INTRODUCTION AND OBJECTIVES: Multigene panel testing has been recently introduced to evaluate hereditary cancer, however, limited information is available regarding its use in kidney cancer. In this study, we describe the outcomes of the first kidney cancer focused panel test.

METHODS: We retrospectively reviewed test results and clinical data of kidney cancer patients who underwent targeted multigene panel testing of 19 genes associated with hereditary kidney cancer from 2013 to 2016. Age of onset, gender, race/ethnicity, and patient/family cancer history were noted. The frequency of positive, inconclusive, and negative results was evaluated. A logistic regression analysis evaluated predictive factors for a positive test.

RESULTS: Patients undergoing testing (n=1,239) had a median age of diagnosis of 46 years, which is significantly younger than the U.S. population of kidney cancer (p<0.0001). Overall, 6.1%, 75.3%, and 18.6% of individuals had positive, negative, and inconclusive results, respectively. The most commonly altered genes included FLCN and FH, which were 1.8% and 1.3% of cases respectively. TSC2, MET, and PMS2 had the highest rates of variants of unknown significance (VUS) with 2.7%, 2.2%, and 1.7% of cases respectively. Early age of onset was the only factor found to be predictive of a positive test on multivariate analysis (OR 0.975, 95% p=0.0052). Furthermore, early age of onset may be the only identifying characteristic of low penetrant syndromes, such as those associated with MITF mutations, which did not have a single definitive histology nor a family history of kidney cancer, but had an early median age of onset of 39.

CONCLUSIONS: Multigene panel tests facilitate the identification of hereditary kidney cancer. This testing modality may be particularly useful when a specific syndrome is not suspected based on clinical/family characteristics. Our results support the use of early age of onset for genetic counseling and/or testing.

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