

## Stratification of Liver Metastasis Burden in Pancreatic Cancer Patients: A Novel 2-2 5-5 Model

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**Background/Aims:** Despite its wide scope, hepatic metastasis has been uniformly regarded as a ‘single-organ metastasis’ in metastatic pancreatic cancer (MPC). We aimed to stratify liver metastasis in MPC based on tumor burden and evaluate their prognosis

**Methods:** Patients with MPC treated at Seoul National University Bundang Hospital between 2011 and 2021 were included as a training cohort, and those from Seoul St. Mary’s Hospital and Hallym University Sacred Heart Hospital were included as an external validation cohort. Liver metastasis burden was stratified based on the number and longest diameter of the metastases according to the CT images at the time of diagnosis. To develop the stratification model, the optimal cutoff of number and size of metastatic liver mass was derived using repeated Cox proportional hazard regression in multi-layer subgroup analyses and modified with chemotherapy regimen. The ‘H category classification’ suggested by the Japanese Society for Cancer of the Colon and Rectum (JSCCR) were also referred to. The stratification criteria were validated using external validation cohort.

**Results:** A total of 1,257 patients were eligible (training cohort 1,084; validation cohort 173). We derived a “two-two five-five” criteria and defined each group as follows: (1) Oligo-metastasis, one or two hepatic metastases and the largest diameter of metastasis  $\leq 2$  cm; (2) Meso-metastasis, as non-Oligo and non-Mega metastasis group; and (3) Mega-metastasis, five or more hepatic metastases or the largest diameter of these metastases  $\geq 5$  cm. Using this criteria, median overall survival (OS) was significantly different among each group: (1) Oligo, 11.4 months; (2) Meso, 9.2 months (HR 1.66, 95% CI 1.14–2.43) and (3) Mega, 5.6 months (HR 2.63, 95% CI 1.94–3.58) in the training cohort. The validation cohort also showed reproducible result, as the median OS of Oligo-metastasis group was 5.8 months and Mega-metastasis group was 1.81 months (HR 1.94, 95% CI 1.16–3.22).

**Conclusions:** The “two-two five-five” criteria successfully stratified MPC patients with hepatic metastasis into three groups according to their survival in both training and validation cohort.

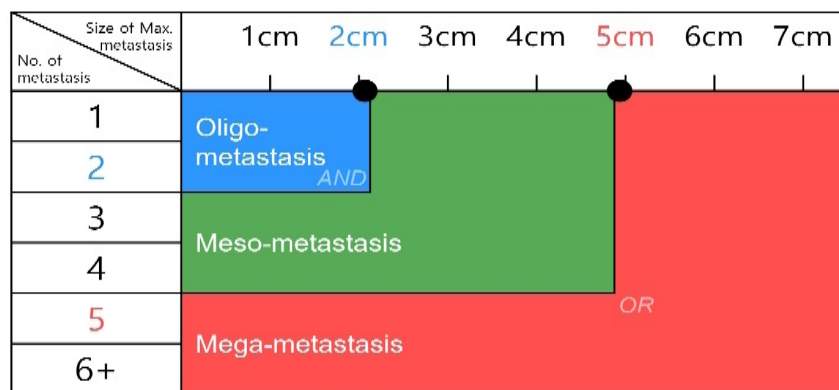


Figure 1. The “two-two five-five” criteria

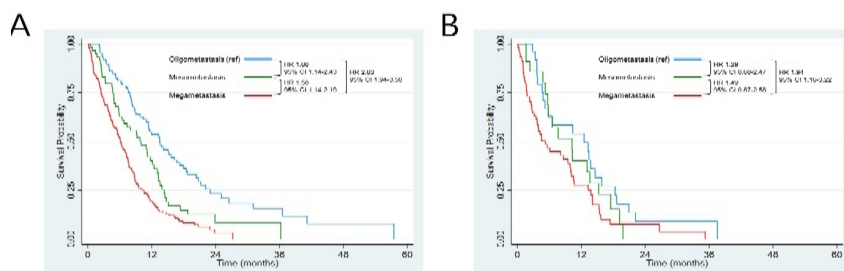


Figure 2. (A) Survival in Training Cohort  
(B) Survival in Validation Cohort