



Pediyatrik Böbrek Naklinde Çapraz Nakil Stratejileri

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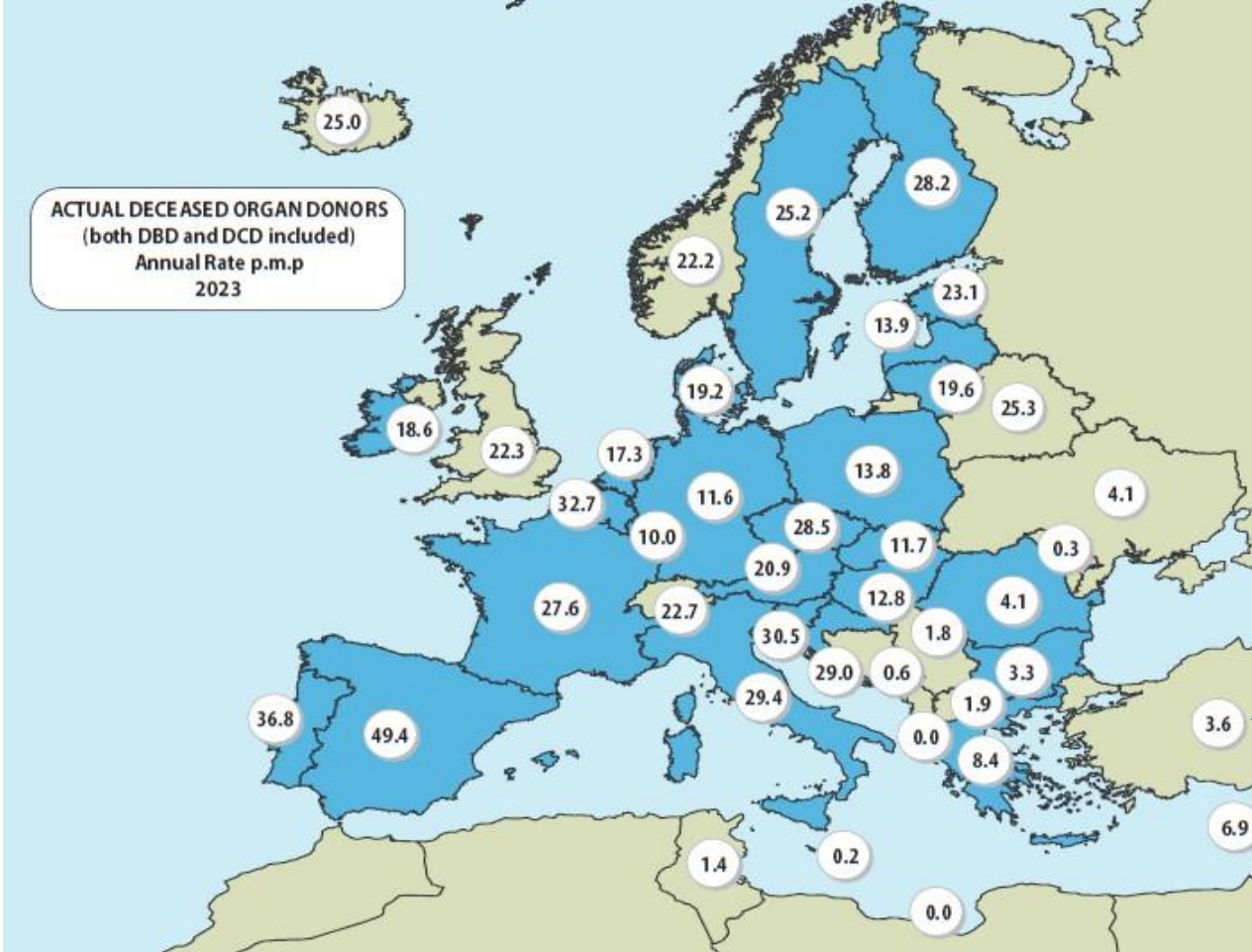


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BAHÇEŞEHİR



isü İSTİNYE
ÜNİVERSİTESİ
İSTANBUL

Keşke



70.000 kronik böbrek hastası

Giriş

- Kadavra Bağış 
- Canlı donör
 - Daha az DGF oranı
 - Daha kısa bekleme süresi
 - Daha az komorbidite oranı
 - Daha iyi hasta ve graft sağkalımı

- Toplumsal farkındalık çalışmaları
- Bağış kampanyaları
- Aile onayı
- Varsayıma dayalı konsent
- Non-heart beating kadavra

Roma: 25 pmp

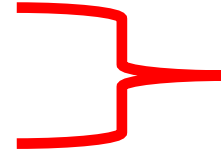
(ESRD). Patients fortunate enough to receive a kidney transplant, on average, live 10 years longer than those who remain on dialysis [1], and it is now clear that a living donor kidney transplant is better than a kidney from a deceased donor. The average deceased donor kidney transplant will function for 8.6 years, while a living donor kidney provides an average of >16 years of dialysis-free survival

Donör havuzunun genişletilmesi

1. Canlı donör havuzunun genişletilmesi stratejisi
 - a. ABO uyumsuz canlı donör nakiller
 - b. HLA uyumsuz canlı donör nakiller
 - c. Çapraz nakiller (KPD)**
2. Canlı donöre uygun olmayan sensitize hastalar için stratejiler
 - a. Uygun mismatch programları
 - b. Kadavra donör aşırı desensitizasyon
 - c. HD'de IVIG/Rituksimab
3. Kadavra donör havuzunu genişleten stratejiler
 - a. Marjinal organların kullanımı**
 - b. Dolaşım durduktan sonra yapılan donasyon

Canlı gönüllü donöre rağmen

- ☐ ABO uyumsuzluğu
- ☐ DSA varlığı/cross (+)



% 30–50

1. ABO uyumsuz nakiller (1998)
2. Desensitizasyon
3. Donör değişimi (**KPD**)
 1. Çapraz canlı nakil
 2. Canlı-kadavra donör değişimi
 3. Altruistik (non-directed) donasyon

- ✓ Pahalı
- ✓ Rejeksiyon riski yüksek
- ✓ Enfeksiyon riski fazla
- ✓ Graft sağkalımı düşük

REVIEW

Allocation and matching in kidney exchange programs

Kristiaan Glorie,¹ Bernadette Haase-Kromwijk,² Joris van de Klundert,³ Albert Wagelmans¹ and Willem Weimar^{2,4}

Avantaj-Dezavantaj

Desensitizasyon

- ✓ Karmaşık bir prosedür
- ✓ Karışık immünolojik testler
- ✓ PF, immunadsorpsiyon ve ritux..
- ✓ Pahalı
- ✓ Hastane yatışı uzun
- ✓ Overimmunsupresyon
- ✓ Ciddi infeksiyonlar
- ✓ Rejeksiyon atakları fazla
- ✓ Graft sağkalımı düşük

Çapraz nakil

- ✓ Basit bir prosedür
- ✓ Daha ucuz
- ✓ Kararında immunsupresyon
- ✓ İnfeksiyon riski az
- ✓ **Lojistik sorunlar**
- ✓ **Aynı anda birden fazla ameliyat**
- ✓ **Son dakika takas sorunları**
- ✓ **Donörü kabul etmeme vb.....**

de Weerd AE, Betjes MGH. ABO-incompatible kidney transplant outcomes: a meta-analysis. *Clin J Am Soc Nephrol* 2018; 13: 1234.
Marfo K, Lu A, Ling M, Akalin E. Desensitization protocols and their outcome. *Clin J Am Soc Nephrol* 2011; 6: 922.
Axelrod D, Lentine KL, Schnitzler MA, et al. The incremental cost of incompatible living donor kidney transplantation: a national cohort analysis. *Am J Transplant* 2017; 17: 3123.

Çapraz nakil

Konvansiyonel çapraz: ABO uyumsuz
Sadece A ve B kan grupları arasında

Ankonvansiyonel çapraz: Cross (+)
O ve AB grubu dahil hepsi çaprazlanabilir

- ▶ O donör
- ▶ Düşük PRA
- ▶ A/B, B/A

Çaprazlaması kolay

- ▶ AB donör
- ▶ Yüksek PRA
- ▶ A donör/O alıcı

Çaprazlaması zor

Çapraz nakil- tarihçe

History of KPD

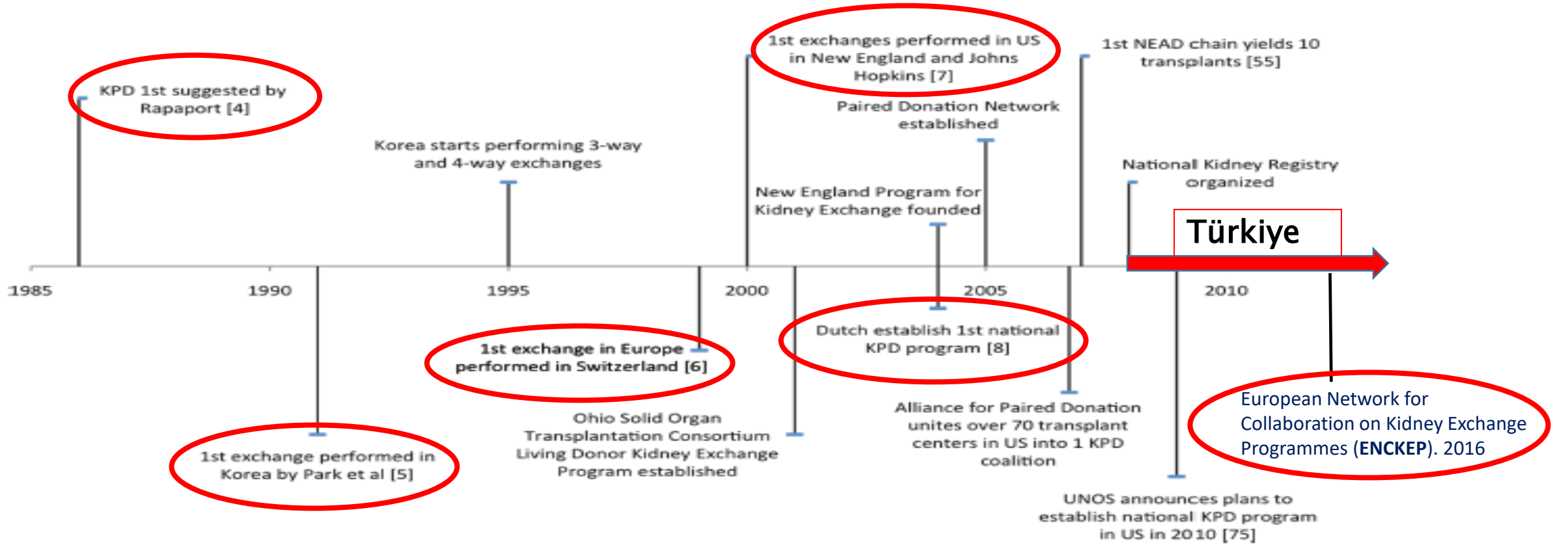


Fig. 1. A history of kidney paired donation from its original proposal by Felix Rapaport to the present day.



Alvin E. Roth.

Linda A. Cicero/Stanford Üniversitesi Fotoğrafçısı

Tam Olarak: Alvin Eliot Roth

Doğmak: 18 Aralık 1951, New York City ,
NY, ABD (73 yaşında)

Ödüller Ve Onurlar: Nobel Ödülü
(2012)

Çalışma Konuları: arz ve talep • oyun
teorisi

Özellikle "oyun teorisi" olarak adlandırılan teoriden ilham aldı." Ertelenmiş kabul " algoritması, Shapley ve Amerikalı ekonomist David Gale tarafından 1960'larda serbest ticaret yapan bir sistemdeki oyuncu çiftlerinin verimli bir şekilde eşleştirilmesini sağlamak için geliştirilen bir dizi kuraldır. 1990'ların ortalarında Roth ve meslektaşları, tıp fakültesi mezunlarını asistan hekim arayan hastanelerle eşleştiren bir sistemi geliştirmek için algoritmayı değiştirdiler. 2003 yılında ekibi, New York'taki lise öğrencileriyle eşleştiren bir sisteme benzer bir çözüm uyguladı. Ayrıca 2003 yılında, böbrek bağışçıların organlarını "takas edebilecekleri" ve amaçlanan alıcılarının uyumlu nakillere sahip olmasını sağlayacak bir sistem tasarlamaya başladı. Çalışmaları, İsveç Kraliyet Bilimler Akademisi tarafından "gerçek dünya sorunlarına pratik çözümler" bulma örneği olarak gösterildi.

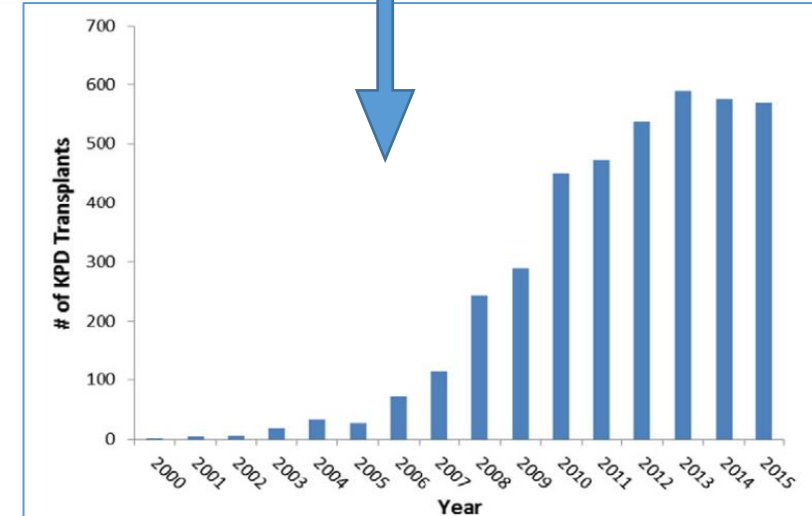


Fig. 1. The number of kidney paired donation (KPD) transplants performed in the United States per year. Data obtained from the OPTN database from the year 2000 to 2015. Patients were listed as non-biological, unrelated paired donations.

Eşleştirme Modelleri

1. Hastalar arası
 - a) Basit eşleşme
 - b) Domino eşleşme
2. Merkezler arası
 - a) Merkez içi/merkezler arası
 - b) Ulusal
 - c) Uluslararası
3. Max zincir uzunluğu
4. Ameliyat zamanlaması
 - a) Eş zamanlı
 - b) Ardışık
5. Yeni Trendler
 - a) Bi-organ çapraz nakil
 - b) Global modeller

Table 1 Types of kidney exchange

Simultaneous anonymous 2-way kidney exchange
3-way, 4-way, n -way exchange ^[13]
Compatible pair ^[14,21]
Non-simultaneous kidney exchange ^[16]
Non-simultaneous extended altruistic donor and domino ^[18]
Kidney exchange + desensitization therapy ^[15]
Kidney exchange + ABO incompatible transplant ^[18]
Acceptable mismatch transplant
Use of A2 donor to O patients ^[18]
Living donor-deceased donor list exchange ^[19]
National kidney exchange ^[20]
International kidney exchange ^[17]
Global kidney exchange ^[18]

REVIEW

Kidney exchange transplantation current status, an update and future perspectives

Hastalar arası basit eşleşme

- İlk başlangıç
- Önce iki sonra çok yönlü
- Çoklu cerrahi
- Teknik olarak zor

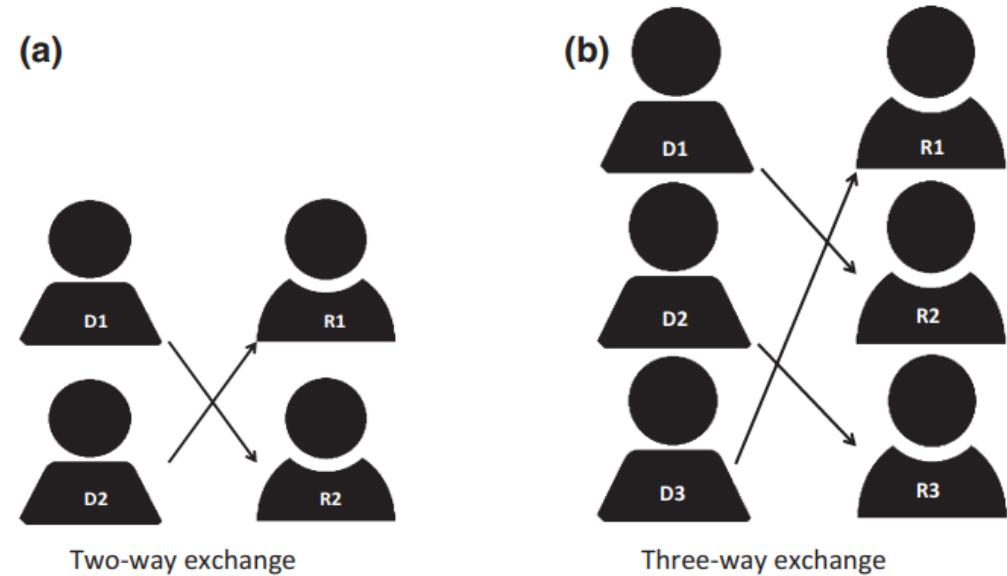
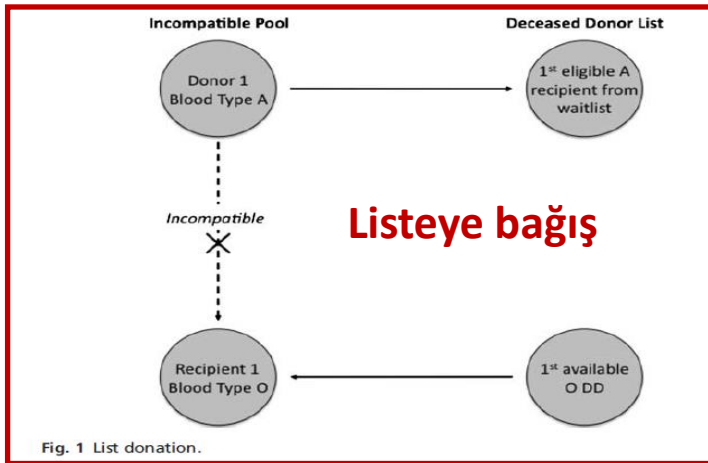


Figure 1 Different types of simple paired kidney exchanges. (a) Two-way exchange, (b) multi (n)-way exchange between multiple pairs.

Hastalar arası domino eşleşme

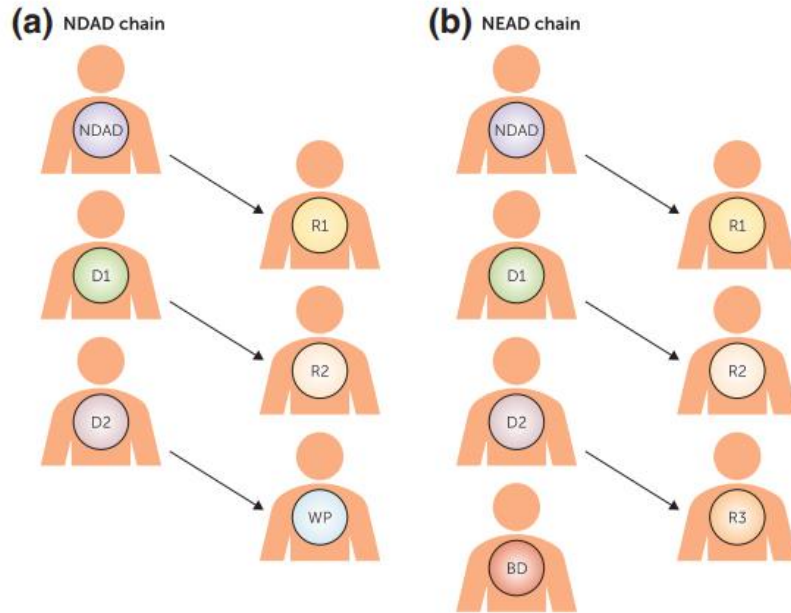


Figure 2 Matching strategies with non-directed anonymous donors (NDAD) – (a) NDAD starting chain ending up with the final kidney donation to a recipient on the waiting list (WP); (b) non simultaneous extended altruistic donor (NEAD) chain ending up as a bridge donor (BD) who can start a new chain.

✓NDAD

- Fedakar bağışçı
- Çok merkezli/ulusal program
- Farklı zaman diliminde ameliyat
- Canlı böbreklerin transportu
- Soğuk iskemi arttı

✓NEAD

- Eşleşmesi zor bridge donörle bitebilir...
- Donör vazgeçebilir(%7)...

Paired kidney exchange transplantation

the sensitization status of the recipients [3]. Alvin Roth & Lloyd Shapley received 2012 Nobel prize in economics for developing the algorithm utilized to match large number of donors and recipients in PKE program [36].

Uyumlu çift ile çapraz nakil

- Uyumlu (gönüllü) çift için max fayda

- Daha genç böbrek
- Boyutu daha iyi
- HLA uyumlu

- Diğer çift için nakil şansı..

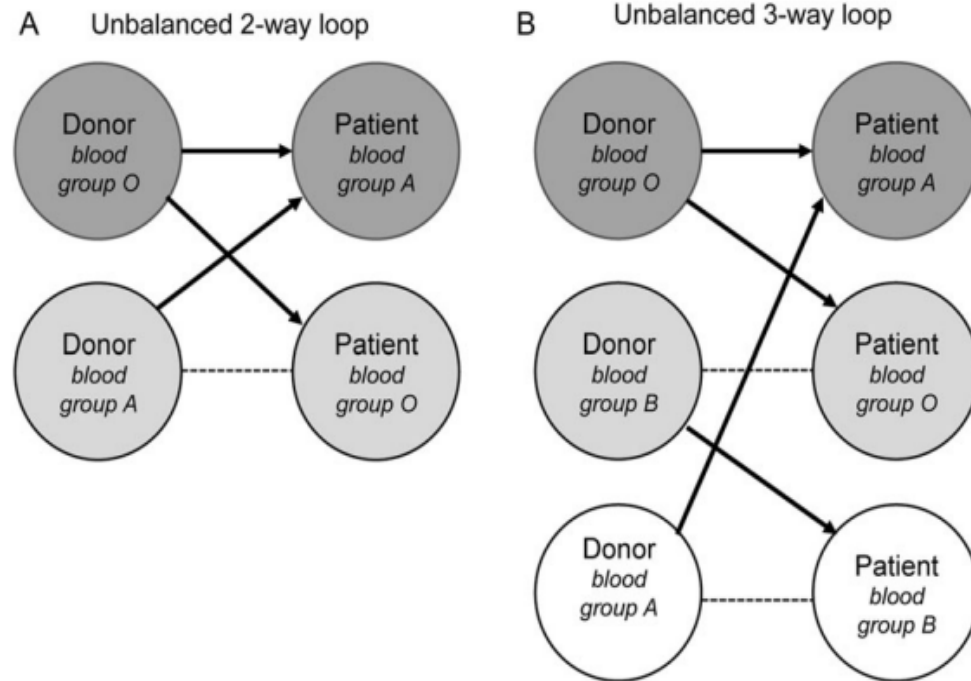
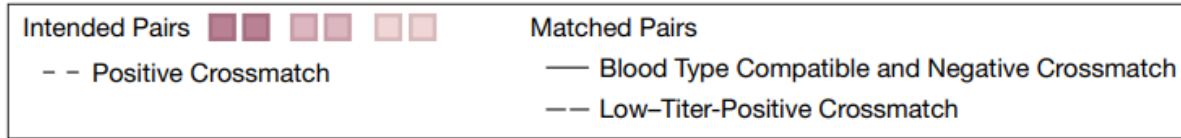


FIGURE 3: Exchange strategies in kidney paired donation. An unbalanced n -way loop exchanges between (A) one compatible and one incompatible donor-recipient pairs or (B) one compatible and two incompatible donor-recipient pairs.

Desensitizasyon ile apraz nakil

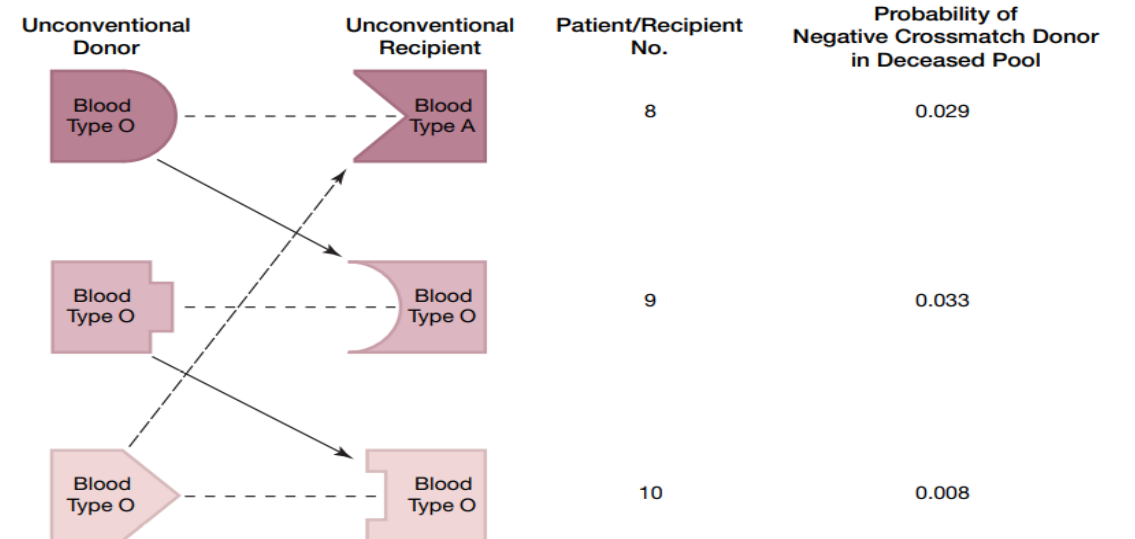
- Kompleks bir soruna iki ynl zm
- Sensitize hastaya daha az sensitize donr
- Karşı iftler iin nakil řansı
- Montgomery ve ark (John Hopkins)



Three intended unconventional donor/recipient pairs are shown. Each recipient has a positive crossmatch to the intended donor, with a titer of 1024 or greater indicating a strong antibody response not amenable to desensitization. The 3 recipients exchange donors such that 3 feasible scenarios are created: 2 negative crossmatches and 1 low-titer-positive crossmatch that can be overcome by desensitization.

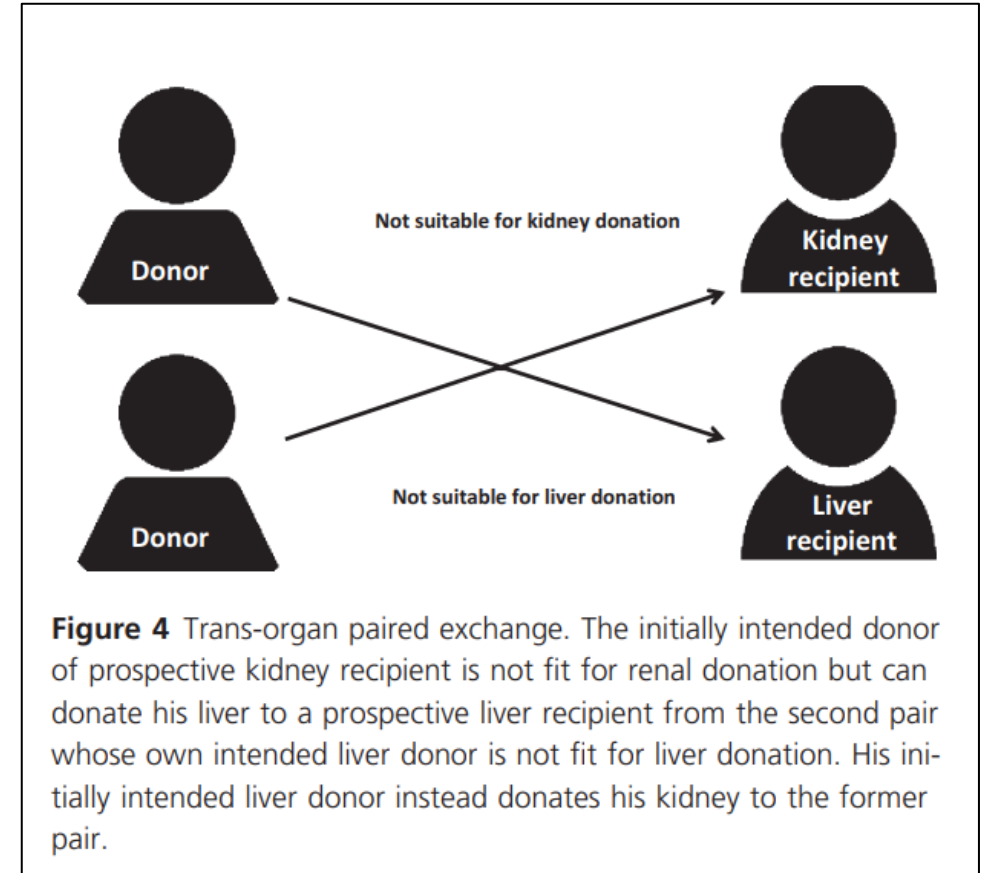
Clinical Results From Transplanting Incompatible Live Kidney Donor/Recipient Pairs Using Kidney Paired Donation

Figure 2. Use of a Triple Match



Yeni trend-Bi organ apraz nakil

- Trans organ apraz nakil yeni bir tanım (Torres 2019)
- ekici bir teklif olsada;
- Cerrahi Risk
 - Bbrek donr:1/3000
 - Karaciğer donr:1/500
- Onam nemli
- Donrler iin ek baskı...



Böbrek-karaciğer takası

- 2017 bir yazıdan esinlenildi.
 - **Dickerson'un simülasyonu**
 - **20-30 ek nakil op/ayda**



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CASE REPORT

AJT

Bi-organ paired exchange—Sentinel case of a liver-kidney swap

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John P. Roberts² | Nancy L. Ascher² | Chris E. Freise² | Brian K. Lee³

- Anne-kız böbrek nakli
- Kız kardeşler karaciğer nakli
- Etik komisyonda tartışılarak

Multi-Organ Exchange: The Whole Is Greater than the Sum of its Parts

John P. Dickerson and Tuomas Sandholm
Computer Science Department
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Pittsburgh, PA 15213

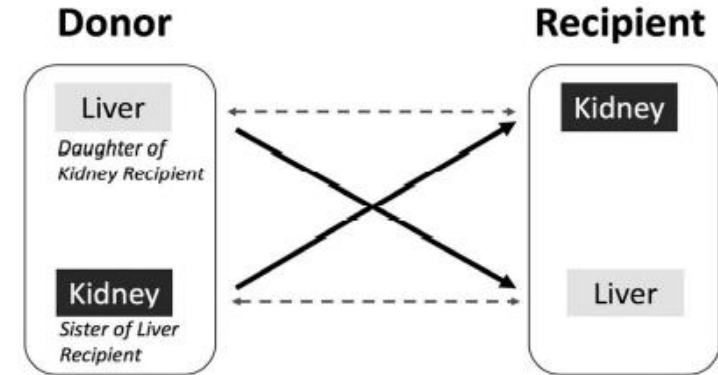


FIGURE 1 Diagrammatic representation of the liver-kidney exchange

TABLE 1 Baseline demographics, pre- and posttransplant laboratory values

	Donor-L	Recipient-K	Donor-K	Recipient-L
Age (yr)	21	42	47	52
Sex	Female	Female	Female	Female
Relationship	Daughter-mother		Sisters	
Height, cm	159	150	158	165
Weight, kg	44.8	64	58.7	57.4
BMI, kg/m ²	17.5	28.5	23.6	21
GRBW ratio, %				0.85
GW/SLV				0.4
Blood type/rhesus	O+	B+	O+	O+
PRA		0%		
Cause of end-organ failure (recipients)		Fibrillary GN		PBC
CMV, donor/recipient immune status		D+/R+		D-/R+
HLA mismatches		5 of 6		
Blood pressure, mm Hg	95/65	125/70	113/71	122/55
Serum creatinine, mg/dL	0.65	PD	0.71	0.56
eGFR predonation, mL/min	126		102	89
UPC predonation, g/g			0.14	
Serum ALT predonation, U/L	12			
Serum AST predonation, U/L	21			
Serum albumin preop, g/dL	4.5			1.7
Platelet count preop, ×10 ⁹ /L	182			106
INR predonation	1.1			
Serum total bilirubin predonation, mg/dL	0.8			
Induction agent		Basilixumab		None
Maintenance immunosuppression		Tac/MMF/pred		Tac/MMF/pred
Blood pressure at 1 yr, mm Hg			117/79	
Estimated blood loss, mL	120	200	50	1700
Serum creatinine at 1 yr, mg/dL	0.78	1.4	0.97	0.79
Serum ALT at 1 yr, U/L	8			7
Serum AST at 1 yr, U/L	19			16
Serum albumin at 1 yr, g/dL	4.0			4.6
Platelet count at 1 yr, ×10 ⁹ /L	217			259
INR at 1 yr	1.0			1.0
Serum total bilirubin at 1 yr, mg/dL	0.8			0.6
UPC at 1 yr, g/g		0.2	Undetectable	

- Sol donör nefrektomi
- Sağ donör hepatektomi

- Etik ???????

Moreover, registry data of 15 000 donor nephrectomies revealed an overall postoperative complication rate of 16.8%, with 7.3% of these being Clavien-Dindo grade III or higher.¹¹ In comparison, liver donation incurs a complication rate of 12%-40%, but only 3.5%-3.8% of which were major (≥Clavien-Dindo grade III).¹⁰

10. Abecassis MM, Fisher RA, Olthoff KM, et al. Complications of living donor hepatic lobectomy—a comprehensive report. *Am J Transplant.* 2012;12(5):1208-1217.

11. Lentine KL, Lam NN, Axelrod D, et al. Perioperative complications after living kidney donation: a national study. *Am J Transplant.* 2016;16(6):1848-1857.

- **Sonuç:** hayal edilebilir, yapılabilir.

Yeni trend=herkese nakil

- ✓ Advanced Donation Program (ADP)
 - ABD 2011'den beri kurgulanmakta
 - Gönüllü bağışçı ile aile için **KUPON** alınır
 - Ancak; alıcı için organ garantisi yok
- ✓ Global Kidney Exchange (GKE)
 - Rees ve ark. 2017'de İlk defa
 - Filipinli ve ABD çiftler arasında

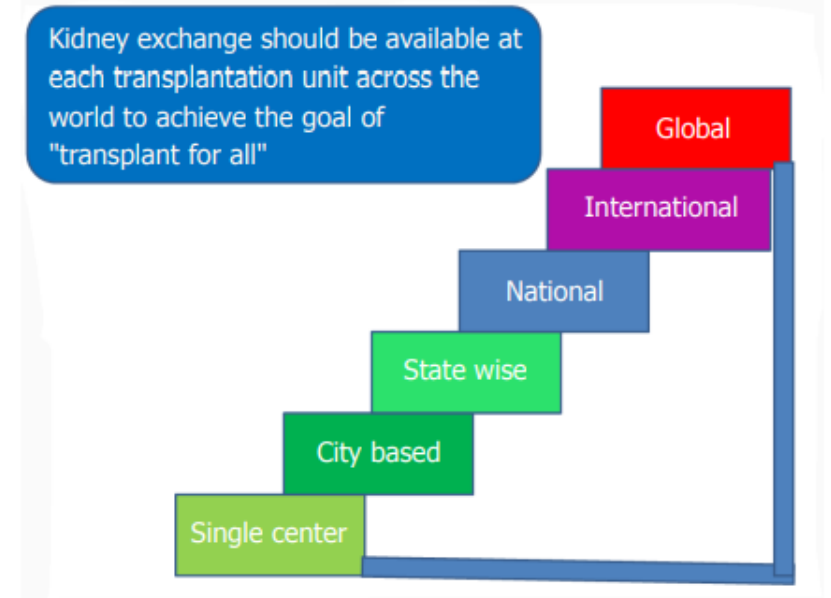
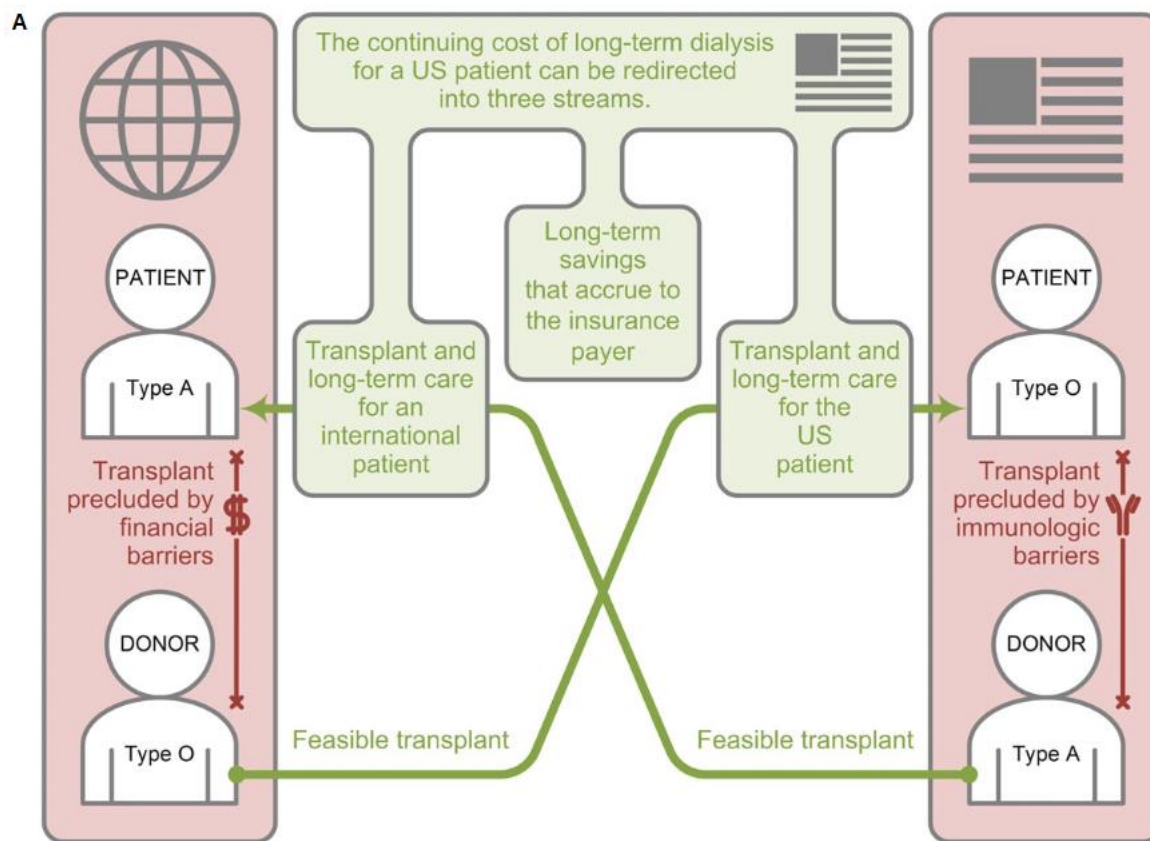


Figure 1 Stepwise progress in kidney exchange.

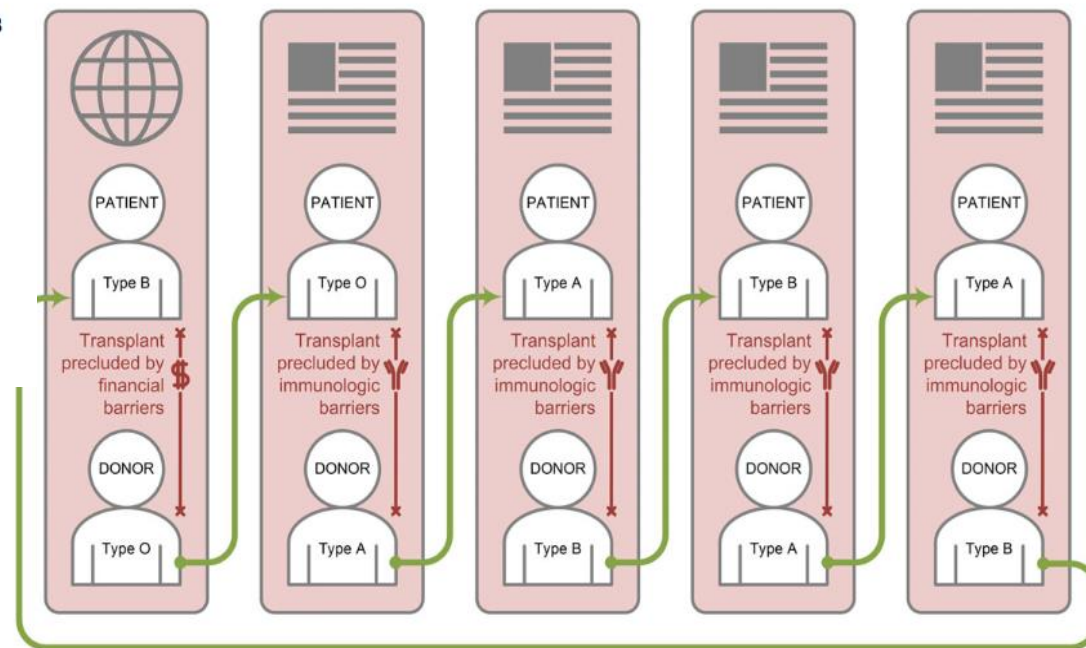
Etik sorunlar
Yasal sorunlar
Organ Ticareti ??

Brief Communication

Kidney Exchange to Overcome Financial Barriers to Kidney Transplantation



B



PATIENTS	1	2	3	4	5	6	7	8	9	10	11
PRA:	28%	68%	0%	22%	1%	93%	1%	95%	58%	0%	1%
Race:	Asian	Caucasian	Caucasian	Caucasian	AfricanAmer	Caucasian	Caucasian	Caucasian	Asian	AfricanAmer	Caucasian
Age:	33 yo	48 yo	32 yo	59 yo	36 yo	59 yo	68 yo	54 yo	63 yo	46 yo	48 yo
Insurance:	Philanthropy	Medicare	Medicare	Medicare	Private	Private	Medicare	Private	Medicare	Medicare	Private
Dialysis start:	Oct 2014	Jan 2012	Sep 2010	Apr 2013	Sep 2014	May 2014	Dec 2014	Preemptive	Jan 2012	Aug 2011	Apr 2015
Transplant:	Jan 2015	Jan 2015	Jan 2015	Mar 2015	Mar 2015	Mar 2015	Mar 2015	Mar 2015	Apr 2015	Aug 2015	Aug 2015
State:	OH	MN	WA	GA	GA	GA	GA	NC	CA	CA	GA
Sex and ABO:	A	O	B	A	A	O	O	O	O	O	B
DONORS	A	O	B	A	A	O	O	O	O	B	A
Sex and ABO:	A	O	B	A	A	O	O	O	O	B	A
Race:	Caucasian	Asian	Caucasian	Caucasian	AfricanAmer	Caucasian	Caucasian	Caucasian	Asian	Caucasian	Caucasian
Age:	53 yo	29 yo	44 yo	54 yo	47 yo	30 yo	42 yo	48 yo	53 yo	60 yo	47 yo
Relationship:	Altruistic	Spouse	Friend	Father-in-law	Brother-in-law	Friend	Child	Friend	Spouse	Sibling	Friend
Barrier:	Financial	ABOI	ABOI	DSA	DSA/Size	DSA	DSA	DSA	DSA	ABOI	ABOI



Finansal bariyer

Max zincirin uzunluğu

- Donör havuzu genişlemeli ve eşit eşleşme olmalı (**DONÖR**)
- Herkesin menfaatine ve ADİL olmalı
- Max. Zincir uzunluğu 3 olmalı
 - İyi kalite eşleşmeyi sağlar
 - 3 yol kısmen daha fazla hastanın sorununu çözer
 - Zinciri uzatıp çok kompleks olmamalı
 - Yeni stratejiler: listeye bağlı..

➡ The National Kidney Registry^{5,6} and Alliance for Paired Donations¹ in the United States have reported on long kidney exchange chains (2–35 pairs) utilizing real-time software.

➡ United States and as a national donor exchange scheme in both The Netherlands and South Korea.^{3–5} The Korean relay system expands the concept of single matched pairs to involve multiples up to a reported peak of seven pairs exchanging grafts over a period of time.⁶

Paired Kidney Exchange in India: Future Potential and Challenges Based on the Experience at a Single Center

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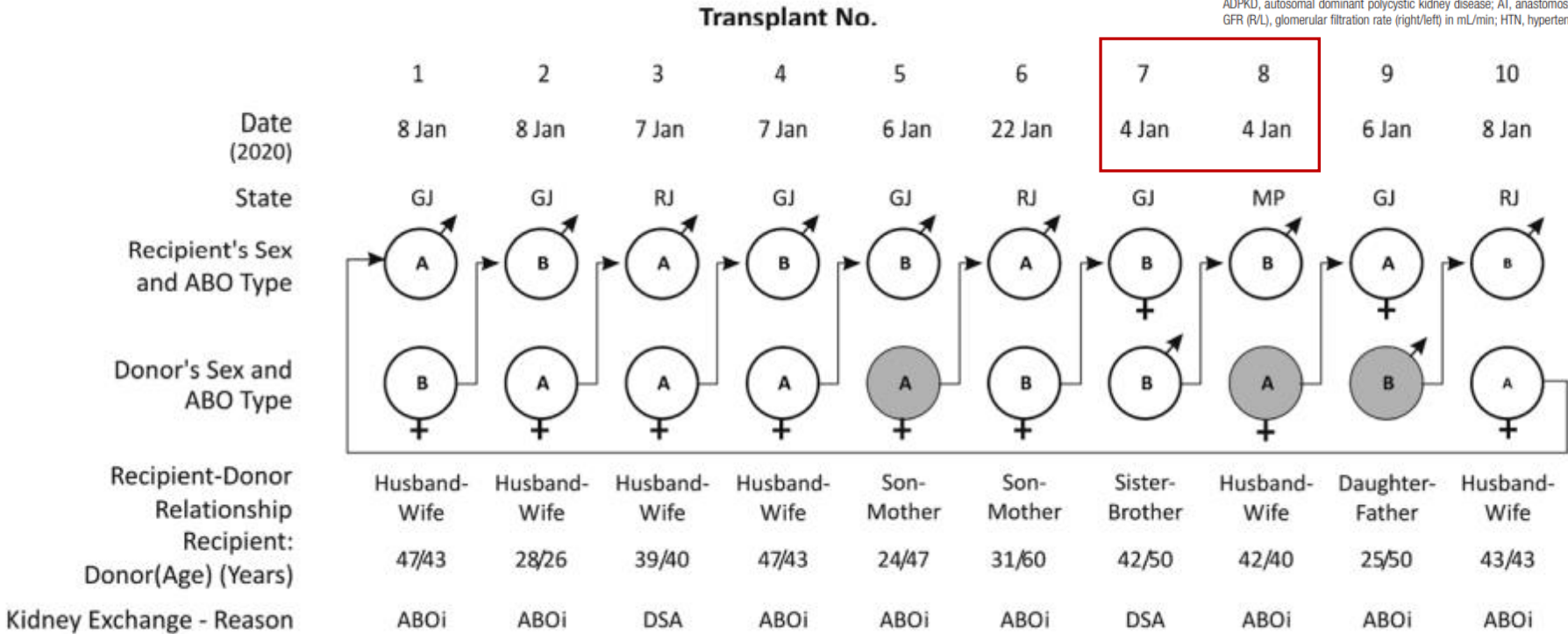
Laparoskopik retroperitoneal donör nefrektomi

TABLE 1.

Demographics of recipient-donor pairs and outcome

Recipient (R)	1	2	3	4	5	6	7	8	9	10
Original disease -ESRD	DN	CGN	CGN	DN	HTN	HTN	HTN	DN	CGN	ADPKD
Dialysis Vintage (mo)	8	12	36	12	3	2	18	17	38	1
Weight (kg)	59	67	48	55	47	47	62	40	47	64
Donor (D)	1	2	3	4	5	6	7	8	9	10
Weight (kg)	81	65	80	63	82	59	60	49	82	63
GFR (R/L)	43/54	50/48	56/50	48/54	55/55	52/49	54/61	50/50	55/55	53/45
S.Creatinine (mg/dL)	0.63	0.57	0.53	0.8	0.9	0.84	1	0.55	1	0.61
Outcome	R1←D10	R2←D1	R3←D2	R4←D3	R5←D4	R6←D5	R7←D6	R8←D7	R9←D8	R10←D9
WIT (s)	67	100	180	193	315	204	257	185	96	125
CIT (min)	24	75	120	114	118	54	110	73	20	82
AT (min)	24	15	29	25	19	39	34	36	22	14
S. Creatinine (mg/dL)	1	1.1	1.1	0.9	1.1	1	1.1	0.7	0.73	0.84

ADPKD, autosomal dominant polycystic kidney disease; AT, anastomosis time; CGN, chronic glomerulonephritis; CIT, cold ischemia time; DN, diabetes nephropathy; ESRD, end-stage renal disease; GFR (R/L), glomerular filtration rate (right/left) in mL/min; HTN, hypertension nephropathy; WIT, warm ischemia time.



- 2000-2020 tek merkez
- 920 kadavra
- 4558 canlı böbrek tx
 - Çapraz tx:440 (%9.6)
 - En uzun zincir: 6
 - Ardışık nakil: 67

FIGURE 1. A nonsimultaneous 10-way kidney exchange cycle. GJ, Gujarat; MP, Madhya Pradesh; RJ, Rajasthan.

Ulusal liste

EFFECTIVENESS

- Ethical, equitable, patient centric policy
- Standard protocols and simple logistics
- Auditing outcome and performance
- Reliable long-term donor-recipient care
- Avoiding commercialization

STATE/NATIONAL KIDNEY EXCHANGE PROGRAM

DONOR POOL

- Compatible pairs
- Incompatible pairs
- Multiple donors registration
- Multicentre ,state, national pool

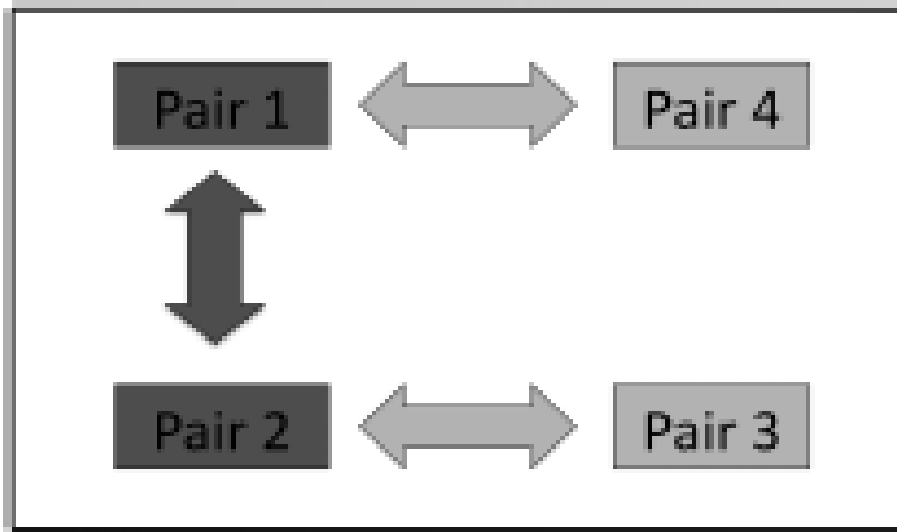
INCREASE MATCHES

- Software allocation
- Optimized chain length
- Optimized match run frequency
- Standardized laboratories

Table 1. Key ingredients of four national kidney paired donation registries

Country	The Netherlands	UK	Canada	Australia
Year established	2004	2007	2009	2010
Name of program	Living Donor Exchange Programme	National Living Donor Kidney Sharing Scheme (NLDKSS)	Canadian Blood Services Kidney Paired Donation Program (CBS-KPD)	Australian paired Kidney eXchange Program (AKX)
Dedicated central support staff	Yes	Yes	Yes	Yes
HLA laboratories involved	Single	Multiple	Multiple	Multiple
Types of exchanges considered	Multiway and domino	Multiway and domino	Multiway and domino	Multiway and domino
Accepts ABO-incompatible donor matching	No	Yes	No	Yes
Donor travel or organ transport	Donor travel	Organ transport	Donor travel (rarely organ transport)	Organ transport
Frequency of match cycles	Every 3 months	Every 3 months	Every 4 months	Every 3 months
Donor allocation algorithm	Virtual cross-match	Virtual cross-match	Virtual cross-match	Virtual cross-match
Primary allocation criteria	Unacceptable antigens based on recipient's serological DSA for HLA-A, B, Bw, DR, DQ	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQB1, DPB1	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1

Ulusal liste avantajı



- ✓ 2 yerine 4 çift nakil şansı yakalar
- ✓ Çocuklar için şans,
- ✓ Yüksek sensitize hastaların şansı artar

Fig. 4. If an exchange between Pair 1 and Pair 2 is performed at one center, only two transplants occur; however, in the larger pool, Pair 1 can exchange with Pair 4 and Pair 2 can exchange with Pair 3 allowing four transplants instead of two.

Kidney paired donation: principles, protocols and programs |

Ameliyat yöntemi

- ✓ Yeterli cerrahi ekip ve ameliyathane donanımı
- ✓ Köprü donör hariç tüm ameliyatlar eşzamanlı
 - ✓ Ardışık ameliyatlar
- ✓ Ulusal sistemde;
Donör transferi
Graft böbrek transferi

Table 3 Key features of national kidney exchange program

Country ^[3-10]	Key features of kidney exchange program
Australia ^[3-4]	High transplant rate for highly sensitized, HLA-incompatible pairs due to accepting ABO-incompatible donor matching with ABO titers $\leq 1:64$, high-resolution HLA identification and virtual cross match
Canada ^[5]	Non-directed anonymous donors facilitate 62% of transplants
South Korea	Favourable due to less sensitized, more compatible pairs, more non-directed anonymous donors, non-O > O patients
United Kingdom ^[8]	Low transplant rate due to less use of altruistic donor, restriction on long chain, permit only ≤ 3 -way exchange, donor travel
Johns Hopkins University, United States	Kidney exchange + desensitization increases transplant rate for difficult to match and difficult to desensitize pairs
San Antonio, United States ^[10]	Use of compatible pairs and A2 donors increases transplant rate even in single center program
National kidney registry, United States	Longer chain are used in matching
Donor vs kidney transport	Donors travel is preferred in Netherlands and Canada, kidney transport is preferred in United Kingdom and Australia
Alliance for paired donation, United States	Global kidney exchange

Çapraz nakil sonuçları

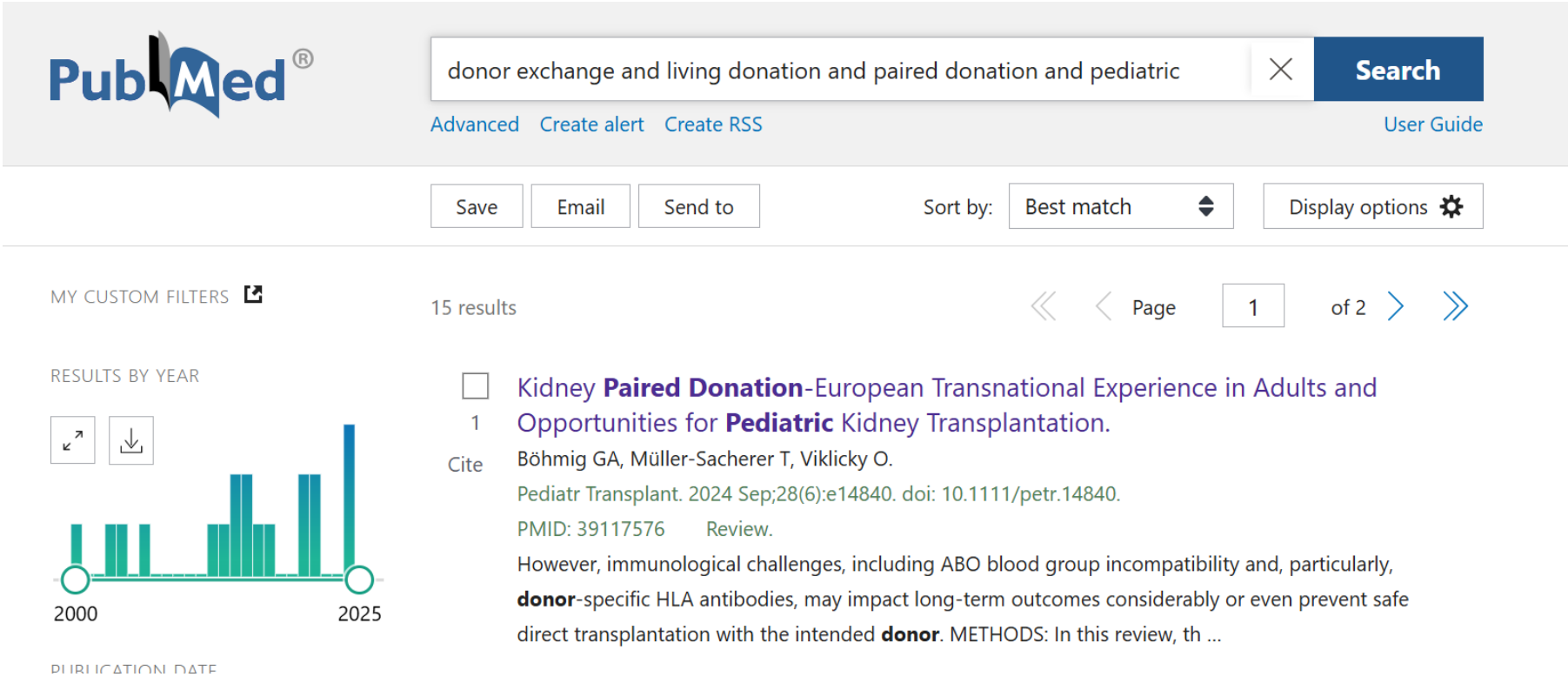
Table 2. Outcomes of various paired kidney exchange studies.

Author and year	Sample	Outcome	Remarks
Leeser et al. 2020 [16] (2008–2017) NKR, USA	2363 NKR PKE compared to control kidney transplant recipients ($n = 54,497$)	Median follow-up 3.7 years Similar graft failure and mortality	NKR registry was relatively high risk – more likely to be black, women, older, >80% PRA, previous transplant and longer time on dialysis
Flechner et al. 2018 [22] NKR, USA	2037 NKR PKE txp (2008–2017) vs. 1. Living donor related txp (49610) (UNOS) 2. Living unrelated txp no. 23310 3. UNOS non-NKR PKE no. 4236	One and 3 year comparable graft survival outcomes and better 5 years graft survival in PKE transplant	
Allen et al. 2018 [69] Australia	First 100 transplants in Australian PKE program	37 exchanges mean operating time 115 ± 44 min. CIT for nonshipped kidneys 2.6 ± 0.6 h vs. 6.8 ± 2.8 for shipped kidneys two DGFs. One year allograft survival 97%	Shipping kidneys rather than donor
Kute et al. 2017 [70] (2000–2016) India Jha et al. 2015 [71] (2010–2013) India	300 of total 3616 LDKT and 561 DDKT; mean follow-up 3 ± 3 years 26 PKE vs. 716 non-PKE Follow-up 20 months	Patient survival 96%, death censored graft survival 83%; Mean serum creatinine 1.3 mg/dl Serum creatinine at 1 month and last follow-up better in PKE Similar graft and patient survival and BPAR	124 two-way, 14 three-way, 1 four-way and 1 six-way transplant All two-way exchanges; reason for exchange – blood group incompatibility
Malik et al. 2014 [12] (2009–2013) Canada Tuncer et al. 2012 [72] (2008–2011) Turkey	235 PKE 57 PKE vs. 1081 living related txp	1-year patient survival 100%, graft survival 98% and BPAR 8% Similar first and second year GFR, AR, graft loss, pt. loss	PKE pts had higher HLA mismatch and age
Leeser et al. 2012 [73] (2007–2011) NKR, USA Bingaman et al. 2012 [19] (3 years) Methodist San Antonio, USA Klerk et al. 2011 [74] (2004–2011) Dutch PKE program	44 pair leading to 50 txp. 134 (117 incompatible and 17 compatible pairs) 187 transplants – 83 blood group incompatible and 104 positive crossmatch pairs	DGF – 6%; 1 year rejection rate – 9.1%; 1 year pt. and graft survival 98% and 94% 3 episodes of rejection, no graft lost due to rejection 5-year uncensored survival – 85%; death censored graft survival – 89%	Blood type incompatibility – 54.4%; sensitization – 43.2% 5 desensitization combined with PKE 44% with PRA >80% 40% of the registered patients got transplanted
Montgomery et al. 2005 [18] (2001–2004) Johns Hopkins, USA	22; median follow-up 13 months	Patient survival 100%; graft survival 95.5%; 6 months creatinine – 1.2 mg/dl; ACR – 18%; no AMRs	Two triple exchanges; 5 patients were highly sensitized

Sonuç;

- Kadavra donörden daha iyi
- Canlı donörler ile aynı

Pediatric çapraz böbrek nakli



Unrecognized opportunities: The landscape of pediatric kidney-paired donation in the United States

Jennifer Verbesey¹ | Alvin G. Thomas^{2,3} | Amy D. Waterman⁴ |
Sunil Karhadkar⁵ | Victoria R. Cassell⁴ | Dorry L. Segev^{3,6} | Julien Hogan^{7,8} |
Matt Cooper⁹

2014 böbrek dağıtım sistemi, pediatrik alıcılar için bekleme sürelerini neredeyse iki katına çıkardı.

2008-2021 KPD sonuçları karşılaştırıldı.

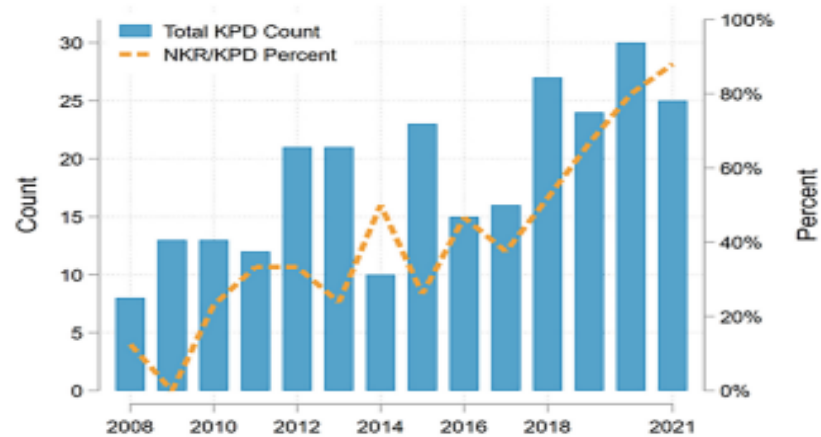


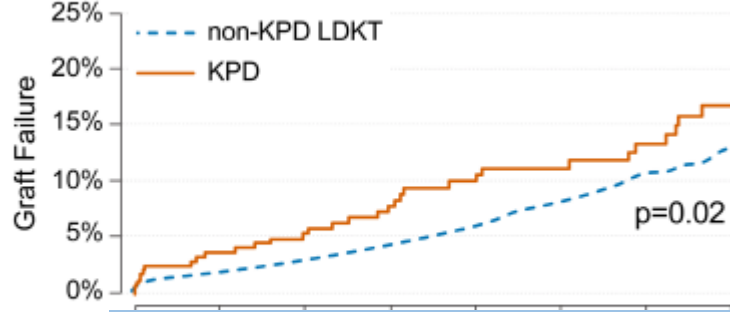
FIGURE 1 Pediatric (Age < 18) Paired Donation Transplants 2008–2021. The dotted line shows the annual proportion of kidney-paired donation (KPD) transplants facilitated by the National Kidney Registry (NKR); the vertical bars indicate total KPD count.

TABLE 1 Study population characteristics.

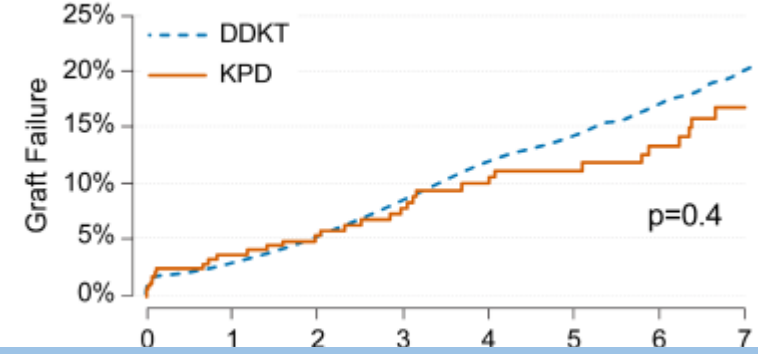
	KPD	Non-KPD LDKT	DDKT
N	258	3447	4987
Recipient characteristics			
Female, %	42.2	38.7	41.5
Black, %	15.1	7.9	23.6
Hispanic, %	15.9	18.4	31.4
Age, Median (IQR)	12.0 (6.0, 15.0)	11.0 (4.0, 15.0)	13.0 (8.0, 16.0)
Preemptive transplant, %	37.6	40.8	24.4
Days on dialysis, Median (IQR)	99 (0, 370)	42 (0, 325)	314 (0, 706)
Public insurance, %	43.8	40.9	70.8
Previous transplant, %	15.5	7	9.6
PRA > 80 at transplant	12	2.8	4.5
eGFR pre-transplant, Median (IQR)	14.6 (8.5, 23.3)	14.9 (9.0, 23.7)	10.8 (6.6, 18.1)
Delayed graft function, %	4.3	3.1	7.9
Donor characteristics			
Female, %	67.4	60.3	30
Black, %	6.2	7.3	13.2
Hispanic, %	12.4	16.6	22.2
Age, Median (IQR)	35.0 (29.0, 43.0)	37.0 (31.0, 43.0)	25.0 (21.0, 30.0)
BMI, Median (IQR)	25.9 (23.5, 28.7)	26.5 (23.6, 29.5)	25.2 (22.4, 28.8)
LKDPI/KDPI, Median (IQR)	1.6 (−9.4, 14.2)	2.0 (−9.5, 13.7)	13.4 (6.6, 23.0)
Blood type			
A, %	31.8	26.8	37.4
AB, %	1.2	0.6	0.8
B, %	12.8	7.7	16.7
O, %	54.3	65	45
Transplant characteristics			
Cold ischemia time, h, Median (IQR)	2.4 (1.2, 8.7)	1.2 (0.9, 2.1)	11.9 (8.2, 16.2)
ABO incompatible, %	1.2	0.4	0.1
HLA mismatches (A, B, DR)			
0, %	1.2	3.6	2.1
1, %	3.9	8.2	0.4
2, %	7	27	3.2
3, %	20.5	37.9	11.2
4, %	25.2	7.3	27
5, %	27.5	9.4	36
6, %	13.6	4.9	20.2

Abbreviations: BMI, body mass index; DDKT, deceased donor kidney transplant; KPD, kidney-paired donation; LDKT, living donor kidney transplant.

KPD vs. non-KPD Living Donor KT

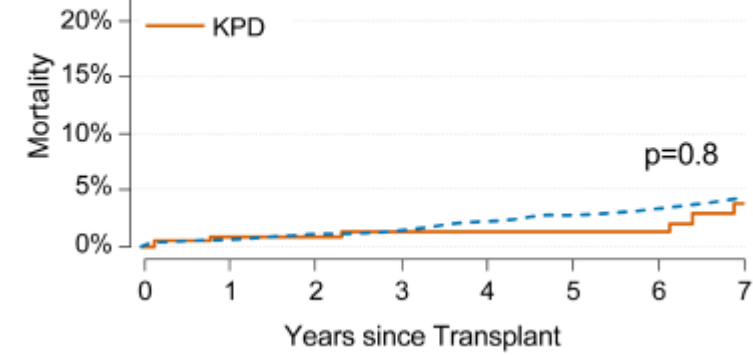
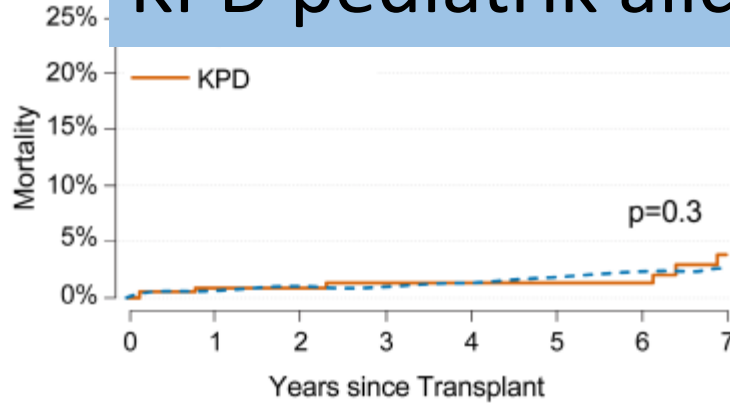


KPD vs. Deceased Donor KT



Nakil sonuçlarında bir fark gözlemlemedik.
Bu sonuçlar göz önüne alındığında,
KPD pediatrik alıcılar için yeterince kullanılmıyor olabilir.

KPD vs. non-K



EDITORIAL

Kidney paired donation

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- ✓ Victoria Cassell ve meslektaşlarının "**Tanınmayan Fırsatlar**" başlıklı makalesinde
 - ✓ Pediatrie **nadir tartışılan** bir konu
 - ✓ KPD oranlarının son yıllarda artmış olmasına rağmen, **genel olarak düşük** olduğunu
 - ✓ **Sonuçların (Non KPD ve DDKT ile) benzer** olduğu
 - ✓ Pediatrik hastalar için **2001'den beri canlı bağış oranı azalmaktadır**;
 - ✓ toplumun sağlık durumunun kötüleşmesi,
 - ✓ canlı bağışçı kriterlerinin katılığı,
 - ✓ finansal engeller ve
 - ✓ canlı bağış avantajları hakkında bilgi eksikliği
- ✓ Pediatrik hastalarda KPD kullanımının artırılmasını, **nakil erişimini genişletmek için bir fırsat** olarak görüyor.

Brief Communication

Optimizing Outcomes in Pediatric Renal Transplantation Through the Australian Paired Kidney Exchange Program

M. P. Sypek^{1,2,3,*}, S. I. Alexander⁴, L. Cantwell⁵,
F. L. Ierino^{1,3,6}, P. Ferrari⁷, A. M. Walker^{1,3,8} and
J. Y. Kausman^{1,2,3,8}

Table 1: Demographics and baseline characteristics of patients

Case	Age at transplantation	Cause of ESKD	No. of runs in AKX	Comorbidities	Sensitizing events	Reason for AKX	Class I cPRA (%)	Class II cPRA (%)	Combined cPRA (%)
1	3 years	ARPKD	3	Liver disease, pulmonary hypoplasia, hypothyroidism	Blood transfusion	DSA	70	25	78
2	14 years	PUVs	13	GERD with fundoplication, anxiety, bilateral native nephrectomies	Previous Tx	DSA	99	94	99.8
3	17 years	Renal hypodysplasia	1	PCOS	Previous Tx	DSA	56	86	92
4	16 years	PUVs/dysplasia	1	Mitrofanoff	Blood transfusion	DSA	86	0	86
5	8 years	Dysplasia/perinatal ischemia	4	Diabetes insipidus, autism spectrum disorder	Blood transfusion	DSA, need for urgent transplant due to HDx complications	86	68	96
6	3 years	Infantile nephrotic syndrome	1	Oral aversion, poor growth, anxiety	Blood transfusion	Hepatitis B core antibody	0	32	32
7	9 years	CAKUT	2	None	None	ABO incompatibility	0	0	0

ESKD, end-stage kidney disease; cPRA, calculated panel reactive antibody; ARPKD, autosomal recessive polycystic kidney disease; DSA, donor-specific antibody; PUV, posterior urethral valve; GERD, gastroesophageal reflux disease; Tx, transplantation; PCOS, polycystic ovarian syndrome; HDx, hemodialysis; CAKUT, congenital abnormalities of the kidney and urinary tract; VUR, vesicoureteric reflux disease.

Table 3: Outcomes for patients transplanted through the AKX

Patient	Duration of follow-up (months)	eGFR (mL/min/1.73 m ²)	Donor-specific antibody (DSA) testing (MFI)	
1	24	94	12 months	Cw4 (1438)
2	26	46	12 months	A32 (1358); DR7 (1324); B64 (<1000) ¹
			18 months	A32 (<1000); DR7 (<1000) ¹
3	22	91	1 month	No DSA
4	12	73	12 months	No DSA
5	9	87	2 weeks	No DSA
6	8	84	Not tested	Not tested
7	54	66	30 months	A29 (<1000) ¹
			54 months	DR18 (<1000) ¹

eGFR, estimated glomerular filtration rate (calculated using the revised Schwartz formula).

¹DSA below cut-off for positive test (>1000).

- ✓ Çocukların yaşamları boyunca birden fazla nakle ihtiyaç duymaları muhtemeldir.
- ✓ Bu nedenle, yüksek düzeyde doku uyumu ve organ kalitesi eşleşmesi temel önceliklerdir.

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Keywords: ABO incompatibility | HLA incompatibility | kidney paired donation | kidney transplantation

COMPREHENSIVE REVIEW OPEN ACCESS

Kidney Paired Donation—European Transnational Experience in Adults and Opportunities for Pediatric Kidney Transplantation

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- ✓ KPD programları yetişkinler için faydalı
- ✓ Son veriler bunun pediatrik hastalar için de geçerli olabileceğini göstermektedir.

Sonuç:

1. Pediatrik KPD az, çünkü kadavra bekleme süresi az
2. Pediatrik KPD nasıl arttırılabilir
 1. Eğitim çalışmaları
 2. Yetişkin aktif KPD programları ile bağlantı
 3. Optimal organ boyutu, yaşı ve eplet eşleşmesi
 4. Cesaret verici uzun dönem sonuçların çıkması

TABLE 1 | Key features of the Czech-Austrian KPD program.

KPD rules	Transnational program (AT: Vienna and Innsbruck; Cz: Prague)	Differences between participating centers
Option of pediatric KPD Tx	Yes (Innsbruck, Prague)	No pediatric kidney Tx in Vienna
Additional centers/countries	Requirements: program harmonization & contract (example: recent exchanges with Israel)	None
Inclusion criteria		
ABO incompatibility	One to two matchruns	None
DSA and/or positive crossmatch	Yes	None
Combined HLA/ABO incompatibility	Yes	None
Repeated mismatch	Optional	None
Other criteria	Optional (e.g., donor age for pediatric recipients)	None
Altruistic donors	Accepted	None
Imputation of multiple donors for one recipient	Accepted	None
Organ travel	Yes (ground or flight transport)	None
Donors travel between centers	No	None
Centralized computer algorithm	Yes (software in Prague)	None
Matching algorithm		
HLA donor/recipient typing	High resolution: A, B, C, DRB1, DQA1, and DQB1	HLA-DPB1: All (A) or subset of (Cz) recipients
Single antigen testing	DSA threshold: MFI >1000–2000	None
ABOi KPD donor	Accepted for HLA-incompatible pairs	None
HLAi KPD donor	Usually not accepted	None
Other factors	Pre-specified for selected recipients (e.g., donor age, HLA mismatch)	None
Match runs	Every 3 months	None
Final crossmatch requirement	Negative T and B cell flow crossmatch	None
Closed loops	Yes	AT: ≤3 simultaneous exchanges per center (participation in larger transnational loops) Cz: No limit (non-simultaneous exchanges)
NEAD chains	Yes	AT: Participation in short bridge donor-linked segments (simultaneous Tx required) Cz: Longer segments (non-simultaneous Tx)
Deceased donor wait list	Wait list inactivation upon match run participation	None
Anonymity	Yes	None

Abbreviations: AT, Austria; ABOi, ABO-incompatible; Cz, Czech Republic; HLAi, HLA-incompatible; KPD, Kidney Paired Donation; MFI, Mean Fluorescence Intensity; NEAD chain, Non-simultaneous Extended Altruistic Donor chain; Tx, Transplantation.

İlk KPD böbrek: 2010

İlk KPD karaciğer: 2013

UKM verileri

YIL	ÇAPRAZ NAKİLLER (PEDIATRİK DAHİL)			TOPLAM ÇAPRAZ PEDIATRİK DAHİL	PEDIATRİK ÇAPRAZ NAKİLLER		TOPLAM PEDIATRİK ÇAPRAZ
	SAĞ BÖBREK	SOL BÖBREK	KARACİĞER		PEDIATRİK BÖBREK	PEDIATRİK KARACİĞER	
2011	30	60		90			0
2012	35	85		120	4		4
2013	12	63	2	77	2	1	3
2014	20	63		83	3		3
2015	24	104		128	1		1
2016	28	95	6	129	6	1	7
2017	19	85		104	1		1
2018	42	139	11	192	4	2	6
2019	31	143	4	178	7		7
2020	28	141	10	179	9		9
2021	21	180	16	217	9	2	11
2022	26	203	33	262	7	8	15
2023	15	139	92	246	7	24	31
2024	21	137	142	300	5	22	27
2025	4	37	65	106	3	12	15
TOPLAM	356	1674	381	2411	68	72	140

İSÜ organ nakli merkezi

Böbrek nakli

	Yetişkin (n 1397)		Pediatrik (n 224)		toplam
Kadavra/Canlı	96	1301	20	204	1621
Çapraz nakil		163		14	177 (%11.7)
Çapraz eşleşme modelleri		Dörtlü: 3 (n 11) Üçlü: 9 (n 24) İkili: 69 (n 128)		Dörtlü: (n 1) Üçlü: (n 3) İkili: (n 10)	Ped: % 6.8
Çapraz nakil nedenleri		ABO uyumsuzluğu İmmunolojik risk Gönüllü		ABO uyumsuzluğu İmmunolojik risk Çoklu arter	
Donörleri		Eş, akraba ve diğer		Ebeveyn: 14	

Vaka Örneđi

- **SG 4 yaşı/12 kg**
- Kan grubu: B poz
- Ety: Senior Loken
- Özg:
 - Ciddi nöromotor gelişim geriliđi
 - Görme kaybı mevcut.
 - Nistagmusu var.
 - Nöbet geçirme öyküsü yok.
- Aşı takvimi: tam

- Donör: baba
- **MG 42 yaşı/80 kg**
- Kan grubu: O poz
- Doku uy: 3 MM
- GFR: 97,5 mL/dk

- Çapraz donör
- **AS 39 yaşı/60 kg**
- Kan grubu: B poz
- Doku uy: 4 MM
- GFR: 113 mL/dk



ABO ve HLA uyumsuzluğunun ötesinde Pediatrik KPD stratejileri

- ✓ Pediatrik hastalarda HLA-DR/DQ eplet uyumsuzluklarının (özellikle ilaç uyumsuzluğu vakalarında) uzun vadeli allotransplant disfonksiyonuna yol açabilecek **de novo DSA oluşumuna** katkıda bulunabilir
- ✓ **İnfeksiyon riskini azaltmak**; HBV viral bulaşma riski olmayan bir donörden yapılan bir KPD nakli
- ✓ Yüksek derecede duyarlı bir pediatrik alıcıda başarılı bir ABO uyumsuz canlı donör (62 yaş) eşleştirilmiş KPD böbrek nakli.
- ✓ **Yaş-kilo-böbrek boyutu eşleşmesi**: En küçük pediatrik alıcılar için böbrek boyutu eşleştirme çabası
- ✓ **Cerrahi riskler**: Küçük pediatrik alıcı donörünün çoklu renal arter varlığı.....

39. C. Wiebe, T. E. Nevins, W. N. Robiner, W. Thomas, A. J. Matas, and P. W. Nickerson, "The Synergistic Effect of Class II HLA Epitope-Mismatch and Nonadherence on Acute Rejection and Graft Survival," *American Journal of Transplantation* 15, no. 8 (2015): 2197–2202, <https://doi.org/10.1111/ajt.13341>.

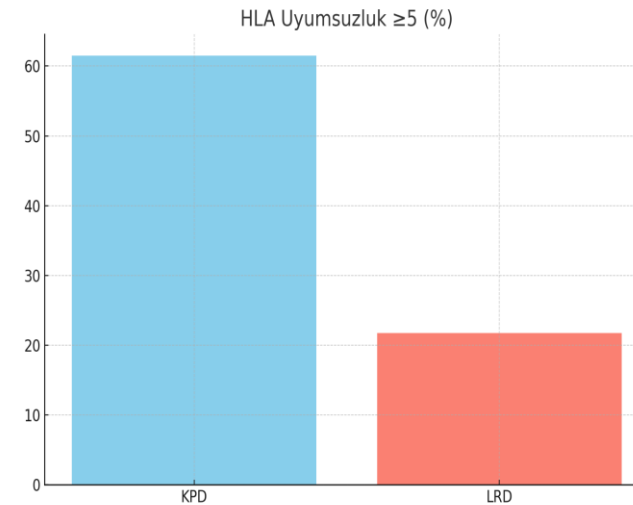
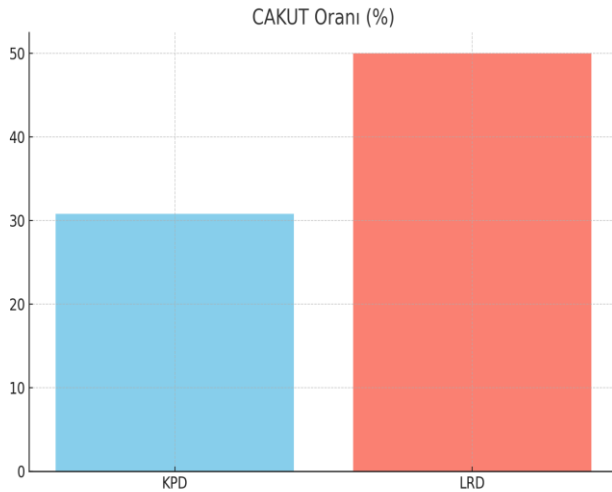
37. M. P. Sypek, S. I. Alexander, L. Cantwell, et al., "Optimizing Outcomes in Pediatric Renal Transplantation Through the Australian Paired Kidney Exchange Program," *American Journal of Transplantation* 17, no. 2 (2017): 534–541, <https://doi.org/10.1111/ajt.14041>.

38. Y. Calzada, I. Revuelta, E. Codina, et al., "Overcoming Limits: First ABO Incompatible Living Donor Paired Kidney Transplant in an Hypersensitized Pediatric Recipient in Spain," *Pediatric Transplantation* 26, no. 8 (2022): e14359, <https://doi.org/10.1111/ptr.14359>.

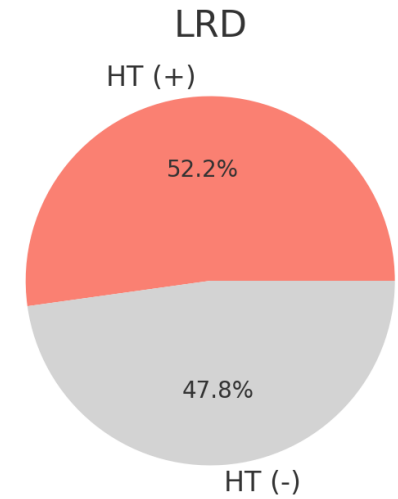
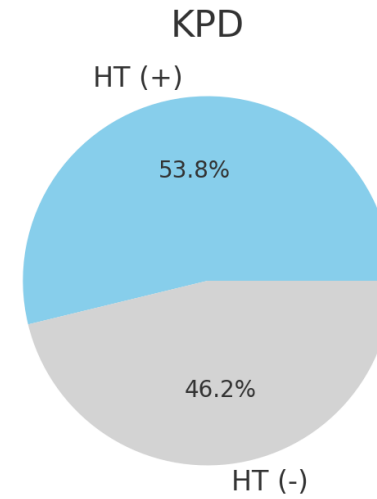
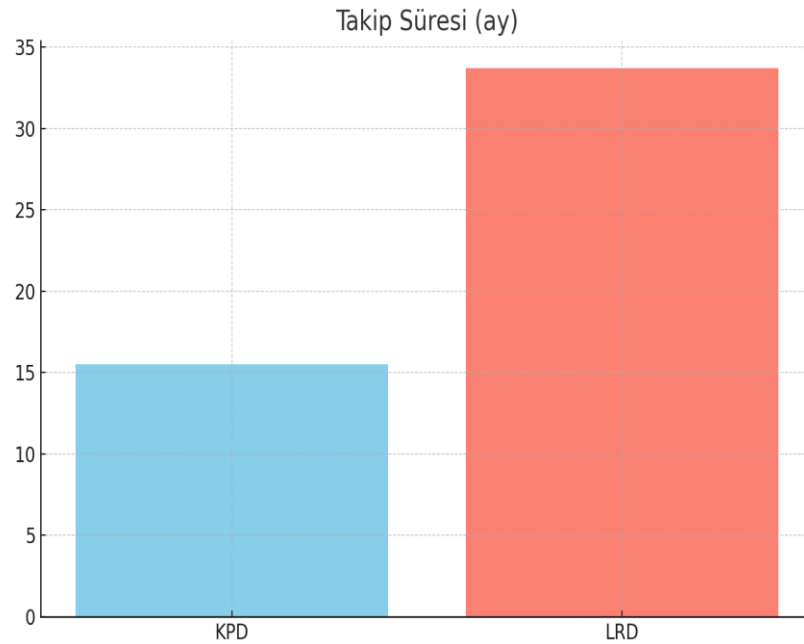
36. J. R. Krissberg and P. S. Verghese, "Kidney Paired Donation," *Pediatric Transplantation* 28, no. 1 (2023): e14667, <https://doi.org/10.1111/ptr.14667>.

Pediatric KPD

Parametre	KPD (N=14)	LRD (N=23)
Alıcı yaşı (yıl)	13.0 (IQR: 12; 2–17)	11.4 (IQR: 12; 2–18)
Verici yaşı (yıl)	50.0 (IQR: 15; 33–65)	37.0 (IQR: 20; 24–70)
Diyaliz süresi (ay)	9.0 (IQR: 34.0; 2.6–72.0)	12.0 (IQR: 42.0; 0.1–130.0)

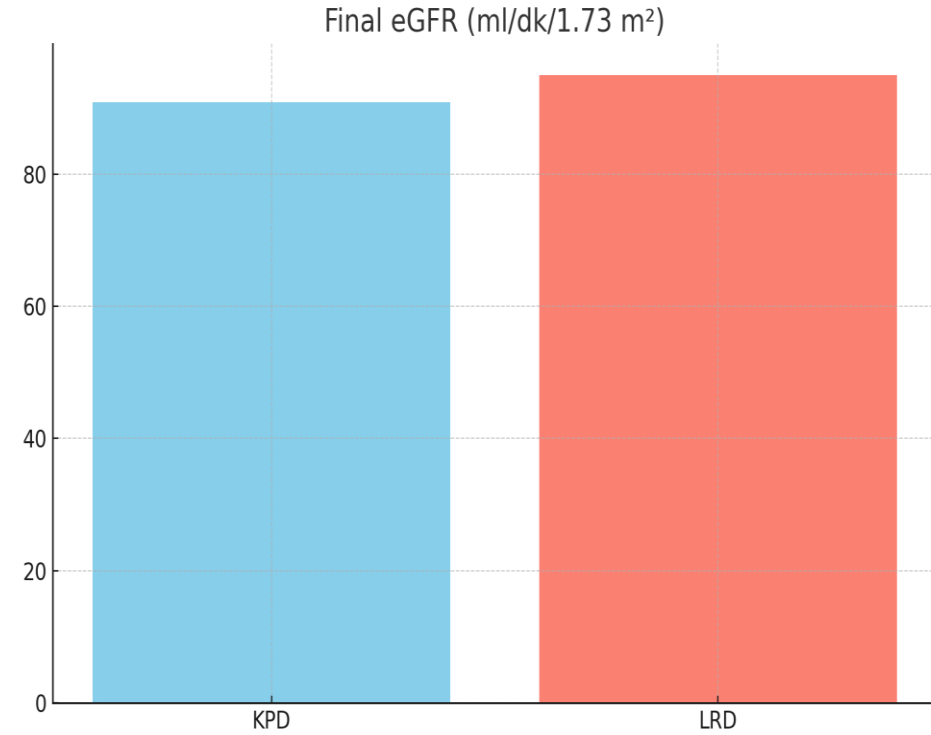


Pediatric KPD takip ve HT



Pediatric KPD

Sonuç



Pediatric KPD özet

- ✓ KPD; tıbbi, etik ve yasal olarak canlı donör havuzunu arttıran en uygun yöntem
- ✓ Avantajları nedeniyle 30 yıldır umut vaad eden bir sistem
- ✓ Yapay zeka uygulaması ile 2 kat fayda sağlanabilir
- ✓ Ulusal listeler pediatrik hastalar için avantaj sağlar
- ✓ Pediatric KPD stratejileri;
 - ✓ ABO uyumsuzluğu ve immünolojik risk (pediatrik hastada riski azaltmak)
 - ✓ Böbrek boyut uyumsuzluğu
 - ✓ Çoklu arter varlığı
- ✓ KPD sonuçları:
 - ✓ Canlı vericili nakiller ile aynı
 - ✓ Kadavra vericili nakillerden daha iyi

KPD, uygun bir donörü olan pediatrik hastalar için canlı donasyona yönelik birçok engeli aşmak için uygulanabilir bir stratejidir ve immünolojik riskleri en aza indirme fırsatı sunar.



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