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Practical Evaluation of Tumor Number-Volume Distribution Predicts Liver-Specific Progression-Free Survival after Surgery for Neuroendocrine Tumor Liver Metastases

Yosuke Kasai^{1,1}; Kenzo Hirose^{1,1}; Carlos Corvera^{1,1}; Grace Kim¹; Brandon Shih¹; Robert Warren^{1,1}; Emily Bergsland^{1,1}; Eric Nakakura^{1,1}

¹University of California, San Francisco

BACKGROUND: Previous reports have ascribed improved outcomes to tumor debulking for patients with neuroendocrine tumor liver metastases (NELM), but the methods used to assess the extent of tumor debulking are ill-defined. Here, we propose a simple and practical method to evaluate the tumor volume that when combined with the liver tumor number--tumor number-volume distribution--reliably predicts liver-specific progression-free survival.

METHODS: Seventy patients who underwent surgery for NELM between 2007 and 2017 were analyzed. Individual liver tumor diameter ≥ 1 cm was measured on preoperative imaging, and the index of the total liver tumor volume was calculated by the sum of the cube of the individual tumor diameter. Extent of debulking was assessed by comparing preoperative and postoperative imaging for the individual tumor. The primary outcome was liver-specific progression-free survival (LSPFS). Progression was determined as defined by RECIST 1.1.

RESULTS: A median of 2 tumors (range 1-28) were debulked, mainly using a parenchyma-sparing technique (69%). Forty-four patients (63%) underwent 100% debulking. The median overall survival was not reached with a median follow-up of 23.1 months. The median LSPFS was 10.5 months. Adjusting by

WHO2017-Grade, tumor number ≥ 4 [hazard ratio (HR): 5.95, 95% confidence interval (CI): 2.15-18.6] and tumor volume index $\geq 40 \text{ cm}^3$ (HR: 2.78, 95% CI: 1.15-7.28) were independent prognostic factors for LSPFS. When tumor number-volume distribution was categorized into low-distribution (LD: tumor number ≤ 3 and tumor volume index $< 40 \text{ cm}^3$), high-distribution (HD: tumor number ≥ 4 and tumor volume index $\geq 40 \text{ cm}^3$), and intermediate-distribution (ID: the others), LSPFS significantly differed based on the tumor number-volume distribution (Table 1).

CONCLUSION: Tumor number-volume distribution calculated by our simple and practical method predicts LSPFS after debulking surgery for NELM.

Table 1:

Liver-specific progression-free survival (LSPFS) stratified by tumor number-volume distribution

Distribution	Median LSPFS	95% CI	Log-rank P-value vs LD/ID/HD
LD (22 patients)	33.8 months	13.1-93.4	-/0.029/< 0.001
ID (21 patients)	16.0 months	7.7-33.6	0.029/-/0.003
HD (27 patients)	4.2 months	2.9-6.5	< 0.001/0.003/-

CI: confidence interval, **LD:** low-distribution, **ID:** intermediate-distribution, **HD:** high-distribution