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Relevance of Serum Chromogranin A as Diagnostic and Prognostic Marker for Well-Differentiated Pancreatic Neuroendocrine Tumors

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Background: Chromogranin A (CgA) is a protein involved in the secretory process of neuroendocrine cells and widely used as neuroendocrine tumor biomarker. In the literature there is no consensus on whether CgA is a reliable marker for diagnosis or prognosis. The aim of this study was to investigate the value of CgA as a diagnostic and prognostic marker for patients with well differentiated pancreatic neuroendocrine tumors (WD-PanNETs).

METHODS: Patients with WD-PanNET and a pre-treatment CgA measurement, between 2011 and 2016 at MSKCC were retrospectively reviewed. The CgA serum value was measured by ELISA assay (reference range ≤ 15 ng/mL). The diagnostic value was evaluated comparing CgA values from WD-PanNETs with values obtained from a healthy control group (n=20). We used Cox regression to investigate the prognostic significance of CgA for OS.

RESULTS: 99 patients with WD-PanNET and a pre-treatment CgA measurement were identified. As a diagnostic test, CgA showed a 95% of specificity, a sensitivity of 66%, and an overall diagnostic accuracy of 70.5%. The PPI use was associated with an increase in CgA level (median 60 vs 44 ng/ml, $p=0.015$) and the exclusion of these patients from the analysis led to a reduction of sensitivity to 60% and of accuracy to 68.2%. Patients with an elevated serum CgA had a higher grade (as measured by Ki67) and more advanced stage of disease (Table

1). For the prognostic value analysis, we found that CgA was not prognostic ($p=0.170$), and only Ki67 ($p=0.016$) and stage of disease (IV) ($p=0.025$) were significantly associated with OS.

CONCLUSION: The results of this retrospective study suggest that CgA has a limited role as a diagnostic biomarker for WD-PanNET, especially in patients with localized disease. In addition, our results suggest that an elevated CgA level may have no prognostic value when compared with other known pathological factors.

Table 1:
Association of CgA pre-treatment value with Clinical and Pathological characteristics of 99 patients with diagnosis of WD-PanNET. UNL indicates Upper Normal Level

Characteristics	CgA values \leq UNL N=34	CgA value $>$ UNL N=65	p-value
Non-Functional, No (%)	32 (94)	58 (89)	0.714
Familial Syndrome, No (%)	6 (18)	2 (3)	0.018
Primitive Site, No (%)			0.281
Head	15 (44)	20 (31)	
Body	10 (29)	18 (28)	
Tail	9 (27)	27 (41)	
Primitive Tumor Size, median (IQR)	cm 3.4 (5)	3.2 (2)	0.591
Positive OctreoScan	8/14 (51)	48/51 (94.1)	<0.001
Ki67 %*, median (IQR)	3.8 (6)	10 (18)	0.025
PPI Use, No (%)	8 (23)	26 (40)	0.122

* Available for 76 patients