Defining the Role of Liver Transplantation in Hepatobiliary Cancers

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Defining the Role of Liver Transplant in Hepatobiliary Cancers

- Hepatocellular cancer
- Cholangiocarcinoma
  - Intrahepatic CCA
  - Extrahepatic CCA

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Hepatocellular Carcinoma

- Most common primary malignancy of the liver
- Number 1 cause of death in cirrhosis

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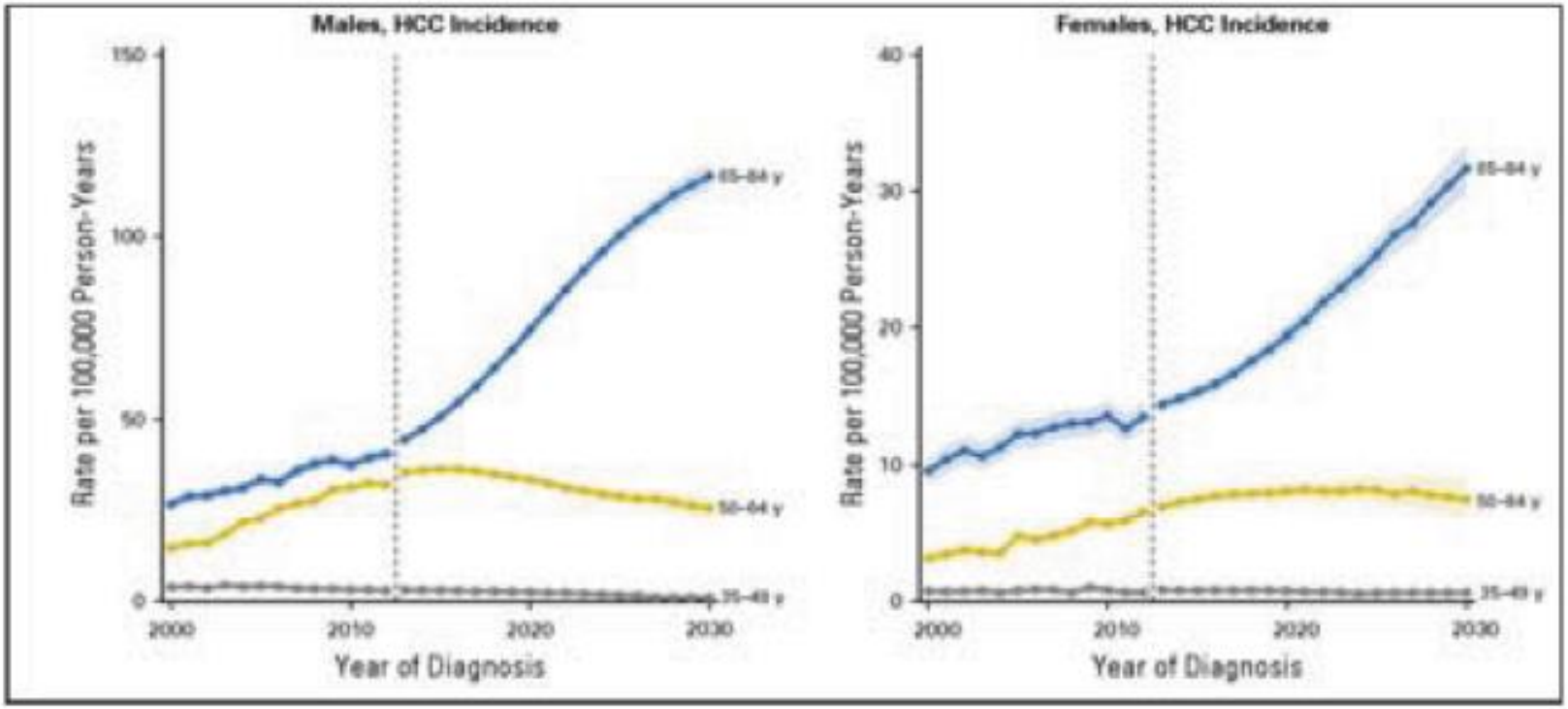
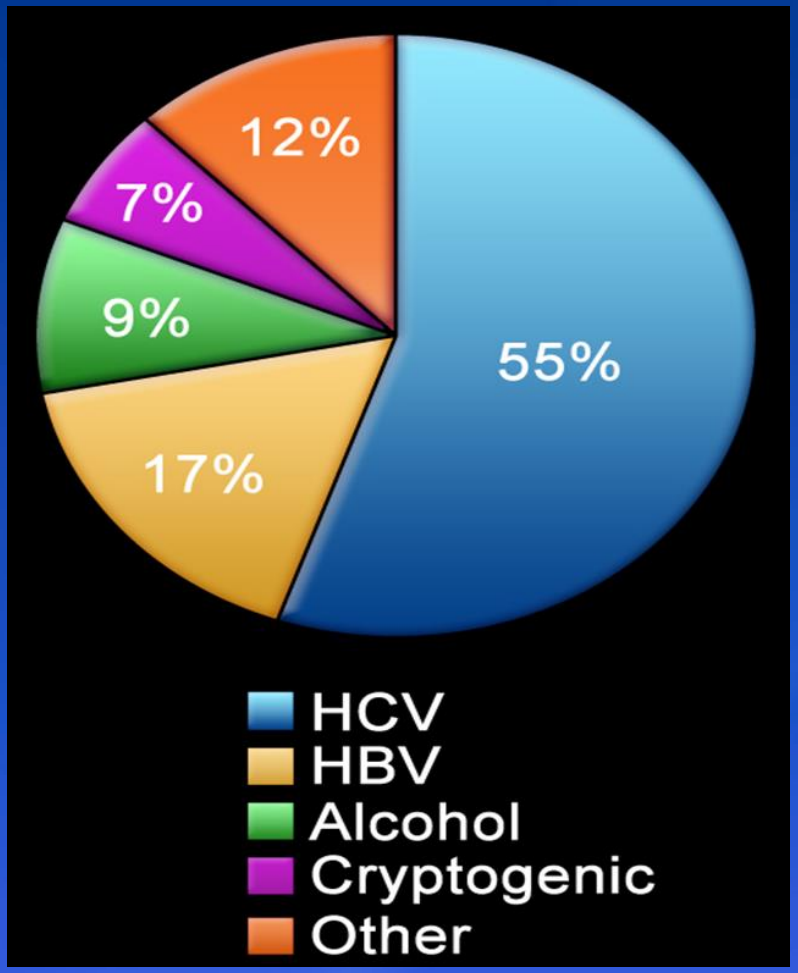
Observed and projected HCC incidence



Jessica L. Petrick et al. JCO doi:10.1200/JCO.2015.64.7412 WWW.AASLD.ORG

HCC: Risk Factor Overview

- **70% - 90% occurs within an established background of chronic liver disease and cirrhosis**
- **Major etiologies of HCC:**
  - Hepatitis C
  - Hepatitis B
  - Alcoholic liver disease
  - Nonalcoholic steatohepatitis



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Management of HCC

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Treatment options

- Surgical resection
- Local therapies (Interventional Radiology)
  - Radiofrequency ablation (RFA)
  - Ethanol or Acetic acid injection
  - Chemoembolization (TACE or DebTACE)
  - ^{90} Yttrium spheres
- Chemotherapy
- Liver Transplant

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Defining the Role of Liver Transplantation in Hepatocellular Cancer

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Liver Transplantation (LT)

- **Curative Treatment for chronic disease and HCC**
- **MELD exception points for HCC**

Survival	
1 year	91%
2 year	75%
5 year Milan Criteria	>70%
5 year Extended criteria	~50%

Surgical Resection

- **Choice of therapy for patients without cirrhosis**
- **5-15% HCC patients eligible**

Survival	
1 year	97%
3 year	84%
5 year	26-57%

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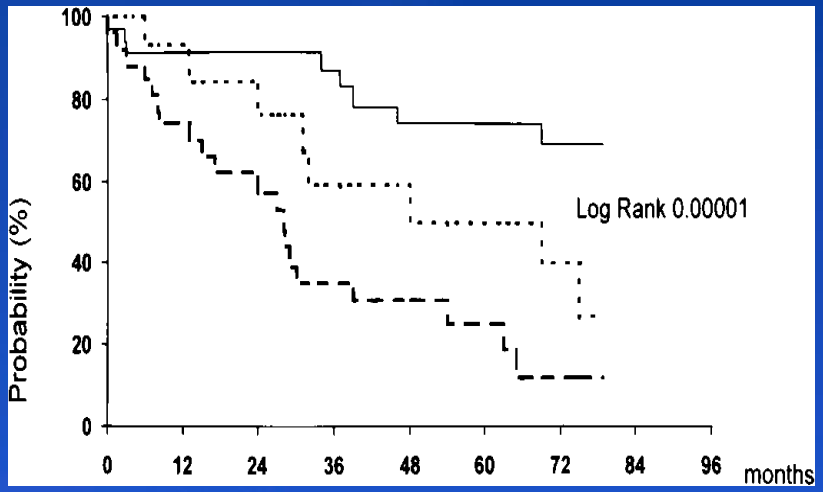
Bolondi L et al. *Gut* 2001;48;251-259., Ikai I, er al. *Cancer* 2004;101;796-802., El-Serag HB, Rudolph KL. *Gastroenterology* 2007;132:2557-2576. Sala M et al. *Lliver Transpl.* 2004;10(Suppl 2):S4-S9., Mazzaferro V et al. *N Engl J Med* 1996;334;693-699., Shetty K et al. *Liver Transpl* 2004;10:911-918., Yao F et al. *Hepatology* 2001;33:1394-1403.

Selection of surgical candidates is key



- Patients with no portal HTN and TB <1mg/dL
- Patients with clinically irrelevant portal HTN and TB <1mg/dL
- Patients with portal HTN and TB >1mg/dL
- Llovet et al, Hepatology 1999

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Liver transplant

- Milan criteria
  - Solitary HCC 2 cm to 5 cm
  - 3 nodules each $\leq$ 3 cm
  - No evidence of vascular invasion
  - No evidence of extrahepatic disease
- Most centers treat lesions upon listing for liver transplant
  - RFA
  - TACE or DebTACE

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Expanding transplant selection criteria

- UCSF criteria
  - Single tumor ≤ 6.5 cm
  - ≤ 3 tumors ≤ 4.5 cm with total ≤ 8 cm

- Patients are treated with local therapy
- Waiting time of 3 months
- If disease activity now within Milan criteria and no new lesions develop, patients are eligible for MELD exception

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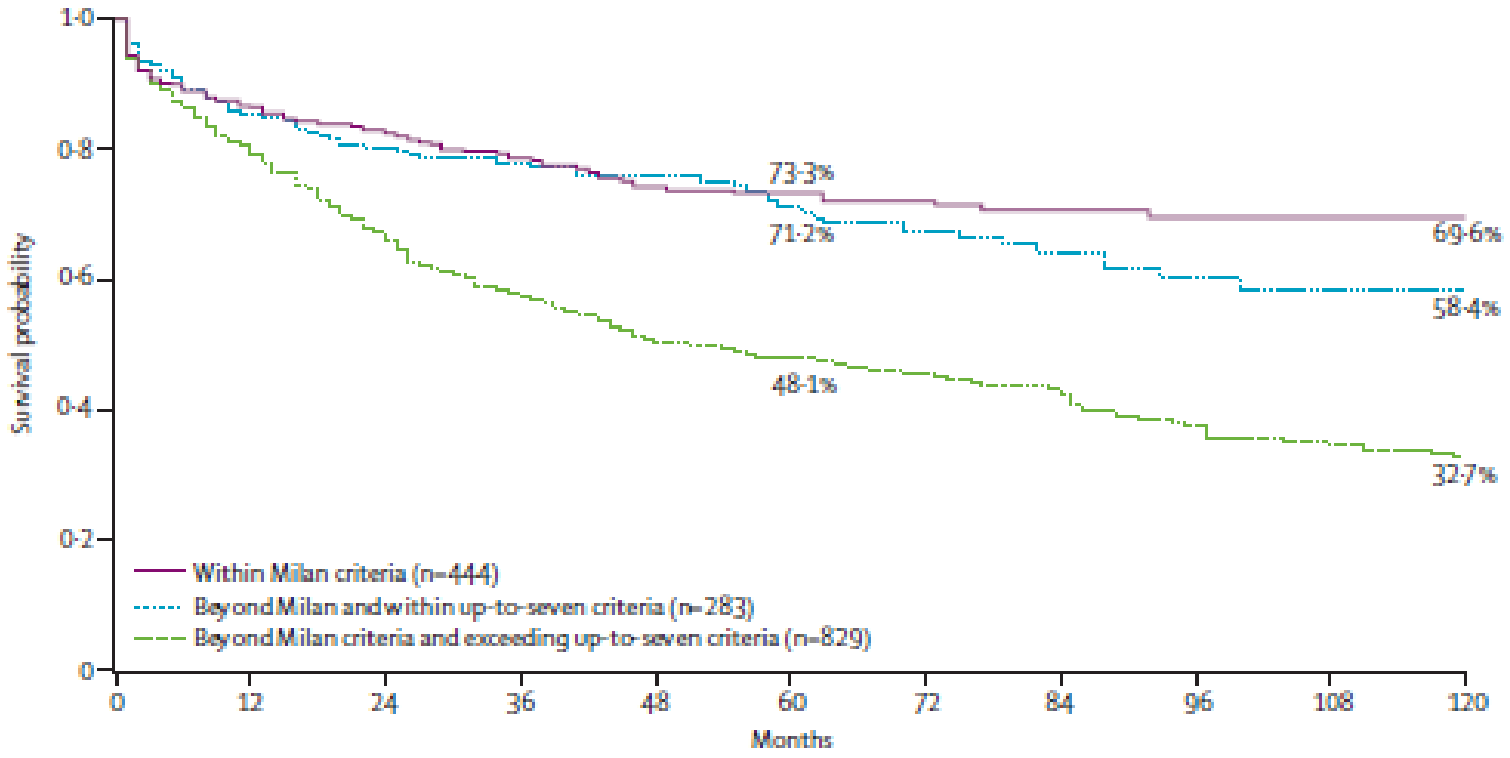
Expanding Milan: Up to 7 criteria

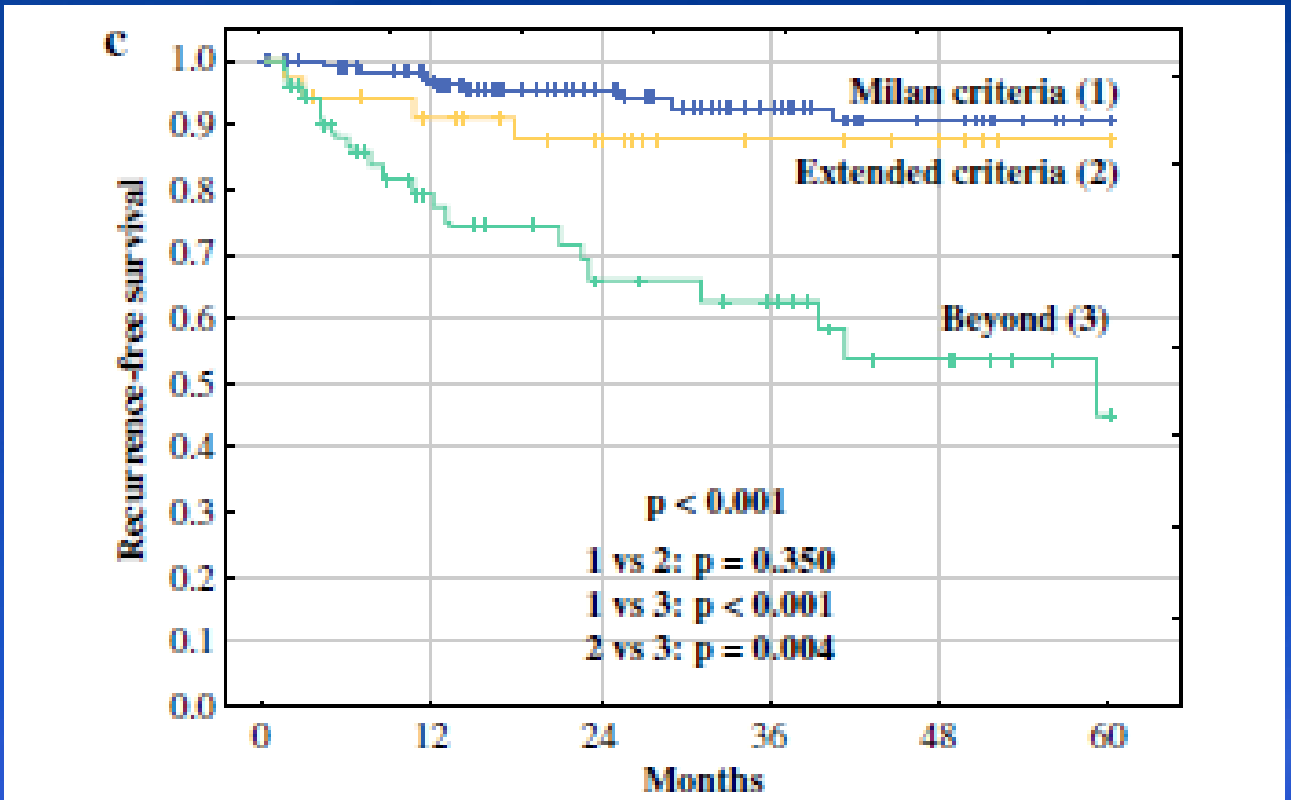
1: 6cm tumor = 1+6 = 7

4 tumors: 1cm+1cm+2cm+3 cm= 7



Patients at risk											
Within Milan criteria	444	340	278	219	176	140	124	94	71	71	71
Beyond Milan within up-to-seven	283	217	173	137	121	90	68	57	44	32	32
Exceeding Milan and up-to-seven	829	593	429	323	250	202	155	120	87	66	48

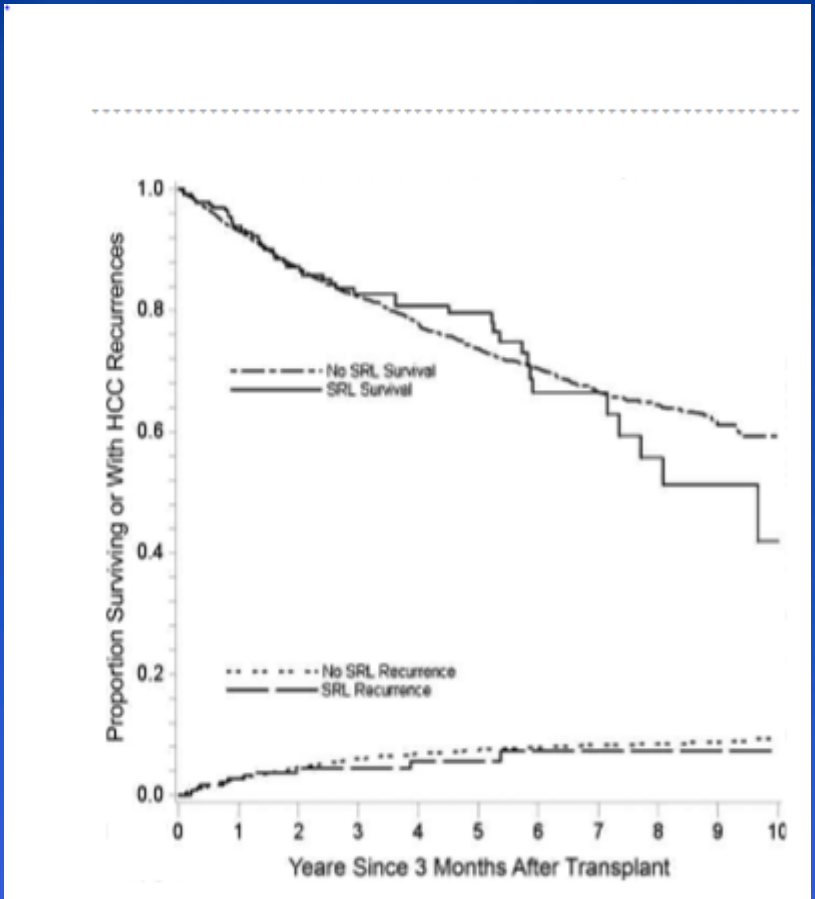
Use of extended selection criteria in liver transplant for HCC



At risk	Baseline	1 year	2 years	3 years	4 years	5 years
(1)	143	109	74	51	37	26
(2)	41	29	23	17	12	9
(3)	56	32	22	18	11	5

M Grat et al. Ann Surg Oncol, August 2016

Immunosuppression: The impact of sirolimus post LT for HCC



- There was no difference in those patients receiving or not receiving sirolimus post LT
- There was a trend to survival improvement in older recipients

- Yanik et al.Hepatology May 2016

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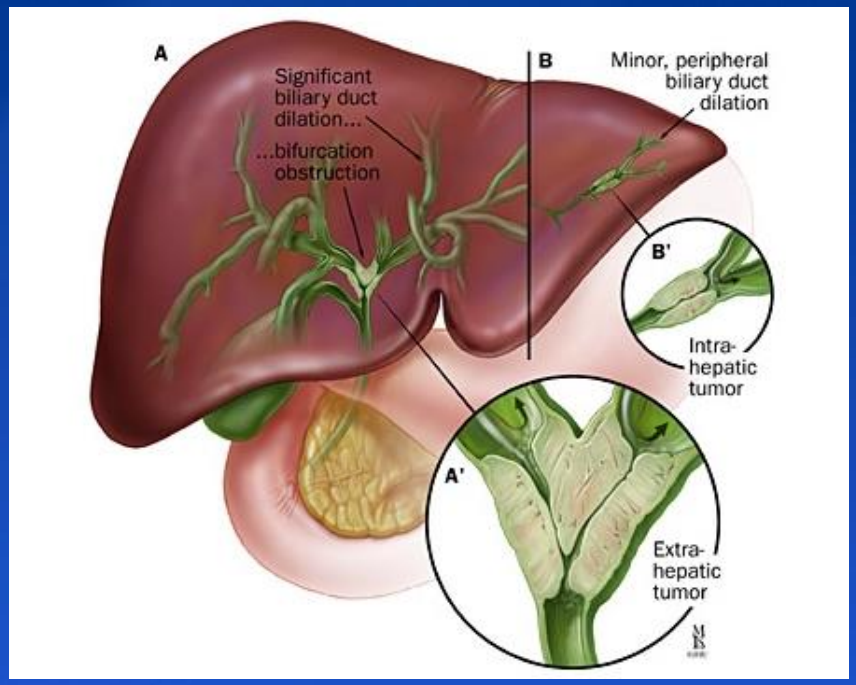

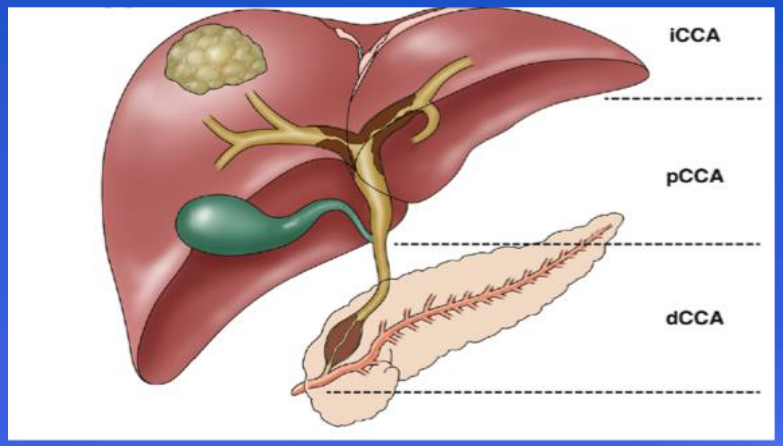

- Cholangiocarcinoma
  - Intrahepatic CCA
    - Mass in the liver
    - Peripheral intraductal
  - Extrahepatic CCA
    - Distal and perihilar

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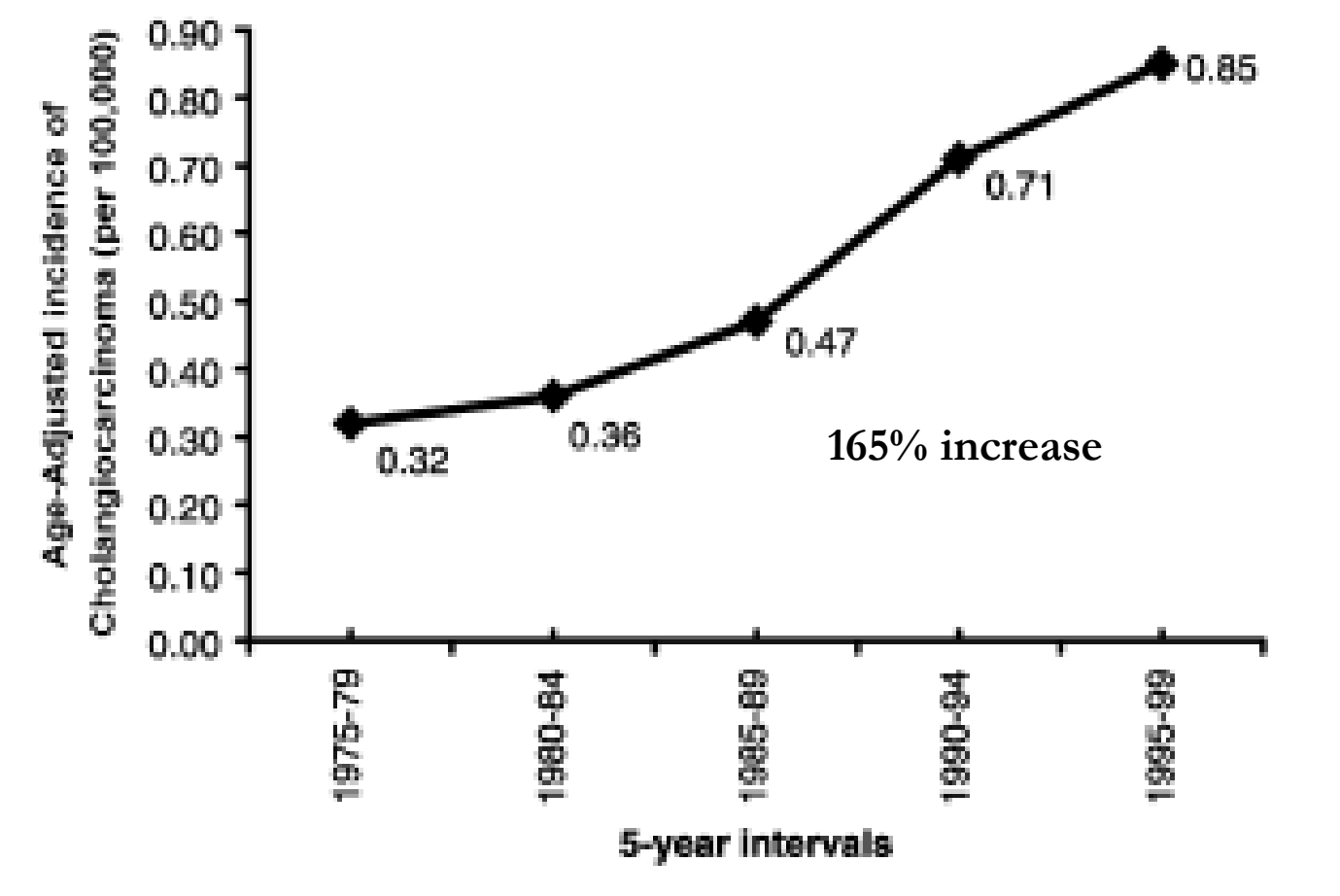
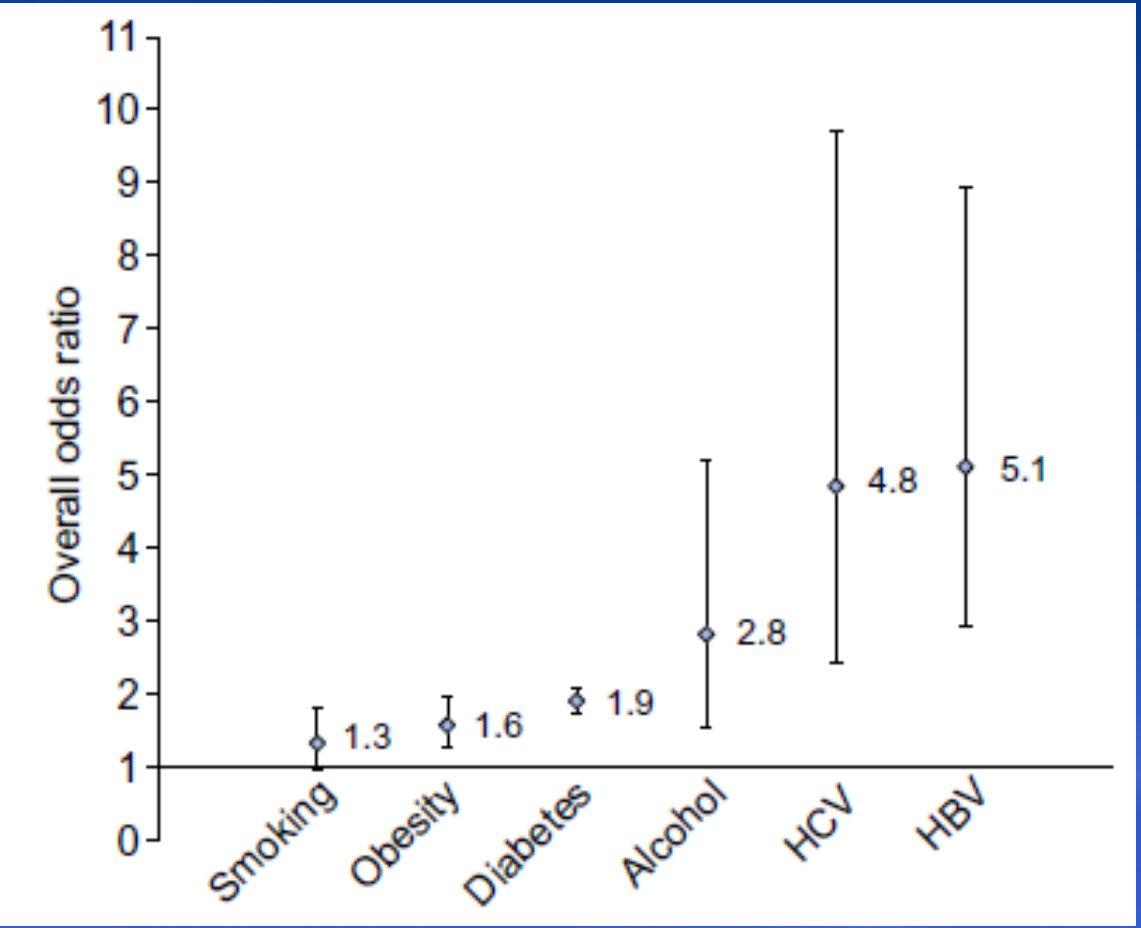
Increasing incidence of *intrahepatic* cholangiocarcinoma in the US



Y.H. Shaib et al. / Journal of Hepatology 40 (2004) 472–477

Pathogenesis of intrahepatic cholangiocarcinoma



Journal of Hepatology **2012** vol. 57 | 69–76

Traditionally outcomes for LT for intrahepatic CCA were poor

- Surgical resection for intrahepatic CCA

Table 1. Selected single-center series of resection for intrahepatic cholangiocarcinoma with more than 70 patients resected

Author	Study period	Resected patients (*n*)	Rate of R0 resections (%)	Mortality rate (%)	3-year survival rate (%)	5-year survival rate (%)
Weimann *et al.* [31]	1978–1996	95	–	5.0	31	21
Jan *et al.* [32]	1977–2001	187	72	6.7	18	10
Paik *et al.* [33]	1994–2005	97	93	–	52	31
Tamandl *et al.* [34]	1994–2007	74	72	9.5	45	28
Endo *et al.* [30]	1990–2006	82	85	1.2	–	–
Jonas *et al.* [5]	1988–2007	195	71	7.2	–	22
Lang *et al.* [4]	1998–2006	83	64	7.1	38	21
Zhou *et al.* [35]	1997–2006	272	–	3.3	30	26

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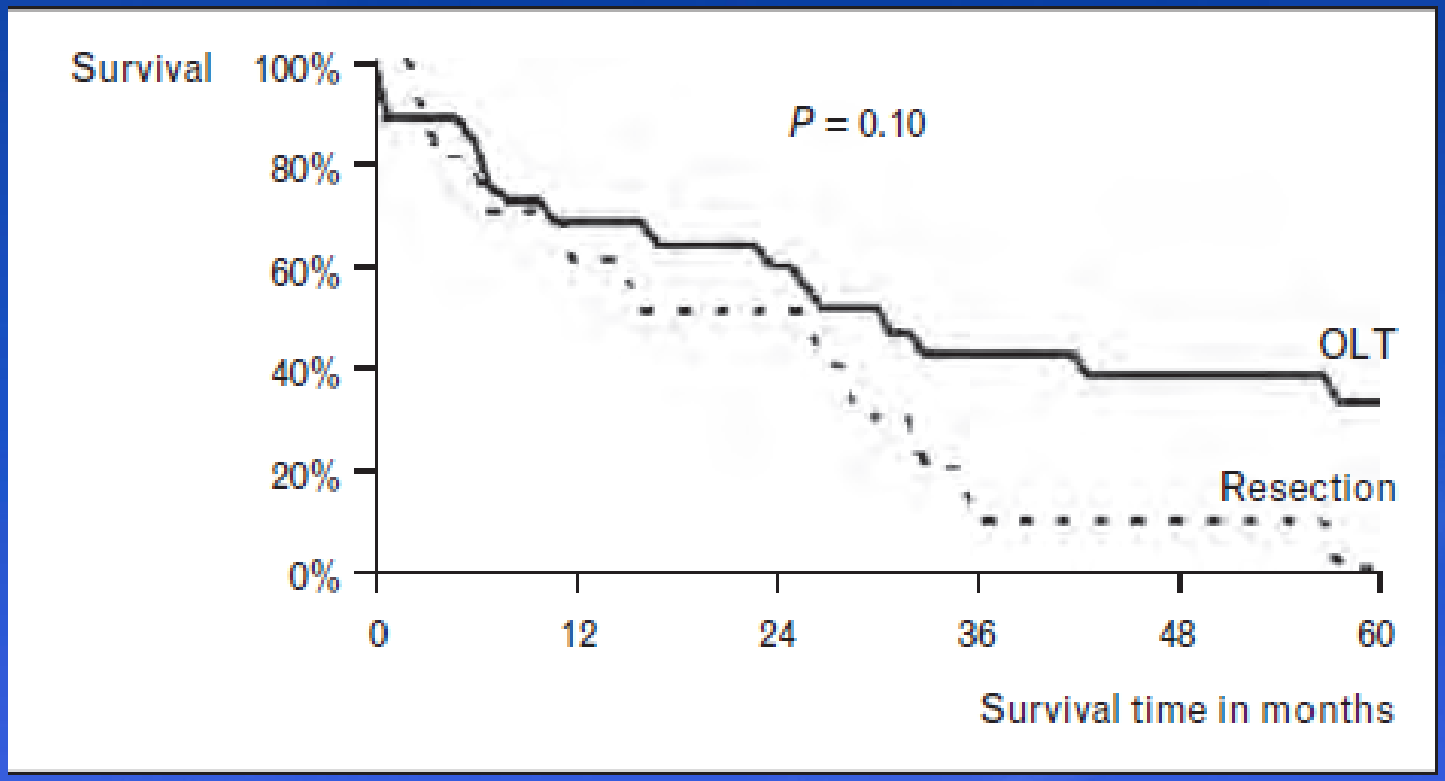
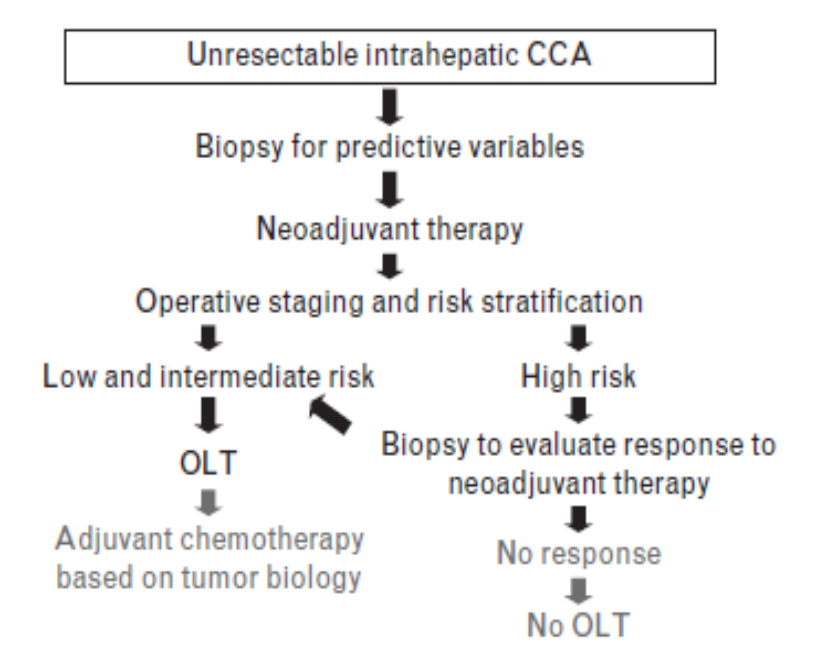
Liver transplant may have superior results to surgical resection for early intrahepatic CCA but there is much more research needed

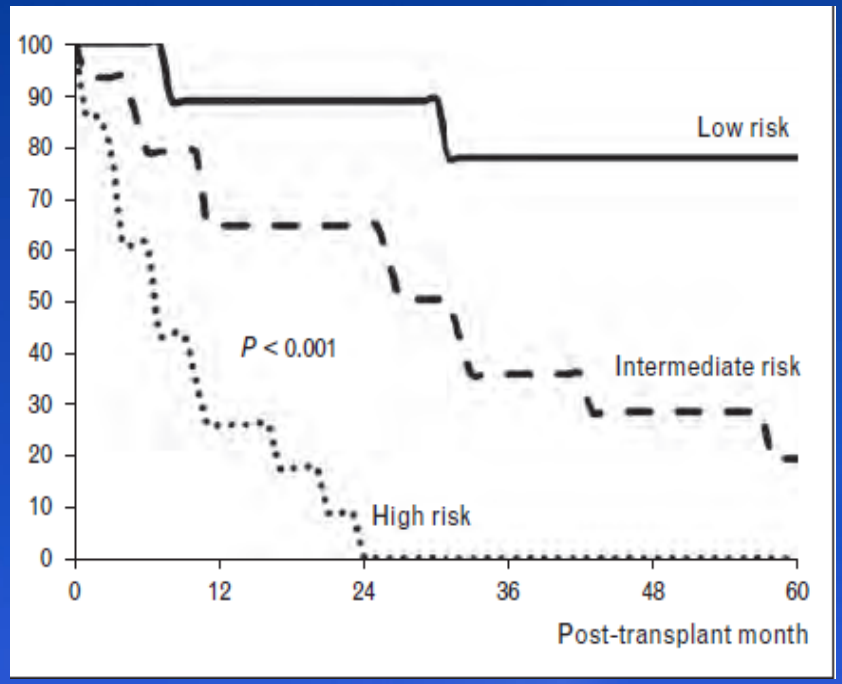


UCLA protocol may challenge role of liver transplant for intrahepatic CCA

Treatment protocol

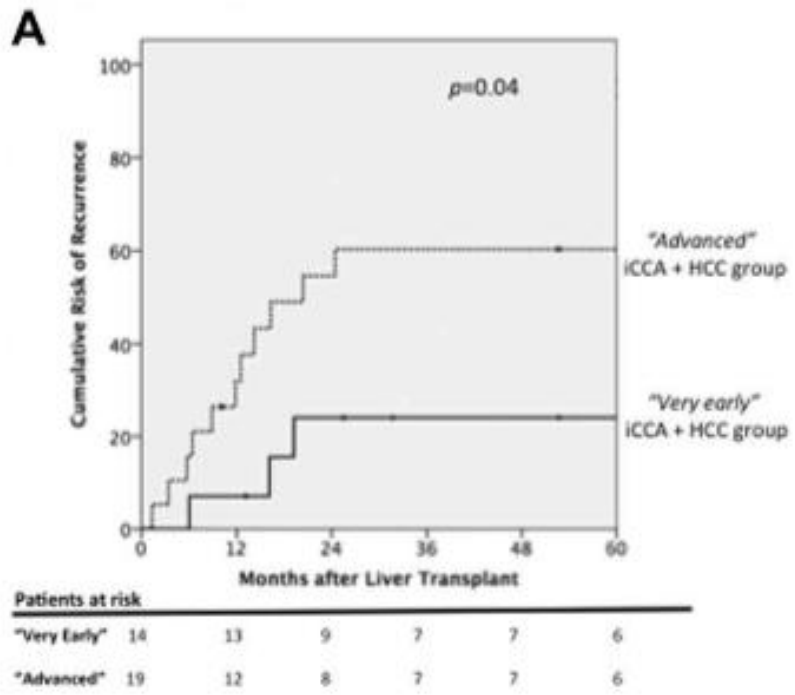


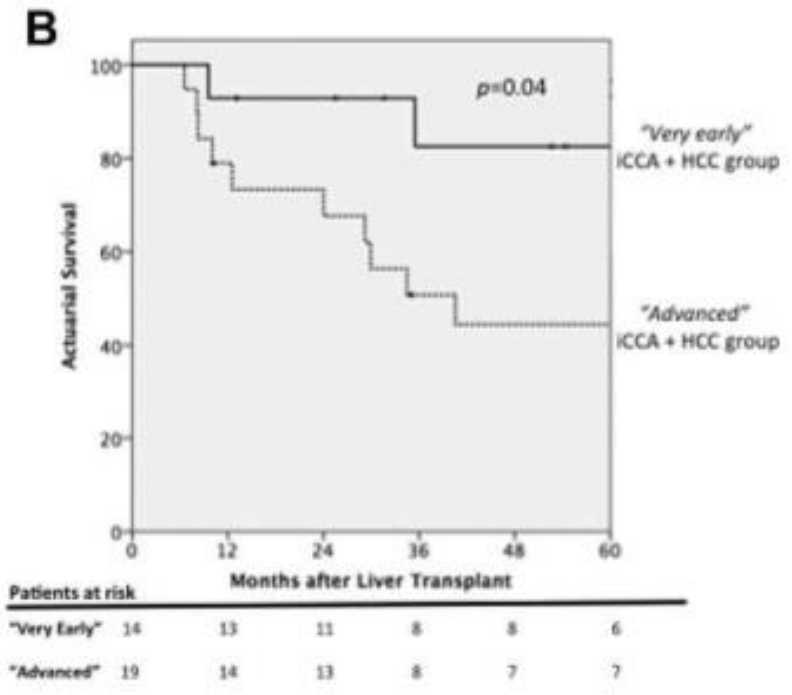
% Disease free survival



Survival is reasonable in very early (single ≤ 2 cm) iCCA with HCC

Early: single lesion < 2cm Advanced: anything beyond





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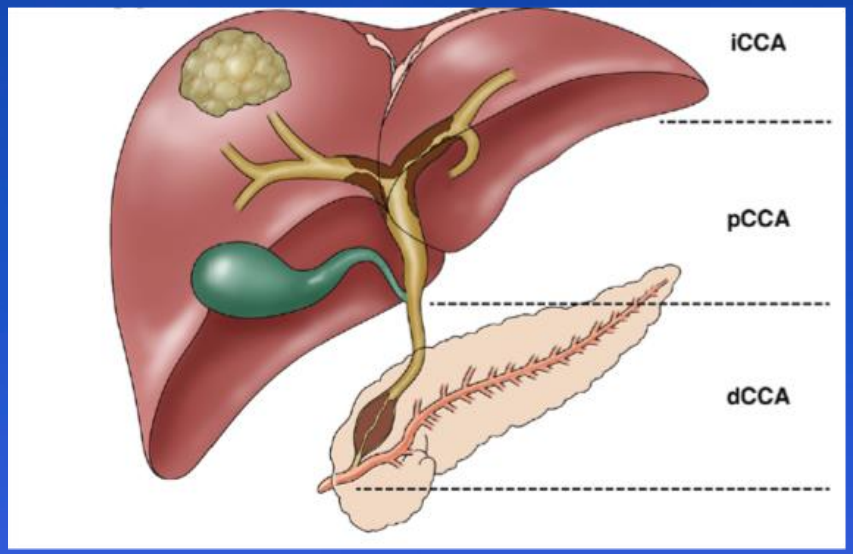
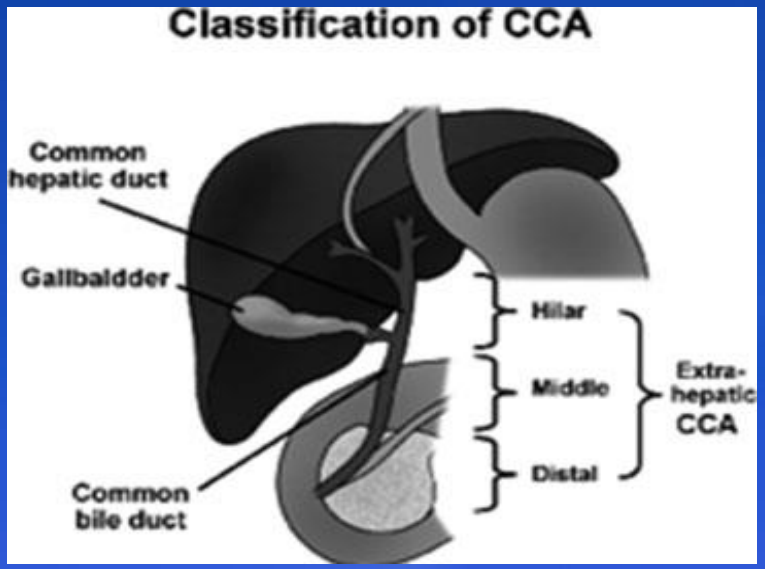
Sapisocin et al. Hepatology 2016

Extrahepatic cholangiocarcinoma

Incidence 1.2 per 100,000 males

Incidence 0.8 per 100,000 females





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Liver transplant for hilar cholangiocarcinoma

Establishing the diagnosis of CCA

- Routine cytology (RC) 15% to 30% sensitivity
- Improves with directed biopsy 50% sensitivity
- FISH improves accuracy of diagnosis
  - Sensitivity from 15% in RC to 34% FISH
  - Specificity equivalent 97%
- Patients considered for transplant can NEVER have EUS or percutaneous biopsy
- Remember to exclude IgG4 cholangiopathy

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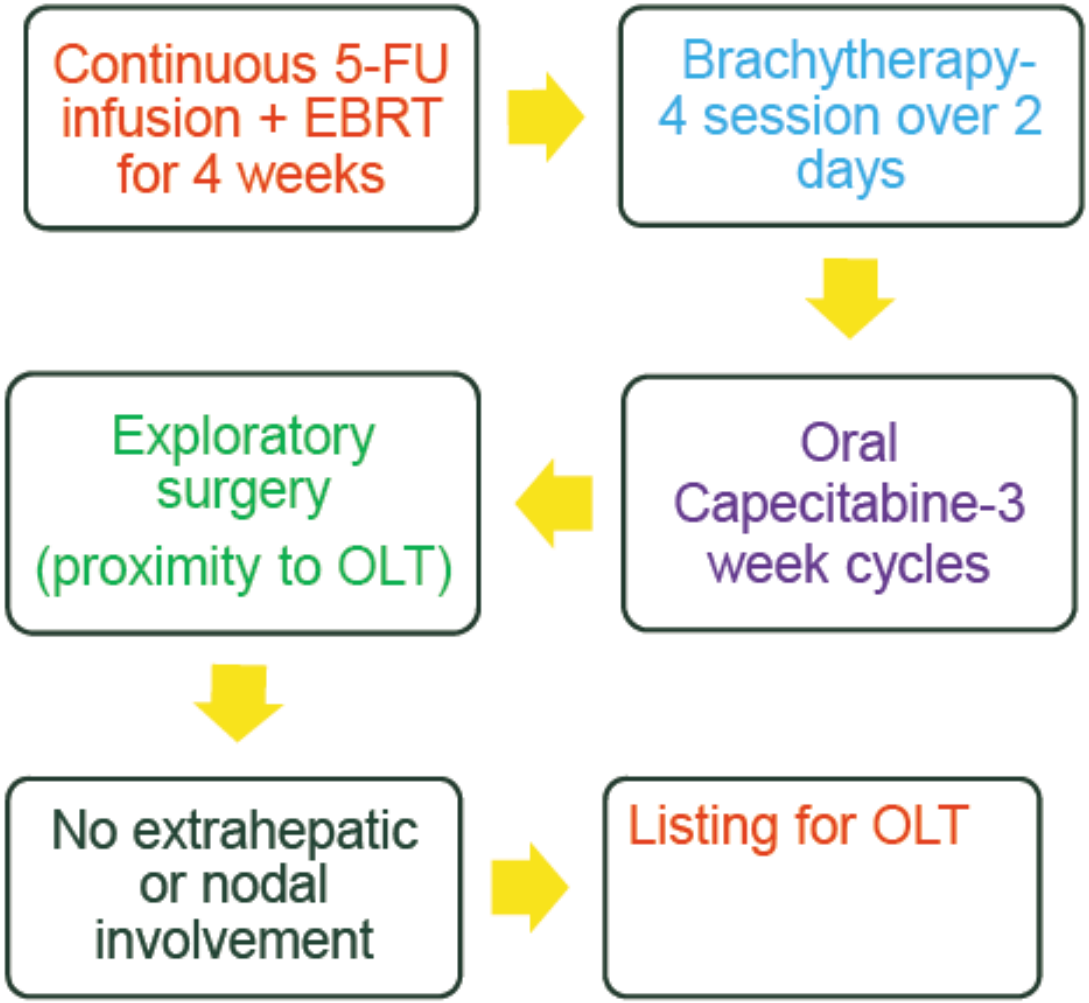
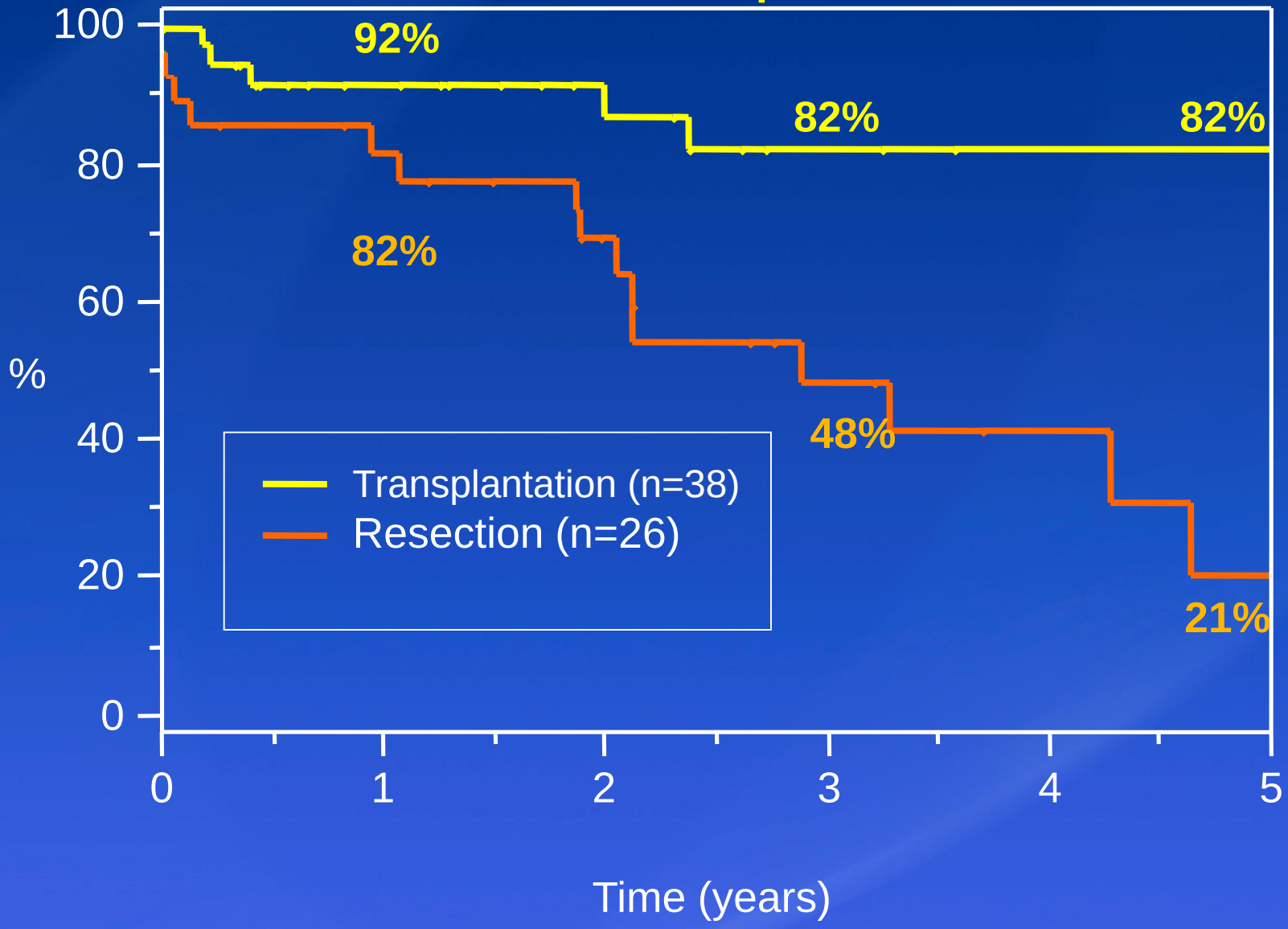
Mayo Transplant Protocol



Survival after liver transplant for CCA



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Liver transplant criteria for hilar CCA

- Established diagnosis of CCA
- Intrahepatic tumor volume ≤ 3 cm
- No evidence of extrahepatic disease
- Lymph node negative (EUS and later surgical exploration)

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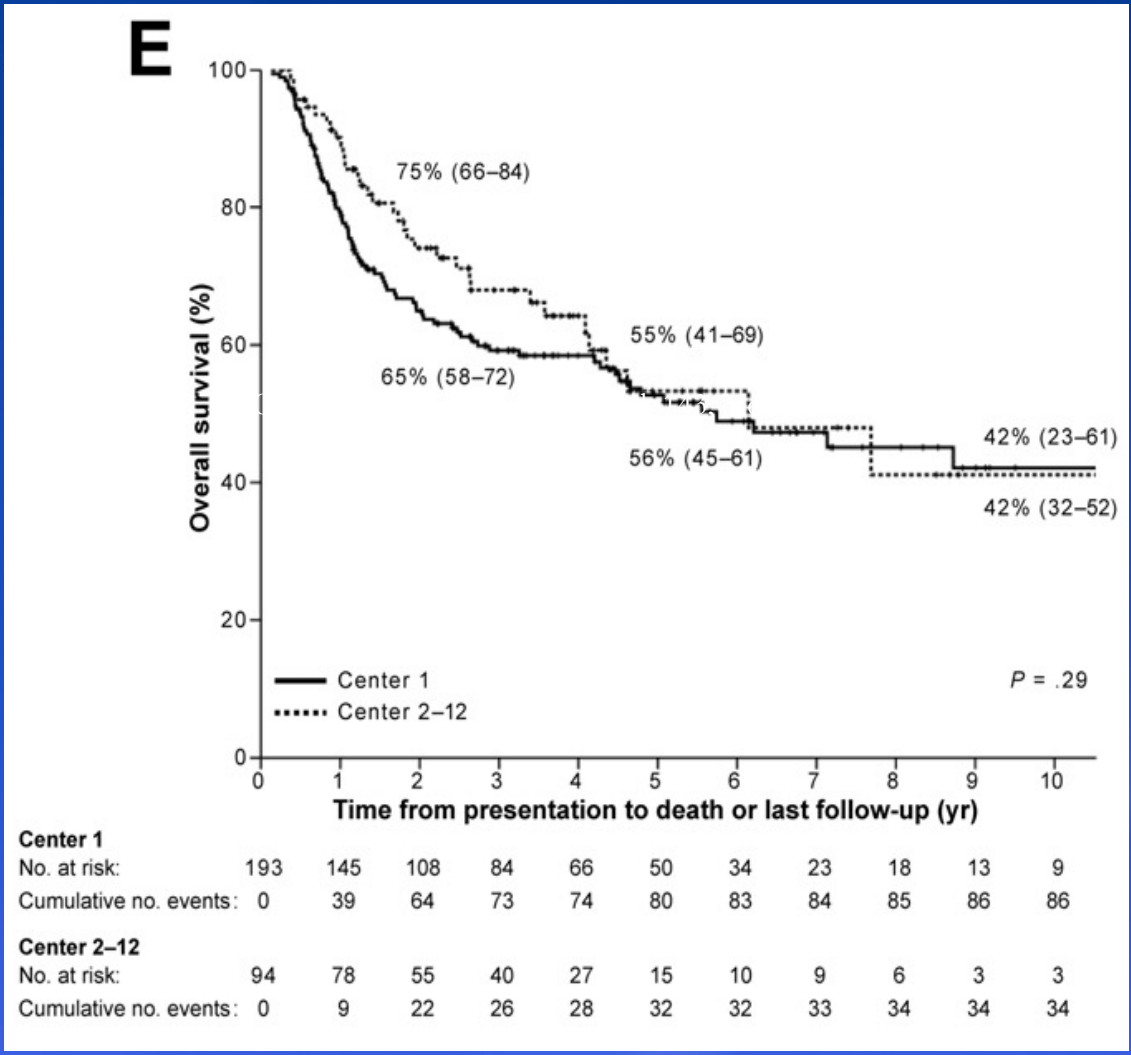
The protocol can be done successfully outside Mayo Clinic



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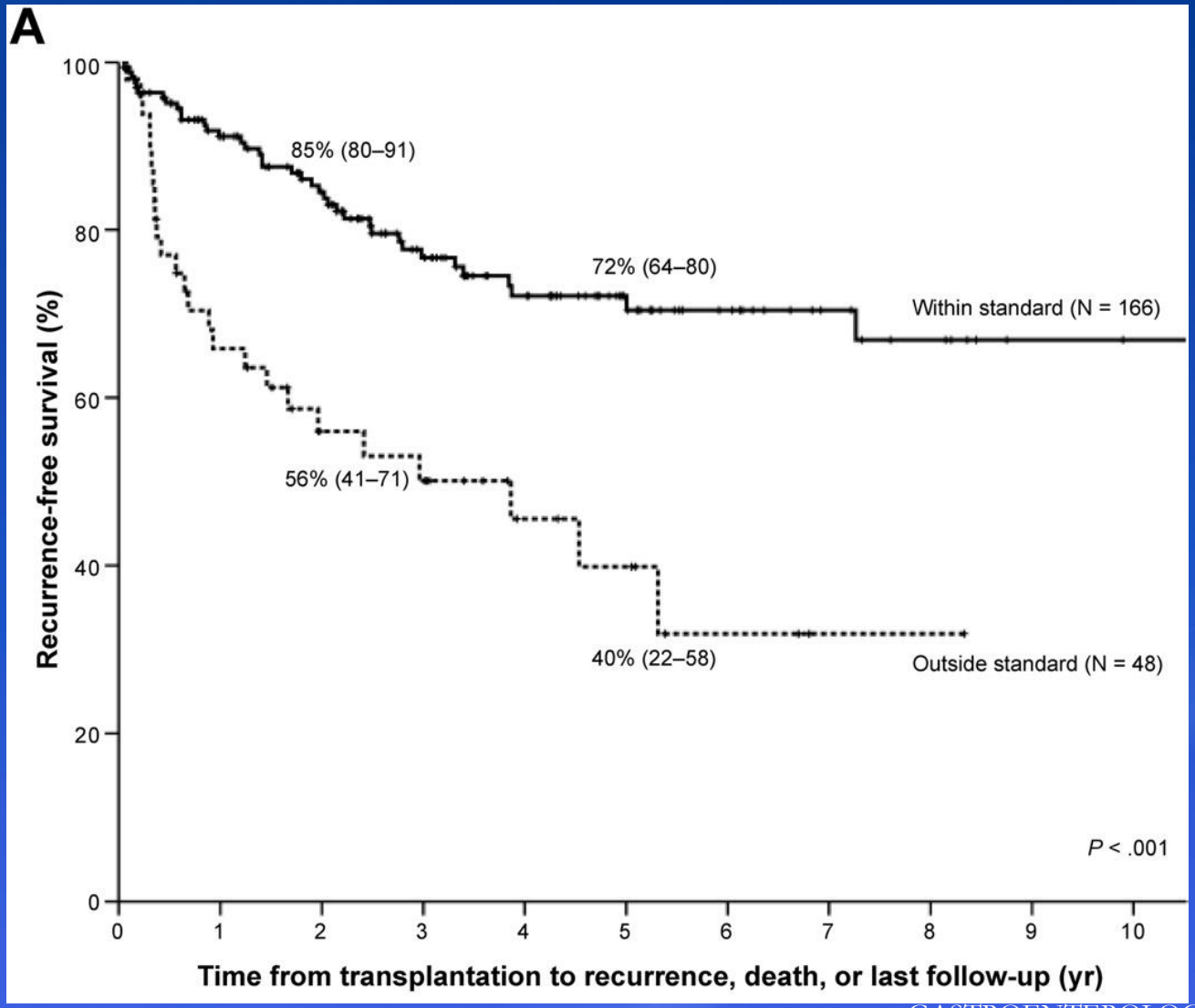
This is a precise protocol…



Thank you

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