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Long-term Survival of Fibrolamellar Hepatocellular Carcinoma Versus Conventional Hepatocellular Carcinoma:

A US Population-based Study

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To the Editor

We read with great interest the article by Weinmann et al,¹ examining the trends in epidemiology, treatment, and survival of a large German cohort of hepatocellular carcinoma (HCC) patients between 1998 and 2009. The International Classification of Diseases for Oncology classifies HCC into HCC not otherwise specified (HCC-NOS), which accounts for the vast majority of HCC, scirrhous HCC, spindle cell variant HCC, clear-cell HCC, pleomorphic HCC, and fibrolamellar HCC (fHCC).² Although, Weinmann and colleagues restricted their analysis to HCC-NOS, we decided to study fHCC in more depth. Fibrolamellar variant of HCC is rare and occurs in a distinctly different group of patients. It occurs in young patients with no sex predominance, unlike common HCC, which occurs 4 to 8 times more often in men.³ It usually does not occur in the setting of hepatitis and cirrhosis unlike common HCC, which usually does.⁴ With the aim of providing more epidemiologic evidence on the differences between fHCC and HCC-NOS, we examined data from the surveillance, epidemiology, and end results (SEER) database. The SEER database was queried to identify patients with fHCC and HCC-NOS from 1998 to 2010. Patients diagnosed within 1 month before death (including patients diagnosed at autopsy or by death certificate) and patients with another malignant primary tumor diagnosed within 5 years before their HCC diagnosis were excluded to minimize the chance that metastatic disease to the liver was misdiagnosed as HCC. Median survival was calculated overall for fHCC and HCC-NOS, and subgroup analyses by treatment modality and stage at diagnosis were also performed. Cumulative survival was calculated using the method of Kaplan and Meier and survival curves were compared using the log-rank test. All analyses were performed using SEER*stat and IBM SPSS version 20.0.

Using the SEER database, 46,417 patients with HCC-NOS and 191 patients with fHCC met our inclusion criteria. The overall median survival was 6 months (95% confidence interval, 5.8-6.2) and 24 months (95% confidence interval, 16.0-32.0) for HCC-NOS and fHCC, respectively. There was a statistically significant increase in median survival for fHCC compared with HCC-NOS (log-rank $P < 0.001$, Fig. 1). Table 1 summarizes the results of our subgroup analysis by stage and treatment modality.

Data from this study suggest that although patients with fHCC seem to have a better overall median survival than HCC-NOS, the survival benefits seem to be limited to patients with higher stages of disease (regional and metastatic spread) and untreated patients. There seems to be no difference in survival outcomes for fHCC and HCC-NOS, when curative treatments (RFA, resection, and transplant) are utilized as therapeutic options.

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Figure 1.
The Kaplan-Meier survival curves comparing fibrolamellar HCC and conventional HCC.
HCC indicates hepatocellular carcinoma.

Table 1
Median Survival by Stage and Treatment Modality for Fibrolamellar HCC Versus HCC-NOS

Variables	Fibrolamellar HCC (N)	Median Survival, 95% CI	HCC-NOS (N)	Median Survival, 95% CI	P
SEER historic stage *					
Localized	64	45.0 (13.9-76.1)	20812	17.0 (16.4-17.6)	0.09
Regional	62	23.0 (6.8-39.2)	12534	5.0 (4.8-5.2)	0.05
Distant	60	16.0 (11.8-20.2)	7267	2.0 (1.9-2.1)	0.001
No reported intervention	95	9.0 (6.3-11.7)	35643	4.0 (3.9-4.1)	0.01
Reported intervention					
RFA, resection, transplant *	91	74.0 (49.1-98.9)	9155	51.0 (48.5-53.5)	0.21

* Radiofrequency ablation (RFA), resection, and transplants combined because of small counts for specific fibrolamellar therapy as treatment with curative intent. Results for other types of surgery that are not potentially curative were not reported.

CI indicates confidence interval; HCC, hepatocellular carcinoma; HCC-NOS, hepatocellular carcinoma not otherwise specified.