

## Optimum Chain Length in Kidney Exchange Program and the Way Ahead

### Why Kidney Exchange?

Kidney exchange is administratively complex but medically straightforward. ABO incompatible kidney transplantation (ABOiKT) and transplant with desensitization therapy are medically complex but administratively straightforward. Current evidence supports the use of kidney exchange over ABOiKT or desensitization therapy.<sup>[1,2]</sup> In a recent meta-analysis, one-year uncensored graft survival was inferior in ABOiKT ( $n = 1346$ ) than ABOcKT ( $n = 4943$ ) (96% vs. 98%;  $P < 0.001$ ); infections were more common in ABOiKT (49% vs. 13%,  $P = 0.02$ ), as were antibody-mediated rejection, severe non-viral infections, and bleeding.<sup>[1]</sup> The patient and graft survival were inferior within the first 3 years after transplantation in ABOiKT than ABOcKT, and though at 5 years, patient and graft survival was similar in the two groups. Awareness of the increased risks of infection, organ rejection, and bleeding could improve care of patients and promote efforts toward paired kidney exchange programs.<sup>[2]</sup> ABOiKT are reported to be twice as expensive and half as good.<sup>[3]</sup> The patient and graft survival was 96-100%, 96%-100%, at 1 year and 83-97%, 96-100%, at 3 year respectively, in the previous four Indian studies ( $n = 384$ ) with 11-16% rejection rates.<sup>[4-7]</sup> The graft and patient survival were each 97% in 45 ABOiKT with a relatively low-cost preconditioning protocol with additional cost of USD-1200.<sup>[8]</sup> The short-term outcome was comparable in ABOiKT ( $n = 20$ ) and ABOcKT ( $n = 669$ ).<sup>[9]</sup> One-third of living, healthy, willing donors are rejected due to ABO blood group incompatibility and sensitization. Institute of Kidney Diseases and Research Center, Institute of Transplantation Sciences (IKDRC-ITS) Ahmedabad, India has completed a total of 6050 kidney transplants including 440 kidney exchange transplants, 925 deceased donor kidney transplants, and 35 ABOiKT. We have shown that kidney exchange increases living donor kidney transplantation (LDKT) rate by 25% in one year despite being a single-center program.<sup>[4]</sup> The outcome of LDKT is always better than deceased donor kidney transplant (DDKT). DDKT is well developed in some states in India such as Tamil Nadu, Gujarat, Maharashtra, and Chandigarh but underdeveloped in many other States such as Bihar, West Bengal, and Uttar Pradesh, which limits its availability as a transplant option.

### Optimum Chain Length in Kidney Exchange Program

We read with interest the recent report entitled "First successful three-way kidney exchange transplantation in North India".<sup>[10]</sup> The kidney exchange chain length should be decided according to the level of development

of kidney exchange program and volume of LDKT and DDKT programs at each center.<sup>[4,11]</sup> Logistics are simple in two-way kidney exchange. The optimum chain length should be three.<sup>[4,10]</sup> Longer chains may not increase the quality of matching but make logistics difficult to manage. The majority of kidney exchanges in India are two-way and less commonly three-way.<sup>[11]</sup> United Network for Organ Sharing, USA and European countries suggest two-way and three-way exchanges for logistical reasons.<sup>[12]</sup> The National Kidney Registry works with all the transplant hospitals in the United States and currently has the largest living donor pool in the world, allowing it to use longer kidney exchange chains. Chain lengths ranged from one to 35 transplants facilitated, with two being the most common chain length even in USA. Three-way kidney exchange should be preferred in advanced programs and two-way kidney exchange should be preferred in new programs in preparation.

From 2000–2020, our center has completed 6045 kidney transplants including 440 kidney exchanges [164 two-way ( $n = 328$ ), 23 three-way ( $n = 69$ ), 4 four-way ( $n = 16$ ), 1 five-way ( $n = 5$ ), 2 six-way ( $n = 12$ ), and 1 ten-way ( $n = 10$ )]. In IKDRC-ITS, short chain (two-way or three-way kidney exchange) exchanges are commonly done but longer kidney exchanges to increase the probability of transplant for difficult to match pairs such as highly sensitized or O blood group patient with non-O donor are also done. Challenges for 3-way or longer kidney exchanges are time required for taking legal permission, requirement for larger surgical teams for simultaneous surgeries, and need of computer software for allocation. As per transplant human organ act 2014 (amended) India, cases of swap donation shall be approved by the Authorization Committee of the hospital or district or state in which transplantation is proposed to be done and donation of organs shall be permissible only from near relatives of the swap recipients. This will help to complete formalities required from different states in longer kidney exchange chain when pairs are from different states. Multicenter kidney exchange will eliminate the need for larger surgical teams when simultaneous surgeries are performed, while increasing the quality and quantity of matching. Two-way kidney exchanges can be done with manual allocation when the donor pool is small. Computer software is required for longer chain allocation to increase the quality of matching and number of transplants as the donor pool increases.

Anonymity is a legal requirement in most European countries, and it is part of the protocol in all countries, except Poland. Non-anonymous allocation is unique to developing countries such as India. This increases

trust between transplant unit, donor-recipient pairs, and transplant coordinator and allocation team.

## The Way Ahead

There is a need to establish regional centers of excellence in kidney exchange which should be tasked with the formation of city-based registries and the ultimate linking of all single center or city-based registries to state-based registry and the national registry. There is a need for amendments to the transplant human organ act to allow kidney exchange between extended family members, and altruistic nondirected kidney donors in kidney exchange. A robust uniform immunological assessment across centers with negative lymphocyte cross-match, flow cross-match, and donor-specific antibody will have to be standardized to improve long-term survival and unequal outcome due to immune injury after transplantation.

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## Conflicts of interest

There are no conflicts of interest.

**Vivek B. Kute, Himanshu V. Patel,  
Vineet V. Mishra, Sanjay K. Agarwal<sup>1</sup>**

*Department of Nephrology, Institute of Kidney Diseases and Research Center and Dr. H L Trivedi Institute of Transplantation Sciences (IKDRC-ITS), Ahmedabad, <sup>1</sup>Department of Nephrology, All India Institute of Medical Sciences, New Delhi, India*

### Address for correspondence:

*Prof. Vivek B. Kute,  
Department of Nephrology, Institute of Kidney Diseases and Research Center and Dr. HL Trivedi Institute of Transplantation Sciences (IKDRC-ITS), Ahmedabad, India.  
E-mail: drvivekkute@rediffmail.com*

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