

Oncology LIVE CM Series

Treatment of Hepatocellular Carcinoma: A Multi-disciplinary Approach

# Treatment options for early-stage HCC surgical resection & OLT

Yuko Kono, MD, PhD

Clinical Professor of Medicine, Hepatology

Clinical Professor of Radiology

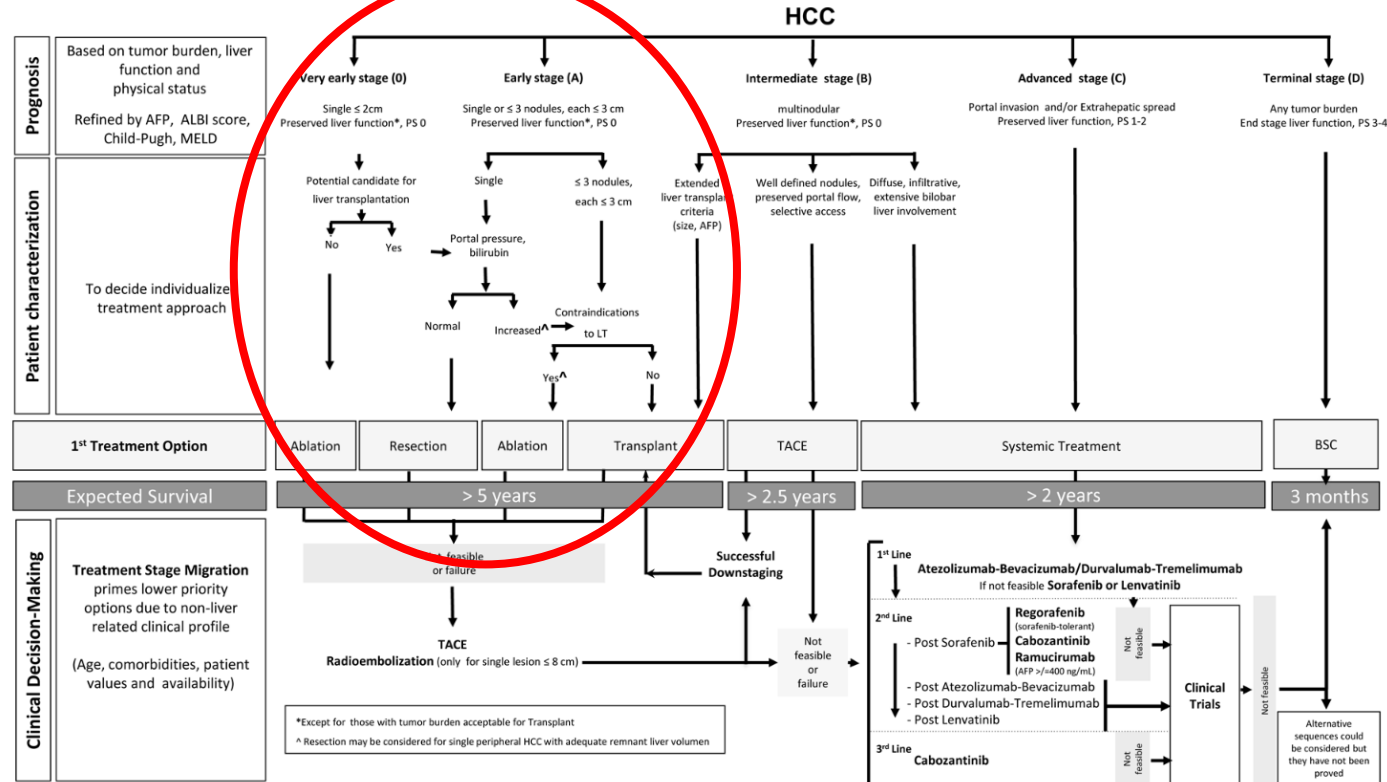
University of California, San Diego

June 12<sup>th</sup>, 2024

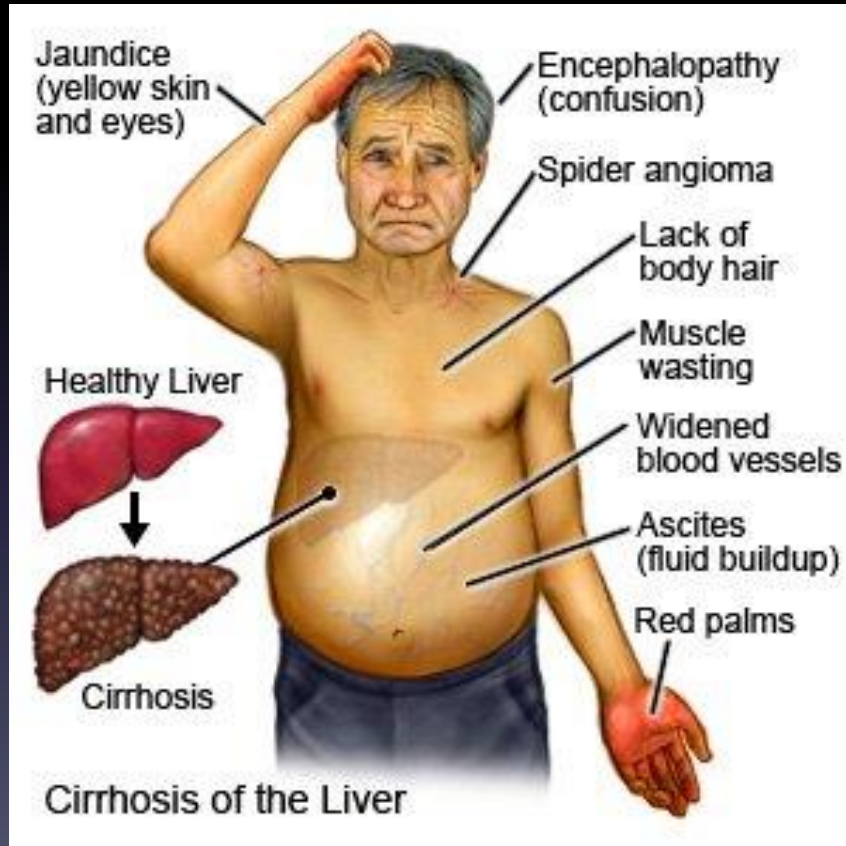
# Disclosures

- Research support: GE Healthcare, Bracco, Canon Medical Systems Inc. Lantheus Medical Imaging
- Grant support: NIH 1R01CA194307, NIH 1R01CA215520-01A1

# BCLC Staging



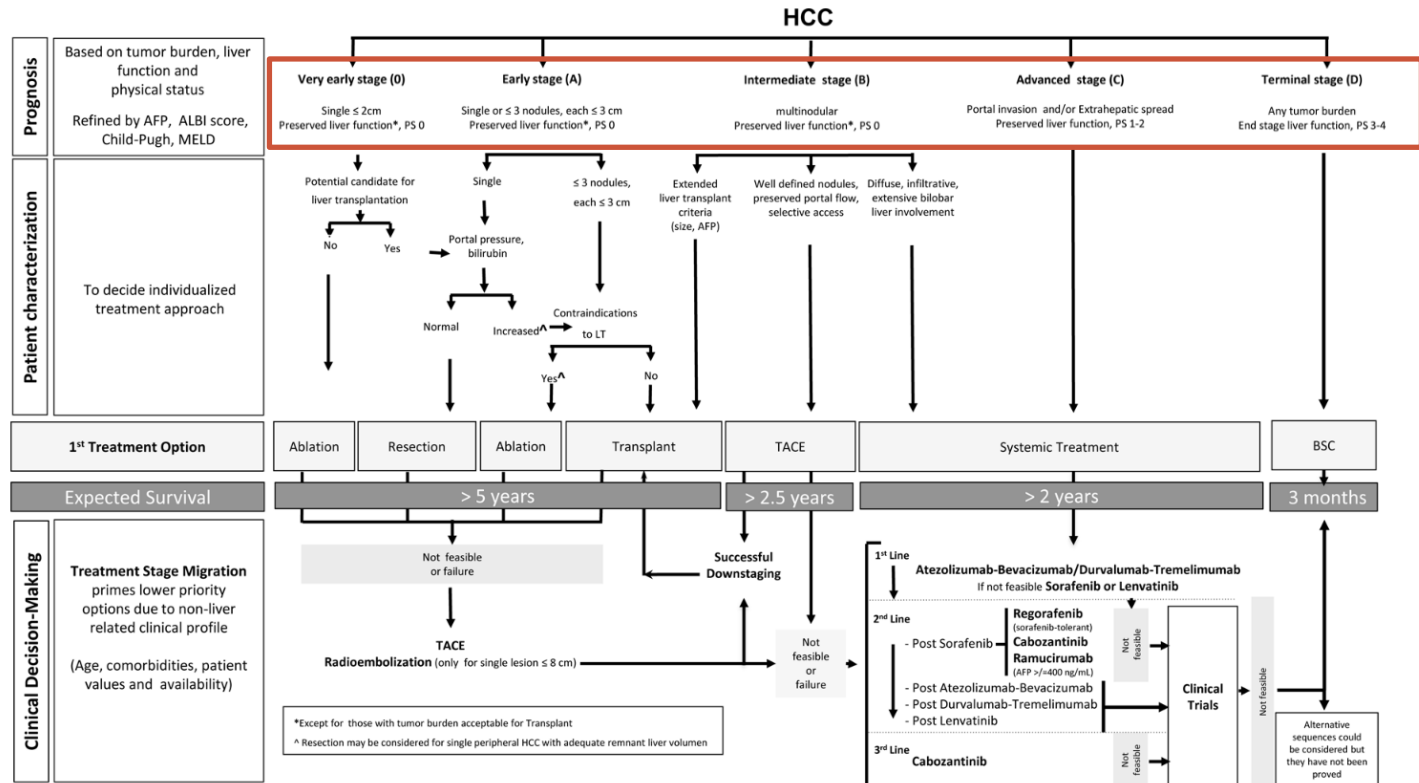
# The Majority of HCC develop in cirrhotic pts



## Poor Liver Function

- Ascites
- Hepatic encephalopathy
- Jaundice
- Variceal bleed

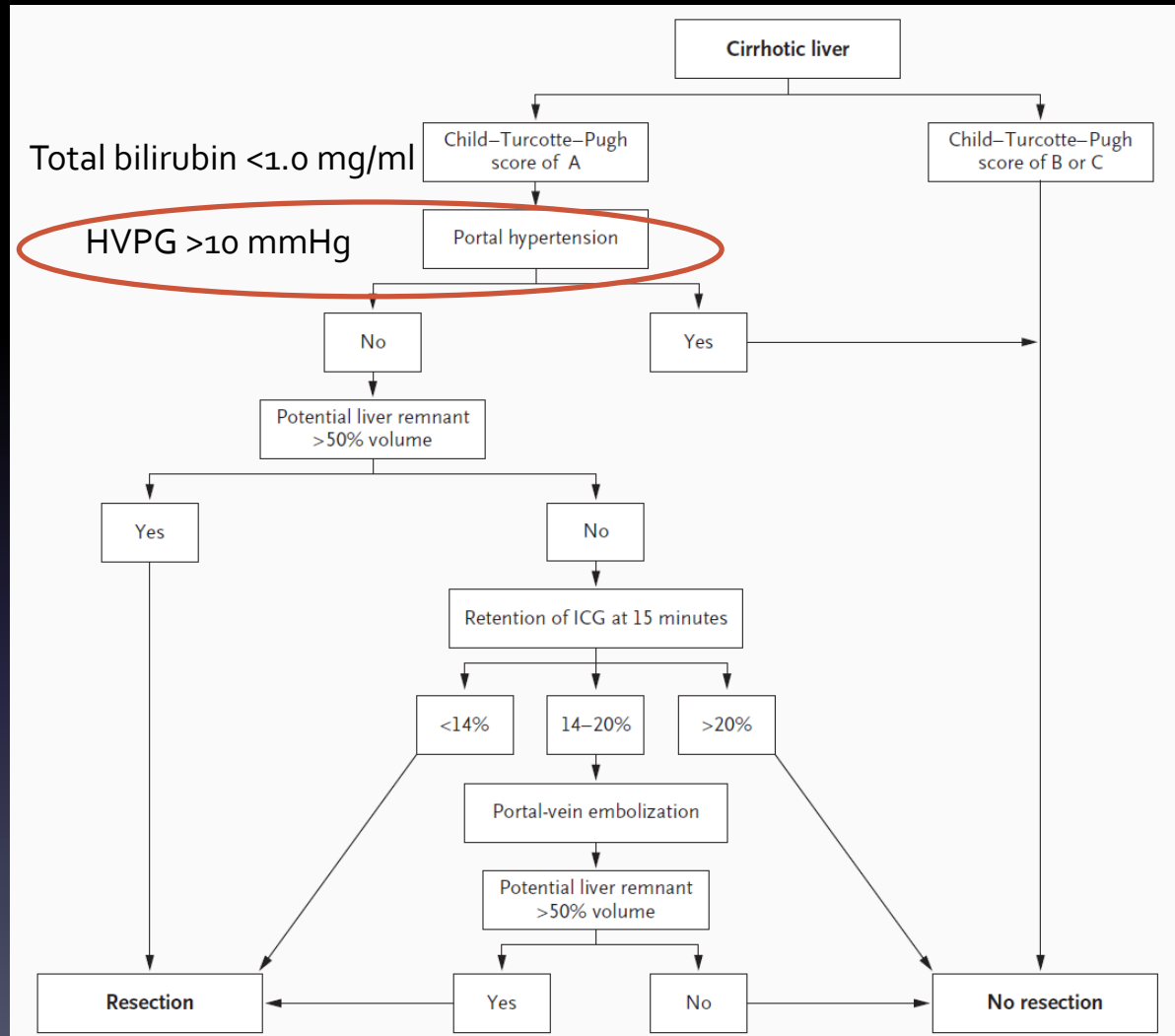
# BCLC Staging



# Surgical Resection: Who can be a candidate?

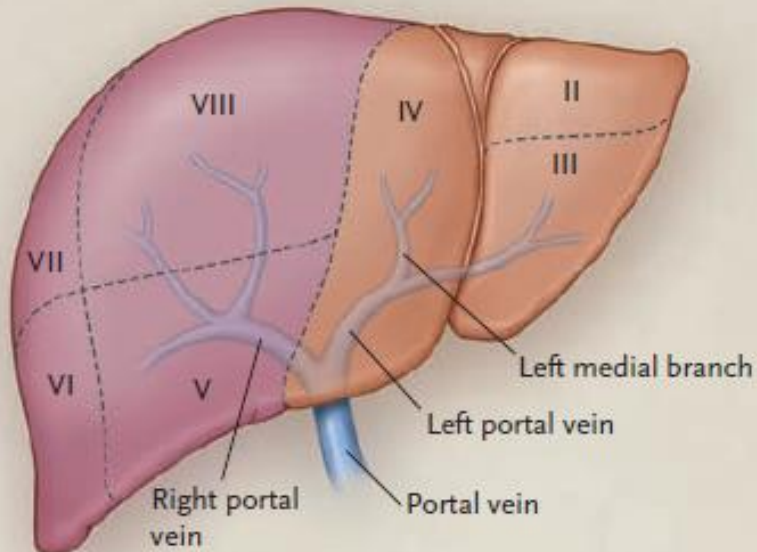
Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
<b>Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)</b> Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

# Liver Resection in Cirrhotic Patients

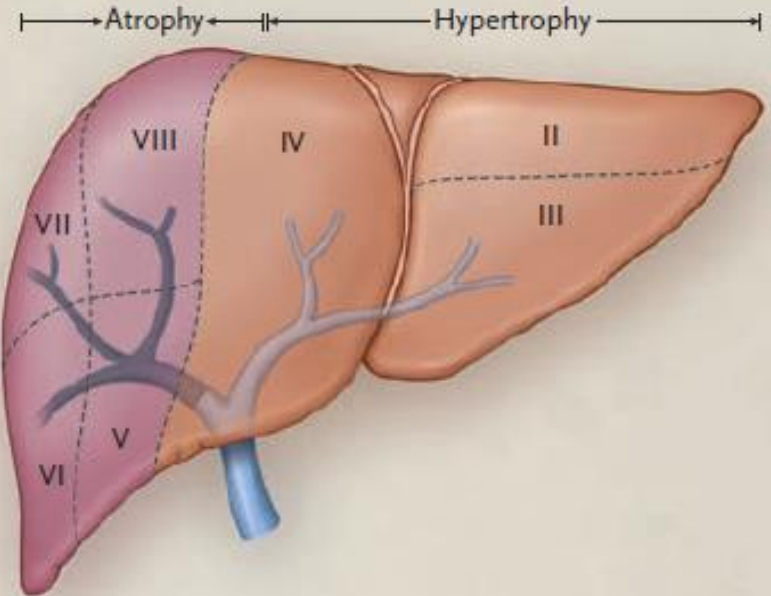


# PVE (portal vein embolization)

**A** Normal anatomy

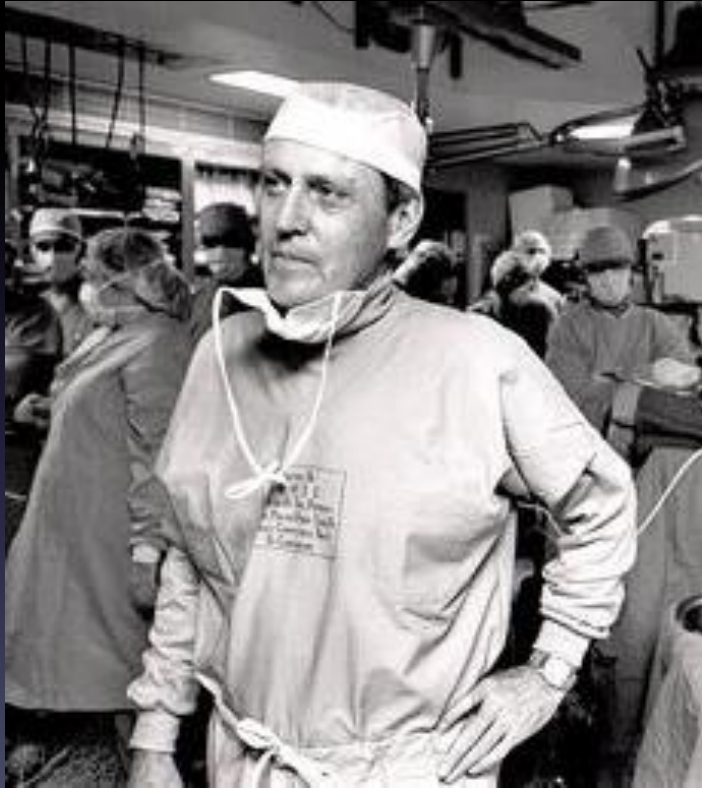


**B** Occlusion of right portal vein





# Liver Transplantation for HCC



SURGERY

DECEMBER 1963

*Gynecology & Obstetrics*

VOLUME 117

NUMBER 6

## HOMOTRANSPLANTATION OF THE LIVER IN HUMANS

T. E. STARZL, M.D., F.A.C.S., T. L. MARCHIORO, M.D., K. N. VON KAULLA, M.D.,  
G. HERMANN, M.D., R. S. BRITTAIN, M.D., and W. R. WADDELL, M.D., F.A.C.S.,  
Denver, Colorado

# Milan Criteria



The NEW ENGLAND  
JOURNAL of MEDICINE

ORIGINAL ARTICLE

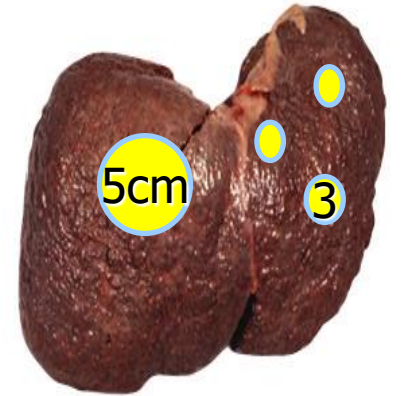
## Liver Transplantation for the Treatment of Small Hepatocellular Carcinomas in Patients with Cirrhosis

**Authors:** Vincenzo Mazzaferro, M.D., Enrico Regalia, M.D., Roberto Doci, M.D., Salvatore Andreola, M.D., Andrea Pulvirenti, M.D., Federico Bozzetti, M.D., Fabrizio Montalto, M.D., Mario Ammatuna, M.D., Alberto Morabito, Ph.D., and Leandro Gennari, M.D., Ph.D. [Author Info & Affiliations](#)

Published March 14, 1996 | N Engl J Med 1996;334:693-700 | DOI: 10.1056/NEJM199603143341104

VOL. 334 NO. 11

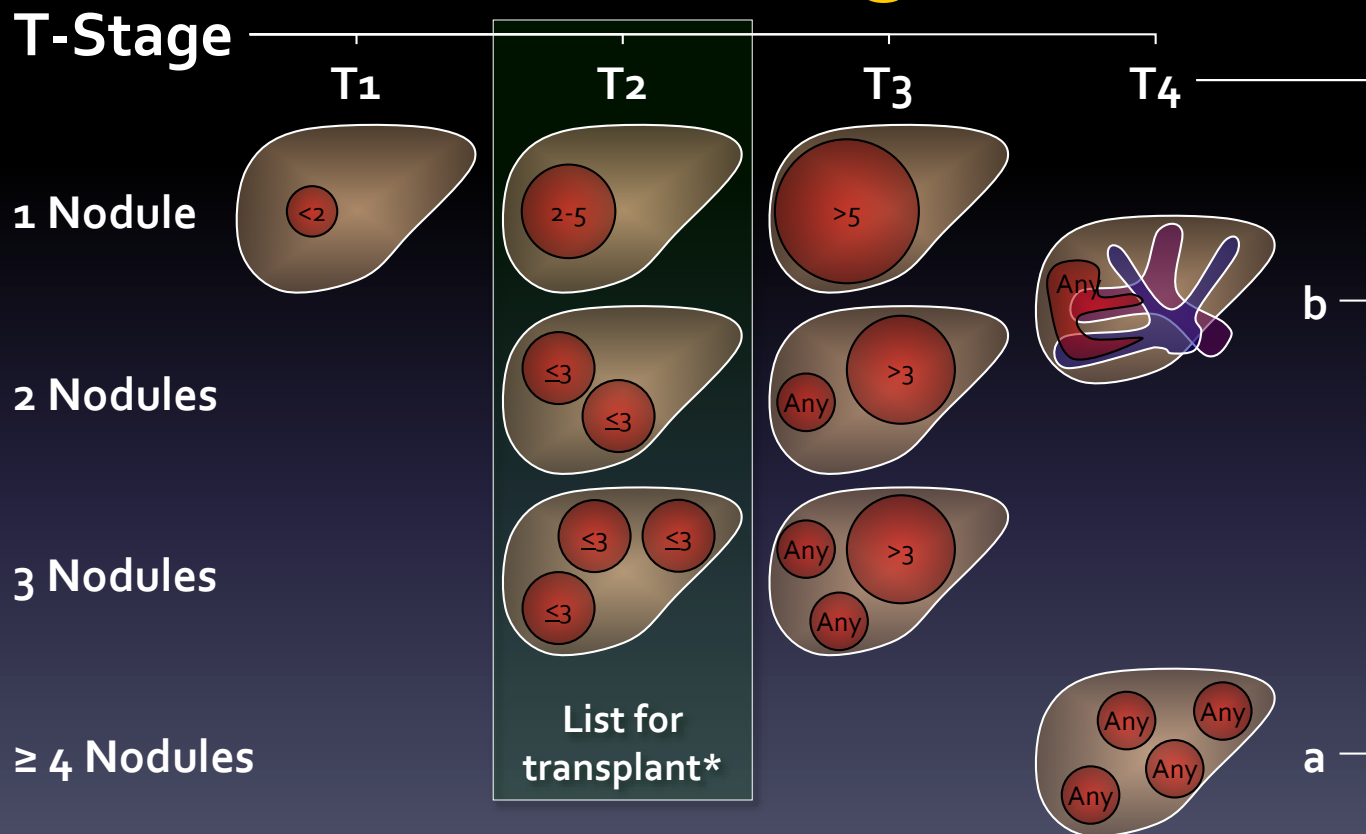
f



n = 48

4- year survival >85%, recurrence 8%

# HCC: T stage



\* > 70% 5-year survival post OLT - Bruix and Sherman. Hepatology. 2005

# MELD (Model for Endstage Liver Disease)

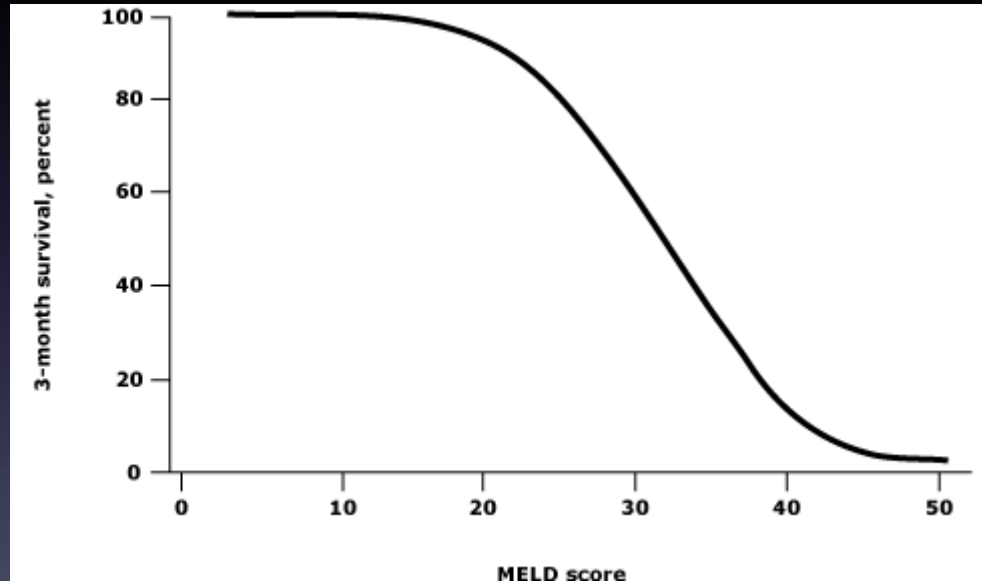
Range 6-40, used for Liver Organ Allocation

- Original MELD: INR, T-bil, Cre
- MELD Na : Original MELD plus Na
- MELD 3.0: MELD Na + gender + albumin

# MELD 3.0

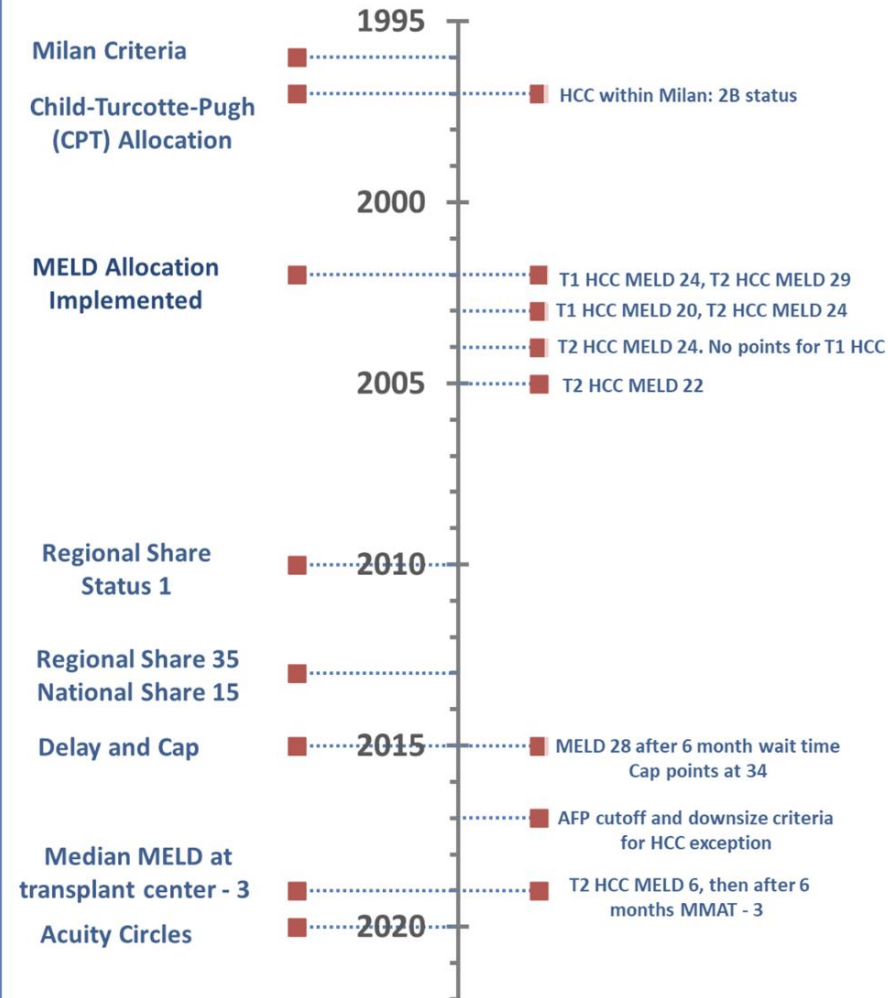
MELD 3.0 = 1.33 (if female) +  $[4.56 \times \log_e(\text{bilirubin})]$  +  $[0.82 \times (137 - \text{Na})]$  –  $[0.24 \times (137 - \text{Na}) \times \log_e(\text{bilirubin})]$  +  $[9.09 \times \log_e(\text{INR})]$  +  $[11.14 \times \log_e(\text{creatinine})]$  +  $[1.85 \times (3.5 - \text{albumin})]$  –  $[1.83 \times (3.5 - \text{albumin}) \times \log_e(\text{creatinine})]$  + 6, which is rounded to the nearest integer.

# Organ allocation and the MELD score



- ❖ 40 or more — 71.3% mortality
- ❖ 30–39 — 52.6% mortality
- ❖ 20–29 — 19.6% mortality
- ❖ 10–19 — 6.0% mortality
- ❖ <9 — 1.9% mortality

# HCC Liver Allocation



# Extended Criteria

**Table 1.** Extended criteria by tumor morphology (diameter and number of HCC).

Criteria	Author	Year	Donor Setting	Institution	Criteria	Cases	Outcome	External Validation
Milan	Mazzaferro [3]	1996	DD	Univ. of Milan, Italy	Single tumor < 5 cm Up to 3 tumors with diameter < 3 cm	48	4-year survival rate: 75%	○
UCSF	Yao [4,5]	2001, 2007	DD	Univ. of California, USA	Solitary tumor < 6.5 cm < 3 nodules with the largest lesion < 4.5 cm and total tumor diameter < 8 cm	168	5-year survival rate: 75.2%	○
Total Tumor Volume (TTV)	Toso [6]	2008	DD	Univ. of Alberta, Canada	TTV less than 115 cm <sup>3</sup>	228	Within Milan: 5-year survival rate: 82% Within TTV: 5-year survival rate: 80%	○
Up-to-7	Mazzaferro [7]	2009	DD	International multicenter	HCCs with seven as the sum of the size of the largest tumor [in cm] and the number of tumors	1556	Within Milan: 5-year survival rate: 73.3 % Within Up-to-7: 5-year survival rate: 71.2%	○
Tokyo	Sugawara [8]	2007	LD	Univ. of Tokyo, Japan	HCC diameter: 5 cm or less, HCC number: 5 or less	78	5-year survival rate: 75%	○
Asan	Lee [9]	2008	LD	Asan Medical Center, Korea	HCC diameter 5 cm or less, HCC number 6 or less	229	5-year survival rate: 76%	○

DD: Deceased donor, LD: Living donor, ○: Externally validated.

All Comers:  
Any size, #  
No TIV  
No Mets



# MELD exception for HCC

- Tumor Burden within Milan Criteria
- Tumors beyond Milan must be down-staged to within Milan
- Median MELD score at Transplant (MMAT)  $\geq 3$  to take effect after 6 months

# HCC and Liver Transplantation

- Patients with the following are contraindications for HCC exception score
  - Macro-vascular invasion of main portal vein or hepatic vein
  - Extra-hepatic metastatic disease
  - Ruptured HCC
  - T<sub>1</sub> stage HCC

# HCC and Liver Transplantation

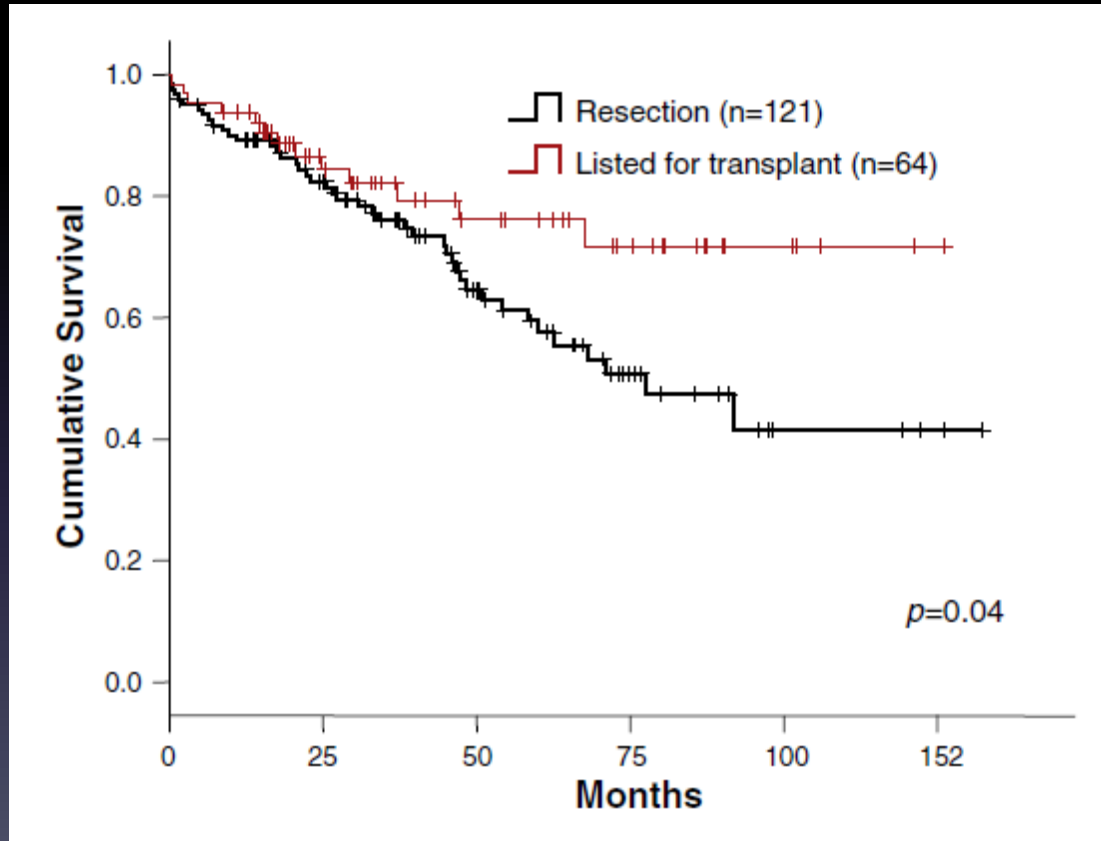
- Ruptured HCC and primary portal vein branch invasion of HCC
  - If stable (minimum of 12 months) interval after treatment for primary portal vein branch invasion or after ruptured HCC may be suitable for consideration
- Down-staging with Immunotherapy
  - use of immunotherapy does not preclude consideration for an HCC exception.

## An Analysis of Resection vs Transplantation for Early Hepatocellular Carcinoma: Defining the Optimal Therapy at a Single Institution

Characteristic	Resection ( <i>n</i> = 121)	OLT ( <i>n</i> = 110)	<i>P</i> value <sup>a</sup>
Tumor size (cm)	4.0 (1–9)	3.1 (1–5)	.08
Tumor number	1.3 (1–3)	2.4 (1–3)	< .001
Pathological vascular invasion	21%	20%	0.77
pTNM			.05
I	2 (2%)	12 (11%)	
II	85 (70%)	50 (46%)	
III	32 (26%)	25 (23%)	
IV	2 (2%)	22 (20%)	
Recurrences	53 (44%)	17 (15%)	.09

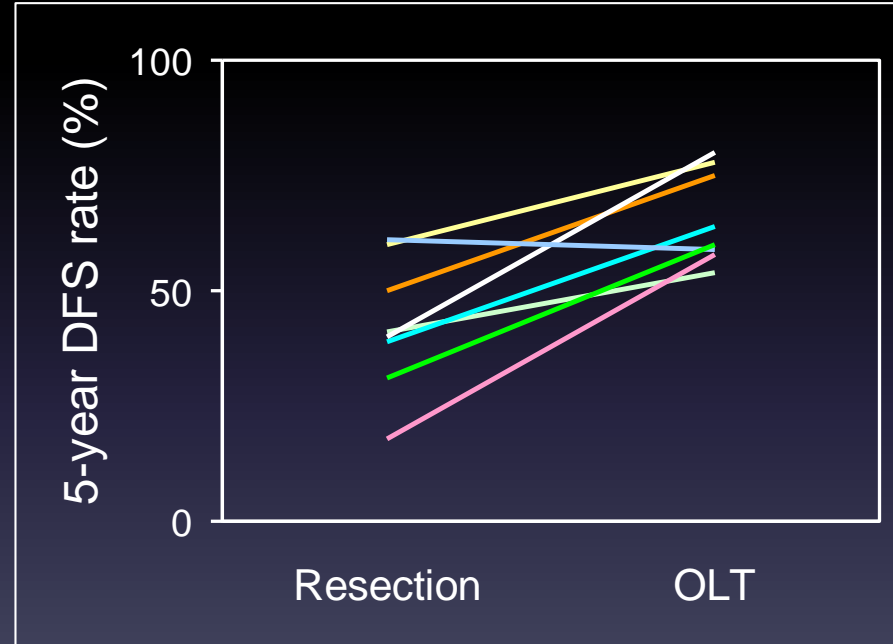
# Overall Survival

From time of Listing or Resection



# Resection vs Transplantation

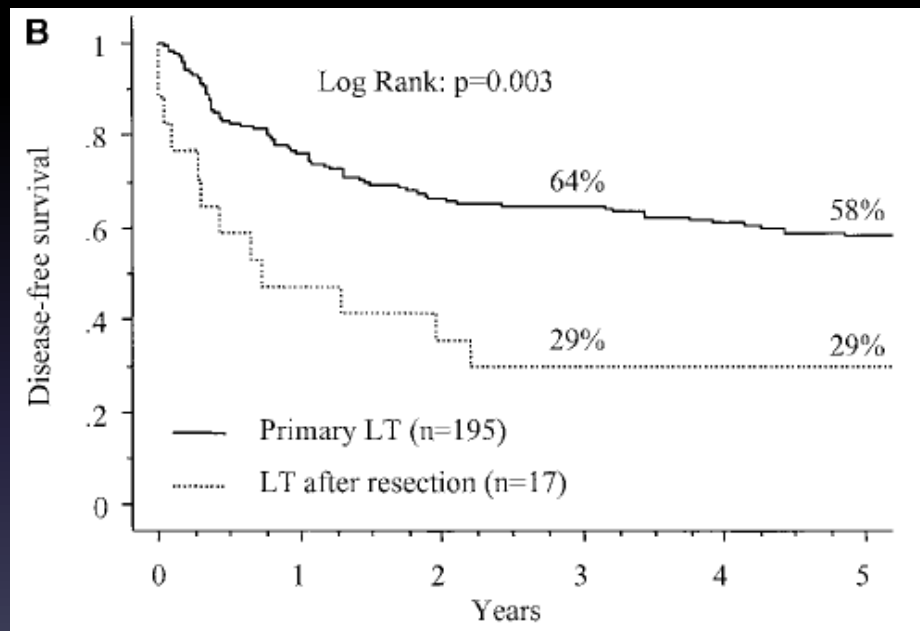
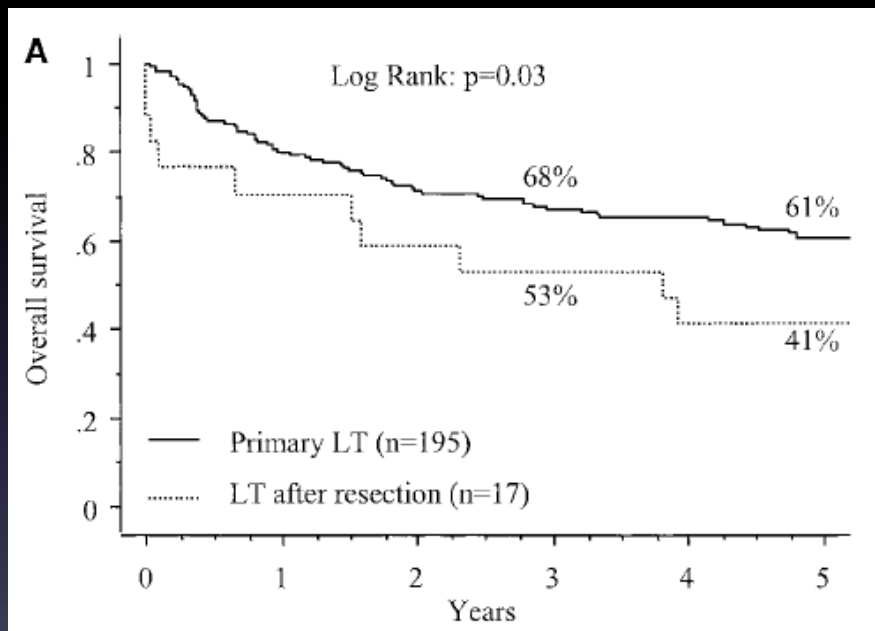
First Author	Year	Primary Therapy	Sample Size	5-year OS Rate	5-year DFS Rate
Lee <sup>85</sup>	2010	Transplantation	78	68%	75%*
		Resection	130	52%	50%
Facciuto <sup>84#</sup>	2009	Transplantation	119	62%	—
		Resection	60	61%	—
Del Gaudio <sup>83</sup>	2008	Transplantation	147	58%	54%
		Resection	80	66%	41%
Shah <sup>82</sup>	2007	Transplantation	140	64%	78%*
		Resection	121	56%	60%
Poon <sup>81</sup>	2007	Transplantation	85	44%	—
		Resection	228	60%	—
Margarit <sup>80</sup>	2005	Transplantation	36	50%	64%*
		Resection	37	78%	39%
Bigourdan <sup>79</sup>	2003	Transplantation	17	71%	80%*
		Resection	20	36%	40%*
Adam <sup>79</sup>	2003	Transplantation	195	61%*	58%*
		Resection	98	50%	18%
Belghiti <sup>77</sup>	2003	Transplantation	70	—	59%
		Resection	18	—	61%
Figueras <sup>78</sup>	2000	Transplantation	85	60%	60%*
		Resection	35	51%	31%



# Resection -> OLT?

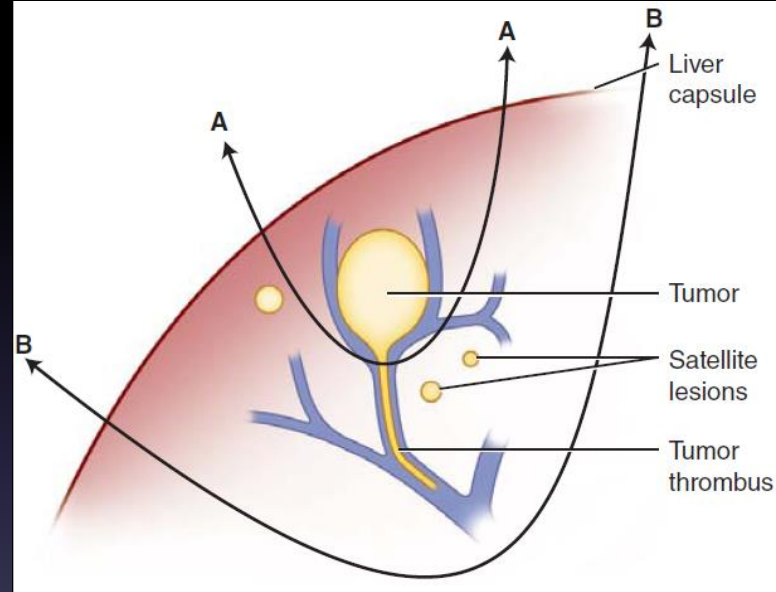
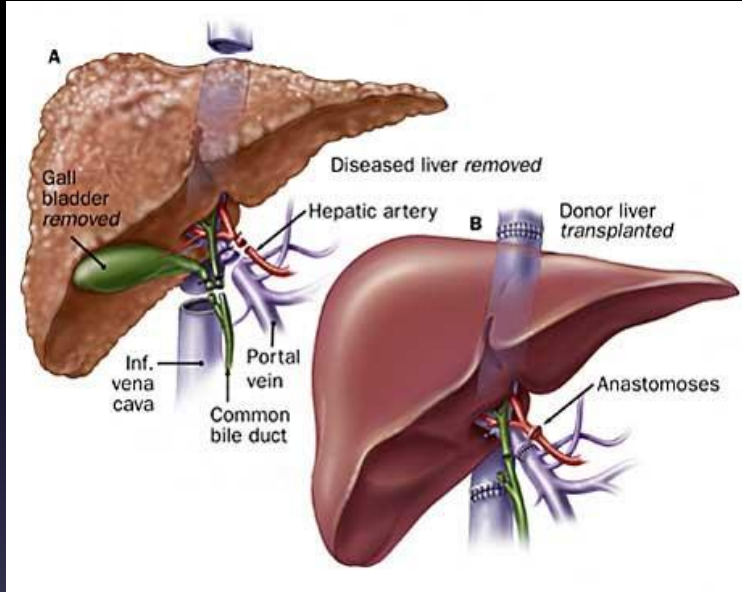
Overall Survival

Disease Free Survival



- 358 patients eligible
- 163 resection / 195 OLT
- Only 20 OLT after resection

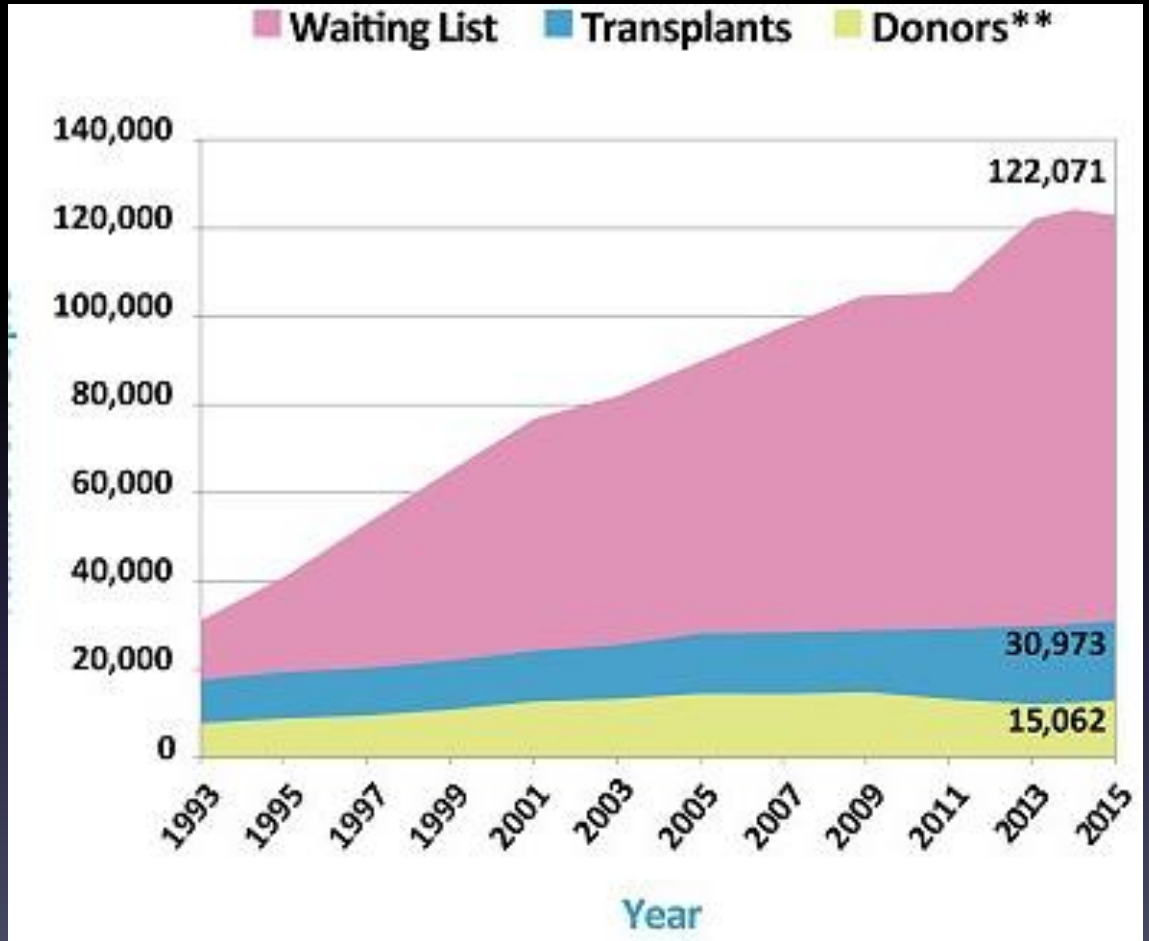
# Why Transplant > Resection?



- Most are multifocal
- Achieves tumor-free margins
- Treats parenchymal & vascular invasion
- Treats underlying liver disease

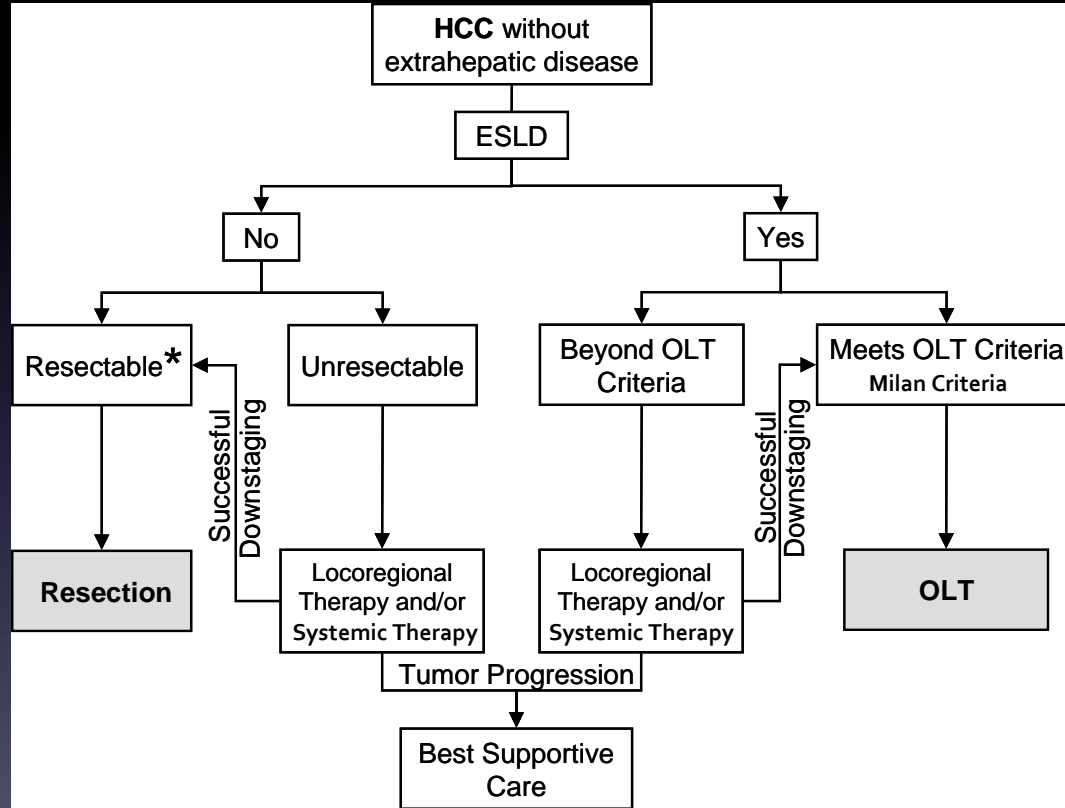


Why not  
transplant  
everyone?



In the US a person is added to the organ transplant wait list every 10 minutes, 20 people a day die waiting

# Resection vs OLT



# Take Home Message

- For early-stage HCC, both resection and liver transplant are considered curative
- Stage T2 HCC: MELD exception point for transplant
  - do not treat stage T1 HCC if patient needs liver transplant
  - All comers: Locally advanced HCC maybe a candidate for down staging for transplant
- Intermediate staging HCC: locoregional therapy: Dr. Berman
- Advanced HCC: systemic therapy: Dr. Burgoyne
- Combination therapy

Question?