New Donor Chains Could Change Approach to Paired Donation

By Eric Seaborg

A new approach aimed at turning one altruistic kidney donation into a never-ending chain could be the next step in increasing the number of transplanted kidneys, a recent report in the New England Journal of Medicine proposes. The new system is called a nonsimultaneous, extended, altruistic donor (NEAD) chain.

"Before this article, everybody in the field of kidney transplantation thought that we had to do everything simultaneously," said lead author Michael Rees, MD, PhD, professor of urology at the University of Toledo and medical director of the Alliance for Paired Donation (APD). "All kidney paired donation transplants had to happen simultaneously because of that great harm that would happen if somebody cheated and somebody was permanently harmed by the loss of their donor."

The insight behind the innovation is that starting a chain with an altruistic donor—someone who volunteers a kidney with no strings attached—fundamentally changes the ethical consequences of a potential donor reneging down the line. Critics, however, contend that the paper downplays these consequences and that the approach widens the gap between patients with incompatible donors and those without.

Paired donation to domino chains
Paired donation began as a way to address the problem that many patients with end stage renal disease have a friend or loved one willing to give them a kidney, but incompatibilities in blood type or human leukocyte antigen (HLA) crossmatching prevent a transplant. Simple swaps between recipient-donor pairs with complementary compatibilities provided a first step in addressing this issue, but the matches were limited in number.

Computer matching programs enabled more complicated swapping

Pre-Dialysis Care Varies by Patient, Center, and Region

Links to First-Year Mortality Warrant Quality Improvement Initiatives

By Timothy O’Brien

For patients with advanced chronic kidney disease (CKD), how much does getting recommended pre-dialysis care affect outcomes? Quite a bit—not only for the individual patient, but also at the level of the dialysis center, according to a study in the May Journal of the American Society of Nephrology.

Based on analysis of U.S. ESRD Network data, the study identified geographic “clusters” where patients are particularly unlikely to receive recommended pre-dialysis care. “Our observations suggest that pre-ESRD care may not vary randomly across communities and that less than optimal care aggregates within some treatment centers, and these centers tend to aggregate geographically,” said lead author William McClellan, MD, of Emory University School of Medicine in Atlanta. “This suggests that assistance to improve pre-ESRD care might be profitably targeted to these treatment centers and the health systems they serve.”

Better pre-dialysis care, better one-year survival
McClellan and his colleagues analyzed data on more than 30,000 patients starting he-
New Donor Chains

Continued from page 1

schemes involving more patients, and altruistic donors enabled "domino" chains in which an altruistic donor might give to recipient A, whose incompatible donor would donate to recipient B, whose incompatible donor would give to recipient C, with the chain ending with a donation to a patient on the United Network for Organ Sharing or similar waiting list who did not have an incompatible donor.

Before the advent of paired donations, an altruistic donor’s kidney would go to the top match on the waiting list, resulting in a single transplant. A domino chain leverages that single donation into several transplant opportunities.

So far, the longest domino chain was a six-way swap involving 12 individuals at Johns Hopkins University in April, done in six operating rooms with nine surgical teams over 10 hours.

Paired donations have always been done simultaneously to prevent the possibility of anyone reneging on a commitment to donate, which could result not only in a would-be recipient missing out on getting an expected kidney, but also losing the "bargaining chip" if her incompatible donor gave a kidney away, removing any chance for a paired donation in the future.

The paper posits that a NEAD chain can change this approach: "When an altruistic donation initiates a chain of transplantation, each subsequent donor makes the donation only after the co-registered recipient in his or her pair has already received a transplant. Thus, although reneging in the middle of a chain would still be problematic, it would not irreparably harm the remaining parts of the chain." Instead of being required to donate immediately, a "bridge donor" can be asked to wait while a solid match is found.

How NEAD works

The chain reported in the NEJM paper was initiated by the APD, a coalition of 70 transplantation programs that pool patients in a single registry. A 28-year-old altruistic donor from Michigan started the chain by traveling to Phoenix to donate to Recipient 1. Eight days later, the husband of Recipient 1 (Donor 2) traveled to Toledo to donate to Recipient 2. Two months later, the mother of Recipient 2 (Donor 3) traveled to Columbus, Ohio, where simultaneous transplants extended the chain to Recipient 3 and Recipient 4.

After finding no matches for Donor 5 for three months, the APD contacted the Incompatible Kidney Transplantation Program at Johns Hopkins University to find Recipient 5. The next three donations were then performed simultaneously, with donations 6 and 7 performed at Johns Hopkins, while the kidney from Donor 8 was shipped by commercial airline to Wake Forest University and transplanted into Recipient 8.

About two weeks later, Donor 9’s kidney was removed at Wake Forest and shipped on a charter flight to Johns Hopkins. On the same day that Recipient 9 received this organ, the kidney of his brother (Donor 10) was flown by commercial airline to Toledo and transplanted into Recipient 10. The chain is still open, pending the identification of the next recipient.

Theoretically, the NEAD chain could go on indefinitely, in contrast to domino chains, which always end with a recipient on the waiting list who does not have an incompatible donor.

Rees said that his group currently has six ongoing NEAD chains, with 13 bridge donors to date, and no one has cheated. The second chain has run to five transplants. "We are so confident that people are not going to cheat that we have let the next four NEAD chains start with only one transplant," he said.

However, one of the paper’s co-authors, Dorry L. Segev, MD, associate professor of surgery at Johns Hopkins University, is less sanguine: "The NEAD has certain risks associated with it. The first is that the donor who is asked to wait around will renge." A Johns Hopkins chain was broken by the first bridge donor.

Although the paper downplays the importance of losing this kidney to others who would have been in the chain, the loss is still "devastating" because it denies a potential recipient this valuable resource, said Ron Shapiro, MD, professor of surgery at the University of Pittsburgh and president of the Paired Donation Network, a consortium of 80 kidney transplant programs.
New Donor Chains

Continued from page 3

programs. The person who loses out can be considered to be a patient on the deceased donor waiting list who might have been a beneficiary at the end of a domino chain.

“The second limitation of NEADs is that we are furthering the disparity between people who have live donors available to them and people who do not and are stuck on the waiting list,” said Segev.

“There are many good things about the chain, but if the chain doesn’t end with a kidney going to somebody on the deceased donor waiting list, then the patients who are waiting for a kidney transplant who don’t have a donor are permanently cheated,” said Shapiro.

Rees counters that if a NEAD works as the first one did, taking 10 people off the waiting list—one four more than the longest domino chain has—almost everyone on the waiting list benefits by moving closer to the top.

As the demand for kidneys continues to outpace the supply, creativity is needed to find the best use of a limited resource, and the appeal of leveraging a donation into a long chain could bring out more altruistic donors. The publicity that the paper has generated—ABC, NBC, CBS, and CNN all covered it—could also make a difference. Following the publicity, more than 500 people have registered at the APD website to donate a kidney.

The paper noted that NEAD chains also increase the universe of possible matches, and thus can improve their quality and provide donors for hard-to-match recipients.

The concept certainly bears watching. Despite his reservations, Shapiro called the paper “a huge contribution” and said that his own transplant institution is negotiating to begin a similar program, although with adaptations to address his concerns.


#### Data Snapshot

**Wait times for kidney transplant**

<table>
<thead>
<tr>
<th>Region Name</th>
<th>Current Waiting List Candidates</th>
<th>Wait Time Index*</th>
<th>Wait Time &gt; 1 Year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Regions</td>
<td>78,957</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Region 1</td>
<td>Connecticu, Maine, Massachusetts, New Hampshire, Rhode Island, Eastern Vermont</td>
<td>2,851</td>
<td>2.53</td>
</tr>
<tr>
<td>Region 2</td>
<td>Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania, West Virginia, Northern Virginia</td>
<td>10,714</td>
<td>2.54</td>
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<tr>
<td>Region 3</td>
<td>Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Puerto Rico</td>
<td>10,479</td>
<td>2.56</td>
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<td>Region 4</td>
<td>Oklahoma, Texas</td>
<td>7,142</td>
<td>2.47</td>
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<td>Region 5</td>
<td>Arizona, California, Nevada, New Mexico, Utah</td>
<td>18,065</td>
<td>2.70</td>
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<td>Region 6</td>
<td>Alaska, Hawaii, Idaho, Montana, Oregon, Washington</td>
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<td>2.6</td>
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<td>Region 8</td>
<td>Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming</td>
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<td>Region 9</td>
<td>New York, Western Vermont</td>
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<td>Region 10</td>
<td>Indiana, Michigan, Ohio</td>
<td>5,613</td>
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<td>Region 11</td>
<td>Kentucky, North Carolina, South Carolina, Tennessee, Virginia</td>
<td>6,921</td>
<td>2.55</td>
</tr>
</tbody>
</table>

* The Wait Time Index measures average wait time on a scale in which 0.5 = <30 days, 1 = 30–90 days, 1.5 = 90 days to 1 year, 2 = 1–2 years, 2.5 = 2–3 years, 3.5 = 3–5 years, and 4 = 5 or more years.

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