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A genetic test could predict future troubles for kidney donors – why not use it?

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Over 100,000 people in the US are waiting for a kidney transplant. Most of the kidneys that were transplanted in 2014 (about 17,000 transplants) are from deceased donors. Kidneys donated from living donors last longer, but the number of living donors has dropped over the past decade.

Ethnic and racial disparities in getting a kidney transplant are common, and African Americans are the hardest hit.

Fewer African-American patients with kidney failure receive a kidney from a living donor compared to European Americans. Kidneys in African-American transplant recipients don't lastas long as in other ethnic/racial groups. And African-American living kidney donors also face a higher risk of post-donation kidney failure than European-American living kidney donors. The estimated risk of getting kidney failure at 15 years post-donation is 74.7 per 10,000 donors in African-American living kidney donors compared to 22.7 per 10,000 donors in European-American living kidney donors.

A genetic change, or "variant," called APOL1, which is chiefly found in African Americans, might play a role in this disparity. Many health care providers and researchers in the transplant community are starting to wonder if African-American potential living kidney donors should be screened for APOL1 variants.

But there are no guidelines about when to use genetic tests and what to

do with the information for organ donation. That means that health care providers might not know how best to evaluate potential living kidney donors in this context.

African Americans have a greater risk of kidney failure

About 19% of African Americans (three million people) have APOL1 variants that put them most at risk of kidney failure.

APOL1 variants are found mostly in people of recent African descent because they helped to protect carriers from infection with sleeping sickness or *trypanosomiasis*.

APOL1 gene variants might affect the health of African-American living kidney donors and might affect the health of their kidney recipient. A recent study reported that APOL1 gene variants in African-American deceased donors increase the chance that the transplanted kidney will fail in the recipient, regardless of the recipient's ethnicity or race.

So APOL1 testing might make sense for African-American potential living kidney donors. But there are many barriers to integrating genetic tests into clinical practice, owing, in part, to the lack of guidelines or data. These tests aren't always covered by insurance, and many people – providers and patients alike – don't know about them. And without guidelines, it's up to individual transplant physicians to decide when someone should be tested. If a genetic test reveals that a potential living donor has the APOL1 variants, doctors might not know how best to advise them.

Why not make APOL1 testing routine?

Some transplants centers already use APOL1 testing routinely for African-American living donors, and others use it on a case-by-case basis.

Those in favor of routine APOL1 testing believe that it could help identify those most at risk, and provide careful counseling to potential living kidney donors about the risks from living donation.

But implementing APOL1 testing into routine clinical practice may be premature. Not all African Americans with APOL1 variants will get kidney failure. And we don't know if this variant poses as much risk to recipients when kidneys come from living donors (who are typically very healthy) as when they come from deceased donors, as critics argue. No long-term scientific studies have tested this. And it would take a long time for studies to answer this question. So that means that we don't yet have all of the information we would need to give people good counseling after APOL1 testing. But, guidelines could at least establish how to handle counseling when information isn't fully available.

To test or not to test: that is the ethical question

Part of the difficulty with genetic tests is that they don't guarantee a definitive result. APOL1 testing, like many other genetic tests, produces a reliable prediction just part of the time.

If APOL1 testing is offered, will potential living kidney donors be subjected to unnecessary distress by getting "positive" results that are not certain? Is it unethical to delay the adoption of APOL1 testing into clinical practice because not using it could cause harm to potential living donors, kidney recipients and public health? Would not using APOL1 testing undermine potential living kidney donors' informed consent for donation?

By undergoing testing, potential living kidney donors with APOL1 variants can learn more about the greater risk donation may pose for them, and make a more informed decision about donating. Those with APOL1 variants who still want to donate could adopt protective lifestyle changes.

Intended recipients from potential living donors with the APOL1 variants would likely need to be informed about their increased risk of kidney failure. While recipients could still benefit from a transplant that lasts just a couple years as opposed to staying on dialysis, the potential living donor may feel undue pressure to donate to help their intended recipient, despite greater risks to themselves by doing so.

However, if those potential living donors with APOL1 choose to not donate in order to reduce their risk of kidney failure, this decision could worsen the known disparities among African Americans who need kidney transplants. It could mean patients need to wait longer to be matched with a suitable donor, which could mean that more people on the waiting list will die before receiving a kidney.

This isn't just about kidneys

As our ability to test for genetic risk factors grows, APOL1 testing could serve as a model for the integration of genetic testing in transplantation.

The National Human Genome Research Institute has launched an initiative to foster genetic literacy in physicians and other providers. This will help medical specialties, like transplantation, incorporate genetic testing into clinical practice. And testing could offer more personalized care, which is consistent with the goals of precision medicine.

Because informed consent is the cornerstone of ethically sound clinical practice, especially in living donation, while we wait for guidelines,

African-American potential living kidney donors should be informed about the option of APOL1 testing.

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