Liver transplantation: Hepatocellular carcinoma

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3r Curso Práctico de Transplante de Órganos Sólidos

Barcelona

Incidence of hepatocellular carcinoma

Incidence and mortality of the 6 most common cancers worldwide

Location	Incidence*	%	Mortality*	%
Lung	1.847	13.0	1.589	19.7
Breast	1.676	11.9	0.521	12.9
Colon/rectum	1.360	9.7	0.693	8.5
Prostate	1.111	7.9	0.307	3.7
Stomach	0.951	6.8	0.723	8.8
Liver**	0.748	5.6	0.745	9.1
All sites	12.667	100	7.571	100

*Numbers of cases (in millions)
**Including HCC and cholangiocarcinoma (< 10%)

Prognostic assessment of HCC patients
Factors that affect prognosis

- Stage, aggressiveness and growth rate of the tumor

- Liver function impairment

- General health of the patient

- The specific intervention (therapy)

Forner A et al. Semin Liver Dis. 2010;30:61-74

Case report
Summary of Liver Disease

Male, 41 years old

1993

- Cirrhosis HCV. Treatment INF plus Rivabirin. No SVR.

2008: Control every 6 months

- Low platelets plus increased AFP

- US: segment IV, nodule of 1.1 cm

Case report

Main lab results

|	Result	Normal range
Total bilirubin	1,5	0 – 2 mg/dl
ALT	126	< 40 IU/l
AST	156	< 40 IU/l
Alkaline phosphatase	271	35 – 104 IU/l
g-glutamyl transpeptidase	98	5 – 36 IU/l
Serum albumin	40	37 – 53 g/L
Prothrombin time	81	70 – 100%
Hematocrit	49	36 - 51 %
Leukocytes	5410	4000 -10000/mm3
Platelets	98.000	150.000 – 400.000/mm3
Creatinine	0.85	0,3 – 1,5 mg/dl
AFP	430	0- 10 ng/dl

Case report
## Radiology: US

January 2008

- US
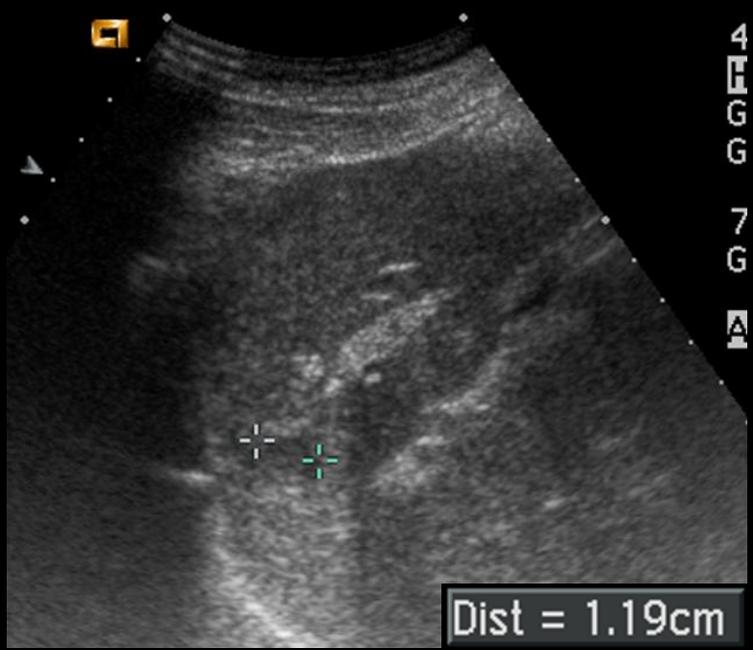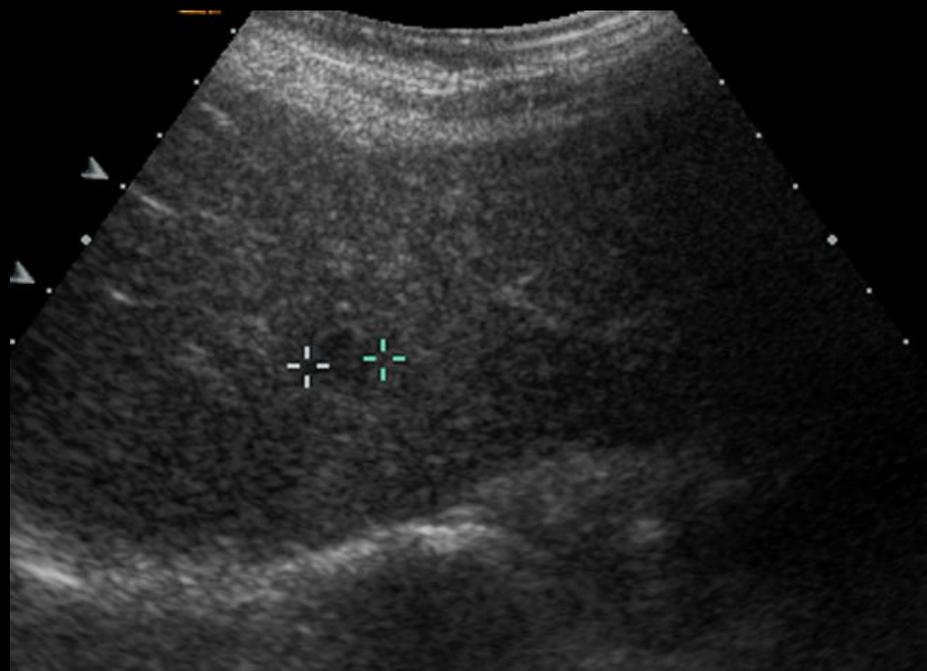
Case report
Radiology: MRI
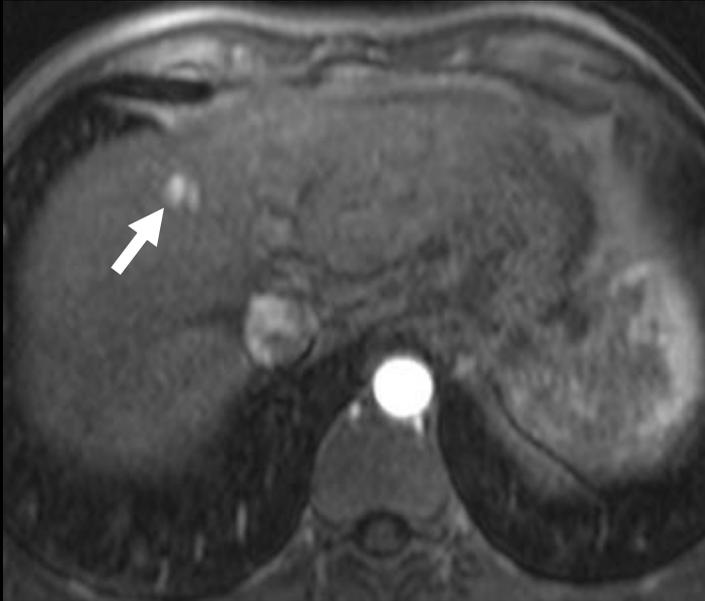
T1-Gd- arterial phase
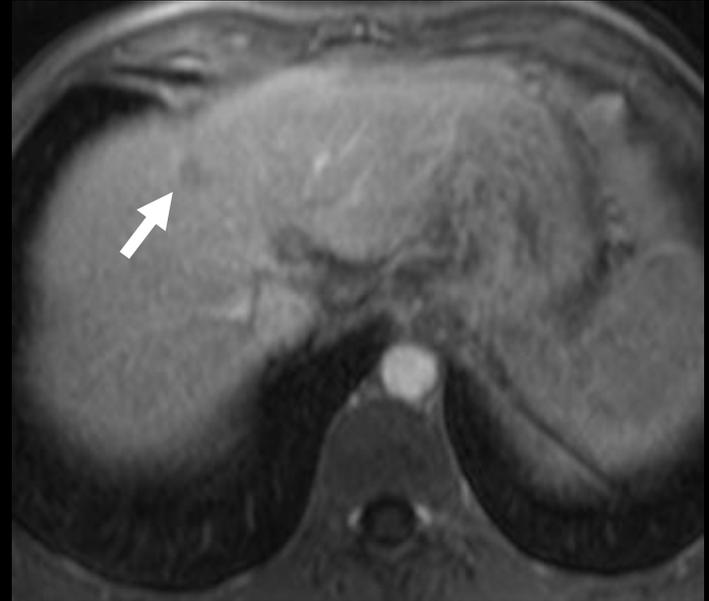
T1-Gd- delayed phase

Diagnostic criteria for HCC
EASL/EORTC Guidelines 2012
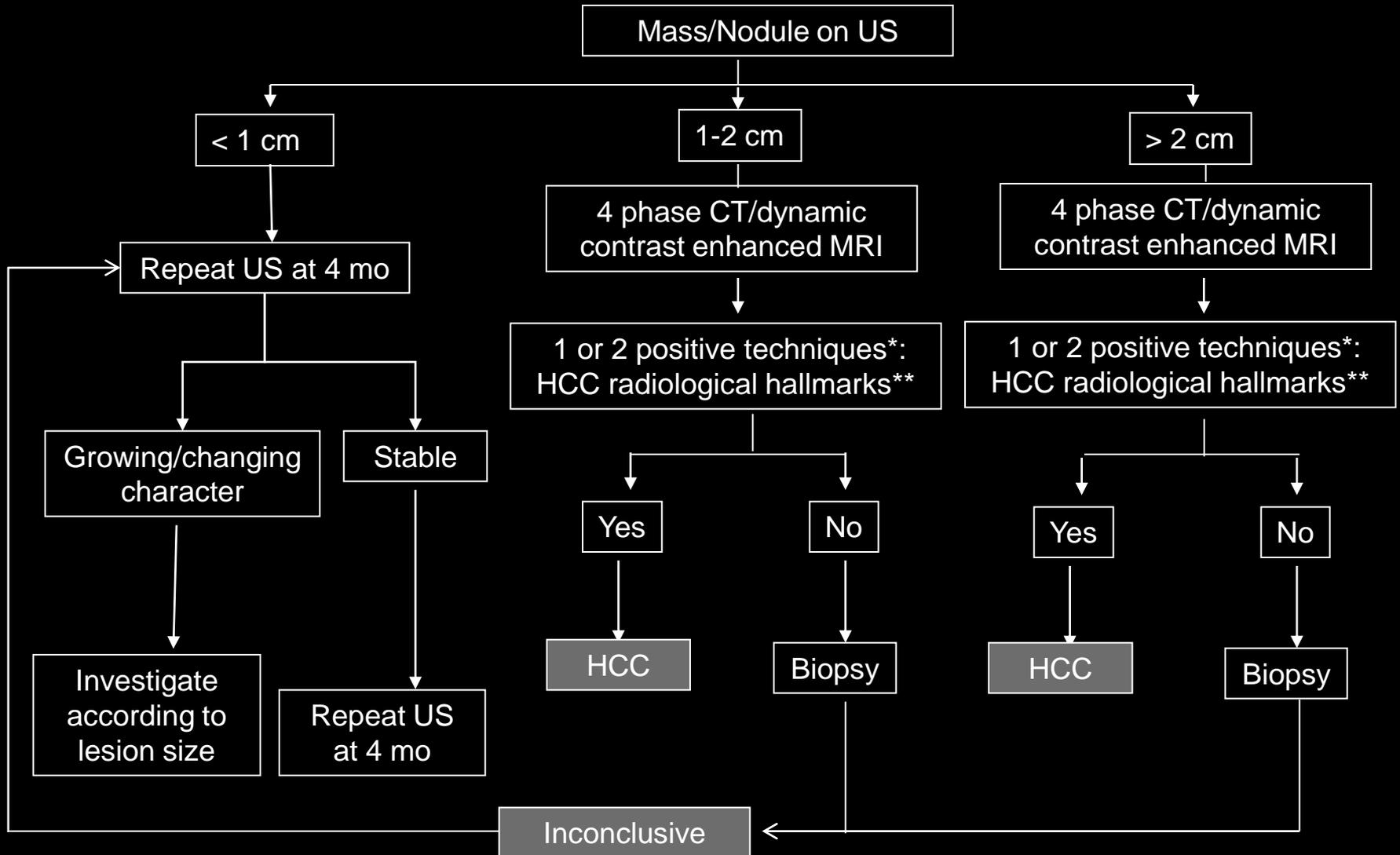
Case report

What would you perform to define the treatment decision?

1. HVPG assessment

2. Surgical resection without further studies

3. Transplantation without further studies

4. CT-chest scanner plus HVPG assessment

Case report
## Results of HVPG and CT-chest scanner

GPVH: 16,5 mmHg

CT-chest scanner: No M1

BCLC Staging and Treatment Strategy, 2012

Forner, et al. Lancet. 2012 Mar 31;379(9822):1245-55. Rodriguez de Lope C, et al. J Hepatol. 2012;56 Suppl 1:S75-87.
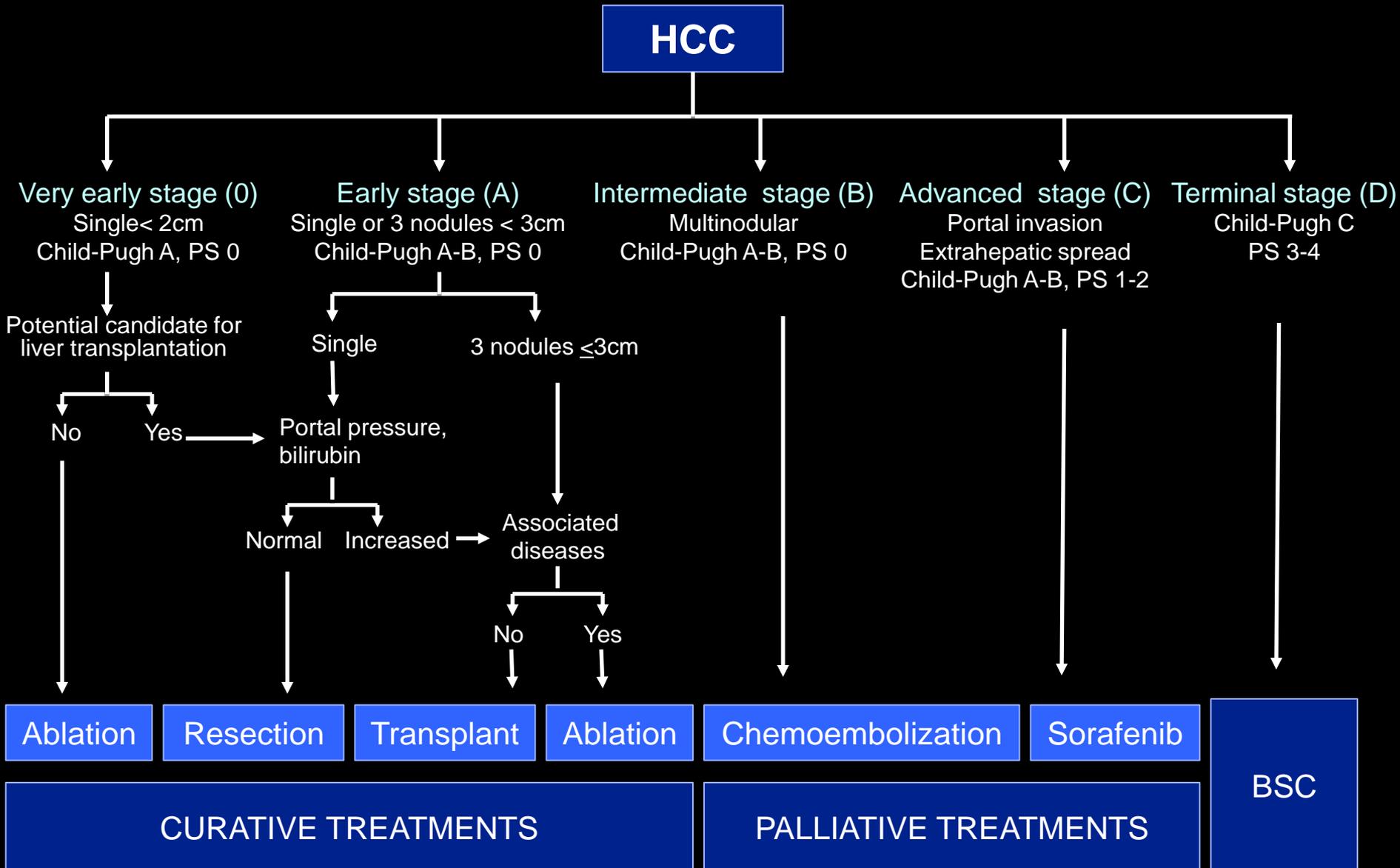
Curative treatments: Surgical Resection
Prognosis of HCC suitable to resection

Best candidates: - Solitary HCC

- Child-Pugh A: No portal hypertension (HVPG < 10 mmHg)

Normal Bilirubin (< 1 mg/dl)

74%

50%

25%

Log Rank 0.00001

Survival (%)

months

0   12   24   36   48   60   72   84   96
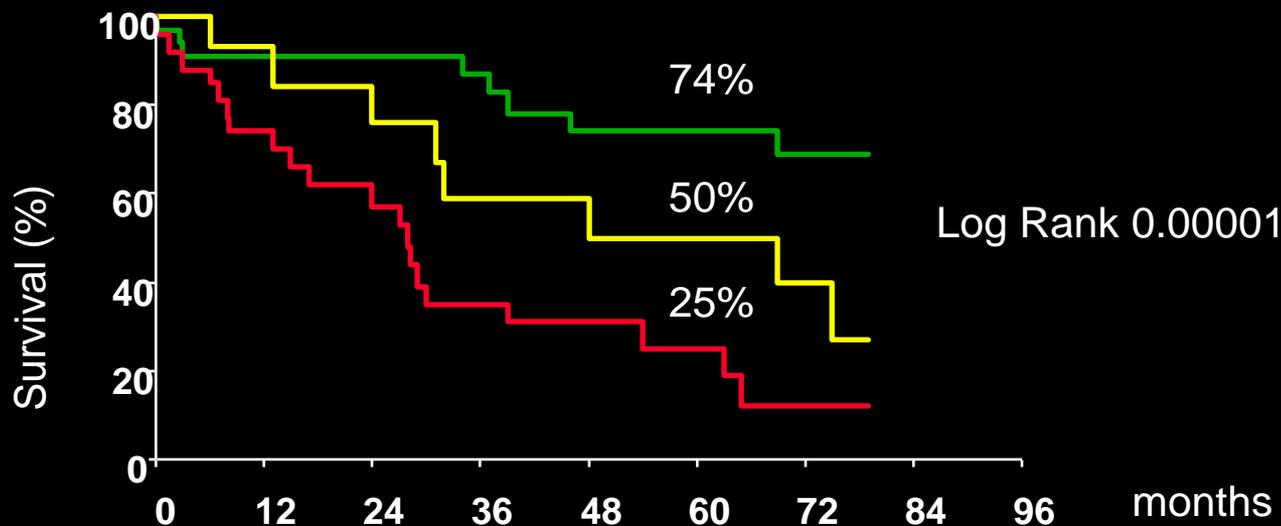
— No portal hypertension and normal bilirubin (n= 35)

— Portal hypertension and normal bilirubin (n=15)

— Portal hypertension and Bilirubin >1 mg/dL (n=27)

Llovet JM, et al. Hepatology. 1999;30:1434-40.

Curative treatments: Surgical Resection
Metanalysis of the impact of CSPH on postoperative outcomes

Panel A: 3-year mortality
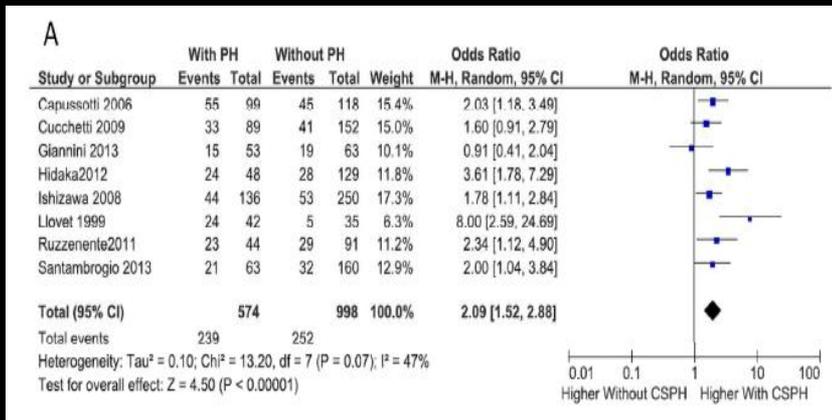
Panel B: 5-year mortality
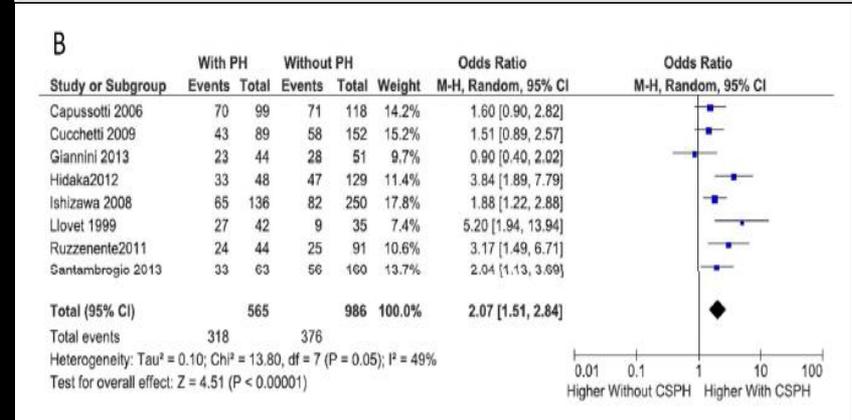
Panel C: clinical decompensation

Berzigotti A, Reig M, et al, Hepatology. 2015 Feb;61(2):526-36.

BCLC Staging and Treatment Strategy, 2012

HCC

Very early stage (0)
Single< 2cm
Child-Pugh A, PS 0

Early stage (A)
Single or 3 nodules < 3cm
Child-Pugh A-B, PS 0

Intermediate stage (B)
Multinodular
Child-Pugh A-B, PS 0

Advanced stage (C)
Portal invasion
Extrahepatic spread
Child-Pugh A-B, PS 1-2

Terminal stage (D)
Child-Pugh C
PS 3-4

Potential candidate for liver transplantation

Single

3 nodules ≤3cm

No

Yes

Portal pressure, bilirubin

Normal

Increased

Associated diseases

No

Yes

Transplant

CURATIVE TREATMENTS

Forner A et al. Lancet. 2012. 2012 Mar 31;379(9822):1245-55.

Curative treatments: Liver Transplantation
Outcomes applying restrictive selection criteria

Authors, year	n	Selection criteria	Recurrence	Survival at 5y
Mazzaferro, 1996	48	Milan	8%	74%*
Jonas, 2001	120	Milan	15%	71%
Cillo, 2004	30	Milan	6.7%	72%
Herrero, 2008	47	Milan	8.5%	70%
Mazzaferro, 2009	444	Milan	5.5%	73.3%

* Survival at 4 years
~ 5-y recurrence rate
¬ 100-(5-y RFS)

Mazzaferro V et al. N Engl J Med. 1996;334:693-9
Jonas S et al. Hepatology. 2001;33:1080-6
Cillo U et al. Ann Surg. 2004;239:150-9
Herrero JI et al. Liver Transpl. 2008;14:272-8
Mazzaferro V et al. Lancet Oncol. 2009;10:35-43
Kulik LM et al. Am J Transplant. 2012;12(11):2997-3007

Curative treatments: Liver Transplantation
Prognosis of patients with HCC waiting for OLT

DROPOUT

ENLISTED

time

TRANSPLANTED

Intention to treat

Per protocol

-Time
-Size
-AFP
-Liver function / MELD

Yao FY, et al. Liver Transplantation. 2003;9(7):684-92.
Freeman RB, et al. Am J Transplant. 2006;6(6):1416-21.
Washburn K, et al. Am J Transplant. 2010;10(7):1643-8.

Curative treatments: Liver Transplantation
Prognosis of patients with HCC waiting for OLT

Mazzaferro V, et al. Lancet Oncol. 2009:10(1):35-43
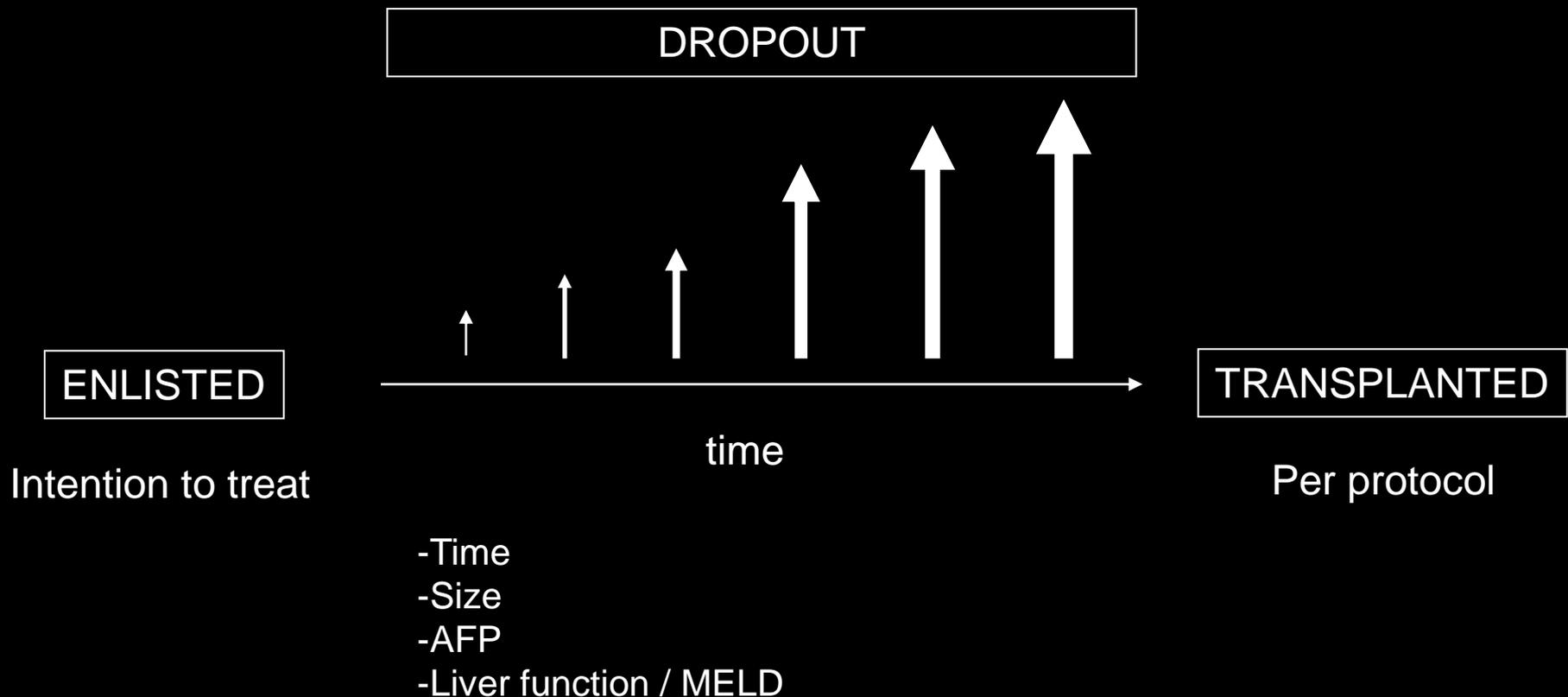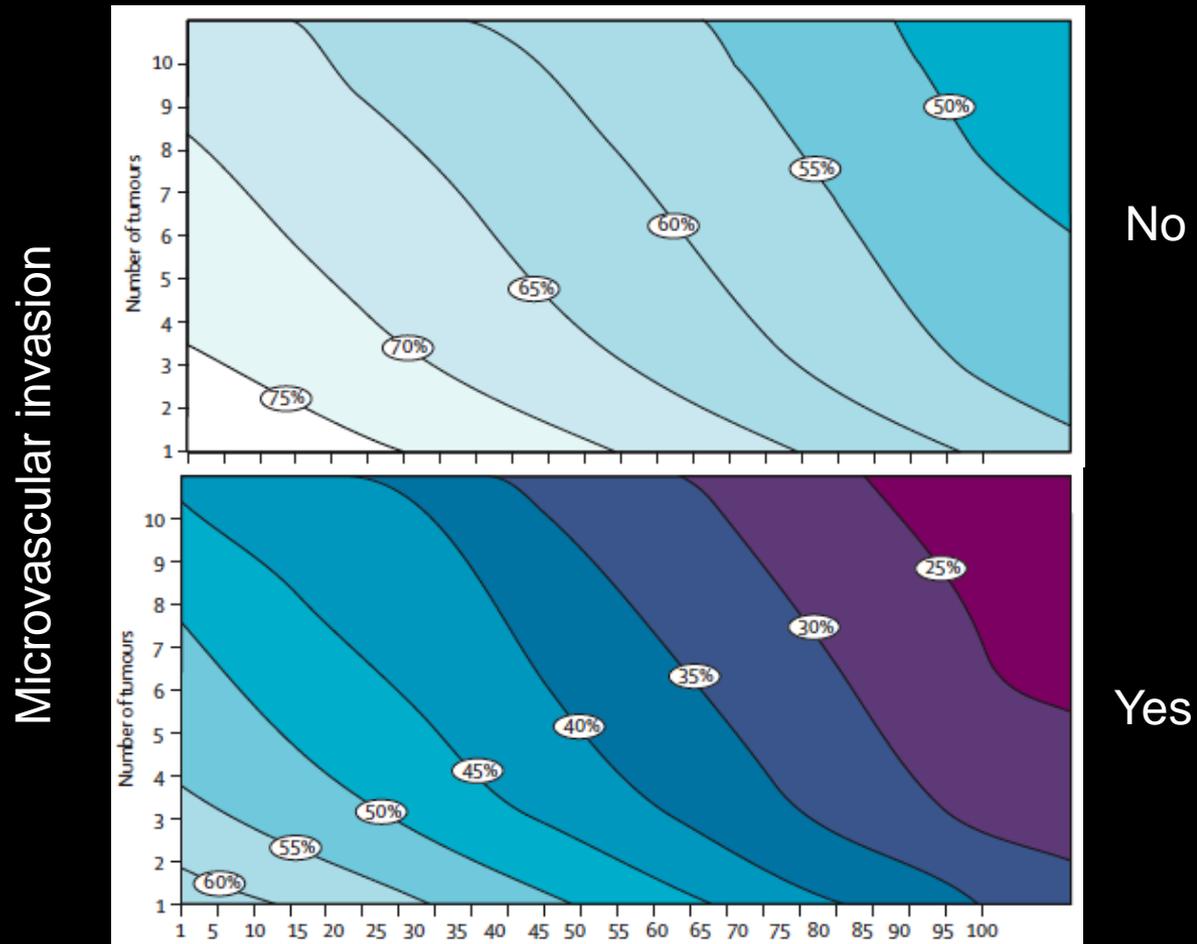
Tumor markers for prognosis assessment
AFP is a criteria for liver transplantation for HCC
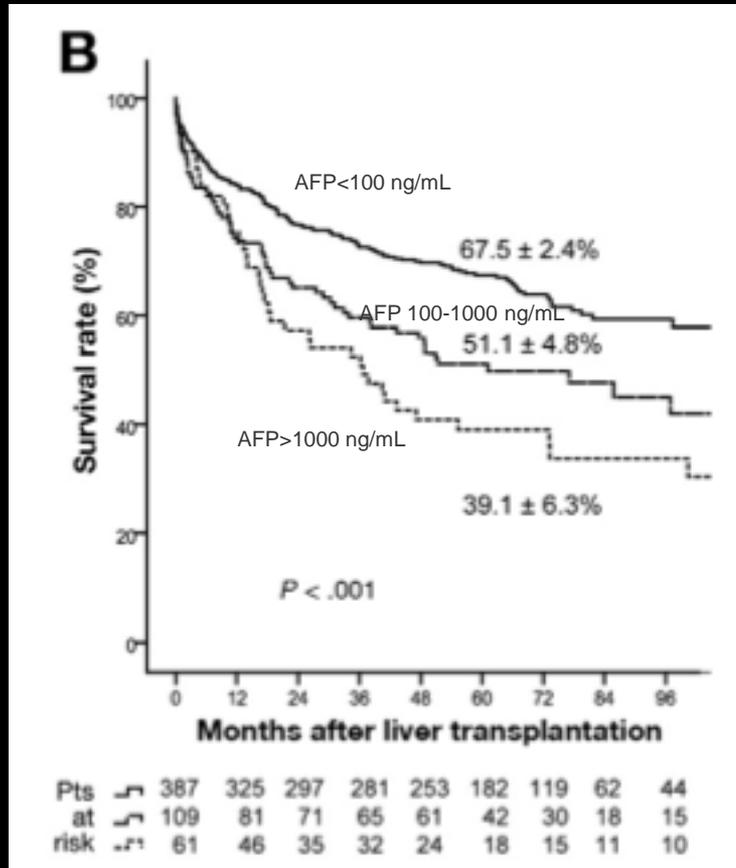
Table 2. Simplified, User-Friendly Version of the AFP Model

Variables	β coefficient	Hazard ratio	Points
Largest diameter, *cm*			
≤3	0	1	0
3–6	0.272	1.31	1
>6	1.347	3.84	4
Number of nodules			
1–3	0	1	0
≥4	0.696	2.01	2
AFP level, *ng/mL*			
≤100	0	1	0
100–1000	0.668	1.95	2
>1000	0.945	2.57	3

Duvoux C et al. Gastroenterology. 2012:143:986-994.

Curative treatments: Liver Transplantation
Strategies to reduce drop-out rate

Cirrhotic patients with early HCC waiting for cadaveric liver transplantation

Increase pool of donors

Priority policies

Is MELD fair/effective?

Adjuvant treatment during waiting time

Living donor liver transplantation

Domino /Split liver transplantation

High risk donors

Phase II trials

Cost-efficacy studies

Chemotherapy

TACE

PEI / RF

Resection/PEI

Curative treatments: Liver Transplantation
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TACE

PEI / RF

Resection/PEI

There are not randomized-controlled trials

Adjuvant treatment during waiting time
Benefit of treatments depends on the waiting time
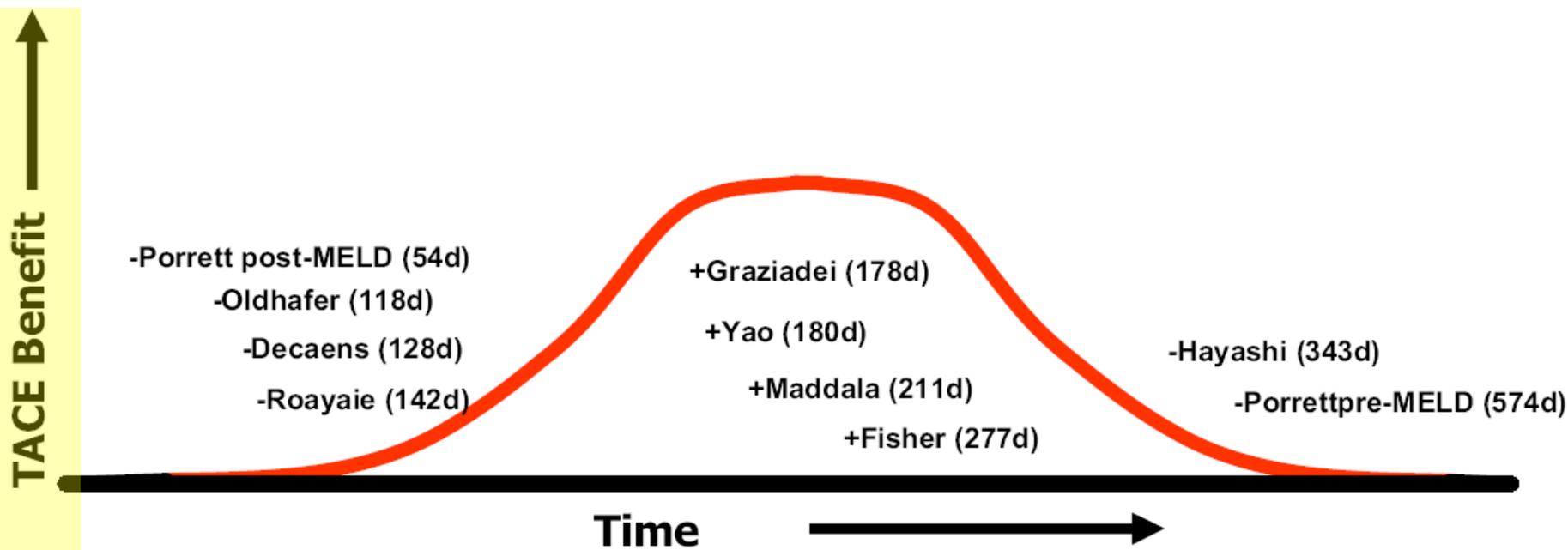
Case report
Treatment

- Laparoscopy, RFA

- Inclusion in waiting list for Liver transplantation

Case report
Evolution during the waiting list

Imaging follow-up every 3 months: Complete response
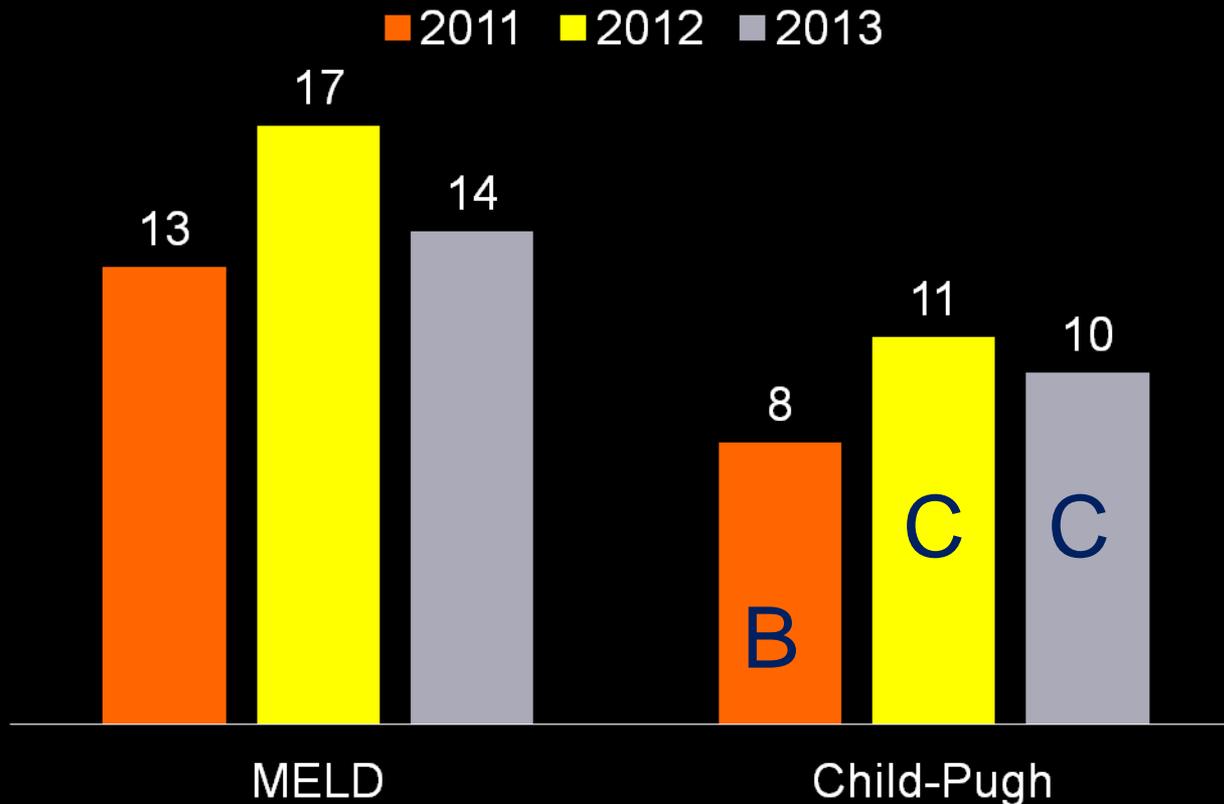
Case report
Evolution during the waiting list

April 2014

Liver donor liver transplantation

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