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PatientVoice

A Patient Perspective on Genetic Testing for ADPKD

The Lack of Complete Genetic Information, Especially Early in the Course of the Disease, Is Harming Adult Autosomal Dominant Polycystic Kidney Disease (ADPKD) Patients

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Introduction

I am honored to have been asked to comment on an article in *CJASN* by York Pei and colleagues, entitled "Insights into Polycystic Kidney Disease from Genetic Studies" (1). Overall, it would be highly desirable to diagnose patients with autosomal dominant polycystic kidney disease (ADPKD) early in life. A complete genetic profile, including whether a truncated gene is present, used in combination with noted side effects such as pain, high BP, or infections, can help an individual patient use and understand the implications from ADPKD progression calculators, such as the Mayo Classification or PROPKD (ADPKD Prognostic) tools. Key areas where patients could benefit from early diagnosis are lifestyle and medication intervention, family planning, living donation information, and increased global knowledge about the disease. However, a thoughtful approach is advised because of important legal, insurance, and emotional issues that arise from disease diagnosis.

Lifestyle and Medication Intervention

A kidney-friendly diet (getting in the habit early of drinking water instead of soda, avoiding excess consumption of energy drinks or high-protein supplements), avoiding nephrotoxic medications such as nonsteroidal anti-inflammatory drugs, avoiding potentially dangerous contact sports, and taking elevated BP in youth seriously (rather than just blowing it off as an aberration or "white coat syndrome") are all positive lifestyle choices that could improve quality of life and possibly extend the time to kidney failure. Without an early diagnosis, it is impossible for an individual to understand the importance of these actions for their long-term health.

"I wish I had known" is a common quote I've heard over the years from newly diagnosed patients, especially those with no family history. Often, this sentiment is expressed with anger or despair, after realizing that some of their lifestyle choices were destructive to their kidneys and may have shortened their time to kidney failure. Because of this, there is a great deal of regret, especially among *de novo* patients, about the lack of a process to diagnose genetic conditions early in life, and corresponding lost opportunities to participate in potentially beneficial clinical trials.

I know many patients with ADPKD whose kidneys failed in their 30s. Every one of these rapid progressors unknowingly engaged in nephrotoxic lifestyle choices such as avoidance of water, disregard of elevated BP readings, very-high-protein intake (usually to boost muscle mass or as part of a fad diet), smoking, excessive alcohol consumption, very-high-caffeine intake, and daily use of NSAIDs for pain and inflammation (usually owing to the strains of a very physical profession or a previous injury). For ADPKD, it would seem sensible to focus on testing siblings and children of previously diagnosed patients with ADPKD. However, because approximately 10% of patients with ADPKD have no family history (they are *de novo* mutations), that approach will leave out these patients. Because early diagnosis can clearly lead to positive early intervention, not only for ADPKD but many other diseases, it is my recommendation that all Americans be tested for genetic diseases. Although speculation about individual patient lifestyle choices is perilous at best, an early-in-life ADPKD diagnosis would at least help physicians provide kidney-friendly advice, and discourage potentially harmful lifestyle choices.

Family Planning

Another key issue with late diagnosis of *de novo* (and some familial) patients with ADPKD is in the area of family planning. Conception frequently occurs before parental ADPKD diagnosis. Although parents of an ADPKD child lovingly welcome their child into the family, of course, many say that if they would have known they could have passed ADPKD to their child, that they would have gone through the preimplantation genetic diagnosis/*in vitro* fertilization process. The commercially available genetic-testing

product, 23andMe, provides results for carriers of the autosomal recessive polycystic kidney disease (ARPKD) gene, which is a great benefit to those in the family-planning phase.

Living Donation

A further benefit to early diagnosis applies to those wishing to be living donors to a patient. I have met multiple parents who have initiated or completed a kidney donation *via* a voucher process, so that their child can receive a living kidney from their transplant center when they need it. Without early diagnosis of their child's ADPKD, which usually occurred as a fluke through imaging ordered because of an injury or an unrelated abdominal condition, these parents would likely have "aged out" as donors before their child was diagnosed with ADPKD.

There are multiple stories about siblings from a parent with ADPKD who did not know if they had ADPKD or not. Some lived life in dread, others in denial. Some believed they did not have ADPKD, but when they got tested to be a donor for their sibling who was approaching kidney failure, they too were diagnosed—a devastating blow.

Increased Knowledge About ADPKD

Widespread genetic testing for ADPKD would also immediately produce an accurate prevalence count. Currently, estimates of ADPKD prevalence in the general population range from 1 in 500 to 1 in 2000. The actual number will have a large bearing on ADPKD research and treatment. If the prevalence is proven to be on the higher side, the case can be made for increased research funding for this "relatively common" disease. If the prevalence is on the lower side, the US Food and Drug Administration classification of "Rare Disease" may apply. This classification would enable a streamlined (*i.e.*, faster) pathway for drug development, which should serve to incentivize pharmaceutical companies to invest in this area, since their costs and time to market will be reduced.

Additionally, a large increase in the number of patients diagnosed at a young age with ADPKD will eventually result in big data, which will lead to more accurate disease progression calculators.

Legal Protection

If the patient protections of the Affordable Care Act 2010 remain in place, patients with polycystic kidney disease (PKD) would not have to worry about health insurance discrimination (higher premiums, lifetime benefit caps, risk of cancellation) owing to their diagnosed pre-existing condition.

The Genetic Information Nondiscrimination Act law (2008) prohibits employment discrimination on the basis of a person's genetic information.

Insurance

There are two clear downsides, both insurance-related, to receiving a diagnosis of ADPKD early in life: long-term care insurance and life insurance. PKD is a condition specifically excluded from most if not all long-term care insurance policies. However, because only approximately 2% of the United States population carries long-term care insurance, this is not currently a high-priority problem for Americans, including patients with PKD. More expensive life insurance is of much higher concern. Patients with PKD will pay higher premiums than those without PKD. More expensive life insurance is a true downside to early diagnosis. This could be partially mitigated through patient education on options such as "term" life insurance policies only for peak earning years, where risks are lower for the underwriters. There are other financial-related ramifications that come with a PKD diagnosis and the resulting increased likelihood for ESKD and shortened lifespan. Comprehensive patient education on these issues would be helpful if received concurrently with genetic test results.

Emotional Support

Perhaps the most controversial aspect of early diagnosis of a slow-progressing disease such as ADPKD is the psychologic effects. Many parents will not want their child or young adult to know they have ADPKD, and every person will react differently. Some teenagers and young adults I have met have taken the diagnosis as an early death sentence and have engaged in self-destructive behavior. Indeed, the top result from a Google search on "Is a PKD diagnosis a death sentence?" yields a quote from a physician that says that it is.

Some young patients, upon being diagnosed, became very serious about taking care of themselves in the hope of "beating" the disease. Many others live in denial of their diagnosis as their chosen healthiest approach to avoid emotional distress. Meanwhile, the parents are usually overprotective and intrusive, creating extra stress in their parent–child relationships. A comprehensive study into how best to provide and manage psychologic support (counseling, intervention, *etc*.) for the entire family, not just for the patient, when diagnosis occurs early in life, is recommended.

Recognizing the factors discussed above, 18 years is a reasonable age to be genetically tested: it is early enough to enable effective intervention that could delay disease progression, but late enough for parents and physicians to provide effective emotional support. Outside of BP control, there is little that a parent can do for a patient with ADPKD who is diagnosed as a minor. The agency of the child should be considered as well. For these reasons, and having discussed this issue with many parents and children over the years, it is my personal opinion that diagnosing ADPKD earlier than 18 years is problematic.

The benefits of receiving comprehensive genetic information early in the course of the disease, along with the related challenges and their possible remedies, are worthy of discussion and planning among researchers, clinicians, patients, caregivers, and policy makers. Planning for optimal scenarios of patient access to genetic information is essential, because the field of commercially available genetic testing is maturing rapidly. Additionally, the continued maturation and expectations of gene editing techniques such as CRISPR predict that patients/parents

will soon demand early genetic testing of children and embryos, to better manage any conditions discovered.

Acknowledgments

Mr. Dwight Odland is an internationally recognized polycystic kidney disease (PKD) patient advocate, has served two terms on the Board of Trustees of the PKD Foundation, and has been the PKD Foundation Los Angeles Chapter Coordinator since 2005, a role that has allowed him to develop relationships with more than 500 patients with PKD. Mr. Dwight Odland was diagnosed with autosomal dominant PKD at 20 years of age, and has no family history of the disease.

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