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HCC SCREENING FOR EARLY DIAGNOSIS: FEASIBILITY AND REALITY?

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PRACTICE GUIDELINES ON SCREENING & SURVEILLANCE FOR HCC

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- At-risk patient groups:
  - Hepatitis B carriers
    - Asian males >40 years
    - Asian females >50 years
    - All cirrhotic hepatitis B carriers
    - Family history of HCC
    - Africans/North American blacks
  - Cirrhosis due to hepatitis C, alcohol, hemochromatosis, PBC, or other causes

Bruix & Sherman. AASLD Practice Guideline: Management of Hepatocellular Carcinoma, Hepatology 2010

MAJOR GUIDELINES RECOGNIZE THE IMPORTANCE OF ROUTINE SURVEILLANCE IN HIGH-RISK POPULATIONS

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Society / Institution	Guidelines
AASLD[1] (American Association for the Study of Liver Diseases)	US every 6 months
EASL[2] (European Association for the Study of the Liver)	US every 6 months
APASL[3] (Asia-Pacific Association for the Study of the Liver)	AFP + US every 6 months
NCCN[4] (National Comprehensive Cancer Network)	AFP + US every 6-12 months
VA[5] (United States Department of Veterans Affairs)	AFP + US every 6-12 months
JSH-HCC[6] (Japan Society of Hepatology)	*High risk:* US every 6 months + AFP/DCP/AFP-L3 every 6 months *Very high risk:* US every 6 months + AFP/DCP/AFP-L3 every 6 months + CT/MRI (optional) every 6-12 months

AFP=alpha-fetoprotein; AFP-L3=*Lens culinaris* agglutinin-reactive fraction of AFP; CT=computerized tomography; DCP=des-γ-carboxyprothrombin; MRI=magnetic resonance imaging

1. Bruix J et al. Hepatology 2011; 53: 1020-1022; 2. EASL, EORTC. J Hepatol 2012; 56(4): 908-943; 3. Omata M et al. Hepatol Int 2010; 4(2): 439-474; 4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers v1.2016. Accessed February 10, 2016; 5. US Dept of Veterans Affairs. Available at: http://www.hepatitis.va.gov/pdf/2009HCC-guidelines.pdf. Accessed September 23, 2015; 6. Kokudo N et al. Hepatol Res 2015; 45.

HCC SURVEILLANCE: EFFECTIVENESS OF TESTS – ULTRASOUND SENSITIVITY ± ALPHA-FETOPROTEIN

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Author	Year	No. patients	No. HCC	No. early HCC	US sensitivity (%)	US + AFP sensitivity (%)
Kobayashi	1985	95	8	6	50	50
Arrigoni	1988	164	16	12	69	75
Oka	1990	140	40	33	68	80
Pateron	1994	118	14	5	23	38
Cottone	1994	147	5	4	87	87
Zoli	1996	164	34	32	91	91
Tradati	1998	40	6	2	33	33
Henrion	2000	94	6	6	67	100
Bolondi	2001	313	61	50	82	82
Santagostion	2003	66	8	2	25	25
Sangiovanni	2004	417	112	55	50	50
Sangiovanni	2006	214	68	34	50	50
Pooled estimates		**1514**	**229**	**170**	**63**	**69 (p=0.65)**

Early stage HCC defined by Milan criteria as 1 nodule <5 cm or 3 nodules each <3 cm in diameter, without gross vascular invasion.

Adapted from Singal A et al. Aliment Pharmacol Ther 2009; 30: 37-47

ULTRASOUND

- In studies reported to be ~60% sensitive for HCC
- Multiple limitations
  - Does not detect infiltrative disease
  - Sensitivity decreased in difficult patients
    - Cirrhotic nodular livers
    - Obesity
    - Abdominal gas
    - Noncompliant with breath-hold
  - Highly operator dependent
- Real life US sensitivity likely much lower than that of studies

PREDICTORS OF ULTRASOUND FAILURE

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- Retrospective study of 1170 patients evaluated causes of failure of US
  - HCC was found beyond Milan criteria in 32.2% of patients surveilled semi-annually with US
  - Single HCCs ⩽2 cm were detected in only 20% of cases
- Nearly half of failures were associated with aggressive HCC
- Increased risk of failure of HCC detection in
  - Men
  - BMI >25
  - Child-Pugh B
  - AFP >200 ng/mL

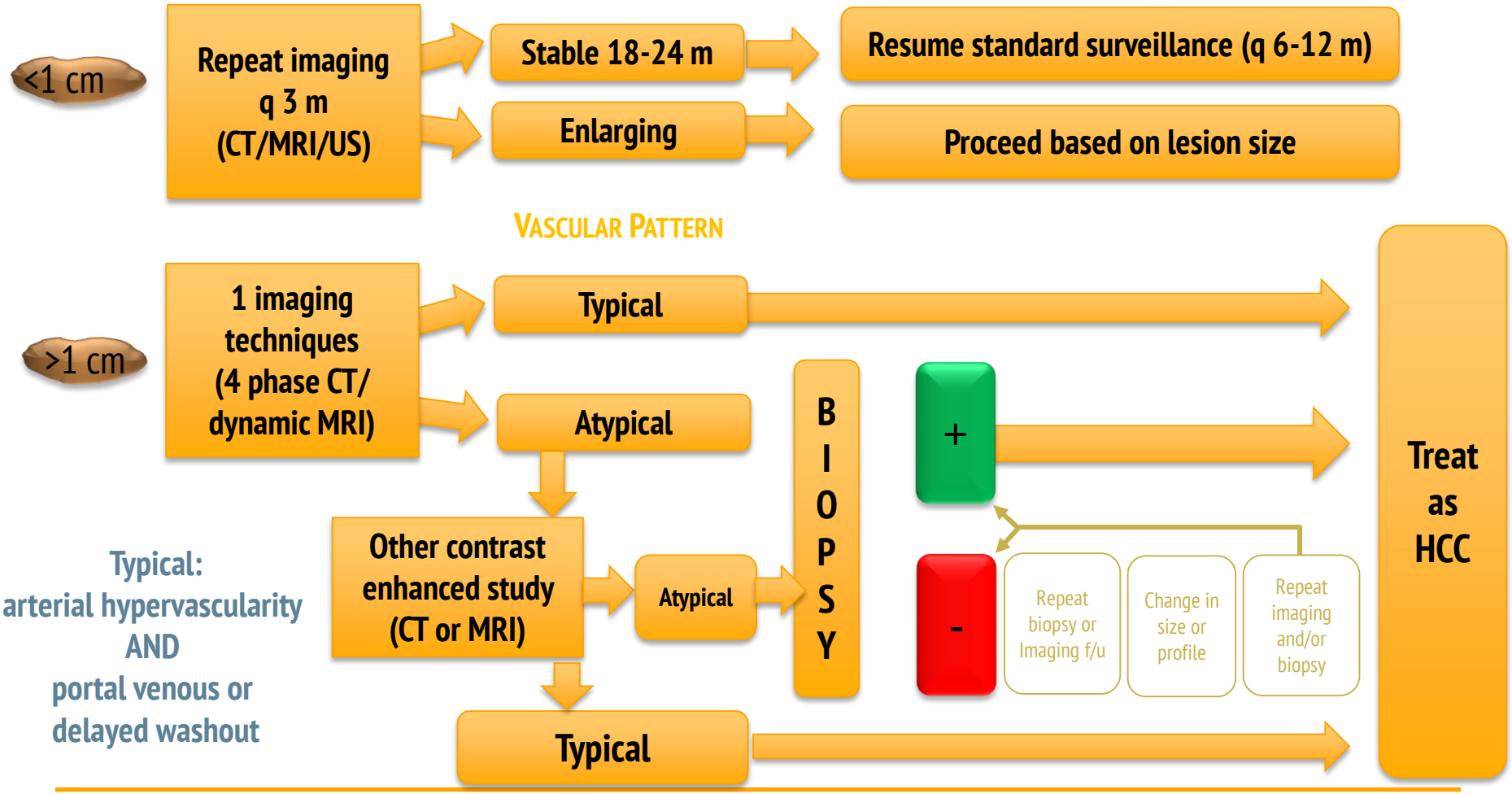
CT SCANNING FOR HCC SURVEILLANCE IS COSTLY

Variable	Ultrasound surveillance (n=83)	CT surveillance (n=80)	*P*
HCC diagnosed	8 (10.8%)	8 (10.0%)	0.86
Proportion of HCC at early stage (BCLC stage A)	5 (55.5%)	5 (62.5%)	0.93
HCC-related mortality	5 (6.0%)	7 (8.8%)	0.46
False positive imaging	3 (3.6%)	9 (5.6%)	0.06
Cost per HCC detected	$17,041	$57,383	

BCLC = Barcelona Clinic Liver Cancer staging; CT = computerized tomography
Pocha C et al. Aliment Pharmacol Ther 2013; 38: 303-312

HCC DIAGNOSIS:

Following detection of mass in cirrhotic liver or with elevation of serum biomarkers



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