

Screening for Hepatocellular Carcinoma (HCC) in HIV/HCV-Coinfected Patients: Impact on Staging, Therapy, and Survival.



Marina Núñez¹, Luciana Kikuchi², Pablo Barreiro³, Mark Nelson⁴, María Eugenia Vispo³, Emma Page⁴, Rena Fox⁵, Edmund J. Bini^{6,7}, Morris Sherman⁸, Norbert Bräu^{9,10}.
The Liver Cancer in HIV Study Group

Wake Forest University, Winston-Salem, NC, USA(1); Universidade de São Paulo, São Paulo, Brazil(2); Hospital Carlos III, Madrid, Spain(3); Chelsea and Westminster Hospital, London, UK(4); University of California San Francisco, San Francisco, CA, USA(5); New York University, New York, NY, USA(6); VA New York Harbor HCS, New York, NY, USA(7); University of Toronto, Toronto, ON, Canada(8); Bronx VA Medical Center(9); Mount Sinai School of Medicine, New York, NY, USA(10)

Background

- Sonographic screening for HCC in patients with chronic hepatitis B has been shown to prolong life.
- This has not yet been proven in HCV-infected patients.
- No studies are available examining the effect of HCC screening in HIV/HCV-coinfected patients
- This multi-center study applied published methods to account for lead time bias of screened subjects.

Methods

- **Retrospective analysis in 20 centers in 5 countries:** Canada, United States, Brazil, United Kingdom, Spain.
- **All HCC cases in HIV/HCV-coinfected patients 1992 – 2009 with data on initial presentation : N=70.** Diagnosis by AASLD criteria (Bruix & Sherman, *Hepatology*, Nov-05)
- **Definitions:**
 - **Screened = asymptomatic, presented with abnormal screening AFP or imaging studies**
 - **Unscreened = symptomatic with work-up initiated by symptoms, not screening results**
- **Analysis of tumor characteristics, staging, therapy, and survival**
- **Estimation of lead time of screened pts. using tumor doubling time method:**
Lead Time (T) = Tumor Doubling Time * 3log (median tumor size unscreened/screened) * 1/ log(2)
 (Schwartz M, *Cancer*, 1961)
Here: T = 112 days * 3log (4.7 cm/3.2 cm) * 1/ log(2)
= 186 days (6.11 mo)
- **Published median HCC tumor doubling time in HIV-negative: 112 days Same in 2 independent studies** (Okada S, *Hepatogastroenterology*, 1993; Chang S, *Am J Roentgenol*, 2005)

Patient Characteristics

	Screened n=39 (57%)	Unscreened n=31 (43%)	P
Age (yrs), Mean ± SD	50.2 (±7.8)	53.3 (±7.4)	0.10
Male Sex	36 (92.3%)	25 (80.6%)	0.17
Race/Ethnicity			0.29
Black	17 (43.6%)	17 (54.8%)	
White	17 (43.6%)	8 (25.8%)	
Latino	5 (25.8)	6 (19.4%)	
Asian	0	0	
Time of HCC Diagnosis Date, median	Mar-2004	Jul-2003	0.38
Alcohol Consumption			0.39
None	13 (34.2%)	8 (26.7%)	
Moderate	11 (28.9%)	6 (20.0%)	
Excessive	14 (36.8%) ^[1]	16 (53.3%) ^[1]	
Unknown			
Liver Function, Mean ± SD Child-Turcotte-Pugh Score	6.56	7.48	0.024
Stage A	24 (61.5%)	11 (35.5%)	
Stage B	12 (30.8%)	15 (48.4%)	0.09
Stage C	3 (7.7%)	5 (16.1%)	
HIV parameters			
CD4+ Cells (per mm ³), Median	308	227	0.25
CD4+ Cells <200 per mm ³	10/37 (27%)	13/31 (42%)	0.20
HIV RNA (Copies/mL), Median	<400	895	0.27
HIV RNA <400 Copies/mL	15/38 (40%)	16/30 (53%)	0.25

HCC Tumor Characteristics

	Screened n=39	Unscreened n=31	P
Hepatic Lesions			0.85
Solitary Tumors	28 (51%)	19 (45%)	
Multiple tumors	25 (46%)	21 (50%)	
Diffusely Infiltrative Tumors	2 (3.6%)	2 (4.8%)	
Median Size Largest Lesion (cm), Range, for Tumor Doubling Time	3.2 (1.5 – 10)	4.7 (2.1 – 16)	0.014
Eligibility for Liver Transplantation			0.27
Meets Milan Criteria	17/32 (53%)	10/26 (39%)	
Meets Expanded Milan Criteria ('up-to-7', Mazzaferro V et al., <i>Lancet Oncology</i> , Jan-09)	25/28 (89%)	11/17 (65%)	0.063
Portal Vein Thrombosis	4 (10.3%)	5 (16.1)	0.50
Extrahepatic Metastases	3 (7.7%)	8 (25.8%)	0.051
AFP level			0.001
Median (ng/mL), Interquartile Range	222 (23 – 1,126)	2,818 (310 – 33,030)	
Normal (≤ ULN), n (%)	3 (7.7%)	4 (14.3%)	0.44

HCC Staging

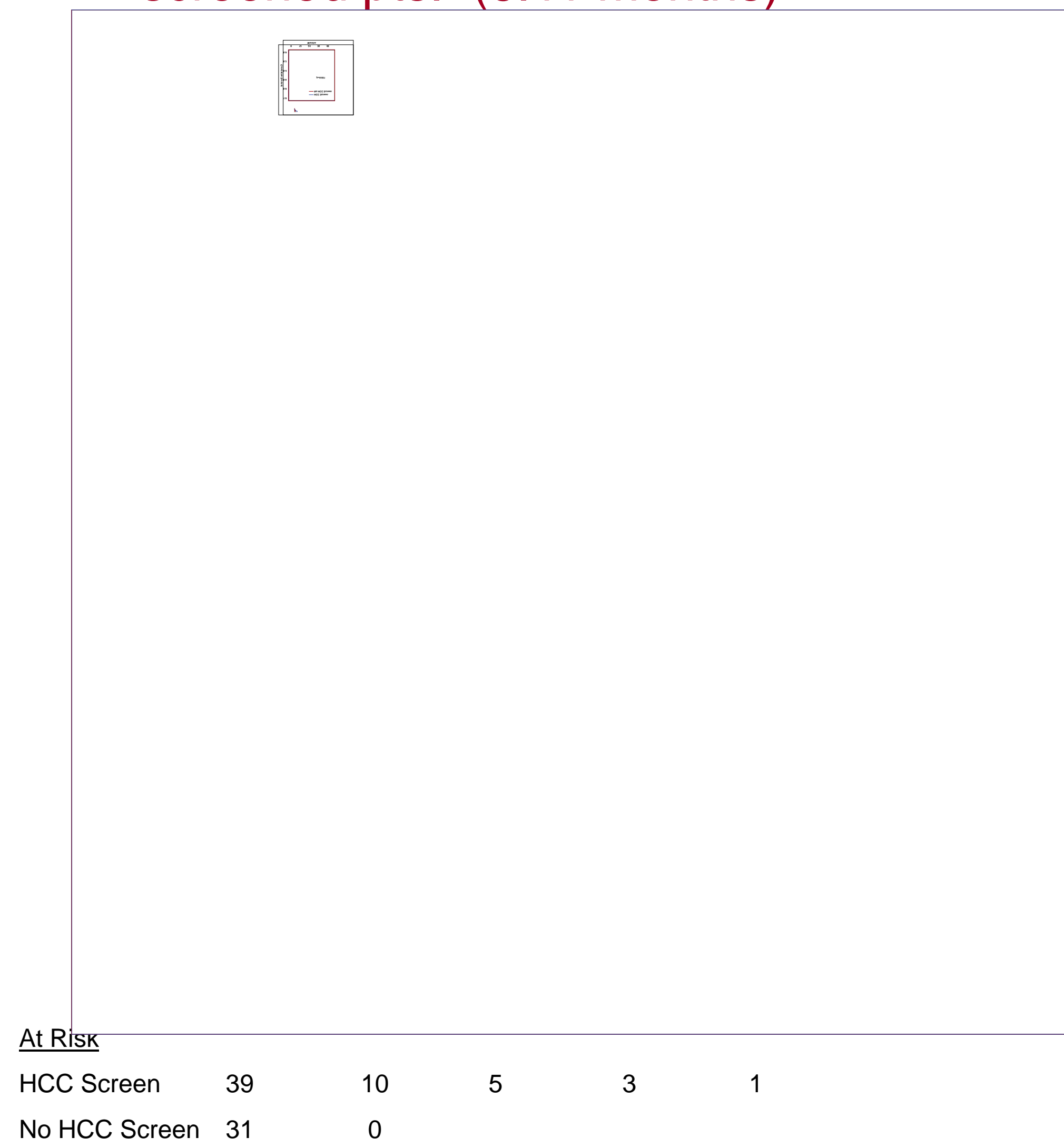
	Screened n=39	Unscreened n=31	P
BCLC Stage, n (%)			
A	18 (46%)	3 (10%)	
B	9 (23%)	3 (10%)	
C } Advanced,	9 (23%)	19 (61%)	0.001
D } Incurable	3 (8%)	6 (19%)	
BCLC Stages C and D	12 (31%)	25 (80%)	<0.001
CLIP Score, Mean ±SD	1.99 (±1.1)	2.45 (±1.4)	0.006

HCC Therapy

	Screened n=39	Unscreened n=31	P
Potentially Curative Therapy	15 (39%)	6 (19%)	
Radiofrequency Ablation (RFA)	9	3	
Ethanol Injections	5	1	
Surgical Resection	1	2	
Liver Transplantation	0	0	
Effective, Non-Curative Therapy	11 (28%)	7 (23%)	0.095
Transarterial Chemoembolization	11	5	
Sorafenib	0	2	
No Therapy	13 (33%)	18 (58%)	
Any Potentially Curative Therapy	15 (39%)	6 (19%)	0.083
Any Effective Therapy	26 (67%)	13 (42%)	0.039

Survival

Adjusted for lead time of screened pts. (6.11 months)



Median Survival:
HCC screen 12.8 months
No HCC screen 3.7 months

Summary and Conclusion

- (1) A large proportion of HIV/HCV-infected patients with HCC (43%) were not screened.
- (2) HCC screening was associated with **better liver function and earlier HCC stages.**
- (3) HCC screening was associated with **higher eligibility for liver transplantation** (by expanded Milan criteria)
- (4) HCC screening was associated with **more frequent use of potentially curative HCC therapy**
- (5) After adjustment of lead time bias, **survival was better** in screened than in unscreened patients.

This study support extension of current guidelines to screen all HCV-infected patients with cirrhosis by ultrasonography every 6-12 months to HIV/HCV-coinfected patients as well

To contribute your cases of HCC in HIV patients for further studies, please contact:

Norbert Bräu norbert.brau@va.gov Tel: (+1) 917-701-3867