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Metabolic Changes in Pheochromocytoma and Paraganglioma: Correlation Between Plasma Hormone Levels, Weight and Diabetes

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BACKGROUND: Pheochromocytomas and paragangliomas (PCC/PGL) are catecholamine-secreting neuroendocrine tumors that cause metabolic and physiologic changes. The goal of this study was to evaluate the relationship between individual plasma hormone levels, body weight, and hemoglobin A1C (HA1C) level during treatment.

METHODS: A retrospective cohort study was performed. PCC/PGL patients with at least one measurement of weight and plasma catecholamines or metanephrines were included. Primary outcome was weight change, and secondary outcome was A1C. Wilcoxon rank-sum tests compared non-parametric, continuous variables; mixed-effect linear modeling (MEM) evaluated relationships between hormones and weight or HA1C.

RESULTS: 360 patients were included, encompassing 7,663 weight measurements and 2,362 hormone observations. Median weight on presentation was 82.2 kg (IQR:66.4-95.6) and median duration of the study was 54.2 months (IQR:19.0-95.1). 75.6% (n=272) underwent surgical resection and 20.6% (n=74) exhibited metastatic and/or recurrent disease (MRD). On multivariable MEM, higher plasma normetanephrine (p=0.049) and dopamine (p=0.045) levels correlated with weight loss, and a history of surgery for PCC/PGL (p=0.004) correlated with weight gain. When stratified by BMI, subjects with higher BMIs demonstrated a less significant decrease in weight with higher normetanephrine levels. In the surgical cohort, weight increased with time from surgery and inversely correlated with normetanephrine level ($p<0.0005$). Patients with elevated normetanephrine/norepinephrine levels were less likely to gain weight (46.2% vs. 70.7%, p=0.0011). MRD status was not independently associated with weight change. Rather, the final hormone levels correlated with overall weight change: if the last norepinephrine level was normal, patients were more likely to gain weight than those with persistently elevated levels (72.4% vs. 33%, $p<0.0005$). Normetanephrine ($p<0.0005$) directly correlated with HA1C.

CONCLUSION: Normetanephrine levels correlate with HA1C, and inversely correlate with weight in PCC/PGL. After surgical resection, declining hormone levels correlate with improving HA1C despite increasing weight; persistently elevated hormone levels and decreasing weight are observed in and may indicate MRD.

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