

## P-5

# Higher Serotonin Levels from Ileum Neuroendocrine Tumors are associated with Mesenteric Mass Progression

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### BACKGROUND

Serotonin produced by ileum neuroendocrine tumors (i-NETs) promotes development of the mesenteric mass (MM) associated with lymph node metastases. We previously reported that more extensive MM progression along the superior mesenteric vessels predicts a lower rate of complete surgical resection. In this study, we hypothesized that tumoral serotonin production is associated not only with the development of MM but also its progression, and we examined serotonin levels and the extent of MM involvement.

### METHODS

One hundred eighty-two patients who underwent resection of primary i-NETs in a single institution between January 2007 and February 2023 were included retrospectively in this study. Serotonin production was measured by urine 24h 5-HIAA before the resection. The extent of MM progression was graded as 0 to 3 based on the distance from the MM and root of the ileocolic vessels. Mesenteric mass volume was calculated as  $\text{diameter}^3 \times \pi / 6$ . Mann-Kendall trend test or linear regression model was utilized to examine the statistical correlations.

### RESULTS

The extent of MM progression correlated with levels of urine 24h 5-HIAA (p-value = 0.0013) in patients without hepatic or ovarian metastasis. However, there was no correlation in those with hepatic or ovarian metastasis (p-value = 0.79). Moreover, MM volume did not correlate with urine 24h 5-HIAA levels ( $R^2 = 0.04$ , p-value = 0.20). Finally, urine 24h 5-HIAA levels were higher in cases with incomplete lymph node resection than in those with complete lymph node resection (mean (SD) 5.7 (3.0) vs 15.4 (10.9) mg/day, p-value = 0.020).

Table. Urine 24h 5-HIAA and MM progression/grade.

MM grade	0: No MM	1: MM > 2cm distant from the root of ICA/V	2: MM < 2cm distant from the root of ICA/V	3: MM involving SMA/V
<b>Liver, Ovary Metastasis (-)</b>	N = 21	N = 34	N = 17	N = 8
<b>Urine 5-HIAA (mg/day)</b>	3.6 (3.0, 5.4)	5.8 (4.7, 7.5)	6.7 (4.8, 9.0)	12.3 (7.5, 19.7)
<b>Liver, Ovary Metastasis (+)</b>	N = 15	N = 42	N = 18	N = 14
<b>Urine 24h 5-HIAA (mg/day)</b>	20 (13, 61)	37 (14, 90)	44 (17, 106)	26 (21, 102)
Median (IQR)				

## CONCLUSIONS

We observed higher urine 24h 5-HIAA levels associated with more extensive MM progression along the superior mesenteric vessels, but not tumor volume in the absence of distant disease. The mechanisms by which local serotonin may promote regional tumor progression are unknown but may provide new therapeutic targets for i-NETs.

## ABSTRACT ID 23711

