

TABLE 6: Identification of hazards for HCC recurrence related deaths by univariate Cox regression,  $n = 199$  (non-HCC recurrence related deaths excluded).

Univariate Cox regressions for HCC recurrence related deaths		$n$	$p$	exp(B)/hazard	95.0% CI	
					Lower	Upper
Underlying disease	Hepatitis B with D	11	0.348	<i>Reference category</i>		
	Hepatitis B	50	0.368	1.964	0.451	8.553
	Hepatitis C	55	0.542	1.584	0.361	6.939
	Hepatitis C with B	6	0.908	0.868	0.079	9.588
	Alcohol	30	0.162	2.919	0.65	13.109
	Cryptogenic cirrhosis	30	0.13	3.151	0.714	13.896
	Other	17	0.433	1.93	0.373	9.979
Tumor vitality	Vital tumor	168	0.083	<i>Reference category</i>		
	Full-necrotic tumor	17	0.147	0.352	0.086	1.442
	No tumor detectable	14	0.084	0.175	0.024	1.264
Tumor morphology	<i>No tumor detectable</i>	14	<0.001	<i>Reference category</i>		
	Uninodular	89	0.323	2.765	0.368	20.791
	Multinodular unilateral	41	0.104	5.354	0.707	40.567
	Multinodular bilateral	55	0.019	10.898	1.488	79.801
UICC-7	<i>No or necrotic tumor</i>	31	<0.001	<i>Reference category</i>		
	UICC I	54	0.688	0.746	0.178	3.124
	UICC II	51	0.402	1.738	0.477	6.327
	UICC IIIA	21	0.003	6.771	1.944	23.584
	UICC IIIB	26	<0.001	12.792	3.791	43.16
	UICC IIIC	6	0.006	8.066	1.800	36.142
	UICC IVA	7	<0.001	226.972	46.041	1118.915
hMILAN	UICC IVB	3	<0.001	91.043	16.824	492.692
	Inside	112		<i>Reference category</i>		
	Outside	87	<0.001	4.701	2.700	8.185
Vascular infiltration	<i>No or necrotic tumor</i>	31	<0.001	<i>Reference category</i>		
	V0	117	0.371	1.733	0.52	5.779
	V1	21	<0.001	9.578	2.769	33.128
	V2	30	<0.001	14.066	4.221	46.866
Neoadj. therapy	No	82		<i>Reference category</i>		
	Yes	117	0.010	0.525	0.321	0.859
Grading	<i>No or necrotic tumor</i>	31	<0.001	<i>Reference category</i>		
	G1	26	0.26	2.179	0.562	8.442
	G2	103	0.061	3.098	0.948	10.124
	G3-4	36	0.001	7.909	2.357	26.542
	Missing data	3	0.007	11.921	1.980	71.774

HCC = hepatocellular carcinoma.

UICC-7 = 7th edition TNM classification of Unité Internationale Contre Cancer.

hMILAN = histologic MILAN classification.

Vascular infiltration: V0 = none, V1 = small vessels, and V2 = large vessels.

Tumor grading: G1 = low, G2 = intermediate, and G3-4 = high to anaplastic.

#### 4. Discussion

The results of this study containing the complete data of our center since 1975 demonstrate that hepatocellular carcinoma can be cured by LT—even in advanced tumor stages. As expected, long-term survival was mainly limited by HCC recurrence (HCCR) ( $p < 0.001$ , exp(B) = 10.156; time-dependent Cox regression) and any covariate with high potency for HCC recurrence therefore was a significant

negative predictor of survival as well. Vice versa, covariates that were not associated with a significantly higher rate of HCC recurrences (e.g., *underlying diseases*) had no significant impact on tumor-free survival. We were surprised though to find that not only intrahepatic HCCRs (some of which might have been de novo HCCs) but extrahepatic HCCR also can occur more than 10 years after LT—without synchronous intrahepatic HCC recurrences. We believe that these tumors must have been dormant metastatic HCC manifestations,