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HIF Expression in Clear-Cell Renal Cell Carcinoma (ccRCC) Tumors of Adults with and without Obstructive Sleep Apnea (OSA)

Olivia Heppell
Wayne State University, hi9325@wayne.edu

Carlos Guerra Londono
Henry Ford Health, cguerra1@hfhs.org

Nilesh Gupta
Henry Ford Health, NGUPTA1@hfhs.org

Introduction: Upregulation of hypoxia-inducible factors (HIF) is an important pathological feature shared by clear cell renal cell carcinoma (ccRCC) and obstructive sleep apnea (OSA). However, it is unclear whether OSA alters the pathogenesis of ccRCC via HIF expression.

Methods: A retrospective cohort of adults undergoing nephrectomy for ccRCC was identified electronically (IRB#16040-1). The diagnosis of OSA was established with preoperative STOP-BANG scores or polysomnography. A consecutive sample of 20 individuals with and 20 without OSA was selected. Clinical characteristics and pathology results were reviewed. Resected tumor sections were immunohistochemically stained for HIF-1& HIF-2 at antibody dilutions of 1:150. Intensity and percentage of staining as determined by an expert uropathologist were used to calculate a histoscore (0-12).

Results: Individuals with OSA exhibited a higher prevalence of hypertension (95% vs. 50%, *p*-value 0.00138) and a greater median BMI (34.8 vs. 29.05, *p*-value 0.00578). Tumor grades and stages were not statistically different between groups. The prevalence of positive HIF-1 expression (histoscore >2) was higher in the OSA group (80% vs. 50%, p=0.0466). Nonetheless, median histoscores were not statistically different (4 vs. 2.5, p = 0.2187) between groups. A suboptimal staining quality precluded reliable HIF-2 histoscores.

Conclusion: In individuals with OSA, ccRCC tumors exhibit a higher prevalence of positive HIF-1 staining. Statistically significant differences in terms of HIF-1 histoscores, tumor grade, and stage were not identified. Future studies can use our results to perform formal sample size calculations, optimize HIF-2 staining procedures, and elucidate the role of OSA in the pathogenesis of ccRCC.