



Hepatocellular Carcinoma Research Agenda

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Epidemiology

- Risk factors well known
 - Cirrhosis of any cause
 - Non- cirrhotic chronic hepatitis B
 - Tyrosinemia
 - Within risk groups there are additional risk factors
 - Age
 - Persistently elevated AFP
 - Histological
 - Nucleolar organizing region
 - Proliferating cell nuclear antigen
 - Small cell dysplasia
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Surveillance

- Zhang BH et al. J Cancer Res Clin Oncol. 2004 (Level I)
 - Randomized controlled trial of screening in chronic hepatitis B
 - Six monthly ultrasound and AFP
 - Treatment was resection
 - Reduction in mortality – 37%
 - Despite less than optimal compliance
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Surveillance

- Results cannot be extrapolated to all causes of cirrhosis
 - Fewer resections possible in cirrhosis
 - Value of ablation not assessed
 - RCT of screening vs no screening not feasible in the West
 - Benefit of screening shown in modeling studies
 - Guidelines indicate all at-risk patients should be screened
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Surveillance

- Research suggestions
 - Value of serological markers
 - US likely to detect much smaller lesions than serological testing
 - Use of CT/MRI for screening
 - Unlikely to add much since US already highly sensitive
 - Intervention unlikely for lesions smaller than 1 cm
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Early Diagnosis

- Cancer is a process
 - No clear distinction between abnormal but non-malignant and malignant
 - Borzio M et al. J Hepatol. 2003 (Level II-3)
 - Description of natural history of dysplastic nodules
 - Kojiro M, Roskams T. Semin Liver Dis. 2005 (Level II-3)
 - Description of the earliest lesions that can be called malignant with some degree of certainty
 - Stromal invasion
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Early diagnosis

- Suggested research agenda
 - Define the risk of progression of HCC for
 - Low grade and high grade dysplasia
 - Cirrhotic nodule
 - Compared to cirrhotic livers in which these diagnoses have not been made
 - Define radiologic appearances of various dysplastic and other nodules
 - CEUS, MDCT, DMRI
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Staging

- No universal agreement on staging
 - Commonly used staging systems
 - BCLC
 - CLIP
 - JIS
 - None of these accurate for very early HCC
 - Research agenda
 - Large scale multinational multicenter prospective study with prospective validation
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Treatment Guidelines

- Bruix J, Sherman M. Hepatology. 2005 (Level III)
 - AASLD Practice Guidelines
 - No RCT's for Resection vs no Rx
 - Chemoembolization superior to no therapy (2 RCT's)
 - No RCT for PEI vs no therapy
 - PEI vs resection 1 RCT – small sample
 - Equivalent results
 - PEI vs RFA
 - 3 RCT's
 - RFA is superior
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Treatment

- Suggested research agenda
 - Ablation vs observation for lesions not proven to be HCC
 - Negative biopsy or dysplastic lesions
 - Atypical appearance on imaging
 - Lack of washout in early or late venous phase
 - Combination therapy
 - Ablation enhancers
 - Doxorubicin (liposomal or non-liposomal)
 - Portal vein balloon
 - Others
 - TACE plus ablation
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