Liver Cancers: Current and Emerging Practices

--Surveillance, Diagnose, Staging--

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I have no disclosures

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HCC-Surveillance

- WHY?
- WHO?
- HOW?

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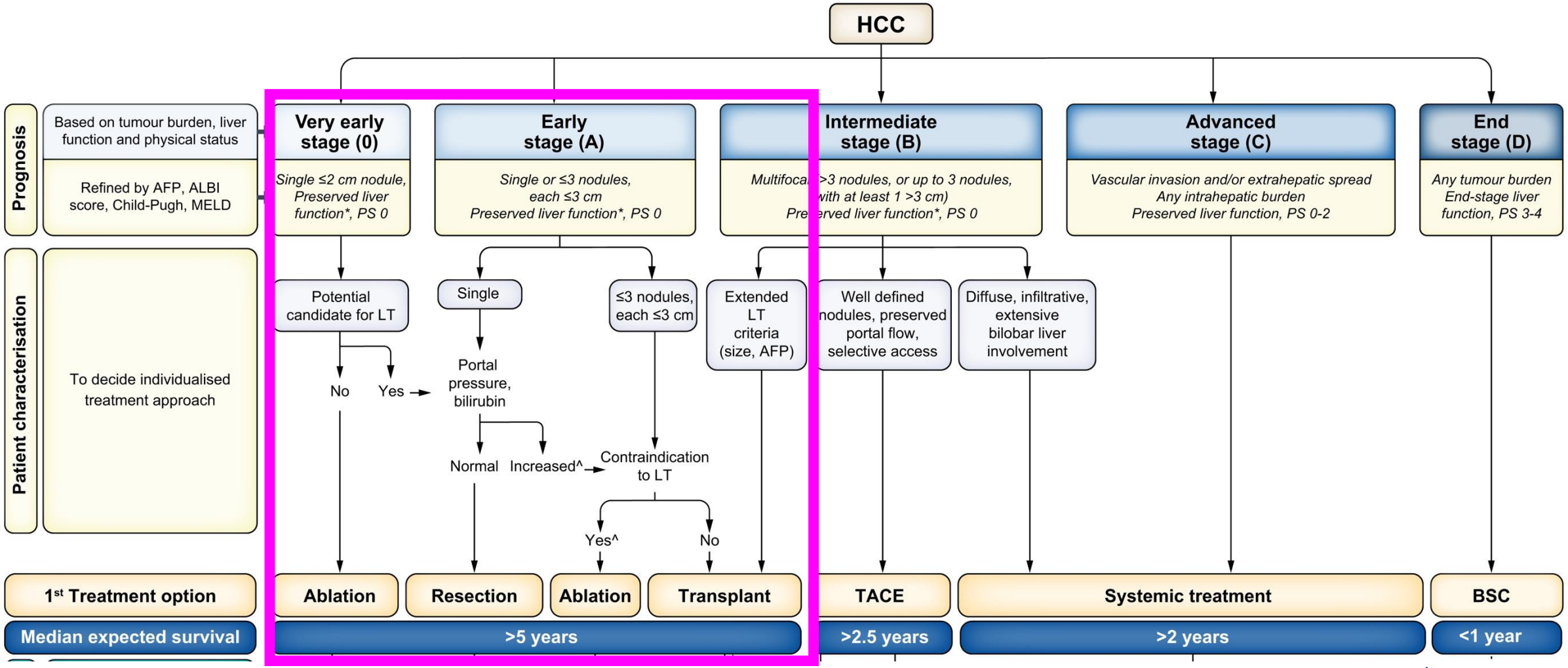
Prognosis is driven by tumor stage at time of diagnosis



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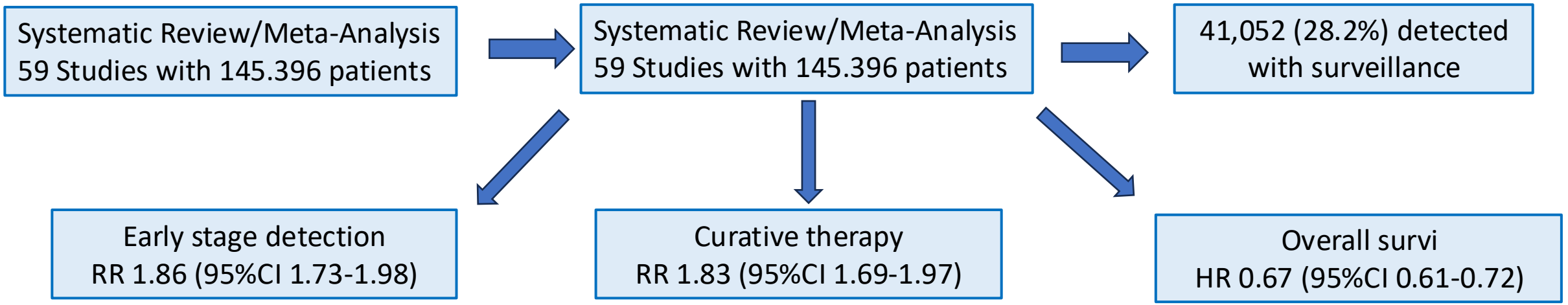
Surveillance associated with improved survival



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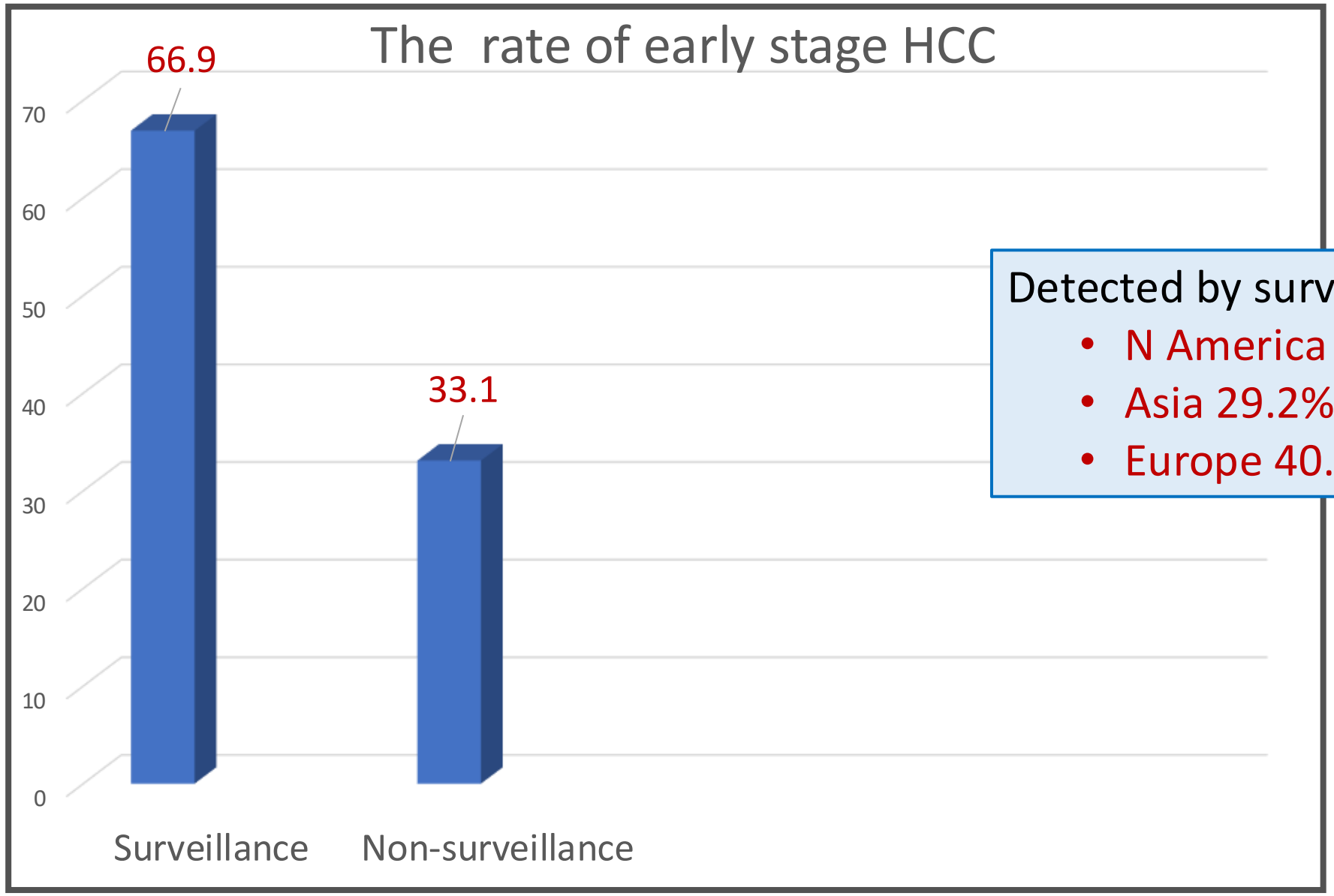

Detected by surveillance

- N America 14%
- Asia 29.2%
- Europe 40.8%

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What AASLD says ?

Guidance statements

7. Patients at high risk of developing HCC (see Table 1) should be entered into HCC surveillance programs, provided they would be candidates for HCC treatment (**Level 2, Strong Recommendation**).
   a. Patients with Child-Turcotte-Pugh class C cirrhosis should not be enrolled in surveillance programs unless they are eligible for liver transplantation (**Level 3, Strong Recommendation**).
   b. All patients listed for liver transplantation should undergo semiannual HCC surveillance because identification of early-stage HCC changes priority for transplantation (**Level 3, Strong Recommendation**).

Population group	Incidence of HCC
Sufficient risk to warrant surveillance	
Child-Pugh A–B cirrhosis, any etiology Hepatitis B Hepatitis C (viremic or post-SVR) Alcohol associated cirrhosis Nonalcoholic steatohepatitis Other etiologies	≥ 1.0% per year
Child-Pugh C cirrhosis, transplant candidate	
Non-cirrhotic chronic hepatitis B Man from endemic country[a] age > 40 y Woman from endemic country[a] age > 50 y Person from Africa at earlier age[b] Family history of HCC PAGE-B score ≥ 10[c]	≥ 0.2% per year

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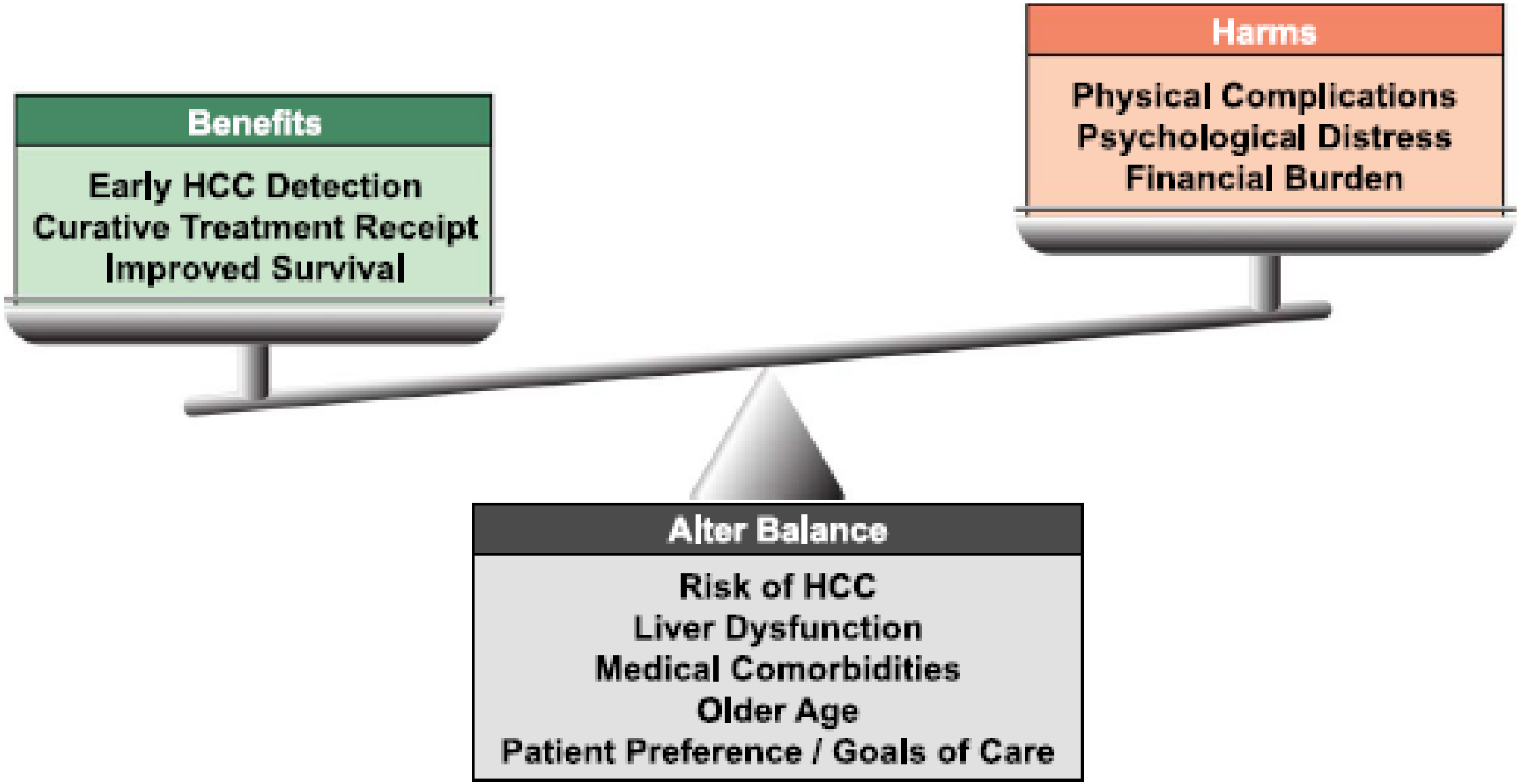

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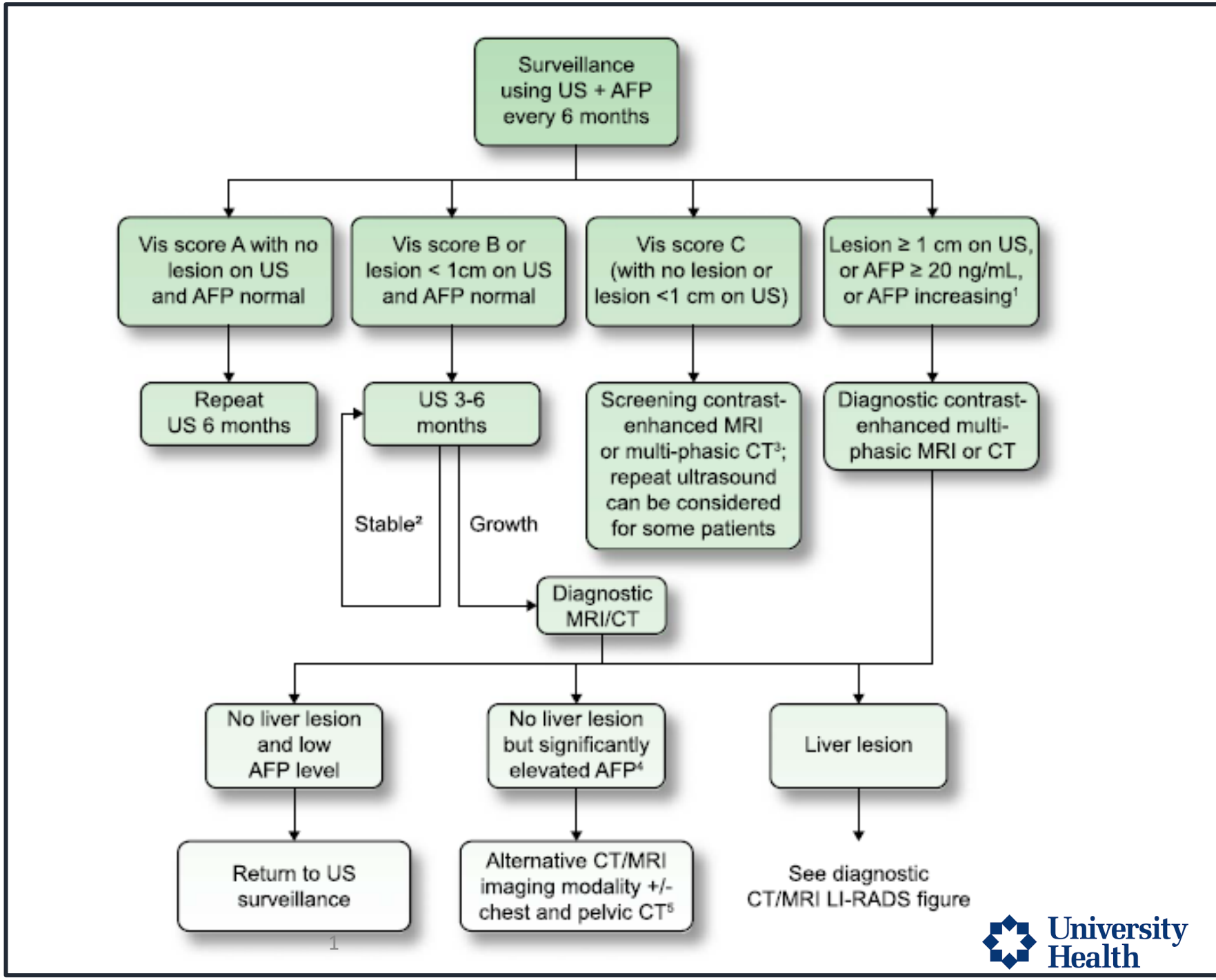
What about special groups?

- Listed patients for LT ? YES
- HCV cirrhosis after SVR ? YES
- Child C cirrhosis, not a candidate for LT? NO
- Non-cirrhotic HCV after SVR? NO, but it depends
- MASH without cirrhosis ? NO, but it depends

How we should?

US+AFP
Sensitivity %63



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About AFP??

- Red flags:
  - >20 ng/ml: most common threshold for HCC surveillance
  - Rising AFP on two consecutive tests
  - Doubling of AFP levels
- AFP ≥ 200 ng/ml but no liver mass on CT or MRI
  - Repeat imaging with other + chest-pelvic imaging
  - PET-CT

Handicaps of Current HCC Screening

- Suboptimal early-stage sensitivity of US
- False positives with subsequent harms
- Inter-operator variability in US performance
- Poor adherence
  - Limited access to imaging
  - Scheduling difficulties
  - Transport problems

USA screening rates of target population for HCC

First year 25%

At least once 35%

Who should be screened more intensly?

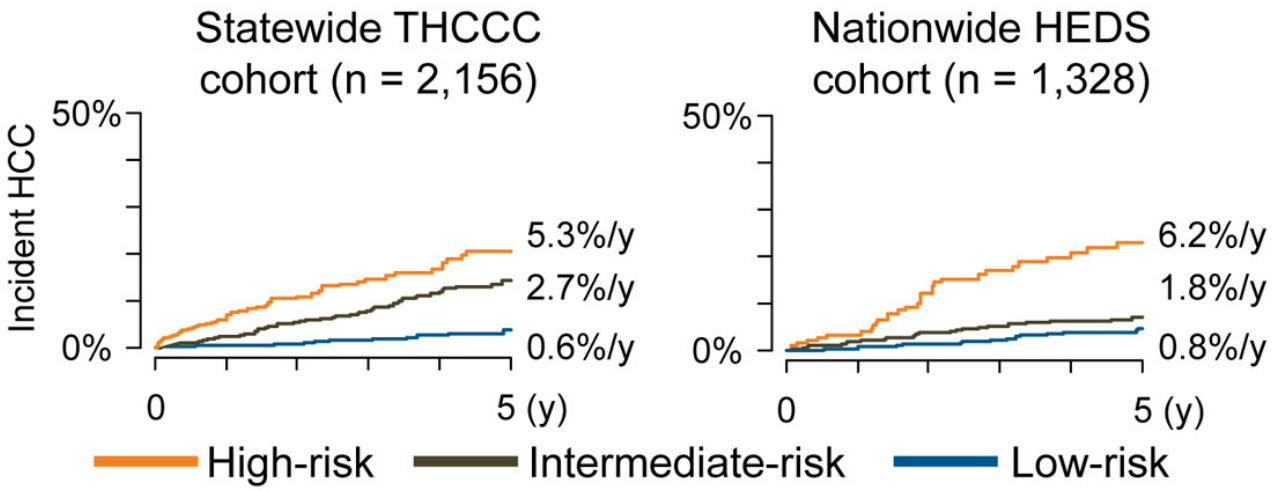
Phase 3 validation of PAaM for HCC risk stratification in cirrhosis

Molecular biomarker
PLSec-**A**FP

Clinical variable-based
aMAP score

Integrative HCC risk score, **PAaM**

Phase 3 biomarker validation studies



PLSec: prognostic liver secretome signature, derived from a thoroughly validated hepatic transcriptome signature

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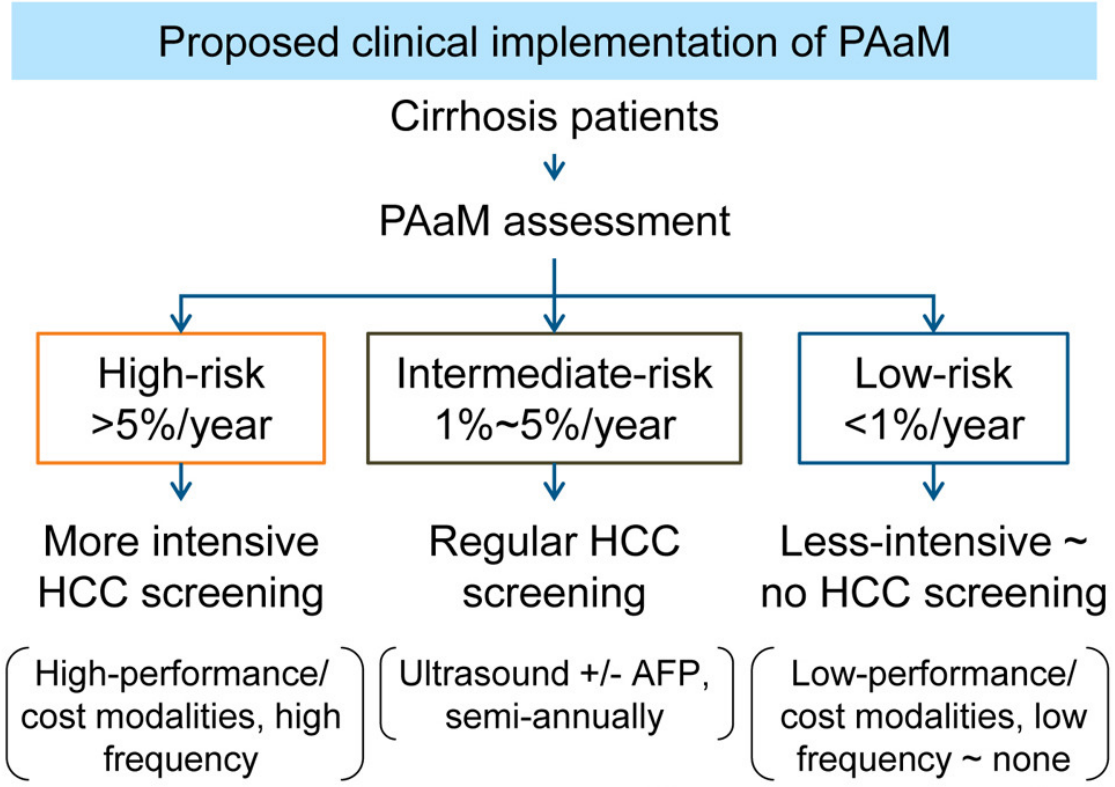
Who should be screened more intensly?

Phase 3 validation of PAaM for HCC risk stratification in cirrhosis



PLSec: prognostic liver secretome signature, derived from a thoroughly validated hepatic transcriptome signature

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Emerging Surveillance Strategies: GALAD

- Gender
- Age
- AFP
- AFP-L3 (lectin binding subfraction)
- DCP (des gamma carboxy prothrombin)

FDA approve for risk stratification not for HCC screening

Sensitivity %65
Specificity %82

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Emerging Surveillance Strategies: Liquid Biopsy

- Cell-free DNA (cfDNA)/DNA methylation
- Extracellular vesicles (EVs)

Test	Sensitivity (%)	Specificity (%)	Current
Oncoguard® (mtHBT)	82	87	Phase II
HelioLiver®	76	91	Phase II
Freenome®	?	?	Phase I
EV chip	94.4	88.5	Phase II

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Emerging Surveillance Strategies: New Biomarkers

Biomarker	Early detection performance	
Osteopontin	Sensitivity:49%	Specificity: 72%
Midikine	Sensitivity:87%	Specificity: 90%
Dikkopf-1	Sensitivity:41%–74%	Specificity: 87%
Glypican-3	Sensitivity:55%	Specificity: >95%
Alpha-1 fucosidase	Sensitivity:55%	Specificity: >95%
Golgi Protein-73	Sensitivity:62%–79%	Specificity:62%–88%

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Emerging Surveillance Strategies: Imaging

- Abbreviated NC-MRI + AFP > US+AFP
  - Sensitivities 80%–90%
  - Specificities 91%–98%
- Contrast-Enhanced US (CHUS) + AFP
  - Sensitivities 82%–84%
  - Specificities 88%–91%

Yakon 2023 Radiol
Jiang 2021 J GI Oncol

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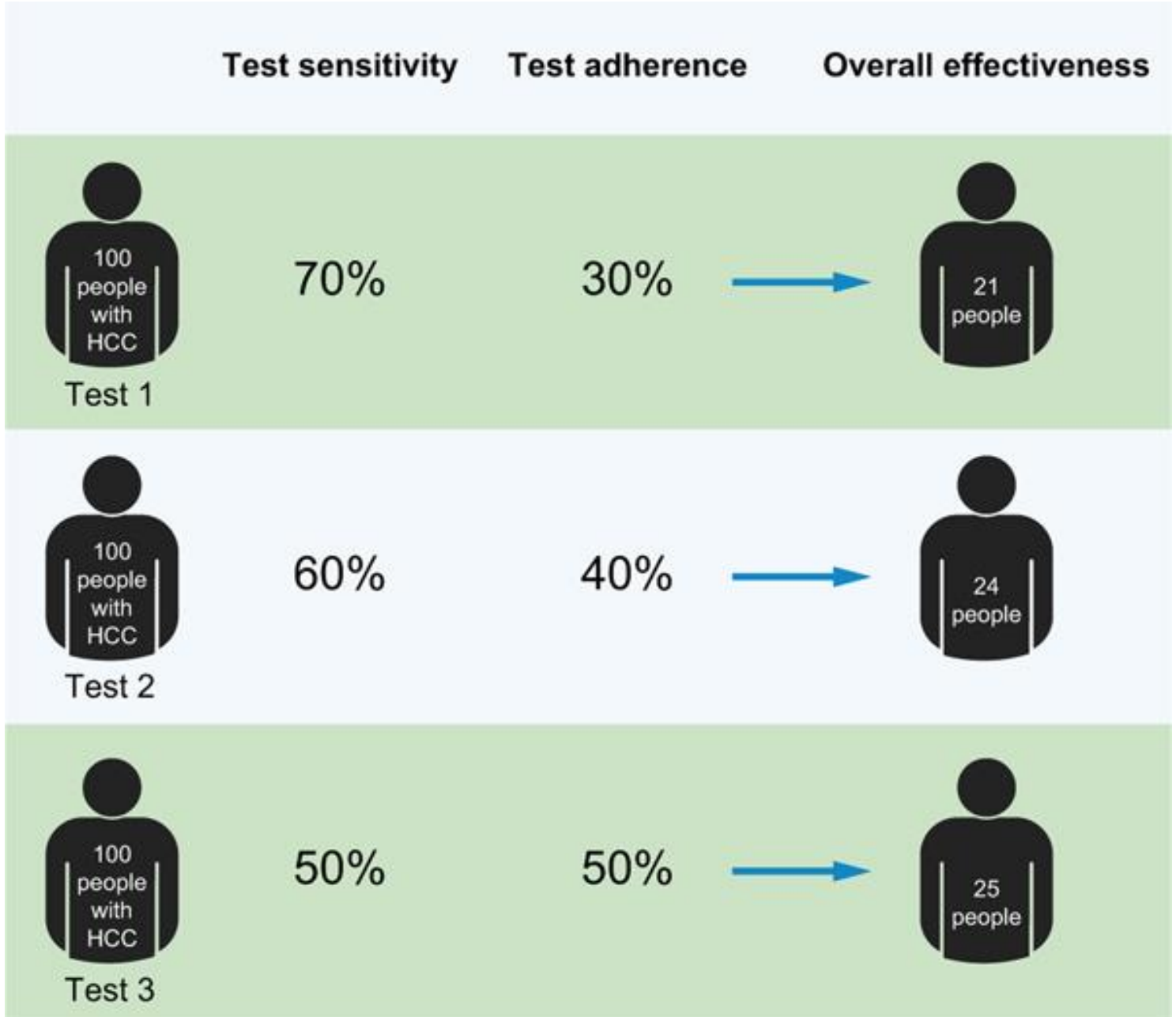

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HCC-Diagnosis

- Imaging
- Pathology
- Biomarkers

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Liver Reporting and Data System (LI-RADS) classification of CT or MRI

CT/MRI Diagnostic Table

Arterial phase hyperenhancement (APHE)		No APHE		Nonrim APHE		
Observation size (mm)		< 20	≥ 20	< 10	10-19	≥ 20
Count additional major features: • Enhancing "capsule" • Nonperipheral "washout" • Threshold growth	None	LR-3	LR-3	LR-3	LR-3	LR-4
	One	LR-3	LR-4	LR-4	LR-4 / LR-5	LR-5
	≥ Two	LR-4	LR-4	LR-4	LR-5	LR-5

LR-4 / LR-5

Observations in this cell are categorized based on one additional major feature:

- LR-4 – if enhancing "capsule"
- LR-5 – if nonperipheral "washout" **OR** threshold growth

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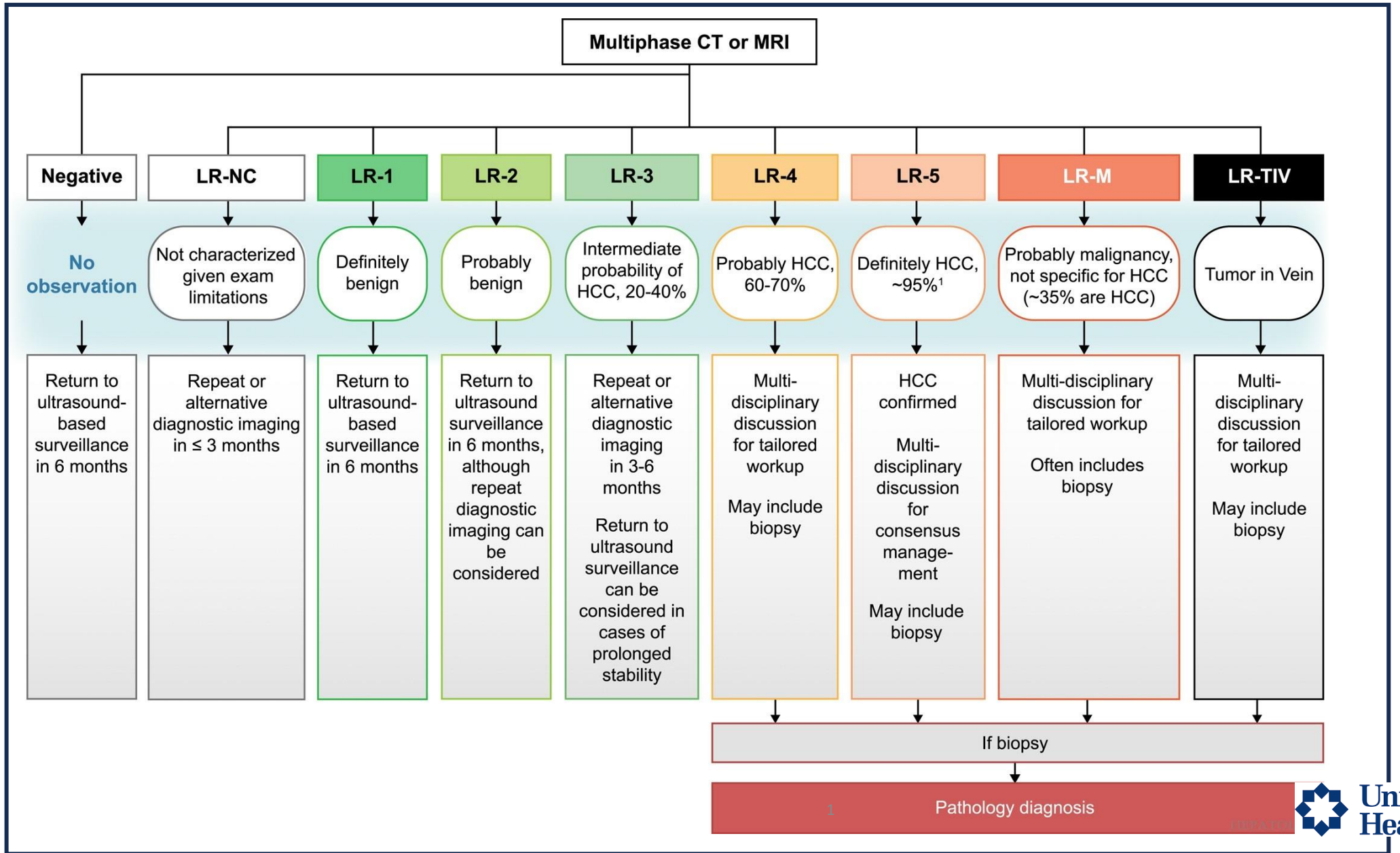
Risk of HCC and recommended management strategy



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Pathological Diagnosis: When ??

- LR-4 and LR-M lesions
- Liver nodules in patients without cirrhosis or without HBV
- Suspicion for mixed HCC-cholangiocarcinoma
- Plan for immunotherapy
  - Molecular and immune classes
  - Oncogenic mutations

Diagnostic Biomarkers:

- AFP; not recommended
- Liquid biopsy; tumor components released by cells
  - CtDNA (methylation profiles, extracellular RNA signatures from exosomes)
  - Circulating tumor cells
  - Extracellular vesicles

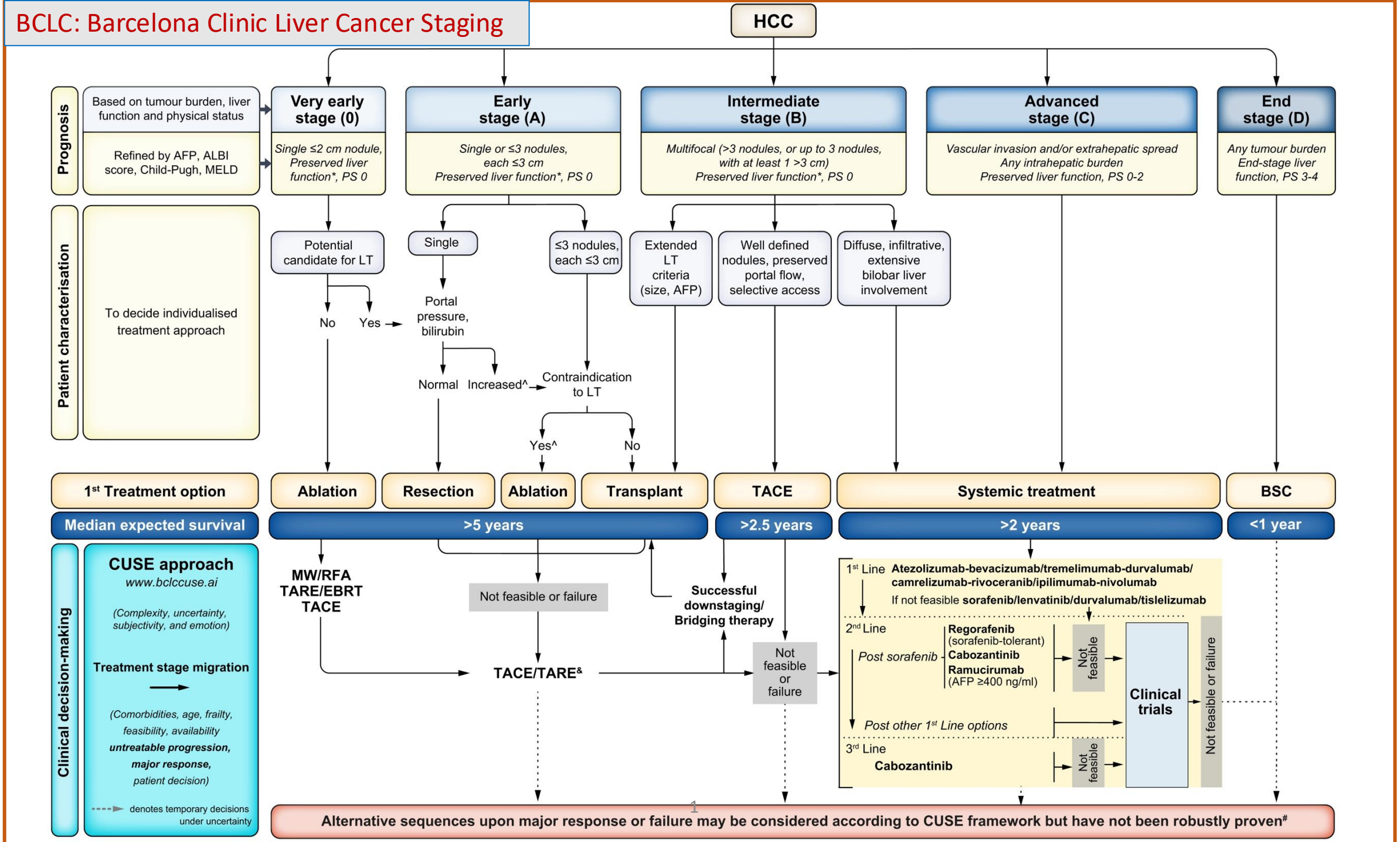
HCC-Staging; what info we need?

- Degree of tumor burden: Imaging
- Severity of liver dysfunction: Child-Pugh, MELD, ALBI
- Performance status: ECOG (0-4)

Tumor Burden and Metastasis

- High-quality multiphase CT or contrast-enhanced MRI
- Non-contrast chest CT (HCC >2cm or BCLC >0)
- Pelvic CT and Bone scan
  - AFP > 1000 ng/ml
  - Macrovascular invasion
  - Multifocal bilobar disease

BCLC: Barcelona Clinic Liver Cancer Staging

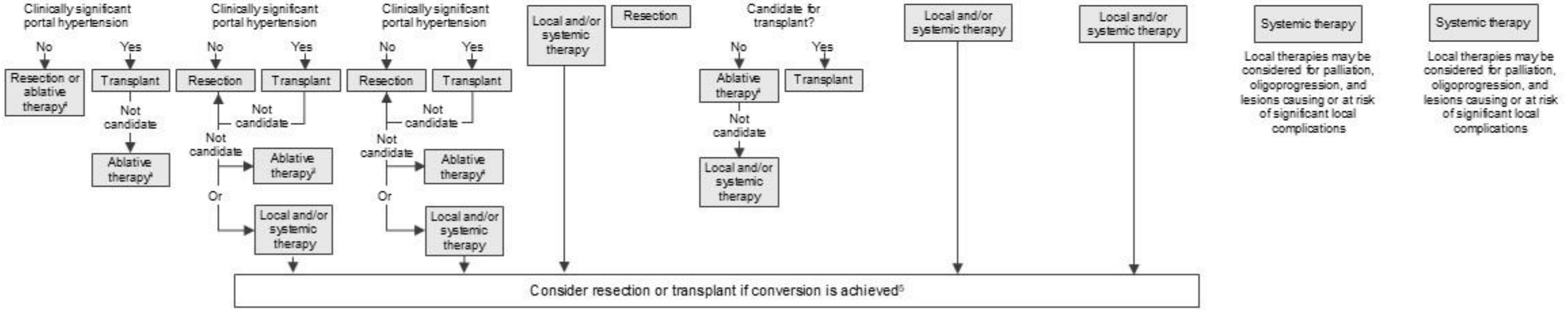


Alternative Staging Proposals

- The Italian Liver Cancer (ITA.LI.CA) system
  - To account for heterogeneity subclassifies BCLC St B into B1/B2/B3
- The HKLC system
  - More nuanced stratification in intermediate- and advanced-stage
- BEACON classification
  - Includes PV thrombosis

BEACON classification

Class	CLASS 1A	CLASS 1B	CLASS 1C	CLASS 1D	CLASS 2	CLASS 3A	CLASS 3B	CLASS 4A	CLASS 4B
Definition	• Solitary • ≤3 cm	• Solitary • 3-8 cm • No high risk feature[2]	• Solitary • ≥1 high-risk feature[2]	• Solitary • Vp1/2, or infiltrative	• Multifocal • ≤3 lesions, ≤3 cm • No high risk feature[2]	• Multifocal • >Class 2, but tumor burden <50% of liver • +/- Vp1/2 or infiltrative	• Solitary, with tumor burden <50% of liver • Vp3/4/hepatic vein invasion, or N1	• Any tumor burden ≥50% of liver, or multifocal with Vp3/4/hepatic vein invasion	Distant Metastasis
Example									
Resection[1]	P*	P*	P*	P	U	U			
Transplant[1]	P*	P*	P*	U	P*	U/P[3]			
RFA, MWA[1]	P*				P				
EBRT[1]	U	U	P	P	U	U	U		
TARE[1]	U	U	P	P	U	P	U		
TACE[1]	U	U*	U*	U	U*	U	U		
Systemic[1]		U	U	P*	U	P*	P*	P*	P*



*These preferred therapies have the highest level of clinical evidence

[1] Patients with decompensated liver disease who are not candidates for liver transplantation, patients with severely limited functional status, or any patient for whom HCC is not life limiting, should receive best supportive care

[2] High risk features: Maximum diameter > 8 cm, AFP >1000 ng/mL, or poorly differentiated (if pathology is known)

[3] Preferred only for liver-confined disease after successful downstaging; may be useful for those with vascular invasion after downstaging with nonviable tumor in vein

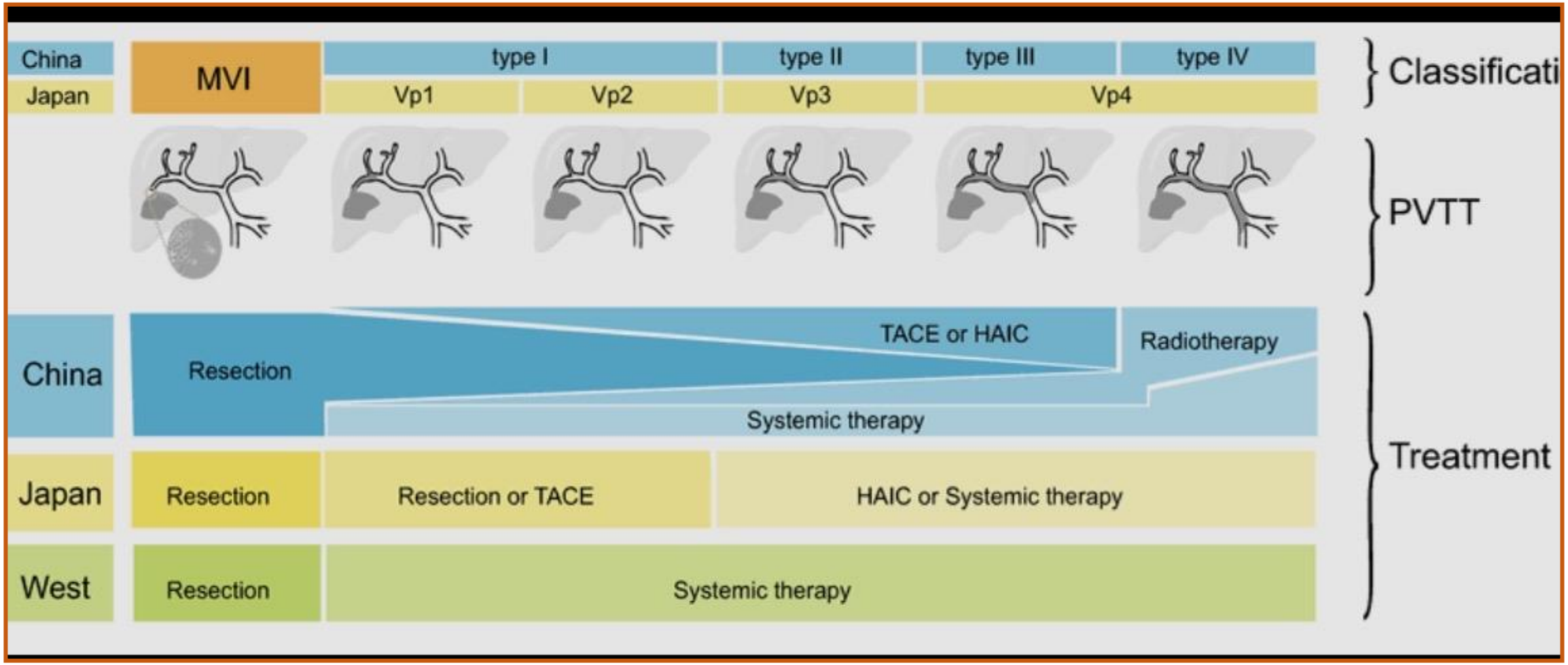
[4] Ablative intent therapies include RFA and MWA; TARE (delivered to 1-2 liver segments) and EBRT may be ablative if sufficiently high radiation dose can be delivered to the tumor

[5] The role of surgery in patients downstaged from unresectable or untransplantable to resectable HCC remains undefined, particularly when imaging suggests nonviable tumor

P = Preferred, U = Useful in some situations

HCC-Live Conference, 2026 California

BEACON classification-Portal Vein Invasion



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SUMMARY

Surveillance

- Target at-risk populations (cirrhosis ± selected HBV)
- Ultrasound ± AFP every 6 months remains standard
- Real-world gap: Only 20-25% receive consistent surveillance
- New researches promising (implementation to practice ?)

Diagnosis

- Imaging-based diagnosis is key (no biopsy in most cases)
- Multiphasic CT/MRI: arterial enhancement + washout
- Use standardized systems (LI-RADS)
- Diagnostic biomarkers; there is hope!

Staging

- Barcelona Clinic Liver Cancer staging system still most popular
- More personalized, flexible treatment strategies are emerging
- Multidisciplinary approach is essential

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