Prise en charge des cholangiocarcinomes hilaires avancés:

Place de la transplantation hépatique

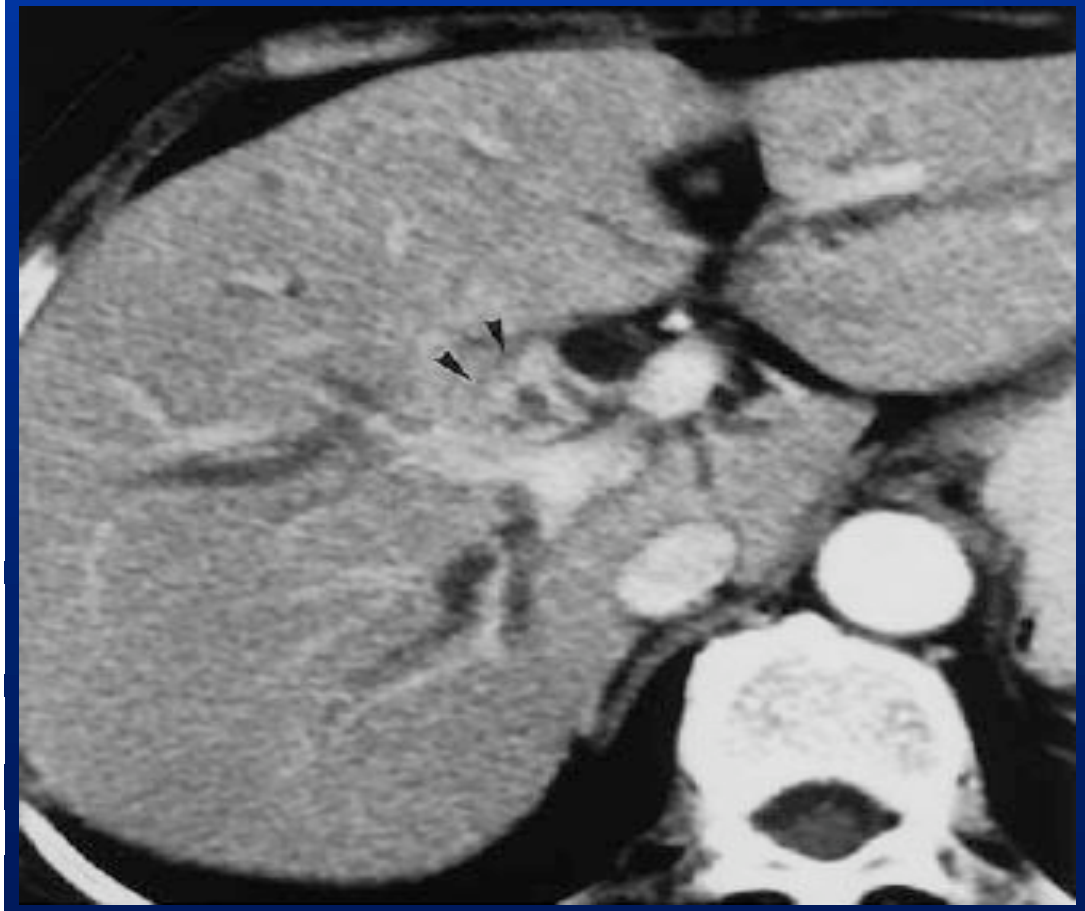
Mircea CHIRICA, Olivier SCATTON et Olivier SOUBRANE

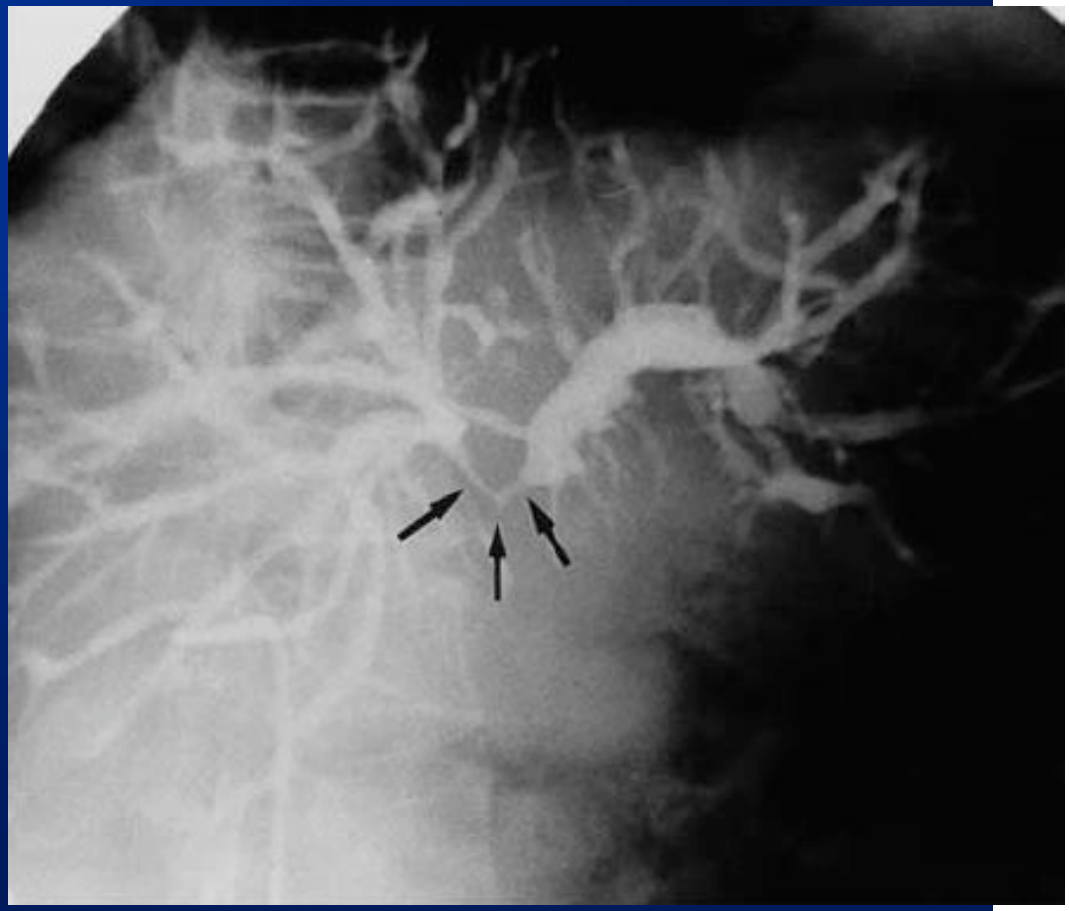
Définition d'un cholangiocarcinome hilaire

- = tumeur de Klatskin = adénocarcinome des gros canaux biliaires, au niveau du hile

- 50-60% des cancers des gros canaux(tiers moyen-17%, inferieur-17%, forme diffuse-7%)

Cholangiocarcinome hilaire
Klatskin





Stratégie diagnostique dans les tumeurs de Klatskin

- Diagnostic de sténose biliaire
- Diagnostic de cancer
- Diagnostic d'extension à distance
- Diagnostic d'opérabilité
- Diagnostic de résécabilité

Diagnostic de sténose biliaire

- Clinique
  - ictère rétentionnel, fonçant rapidement
- Examens biologiques
  - Cholestase : augmentation des phosphatases alcalines, de la GGT
  - baisse du TP avec un facteur V normal
- Examens morphologiques

  Échographie, scanner, IRM

Diagnostic de cancer

- les marqueurs tumoraux : augmentation de l'ACE et CA 19-9
- Cytologie de la bile ou brossage
  - sensibilité 75%, spécificité 100%

    Mansfield et coll Gut 1997
- Biopsie sous cholangioscopie percutanée
  - sensibilité 96%

    Nimura et coll Endoscopy 1993
- Echoendoscopie

En fait, le plus souvent la clinique

! cholangite sclérosante localisée

dans 10 à 15 % des cas

risque d'une chirurgie majeure pour maladie mineure

Diagnostic d ’extension à distance

- Scanner abdominal
- Scanner thoracique

En fait, l ’extension à distance est rare!

^{18}F-fluorodeoxyglucose Positron Emission Tomography Influences Management Decisions in Patients with Biliary Cancer

Carlos U Corvera, MD, FACS, Leslie H Blumgart, MD, FACS, Timothy Akhurst, MD, Ronald P DeMatteo, MD, FACS, Michael D'Angelica, MD, FACS, Yuman Fong, MD, FACS, William Robert Jarnagin, MD, FACS

(J Am Coll Surg 2008;206:57–65.

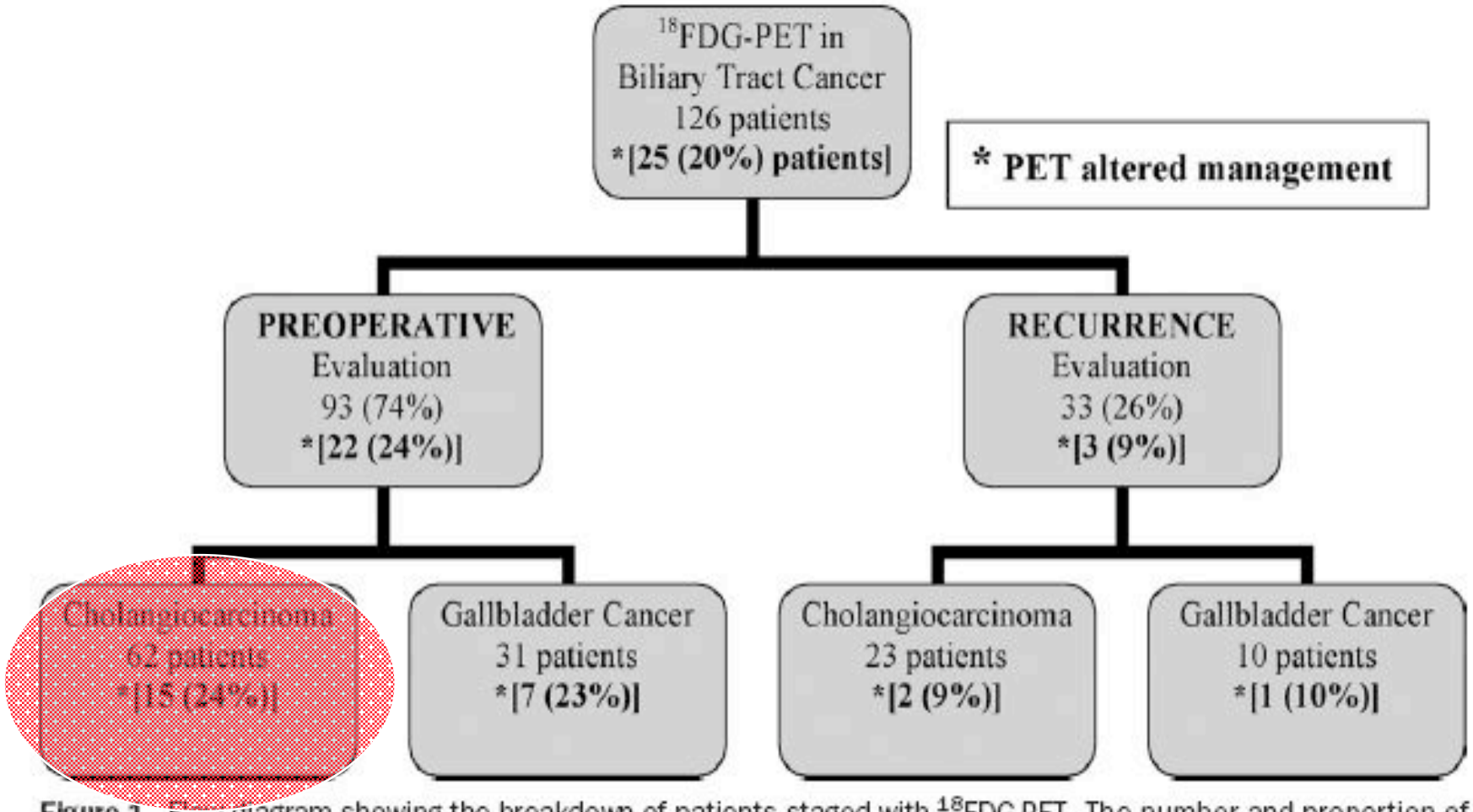
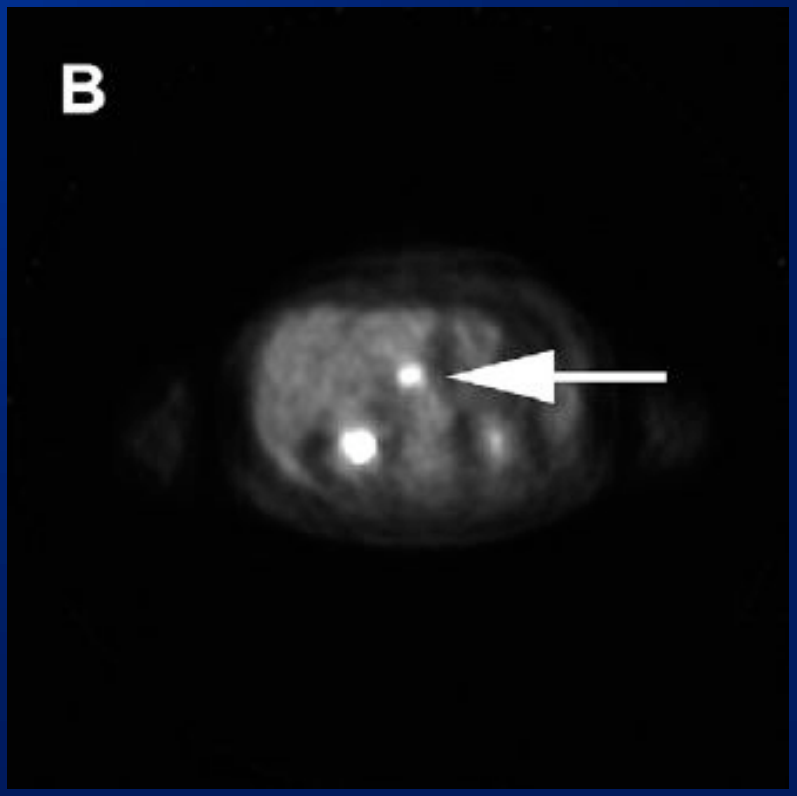


Figure 1. Flow diagram showing the breakdown of patients staged with ^{18}FDG-PET. The number and proportion of patients whose management was altered by the PET scan are indicted by the asterisks. ^{18}FDG-PET, ^{18}Fluorodeoxygluose-positron emission tomography.

PET	Sensibilité	Spécificité
Tumeur	78%	75%
Métastases	96%	89%

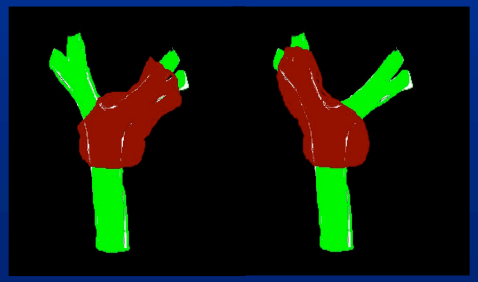


Diagnostic d'extirpabilité

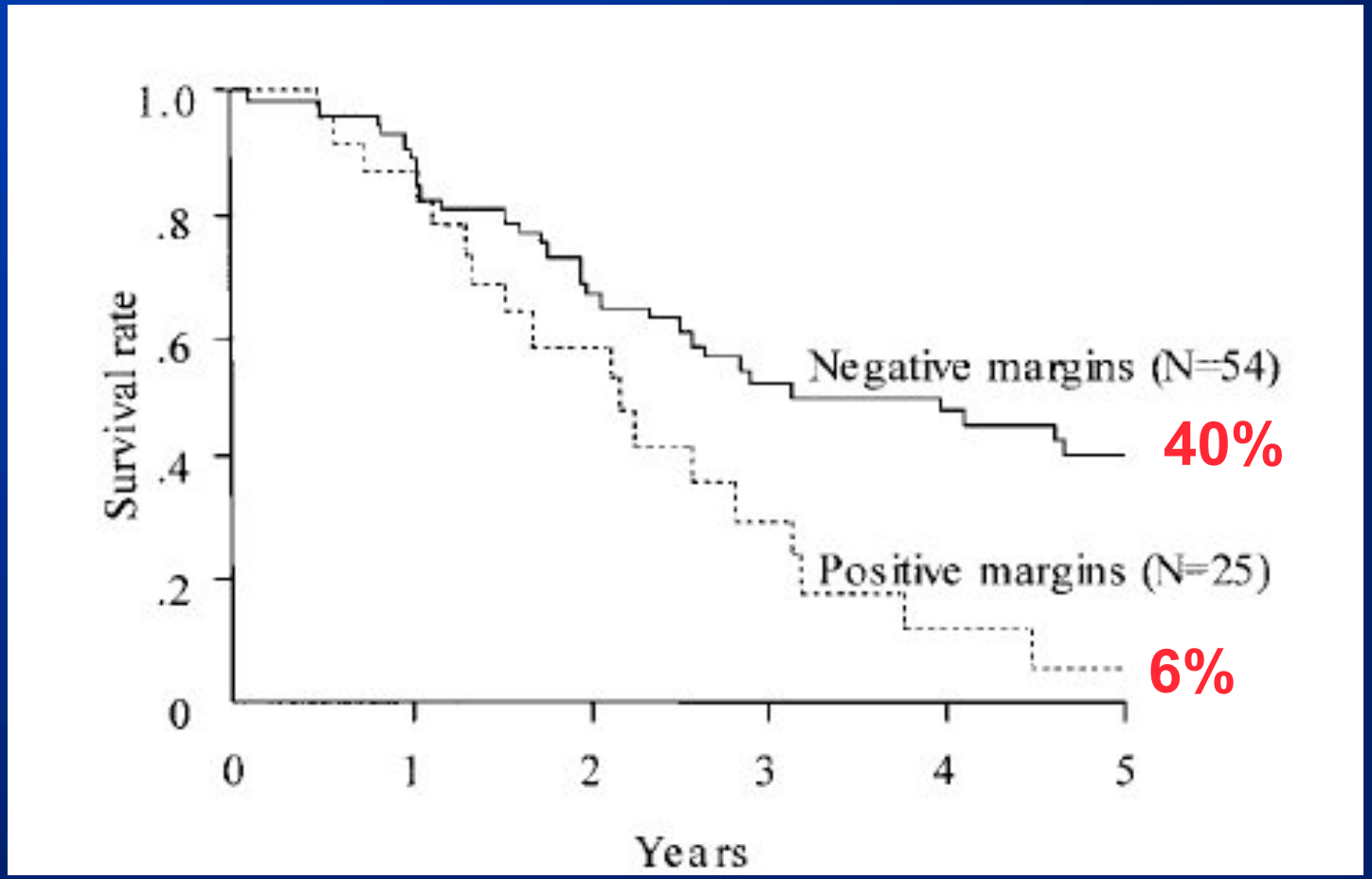
Le seul traitement curateur est la résection chirurgicale !

- **Envahissement biliaire**
  - **plus le niveau haut de la lésion que le niveau bas**
- **Envahissement porte**
  - **envahissement sur la paroi antérieure**
- **Envahissement artériel**
- **Parenchyme hépatique fonctionnel**

Stratégie chirurgicale



- Laparoscopie exploratrice
- Drainage biliaire coté restant
- Embolisation porte
- Hepatectomie D/G± segm IV
- Resection systematique segm I
- Resection VBP
- Curage ganglionnaire
- ± resection-reconstruction porte
- Pas de resection arterielle



Kawasaki et al Ann Surg 2003

Transplantation hépatique

Cholangiocarcinome hilaire:

- Évolution locale
- Difficilement resecable
- Métastases rares et tardives

TH:

- Marges négatives
- Ablation foie natif (cholangite sclérosante)

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Role of Liver Transplantation in Cancer Therapy

SHUNZABURO IWATSUKI, M.D., ROBERT D. GORDON, M.D., BYERS W. SHAW, JR., M.D., THOMAS E. STARZL, M.D., PH.D.

Transplantés pour Klatskin: 5 malades

Récidive: 4 malades

Survie a 2 ans: 0 malades

Spanish Experience in Liver Transplantation for Hilar and Peripheral Cholangiocarcinoma

Ricardo Robles, MD, PhD, Joan Figueras, MD, PhD,† Victor S. Turrión, MD, PhD,‡ Carlos Margarit, MD, PhD,§ Angel Moya, MD,** Evaristo Varo, MD, PhD, †† Javier Calleja, MD,‡‡ Andres Valdivieso, MD, PhD,§§ Juan Carlos G. Valdecasas, MD, PhD,*** Pedro López, MD,††† Manuel Gómez, MD,‡‡‡ Emilio de Vicente, MD,§§§ Carmelo Loinaz, MD,**** Julio Santoyo, MD, Manuel Fleitas, MD, PhD, Angel Bernardos, MD,§§§§ Laura Lladó, MD,† Pablo Ramírez, MD, PhD,* F.S. Bueno, MD, PhD,* Eduardo Jaurrieta, MD, PhD,† and Pascual Parrilla, MD, PhD**

(*Ann Surg* 2004;239: 265–271)

Transplantation pour Klatskin

- 36 malades
- 4 découvertes sur pièce
- Récidive 53% après médiane 21 mois
- Survie 5 ans: 30%
- Si pas de récidive survie 5 ans : 71%
- Mauvais pronostic: stades III,IV et envahissement vasculaire

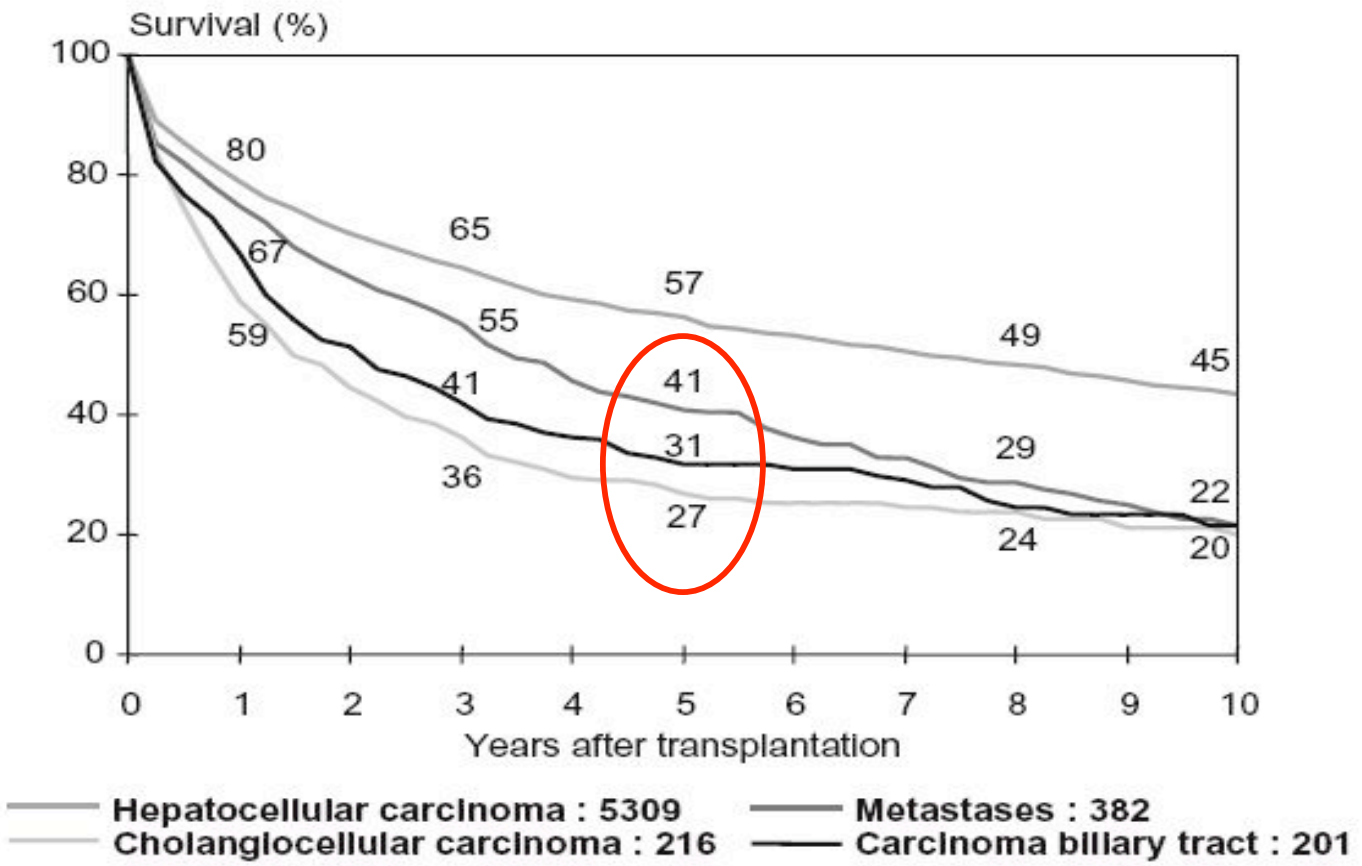


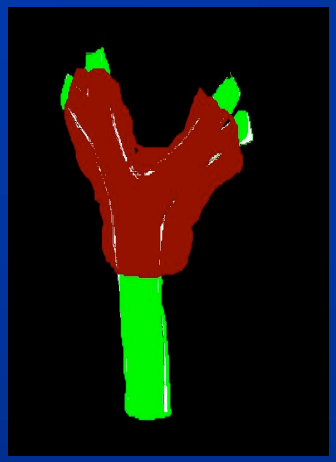
Fig. 3. Cumulative survival of 201 patients who received liver transplantation for hilar cholangiocarcinoma between May 1968 and December 2004 in European Liver Transplant Registry (ELTR) countries[46]

Liver Transplantation with Neoadjuvant Chemoradiation is More Effective than Resection for Hilar Cholangiocarcinoma

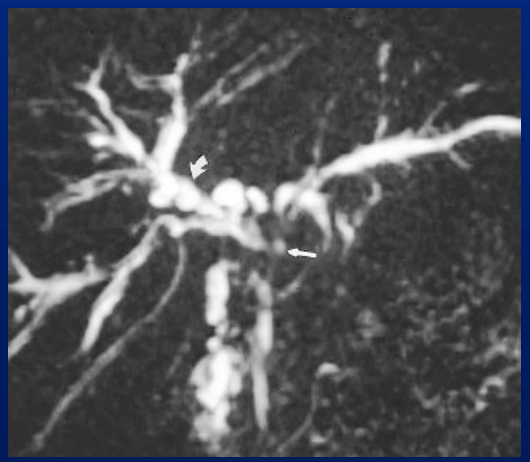
David J. Rea, MD, Julie K. Heimbach, MD,† Charles B. Rosen, MD,† Michael G. Haddock, MD,‡ Steven R. Alberts, MD,§ Walter K. Kremers, PhD,† Gregory J. Gores, MD,¶ and David M. Nagorney, MD**

(*Ann Surg* 2005;242: 451–461)

1. Cholangiocarcinome hilaire localement irresecable



2. Cholangiocarcinome hilaire sur cholangite sclérosante



Patients enrolled: Unresectable HC or HC in the setting of PSC

↓

Diagnosis established by any of the following

- Intraluminal brush cytology / biopsy
- CA 19.9 > 100 ng/ml in the setting of a radiographic malignant stricture
- Biliary aneuploidy demonstrated with digital image analysis (DIA) and fluorescent in-situ hybridization (FISH)

↓

Staging investigations

- CT scan of chest and abdomen
- Liver ultrasound
- Bone scan
- Endoscopic ultrasound with FNAC of suspicious lymph nodes

↓

Exclusion criteria

- Previous chemotherapy/radiotherapy
- Uncontrolled infection
- Previous malignancy (other than skin or cervical cancer) within preceding 5 years
- Medical comorbidity precluding transplantation
- Extrahepatic disease (including regional nodal metastasis)
- Operative biopsy or attempted resection

EBRT 4500 cGy, 150 cGy twice daily+bolus 5-FU iv (500 mg/sqm/d)×3 days

↓

Intraluminal boost using transcatheter Iridium-192 brachytherapy wire (2000 - 3000 cGy at 1 cm radius)

↓

Infusional 5-FU (225 mg/sqm/d) daily or oral Capecitabine 2000 mg/sqm/d in 2 divided doses, 2 out of every 3 weeks; continued till transplantation

↓

Exploratory laparotomy

- Right or bilateral subcostal incision
- Thorough abdominal exploration with biopsy of any abnormal lymph nodes or nodules
- Palpation of the hilum to determine inferior extension of tumor
- Examination of caudate to assess resectability with caval-sparing hepatectomy
- Biopsy of lymph nodes overlying common hepatic artery at the take-off of the gastroduodenal artery and others along the common bile duct (CBD) above duodenum
- Extrahepatic metastases, lymph node metastases, and local extension of disease to adjacent organs or tissues precluded liver transplantation

↓

Liver transplantation

Transplantation pour Klatskin

- 71 malades
- 61 laparotomie de stadialisation
- 14(23%) récusées après laparotomie
- 38 transplantés
- 16 cas=pas de tumeur sur la pièce

Transplantation pour Klatskin

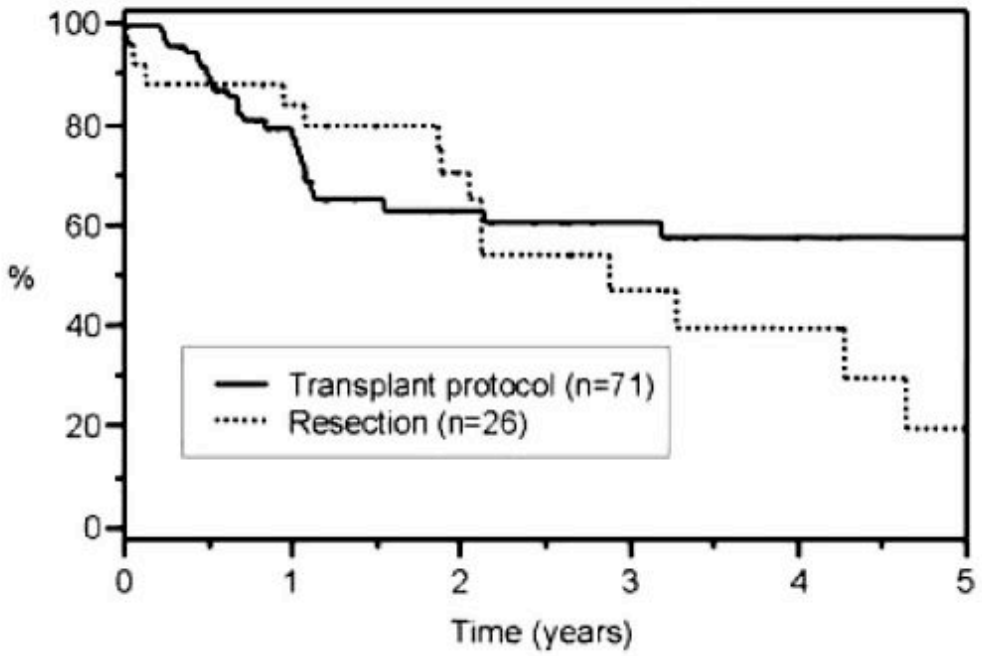


FIGURE 1. Patient survival from start of neoadjuvant therapy (all 71 patients in transplant protocol) or resection.

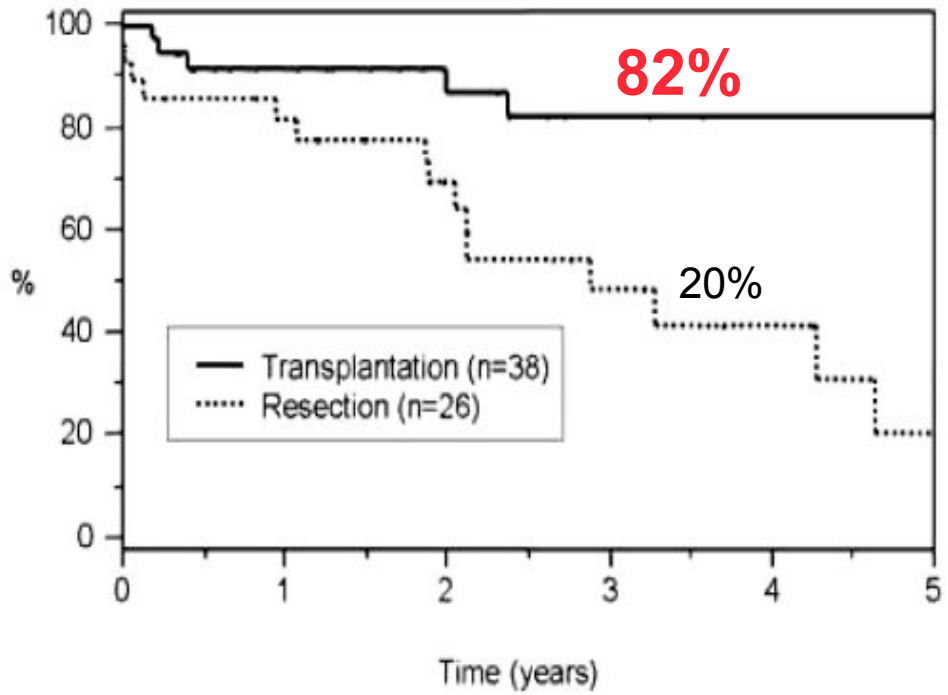


FIGURE 2. Patient survival from operation.

Predictors of Disease Recurrence Following Neoadjuvant Chemoradiotherapy and Liver Transplantation for Unresectable Perihilar Cholangiocarcinoma

Julie K. Heimbach,[1,5] Gregory J. Gores,[1] Michael G. Haddock,[2] Steven R. Alberts,[3] Rachel Pedersen,[4] Walter Kremers,[1,4] Scott L. Nyberg,[1] Michael B. Ishitani,[1] and Charles B. Rosen[1]

(*Transplantation* 2006;82: 1703–1707)

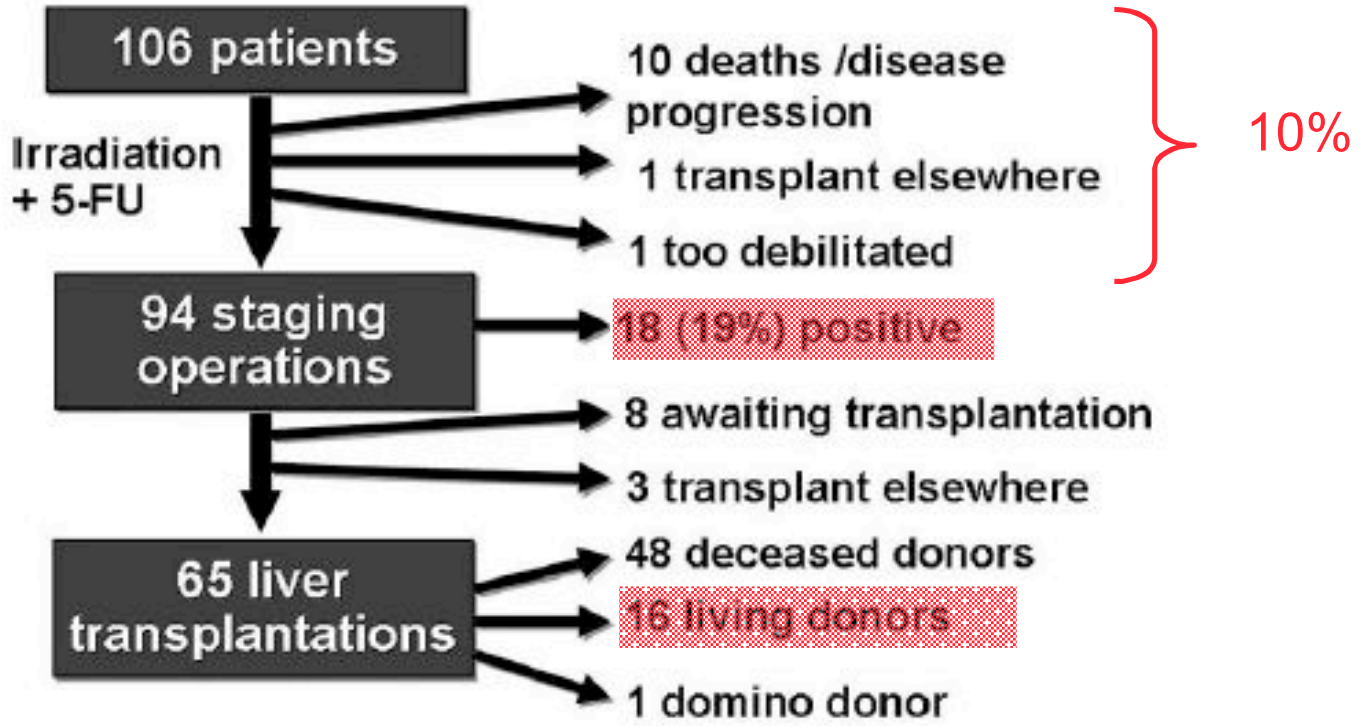


FIGURE 1. Patients with hilar CCA enrolled in combined chemotherapy, EBRT, brachytherapy, staging laparotomy, and liver transplantation protocol.

Récidive

- 11 malades (17%)
- Intervalle 22 mois (7-65)
- Métastases a distance: n=8
- Récidive locorégionale: n=3

Facteurs de risque récidive

Pré transplantation:

- Age >45 ans
- CA 19.9>100 (après drainage)
- ATCD de cholécystectomie
- Tumeur visible

Anatomopathologie foie explanté:

- Tumeur >2cm
- Grade tumoral
- Envahissement perinerveux

- **Intervalle listing-greffe >100j**

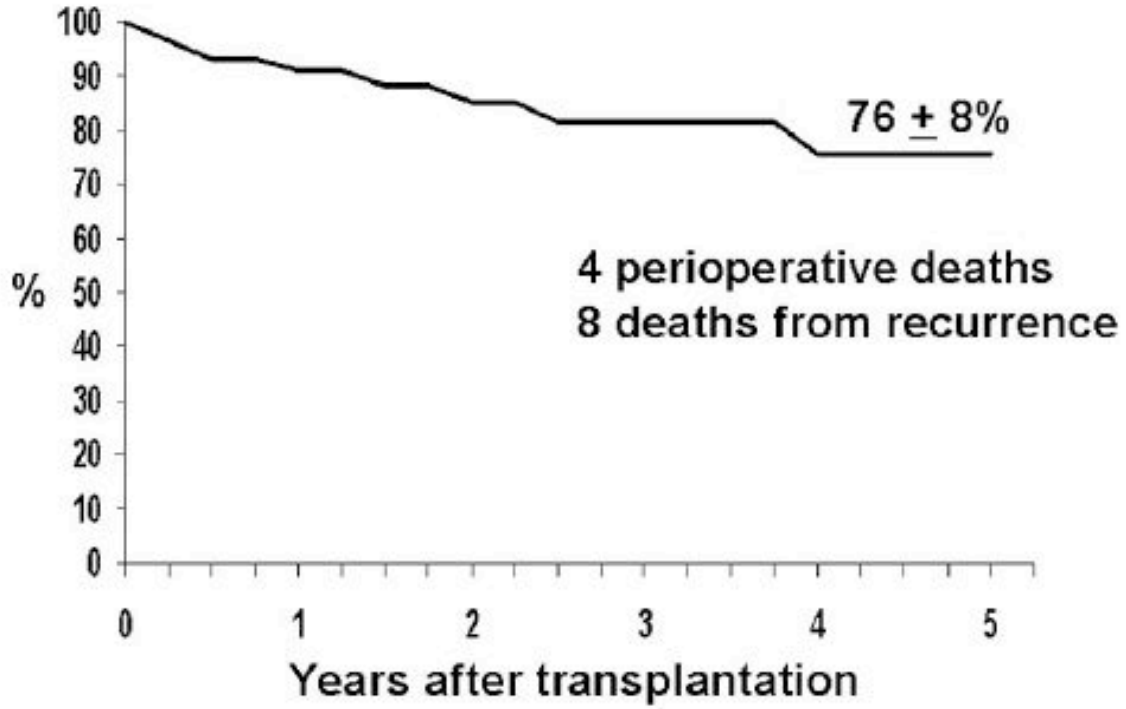


FIGURE 2. Survival rates since time of diagnosis for patients enrolled in the combined protocol who received liver transplantation for hilar CCA. Mean follow-up is 32 months, median 18 months (range 2 days-13 years.)

Vascular Complications After Orthotopic Liver Transplantation After Neoadjuvant Therapy for Hilar Cholangiocarcinoma

Hendrik T.J. Mantel,[1] Charles B. Rosen,[1] Julie K. Heimbach,[1] Scott L. Nyberg,[1] Michael B. Ishitani,[1] James C. Andrews,[2] Michael A. McKusick,[2] Michael G. Haddock,[3] Steven R. Alberts,[4] and Gregory J. Gores[1]

LIVER TRANSPLANTATION 13:1372-1381, 2007

Complications vasculaires

- 40% complications vasculaires
- Artérielles:21%
  - Tardives, donneur vivant
- Veine porte: 22%
  - Tardives 3-12 mois
- Veines sus hépatiques /veine cave:12%

Conclusion

- **Résection:** mauvais pronostic
- **Transplantation: nouvelle indication!**
- **Début du programme à Cochin…**
- Photothérapie dynamique
- Nouvelles chimiothérapies