Utilization of Hepatocellular Carcinoma Surveillance in Patients with Cirrhosis: A Systematic Review and Meta-Analysis

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BACKGROUND

- Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer related death worldwide.
- Studies have demonstrated an association between receipt of HCC surveillance and improved survival.
- Prior studies have demonstrated that only a minority of patients with cirrhosis undergo HCC surveillance
- Lower surveillance rates have been attributed to poor provider knowledge of surveillance guidelines, under-recognition of liver disease, and patient-reported barriers.

AIMS

- Quantify HCC surveillance utilization in patients with cirrhosis, examine socio-demographic correlates of HCC surveillance, and summarize intervention efforts to increase surveillance receipt

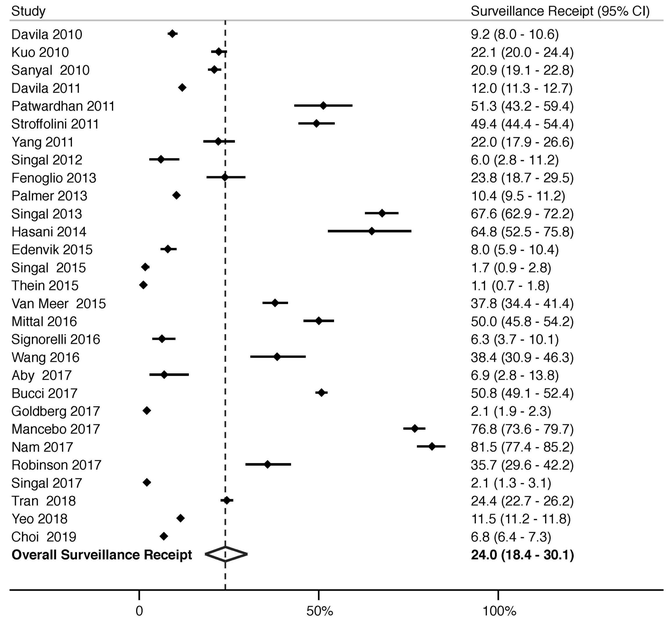
METHODS

- We conducted a search with Medline from January 2010- August 2018 with keyword combinations: [screen$ or surveillance or detect$ or diagnosis] AND [liver ca$ or hepatocellular ca$ or hcc or hepatoma].
- We searched relevant conference abstracts from 2017 and 2018, performed manual searches of references from relevant articles and consulted expert hepatologists to identify additional references or unpublished data.
- Inclusion criteria included cohort studies that described receipt of surveillance in patients with cirrhosis. Excluded studies characterized receipt of one-time screening and those utilizing patient survey or self-reported methodology.
- Surveillance receipt was defined as the proportion of patients with repeated imaging and/or AFP prior to HCC diagnosis.
- We collected data regarding study period, region, population of interest, surveillance definition and interval, duration of follow-up, and potential correlates of surveillance receipt.
- We recorded a description of the intervention and surveillance receipt in the intervention and control groups for studies assessing interventions to increase surveillance receipt.
- We assessed the risk of bias for each study using a modified Newcastle-Ottawa scale .
- Primary outcome was HCC surveillance rates among patients with cirrhosis.
- Weighed pooled estimate of overall surveillance and subgroup analysis was computed.

RESULTS

12,728 citations found → 855 abstracts reviewed → 69 full texts reviewed → 29 surveillance + 7 intervention articles

Figure 1: Pooled Surveillance Utilization



- Lowest surveillance observed among U.S. studies vs. Europe and Asia (17.8% vs. 43.2% vs. 34.6%, p<0.001)
- Highest surveillance noted in cohorts from Gastroenterology and Hepatology clinics vs. those followed by subspecialty and primary care, or population-based cohort studies (73.7% vs. 29.5% vs. 8.8%, p<0.001)

Table 1: Correlates of Surveillance Utilization

Author, year	Age	Gender	Race	Alcohol abuse	NAFLD	Hepatology care
Davila 2010						+
Davila 2011	– (<50)	NS	– (Black)	–	–	
Patwardhan 2011	NS	NS	NS	NS	NS	+
Singal 2012	NS	NS	NS	–	NS	+
Fenoglio 2013				–	–	
Palmer 2013	NS	+ (F)	NS			
Singal 2013	NS	NS	NS	NS		
Hasani 2014	NS	NS		NS	NS	NS
Edenvik 2015	NS	NS		–	–	
Singal 2015	NS	+ (M)	NS	NS	–	
Thein 2015	NS	NS		–	NS	
Wang 2016	NS	NS				
Goldberg 2017	+(older)		– (Black)	–	–	
Mancebo 2017	NS	NS		–		
Robinson 2017		NS	NS		+	
Singal 2017	NS	NS	NS	–	–	+
Tran 2018	+ (>54)	NS	+ (Asian)	NS		

- Consistently positive correlates were number of clinic visits and receipt of hepatology subspecialty care
- Lower surveillance observed in patients with NASH or alcohol-related cirrhosis than other etiologies

Table 2: Implemented Interventions and Outcomes

Author Year	Intervention	Outcome	Pre-Intervention	Post-Intervention	Absolute Difference
Aberra 2013	Nurse base protocol	One-time abdominal imaging	119/160 (74.4%)	331/355 (93.2%)	18.8%
Kennedy 2013	PCP patient education, system redesign	Semi- annual US + AFP for 2 years	0/22 (0%)	14/22 (63.6%)	63.6%
Beste 2015	EMR Reminder	≥2 abdominal imaging in 18 months	103/564 (18.2%)	218/790 (27.6%)	9.4%
Del Poggio 2015	PCP Education	HCC diagnosed by surveillance	85/244 (34.8%)	105/190 (55.3%)	20.5%
Nazareth 2016	Nurse-led clinic	Semi-annual US	-	40/76 (52.6%)	-
Farrell 2017	Radiology led recall	Semi-annual US	-	368/804 (45.8%)	-
Bui 2017	Physician extender	3 abdominal imaging in 2 years	51/224 (22.8%)	183/224 (81.7%)	58.9%
Singal 2019	Mailed outreach	Semi-annual US in 18 months	44/600 (7.3%)	247/1200 (20.6%)	13.3%

- Both in-reach and outreach interventions appear to increase HCC surveillance utilization in patients with cirrhosis – including those followed in academic centers with high baseline surveillance receipt

CONCLUSION

- HCC surveillance continues to be underutilized, with only 1 in 4 patients with cirrhosis receiving surveillance.
- Surveillance underuse is more prominent in patients with non-viral cirrhosis and those followed by primary care providers or outside academic centers.
- Interventions utilizing provider and patient education, reminder systems, and outreach can improve HCC surveillance rates.

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