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TRANSuMmIT TALKS
Transmitting Ideas...Transforming Lives
EXCERPTS FROM INDIA SPEAKER TOUR IN OCT. 2022

SPEAKER

Dr. Dorry L Segev
Professor of Surgery and Population Health Vice Chair, Department of Surgery; Director, Center for Surgical and Transplant Applied Research, NYU Langone Health, USA

Hot Topics in Kidney Transplantation: New Living Donor Tools and More

Old Paradigm:
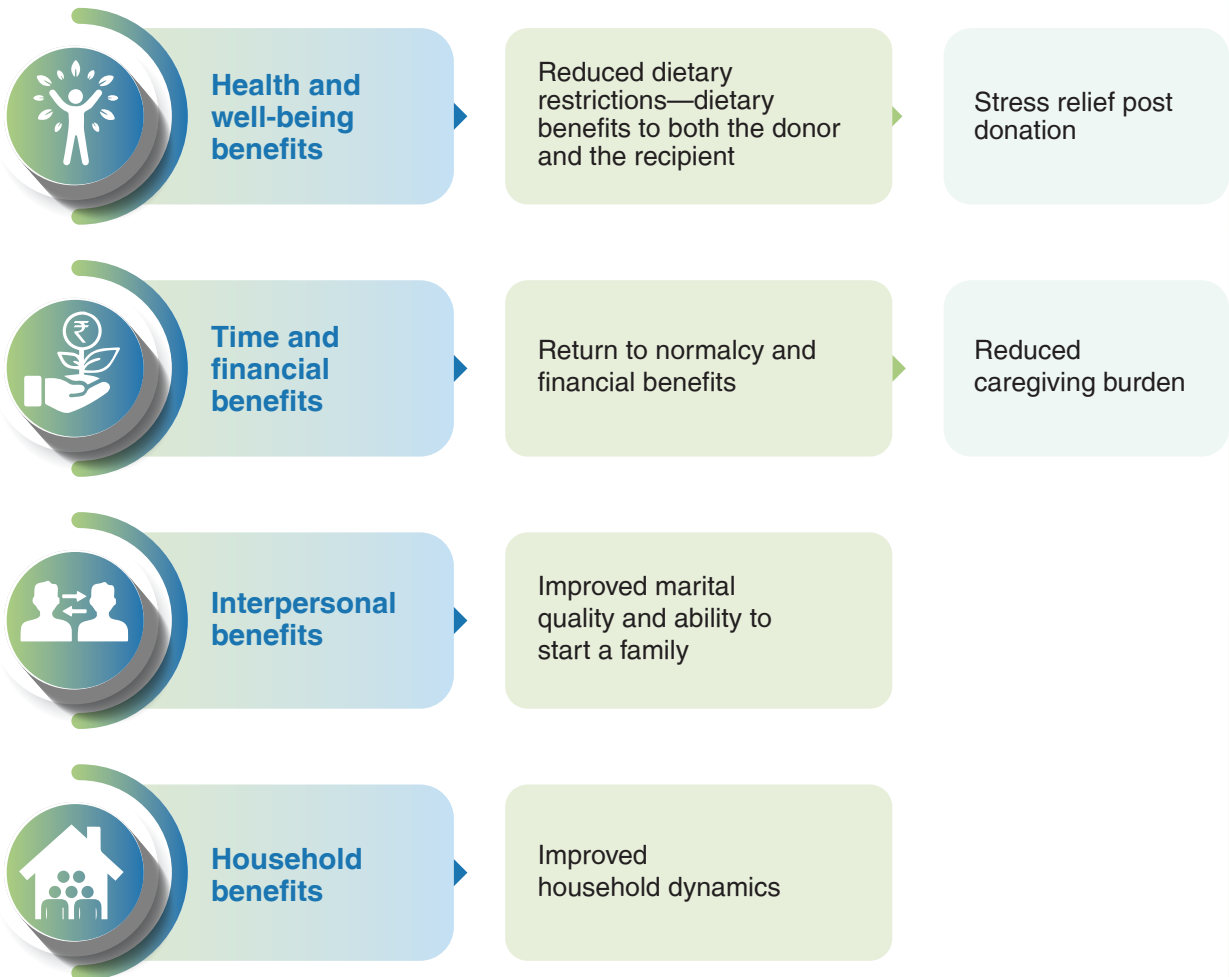Risk of ESRD in donors is no higher than in the general population.[1]

New Paradigm:
There is attributable risk to donating, which can be estimated using big data.[1]

ESRD: End-stage renal disease.

Old Paradigm:
A normal healthy person was to be subjected to a major surgical operation not for his own benefit.[1]

New Paradigm:
Tangible benefit and interdependent donors.[1]

Tangible Benefit With Interdependent Donors' Selection[2]

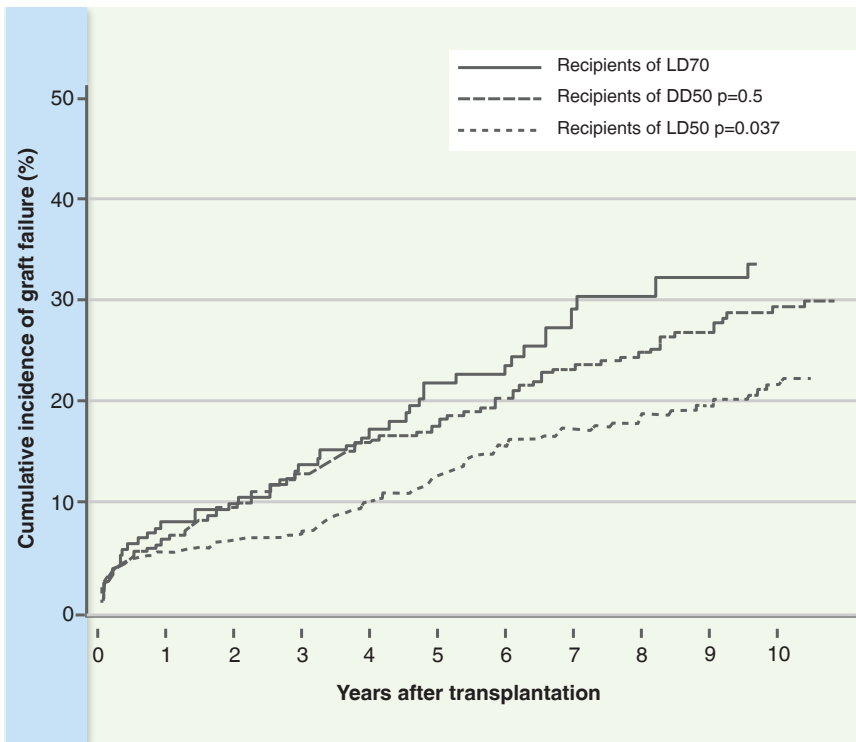| Health and well-being benefits	Reduced dietary restrictions—dietary benefits to both the donor and the recipient	Stress relief post donation
Time and financial benefits	Return to normalcy and financial benefits	Reduced caregiving burden
Interpersonal benefits	Improved marital quality and ability to start a family	
Household benefits	Improved household dynamics	

Old Paradigm:
All live kidney donors are basically equivalent and better than any deceased donor.[1]

New Paradigm:
Live donor kidney donor profile index.[1]

Younger Donors = Better Outcomes[3]

Legend:
Recipients of LD70
Recipients of DD50 p=0.5
Recipients of LD50 p=0.037

Y-axis: Cumulative incidence of graft failure (%) — 0, 10, 20, 30, 40, 50
X-axis: Years after transplantation — 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10

p=0.005

Recipients of live donor kidneys aged >70 had a significantly higher rate of graft loss compared with recipients of younger live donor kidneys aged 50 to 59.[3]

DD50: Deceased donors aged 50 to 59; LD50: Live donors aged 50 to 59; LD70: Live donors ≥70.
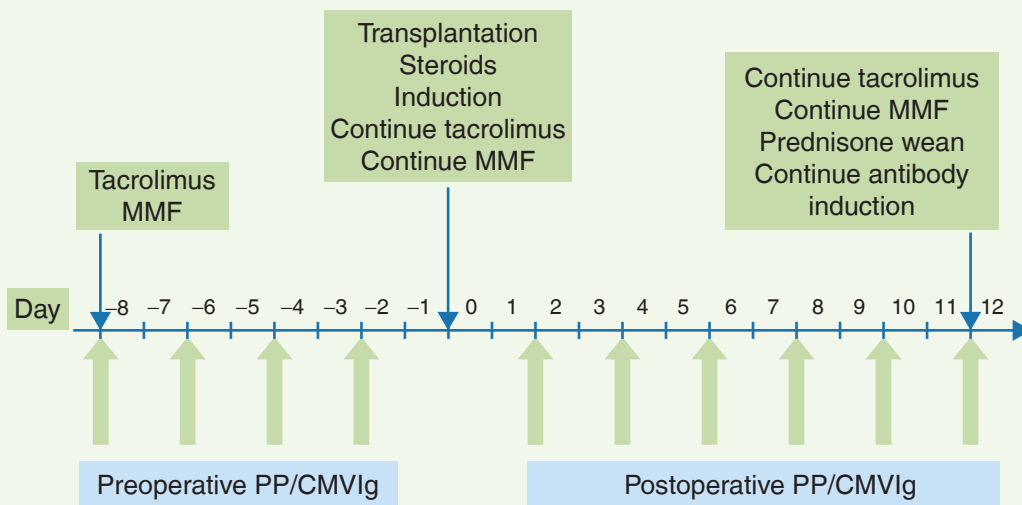
Old Paradigm:
The result of a kidney exchange needs to be compatible.[1]

New Paradigm:
Combining kidney exchange and desensitization is the best of both worlds.[1]

Desensitization:[4]

Day

Tacrolimus
MMF

Transplantation
Steroids
Induction
Continue tacrolimus
Continue MMF

Continue tacrolimus
Continue MMF
Prednisone wean
Continue antibody
induction

−8 −7 −6 −5 −4 −3 −2 −1 0 1 2 3 4 5 6 7 8 9 10 11 12
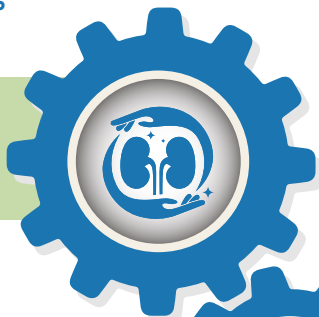
Preoperative PP/CMVIg

Postoperative PP/CMVIg

Live donor transplantation after desensitization provided a significant survival benefit for patients with HLA sensitization, as compared with waiting for a compatible organ.

CMVIg: Cytomegalovirus immune globulin prophylaxis; HLA: Human leukocyte antigen;
MMF: Mycophenolate mofetil; PP: Patient preparation.

Eplet Matching[5]

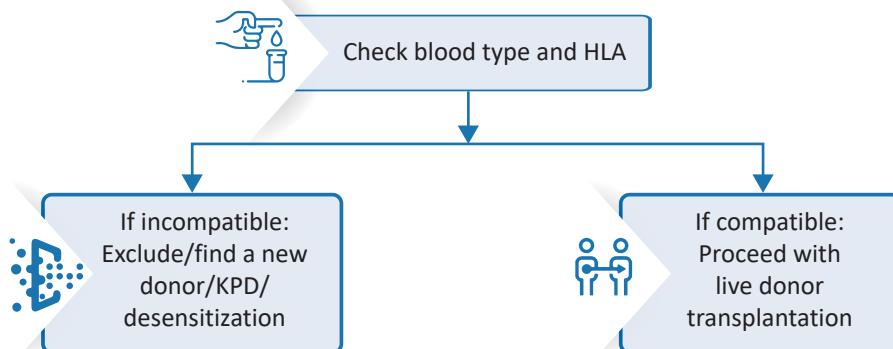Improve transplant outcomes by decreasing DSA formation/rejection

Potentially provide an opportunity to lower immunosuppression in well-matched transplants
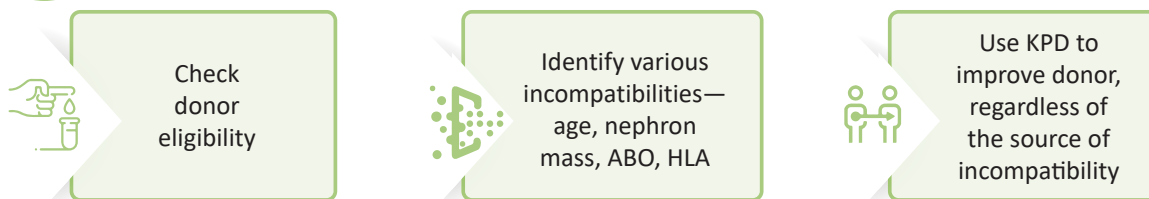
HLA eplet compatibility helps in better representation of the immunological risk
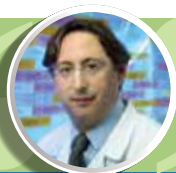
Old compatibility paradigm[1]

Check blood type and HLA

If incompatible: Exclude/find a new donor/KPD/desensitization

If compatible: Proceed with live donor transplantation

New compatibility paradigm[1]

Check donor eligibility

Identify various incompatibilities—age, nephron mass, ABO, HLA

Use KPD to improve donor, regardless of the source of incompatibility

ABO: ABO blood group system; DSA: Donor-specific antibodies; HLA: Human leukocyte antigen;
KPD: Kidney paired donation.

Discussion With Dr. Dorry Segev

Q **WHAT ARE THE PARADIGMS AND HOW CAN WE CHANGE THEM?**

A The old paradigm states that the risk of ESRD in living donors is no greater than that in the general population with some attributable risk. The approach should be based on what kind of donors they are, in case of interdependent donors there are tremendous and tangible benefits to the donors, by donation. Also, the compatibilities of the donor and recipient, the approach to desensitization, etc. should be considered.

Q **CAN WE USE A DONOR WHO MAY BE ANTIGENICALLY MISMATCHED?**

A Repeat mismatches must be avoided because of the risk of B cell-mediated immunological response. So, the patients must be accessed depending on their condition, as to how long can they wait for a compatible donor.

Q **SHOULD DESENSITIZATION BE THE GO-TO OPTION BETWEEN THE UNDESIRABLE AND UNACCEPTABLE BONDS?**

A The decision should be made based on how broadly the person is sensitized and how well they are doing in dialysis. The points to be kept in mind are if the patient wants to be desensitized or can wait for a little longer.

ESRD: End-stage renal disease.

References: 1. Data taken from Dr Dorry L Segev's presentation on 'Hot topics in kidney transplantation: New living donor tools and more-Excerpts from India Speaker Tour Held in October 2022. **2.** Van Pilsum Rasmussen SE, Henderson ML, Segev DL, *et.al.* Considering tangible benefit for interdependent donors: extending a risk-benefit framework in donor selection. *Am J Transplant.* 2017;17(10):2567–2571. **3.** Berger JC, Muzaale AD, James N, *et.al.* Living kidney donors ages 70 and older: Recipient and donor outcomes. *Clin J Am Soc Nephrol.* 2011;6(12):2887–2893. **4.** Montgomery RA, Lonze BE, King KE, *et.al.* Desensitization in HLA-incompatible kidney recipients and survival. *N Engl J Med.* 2011;365(4):318–326. **5.** Charnaya O, Levy E D, Amaral S, *et.al.* Pediatric Kidney Transplantation-Can We Do Better? The Promise and Limitations of Epitope/Eplet Matching. *Front Pediatr.* 2022 Jun 3;10:893002.

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