HCC Surveillance is Associated with Potential Harms

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Background

• Hepatocellular carcinoma (HCC) is the leading cause of death in patients with cirrhosis.

• Surveillance using ultrasound every 6 months is recommended in patients with HCC.

• HCC surveillance is associated with improved rates of early tumor detection, curative treatment and overall survival.

• Experiences with breast and prostate cancer screening, in which data regarding harms created controversy about screening guidelines, highlight the importance of evaluating harms associated with HCC surveillance.

• We currently lack a high-quality assessment of potential harms associated with HCC surveillance to comprehensively inform decisions regarding HCC surveillance in patients with cirrhosis.

Aims

• To characterize and quantify potential harms of HCC surveillance among a large cohort of patients with cirrhosis

Methods

• We conducted a retrospective cohort study among patients followed at large safety-net health system.

• Inclusion criteria: Patients with cirrhosis, confirmed by chart review, with ≥1 outpatient clinic visit between January 2010 and July 2011

• Exclusion criteria: History of HCC or liver transplantation

• We recorded HCC surveillance imaging and/or alpha fetoprotein (AFP) testing between January 2010 and December 2013.
  • False positive surveillance tests were defined as suspicious mass on ultrasound or AFP ≥ 20 ng/mL with no HCC diagnosis during follow-up evaluation.

• We recorded potential harms of HCC surveillance as follows:
  • False positive tests with diagnostic CT or MRI scans (associated with contrast injury and radiation exposure)
  • False positive tests with diagnostic biopsy (associated with risks of pain, bleeding, and bile leak)
  •False positive tests with potential for psychological distress (e.g. anxiety and/or depression)
  • Potential for over-diagnosis, in which detected tumors would be of minimal clinical significance given competing risk of liver-related mortality

• Predictors of harms were identified using logistic regression analysis, with significance defined as $p < 0.05$.

Results

•We identified 571 patients with cirrhosis, with median follow-up of 2.8 years.

Table 1: Patient Characteristics

Variable	All Pts (n=571)
Age (years)	53.0 ± 12.6
Gender (% male)	384 (67.3%)
Race	
Caucasian	205 (35.9%)
Black	94 (16.5%)
Hispanic	255 (44.7%)
Asian	15 (2.6%)
Etiology of liver disease	
Hepatitis C	288 (50.4%)
Hepatitis B	20 (3.5%)
Alcohol-induced	175 (30.7%)
Nonalcoholic steatohepatitis	71 (12.4%)
Other	17 (3.0%)
Insurance Status	
Medicare	165 (28.9%)
Medicaid	123 (21.6%)
Private Insurance	20 (3.5%)
Uninsured/Dallas County Subsidy Program	262 (46.0%)
Child Pugh Class	
Child Pugh A	170(29.8%)
Child Pugh B	328 (57.4%)
Child Pugh C	73 (12.8%)
Receipt of Hepatology Subspecialty Care	269 (47.6%)

• HCC surveillance had been performed in 551 (96.5%) patients
  • 431 had at least one surveillance ultrasound
  • 425 had at least one surveillance AFP level

• 155 (28.1%) patients had ≥ 1 false positive surveillance test
  • 110 patients had false positive surveillance ultrasound
  • 57 patients had false positive AFP level ≥ 20 ng/mL

• 123 (22.3%) patients had at least one diagnostic cross sectional imaging study (4-phase CT or MRI)
  • 49 (8.9%) patients had multiple CT or MRI studies
  • 2 (0.4%) patients underwent biopsy after 8 CT/MRI scans
  • 1 (0.2%) patient underwent angiogram after 7 CT/MRI studies

Table 2: Triggers for Diagnostic Evaluation

Surveillance Tests	All Pts (n=123)
Coarse echotexture without mass on ultrasound	27 (22.0%)
Subcentimeter mass on ultrasound	14 (11.4%)
Hepatic mass ≥ 1 cm on ultrasound	42 (34.1%)
AFP level > 20 ng/mL	31 (25.2%)
Coarse echotexture on ultrasound and AFP ≥ 20 ng/mL	3 (2.4%)
Subcentimeter mass on ultrasound and AFP ≥ 20 ng/mL	1 (0.8%)
Hepatic mass ≥ 1 cm on ultrasound and AFP ≥ 20 ng/mL	5 (4.1%)

Results

Figure 1: Prevalence of Harms Related to HCC Surveillance

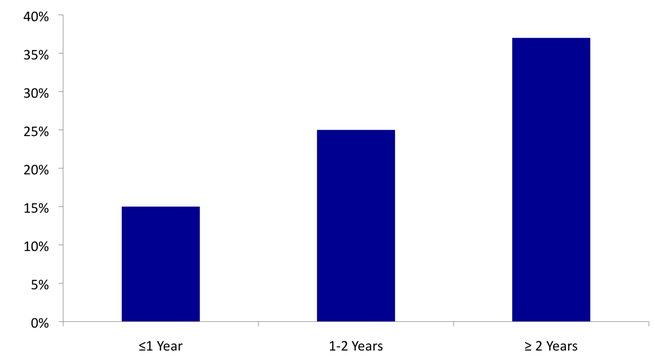

Table 3: Predictors of HCC Surveillance Harms

Variable	Univariate OR (95% CI)	Multivariate OR (95% CI)
Male gender	0.94 (0.64 – 1.37)	
Caucasian race	0.83 (0.57 – 1.21)	
Viral liver disease*	1.41 (0.98 – 2.03)	1.60 (1.04 – 2.46)
County Subsidy Program*	2.23 (1.48 – 3.38)	2.21 (1.45 – 3.40)
Child Pugh A cirrhosis	0.74 (0.50 – 1.11)	
Receipt of Hepatology care*	2.15 (1.49 – 3.11)	2.32 (1.52 – 3.59)

* Included in multivariate model

• Surveillance harms were observed in 40% of patients covered by the county healthcare subsidy plan compared to 23% of patients with health insurance.

• Patients evaluated in Gastroenterology clinic were more likely to have harms from HCC surveillance than patients seen in other clinics (39% vs. 23%).

• Surveillance harms were more likely in patients with viral liver disease than non-viral etiologies (33% vs. 26%).

Conclusions

• Over one-fourth of patients with cirrhosis have false-positive HCC surveillance tests.

• Over one-fifth of patients undergo harms from HCC surveillance, with nearly 10% having multiple diagnostic exams.

• Ultrasound results in more HCC surveillance harms than AFP in clinical practice.

• Better HCC surveillance tools, with higher specificity, are urgently needed.