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Embolotherapy for Neuroendocrine Tumor Liver Metastases: Prognostic Factors for Hepatic Progression-free Survival and Overall Survival

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Background: Embolotherapies play an important role in the management of neuroendocrine tumor (NET) liver metastases, but available data on prognostic factors remains limited and controversial, leading to wide practice variations and uncertainty regarding optimal embolotherapy modality. The purpose of this study was to evaluate disease and treatment related variables in a modern context for factors affecting outcomes following embolotherapy.

Methods: This was a multicenter retrospective study of patients with NET liver metastases, who were treated with conventional transarterial chemoembolization (TACE), transarterial embolization (TAE), or selective internal radiation therapy (SIRT) between 2004-2015. The primary endpoints were hepatic progression-free survival (HPFS) and overall survival (OS). Survival analysis with Cox proportional hazards models was performed to evaluate tumor and treatment related factors including WHO 2010 grade, tumor type, and embolotherapy modality.

Results: 184 cases with mean follow-up time of 28 months were analyzed. Univariate and multivariate Cox proportional hazards models are shown in table 1. Higher tumor grade conferred significantly higher hazard ratios (HR) for HPFS and OS on univariate analysis, but the associations weaken on multivariate analysis. Tumor burden of 50% liver volume or greater conferred significantly higher HRs for HPFS and OS in multivariate analyses. No significant differences in HRs for HPFS or OS were seen among tumor types. In grade 1 and 2 tumors, SIRT conferred significantly lower HR for HPFS. In grade 3 tumors, SIRT conferred significantly higher HR for HPFS and OS than TACE.

Conclusion: Higher WHO 2010 grade and hepatic tumor burden of 50% or greater were negative prognostic factors for HPFS and OS following liver-directed embolotherapy. Tumor type was not a significant prognostic factor for HPFS or OS. SIRT demonstrated improved HPFS for grade 1 and 2 tumors, but worsened OS versus TACE for grade 3 tumors.

Table 1. Univariate and multivariate Cox proportional hazards analysis for hepatic progression-free survival and overall survival following embolotherapy

	Hepatic progression-free survival				Overall survival			
	Univariate		Multivariate		Univariate		Multivariate	
	HR	P-value	HR	P-value	HR	P-value	HR	P-value
WHO 2010 Grade								
Grade 1	1	N/A	1	N/A	1	N/A	1	N/A
Grade 2	1.61	**0.02**	1.99	0.09	2.1	**0.01**	1.72	0.36
Grade 3	4.02	**0.00**	1.43	0.52	6.9	**0.00**	1.92	0.42
Embolotherapy by grade								
Grade 1	1	N/A	1	N/A	1	N/A	1	N/A
TACE	0.49	0.06	0.47	**0.05**	0.80	0.69	0.53	0.30
SIRT	0.70	0.33	0.61	0.24	0.66	0.49	0.34	0.10
TAE								
Grade 2	1.37	0.41	1	N/A	1.39	0.54	1	N/A
TACE	0.94	0.89	0.41	**0.03**	2.03	0.20	0.73	0.53
SIRT	0.76	0.56	0.55	0.20	1.51	0.54	1.17	0.81
TAE								
Grade 3	1.82	0.19	1	N/A	3.02	0.09	1	N/A
TACE	5.61	**0.001**	4.92	**0.01**	13.58	**0.000**	10.02	**0.002**
SIRT	5.83	0.10	3.88	0.24	13.97	**0.02**	5.71	0.17
TAE								
Tumor type								
Pancreatic NET	1	N/A	1	N/A	1	N/A	1	N/A
Gut NET	0.93	0.66	1.12	0.64	1.26	0.34	1.85	0.09
Bronchial NET	2.48	0.36	1.31	0.63	1.53	0.42	0.69	0.62
Other	0.69	0.38	0.40	0.11	0.71	0.53	0.20	0.13
Tumor burden								
< 25%	1	N/A	1	N/A	1	N/A	1	N/A
25-50%	1.29	0.21	1.69	**0.05**	0.90	0.70	1.56	0.28
50-75%	1.83	**0.02**	2.32	**0.008**	2.35	**0.01**	3.50	**0.008**
> 75%	1.69	0.14	2.99	**0.01**	1.67	0.25	5.08	**0.003**
Prior hepatic resection or ablation	1.26	0.26	2.16	**0.004**	1.05	0.84	1.87	0.09
Extrahepatic metastases	0.99	0.94	0.81	0.38	1.02	0.29	1.04	0.91
Systemic therapy								
Octreotide	0.56	**0.003**	0.57	**0.03**	0.58	**0.03**	0.80	0.55
Biologic	1.56	**0.03**	1.49	0.16	1.51	0.10	1.35	0.48
Cytotoxic	1.62	**0.01**	1.01	0.98	2.31	**0.000**	1.72	0.20

Abbreviations: HR – hazard ratio, TACE – transarterial chemoembolization, SIRT – selective internal radiation therapy, TAE – transarterial embolization, NET – neuroendocrine tumor