Principles of surgery in Hepatic Tumours

Defining operable , borderline and Inoperable

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Principles of surgery in Hepatic Tumours

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Principles of surgery in Hepatic Tumours

Plan

- Brief history of modern liver surgery
- General Principles of liver Surgery
- Staging System for HCC
- Surgical Management of HCC
- Extended criteria for management of HCC , role of TAce and SBRT

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Milestones in liver surgery

Mystic Organ to a Transparent Organ

The liver surgery has progressed tremendously in the last 50 years

From mortalities ranging from 10-20 % it is now < 2 %

A better knowledge of Liver segmental Anatomy , and Inventions in Imaging techniques and techniques of Surgeryand post operative management

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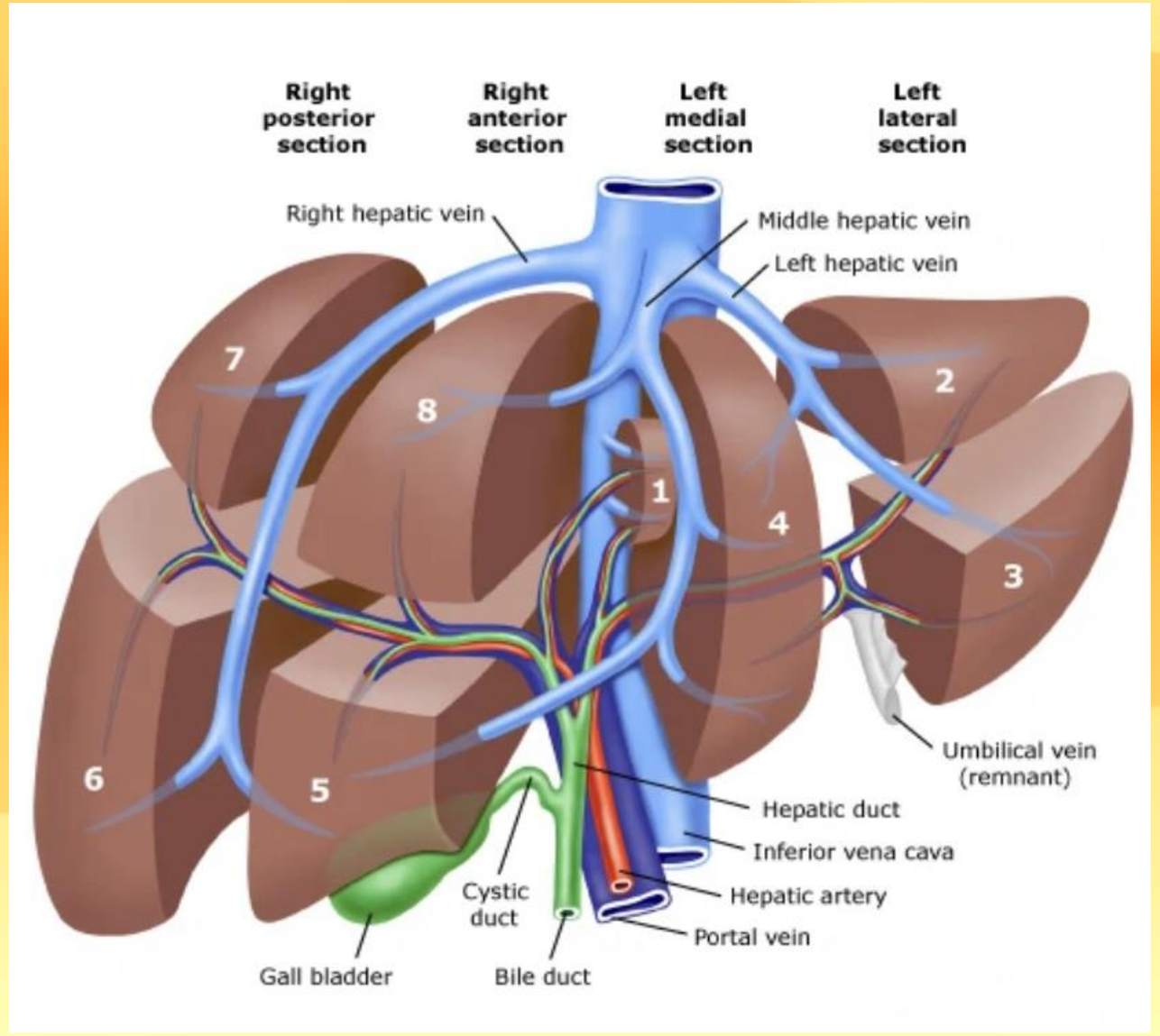
Couinaud's classification 1954



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Milestones in liver surgery

Henry Bismuth introduce the concept of Anatomical resections

IOUS - 1984

Thomas E Starzl performed the first liver transplantation in1963

Strong First LDLT from adult to child in july1989 was performed in Australia

Lo , First Adult LDLT in1996

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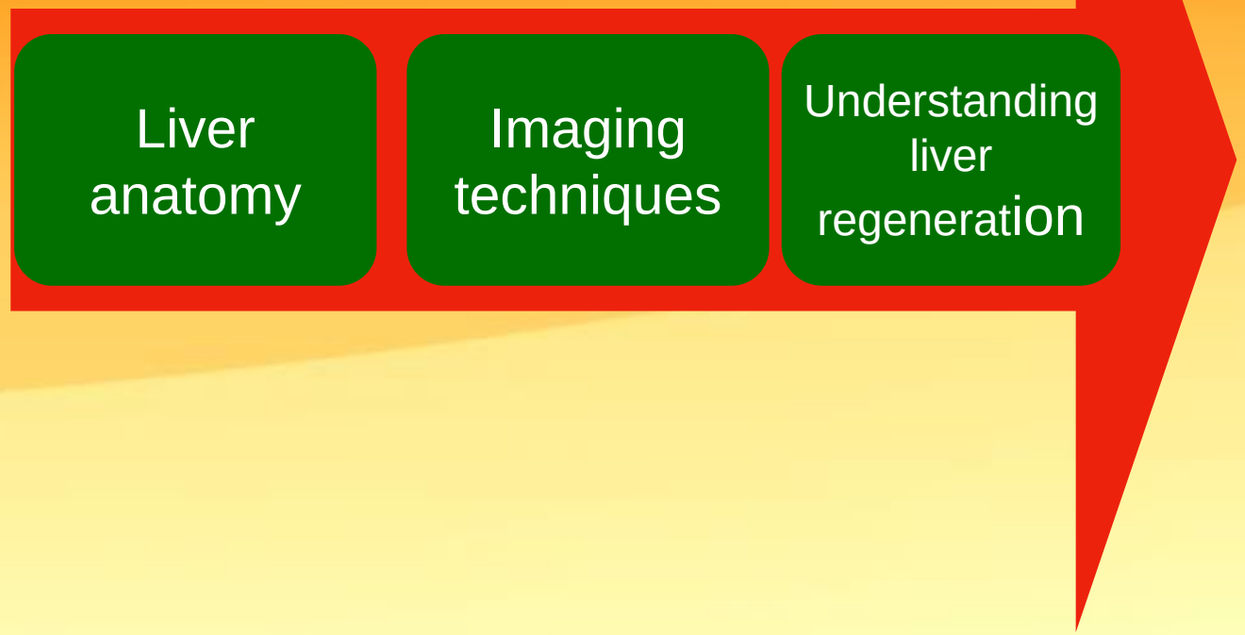
- **A good knowledge of the anatomy is a prerequisite**



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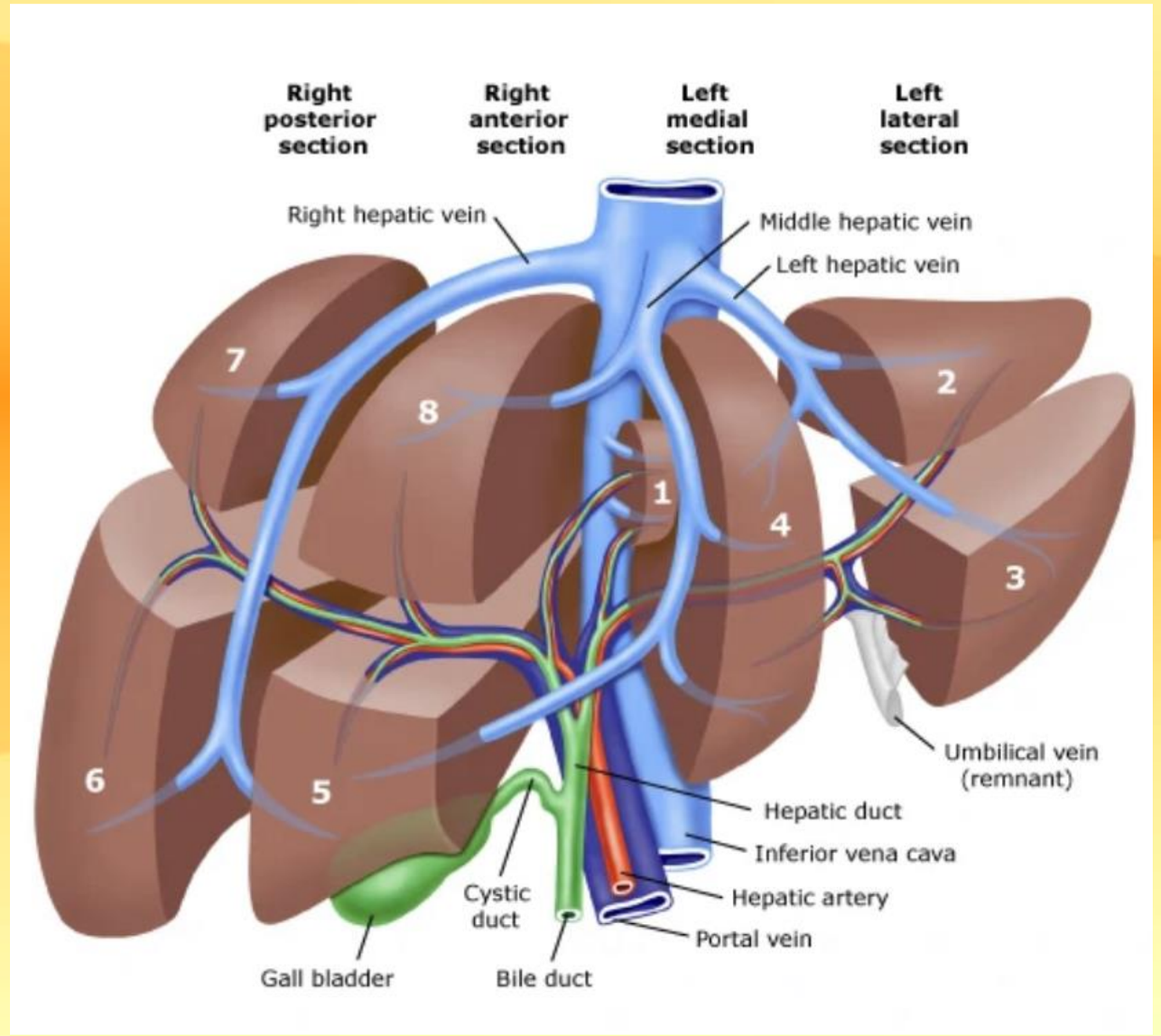
Liver anatomy

- Right hepatic vein divides the right lobe into anterior and posterior segments
- Middle hepatic vein divides the liver into right and left lobe , this runs from IVC to GB fossa an dis called cantle's line
- Left hepatic vein divides the left lobe into medial and lateral part
- Portal vein divides the liver into upper and lower part



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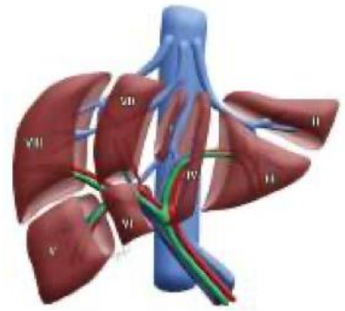

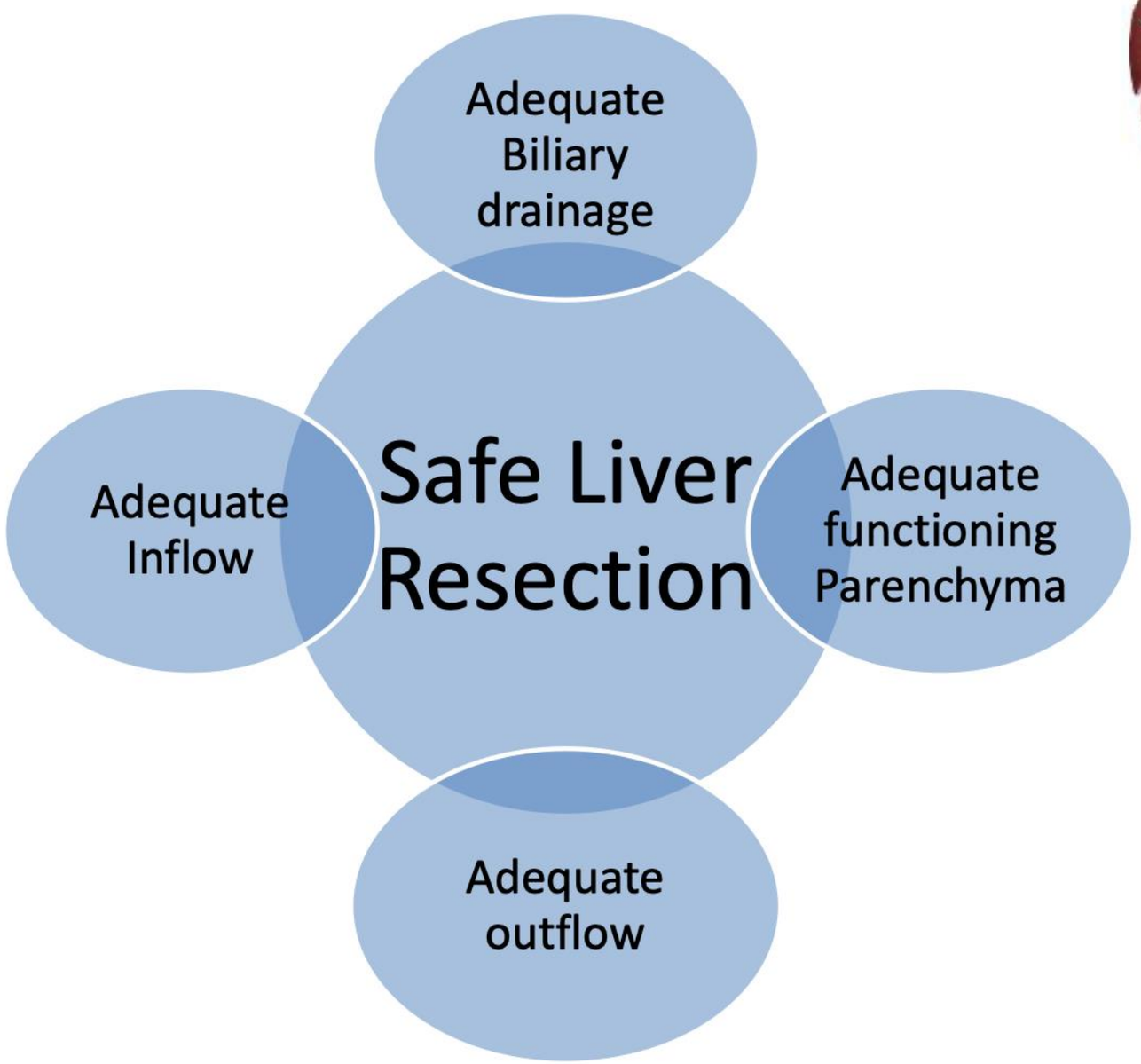

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Risk Factors for Resection

Advanced Age

Co morbidities

Chronic liver Disease

Cholestatic Disease

Post Chemotherapy

Extent and Complexity of the Liver Resection

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Imaging of the liver

Pre operative simulation using a **triple phase Contrast CT scan**

Accurate assessment of the segmental anatomy

Liver Vasculature

Volumetry

MRCP -Biliary Tree

MR spectrography/ Fibroscan -

Functional Status - ICG

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- POST OPERATIVE LIVER FAILURE IS THE COMMONEST CAUSE OF MORTALITY

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- **Cause of Post op Liver failure**

Impaired Functional reserve

Inadequate residual volume

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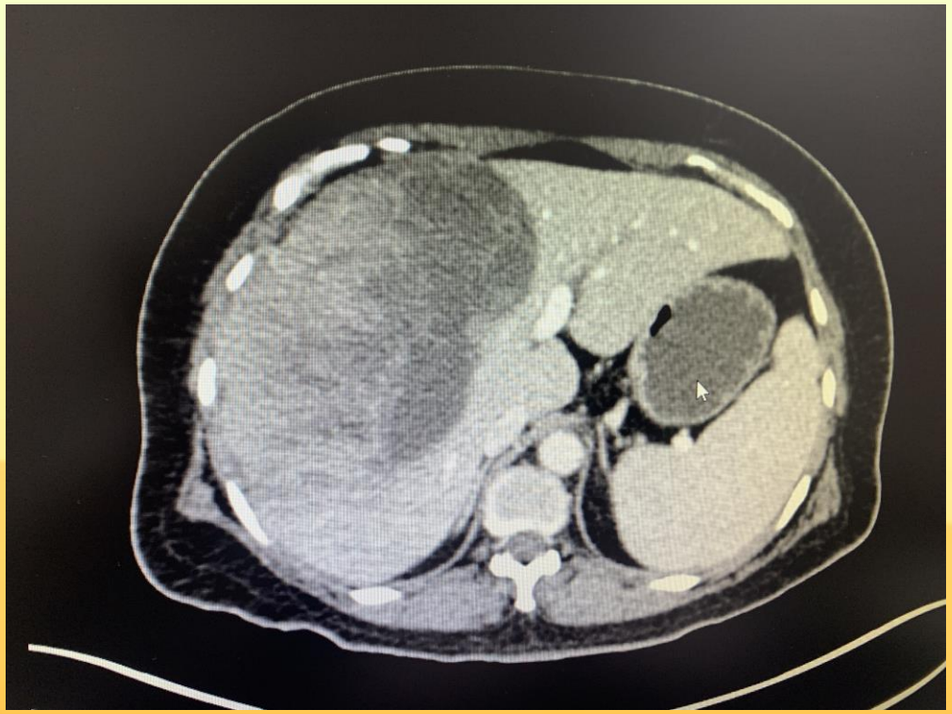
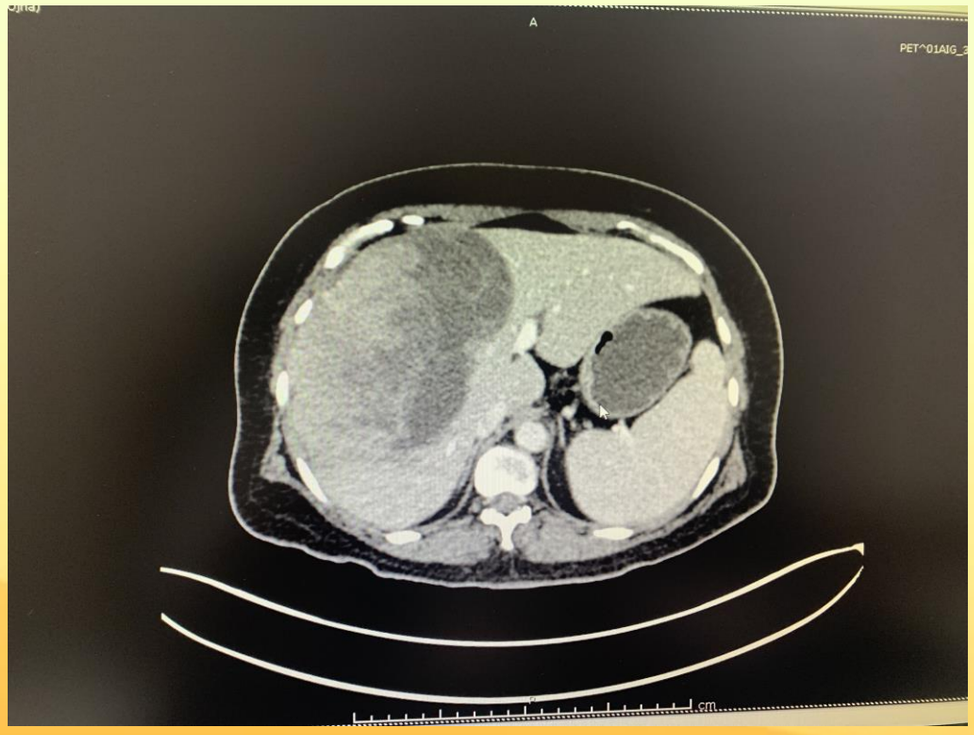
Residual volume

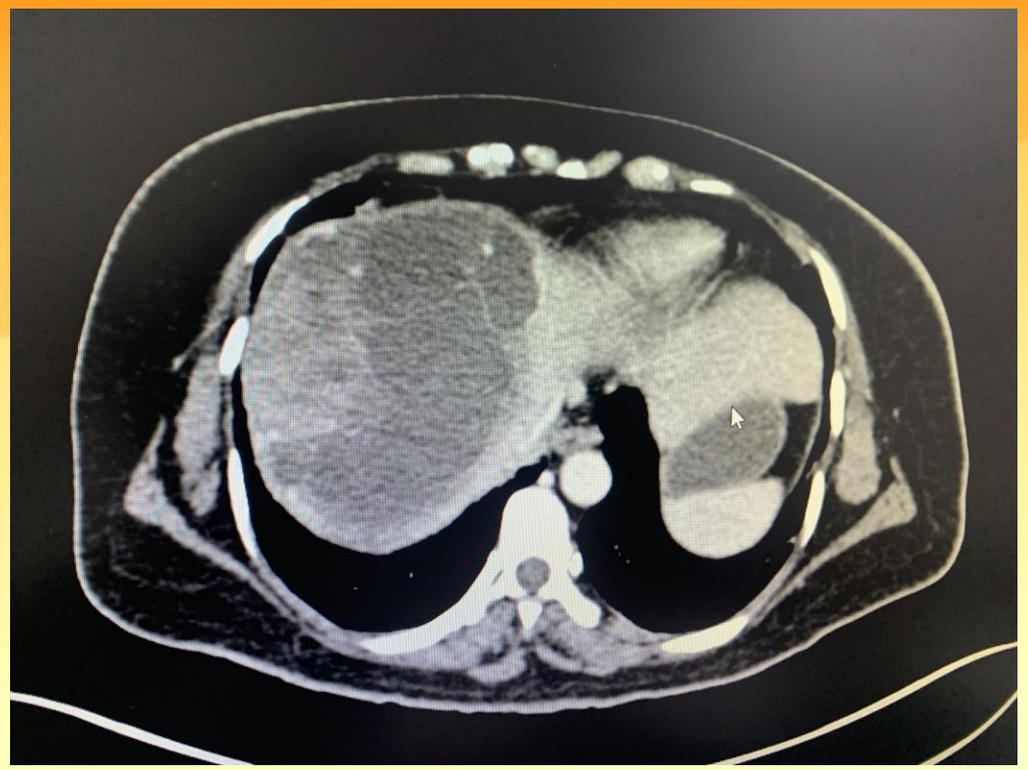
Future Remnant Liver Volume FLR

$$FLRV = \frac{\text{Residual Liver Volume}}{\text{Total liver Volume - tumour volume}}$$





- Total liver volume 2625
- Right lobe without MHV 1840 (70%)
- Left lobe with MHV 785.9(30%)
- Left lateral 546(20.81)%
- Tumour volume 1253



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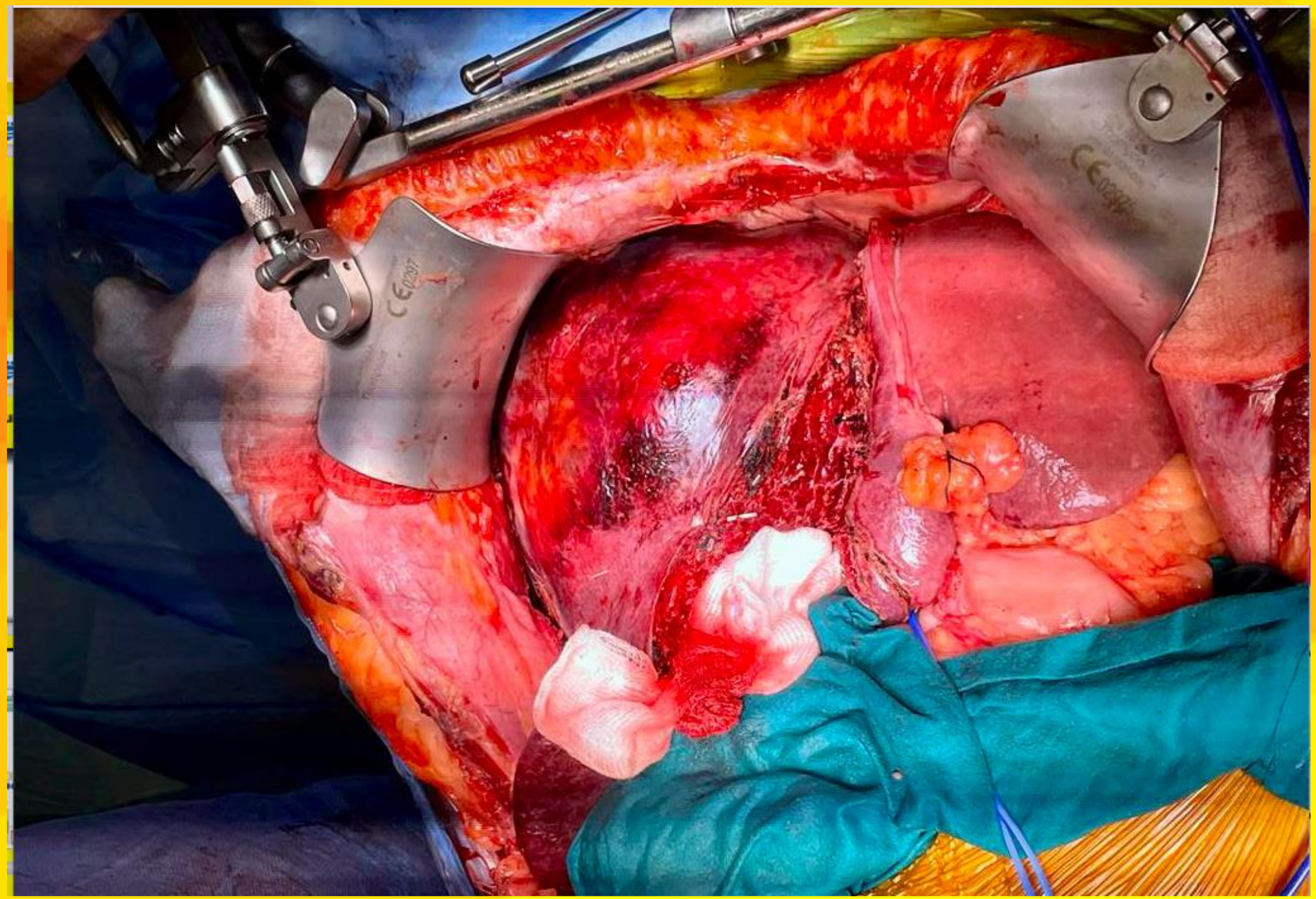
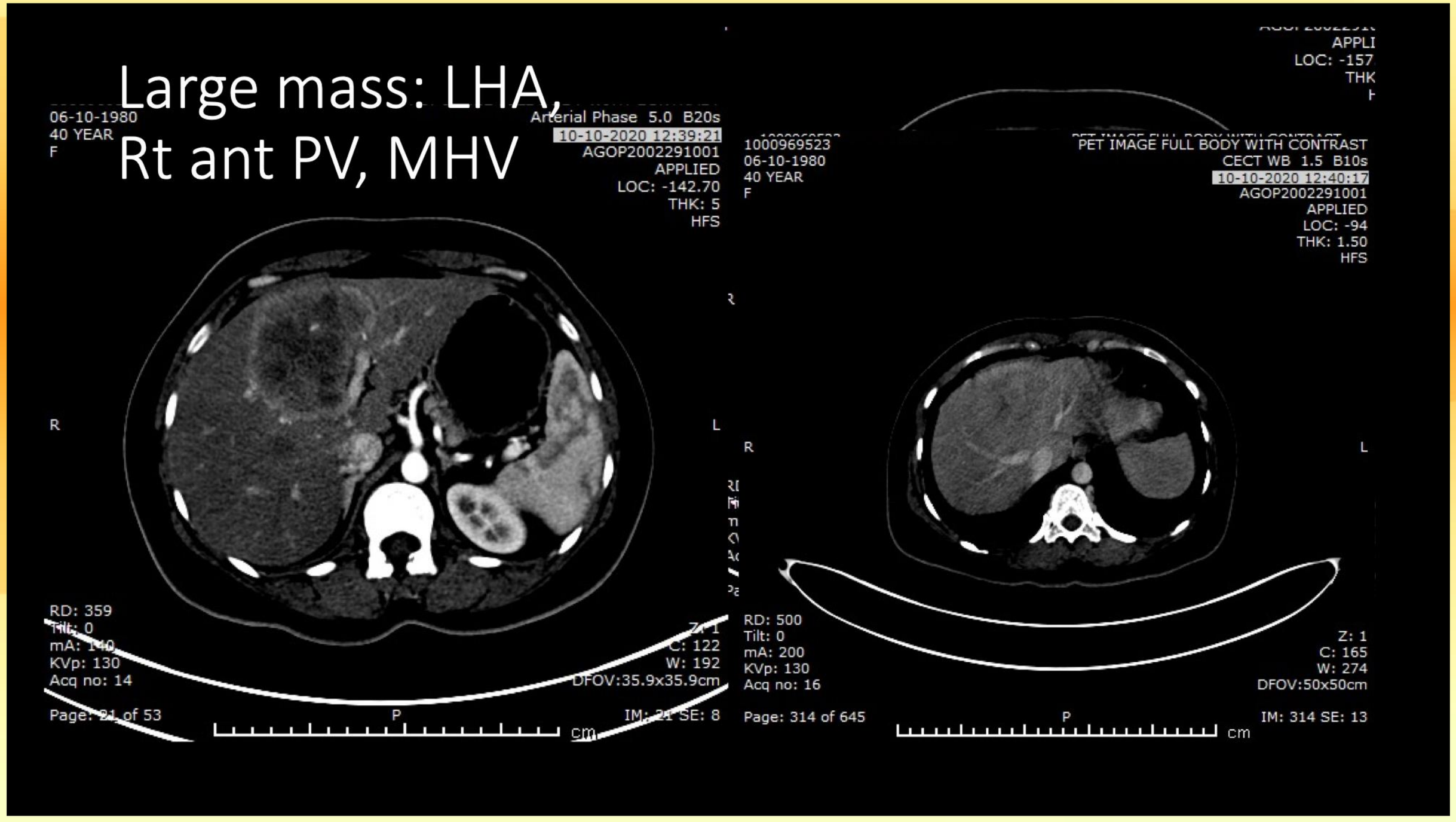
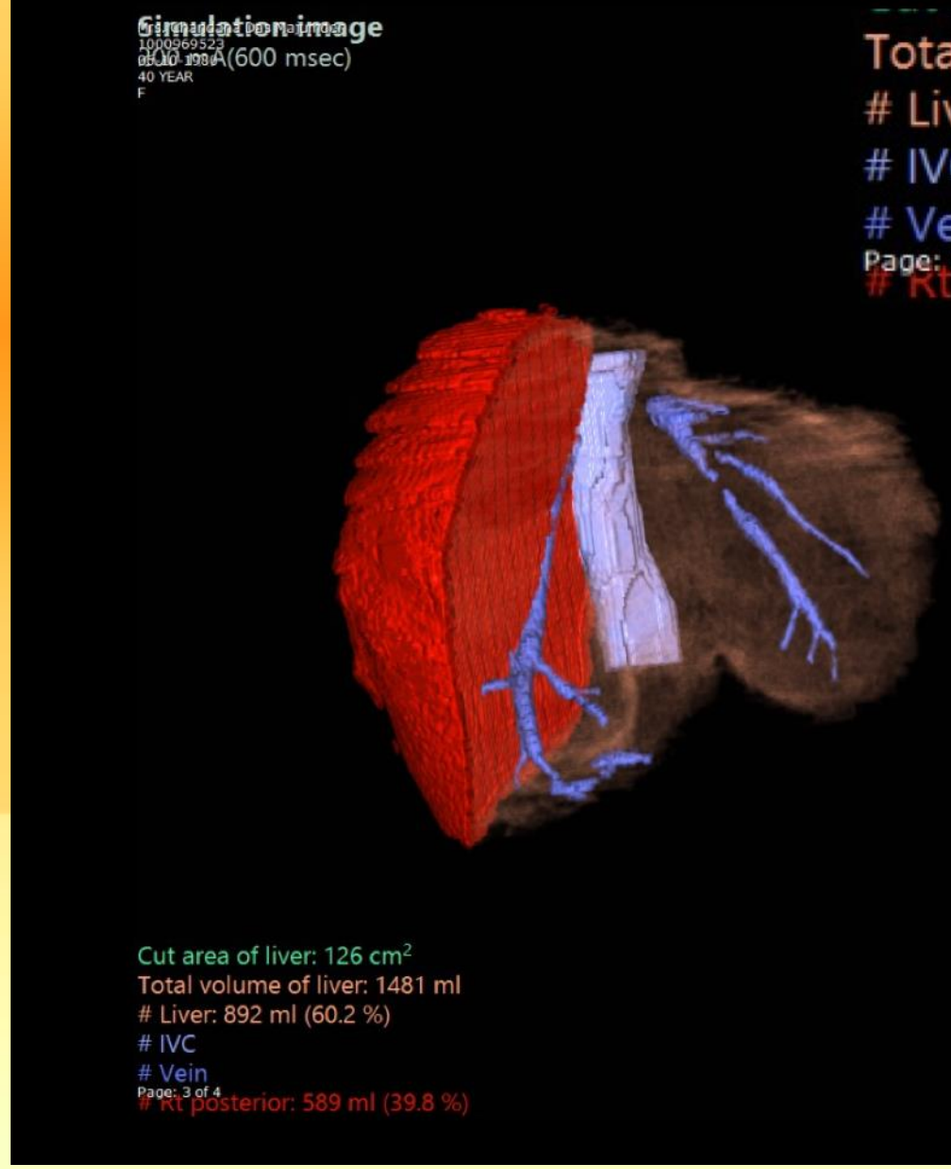


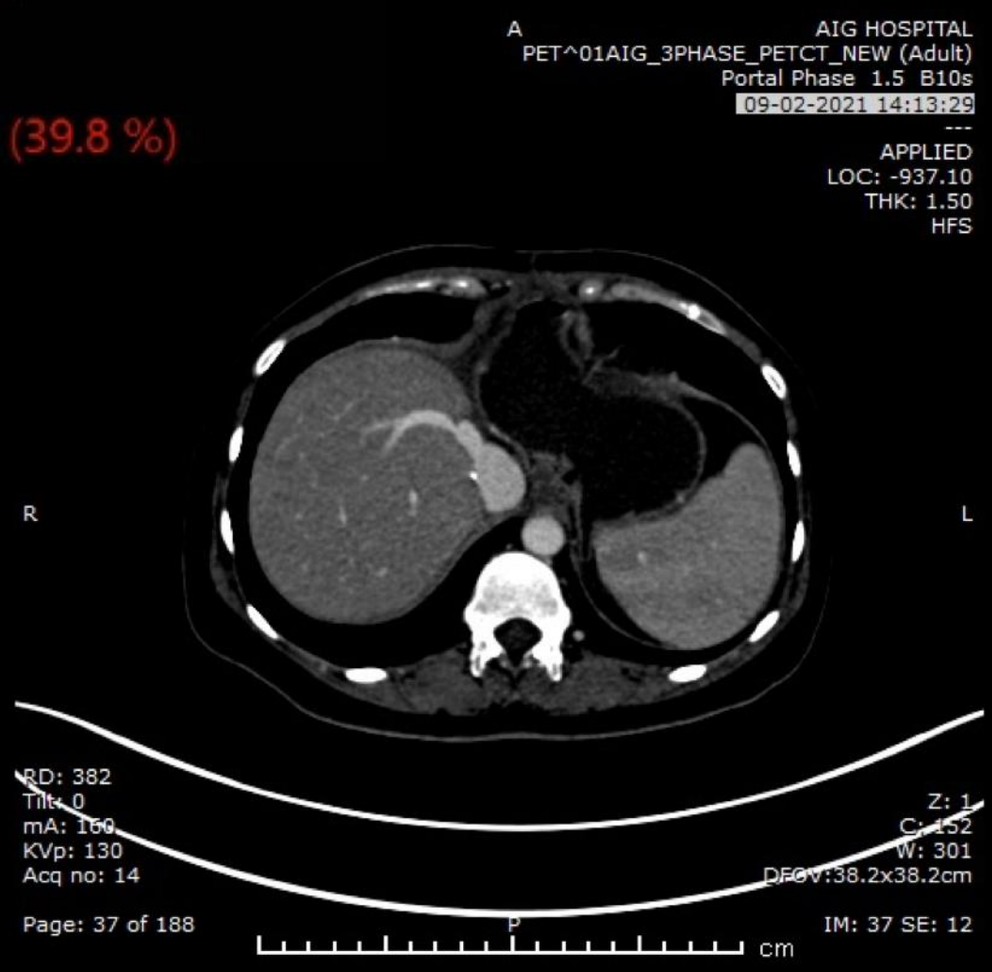
Volumetry


Large mass: LHA,
Rt ant PV, MHV
06-10-1980
40 YEAR
F
Arterial Phase 5.0 B20s
10-10-2020 12:39:21
AGOP2002291001
APPLIED
LOC: -142.70
THK: 5
HFS
R
L
RD: 359
Tilt: 0
mA: 140
KVp: 130
Acq no: 14
Z: 1
C: 122
W: 192
DFOV:35.9x35.9cm
Page: 21 of 53
P
cm
IM: 21 SE: 8
1000969523
06-10-1980
40 YEAR
F
PET IMAGE FULL BODY WITH CONTRAST
CECT WB 1.5 B10s
10-10-2020 12:40:17
AGOP2002291001
APPLIED
LOC: -94
THK: 1.50
HFS
R
L
RD: 500
Tilt: 0
mA: 200
KVp: 130
Acq no: 16
Z: 1
C: 165
W: 274
DFOV:50x50cm
Page: 314 of 645
P
cm
IM: 314 SE: 13

Plan – extended left hepatectomy



Post op



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Strategies to deal with Impaired Functional reserve

- Parenchymal sparing resection
- Resection after PVE
- Resection in combination with RFA
- Two staged Resection ALLPS
- Resection after chemo
- Resection after TACE

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Augmentation of FLRV

PVE

PV ligation

Repeat CT after 3 weeks

FLRV increases by 20- 46 %

Resectability 70 -100%

Can be used as a dynamic test for Liver Regeneration

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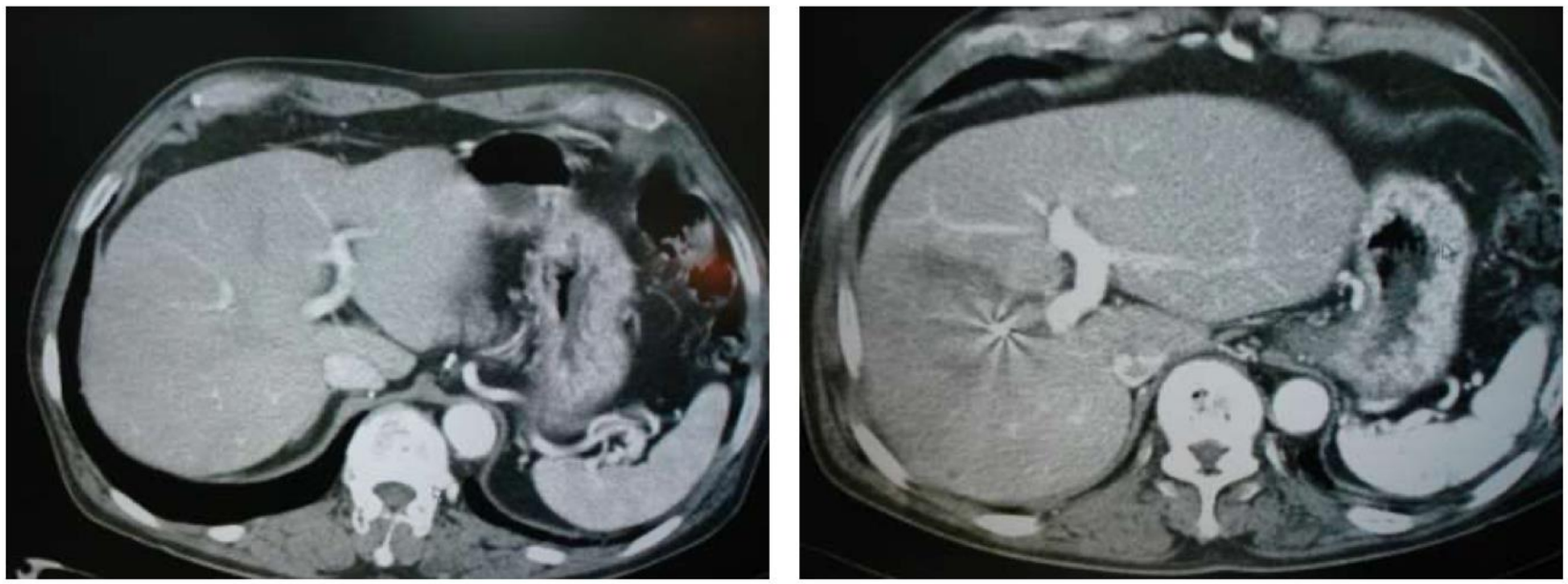
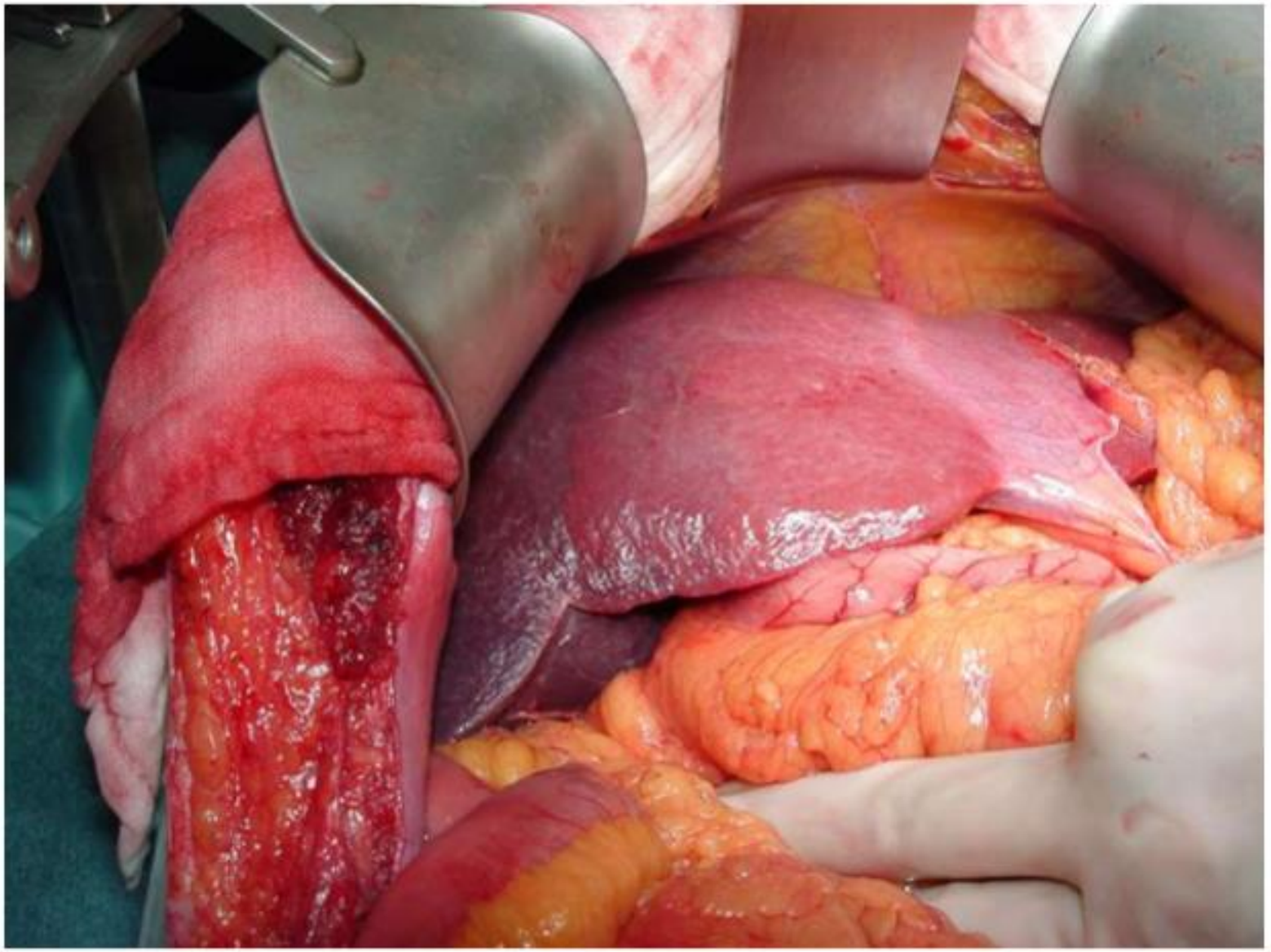
Portal vein embolisation





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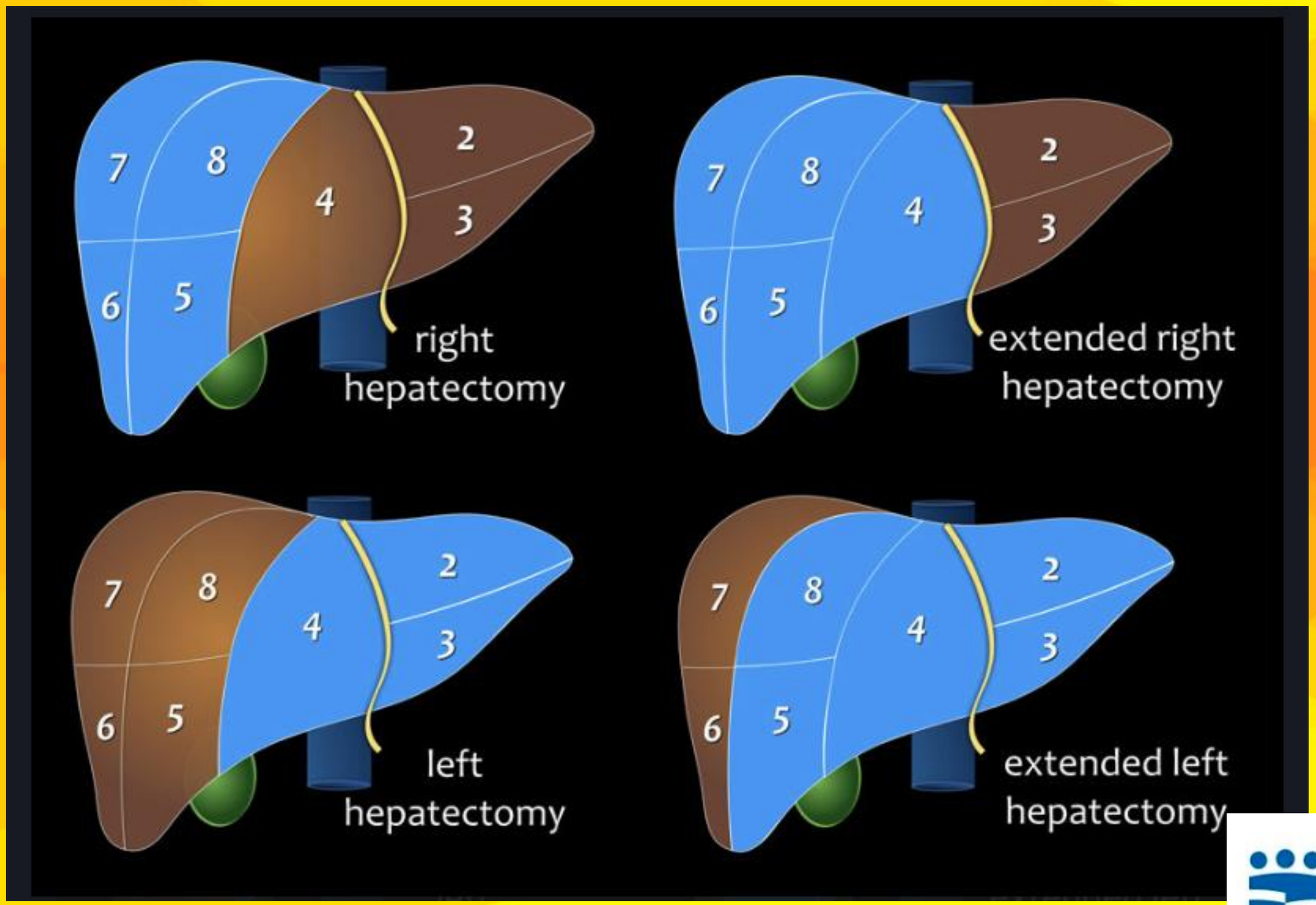
Anatomic VS Non Anatomic Resections

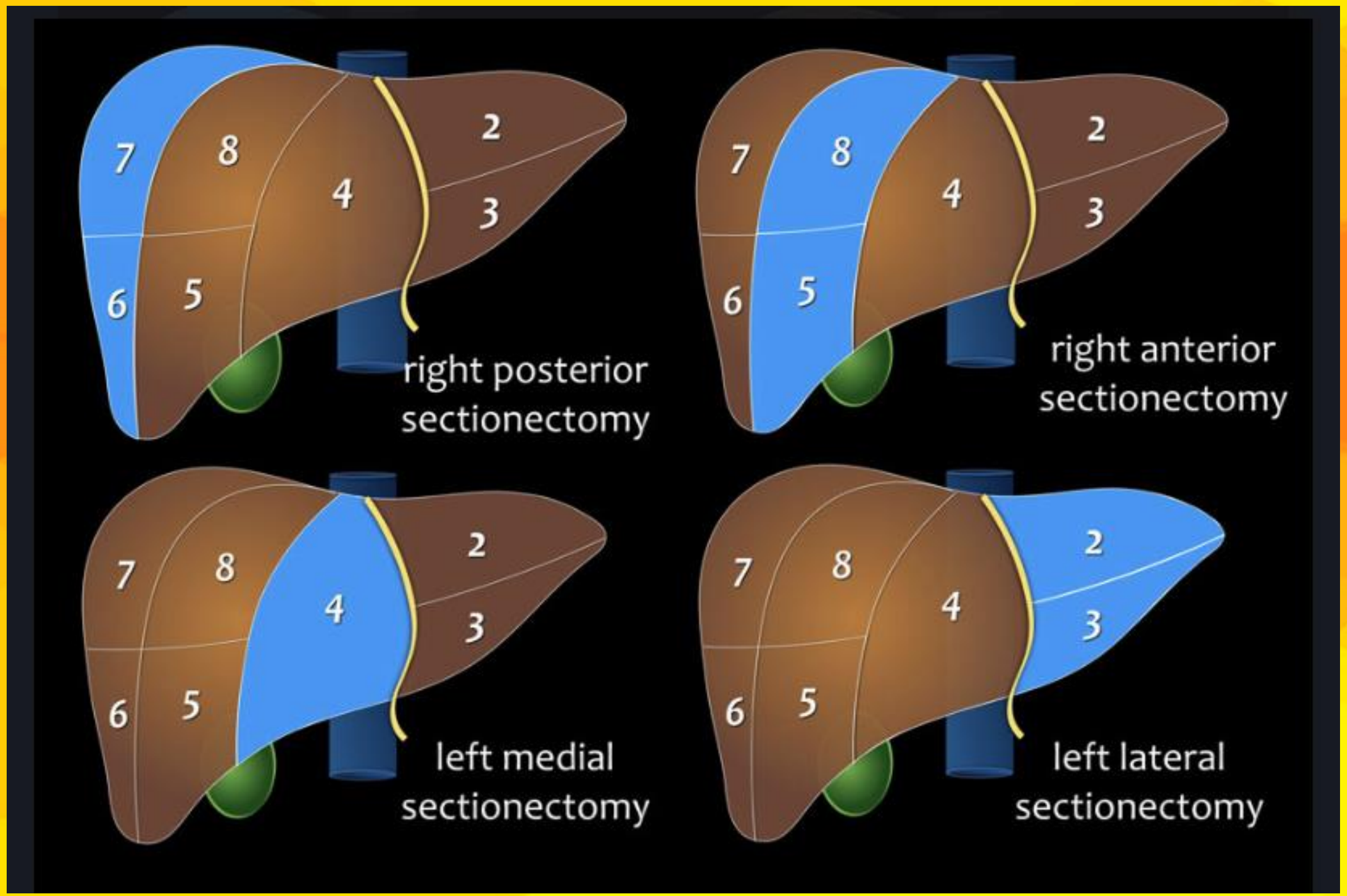
Anatomic vs non-anatomic resections

- Anatomic resections preferred for malignancies
  - ↑ Ro resections
    - (Anatomical vs non-anatomical: 2% positive margins vs 60%)
  - ↓ blood loss
- Non-anatomic resections
  - Preserve parenchyma
  - Indications:
    - Benign hepatic tumours
    - Malignancies in cirrhotic pts
- Margin width? >1mm shown to be adequate

AIG HOSPITALS

ANATOMIC VS NON ANANTOMIC RESECTIONS




7
8
4
2
3
6
5
right posterior
sectionectomy
7
8
4
2
3
6
5
right anterior
sectionectomy
7
8
4
2
3
6
5
left medial
sectionectomy
7
8
4
2
3
6
5
left lateral
sectionectomy

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HEPATOCELLULAR CARCINOMA

Challenges

5th most common cancer world wide

80% of the times develops in a diseased organ.

Disease free survival is relative

Time to symptomatic progression is confounded

Surgical resection or liver transplant - curative

Surgery Remains the Gold Standard

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Resection in Cirrhotics

Best in Single lesions , Asymptomatic

Absent Portal Hypertension

HVPG <10 mm of Hg

Platelet >1L

Normal bilirubin

No Varices

70 % survival at 5 yrs

Only 5-10 % meet the criteria

Lloveet al resection vsTx Hepatology 1999

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Criteria for selection and operability

Anatomical

- Imaging
- Simulation

Functional

- Clinical
- Biochemical
- Functional

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Hepatocellular carcinoma

PRACTICAL APPROACH

Diagnosis - is tissue and issue

Staging (prognosticating) - which system?

Treatment Indications (fitting the treatment to the tumour and the underlying liver disease) - which service knows the best

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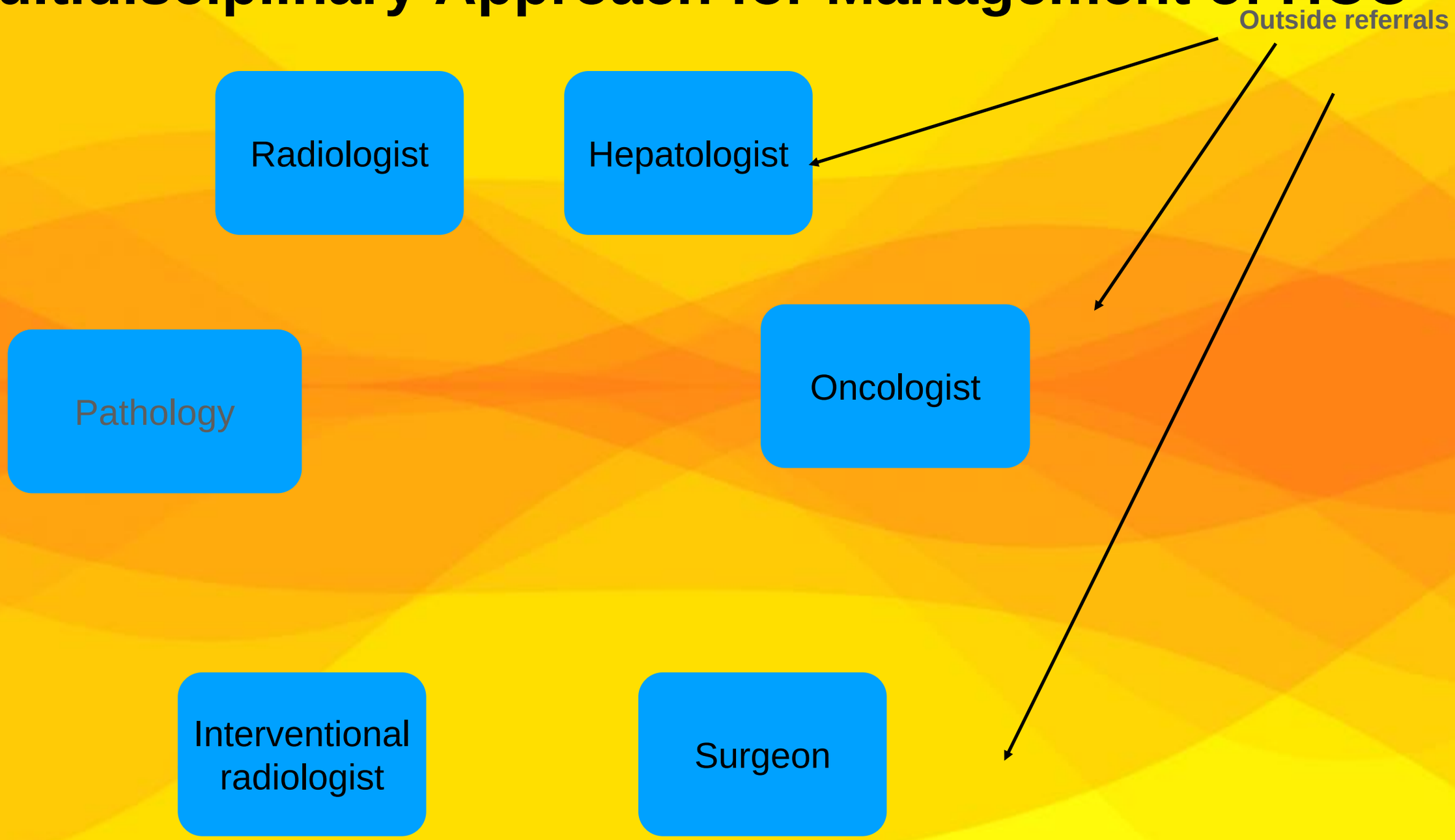
Multidisciplinary Approach for Management of HCC



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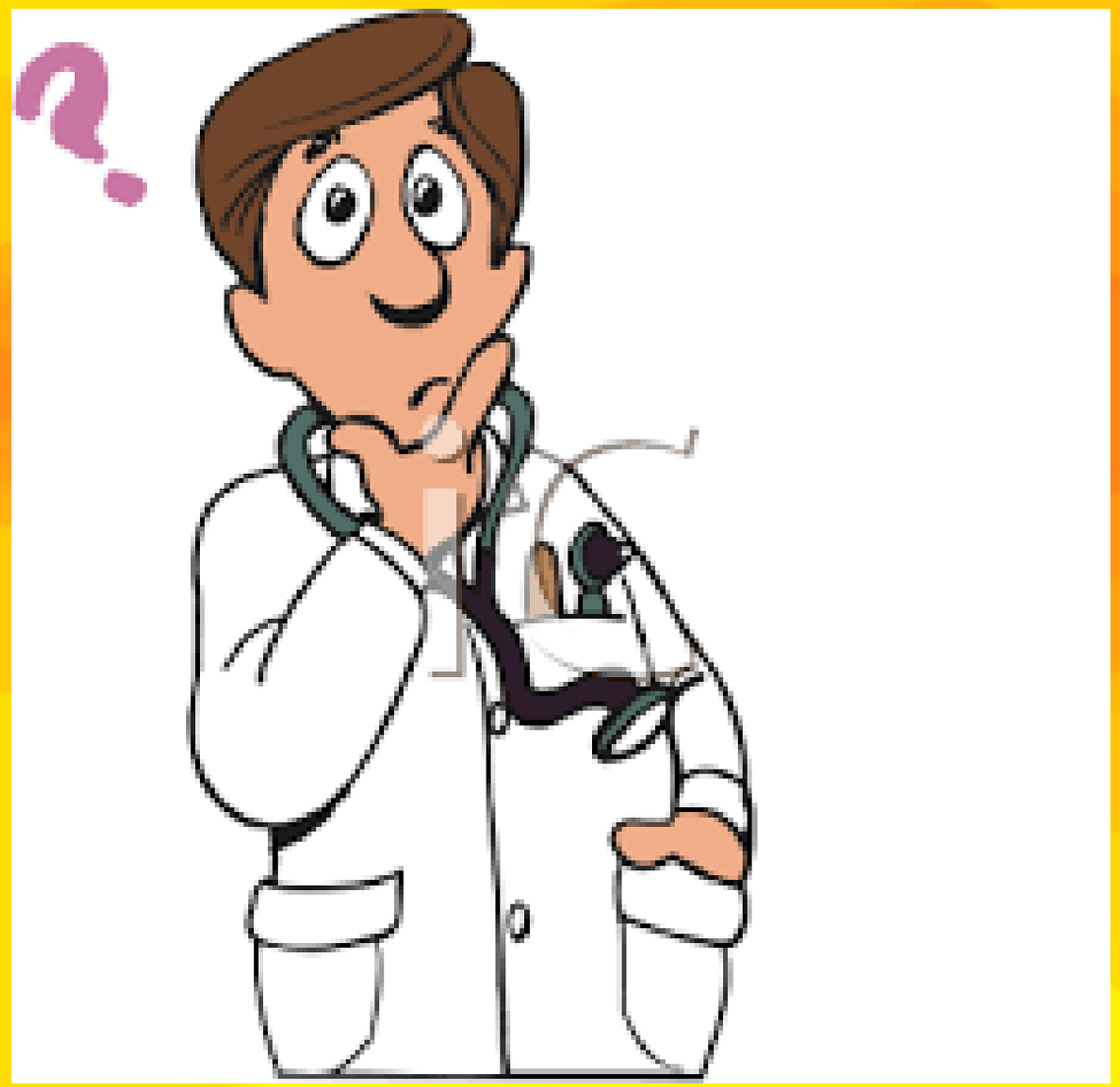
INDIVIDUALISED CARE

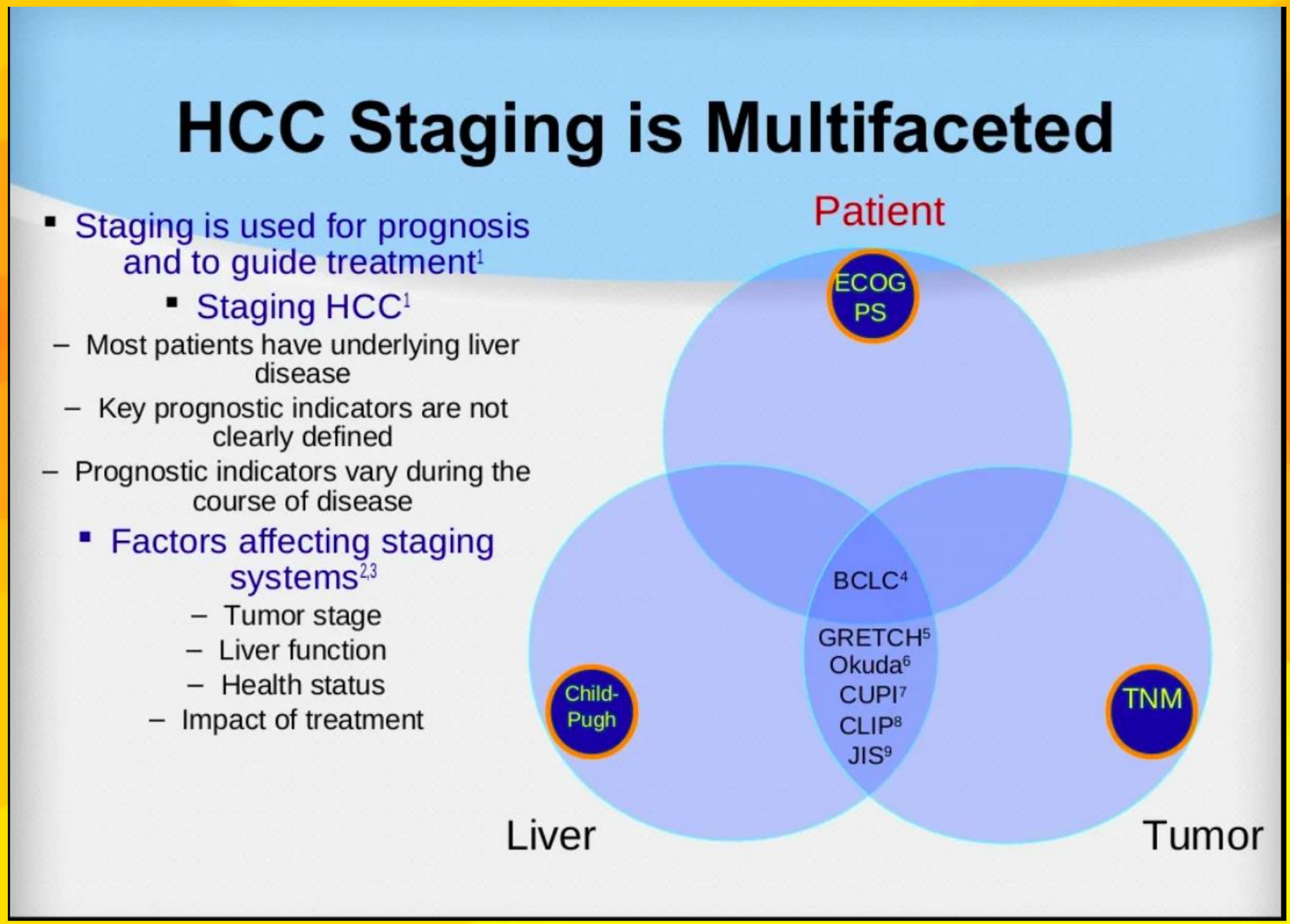
No single staging system with arrows connecting the stage to treatment will be a substitute replace the need to have a thinking clinician

Jordi Bruix, MD;



HCC

Staging


HCC Staging is Multifaceted
Staging is used for prognosis and to guide treatment[1]
Staging HCC[1]
– Most patients have underlying liver disease
– Key prognostic indicators are not clearly defined
– Prognostic indicators vary during the course of disease
Factors affecting staging systems[2,3]
– Tumor stage
– Liver function
– Health status
– Impact of treatment
Patient
ECOG PS
BCLC[4]
GRETCH[5]
Okuda[6]
CUPI[7]
CLIP[8]
JIS[9]
Child-Pugh
TNM
Liver
Tumor

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STAGING

- STAGING
- No single universally accepted staging system (>10 in use)
- Many (AASLD) have adopted the BCLC (validated)
- 5 stages
- Variables
- Tumor stage
- Physical and liver functional status
- Cancer related symptoms
- Treatment Algorithm

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STAGING SYSTEMS

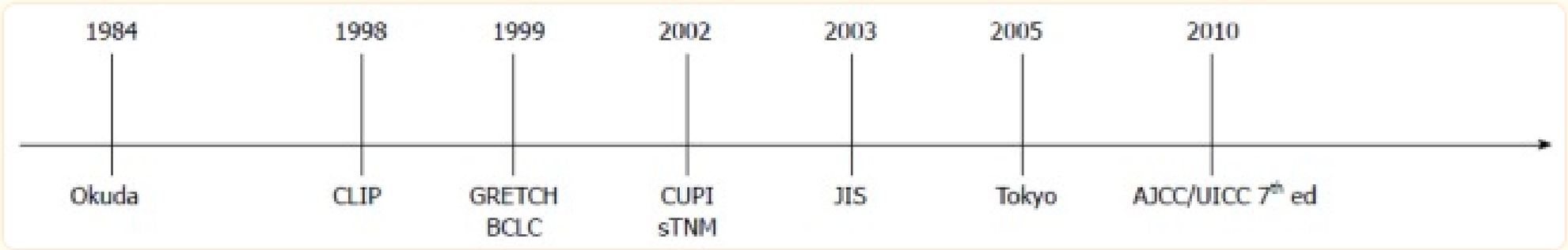

Figure 1

Timeline of hepatocellular carcinoma staging system. AJCC: American Joint Committee on Cancer; UICC: International Union Against Cancer; CLIP: Cancer of the Liver Italian Program; GRETCH: Groupe d'Etude et de Traitement du Carcinome Hépatocellulaire; BCLC: Barcelona Clinic Liver Cancer; CUPI: Chinese University Prognostic Index; JIS: Japan Integrated Staging Score; TNM: Tumor Node Metastasis.

Table 2

Variables included in the main prognostic systems

Variables	Prognostic scores						
	Okuda[13]	CLIP[14]	GRETCH[21]	BCLC[16]	CUPI[23]	JIS[24]	Tokyo[22]
Child-Pugh score		X		X		X	
Ascites	X				X		
Albumin	X						X
Total Bilirubin	X		X		X		X
Alkaline phosphatase			X		X		
Alpha-fetoprotein		X	X		X		
Tumor size	X	X		X			X
Numbers of nodules		X		X			X
TNM stage					X	X	
Portal vein thrombosis		X	X	X			
Metastasis				X			
Portal hypertension				X			
Presence of symptoms and/or General Status			X	X	X		

CLIP: Cancer of the Liver Italian Program; GRETCH: Groupe d'Etude et de Traitement du Carcinome Hépatocellulaire; BCLC: Barcelona Clinic Liver Cancer; CUPI: Chinese University Prognostic Index; JIS: Japan Integrated Staging Score; TNM: Tumor Node Metastasis.

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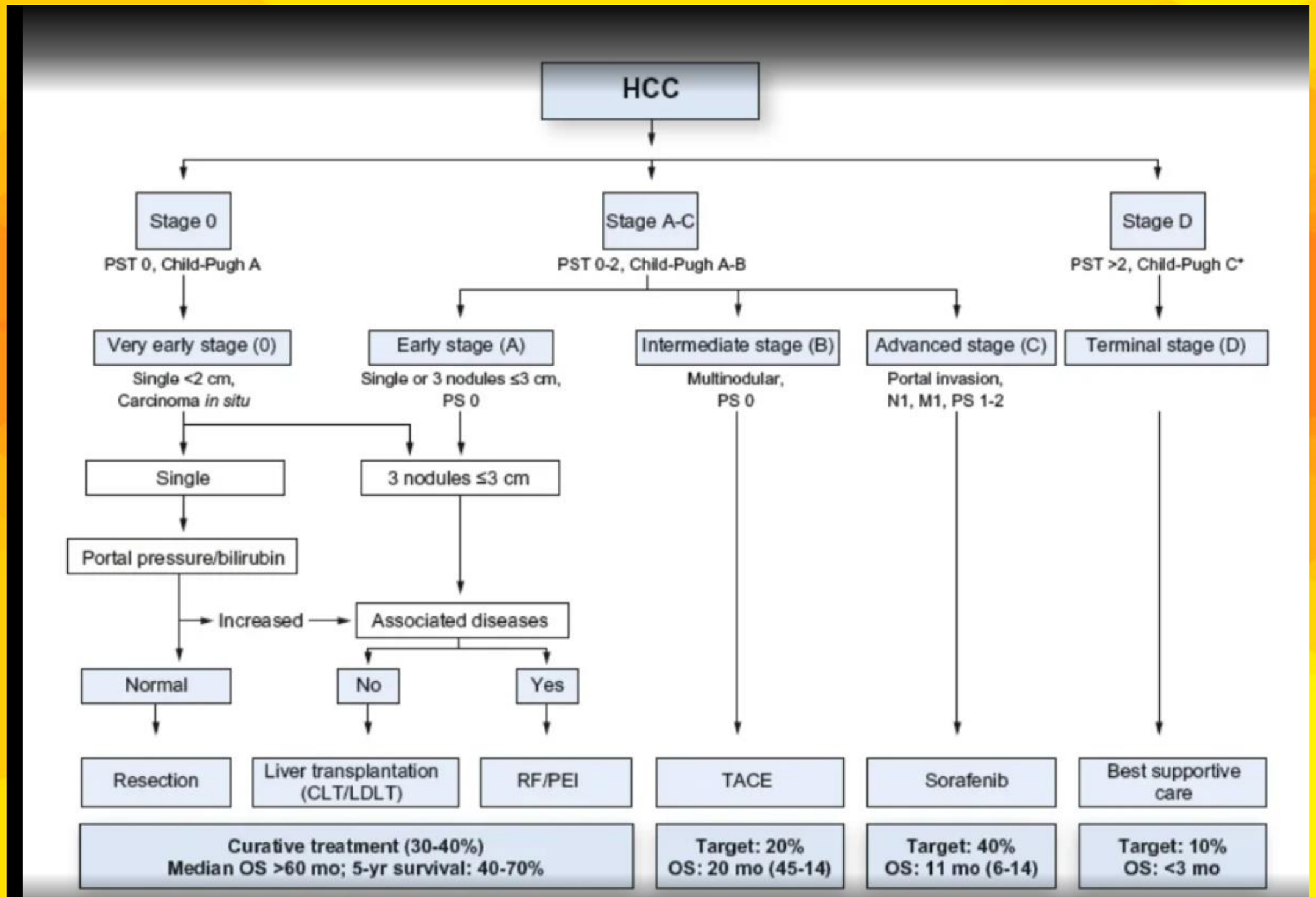
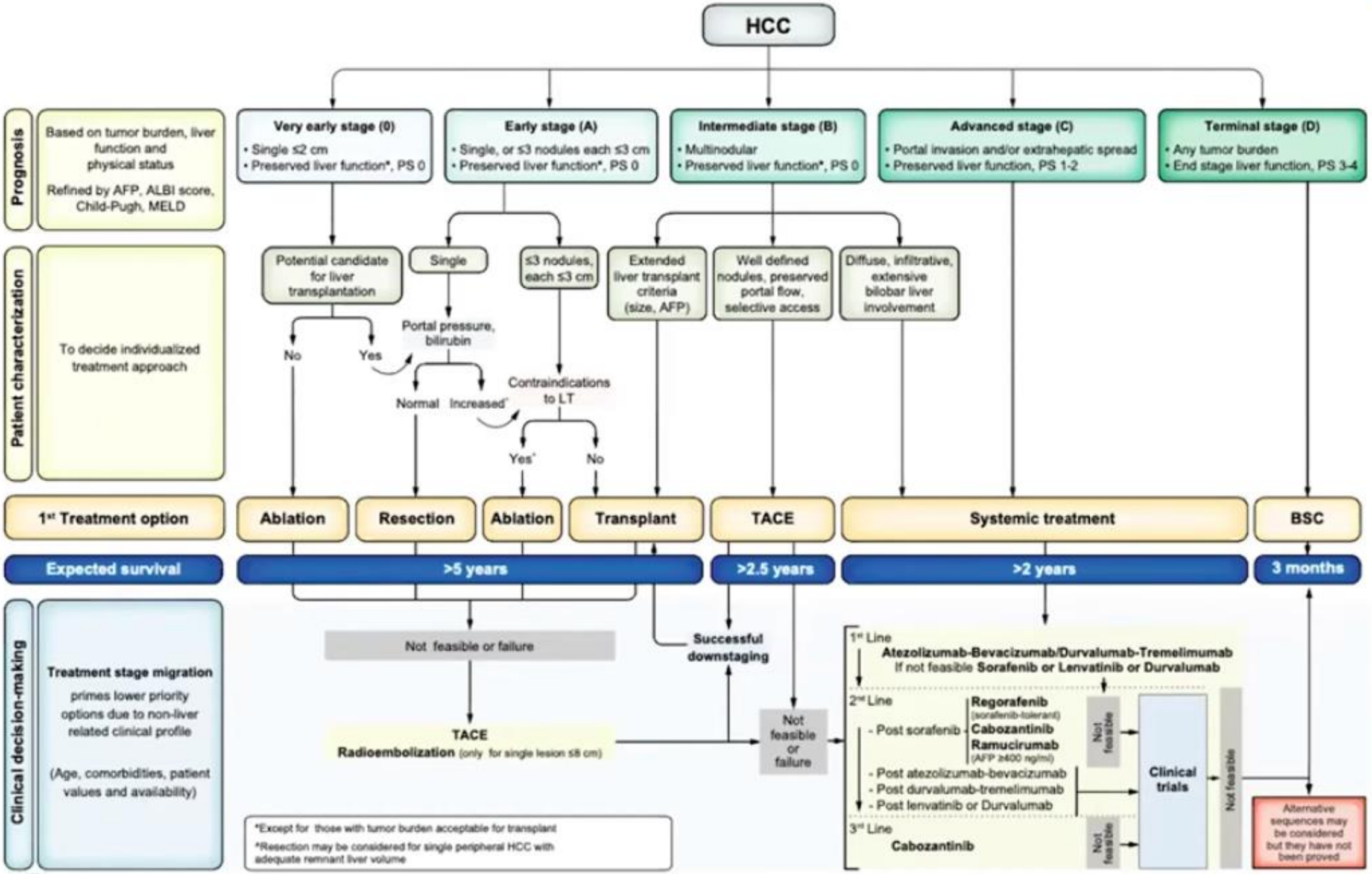
BARCELONA CANCER



BCLC 2022

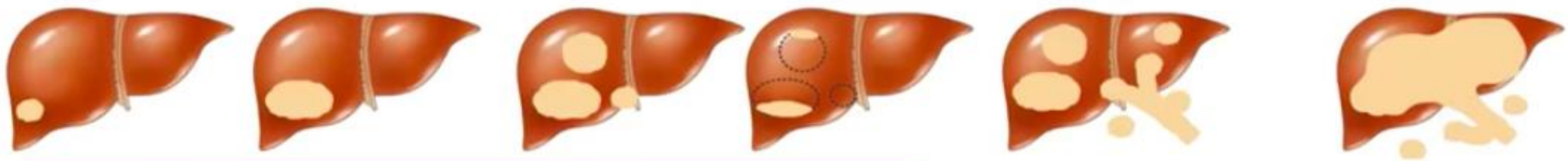

HCC
Prognosis
Based on tumor burden, liver function and physical status
Refined by AFP, ALBI score, Child-Pugh, MELD
Very early stage (0)
• Single ≤2 cm
• Preserved liver function*, PS 0
Early stage (A)
• Single, or ≤3 nodules each ≤3 cm
• Preserved liver function*, PS 0
Intermediate stage (B)
• Multinodular
• Preserved liver function*, PS 0
Advanced stage (C)
• Portal invasion and/or extrahepatic spread
• Preserved liver function, PS 1-2
Terminal stage (D)
• Any tumor burden
• End stage liver function, PS 3-4
Patient characterization
To decide individualized treatment approach
Potential candidate for liver transplantation
Single
≤3 nodules, each ≤3 cm
Extended liver transplant criteria (size, AFP)
Well defined nodules, preserved portal flow, selective access
Diffuse, infiltrative, extensive bilobar liver involvement
No
Yes
Portal pressure, bilirubin
Normal
Increased*
Contraindications to LT
Yes*
No
1st Treatment option
Ablation
Resection
Ablation
Transplant
TACE
Systemic treatment
BSC
Expected survival
>5 years
>2.5 years
>2 years
3 months
Clinical decision-making
Treatment stage migration
primes lower priority options due to non-liver related clinical profile
(Age, comorbidities, patient values and availability)
Not feasible or failure
Successful downstaging
TACE
Radioembolization (only for single lesion ≤8 cm)
Not feasible or failure
1st Line
Atezolizumab-Bevacizumab/Durvalumab-Tremelimumab
If not feasible Sorafenib or Lenvatinib or Durvalumab
2nd Line
- Post sorafenib
Regorafenib (sorafenib-tolerant)
Cabozantinib
Ramucirumab (AFP ≥400 ng/ml)
- Post atezolizumab-bevacizumab
- Post durvalumab-tremelimumab
- Post lenvatinib or Durvalumab
3rd Line
Cabozantinib
Not feasible
Not feasible
Clinical trials
Not feasible
Alternative sequences may be considered but they have not been proved
*Except for those with tumor burden acceptable for transplant
*Resection may be considered for single peripheral HCC with adequate remnant liver volume

Prognosis

Based on tumor burden, liver function and physical status

Refined by AFP, ALBI score, Child-Pugh, MELD

Very early stage (0)	Early stage (A)	Intermediate stage (B)	Advanced stage (C)	Terminal stage (D)
• Single ≤2 cm • Preserved liver function*, PS 0	• Single, or ≤3 nodules each ≤3 cm • Preserved liver function*, PS 0	• Multinodular • Preserved liver function*, PS 0	• Portal invasion and/or extrahepatic spread • Preserved liver function, PS 1-2	• Any tumor burden • End stage liver function, PS 3-4



Preserved liver function*

*Except for those with tumour burden acceptable for Transplant

Child-Pugh score

- **Ascites**
  - ✓ Minor ascites, easy to treat
  - ✓ Tense ascites, high diuretics dosing
  - ✓ Refractory ascites, hyponatremia
  - ✓ Spontaneous bacterial peritonitis
- **Encephalopathy**
  - ✓ Secondary due to infection, constipation, etc
  - ✓ Recurrent encephalopathy
- Bilirubin
- Prothrombin time
- Albumin

Pugh et al. Br J Surg 1973.

ALBI score

- Albumin
- Bilirubin

Johnson et al. J Clin Oncol 2015

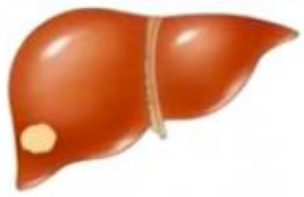
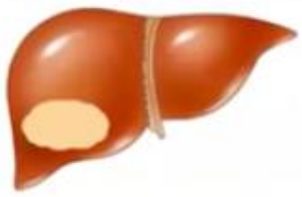
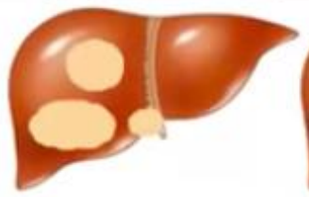
MELD/MELD-Na score

- Creatinine
- Bilirubin
- INR
- Sodium

Kamath et al. Hepatology 2001; Kim et al. N Engl J Med 2008

Alfafeto-Protein (AFP)

Takayasu et al Gastroenterology 20216;
et al. Gastroenterology 2021;
Cabibbo et al.World JHepatol 2012

Prognosis	Based on tumor burden, liver function and physical status Refined by AFP, ALBI score, Child-Pugh, MELD	**Very early stage (0)** • Single ≤2 cm • Preserved liver function*, PS 0	**Early stage (A)** • Single, or ≤3 nodules each ≤3 cm • Preserved liver function*, PS 0	**Intermediate stage (B)** • Multinodular • Preserved liver function*, PS 0	**Advanced stage (C)** • Portal invasion and/or extrahepatic spread • Preserved liver function, PS 1-2	**Terminal stage (D)** • Any tumor burden • End stage liver function, PS 3-4
						
ALBI score						
Child-Pugh score		✓	✓	✓	✓	✓
MELD		✓	✓	✓		
AFP		✓	✓	✓	✓	

- Variceal bleeding
- Malnutrition
- Hepatorenal syndrome
- Arterial hypotension

Child-Pugh, MELD, ALBI do not identify
100% of endstage patients

Clinical Decision-Making

Johnson et al. J Clin Oncol 2015; Pinato et a. J Hepatol 2017; Pugh et al. Br J Surg 1973; Kamath et al. Hepatology 2001; Kim et al. N Engl J Med 2008Kim et al. Gastroenterology 2021.

de Franchiset al.J Hepatol 2015; D'Amico et al. J Hepatol 2018;Garcia-Tsaoet al.Hepatology 2010;Tonon et al. Clin Gastroenterol Hepatol 2021; Llach J et al. Gastroenterology 1988

Downstaging in BCLC 2022 approach

The goal of downstaging is to reduce tumour burden in order for residual viable tumours to fall within acceptable LT criteria,
with Milan Criteria being the commonest endpoint of downstaging

TACE?
TARE?
SBRT?

Mazzaferro et al Lancet Oncol 2020; Yao et al. Hepatology 2015

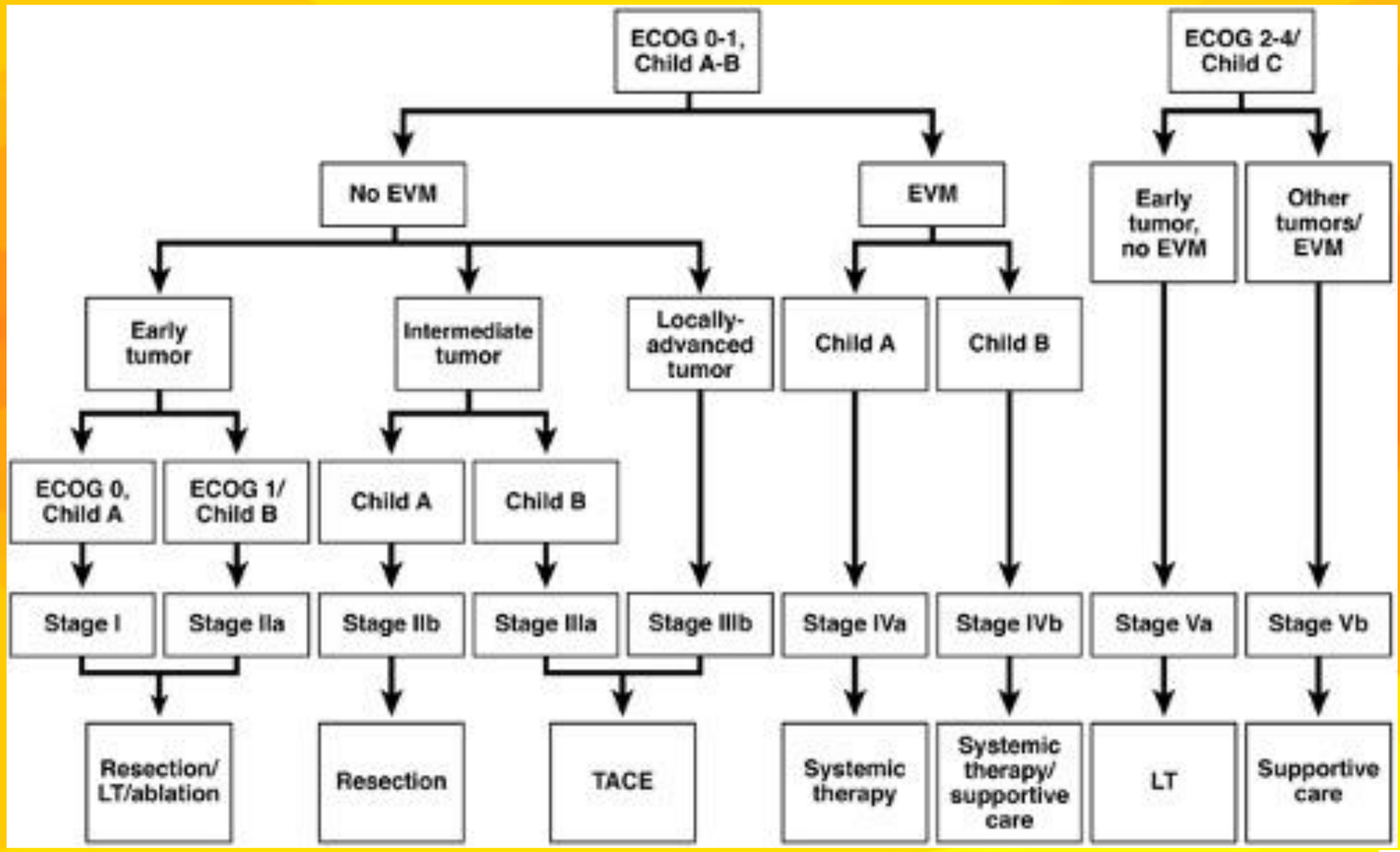
- The upper limit of where a downstaging approach is considered varies across LT regions.
- This also affects the specific imaging criteria used to define baseline and post-treatment staging and evaluation of response.
- There is need to develop further studies to validate such approach and establish how to best apply a downstaging protocol.

Patients with an AFP >1000 ng/mL who experienced biochemical response (at least a decrease to >500 ng/mL) to locoregional therapies have a post-LT outcome comparable to the reported within MC

Mehta et al. Hepatology 2019; Mehta et al. Transplantation 2020

HCC

Hongkong liver cancer staging system



Gastroenterology 2014 1461691-1700.e3DOI: (10.1053/j.gastro.2014.02.032)

Gastroenterology 2014 1461691-1700.e3DOI: (10.1053/j.gastro.2014.02.

AIG HOSPITALS

Prognosis

Based on tumor burden, liver function and physical status

Refined by AFP, ALBI score, Child-Pugh, MELD

Patient characterization

To decide individualized treatment approach

1st Treatment option

Expected survival

Clinical decision-making

Treatment stage migration

primes lower priority options due to non-liver related clinical profile

(Age, comorbidities, patient values and availability)

Evidence-based

Clinical-Practice

QUESTIONS TO BE ASKED IN CLINICAL PRACTICE

TUMOR CHARACTERISTICS

Diagnosis , is biopsy needed

Segmental anatomy

Tumour size and no

Extra hepatic spread

CONDITION OF THE LIVER

Functional status

Is there e/o Portal hypertension

What is the FLRV

PATIENT FACTORS

Age

Co morbidities

Performance status

FITTING THE TREATMENT TO THE TUMOUR AND THE UNDERLYING LIVER DISEASE

EVALUATION OF THE HEPATIC RESERVE OF PATIENTS WITH HCC

Quantity and Quality of the FLRV

Quantity

>25% for normal liver

>40 % for Cirrhotic Liver

(Schindl MJ et , Gut 2005 adnd Shoup et al J gastrointest Surg 2003)

Quality -

LFT (alb , INR Platelets

HVPG

OGD

Liver Biopsy

HCC

Resection for HCC

NON CIRRHOTIC. - Only 5-10 % of the patients

Extended Resections can be done after proper evaluation

CIRRHOTIC — Child s A - Major hepatectomy(Avoid R hepatectomy)

Child s B - segmental or subsegmental resection

Child S C - contraindication for resections

HCC

Resection for HCC

5 years Survival after Resection

Function	Single		Multiple	
	PHT**	No PHT	PHT	No PHT
Child-Pugh A	68%	71%	58%	56%
Child-Pugh B	Over all 5 year survival 19%			
Resection after recurrence*	79%	81%	73%	73%

*3 year survival

**PHT defined as varices and or platelets less than 100000

Ishizawa T, Gastroenterology. 2008;134:1908–16.

Resection after Downstaging

Neoadjuvant and down staging prior to resection

Not recommended if the tumour is resectable

Delay

Technically more difficult

May be associated with more morbidity

Not resectable due to anatomic reasons , 6-28% become resectable

Recurrence rate is 40 -85 %

Survival , 5 year 25 to 60 %

HCC

Practicality of liver resections

- 20 % who meet the current EASL/AASLD criteria are denied surgery and this increases mortality
- Common practice is to offer surgery beyond the criteria
- Down staging and LR is offered for patients who have locally advanced tumour
- Downstaging and LR has better survival compared to locaregional therapies like TACE
- In real life LR for HCC is based on individual componentsand local conditions which are not captured by guidelines

HCC

WHAT EXTENT CAN WE GO ?

Surgical treatment of hepatocellular carcinoma

HEPATOLOGY

AASLD

CORRESPONDENCE HEPATOLOGY, March 2016

Hepatic Surgeons Are Like the Child Who Rescued Dying Fish

TO THE EDITOR:

Let us first share with you a story. Under a scorching sun, numerous fish were stranded on the beach after a receding tide, waiting to die. A child picked these fish up one by one and threw them back into the sea. An old man asked the child, "There are so many of them, who cares for one or two fish?" The child did not stop his work and replied, "Look, this one cares, and that one cares too."

We, hepatic surgeons, are like this child. We are aware that we are unable to cure all our patients with hepatocellular carcinoma (HCC), but we never stop to give a chance of cure to them by surgery. Although the current European and American guidelines for HCC do not recommend hepatic resection for patients with intermediate or advanced HCCs, with Child B liver function, or concurrent portal hypertension, many hepatic surgeons around the world still operate on such patients on a selective basis provided the perioperative mortality and morbidity rates are estimated to be low.[1-3] In real life, a significant proportion of these patients would also choose surgical resection because of the potential cure despite a high tumor recurrence rate after resection.

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Second Military Medical University
Shanghai, China
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Hong Kong SAR, China

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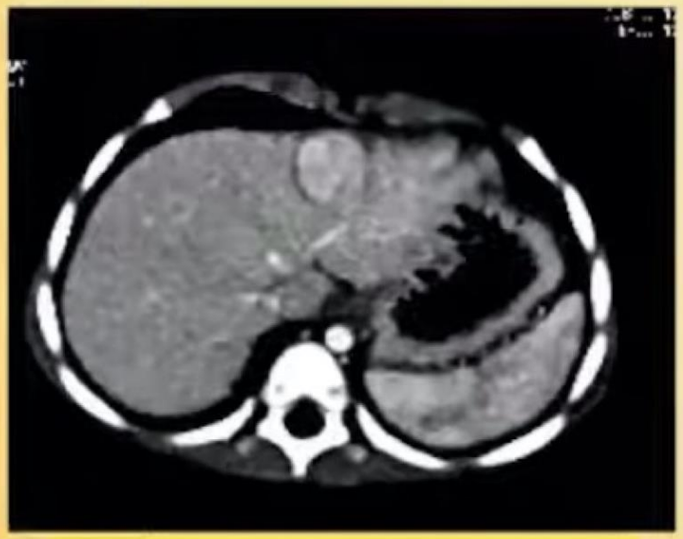
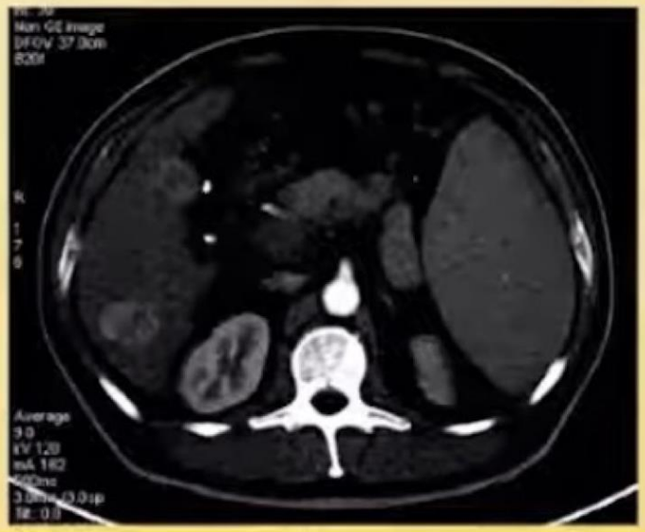
Liver Transplantation for HCC

Liver Transplantation for HCC

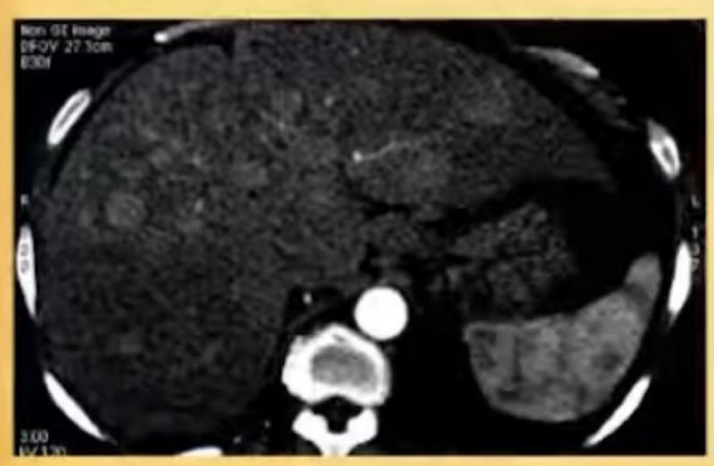
HCC – A wide Spectrum



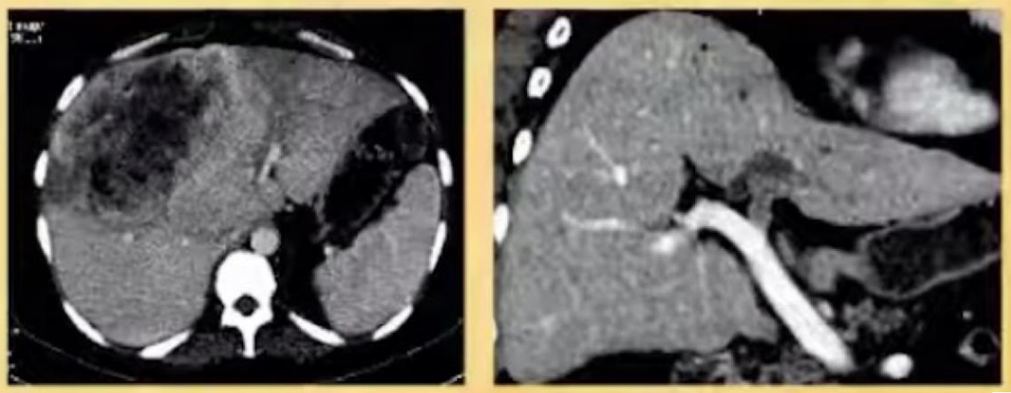
Early HCC, single lesion



< 3 tumours < 3 cm max dia



Multifocal HCC



Large HCC with vascular involvement

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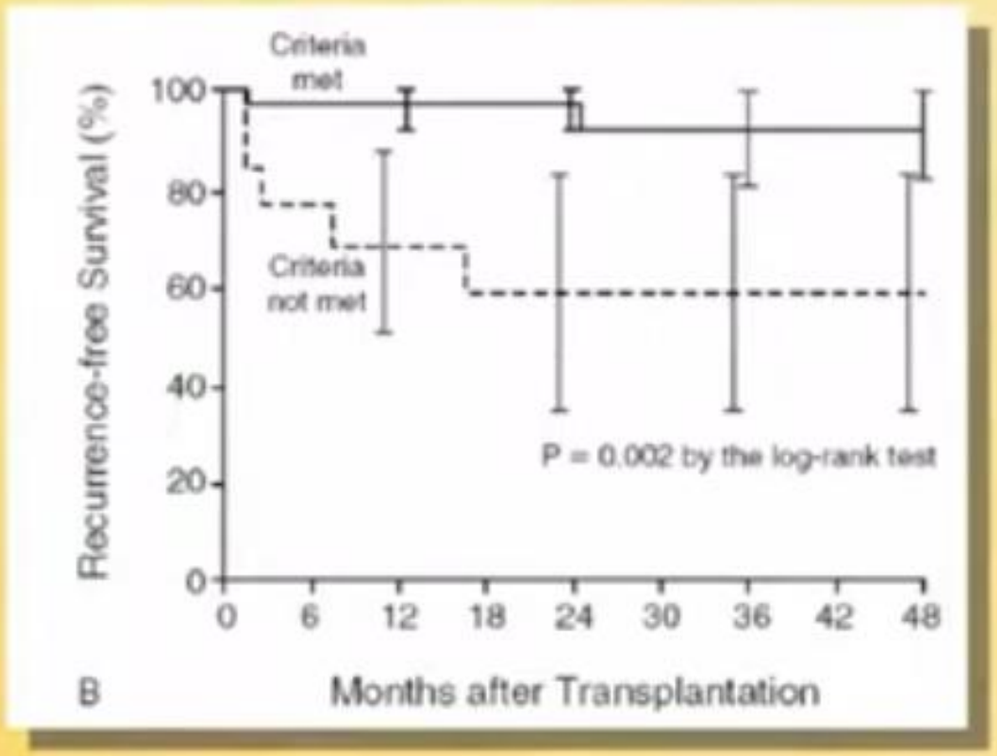
LIver Transplantation for HCC

Conventional Criteria – LT for HCC

Milan group -- *single ≤ 5cm, ≤ 3 tumours ≤ 3cm (on imaging)*

***Mazaffero et al, NEJM 1996*



4yr OS 75%
DFS 83%

~ Accepted by UNOS as "Conventional Criteria" since 1998

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UCSF Criteria

- Lesion <6.5cm
- 2-3 lesions
  - -Largest <4.5cm
  - -total dia <8cm
- No vascular invasion
- No extrahepatic metastases
- One yr survival 90%
- Five yr survival 75%

Yao FY etal.Hepatology2001;33: 1394-403

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Liver Transplantation for HCC

EXPANDED CRITERIA

Published expanded criteria – DDLT

Criteria Name, year	Criteria	No. of patients	OS / RFS using expanded criteria	OS / RFS for within Milan	Prognostic factors
Pamplona Criteria, 2001	1 nodule ≤ 6 cm or 2-3 nodules ≤ 5 cm	63 pts, 12 beyond Milan	79% OS at 5 yrs in entire group, 70% RFS	NA	-
Mt.Sinai criteria, 2002	≥ 1 nodule 5-7 cm (with neoadjuvant Chemo + TACE)	31 pts in expanded criteria	55% 5 yr OS in pts beyond Milan and within Mt.Sinai	NA	-
Edmonton Criteria, 2004	1 nodule <7.5 cm, or any number < 5 cm	40 pts, 21 pts beyond Milan	83% 4 yr OS and 77% RFS	87% OS at 4 yrs	Sirolimus helps in beyond criteria
UCSF Criteria, 2007	Single tumour ≤ 6.5 or ≤ 3 nodules ≤ 4.5 and TTD ≤ 8 cm	168, 38 beyond Milan	75% OS at 5 yrs, RFS 93%	80% OS 5 yrs, RFS 90%	-
Up to Seven, 2009	Seven as sum of largest tumour dia (cm) and no. of tumours	1556 pts, 1112 beyond Milan	71.2% OS at 5 yrs	73% OS for within Milan	MVI significantly affects survival
UNOS Region 4,R4T3 Criteria. 2010	1 lesion <6 cm; ≤3 lesions, none >5 cm and total dia <9 cm	445 pts, 363-MC and 82 expanded	3 yr OS 77.1%, RFS 86.9%	3 yr OS 72.9%, RFS 90.5%	-

Upto 3 nodules, upto 7.5cm max dia

31 to 1556 pts

> 70 % 5-yr OS in most

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Liver Transplantation for HCC

EXPANDED CRITERIA

Published expanded criteria – LDLT

Criteria Name, year	Criteria	No. of patients	OS / RFS using expanded criteria	OS / RFS for within Milan	Prognostic factors
Tokyo (5-5 rule), 2007	≤ 5 nodules and ≤ 5 cm	Total 78 patients	5-yr OS 75% 5-yr RFS 94%	-	-
Kyoto Criteria, 2007	≤ 10 nodules , all ≤ 5 cm and DGCP (PIVKA II) ≤ 400 mAU/ml	Total 136, 62 beyond Milan	87% OS and 5% recurrence rate at 5 yrs	10% recurrence rate at 5 yrs for tumours in Milan	-
Asan Criteria, 2008 (on explant path)	tumor diameter ≤ 5 cm, ≤ 6 lesions, no gross vascular invasion	221 patients	82% 5 yr OS	76% for within Milan	Higher discriminatory power compared to Milan and UCSF
Kyushu Criteria, Japan, 2009	Any number of tumours, < 5 cm in size, PIVKA II <300	90 pts, 54 pts beyond Milan	83% OS at 5 yrs 87% RFS at 5 yrs	95.6% OS at 5 years	Pre-op DGCP ≥ 300 mAU/mL and tumour size ≥ 5 cm
Hangzhou, 2008	Tumour size <8 cm in total, any tumour number. If >8 cm, gr I/II + AFP <400 ng/mL	92 patients	72% 5-yr OS		Preop AFP and tumour differentiation
Toronto Criteria, 2011	No number-size criteria. Poor tumour differentiation as exclusion	294 patients	70% OS and 70% DFS at 5 yrs	72% OS at 5 years	-

71 to 221 pts | Upto 10 cm, upto any no. | > 75% OS, > 70 % RFS | Outcomes comparable to within Milan

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LIVER TRANSPLANTATION FOR HCC

EXTENDED CRITERIA

Published expanded criteria – LDLT

Criteria Name, year	Criteria	No. of patients	OS / RFS using expanded criteria	OS / RFS for within Milan	Prognostic factors
Tokyo (5-5 rule), 2007	≤ 5 nodules and ≤ 5 cm	Total 78 patients	5-yr OS 75%	-	-
Kyoto Criteria, 2007					-
As					
Jap					≥ 5 cm
Hangzhou, 2	number. If >8 I/II + AFP <400 ng/mL				AFP and tumour differentiation
Toronto Criteria, 2011	No number-size criteria. Poor tumour differentiation as exclusion	294 patients	70% OS and 70% DFS at 5 yrs	72% OS at 5 years	-

~ Significant expansion beyond Milan

~ Mostly from the Asian countries where DDLT is not common

~ Main impetus -- No EHD and no gross vascular invasion (not so much number/size)

~ Use of tumour markers in prediction of outcomes – tumour biology

71 to 221 pts | Upto 10 cm, upto any no. | > 75% OS, > 70 % RFS | Outcomes comparable to within Milan

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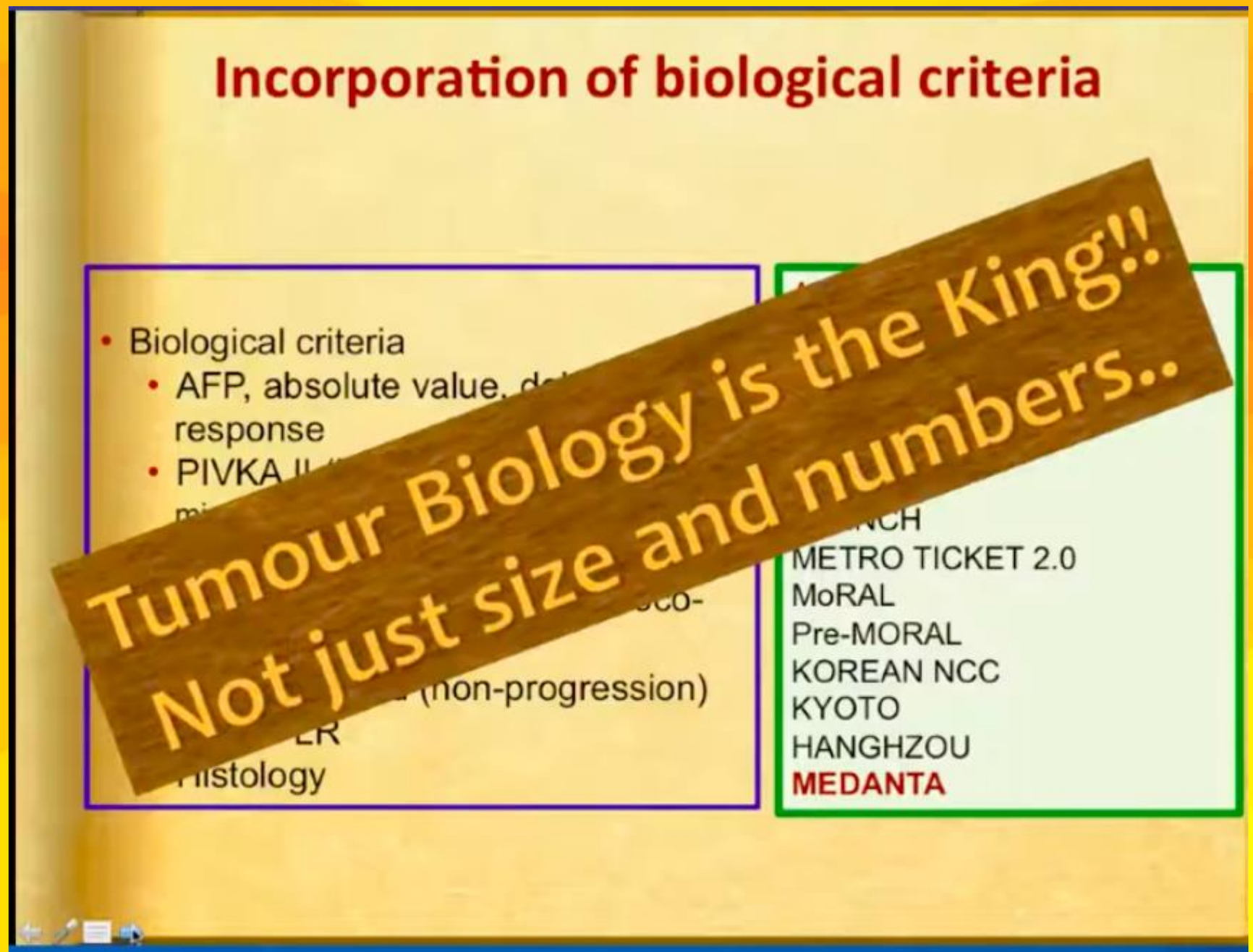
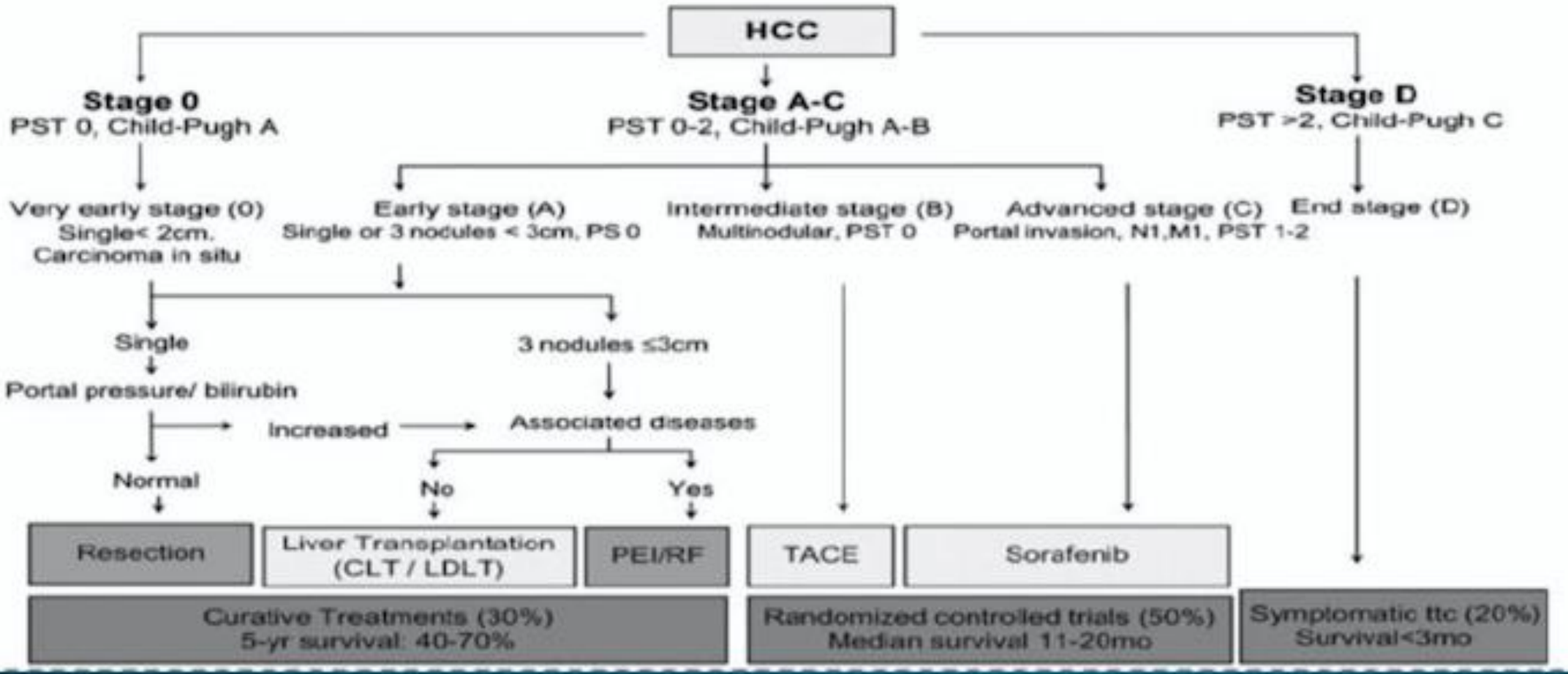
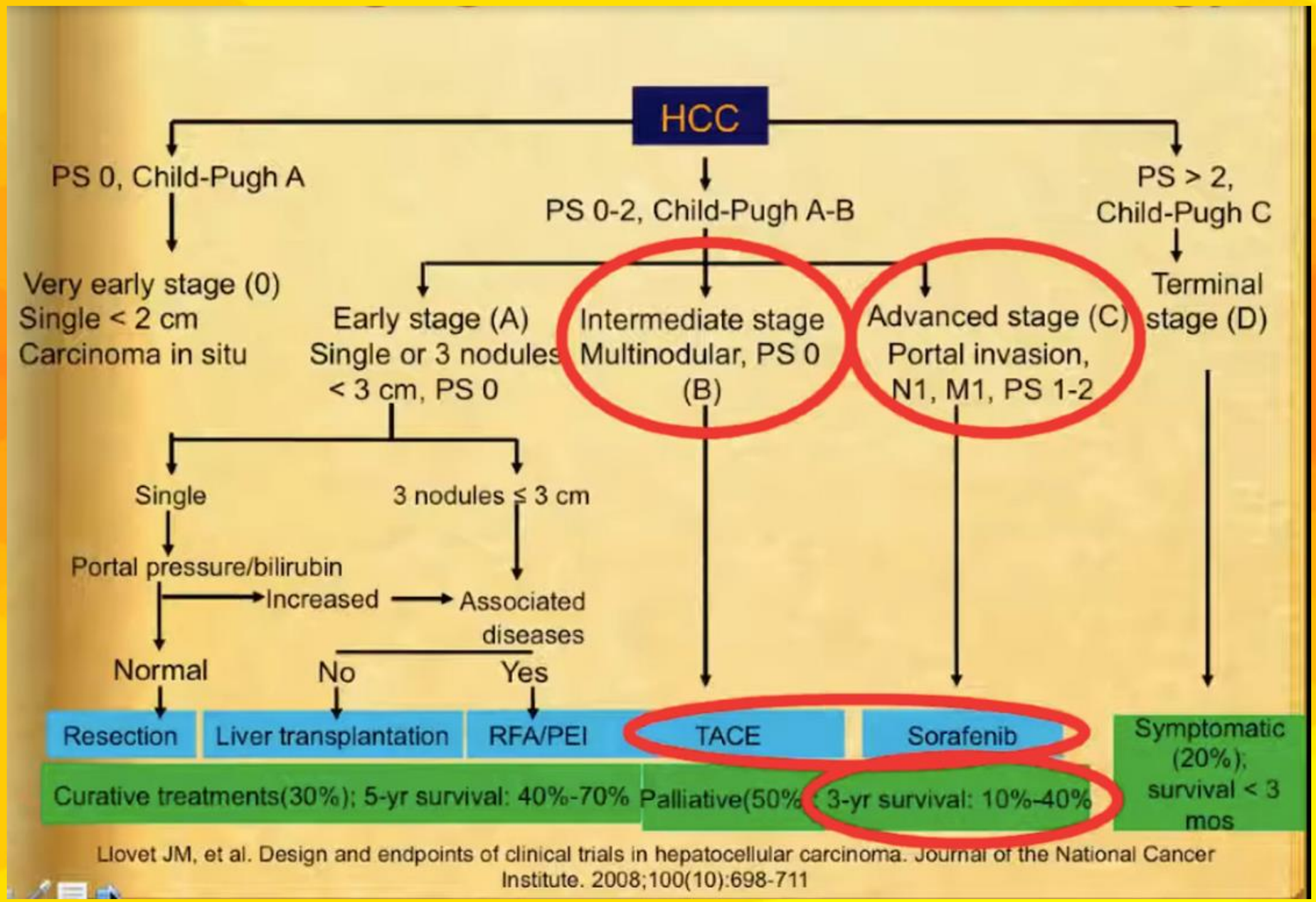
LIVER TRANSPLANTATION FOR HCC




HCC
Stage 0
PST 0, Child-Pugh A
Stage A-C
PST 0-2, Child-Pugh A-B
Stage D
PST >2, Child-Pugh C
Very early stage (0)
Single< 2cm,
Carcinoma in situ
Early stage (A)
Single or 3 nodules < 3cm, PS 0
Intermediate stage (B)
Multinodular, PST 0
Advanced stage (C)
Portal invasion, N1,M1, PST 1-2
End stage (D)
Single
3 nodules ≤3cm
Portal pressure/ bilirubin
Increased
Associated diseases
Normal
No
Yes
Resection
Liver Transplantation
(CLT / LDLT)
PEI/RF
TACE
Sorafenib
Curative Treatments (30%)
5-yr survival: 40-70%
Randomized controlled trials (50%)
Median survival 11-20mo
Symptomatic ttc (20%)
Survival<3mo
Where RT fits
Unsuitable for resection, transplant or RF
Definitive RT
Unsuitable/refractory to TACE
Definitive RT ◆
Symptomatic
Low dose RT ◆
RT as bridge to transplant
Portal invasion
Definitive RT & sorafenib ◆

EXTENDED CRITERIA

ROLE OF SBRT /TACE /TARE



Llovet JM, et al. Design and endpoints of clinical trials in hepatocellular carcinoma. Journal of the National Cancer Institute. 2008;100(10):698-711

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LIVER TRANSPLANTATION FOR HCC

DOWNSTAGING

- Conventionally **PVTT** is contraindication for Liver Transplant
- With **Downstaging,** even this group can have long time survival with Resection and or LT.
- **Double Equipoise concept (maximum recipient benefit with minimum donor risk)**
- **Downstaging** recommended in LDLT even if Adverse Biological factors
- Minimal recipient survival is contentious and **TRansplant Benefit**, a better metric

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LIVER TRANSPLANTATION FOR HCC

DOWNSTAGING FOR LOCALLY ADVANCED HCC

HCC WITH PVTT- LT POST DOWN STAGING WITH RT+TACE/CR

Down-Staging of Hepatocellular Carcinoma via External-Beam Radiotherapy With Subsequent Liver Transplantation: A Case Report

Alan Wigg,[1,2] **Kenneth Hon,**[1,2] **Leigh Mosel,**[3] **Nicole Sladden,**[4] **and Kevin Palumbo**[5]
[1] *Hepatology and Liver Transplant Medicine Unit,* [2] *South Australian Liver Transplant Unit,* [3] *Department of Medical Imaging, and* [4] *Department of Anatomical Pathology, Flinders Medical Centre, Bedford Park, Australia, and* [5] *Adelaide Radiotherapy Centre, Adelaide, Australia*

Living Donor Liver Transplantation for Advanced Hepatocellular Carcinoma with Portal Vein Tumor Thrombosis after Concurrent Chemoradiation Therapy

Dai Hoon Han,[1,2] Dong Jin Joo,[1,2,3] Myoung Soo Kim,[1,3] Gi Hong Choi,[1,2,3] Jin Sub Choi,[1,2,3] Young Nyun Park,[2,4] Jinsil Seong,[2,5] Kwang-Hyub Han,[2,6] and Soon Il Kim[1,3]

Liver Transplantation After Transarterial Chemoembolization and Radiotherapy for Hepatocellular Carcinoma with Vascular Invasion

Yuri Jeong[1] · Min-Ho Shin[2] · Sang Min Yoon[1] · Gi-Won Song[2] · Ki-Hun Kim[2] · Chul-Soo Ahn[2] · Deok-Bog Moon[2] · Shin Hwang[2] · Jin-hong Park[1] · Jong Hoon Kim[1] · Sung-Gyu Lee[2]

LIVER TRANSPLANTATION FOR HCC

DOWNSTAGING FOR LOCALLY ADVANCED HCC

Successful pre-Tx downstaging of HCC-PVTT gives good results after LDLT

AMC, Seoul *Jeong Y, Lee SG et al., J Gastrointest S 2016*

17 HCC patients with PVTT
underwent DS with TACE and radiotherapy, and LDLT
the 3-year DFS and OS were 57.8 and 60.5 %, respectively.

J Gastrointest Surg

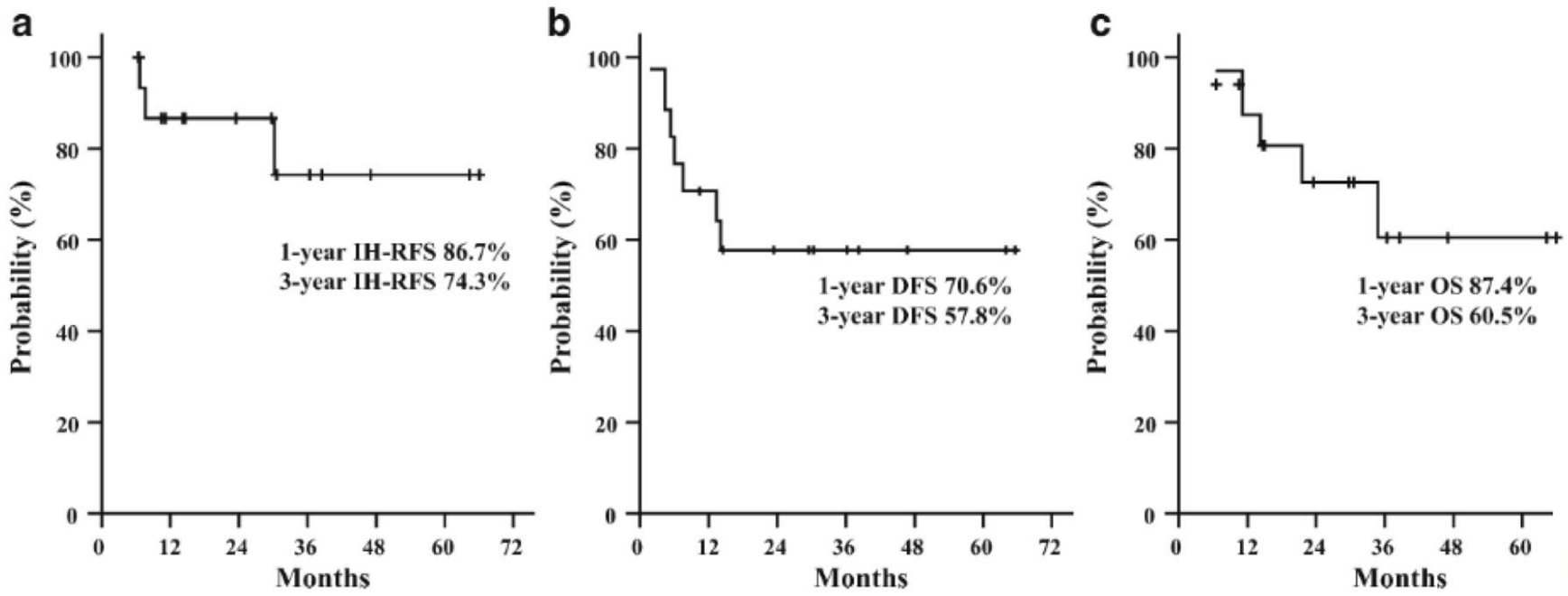

Fig. 1 Survival outcomes. **a** Intrahepatic recurrence-free survival (*IH-RFS*) rate. **b** Disease-free survival (*DFS*) rate. **c** Overall survival (*OS*) rate

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LIVER TRANSPLANTATION FOR HCC

DOWNSTAGING FOR LOCALLY ADVANCED HCC

Original Clinical Science—Liver

ILTS

Experience With LDLT in Patients With Hepatocellular Carcinoma and Portal Vein Tumor Thrombosis Postdownstaging

Arvinder S. Soin, MS, FRCS,[1] Prashant Bhangui, MS,[1] Tejinder Kataria, MD,[2] Sanjay S. Baijal, MD,[3] Tarun Piplani, MD,[3] Dheeraj Gautam, MD,[4] Narendra S. Choudhary, DM,[1] Srinivasan Thiagarajan, MS,[1] Amit Rastogi, MS,[1] Neeraj Saraf, MD,[1] and Sanjiv Sajgal, DM[1]

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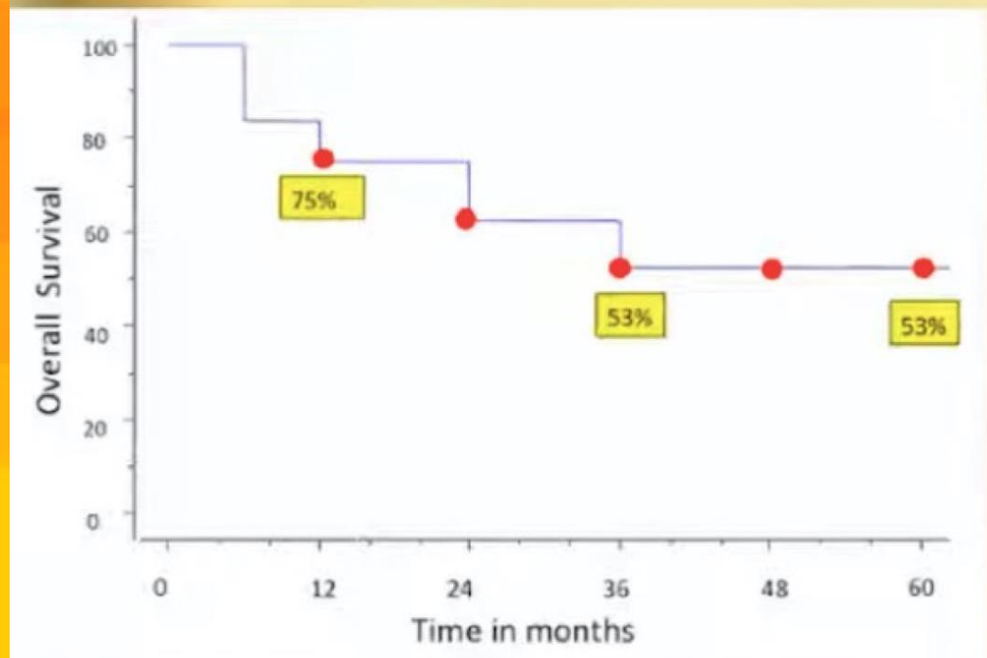
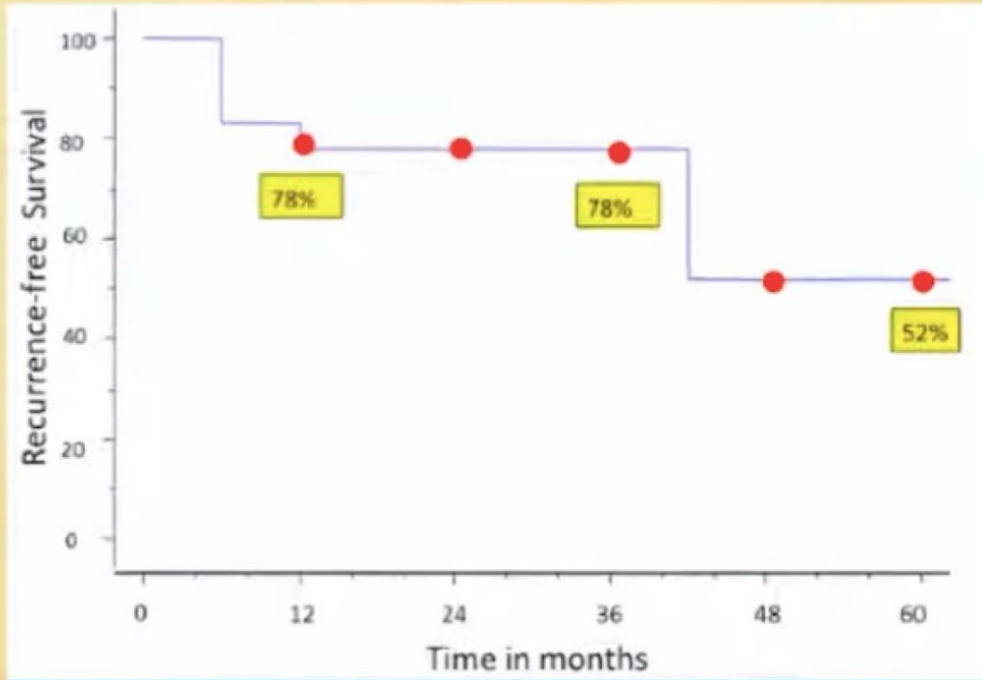
LIVER TRANSPLANTATION FOR HCC

Survival in 25 HCC PVTT patients following LDLT Postdownstaging



No. of patients exposed	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
Downstaged patients (25)	15	8	4	2	2



No. of patients exposed	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
All Downstaged patients (25)	13	7	4	2	1

Soin AS, Bhangui P. et al. Transplantation 2020

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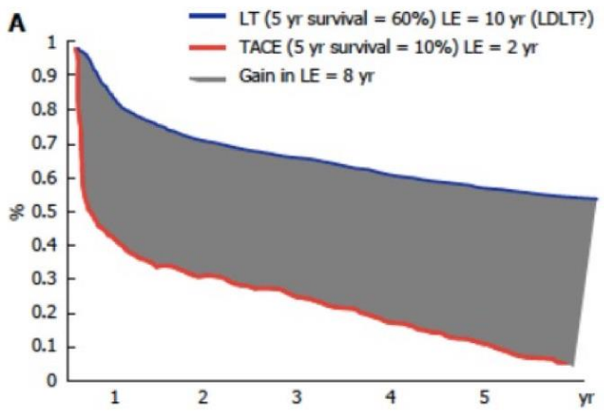
LIVER TRANSPLANTATION FOR HCC

Selection criteria based on Transplant benefit

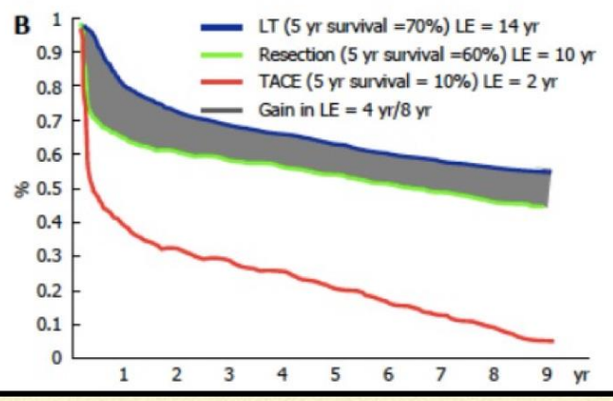
INTERNATIONAL LIVER TRANSPLANTATION SOCIETY

ILTS CONSENSUS CONFERENCE 2019
ROTTERDAM | NETHERLANDS
FEBRUARY 7, 2019

Transplant benefit = gain offered by LT in comparison with the best alternative therapy



40/M, Childs B, HBV
2 HCC nodules, largest 6 cm
Outside Milan/UCSF



65/M, Child A, HCV
1 HCC nodule, 4 cm
Within Milan/UCSF

Vitale A, Volk M, Cillo U. Transplant benefit for patients with Hepatocellular Carcinoma World J Gastroenterol 2013

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LIVER TRANSPLANTATION FOR HCC

TRANSPLANT BENEFIT

MC-in HCC , Child's C – 3/5 yr post Tx survival 85/80%;
No transplant - 3/5 yr survival 25/0%

8cm, 7 tumors, no PVTT – 3/5 yr post Tx survival 75/65%;
No transplant – 3/5 yr survival 10/0%

HCC+PVTT –DS (TARE+SBRT)+LDLT –3/5 yr post Tx surv 65/55
No transplant – 3/5 yr survival 0/0%

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LIVER TRANSPLANTATION FOR HCC

CASE REPORTS

CASE I (TARE + LDLT)

	26/12/19	31/1/20	16/3	23/4
AFP	7.2	11.5	6.9	
PIVKA	**25453**	8600	2793	**166**

- 65 yr old , **Lyricist** ,
- NASH related CLD(child s A) detected to have Advanced HCC (VP 2-3)

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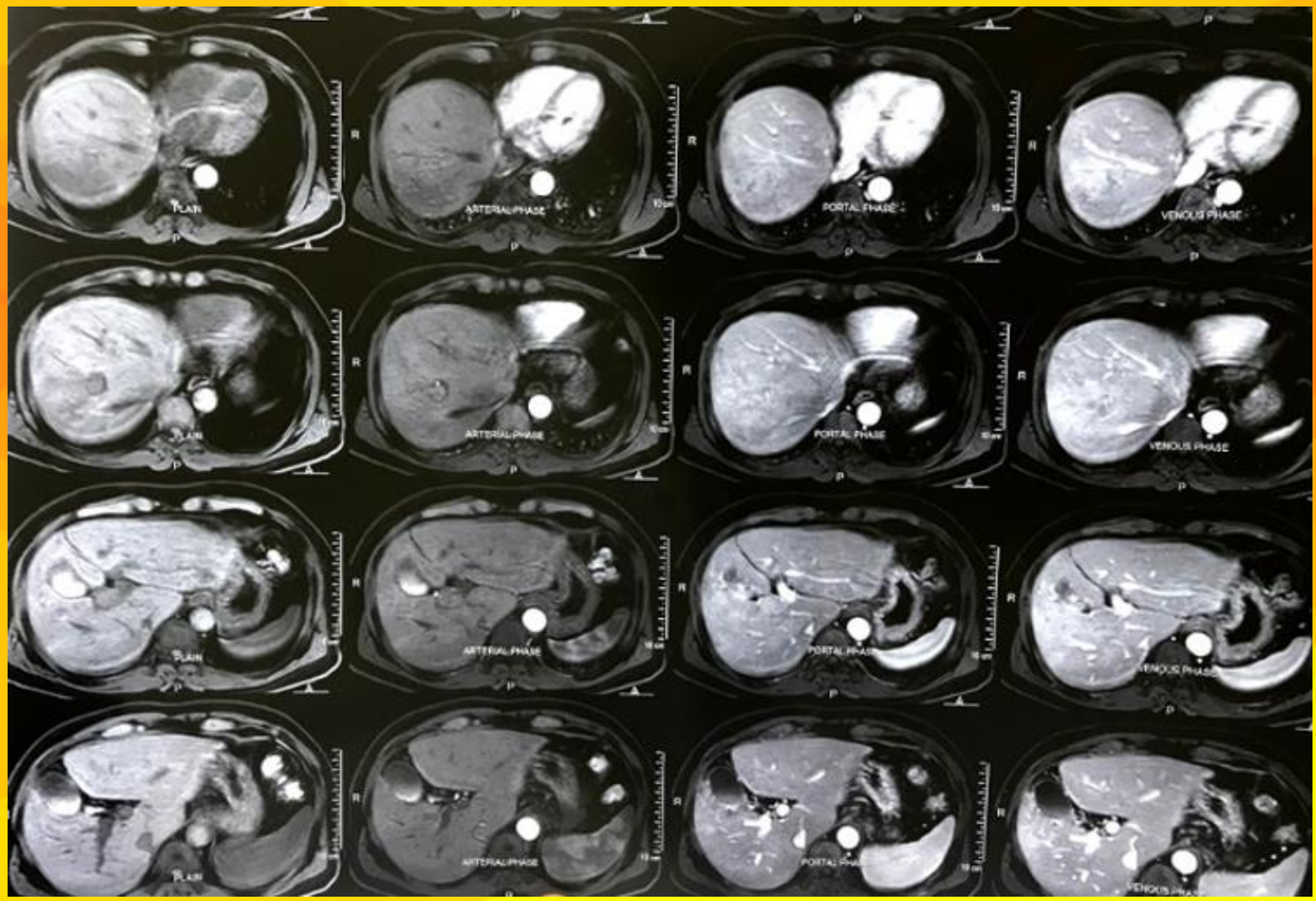
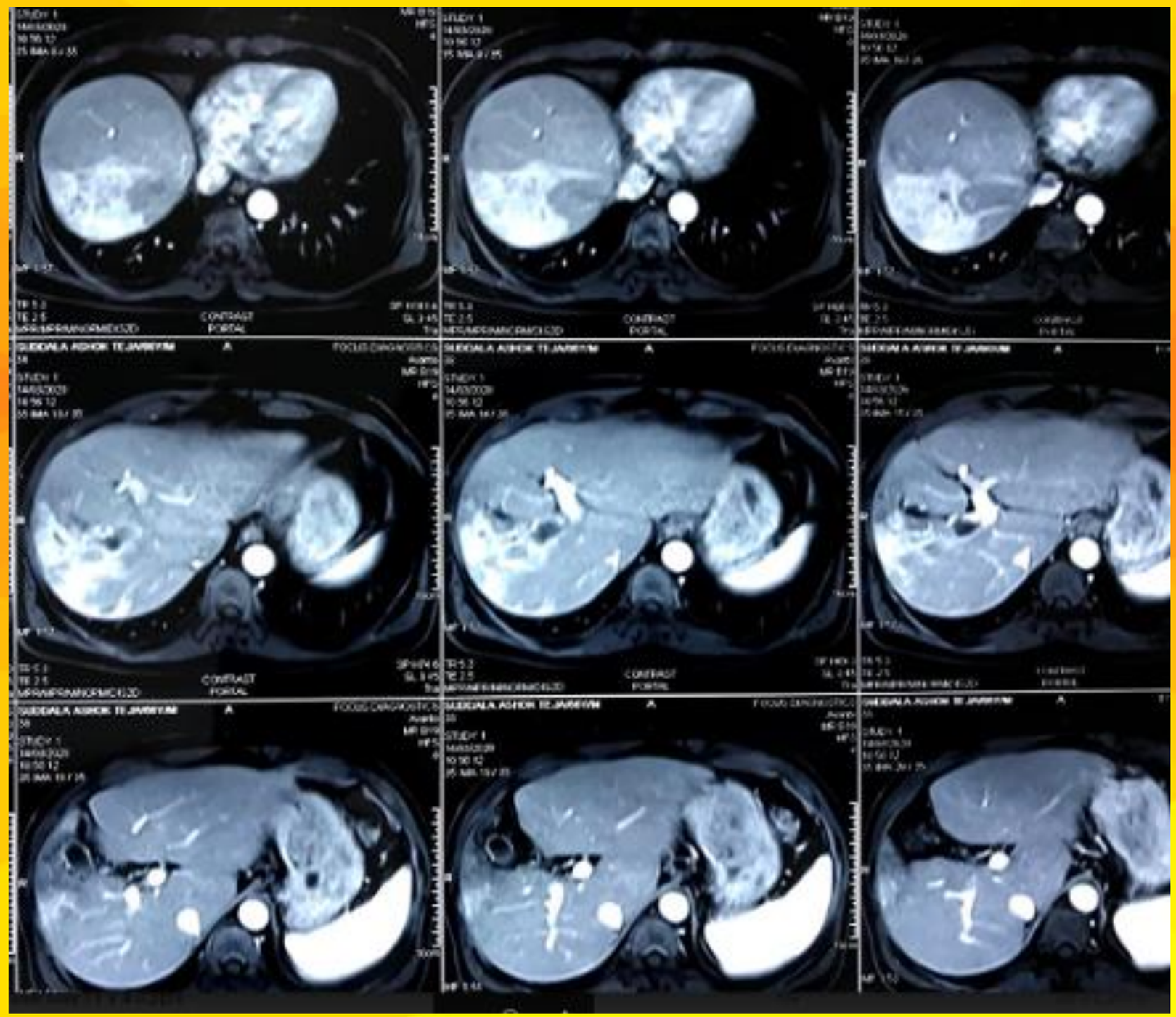

PLAIN
ARTERIAL PHASE
PORTAL PHASE
VENOUS PHASE
PLAIN
ARTERIAL PHASE
PORTAL PHASE
VENOUS PHASE
PLAIN
ARTERIAL PHASE
PORTAL PHASE
PLAIN
ARTERIAL PHASE

LIVER TRANSPLANTATION FOR HCC



LIVER TRANSPLANTATION FOR HCC

Tumor size reduced **9.1x 7.2 cm** **4.7 x 3.7 cm**

PVTT —— Complete metabolic resolution and enhancement of filling defect

NO EXTRA HEPATIC DISEASE

Pathology

WELL DIFFERENTIATED TUMOR

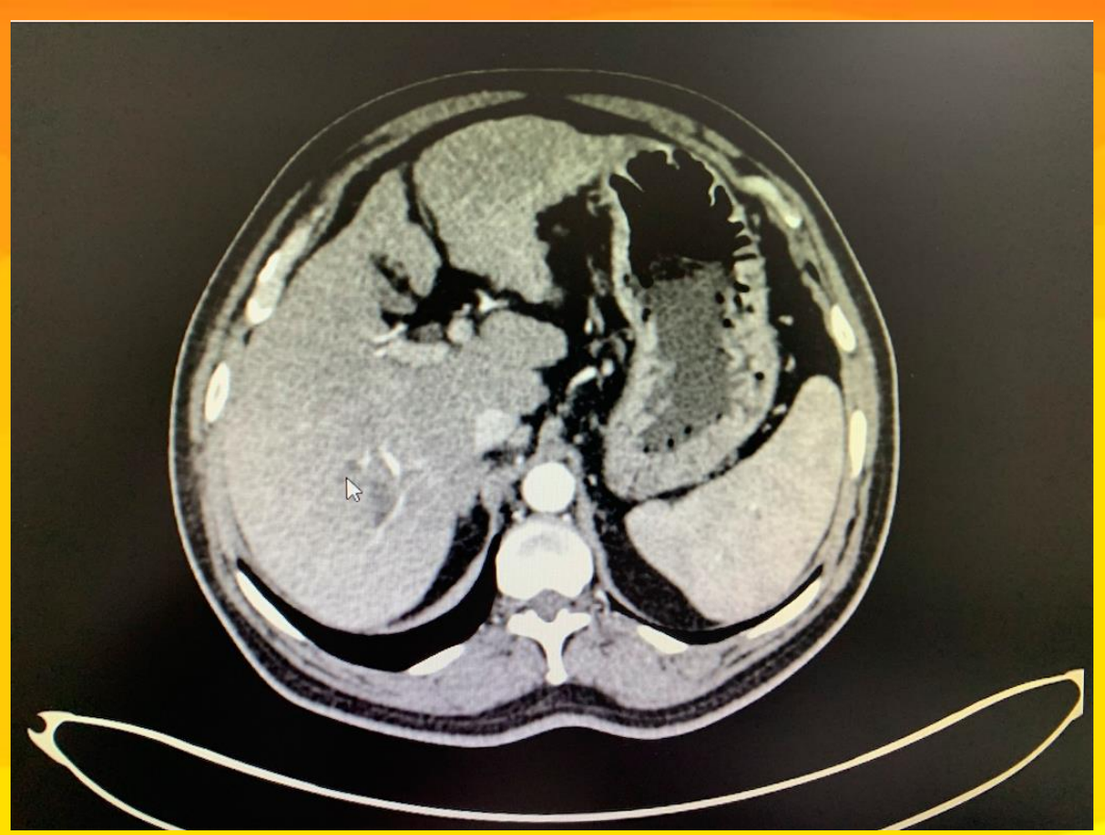
THE SIZE OF THE TUMOR - <2 CMS WITH MORE THAN

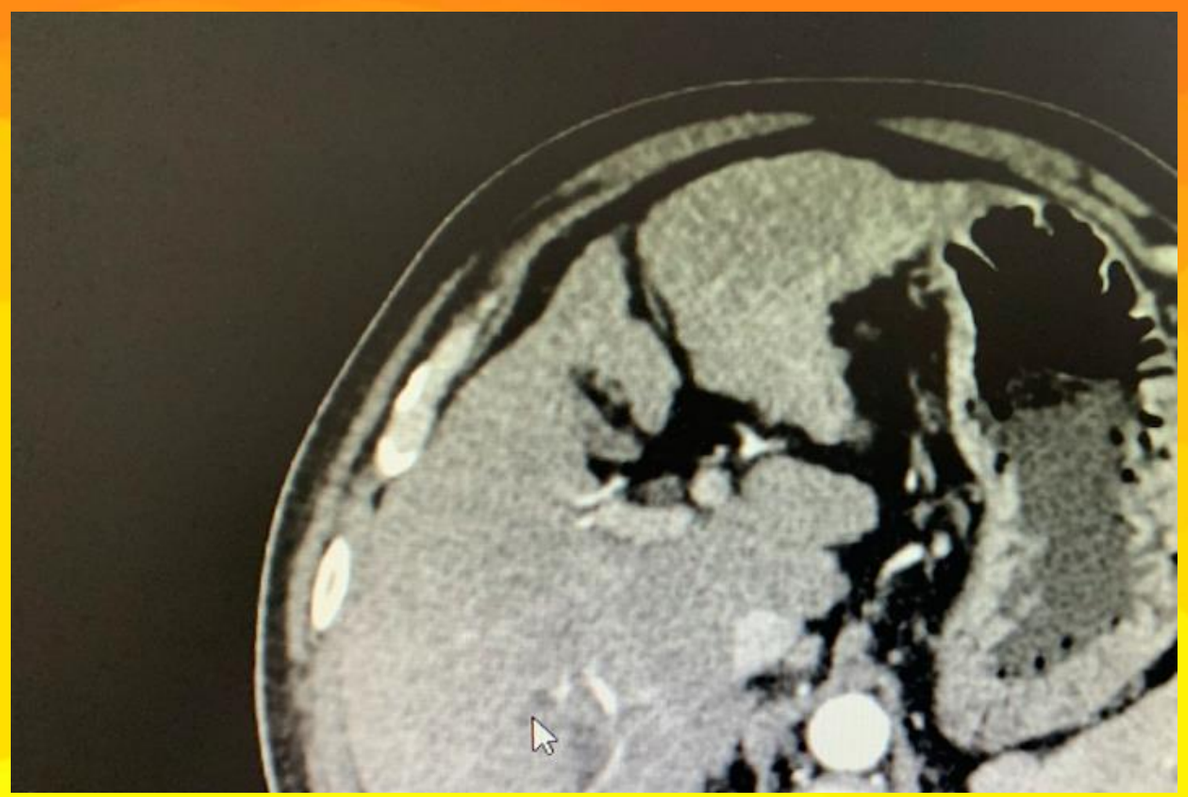
AND NO E/O TUMOR IN THE PV .

Liver Transplantation for HCC

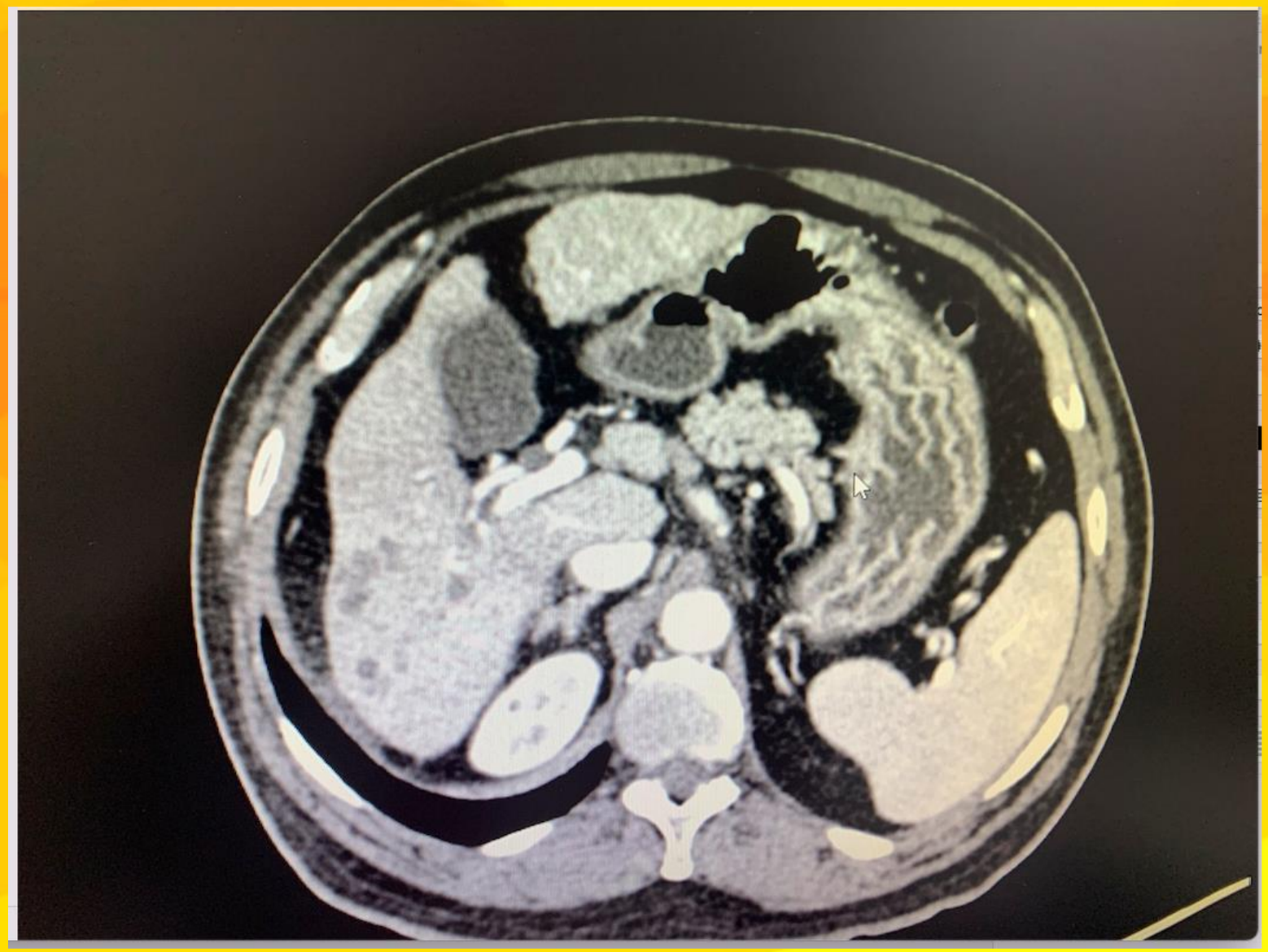
Case report

- Case 2 ,
- 61 yrs old NASH related CLD Childs A, with HCC





SBRT for down staging for Ltx



Surgery for HCC

Conclusion

Surgical Management of HCC is evolving

Potential cure is increasing with down staging modalities like TACE , TARE, SBRT followed by LR or LT ,

Patients with PVTT or locally advanced tumours -have not hit the end of the road .

multidisciplinary approach

Genomics is becoming a part of prognostication and diagnosis

Personalised medicine and individualised treatment is the future

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Liver Transplant for HCC

Some downstage patients with good tumour biology do well with LR and LT

When we expand the criteria for LDLT ,

Double Equipoise ,(recipient outcomes and donor safety) Should be strictly followed

Minimum Acceptable recipient survival is contentious and Transplant Benefit , a better metric

Liver Transplant for HCC

Multidisciplinary Approach for Management of locally advanced HCC

Radiologist

Hepatologist

Pathology

Oncologist

Interventional radiologist

Surgeon

Radiation Oncologist

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Seeking Optimal Outcomes in an Era of Personalised Medicine and Transplant Oncology …. Beyond Convention Yet Evidence Based

THANK YOU

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