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HCC EARLY DETECTION AND SCREENING

DISCLAIMER

Please note:

The views expressed within this presentation are the personal opinion of the author. They do not necessarily represent the views of the author's academic institution or the rest of the HCC CONNECT group

HCC SURVEILLANCE USING ULTRASOUND AND AFP IMPROVES EARLY DETECTION AND SURVIVAL IN PATIENTS WITH CIRRHOSIS

Nicole E. Rich et al. AASLD Washington DC 2017

STUDY DESIGN

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Aims:

- Identify correlates for receipt of HCC surveillance
- Characterize association between HCC surveillance and early tumor detection
- Evaluate benefit of adding AFP to ultrasound-based surveillance

Methods:

- Retrospective cohort study of 932 patients diagnosed with HCC from 2 health systems in the U.S – 359 surveillance-detected and 573 incidental/symptomatic

AFP: alpha feto-protein
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PREDICTORS FOR SURVEILLANCE DETECTED HCC

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	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Male gender	1.41 (1.04 – 1.91)	1.46 (0.98 – 2.18)
Race		
Non-Hispanic White	Reference	Reference
Black	0.77 (0.55 – 1.08)	1.25 (0.80 – 1.95)
Hispanic	0.84 (0.61 – 1.17)	1.0 (0.66 – 1.52)
Liver disease etiology		
Viral hepatitis	Reference	Reference
Alcohol-related cirrhosis	0.65 (0.43 – 1.00)	**0.57 (0.34 – 0.96)**
Non-alcoholic steatohepatitis	0.58 (0.38 – 0.89)	**0.27 (0.16 – 0.49)**
Child Pugh Class		
Child Pugh A	Reference	Reference
Child Pugh B	0.63 (0.47 – 0.84)	**0.58 (0.41 – 0.83)**
Child Pugh C	0.46 (0.30 – 0.70)	**0.45 (0.26 – 0.76)**
Hepatology care, year prior to diagnosis	7.90 (5.69 – 10.9)	**6.76 (4.67 – 9.79)**
Primary care visit, year prior to diagnosis	3.55 (2.67 – 4.69)	**4.65 (3.17 – 6.81)**
Safety net-health system (vs. tertiary care center)	0.54 (0.41 – 0.73)	**0.30 (0.20 – 0.46)**

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RESULTS

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- Patients detected by surveillance were significantly more likely to be found at an early stage than those who presented incidentally or symptomatically
  - Within Milan: 255 (71.0%) vs. 157 (27.5%), p<0.001
  - Stage BCLC 0/A: 237 (66.2%) vs. 151 (26.4%), p<0.001
- Surveillance-detected tumors were found by ultrasound alone in 190 (52.8%) of cases, AFP alone in 47 (13.1%), and both ultrasound and AFP in 123 (34.2%)
- Adding AFP to ultrasound significantly increased sensitivity for early tumor detection compared to ultrasound alone: 313/933 (33.5%) vs. 360/933 (38.6%), p=0.02

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CONCLUSIONS

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- HCC surveillance is associated with increased early detection and improved survival
- However, most HCC patients, particularly those outside of hepatology subspecialty care, are detected outside of surveillance programs so efforts are needed to improve surveillance utilization
- Using AFP with ultrasound increases HCC detection at an early stage, when curative therapies are still available
- However, over one-fourth of surveillance-detected HCC are found beyond an early stage, highlighting the need for better surveillance imaging tests and biomarkers

FREQUENCY, EVALUATION, AND SUBSEQUENT CLINICAL OUTCOMES OF CIRRHOSIS PATIENTS WITH ABNORMAL IMAGING FINDINGS DURING SURVEILLANCE FOR HCC

Neehar D. Parikh et al. AASLD Washington DC 2017

STUDY OVERVIEW

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Background:

- Value of a screening program must balance benefits (early tumor detection) and potential harms, including physical harms from false positive findings

Aims:

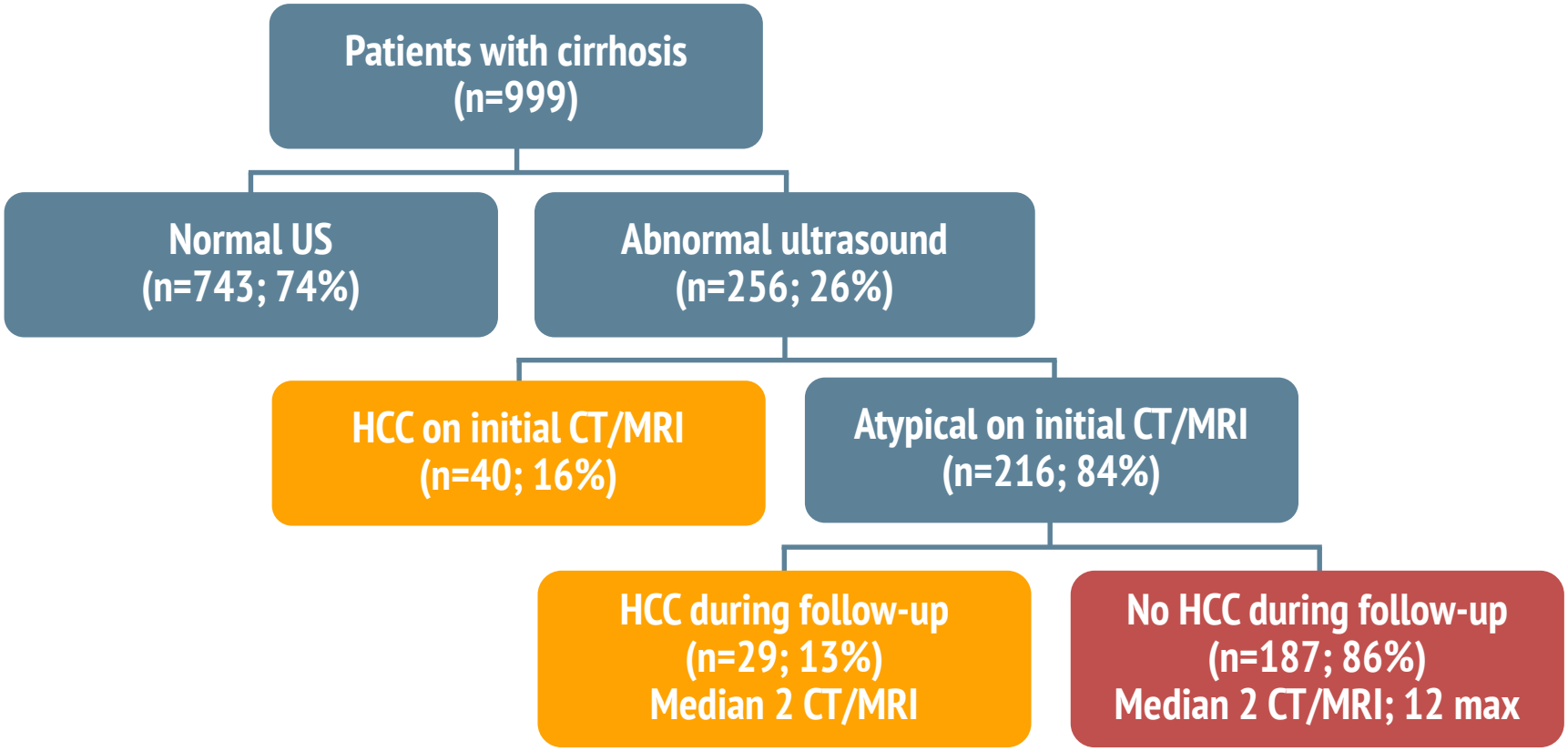
- Single-center retrospective cohort study among patients in an organized surveillance program using electronic medical record reminders

METHODS

- Of 999 patients, surveillance was completed every 6, 9, and 12 months in 46%, 51%, and 68% of patients during median follow-up of 2.2 years

- There were 256 (26%) patients with at least one abnormal imaging study
  - 40 patients diagnosed with HCC on initial imaging
  - 29 diagnosed with HCC during follow-up imaging
  - 144 had false positive and returned to US-based surveillance
  - 43 continued to be followed by CT/MRI for indeterminate nodules
  - Of the 69 HCC patients, 78% were within Milan Criteria at diagnosis

STUDY DESIGN



US: ultrasound

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CONCLUSIONS

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- False positive findings are common in HCC surveillance programs, resulting in potential physical, psychological, and financial harms
- Risk stratification tools to better target HCC surveillance programs to patients with cirrhosis at highest risk for HCC could improve surveillance value
- Better imaging and biomarkers with improved sensitivity for early tumor detection *and* improved specificity to reduce surveillance-related harms are needed

RCT OF MAILED OUTREACH AND PATIENT NAVIGATION TO INCREASE HCC SURVEILLANCE IN PATIENTS WITH CIRRHOSIS

Amit Singal et al. ILCA Seoul 2017

STUDY OVERVIEW

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Background:

- Fewer than 20% of patients with cirrhosis undergo HCC surveillance in clinical practice
- The most common reason for lack of HCC surveillance is lack of orders by clinic providers

Aims:

- Evaluate effectiveness of a mailed outreach intervention +/- patient navigation to increase repeat HCC surveillance rates over 18 months

METHODS

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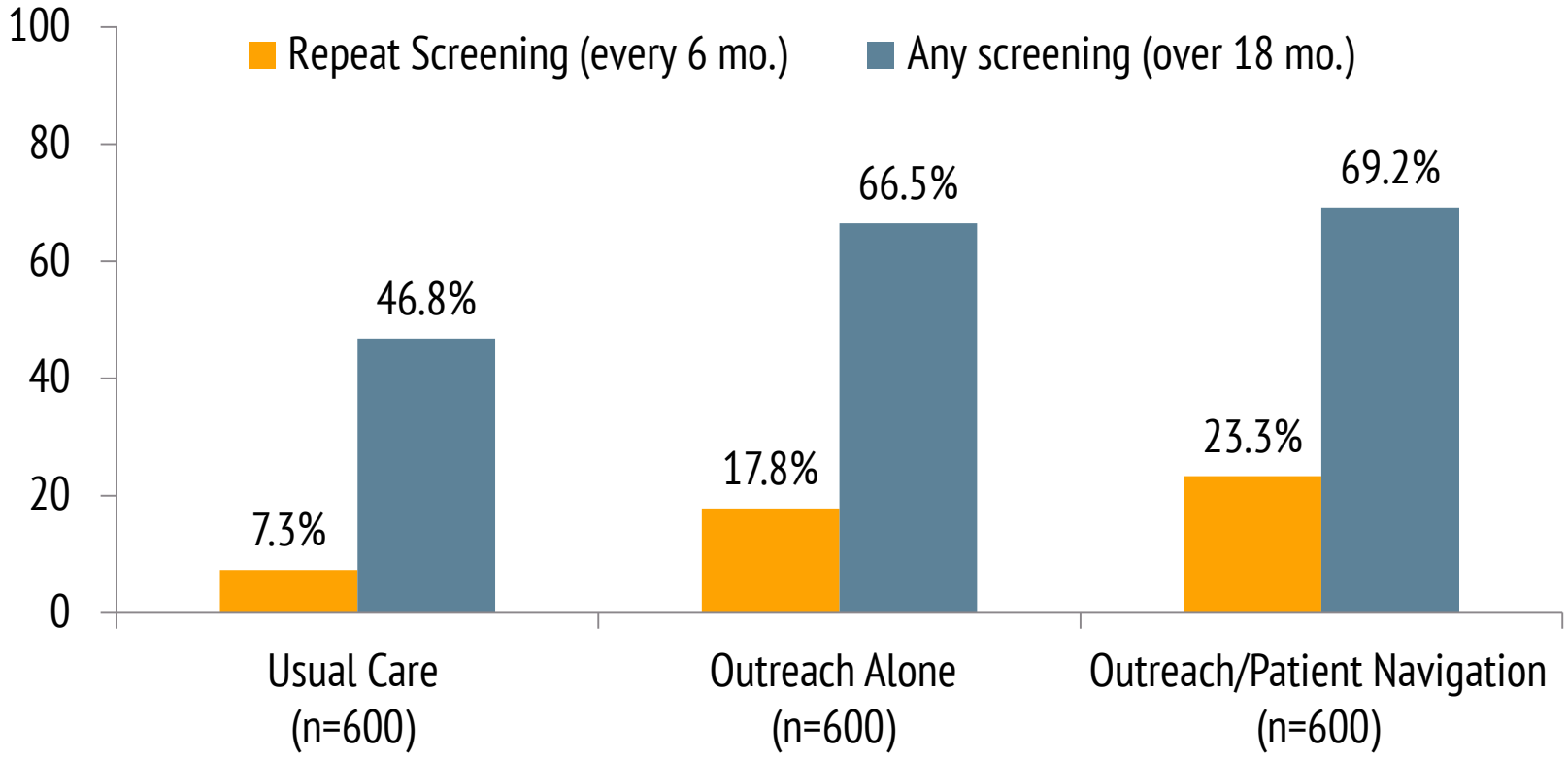
- Pragmatic randomized trial comparing 3 strategies for HCC surveillance
  - **Arm 1:** Usual visit-based surveillance by clinic providers
  - **Arm 2:** Mailed surveillance outreach
  - **Arm 3:** Mailed surveillance outreach + patient navigation
  - Arms 2 and 3 received one-page letter with HCC risk information and invitation for ultrasound

- Included patients with documented or suspected cirrhosis with an outpatient visit in prior year
  - **Documented cirrhosis** was defined using ICD-9 codes for cirrhosis or cirrhosis-related complications
  - **Suspected cirrhosis** defined as AST to platelet ratio index (APRI) $\geq$1.5 in the presence of liver disease

RESULTS


100
80
60
40
20
0
Repeat Screening (every 6 mo.)
Any screening (over 18 mo.)
7.3%
46.8%
17.8%
66.5%
23.3%
69.2%
Usual Care
(n=600)
Outreach Alone
(n=600)
Outreach/Patient Navigation
(n=600)

CONCLUSIONS

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- Outreach strategies can significantly increase consistent HCC surveillance completion among patients with cirrhosis
  - Can be a viable method of HCC surveillance delivery for large health systems

- Addition of patient navigation to an outreach strategy *may* be of additional benefit

PHASE III BIOMARKER STUDY FOR HCC SURVEILLANCE USING AFP, AFP-L3, AND DCP: A PROSPECTIVE COLLECTION WITH RETROSPECTIVE BLINDED EVALUATION

Hashem B. El-Serag et al. AASLD Washington DC 2017

STUDY OVERVIEW

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Background:

- AFP, AFP-L3% and DCP are used for HCC surveillance in Japan and have been evaluated in phase II biomarker studies; however there are fewer longitudinal phase III data

Aims:

- To evaluate AFP, AFP-L3% and DCP for identification of HCC among patients with cirrhosis

Methods:

- Interim results from cohort study at a single center between August 2014 and July 2017
- Prospective sample collection with retrospective blinded assays for biomarkers

DCP: Des-gamma carboxyprothrombin

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RESULTS

- Of 615 patients, 29 have developed HCC
  - 26 had abnormal surveillance imaging
- HCC unifocal in 62% of cases and mean tumor size 2.0 cm
- Curative treatment in 29%, TACE 17%, and 38% no treatment

	HCC within 6 months		HCC within 12 months	
	True positive rate	False positive rate	True positive rate	False positive rate
AFP >20 ng/mL	0.29	0.05	0.28	0.05
AFP-L3% >10%	0.43	0.06	0.44	0.06
DCP >2 ng/mL	0.43	0.11	0.48	0.11
Any of the above	0.71	0.20	0.68	0.19
GALAD >-0.63	0.86	0.27	0.84	0.26

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CONCLUSIONS

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- In a North American cohort of patients with cirrhosis, novel biomarkers including AFP-L3% and DCP may improve HCC detection; however, are also associated with increased false positives
- Further studies are needed to determine the ideal cut-offs to optimally balance early detection of HCC and potential surveillance-related harms
- Future studies should focus on early HCC detection, not any stage detection, and benefit of biomarkers when combined with ultrasound

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