Patients with Protein-Truncating PKD1 Mutations and Mild ADPKD

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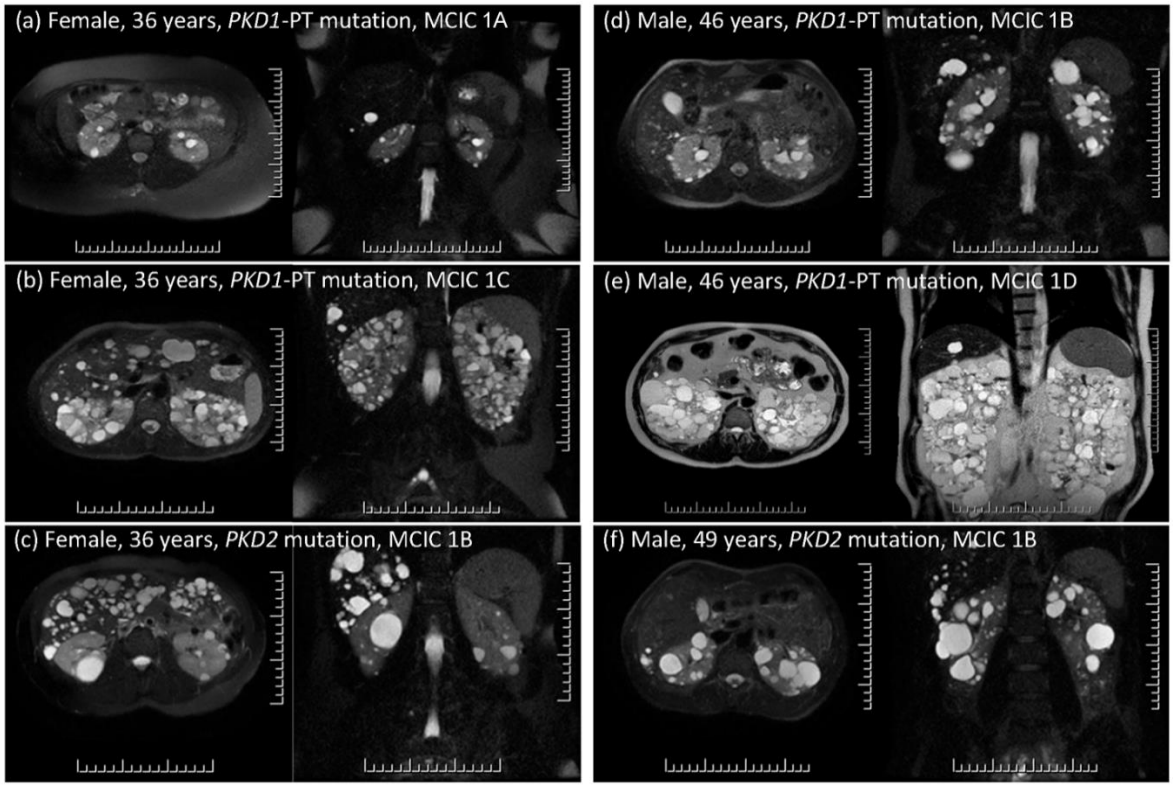
Supplemental Material. Mutation screening in study cohort.

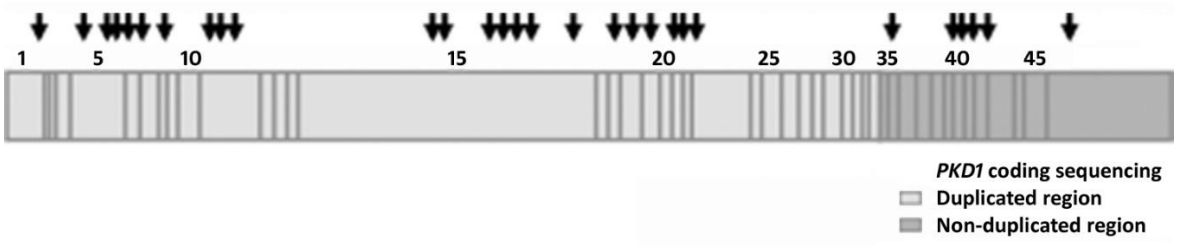
DNA samples were collected from all study patients and screened by bidirectional Sanger sequencing of the coding regions and splice junctions of both *PKD1* and *PKD2* using a validated long range PCR protocol (1). Since March 2016, targeted exome sequencing (tES) was used for our mutation screening of both genes using a published protocol (2). All pathogenic mutations identified through tES were confirmed by Sanger sequencing using a validated PCR protocol (1).

All nonsense, frameshift, and canonical splice site mutations were grouped as protein-truncating mutations, and non-synonymous missense or atypical splice site mutations were grouped as non-truncating mutations. In-frame insertions/deletions (IF-Indels) were classified separately. Non-truncating mutations were evaluated for their pathogenicity using bioinformatics prediction algorithms (Align GVGD, PolyPhen-2, SIFT, PROVEAN, and Human Splicing Finder), review of the PKD mutation database (http://pkdb.mayo.edu), and evaluation of familial co-segregation when possible (1). All mutation-negative patients were re-screened by multiplex ligation–dependent probe amplification for detection of large gene rearrangements (3).

1. Iliuta I-A, Kalatharan V, Wang K, Cornec-Le Gall E, Conklin J, Pourafkari M, et al.: Polycystic Kidney Disease without an Apparent Family History. *J Am Soc Nephrol.* 28: 2768–2776, 2017
2. Rossetti S, Hopp K, Sikkink RA, Sundsbak JL, Lee YK, Kubly V, et al.: Identification of gene mutations in autosomal dominant polycystic kidney disease through targeted resequencing. *J Am Soc Nephrol* 23: 915-933, 2012
3. Consugar MB, Wong WC, Lundquist PA, et al. Characterization of large rearrangements in autosomal dominant polycystic kidney disease and the PKD1/TSC2 contiguous gene syndrome. *Kidney Int.* 74: 1468–1479, 2008



Supplemental Figure 1. Representative axial (left) and coronal (right) magnetic resonance images comparing age-matched cystic disease severity by Mayo class in patients with different mutation types. (a) 36 year-old female with a *PKD1* truncating mutation, and Mayo clinic imaging class (MCIC) 1A; (b) 36 year-old female with a *PKD1* truncating mutation, ht-TKV = 673 ml/m, and MCIC 1C; (c) 36 year-old female with a *PKD2* mutation, ht-TKV = 279 ml/m, and MCIC 1B; (d) 46 year-old male with a *PKD1* truncating mutation, ht-TKV = 464 ml/m, and MCIC 1B; (e) 46 year-old male with a *PKD1* truncating mutation, ht-TKV = 2121 ml/m, and MCIC 1D; (f) 49 year-old male with a *PKD2* mutation, ht-TKV = 534 ml/m, and MCIC 1B. PT: protein truncating; MCIC: Mayo Clinic imaging classification; Ht-TKV: height adjusted total kidney volume.



Supplemental Figure 2. Location of *PKD1* truncating mutations and mild Mayo imaging class.