# Genetic analysis sheds light on the role of IFT140 in polycystic kidney disease

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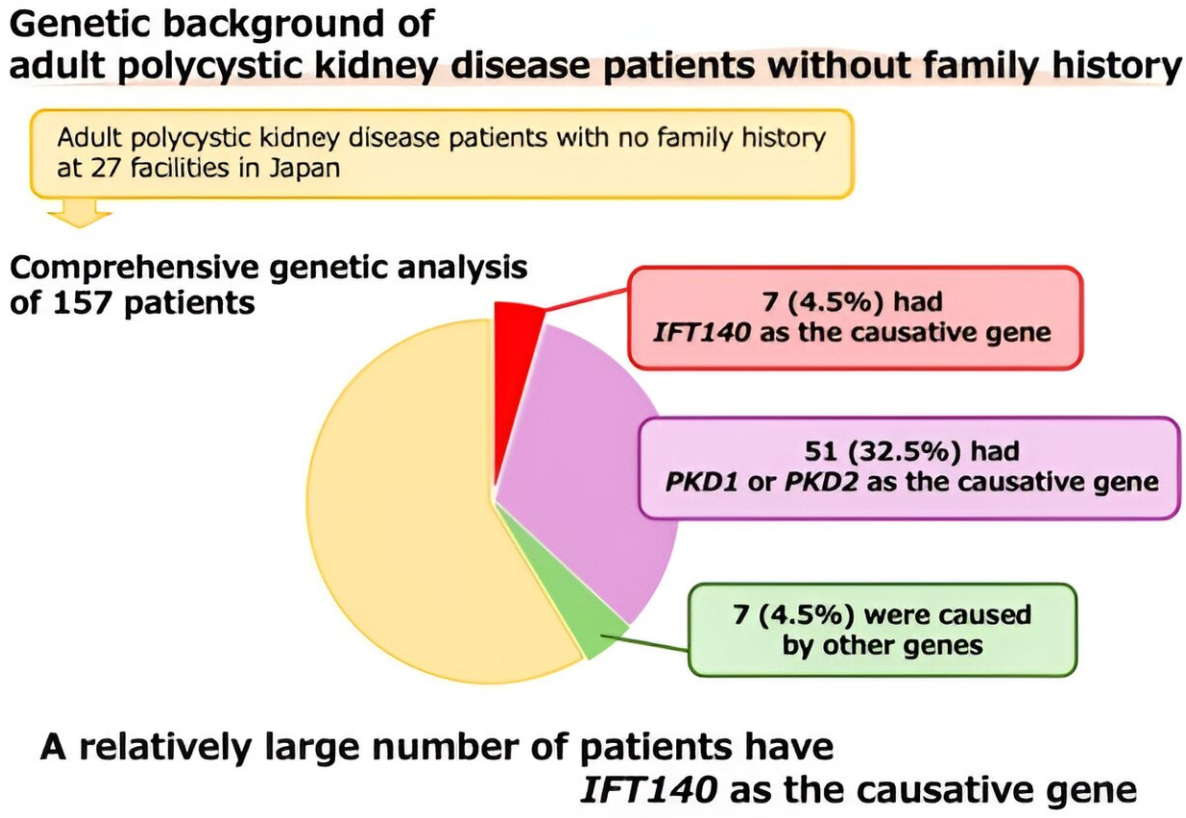


Through a comprehensive genetic analysis of patients with PKD but no family history of the disease, researchers found that a mutation in the *IFT140* gene was significantly prevalent. Compared to patients with mutations in more commonly affected genes, PKD in people with an *IFT140* mutation usually manifested in a milder form—their total kidney volume (TKV) was lower, and the cysts were sometimes asymmetric. Credit: Department of Nephrology, TMDU

Polycystic kidney disease (PKD) is an intractable disorder that causes fluid-filled cysts to grow in the kidneys. It is typically seen in adults. As one of the most prevalent hereditary kidney diseases, the autosomal dominant form of PKD is usually caused by mutations in the PKD1 and PKD2 genes.

However, one out of ten patients with this condition typically exhibit no family history of the disease and lack mutations in these well-known genes. This raises an important question about the other genetic factors that may be contributing to PKD in these cases.

In a study published online on 16 July 2024 in *Kidney International Reports*, researchers from Tokyo Medical and Dental University (TMDU) addressed a key gap in understanding PKD. They performed a comprehensive genetic analysis of patients with PKD focusing exclusively on those without a family history of polycystic kidneys.

A total of 157 adult patients were recruited in the study from 2014 to 2023, coming from 27 Japanese institutions. These patients underwent genetic testing using next-generation sequencing, covering up to 92 genes depending on the panel used for the assay. These genes were all associated with inherited kidney cystic diseases.

The results pinpointed a potential cause for PKD in a part of the cohort. "Our comprehensive genetic analysis revealed that seven patients (4.5%) had mutations in the IFT140 gene, a recently identified gene associated with PKD," says Dr. Eisei Sohara from TMDU, while discussing the results. This was in stark contrast to previous findings on IFT40.

"The proportion of monoallelic loss-of-function IFT140 variants in this cohort was higher than that in previously reported cohorts with polycystic kidneys who had a positive family history," he adds.

To shed further light on this issue, the researchers analyzed various relevant clinical characteristics of the patients. Interestingly, the kidneys of patients with mutations in the ITF140 gene were usually in a better state than those with PKD1 in terms of kidney function and cyst size.

"Because the phenotype of polycystic kidneys caused by the IFT140 gene is mild, parental kidney disease may be overlooked. Therefore, patients without a positive family history are more likely to carry pathogenic variants in IFT140," highlights Dr. Takayasu Mori from TMDU.

Explaining further, he says, "Patients with IFT140-related polycystic kidneys are also likely to be underdiagnosed because of relatively high glomerular filtration rate, smaller kidney volume, and atypical kidney cysts."

Overall, the results of this study help paint a clearer picture of the genetic landscape surrounding autosomal dominant PKD, which affects over 30,000 people in Japan alone.

"Our findings may impact clinical practice, including diagnosis, drug therapy selection, and genetic counseling for adult PKD patients without a family history," concludes Dr. Takuya Fujimaru from TMDU.

**More information:** Takuya Fujimaru et al, Importance of IFT140 in Patients with Polycystic Kidney Disease Without a Family History, *Kidney International Reports* (2024). DOI: 10.1016/j.ekir.2024.06.021

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