et al. Ann Surg Oncol 2015*

# Extended liver resections for intrahepatic cholangiocarcinoma: Friend or foe?






*Bergeat D, et al. Surgery 2015*

# Λεμφαδενεκτομή

- Ακόμη αμφιλεγόμενη
- Μόνο 55% έχουν εκτίμηση τουλάχιστο 1 LN
- Δεν επηρεάζει την Συνολική Επιβίωση
- 40% των εκτομών έχουν LN (+)
- LN (+): πλέον ισχυρός δείκτης έκβασης
- Consensus: ΠΑΝΤΑ στο χρόνο της ηπατεκτομής
- Σταδιοποίηση - Πρόγνωση
- Κριτήριο επικουρικής ΧΜΘ
- ΠΡΟΣΟΧΗ: Απαγγείωση του CBD!!!
  ↑ Νοσηρότης σε Κίρρωση

*Bagante F, et al. World J Surg 2018*

# Cholangiocarcinoma

## Intrahepatic CCC (n=150)

| | All | R0 | | | | R1 |
|---|---|---|---|---|---|---|
| Preoperative chemotherapy | **11** | 3 | – | 2 | 3 | 2 |
| **UICC stage (TNM 8th Ed.)** [b] | | | | | | |
| IA | **15** | 3 | 4 | 4 | 4 | – |
| IB | **19** | 6 | – | 6 | 4 | 3 |
| II | **36** | 6 | 2 | 10 | 13 | 5 |
| IIIA | **8** | 1 | – | 3 | 3 | 1 |
| IIIB | **47** | 4 | 2 | 16 | 18 | 7 |
| IV | **8** | 2 | 1 | 1 | 3 | 1 |

| | | Kaplan Meier Model | | Multivariate Cox regression model | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | OS | RFS | OS | | | RFS | | |
| | | | | HR | 95% CI | *p*-value | HR | 95% CI | *p*-value |
| **Resection margin** | > 0.5 cm / 0.49–0.1 cm / R1 | 0.230 | 0.111 | | | | | | |
| | > 0.5 cm / < 0.49 cm | 0.087 | 0.052 | 0.754 | 0.428–1.326 | 0.326 | **0.557** | **0.331–0.936** | **0.027** |
| | ≤0.1 cm / > 0.1 cm | 0.291 | 0.458 | | | | | | |
| **Tumor distance to liver capsule** | dist./cl. + infil./perf./pd. Infil. | **0.033** | 0.136 | **1.271** | **1.058–1.525** | **0.010** | | | |
| **Age** | < 65 / > 65 | 0.073 | 0.175 | **1.536** | **1.026–2.300** | **0.037** | | | |
| **Gender** | Woman / Man | 0.283 | 0.472 | | | | | | |
| **Extended resection** | yes / no | **0.009** | **0.024** | 0.848 | 0.514–1.400 | 0.519 | 0.884 | 0.553–1.413 | 0.606 |
| **Major resection** | yes / no | **0.045** | **0.008** | **0.573** | **0.351–0.936** | **0.026** | 0.735 | 0.464–1.165 | 0.191 |
| **Tumor size** | ≤5 cm / > 5 cm | 0.108 | **0.008** | | | | | | |
| | ≤ 10 cm / > 10 cm | **0.014** | **0.002** | **1.609** | **1.007–2.570** | **0.047** | **1.973** | **1.272–3.061** | **0.002** |
| **Multifocality** | yes / no | 0.262 | **0.014** | | | | **1.593** | **1.069–2.374** | **0.022** |
| **T-stage** | T1 + T2 / T3 + T4 | 0.102 | 0.347 | | | | | | |
| **N-stage** | N0 / N+ / NX | **0.016** | 0.085 | **1.258** | **1.027–1.541** | **0.026** | 1.147 | 0.931–1.412 | 0.197 |
| **V-stage** | V0 / V1 + V2 | 0.149 | 0.818 | | | | | | |
| **L-stage** | L0 / L1 | 0.369 | 0.673 | | | | | | |
| **Pn-stage** | Pn0 / Pn1 | **0.027** | 0.091 | 1.401 | 0.882–2.227 | 0.154 | 1.157 | 0.748–1.789 | 0.512 |
| **M-stage** | M0 / M1 | 0.125 | **0.002** | | | | **2.984** | **1.347–6.612** | **0.007** |
| **R-stage** | R0 / R1 | 0.655 | 0.254 | | | | | | |
| **Grading** | G1 + G2 / G3 + G4 | 0.347 | 0.535 | | | | | | |

Bartsch, Heinrich & al. BMC Surg 2020; 20: 61

## Perihilar CCC (n=250)

| | Extrahepatic tumours (*n* = 167) | Intrahepatic tumours (*n* = 83) | *P** |
|---|---|---|---|
| pT classification | | | < 0·001 |
| pT1 | 10 (6·0) | 2 (2) | |
| pT2 | 45 (26·9) | 5 (6) | |
| pT3 | 59 (35·3) | 32 (39) | |
| pT4 | 53 (31·7) | 44 (53) | |
| pN classification | | | 0·008 |
| pN0 | 90 (53·9) | 29 (35) | |
| pN1 | 77 (46·1) | 54 (65) | |
| pM classification | | | 0·638 |
| pM0 | 135 (80·8) | 65 (78) | |
| pM1 | 32 (19·2) | 18 (22) | |
| Stage | | | 0·002 |
| I | 41 (24·6) | 6 (7) | |
| IIA | 26 (15·6) | 12 (14) | |
| IIB | 37 (22·2) | 16 (19) | |
| III | 31 (18·6) | 31 (37) | |
| IV | 32 (19·2) | 18 (22) | |

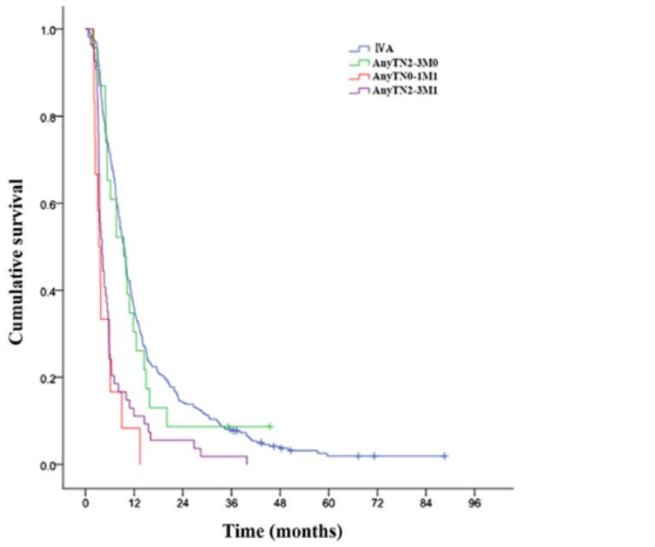
| | Extrahepatic tumours (*n* = 167) | Intrahepatic tumours (*n* = 83) | *P** |
|---|---|---|---|
| Bismuth classification | | | < 0·001 |
| Type I | 12 (7·2) | 0 (0) | |
| Type II | 22 (13·2) | 1 (1) | |
| Type III | 68 (40·7) | 37 (45) | |
| Type IV | 65 (38·9) | 45 (54) | |
| Liver invasion | 103 (61·7) | 75 (90) | < 0·001 |
| Portal vein invasion | 39 (23·4) | 43 (52) | < 0·001 |
| Hepatic artery invasion | 19 (11·4) | 14 (17) | 0·227 |
| Lymphatic invasion | 127 (76·0) | 72 (87) | 0·048 |
| Venous invasion | 61 (36·5) | 48 (58) | 0·001 |
| Perineural invasion | 141 (84·4) | 75 (90) | 0·198 |
| Positive surgical margin | 36 (21·6) | 18 (22) | 0·370 |
| Intrahepatic metastasis | 5 (3·0) | 4 (5) | 0·466 |
| Nodal metastasis | 77 (46·1) | 54 (65) | 0·005 |
| Regional | 60 (35·9) | 37 (45) | |
| Para-aortic | 17 (10·2) | 17 (20) | |
| Histological grade | | | 0·165 |
| Well differentiated | 51 (30·5) | 16 (19) | |
| Moderately differentiated | 105 (62·9) | 61 (73) | |
| Poorly differentiated | 11 (6·6) | 6 (7) | |

N+ ~30-50%

**M1, R1, N+,** L+, Pn+

Ebata & al. Br J Surg 2009; 96: 626-634

# Liver resection for intrahepatic cholangiocarcinoma in AJCC-stage IV: An evaluation of the survival benefit and prognostic accuracy of current AJCC staging system on N and M classification

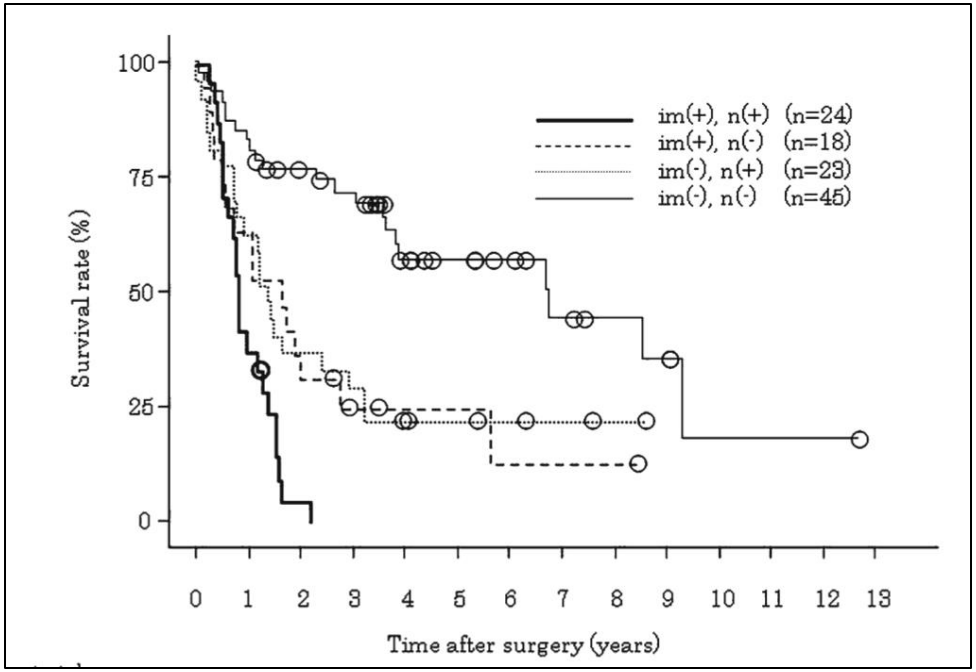



| No. at risk | 0 month | 12 months | 24 months | 36 months | 48 months | 60 months | 72 months | 84 months |
|---|---|---|---|---|---|---|---|---|
| IVA | 298 | 107 | 43 | 22 | 8 | 3 | 1 | 1 |
| AnyTN2-3M0 | 23 | 7 | 2 | 1 | 0 | 0 | 0 | 0 |
| AnyTN0-1M1 | 12 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| AnyTN2-3M1 | 54 | 6 | 3 | 1 | 0 | 0 | 0 | 0 |

Figure 3. OS for patients with ICC in different subgroups after surgery. The 1-, 3- and 5-year OS rates for patients with stage IVA tumors were 35.9, 7.7 and 1.9%, respectively, better than corresponding rates of 30.4, 8.7 and 0%, respectively, for patients with tumors in stage AnyTN2-3M0; much better than 8.3, 0 and 0%, respectively, for patients with tumors in stage AnyTN0-1M1; and than 11.1, 1.9 and 0%, respectively, for patients with tumors in stage AnyTN2-3M1 (P<0.001).

*Yuan L, et al. Oncol Rep 2016*

## Indications for surgical treatment of intrahepatic cholangiocarcinoma with lymph node metastases

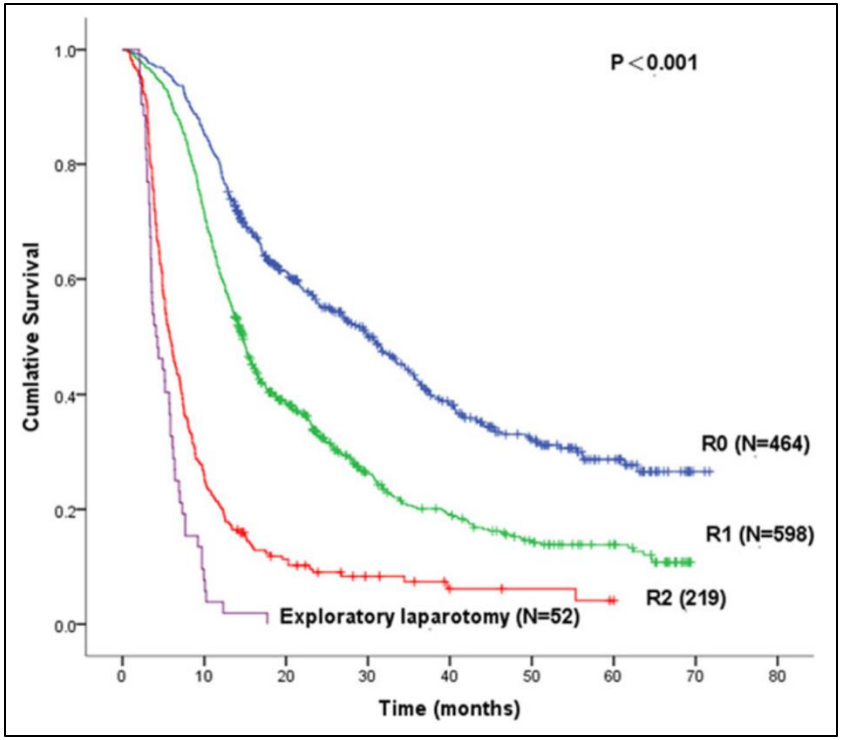


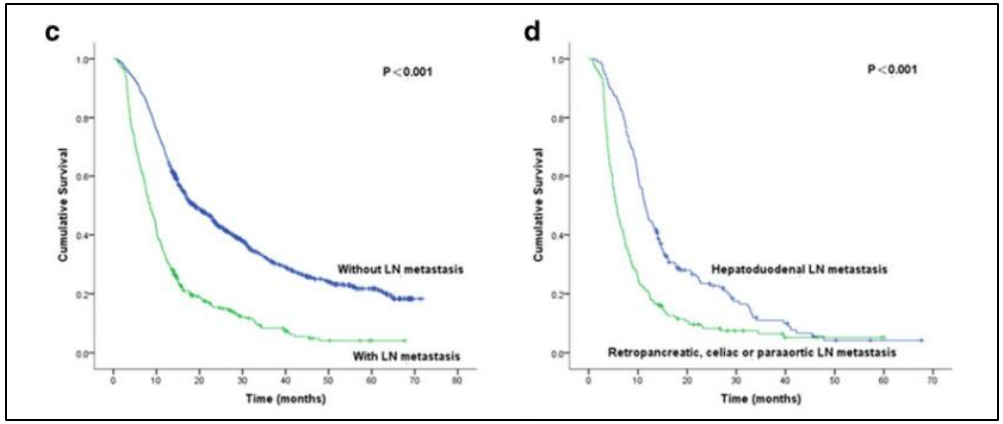

3-year OS 35% vs. 0%

*Uenishi T, et al. J Hepatobiliary Pancreat Surg 2008*

# Survival Outcomes and Prognostic Factors of Surgical Therapy for All Potentially Resectable Intrahepatic Cholangiocarcinoma: a Large Single-Center Cohort Study

Cohort Study of 1333 pts with ICC surgically treated




*…in the presence of LN metastasis, pts had similar survival whether they obtained an R0 or R1 resection…*

*Luo X, et al. J Gastrointest Surg 2014*

# Is there a role for systematic hepatic pedicle lymphadenectomy in intrahepatic cholangiocarcinoma? A review of 17 years of experience in a tertiary institution

215 pts with ICC

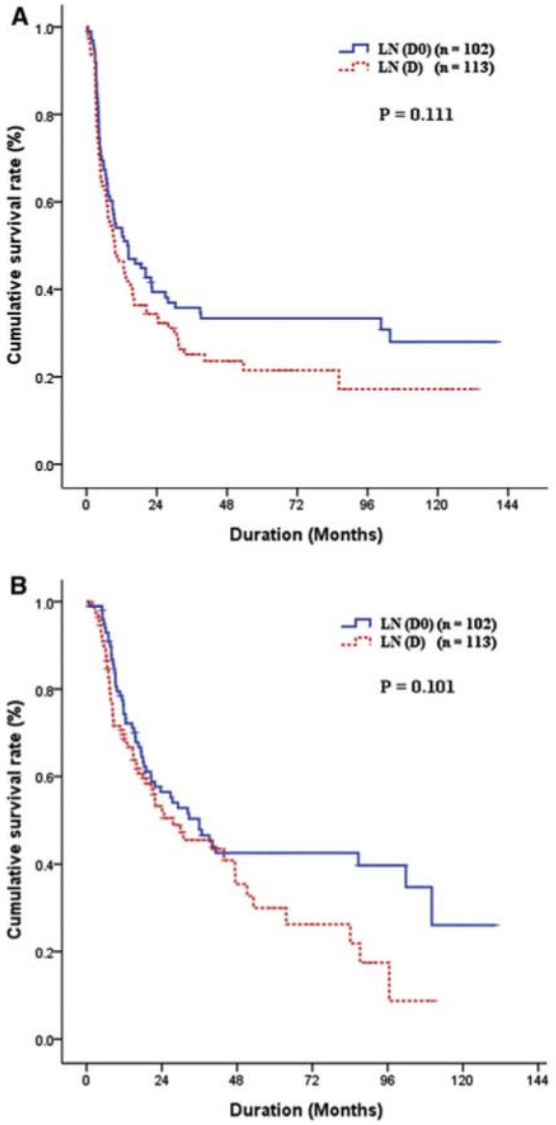



**Fig 1.** (*A*) Disease-free and (*B*) overall survival in patients with or without lymph node dissection.

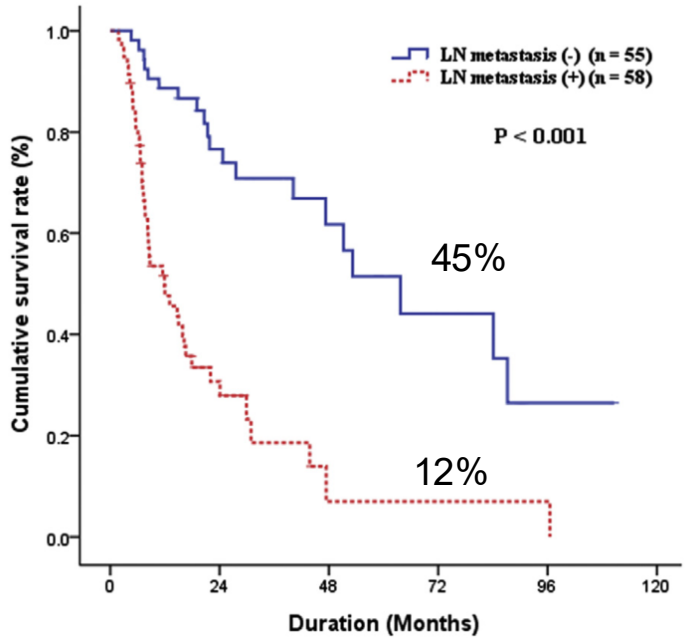
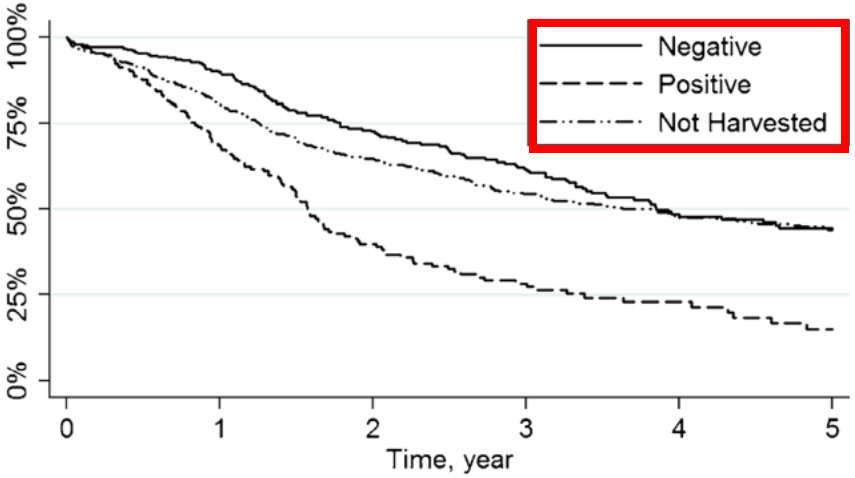


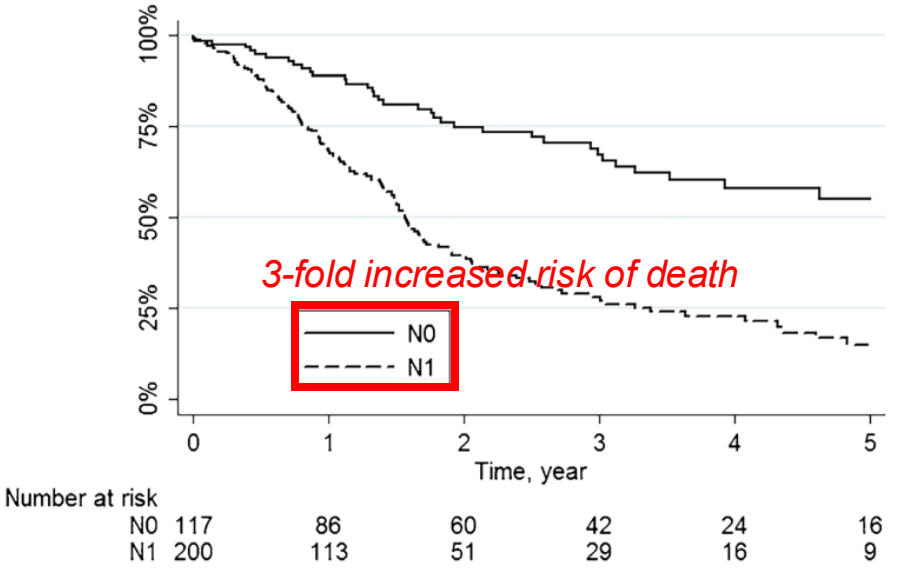

**Fig 2.** Overall survival in the lymph node (LN) patient group with lymph node dissection according to the presence of LN metastasis. Survival in the node-negative group was significantly higher than in the group with nodal involvement.

*Kim DH, et al. Surgery 2015*

# Assessment of the Lymph Node Status in Patients Undergoing Liver Resection for Intrahepatic Cholangiocarcinoma: the New Eighth Edition AJCC Staging System

| | Radiological modal status | | | *p* value |
|---|---|---|---|---|
| | Negative | Suspicious | Positive | |
| Pathological nodal status[a] | | | | <0.001 |
| Negative | 127 (66.5%) | 34 (42.5%) | 16 (34.8%) | |
| Positive | 64 (33.5%) | 46 (57.5%) | 30 (65.2%) | |
| AJCC seventh edition T stages[b] | | | | <0.001 |
| T1/T2a/T2b | 471 (77.5%) | 74 (62.7%) | 31 (52.5%) | |
| T3/T4 | 137 (22.5%) | 44 (37.3%) | 28 (47.5%) | |
| AJCC eighth edition T stages[b] | | | | 0.003 |
| T1a/T1b/T2 | 406 (66.8%) | 70 (59.3%) | 27 (45.8%) | |
| T3/T4 | 202 (33.2%) | 48 (40.7%) | 32 (54.2%) | |




1990 – 2015
1154 pts surgically treated for ICC

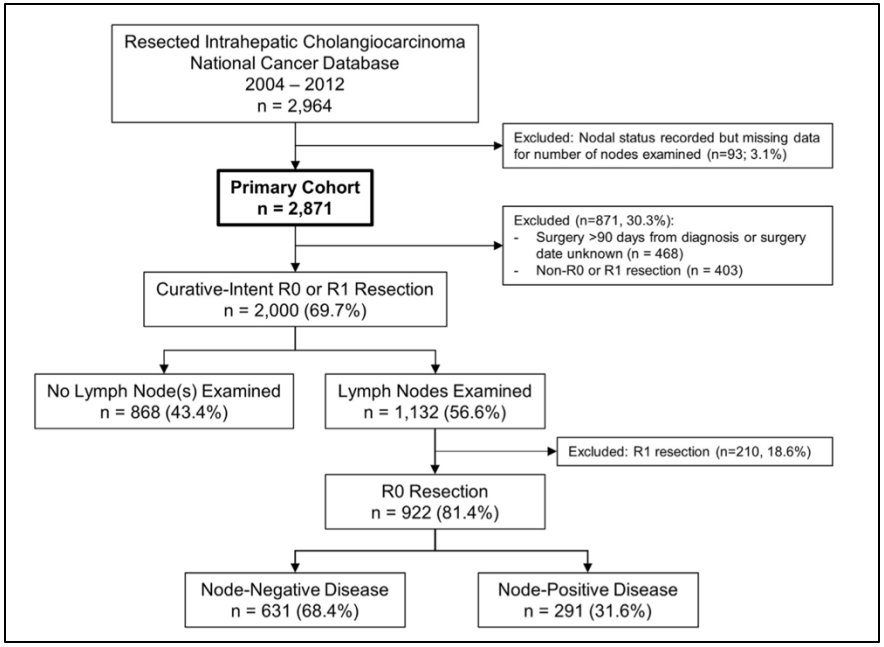
Innacurate radiological LN staging 40%
NOT an alternative to lymphadenectomy

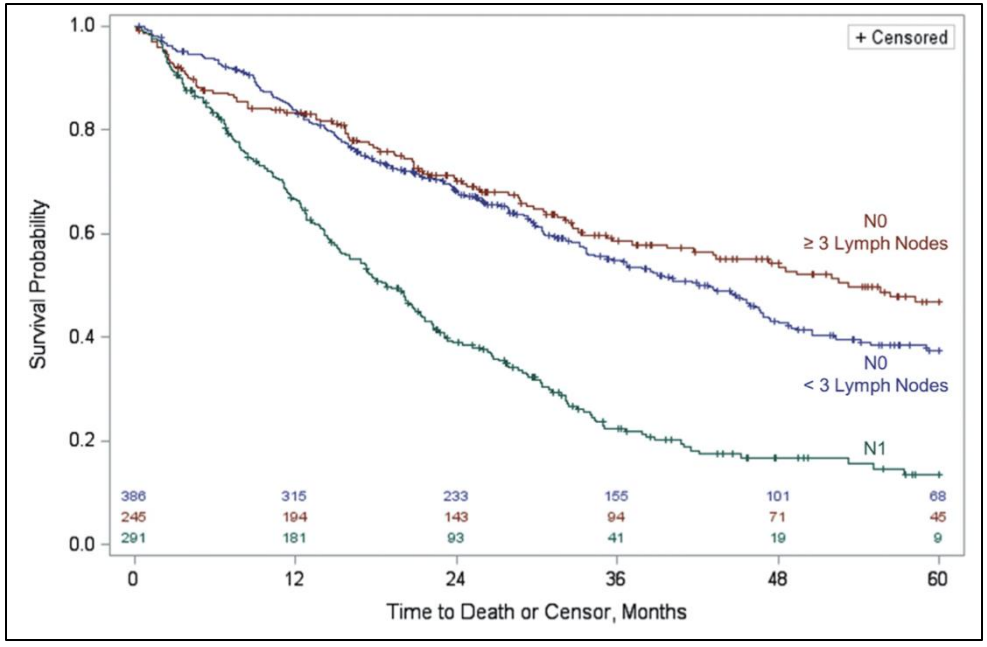
*Bagante F, et al. J Gastrointest Surg 2018*

ORIGINAL ARTICLE

# Optimal extent of surgical and pathologic lymph node evaluation for resected intrahepatic cholangiocarcinoma

David G. Brauer[1], Ryan C. Fields[1], Benjamin R. Tan Jr.[2], M.B. Majella Doyle[1], Chet W. Hammill[1], William G. Hawkins[1], Graham A. Colditz[1] & William C. Chapman[1]

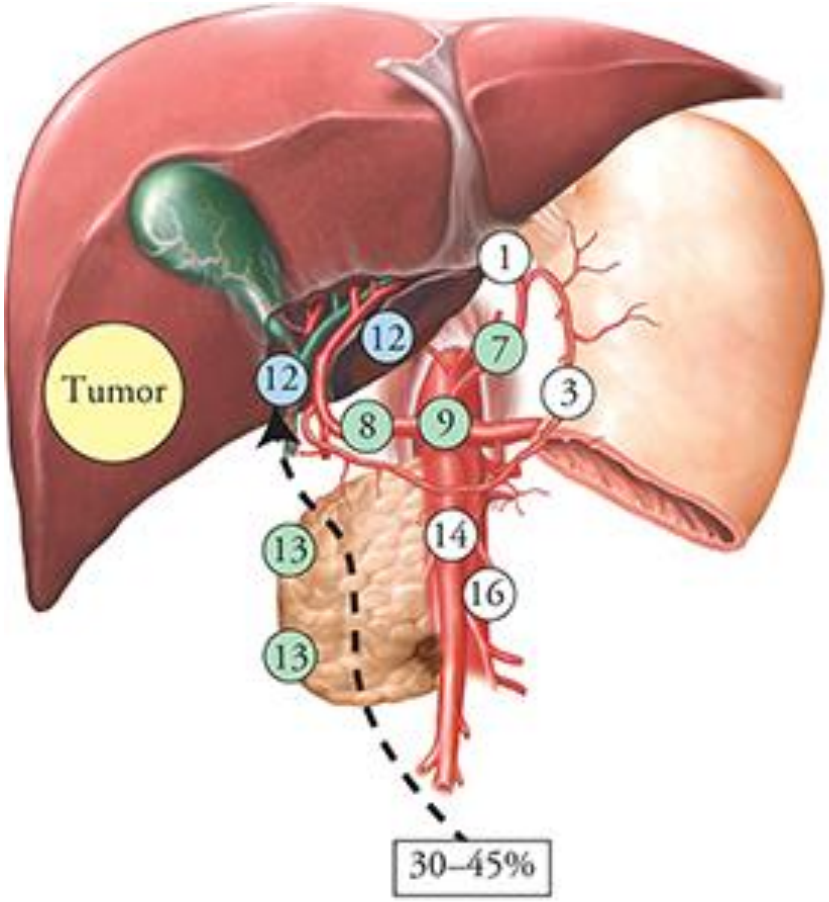


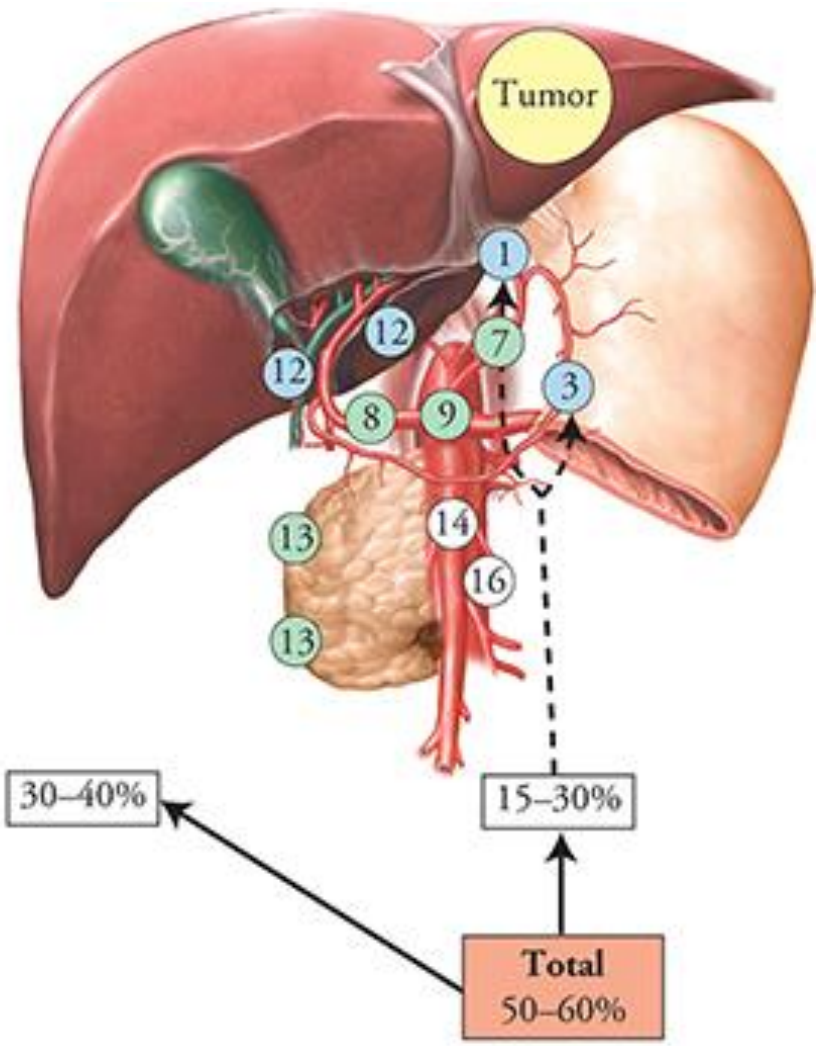




>6 LNs σύμφωνα με *AJCC 8th Edition*

*Brauer DG, et al. HPB 2017*

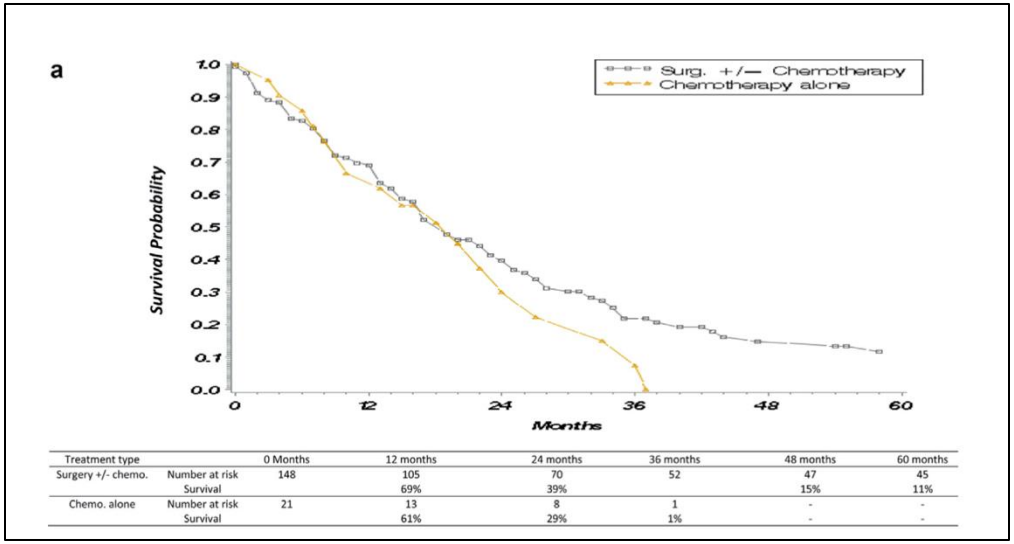
# Λεμφαδενεκτομή στο ICC



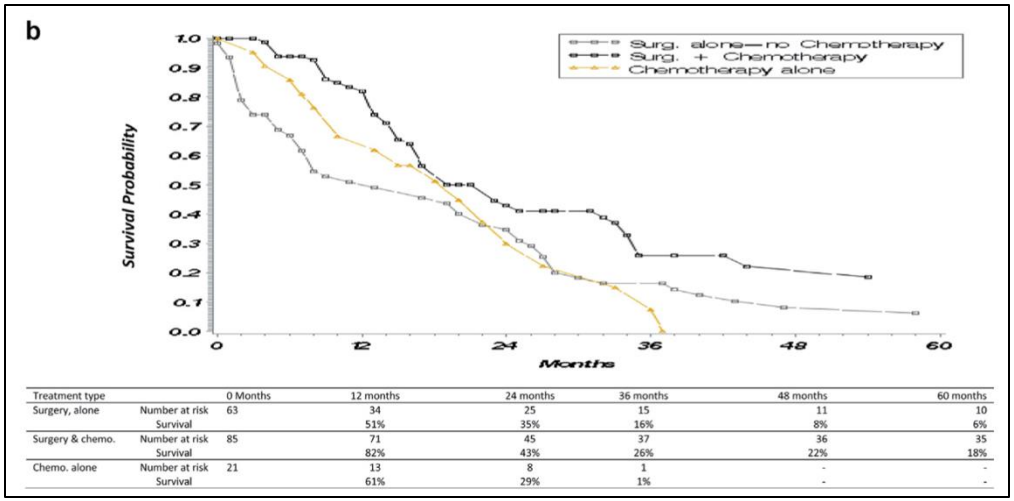



ORIGINAL ARTICLE

# Surgical resection of lymph node positive intrahepatic cholangiocarcinoma may not improve survival




| Treatment type | | 0 Months | 12 months | 24 months | 36 months | 48 months | 60 months |
|---|---|---|---|---|---|---|---|
| Surgery +/- chemo. | Number at risk | 148 | 105 | 70 | 52 | 47 | 45 |
| | Survival | | 69% | 39% | | 15% | 11% |
| Chemo. alone | Number at risk | 21 | 13 | 8 | 1 | - | - |
| | Survival | | 61% | 29% | 1% | - | - |




| Treatment type | | 0 Months | 12 months | 24 months | 36 months | 48 months | 60 months |
|---|---|---|---|---|---|---|---|
| Surgery, alone | Number at risk | 63 | 34 | 25 | 15 | 11 | 10 |
| | Survival | | 51% | 35% | 16% | 8% | 6% |
| Surgery & chemo. | Number at risk | 85 | 71 | 45 | 37 | 36 | 35 |
| | Survival | | 82% | 43% | 26% | 22% | 18% |
| Chemo. alone | Number at risk | 21 | 13 | 8 | 1 | - | - |
| | Survival | | 61% | 29% | 1% | - | - |

…preop radio- evaluation for LN involvement…..

EUS-FNAB

PET scan?

*ICC and LN+* should be considered for neoadjuvant chemo…

*Kizzy S, et al. HPB 2019*

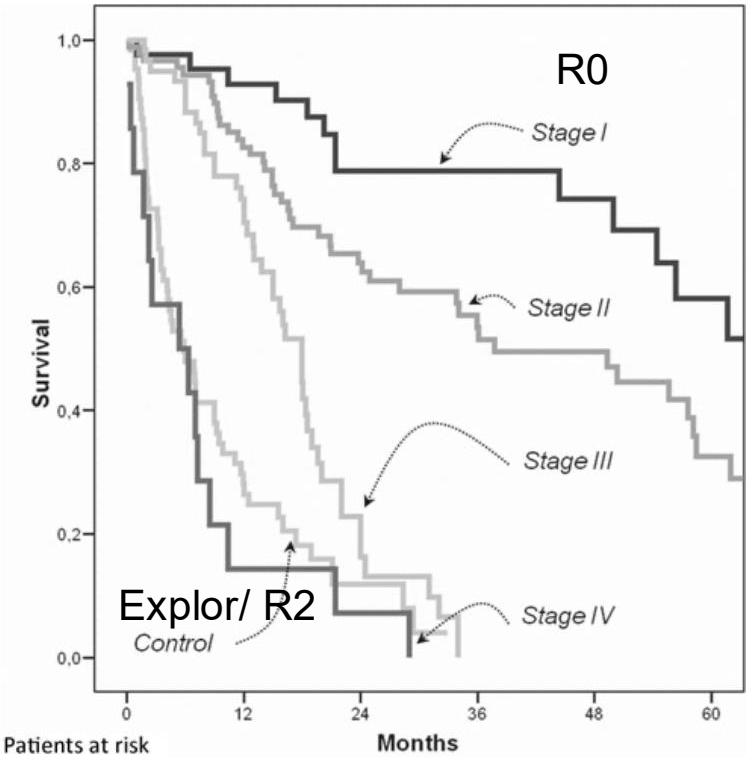
# Χειρουργικό Όριο Εκτομής

- R0 όρια εκτομής (50 – 96%)
- Τεχνικά δυσχερές
- Μεγάλο μέγεθος – Διηθητικός χαρακτήρας του ICC
- Βελτίωση OS
- Προγνωστική αξία σε ασθενείς N0
- Συνιστώμενο  όριο εκτομής ≥ 10mm
- Σε R1 ή οριακές εκτομές  επικουρικές θεραπείες

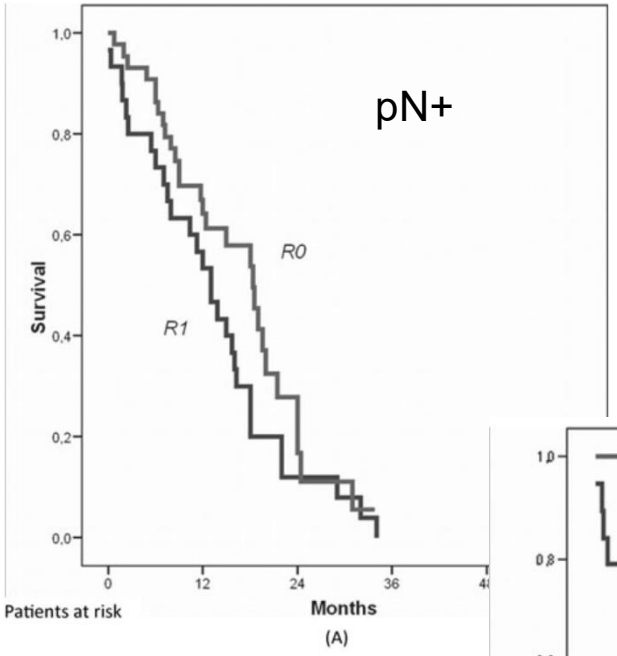
# Influence of Surgical Margins on Outcome in Patients With Intrahepatic Cholangiocarcinoma

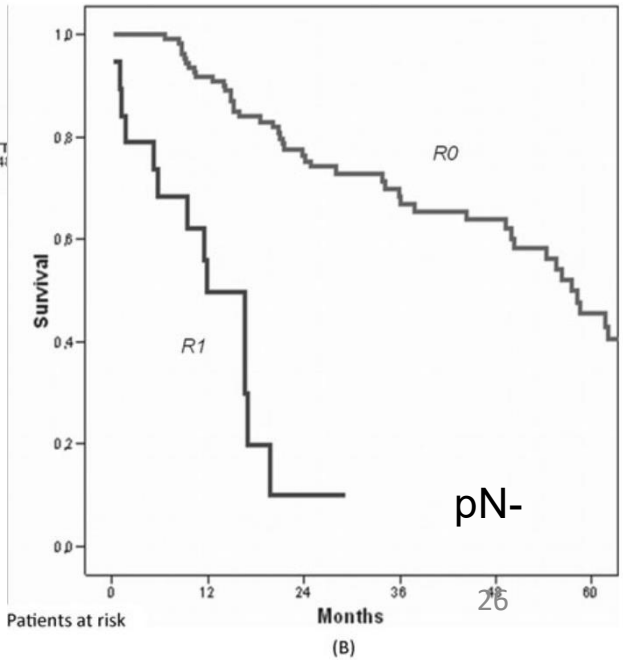
*A Multicenter Study by the AFC-IHCC-2009 Study Group*

212 pts with ICC




pN+




*Farges O, et al. Ann Surg 2011*

# Surgical Approach for Long-term Survival of Patients With Intrahepatic Cholangiocarcinoma

*A Multi-institutional Analysis of 434 Patients*

*Italian Intrahepatic Cholangiocarcinoma Study Group*

**Table 3. Predictors of Overall Survival: Univariate and Multivariate Analyses[a]**

| | Survival Rate, % | | | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|---|---|
| Variable | 1 y | 3 y | 5 y | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value |
| Sex | | | | | | | |
| Female | 82.9 | 53.0 | 37.8 | 1 [Reference] | | | |
| Male | 82.0 | 45.5 | 31.2 | 1.22 (0.92-1.63) | .17 | | |
| Age, y | | | | | | | |
| ≤65 | 80.2 | 43.4 | 25.0 | 1 [Reference] | | 1 [Reference] | |
| >65 | 84.4 | 52.7 | 42.6 | 0.77 (0.58-1.02) | .07 | 0.79 (0.59-1.07) | .13 |
| CEA level | | | | | | | |
| Normal | 87.1 | 51.1 | 37.2 | 1 [Reference] | | | |
| Elevated | 71.1 | 40.5 | 34.5 | 1.25 (0.85-1.83) | .27 | | |
| CA 19-9 level | | | | | | | |
| Normal | 93.4 | 59.8 | 41.3 | 1 [Reference] | | 1 [Reference] | |
| Elevated | 75.0 | 39.8 | 30.1 | 1.79 (1.26-2.53) | .001 | 1.62 (1.15-2.30) | .006 |
| Macroscopic type | | | | | | | |
| Intraductal IHC | 83.3 | 40.0 | 14.3 | 1 [Reference] | | | |
| Mass-forming IHC | 82.3 | 48.8 | 34.3 | 0.81 (0.41-1.59) | .55 | | |
| Mixed forms | 64.8 | 38.9 | 31.3 | 0.82 (0.35-1.92) | .64 | | |
| PI IHC | 100 | 42.0 | 42.0 | 0.90 (0.40-2.03) | .79 | | |
| Grading | | | | | | | |
| G1-2 | 83.7 | 52.9 | 37.9 | 1 [Reference] | | 1 [Reference] | |
| G3-4 | 77.8 | 39.5 | 22.7 | 1.50 (1.10-2.04) | .01 | 1.21 (0.88-1.67) | .24 |
| Lymph node status | | | | | | | |
| N0 | 85.6 | 57.3 | 38.2 | 1 [Reference] | | 1 [Reference] | |
| N1 | 70.5 | 22.4 | 15.9 | 2.56 (1.82-3.61) | <.001 | 2.21 (1.55-3.15) | <.001 |
| Perineural invasion | | | | | | | |
| Absent | 80.2 | 52.9 | 39.1 | 1 [Reference] | | | |
| Present | 81.1 | 42.4 | 24.7 | 1.29 (0.94-1.77) | .11 | | |
| Vascular invasion | | | | | | | |
| Absent | 84.2 | 56.1 | 41.2 | 1 [Reference] | | 1 [Reference] | |
| Present | 79.4 | 41.0 | 24.9 | 1.51 (1.11-2.04) | .008 | 1.05 (0.75-1.47) | .77 |
| Tumor number | | | | | | | |
| Single | 85.1 | 55.5 | 40.4 | 1 [Reference] | | 1 [Reference] | |
| Multiple | 76.8 | 32.8 | 20.6 | 1.83 (1.37-2.46) | <.001 | 1.50 (1.11-2.04) | .009 |
| Tumor size, cm | | | | | | | |
| ≤5 | 84.2 | 54.0 | 41.2 | 1 [Reference] | | 1 [Reference] | |
| >5 | 80.6 | 43.2 | 27.7 | 1.47 (1.10-1.98) | .01 | 1.25 (0.91-1.72) | .17 |
| Radical resection | | | | | | | |
| No | 67.5 | 37.1 | 8.2 | 1 [Reference] | | 1 [Reference] | |
| Yes | 84.4 | 49.9 | 37.5 | 0.46 (0.32-0.67) | <.001 | 0.75 (0.49-1.13) | .17 |
| Adjuvant therapy | | | | | | | |
| No | 80.2 | 49.2 | 34.1 | 1 [Reference] | | | |
| Yes | 86.8 | 41.9 | 33.1 | 0.99 (0.72-1.37) | .96 | | |

R0 vs. R1

↓↓ Risk of recurrence

↑↑ 5-year OS

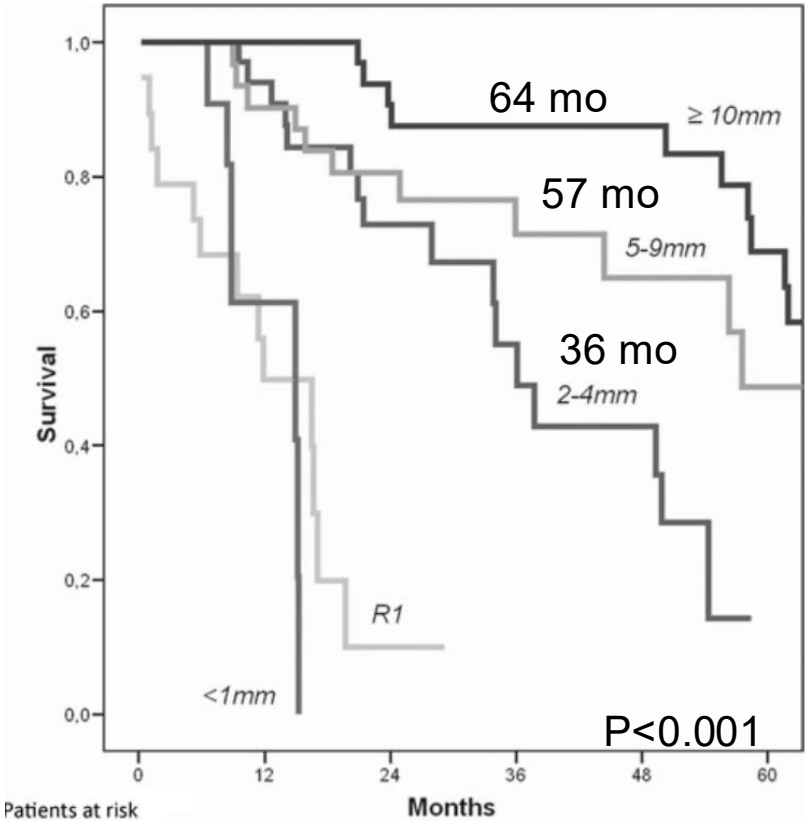
Increasing margin width in R0 NOT associated with:

1. Risk of recurrence
2. Site of recurrence
3. Survival

*Ribero D, et al. Arch Surg 2012*

# Influence of Surgical Margins on Outcome in Patients With Intrahepatic Cholangiocarcinoma

*A Multicenter Study by the AFC-IHCC-2009 Study Group*




Characteristics of the 116 pN0 Patients With IHCC Undergoing R0 Resection

| Margin's Width | ≤1 mm | 2–4 mm | 5–9 mm | ≥10 mm | *P* |
|---|---|---|---|---|---|
| No. patients | 14 | 34 | 32 | 36 | |
| Tumor size | 66 mm | 72 mm | 81 mm | 70 mm | 0.49 |
| Major hepatectomy | 85% | 94% | 93% | 81% | 0.20 |
| Vascular resection | 8% | 6% | 6% | 8% | 0.76 |
| Common bile duct resection | 27% | 9% | 27% | 23% | 0.39 |
| Multiple lesions | 62% | 71% | 50% | 44% | 0.10 |
| Vascular invasion | 25% | 47% | 39% | 36% | 0.69 |
| Neoadjuvant chemotherapy | 13% | 12% | 6% | 2% | 0.40 |
| Adjuvant chemotherapy | 35% | 41% | 31% | 30% | 0.98 |

*Farges O, et al. Ann Surg 2011*

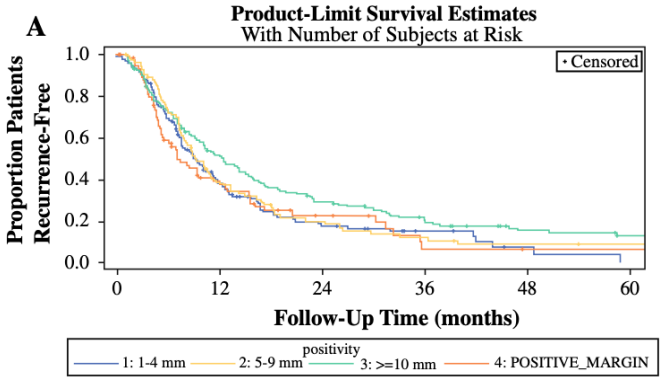
# The Impact of Surgical Margin Status on Long-Term Outcome After Resection for Intrahepatic Cholangiocarcinoma

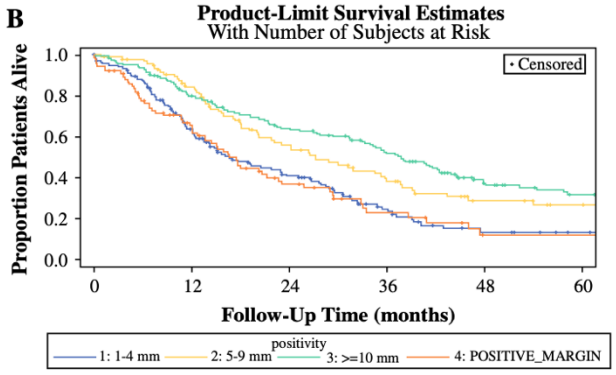
584 pts with ICC

*Spolverato G, et al. Ann Surg Oncol 2015*

Median, 1-, 3-, and 5-year recurrence-free survival and overall survival in all subjects and according to tumor margin status and width

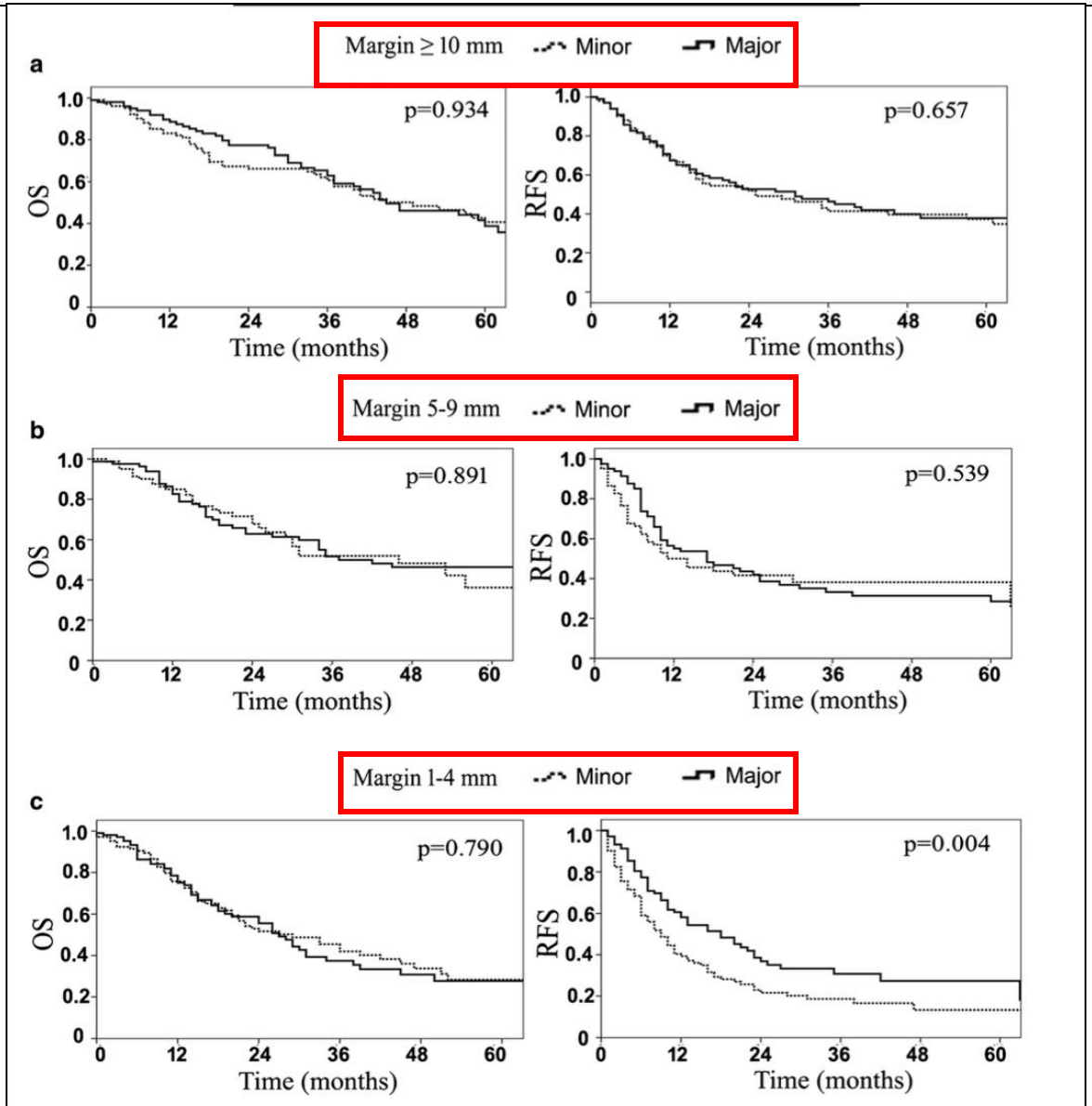
| | All subjects | Positive | 1–4 mm | 5–9 mm | ≥1 cm | *p* value |
|---|---|---|---|---|---|---|
| Recurrence-free survival | | | | | | |
| Median (months) | 10.0 | 7.4 | 8.9 | 9.0 | 12.4 | 0.13 |
| 1-year (%) | 42.8 | 40.1 | 38.3 | 37.3 | 51.1 | |
| 3-year (%) | 15.2 | 7.9 | 15.2 | 12.3 | 19.4 | |
| 5-year (%) | 9.2 | 7.9 | 0.0 | 9.0 | 13.2 | |
| Overall survival | | | | | | |
| Median (months) | 26.4 | 17.6 | 16.7 | 27.3 | 37.7 | <0.001 |
| 1-year (%) | 73.7 | 69.0 | 63.3 | 83.9 | 79.8 | |
| 3-year (%) | 37.3 | 22.4 | 24.9 | 39.6 | 52.0 | |
| 5-year (%) | 23.0 | 13.1 | 13.8 | 27.0 | 32.2 | |



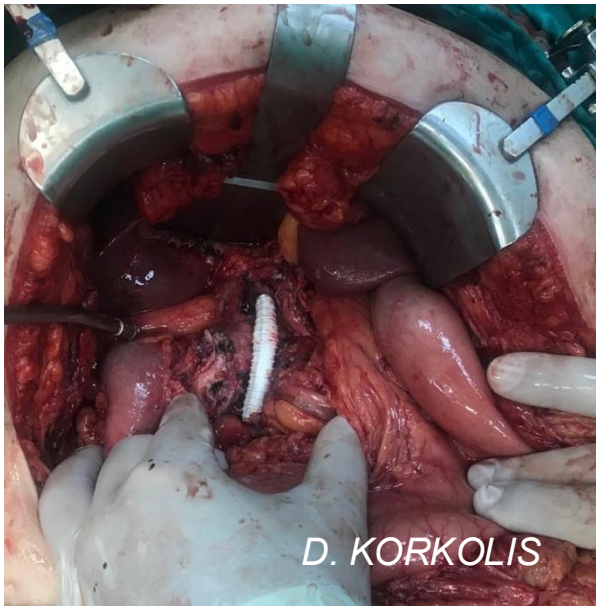
# Perioperative and Long-Term Outcome for Intrahepatic Cholangiocarcinoma: Impact of Major Versus Minor Hepatectomy

*Zhang et al. J Gastrointest Surg 2017*



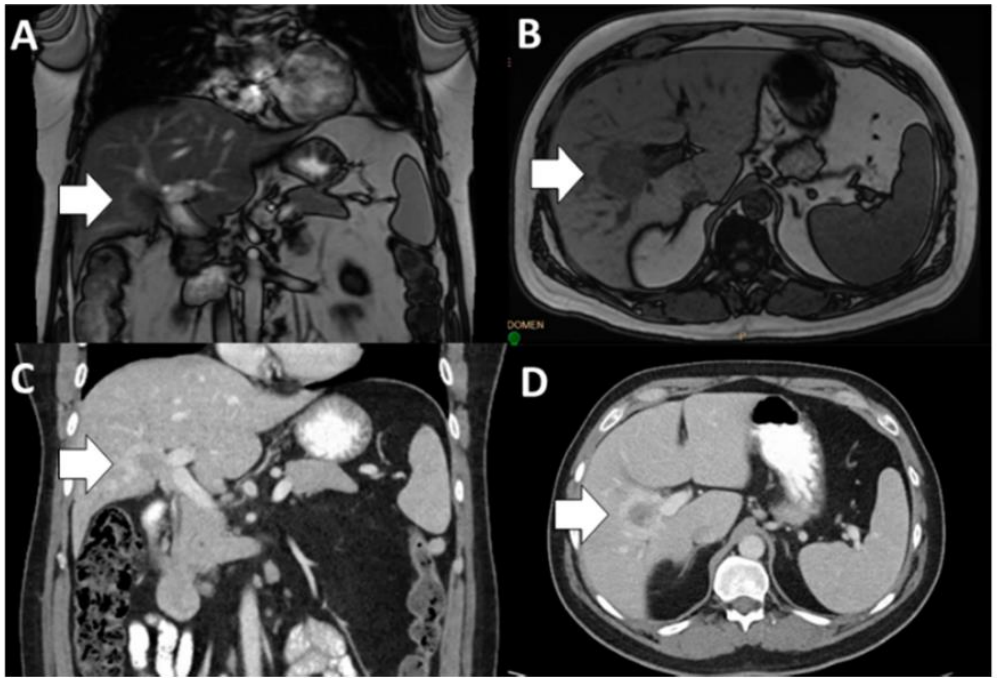
# Αγγειακές Εκτομές

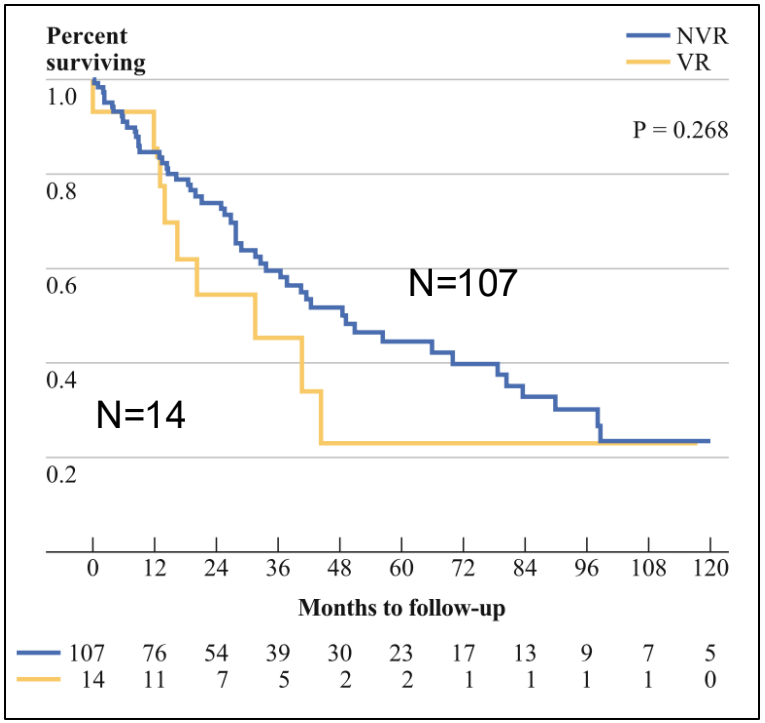
- Συχνή αγγειακή εμπλοκή λόγω διηθητικού χαρακτήρα
- Αγγειακές εκτομές 9 – 15% για R0
- Ανάλογες επιβιώσεις
- Συγκρίσιμη νοσηρότης και θνητότης
- Επιλεγμένοι ασθενείς και Κέντρα




# Role of Major Vascular Resection in Patients with Intrahepatic Cholangiocarcinoma

**Shahzad M. Ali, MD, Clancy J. Clark, MD, Victor M. Zaydfudim, MD, MPH, Florencia G. Que, MD, and David M. Nagorney, MD**



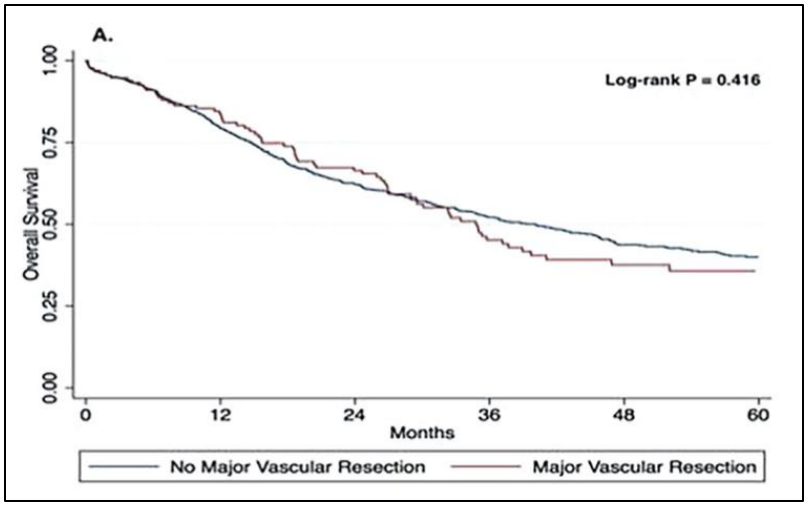



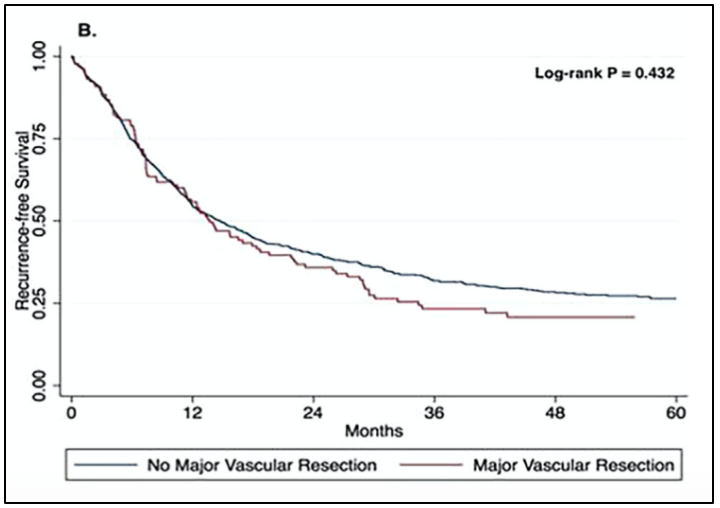

14 pts (12%) required VR
PVR 5pts
IVC 9pts

*Ann Surg Oncol 2015*

# Impact of major vascular resection on outcomes and survival in patients with intrahepatic cholangiocarcinoma: A multi-institutional analysis

1087 pts ICC – 128 (12%) VR



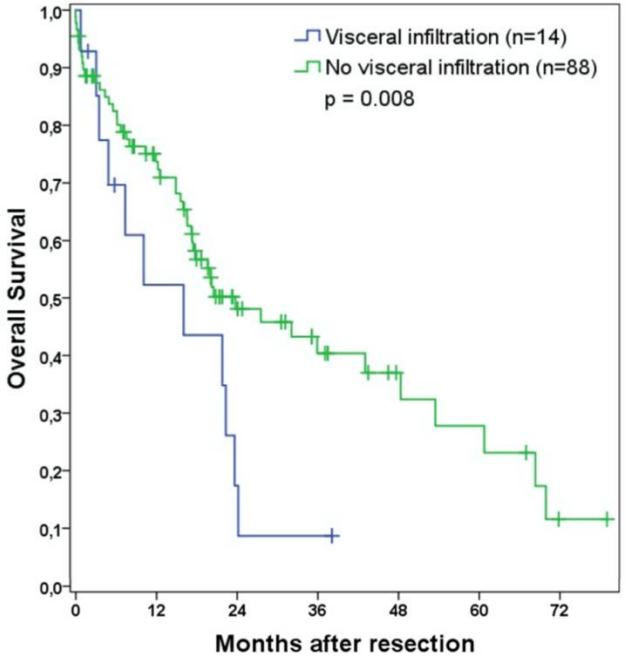

| Perioperative outcomes | Unadjusted rates no. (%) | | Major vascular resection odds ratio (95%CI) | *P*-value |
|---|---|---|---|---|
| | No major vascular resection (*N* = 959) | Major vascular resection (*N* = 128) | | |
| Death at 30 days | 46 (4.8) | 6 (4.7) | 1.05 (0.32-3.47) | 0.93 |
| Death at 90 days | 79 (8.2) | 9 (7.0) | 0.78 (0.21-2.84) | 0.70 |
| Any complication | 401 (41.9) | 71 (55.5) | 0.68 (0.32-1.45) | 0.32 |
| Severe complication | 173 (18.0) | 34 (26.6) | 0.95 (0.45-2.00) | 0.89 |
| **Oncologic outcomes** | **Unadjusted time-to-event (median months)** | | **Major vascular resection hazard ratio (95%CI)** | |
| Overall survival | 40.2 | 33.4 | 0.709 (0.36-1.40) | 0.32 |
| Recurrence-free survival | 14.7 | 14 | 0.737 (0.49-1.10) | 0.14 |

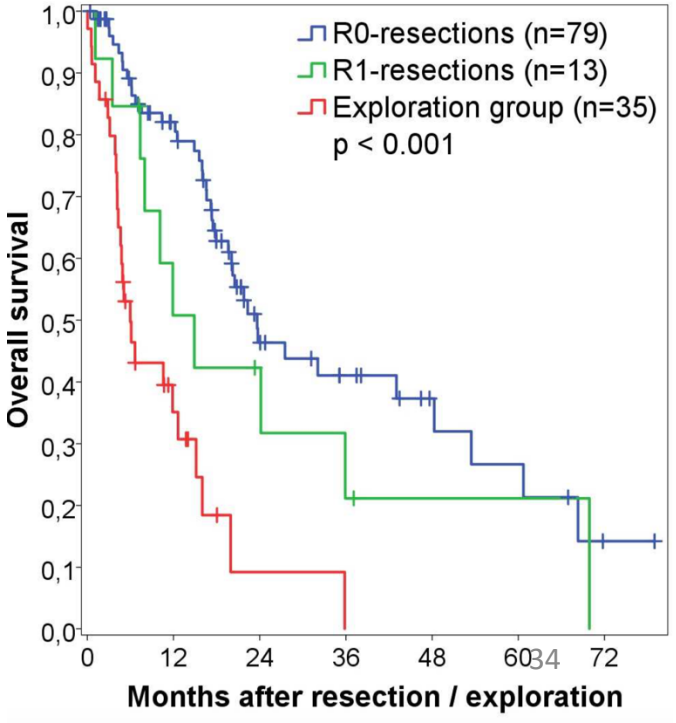
*Reames BN, et al. J Surg Oncol 2017*

## Visceral infiltration of intrahepatic cholangiocarcinoma is most prognostic after curative resection

**- Retrospective cohort study of 102 consecutive Liver Resections from a single center -**

| | Suspected infiltration | Proven infiltration | |
|---|---|---|---|
| **Vascular invasion** | **28** | **12** | **42.9%** |
| Hepatic artery | 0 | 0 | - |
| Portal vein | 10 | 4 | 40% |
| Major hepatic vein | 8 | 3 | 37.5% |
| Vena cava inferior | 10 | 5 | 50% |
| **Visceral invasion** | **35*** | **16** | **45.7%** |
| Diaphragm | 9 | 2 | 22% |
| Adrenal gland | 1 | 1 | 100% |
| Hilar bifurcation | 22 | 11 | 50% |
| Pericardium | 1 | 1 | 100% |
| Duodenum | 1 | 1 | 100% |
| Colon | 1 | 1 | 100% |
| **Total** | **63** | **28** | **44.4%** |





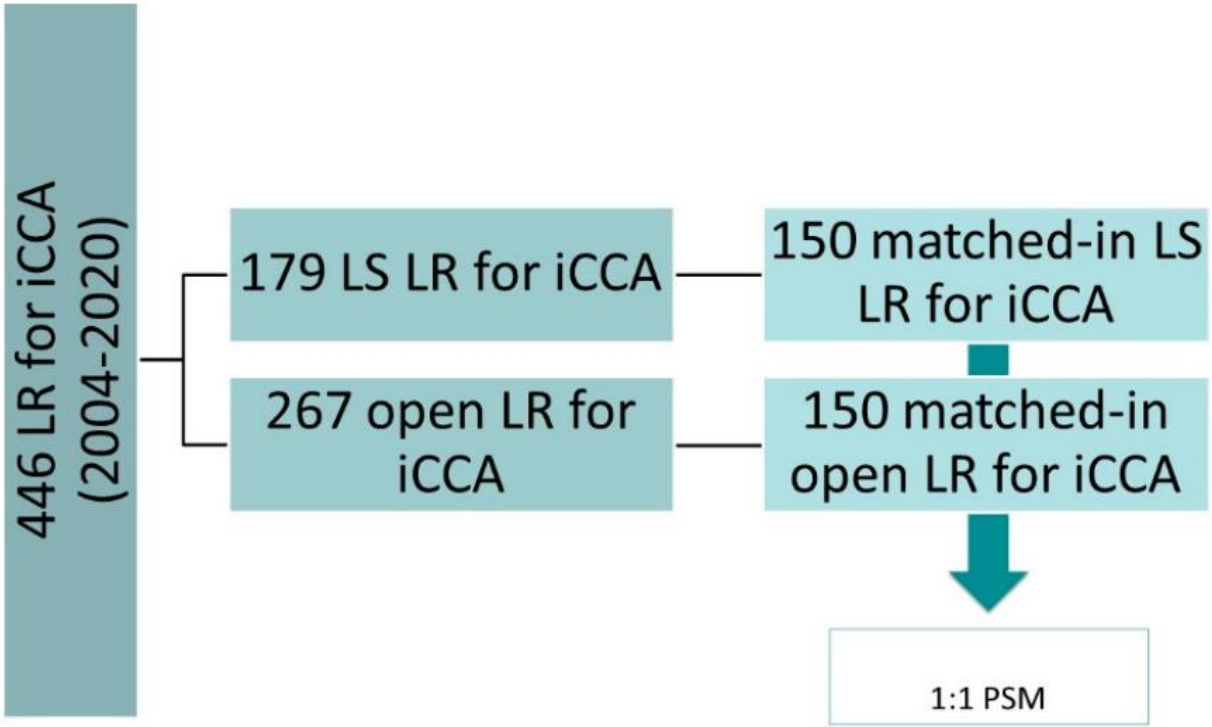

*Bartsch F, et al. Int J Surg 2018*

# LLR vs OLS for ICC

| Author | Year | LLR N | OLR N | Short-Term Outcomes | Long-Term Outcomes |
|---|---|---|---|---|---|
| Wu et al. [55] | 2020 | 18 | 25 | LLR decreased EBL, LOS; no difference 30-day morbidity or mortality | No difference median, 1-or 3-year RFS/OS |
| Haber et al. [56] | 2020 | 27 | 31 | LAD LLR 85%/OLR 94%; R0 LLR 89%/OLR 74%; hospital LOS LLR 10/OLR 12 days; overall complications LLR 30%/OLR 58%, no difference in major complications | |
| Ratti et al. [57] | 2016 | 20 | 60 | EBL LLR 200/OLR 350 mL, despite less use of Pringle; No difference perioperative morbidity or mortality; Functional recovery LLR 3/OLR 4 days | No difference in DFS/OS; Number of harvested nodes comparable |
| Zhu et al. [58] | 2019 | 20 | 63 | Large (≥5 cm)/multiple (≥2) ICC; After PSM—OR time LLR 225/OLR 190 min; occlusion time LLR 50/OLR 35 min; LLR completed in 18; no difference proportion major liver resection, EBL, transfusion rate, major complications, hospital LOS | No difference in recurrence rate, DFS/OS between LLR and OLR |
| Uy et al. [59] | 2015 | 11 | 26 | EBL OLR > LLR; no difference in transfusions, OR time, resection margin, LOS | No difference in 3- or 5-year OS/DFS |
| Lee et al. [60] | 2016 | 14 | 23 | LLR less frequent Pringle maneuver, blood loss; no differences in complication rate, hospital stay, tumor size, lymph node metastasis, number of retrieved lymph nodes | No difference in 3-year OS or RFS |

# Laparoscopic Surgery for Intrahepatic Cholangiocarcinoma: A Focus on Oncological Outcomes

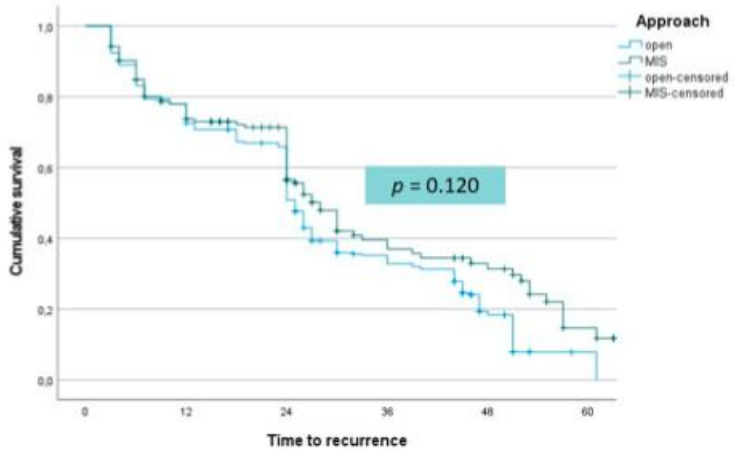
Francesca Ratti [1,*], Andrea Casadei-Gardini [2], Federica Cipriani [1], Guido Fiorentini [1], Federica Pedica [3], Valentina Burgio [2], Stefano Cascinu [2] and Luca Aldrighetti [1]

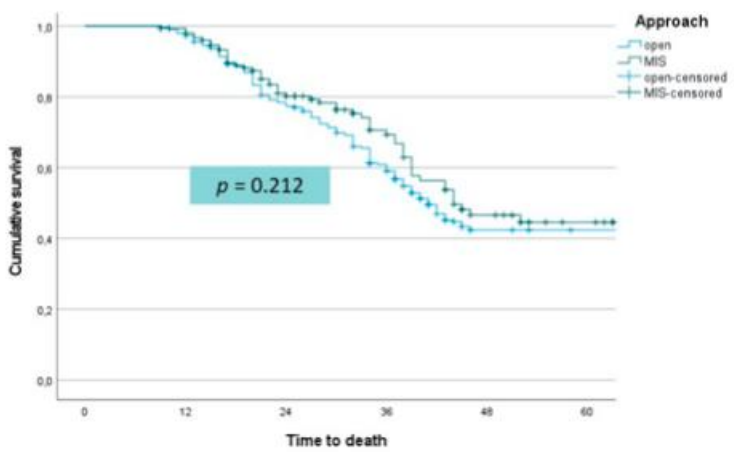


| | | LS Group ($n$ = 150) | Open Group ($n$ = 150) | $p$ |
|---|---|---|---|---|
| Procedure, $n$ (%) * | | | | ns |
| | Minor resection | 99 (66) | 95 (63.3) | |
| | Major resection | 51 (34) | 55 (36.7) | |
| Pringle Manuevre, $n$ (%) | | | | ns |
| | Not performed | 17 (11.3) | 14 (9.3) | |
| | Performed | 133 (88.7) | 136 (90.7) | |
| Lenght of surgery (min) | Mean ± SD | 270 ± 65 | 230 ± 60 | ns |
| Blood loss (mL) | Mean ± SD | 150 ± 100 | 350 ± 250 | 0.021 |
| Number of retrieved nodes | Median (range) | 9 (5-11) | 7 (5–14) | ns |
| Surgical margin, $n$ (%) | | | | ns |
| | R0 | 146 (97.3) | 143 (95.3) | |
| | R1 | 4 (2.7) | 7 (4.7) | |
| Conversion, $n$ (%) | | 17 (11.3) | n.a. | |
| Surgical margin (mm) | Mean ± SD | 6 ± 4 | 7 ± 4 | ns |
| Intraoperative blood transfusions, $n$ (%) | | | | 0.04 |
| | No | 144 (96) | 138 (92) | |
| | Yes | 6 (4) | 12 (8) | |
| Postoperative blood transfusions, $n$ (%) | | | | 0.03 |
| | No | 140 (93.3) | 128 (85.3) | |
| | Yes | 10 (6.7) | 22 (14.7) | |
| Complications, $n$ (%) | | | | |
| | Hemorrhage | 0 | 3 (2) | ns |
| | Wound infection | 2 (1.3) | 6 (4) | 0.02 |
| | Ileus | 2 (1.3) | 7 (4.7) | 0.01 |
| | Biliary fistula | 6 (4) | 12 (8) | 0.03 |
| | Transient liver failure | 4 (2.7) | 7 (4.7) | ns |
| | Ascites | 10 (6.7) | 16 (10.7) | 0.03 |
| | Pleural effusion | 10 (6.7) | 14 (9.3) | 0.04 |
| | Pneumonia | 2 (1.3) | 4 (2.7) | ns |
| | Fever | 6 (4) | 9 (6) | ns |
| | Pancreatitis | 3 (2) | 3 (2) | ns |
| | Lymphatic fistula | 3 (2) | 10 (6.7) | 0.03 |
| | Arrhythmia | 4 (2.7) | 6 (4) | 0.04 |
| | DVT/PE | 2 (1.3) | 3 (2) | ns |
| Overall complication rate, $n$ (%) | | 22 (14.7) | 36 (24) | 0.015 |
| Grade of complications, $n$ (%) * | | | | 0.03 |

*J Clin Medicine 2021*

| | | LS Group ($n$ = 150) | Open Group ($n$ = 150) | $p$ |
|---|---|---|---|---|
| Minor | I grade | 4 (2.7) | 7 (4.7) | |
| | II grade | 12 (8) | 17 (11.3) | |
| Major | III grade | 4 (2.7) | 9 (6) | ns |
| | IV grade | 2 (1.3) | 3 (2) | |
| Mortality, $n$ (%) | | 2 (1.3) | 2 (1.3) | ns |
| Functional recovery (days) | Median (range) | 3 (1–5) | 5 (3–10) | 0.032 |
| Lenght of stay (days) | Median (range) | 4 (2–10) | 6 (3–21) | 0.046 |
| Interval surgery-adjuvant treatment (days) | Median (range) | 35 (30–55) | 49 (37–63) | 0.03 |
| Systemic adjuvant therapy, $n$ (%) | | 124 (82.7) | 116 (77.3) | 0.05 |

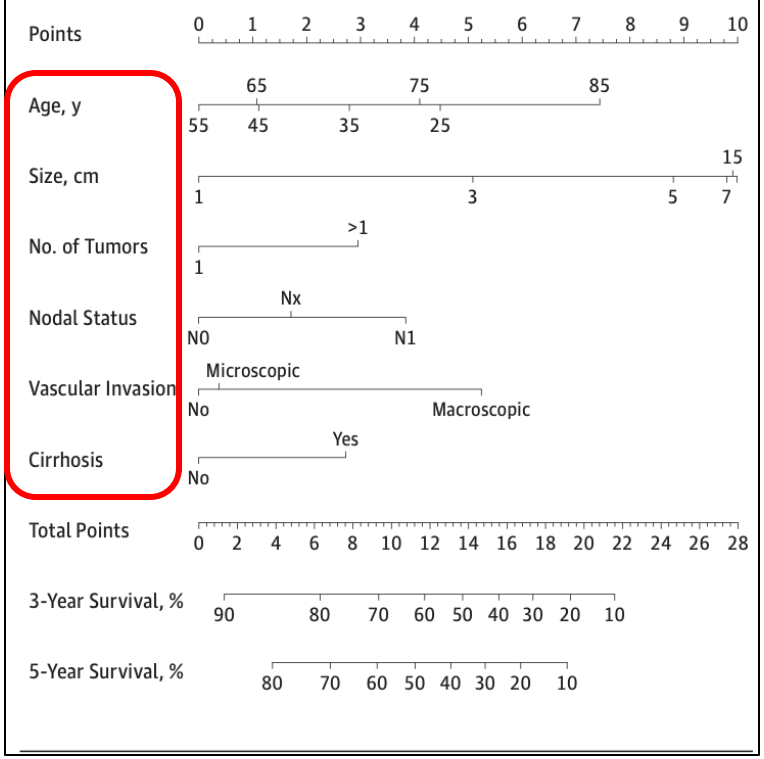



*J Clin Medicine 2021*

# A Nomogram to Predict Long-term Survival After Resection for Intrahepatic Cholangiocarcinoma
## An Eastern and Western Experience

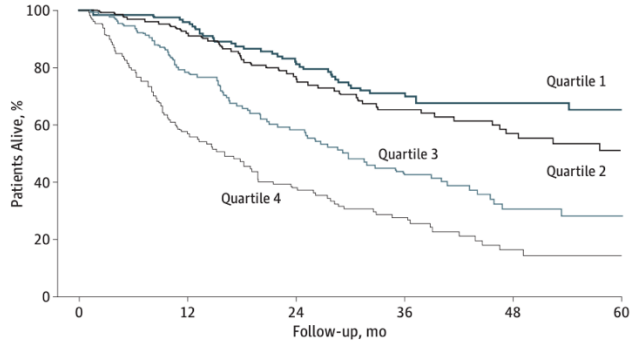
**Figure 2. A Nomogram for Predicting Postsurgery Survival of Patients With Resectable Intrahepatic Cholangiocarcinoma**




514 pts ICC 1990 - 2011

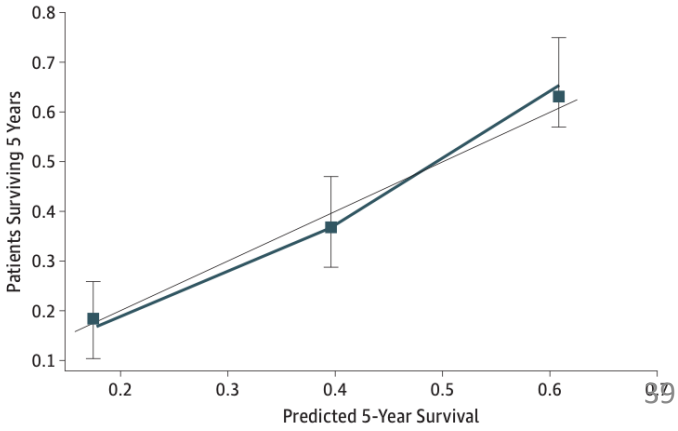
*Hyder O, et al. JAMA Surgery 2014*

**Figure 3. Kaplan-Meier Survival Curves and Patients at Risk at Each Year According to Quartiles of the Predicted Survival**

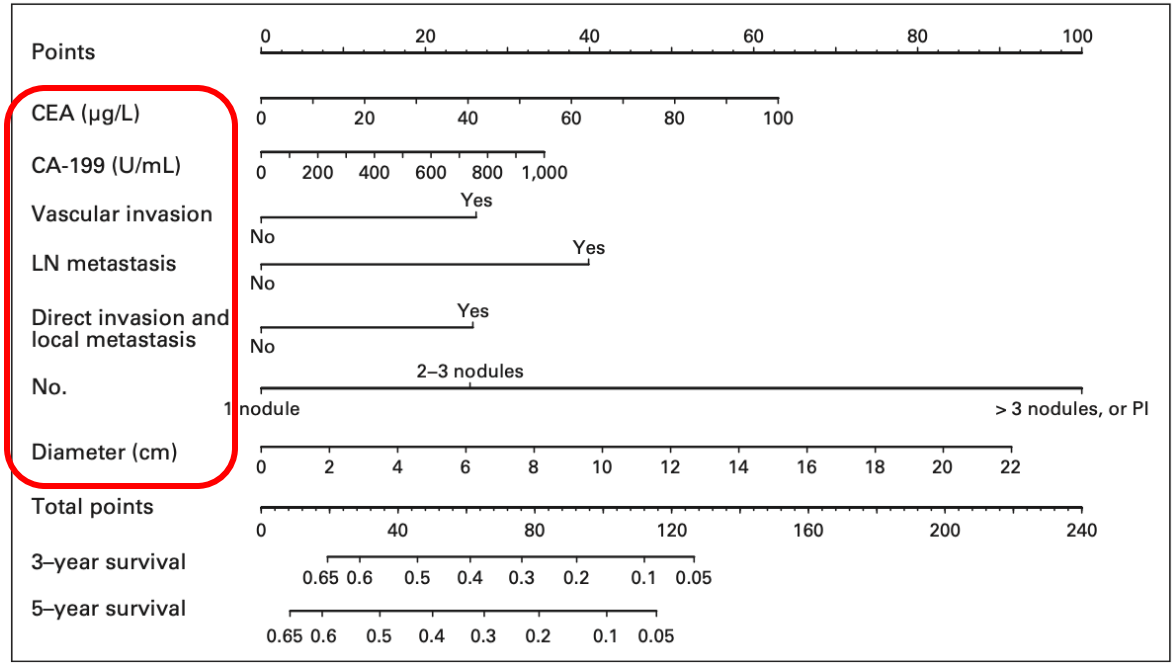



| | | | | | | |
|---|---|---|---|---|---|---|
| Quartile 1 | 129 | 115 | 90 | 67 | 33 | 18 |
| Quartile 2 | 128 | 108 | 75 | 57 | 37 | 19 |
| Quartile 3 | 129 | 89 | 59 | 39 | 17 | 8 |
| Quartile 4 | 128 | 67 | 40 | 27 | 9 | 4 |

**Figure 4. Calibration Plot Comparing Predicted and Actual Survival Probabilities at 5 Years of Follow-up**

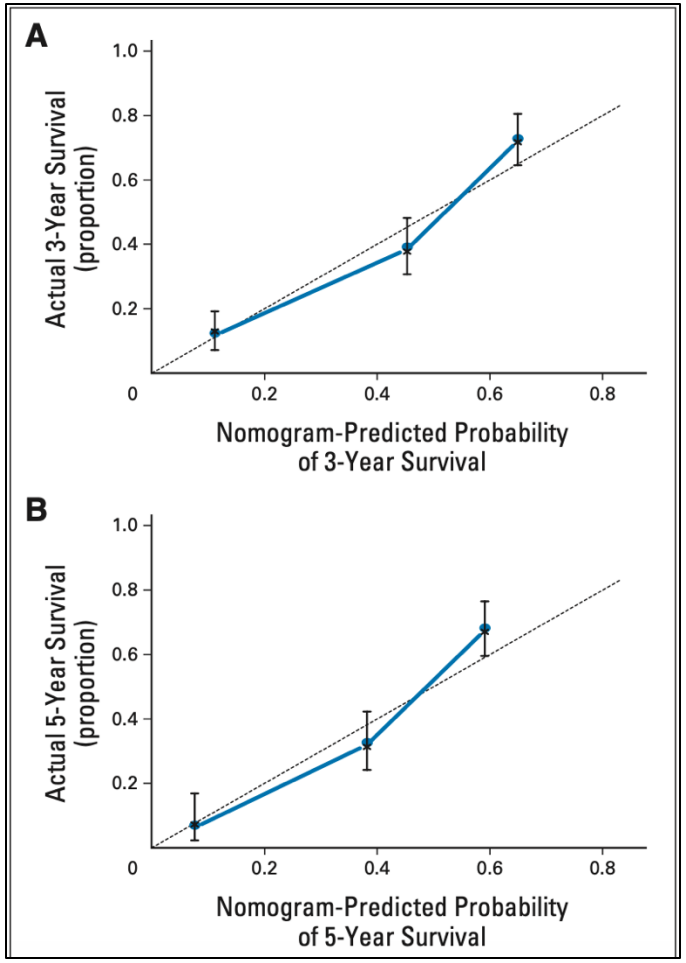


# Prognostic Nomogram for Intrahepatic Cholangiocarcinoma After Partial Hepatectomy




Cohort study 367 consecutive pts with ICC Partial Hepatectomy between 2002 - 2007

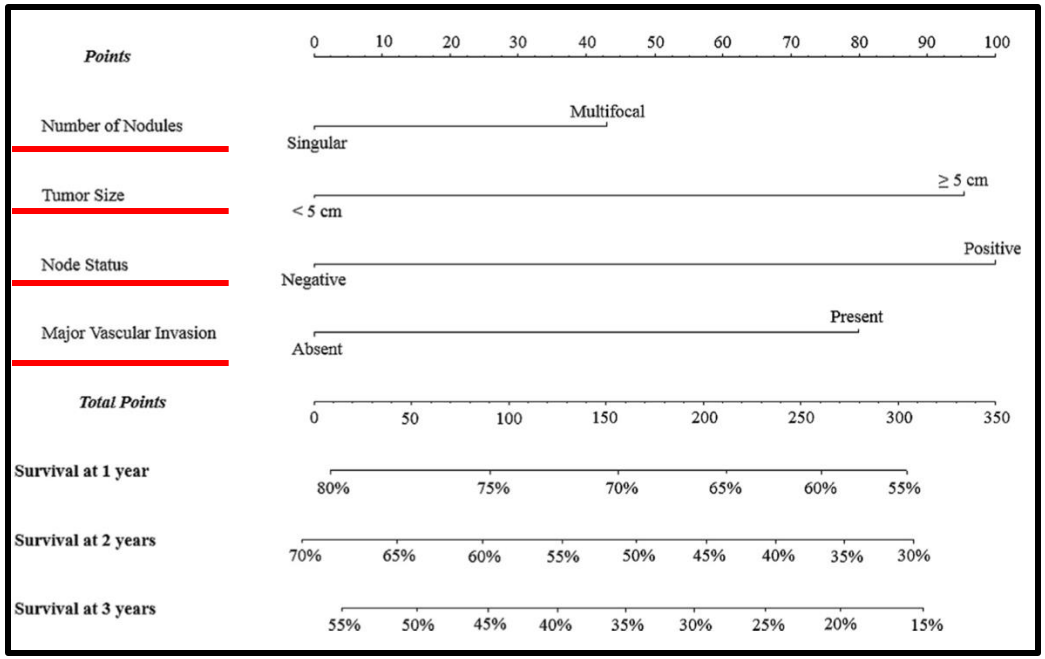
*Concordance Index (C-Index): 0.74!!!*




*Wang Y, et al. J Clin Oncol 2013*

# Defining when to offer operative treatment for intrahepatic cholangiocarcinoma: A regret-based decision curves analysis

*Bagante et al. Surgery 2016*




| | |
|---|---|
| Case 1 | |
| Patients Characteristics | |
| Tumor Size: 5 cm | 96 |
| Node Status: 1 suspicious for metastasis | 100 |
| Vascular Invasion: No | 0 |
| Number of Tumors: Singular | 0 |
| Total Points | 196 |
| Model Predicted Survival | |
| 1 y | 70% |
| 2 y | 45% |
| 3 y | 30% |
| Case 2 | |
| Patients Characteristics | |
| Tumor Size: 3 cm | 0 |
| Node Status: 0 suspicious for metastasis | 0 |
| Vascular Invasion: No | 0 |
| Number of Tumors: Singular | 0 |
| Total Points | 0 |
| Model Predicted Survival | |
| 1 y | 85% |
| 2 y | 70% |
| 3 y | 55% |
| Case 3 | |
| Patients Characteristics | |
| Tumor Size: >5 cm | 96 |
| Node Status: 1 suspicious for metastasis | 100 |
| Vascular Invasion: Yes | 80 |
| Number of Tumors: 3 Nodules | 43 |
| Total Points | 319 |
| Model Predicted Survival | |
| 1 y | 52% |
| 2 y | 28% |
| 3 y | 12% |

# Liver Resection for Advanced Intrahepatic Cholangiocarcinoma: A Cost-Utility Analysis

Umberto Cillo[1] · Gaya Spolverato[2] · Alessandro Vitale[1] · Aslam Ejaz[2] · Sara Lonardi[3] · David Cosgrove[4] · Timothy M. Pawlik[2]

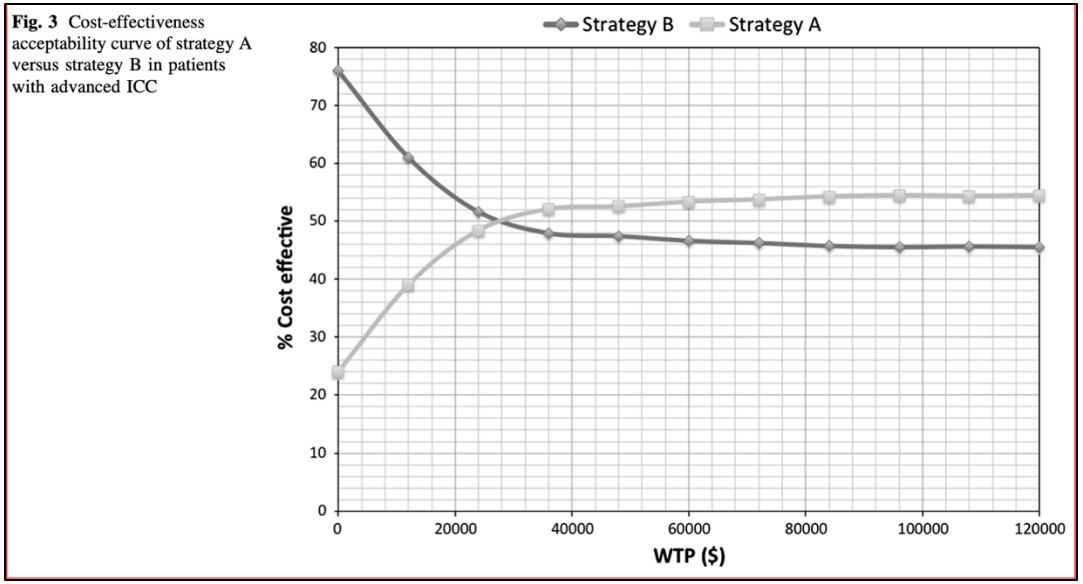



**Fig. 3** Cost-effectiveness acceptability curve of strategy A versus strategy B in patients with advanced ICC

## *Cost- effective Analysis*

Size > 6cm - Vascular invasion(+): HR > sCT
Multifocal disease(+): sCT > HR

*World J Surg 2015*

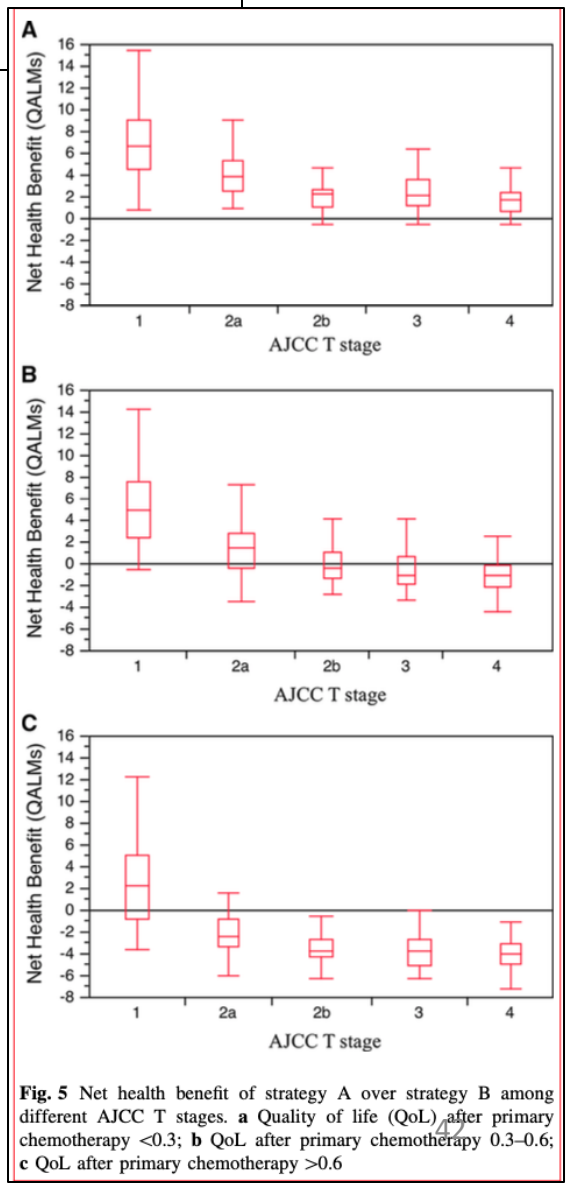
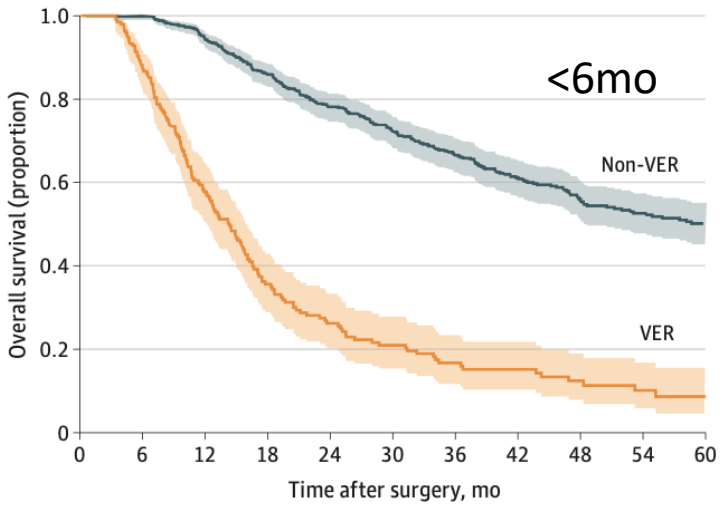



**Fig. 5** Net health benefit of strategy A over strategy B among different AJCC T stages. **a** Quality of life (QoL) after primary chemotherapy <0.3; **b** QoL after primary chemotherapy 0.3–0.6; **c** QoL after primary chemotherapy >0.6

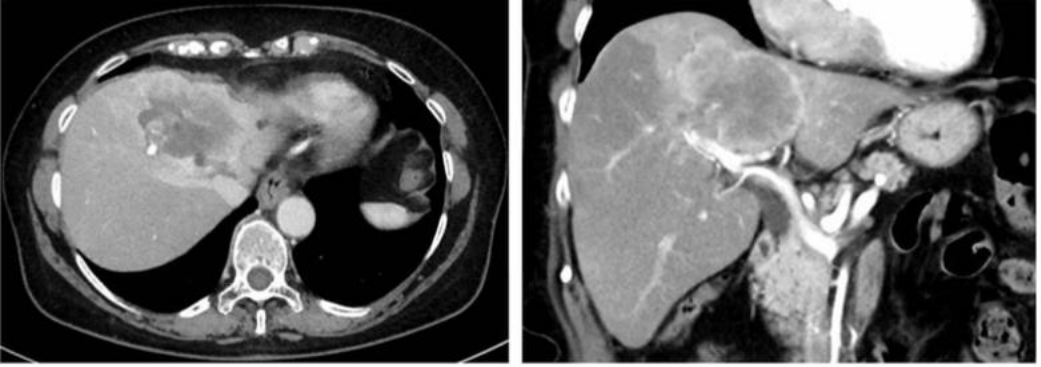
# Very Early Recurrence After Liver Resection for Intrahepatic Cholangiocarcinoma Considering Alternative Treatment Approaches

**Figure 1. Kaplan-Meier Curve Demonstrating the Differences in Overall Survival Between Patients With and Without Very Early Recurrence (VER)**

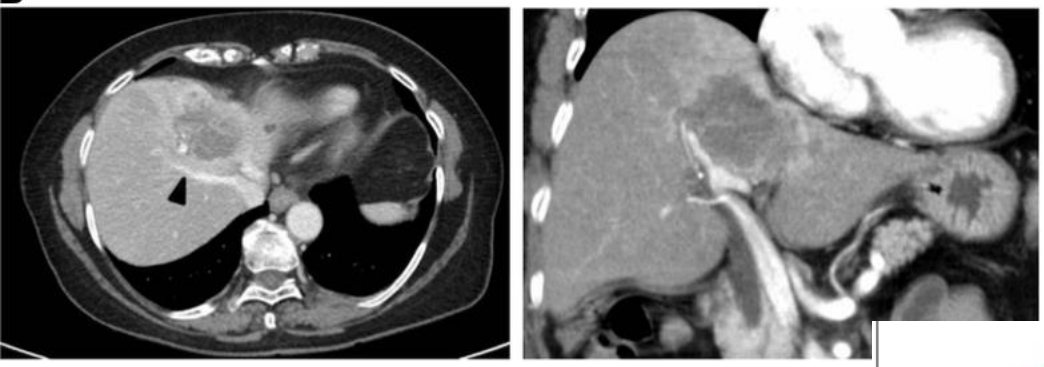



| Variable | Bivariate analysis OR (95% CI) | *P* value |
|---|---|---|
| Age | 0.96 (0.95-0.98) | <.001 |
| Race | | |
| White | 1 [Reference] | NA |
| Person of color | 1.70 (1.23-2.34) | .001 |
| Liver cirrhosis | 2.03 (1.29-3.21) | .002 |
| Ln CA19-9 | 1.11 (1.02-1.22) | .02 |
| Tumor size (cm) | 1.10 (1.06-1.15) | <.001 |
| No. of lesions | 1.37 (1.18-1.58) | <.001 |
| Microvascular invasion | 1.51 (1.07-2.13) | .02 |
| LNM on imaging | | |
| No | 1 [Reference] | .004 |
| Suspicious or positive | 1.72 (1.19-2.50) | |
| AJCC N category | | |
| N0 | 1 [Reference] | NA |
| N1 or Nx | 1.83 (1.26-2.67) | .001 |
| R1 margin | 1.63 (1.04-2.56) | .03 |

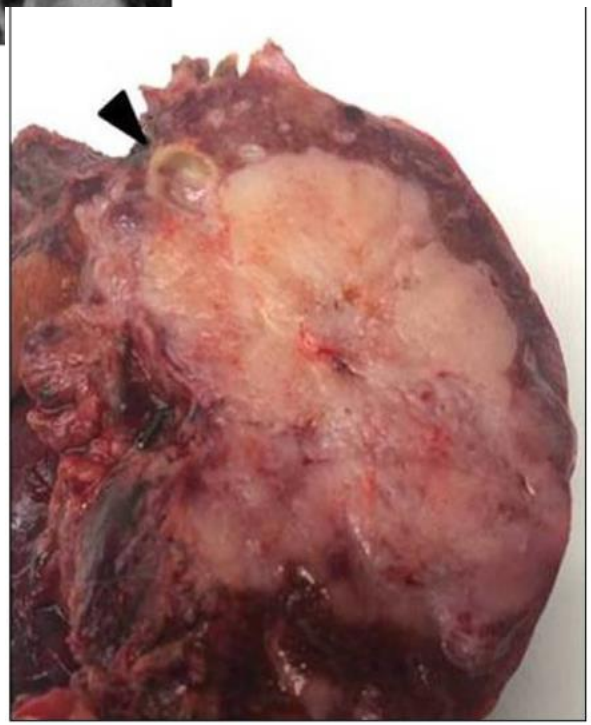
*JAMA Surg 2020*

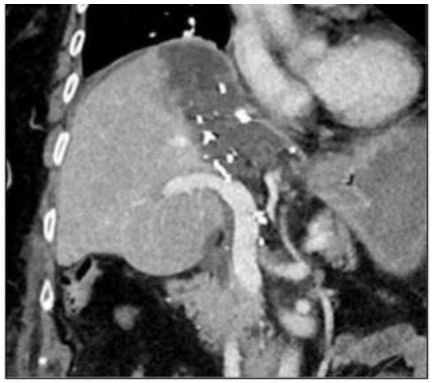


B



Neo – Adjuvant
Chemo-Radiotherapy

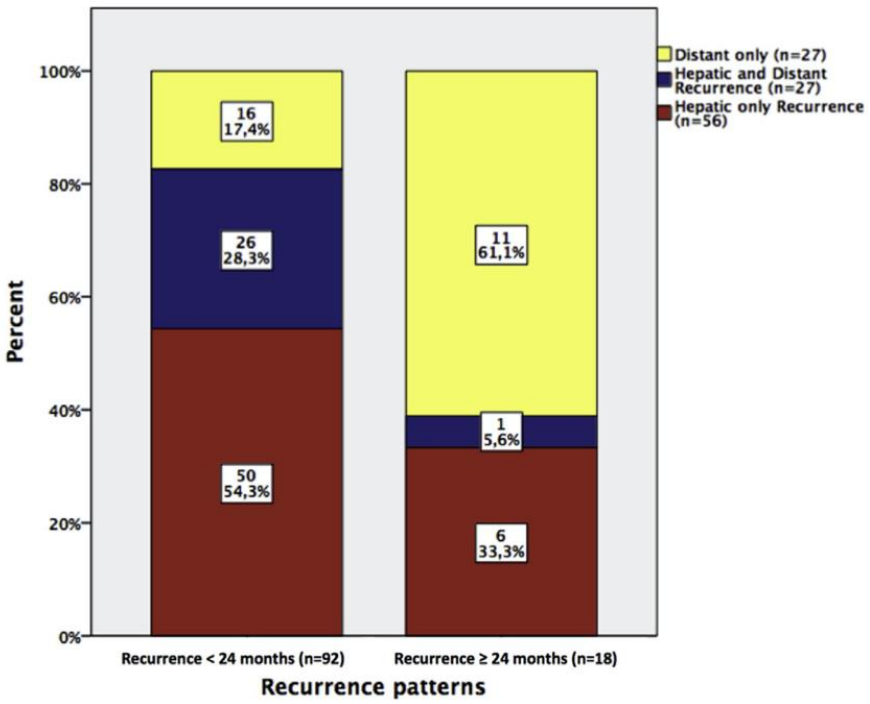


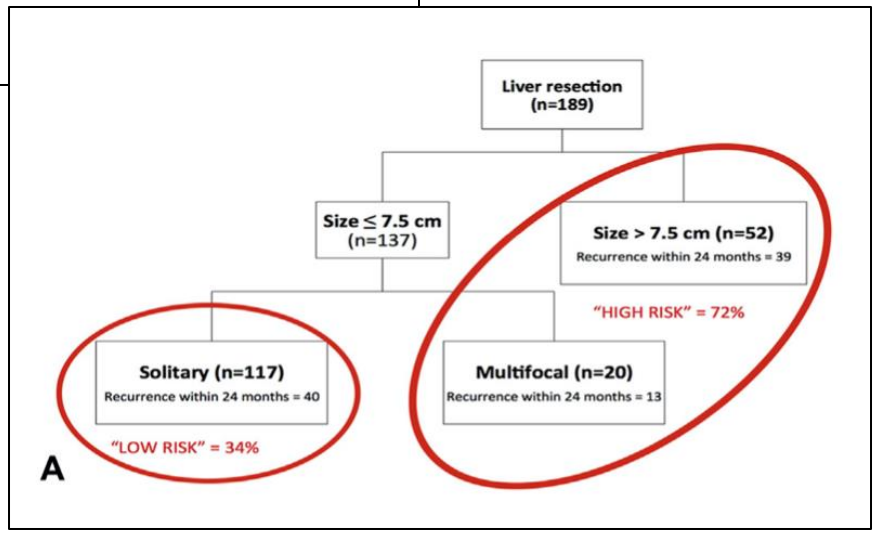


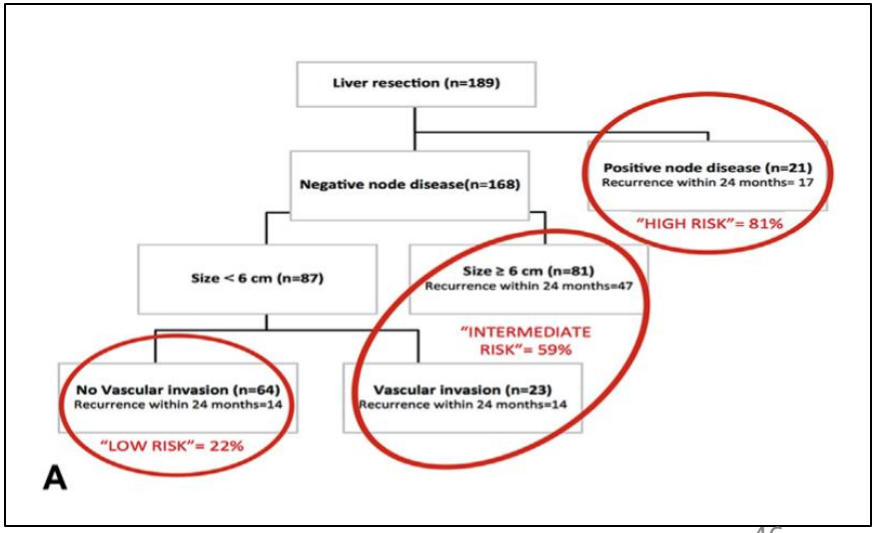
# Υποτροπή

- Υποτροπή στην 5ετία: 50% - 79%
- Ενδοηπατική: 60 – 80%
- Περιτοναική – Απομακρυσμένες Μεταστάσεις (15 – 30%)
- Ηπατεκτομή στην ενδοηπατική υποτροπή
- TACE – HAIP - Χημειοθεραπεία - Ανοσοθεραπεία
- Ραδιοεμβολισμός με Y- 90
- RFA - MWA

# Recurrence Patterns and Disease-Free Survival after Resection of Intrahepatic Cholangiocarcinoma: Preoperative and Postoperative Prognostic Models




*Doussot A, et al. J Am Coll Surg 2016*

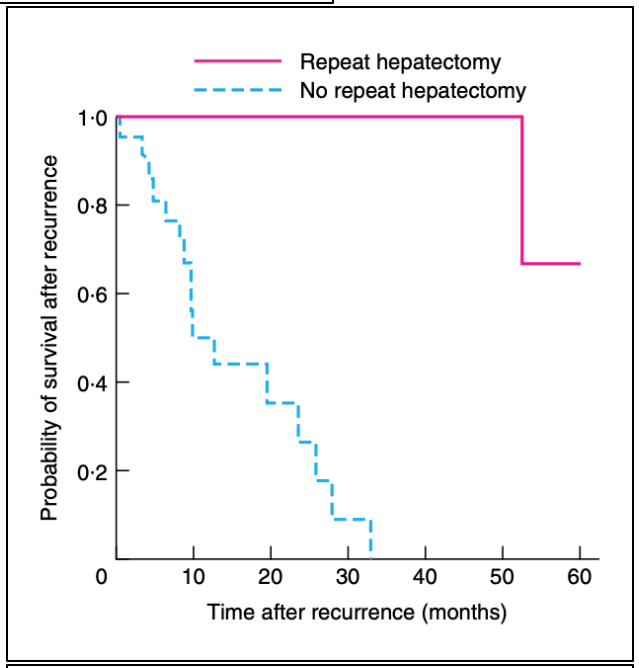
# Treatment of recurrent intrahepatic cholangiocarcinoma

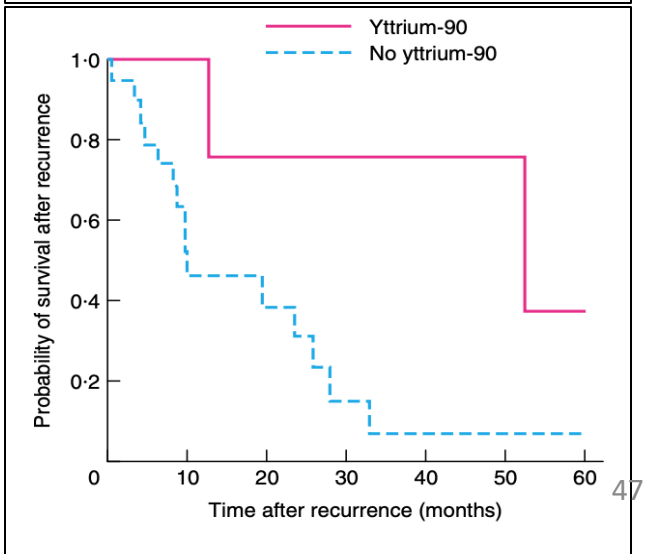
L. Sulpice[1,3], M. Rayar[1], E. Boucher[2,3], M. Pracht[2], B. Meunier[1] and K. Boudjema[1,3]

*Br J Surg 2012*

**Table 2** Clinicopathological factors and 3-year survival after recurrence of intrahepatic cholangiocarcinoma following partial hepatectomy with curative intent

| | 3-year survival after recurrence | | |
|---|---|---|---|
| | Yes ($n = 5$) | No ($n = 40$) | $P$* |
| Sex ratio (F : M) | 0 : 5 | 9 : 31 | 0·566 |
| Age (years) | | | 0·617 |
| ≥ 60 | 3 (60) | 29 (73) | |
| < 60 | 2 (40) | 11 (28) | |
| Body mass index (kg/m$^2$) | | | 0·166 |
| ≥ 25 | 2 (40) | 29 (73) | |
| < 25 | 3 (60) | 11 (28) | |
| Major hepatectomy | 3 (60) | 34 (85) | 0·211 |
| Tumour size > 5 cm | 1 (20) | 30 (75) | 0·027 |
| Satellite nodules | 0 (0) | 12 (30) | 0·303 |
| Microvascular invasion | 2 (40) | 18 (45) | 1·000 |
| Perineural infiltration | 3 (60) | 10 (25) | 0·136 |
| Positive hilar lymph node | 1 (20) | 12 (30) | 1·000 |
| R1 resection | 2 (40) | 11 (28) | 0·617 |
| Adjuvant chemotherapy | 1 (20) | 6 (15) | 0·571 |
| Haemochromatosis | 1 (20) | 7 (18) | 1·000 |
| Cirrhosis | 0 (0) | 13 (33) | 0·301 |
| Cirrhosis and/or haemochromatosis | 1 (20) | 18 (45) | 0·378 |
| Surgery for recurrence | 4 (80) | 3 (8) | 0·001 |
| Chemotherapy for recurrence | 2 (40) | 20 (50) | 1·000 |
| Yttrium-90 | 2 (40) | 4 (10) | 0·125 |



# Management and Outcomes of Patients with Recurrent Intrahepatic Cholangiocarcinoma Following Previous Curative-Intent Surgical Resection

*Spolverato G, et al. Ann Surg Oncol 2015*

**TABLE 1** Patterns of recurrence following curative-intent surgery of intrahepatic cholangiocarcinoma

| Characteristic | Recurrence ($n$ = 400) |
|---|---|
| Intrahepatic only | 239 (59.8) |
| Extrahepatic only | 58 (14.5) |
| Intrahepatic and extrahepatic | 103 (25.7) |
| Site of extrahepatic recurrence | $n$ = 161 |
| Lung | 48 (29.8) |
| Adrenal | 4 (2.5) |
| Bone | 16 (9.9) |
| Peritoneum | 34 (21.1) |
| Lymph node | 38 (23.6) |
| Other | 21 (13.0) |

Total 563 pts

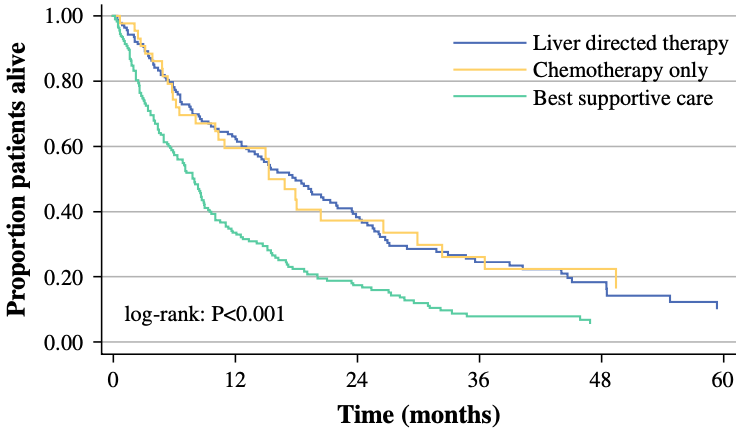



**FIG. 2** Five-year overall survival stratified by type of treatment of recurrent disease

| | |
|---|---|
| 5yr recurrence | 71% |
| 5yr OS | 23.6% |
| Intrahepat Rec | 60% |
| Median OS: | 11.1mo |
| Re-resection | 26.7mo |
| IAT | 9.6mo |

| | Liver directed therapy | Chemotherapy only | Best Supportive Care |
|---|---|---|---|
| Treatment | 75.8% | 24.2% | 52.5% |
| Median Survival | 18mo | 16.8mo | 8.0mo |

# Characterization of intrahepatic cholangiocarcinoma after curative resection: outcome, prognostic factor, and recurrence

Kun-Ming Chan*, Chun-Yi Tsai, Chun-Nan Yeh, Ta-Sen Yeh, Wei-Chen Lee, Yi-Yin Jan* and Miin-Fu Chen

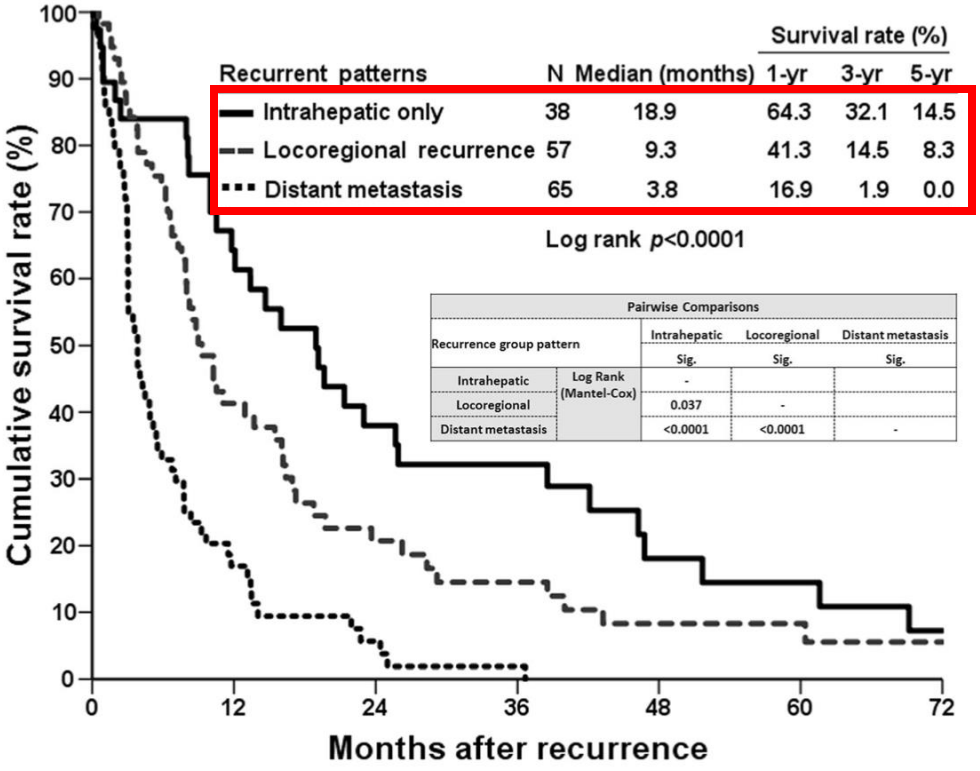



**Fig. 2** Among patients with postoperative recurrence, the survival curves are compared according to recurrent patterns. Patients with only intrahepatic recurrence had a significantly better survival curve than other two recurrent patterns ($p < 0.0001$)

*BMG Gastroenterology 2018*

# Characterization of intrahepatic cholangiocarcinoma after curative resection: outcome, prognostic factor, and recurrence

Kun-Ming Chan*, Chun-Yi Tsai, Chun-Nan Yeh, Ta-Sen Yeh, Wei-Chen Lee, Yi-Yin Jan* and Miin-Fu Chen

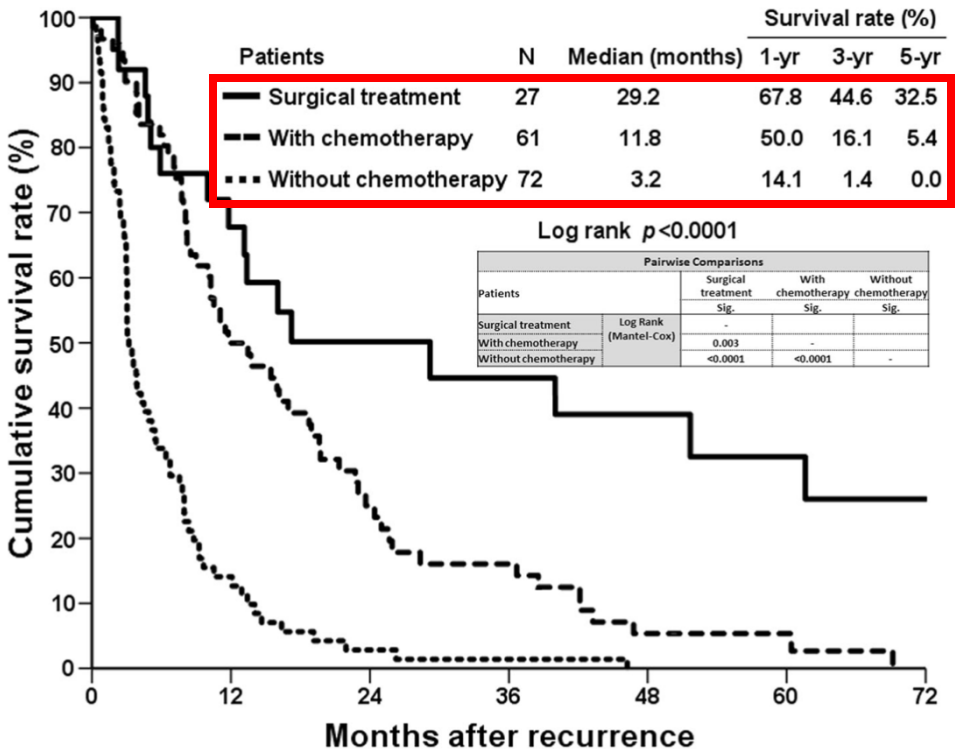


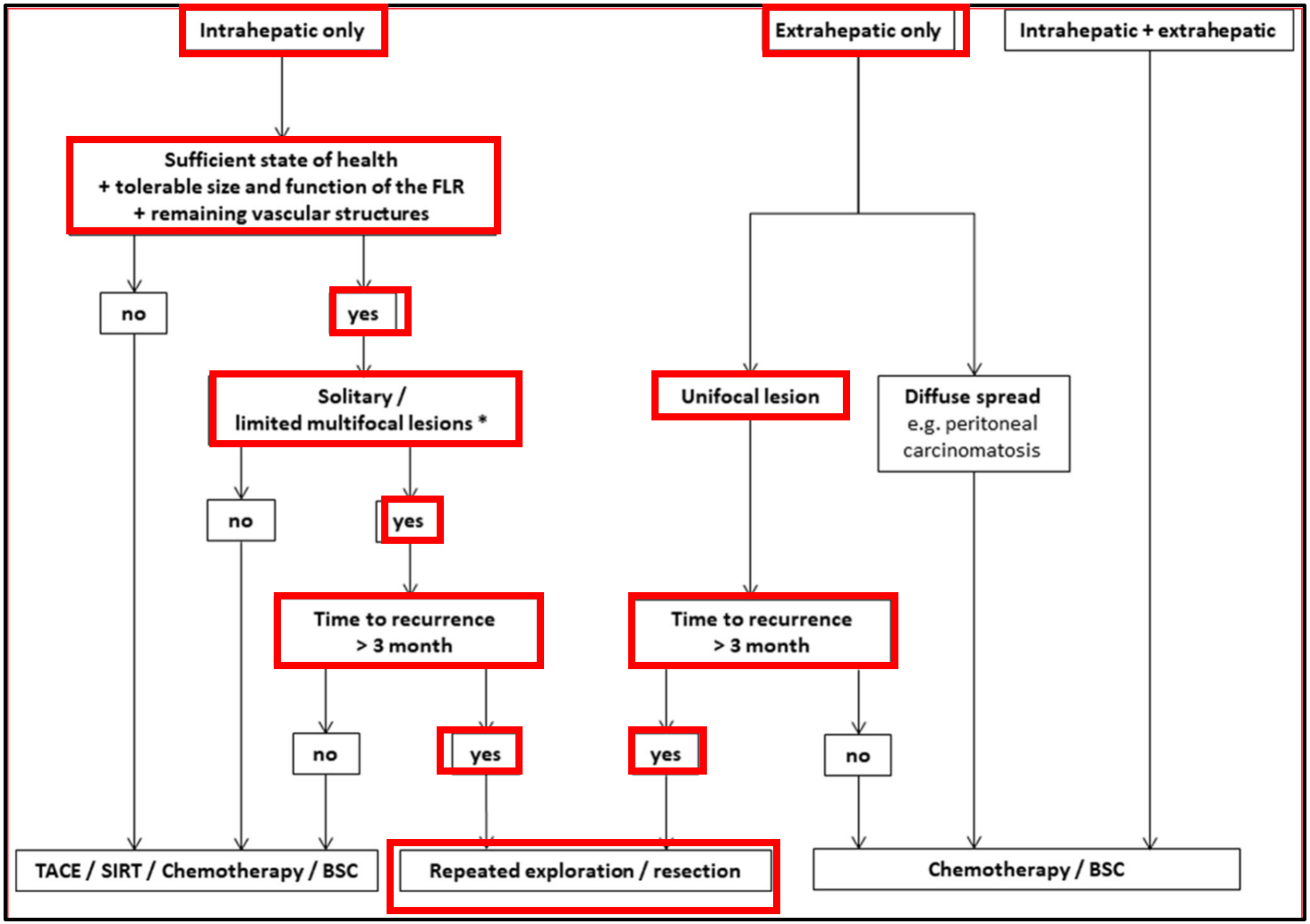

**Fig. 3** Kaplan-Meier survival curves of the patients with cholangiocarcinoma recurrence after curative resection. The patients who underwent surgical resection for recurrent cholangiocarcinoma had a significantly better survival curve than those who did not undergo surgical resection for recurrent cholangiocarcinoma. Among patients without surgical treatment for recurrent cholangiocarcinoma, the survival curve of patients who had received palliative chemotherapy was better than that of patients without palliative chemotherapy ($p < 0.0001$)

# Surgical Resection for Recurrent Intrahepatic Cholangiocarcinoma

Fabian Bartsch[1] · Markus Paschold[1] · Janine Baumgart[1] · Maria Hoppe-Lotichius[1]
Stefan Heinrich[1] · Hauke Lang[1]

World Journal of Surgery

*World J Surg 2018*



# ΜΕΤΑΜΟΣΧΕΥΣΗ

- Αντένδειξη προ 2015 (2ετής επιβίωση <30%)
- Απουσία: α. Κριτήρια επιλογής
  β. Νεοεπικουρικές θεραπείες

- Ενδείξεις:

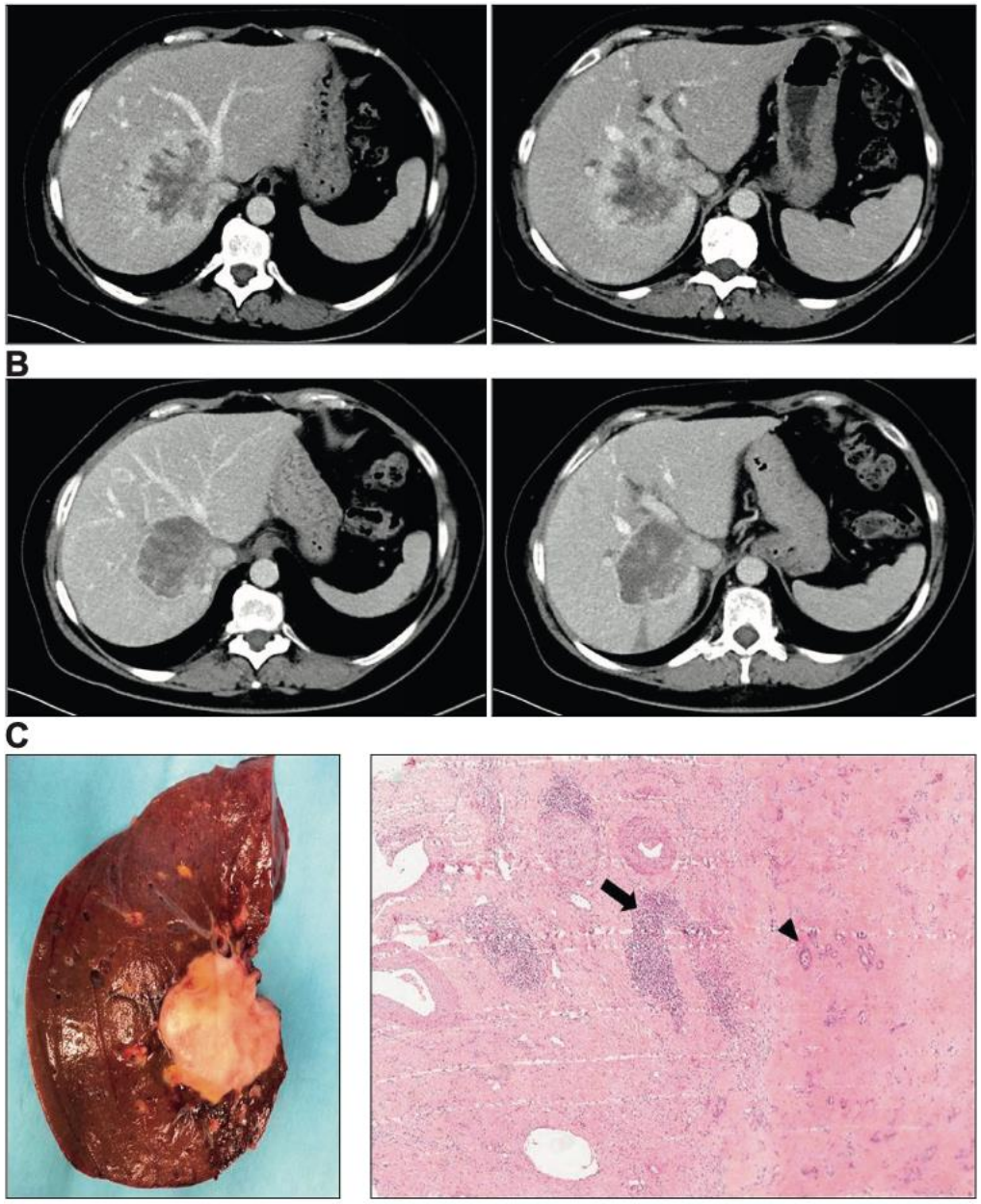
1. Very-early iCCA <2cm non LR (cirrhosis) 5yr OS 65%
2. Unresectable Locally Advanced iCCA with no LNs, no mets
3. Responders to neoadjuvant CRT

*J Hepatol 2020*

# ΜΕΤΑΜΟΣΧΕΥΣΗ

*Hepatology 2022*

| | Liver resection | Liver transplantation |
|---|---|---|
| Age, PS, comorbidities | Case-by-case evaluation to be balanced with resect ability criteria based on extent of liver tissue to be removed *vs.* volume and function of the liver remnant | <65 years, absence of comorbidities contraindicating LT |
| Histology confirmation | Recommended | Mandatory |
| Ca19.9 | Relative contraindication for Ca19.9 >500 ng/ml in the absence of jaundice | To be defined |
| Tumour staging | Single resectable mass any size, if resectability is provided according to point 1<br>Unilateral multifocal disease | Unresectable <2 cm very-early tumour arisen in chronic liver disease/cirrhosis (*i.e.* solid data available and trial ongoing)<br>Unresectable >2 cm lesion with sustained response to chemotherapy ± RT (experimental, within prospective protocols) |
| Chronic liver disease/cirrhosis/PH | Relative/absolute contraindication | No limitation regarding liver function |
| Macrovascular invasion | Relative contraindication (vascular reconstructions are allowed if R0 resection is achievable) | Contraindication in case of intra-/extrahepatic vascular invasion. Questionable in case of extravascular growth with encasement of major inflow/outflow tributaries (experimental) |
| Preoperative lymph node assessment | Recommended | Mandatory to rule out nodal disease |
| Multifocality* | Relative contraindication | To be defined. |
| Neoadjuvant treatment | Experimental | Very-early iCCA: experimental<br>Advanced iCCA: recommended as selection tool (sustained responses may be selected for transplant consideration) |
| Additional procedures | PVE, ALPPS and biliary reconstructions can be added, though associated to higher morbidity/mortality | DCD, marginal grafts in pts with preserved liver function and LDLT can be proposed |
| Adjuvant treatment | Advisable in high-risk patients | To be defined |
| Future studies | - Prospective investigations on neoadjuvant "downstaging" chemotherapy ± targeted agents ± RT (EBRT *vs.* SIRT) schemes able to convert advanced liver-only tumours to resectability<br>- Prospective randomised investigations on adjuvant CT in R1 resections and in patients at high risk of recurrence | Prospective parallel studies with matched patients co-horts (based on tumour burden and biology) to assess survival benefit of LT (± downstaging treatments) *vs.* other treatment options |
| Study endpoints | OS, RFS | Transplant benefit, OS (ITT), RFS and cancer-related survival |




OLT μετά από μερική ανταπόκριση σε νεοεπικουρική χημειο- και ακτινοθεραπεία

*Hepatology 2022*

# ΣΥΜΠΕΡΑΣΜΑΤΑ

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- Επιλεκτική αντιμετώπιση της υποτροπής
- Μεταμόσχευση
- *Biology first!!!*