C-34

Risk for Malignancy by Using VHL Genotype-Directed Protocol for the Surveillance of PNETs in Patients with Von Hippel-Lindau Disease

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BACKGROUND: About 20% of patients with von Hippel-Lindau disease (vHLd) harbor pancreatic neuroendocrine tumors (PNETs), which require annual CT scan for surveillance. There has been significant literature that demonstrate radiation from imaging studies increases the risk of future cancer. Based on a natural history study of surveillance in patients with vHLd-associated PNETs we have proposed an evidence based surveillance program: patients having small PNETs (<1.2 cm diameter), and either non-missense and/or non-exon 3 VHL mutations ("low risk genotype") are followed every two years, based on their low risk for metastases and/or intervention. In the current analysis, we analyzed the lifetime cumulative radiation exposure (CRE) and the excess lifetime risk for developing colon cancer (ELC) based on the current vs. former surveillance protocols.

METHODS: A prospective study (median follow-up 54 months, range 12-84), including patients with vHLd and pancreatic lesions undergoing surveillance imaging follow-up. Lifetime CRE was calculated by multiplying each patient mean scans/year by 48 years (age 18-65 years), and by 19 mSv (median 3-phasic CT scan radiation). This was compared to the predicted CRE according to the

change in the surveillance protocols implemented. ELC was calculated using a radiation risk assessment tool (RadRAT 4.1.1).

RESULTS: 381 surveillance intervals in 124 patients (mean age 50.0±12.9 years) were included in the current analysis (median interval 12 months, range 6-55). The proposed new surveillance algorithm based on tumor size and VHL genotype reduces the lifetime CRE of patients with small PNETs (p=0.00003), and of those with lesion diameter 1.2-3 cm and low-risk VHL genotype (p=0.00005). In addition, a decrease in CT scan rate from annual to biannual rate would significantly decrease the ELC for one patient after ≥10 years of exposure (p=0.02).

CONCLUSION: VHL genotype based surveillance algorithm for PNETs in patients with vHLd is expected to decrease the CRE, with a potential decrease in ELC.