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Titel des Beitrags: Genetic spectrum and clinical correlates of somatic mutations in aldosterone-producing adenoma.

Abstract: Primary aldosteronism is the most common form of secondary hypertension. Somatic mutations in KCNJ5, ATP1A1, ATP2B3, and CACNA1D have been described in aldosterone-producing adenomas (APAs). Our aim was to investigate the prevalence of somatic mutations in these genes in unselected patients with APA (n=474), collected through the European Network for the Study of Adrenal Tumors. Correlations with clinical and biochemical parameters were first analyzed in a subset of 199 patients from a single center and then replicated in 2 additional centers. Somatic heterozygous KCNJ5 mutations were present in 38% (180/474) of APAs, whereas ATP1A1 mutations were found in 5.3% (25/474) and ATP2B3 mutations in 1.7% (8/474) of APAs. Previously reported somatic CACNA1D mutations as well as 10 novel CACNA1D mutations were identified in 44 of 474 (9.3%) APAs. There was no difference in the cellular composition of APAs or in CYP11B2, CYP11B1, KCNJ5, CACNA1D, or ATP1A1 gene expression in APAs across genotypes.
Patients with KCNJ5 mutations were more frequently female, diagnosed younger, and with higher minimal plasma potassium concentrations compared with CACNA1D mutation carriers or noncarriers. CACNA1D mutations were associated with smaller adenomas. These associations were largely dependent on the population structure of the different centers. In conclusion, recurrent somatic mutations were identified in 54% of APAs. Young women with APAs are more likely to be KCNJ5 mutation carriers; identification of specific characteristics or surrogate biomarkers of mutation status may lead to targeted treatment options.