Living donors are better than deceased donors; a Fact or Fiction?

SHAHRZAD OSSAREH- M.D.

HKC- IUMS

OUTLINES

- Patient and graft survival
- Economic burden of deceased and living Tx on the community and recipients
- Influences of living and deceased donors on the recipient Immunology
- General Debates

Introduction

- Kidney transplantation is the treatment of choice for end-stage renal disease.
- A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients when compared with maintenance dialysis.

National Kidney Foundation®

- **On average:**
- Over **3,000** new patients are added to the kidney waiting list each month.
- Every **14** minutes someone is added to the kidney transplant list.
- **13** people die each day while waiting for a life-saving kidney transplant.
- In 2014, **4,761** patients died while waiting for a kidney transplant.
- Another, **3,668** people became too sick to receive a kidney transplant.

2014 Donor Profile

	Living	Deceased
Age	All living donors in the United States must be at least 18 years old to consent to donation. There were 5,538 living donors in 2014. <1: 0 1-5: 0 6-10: 0 11-17: 0 18-34: 1,627 35-49: 2,258 50-64: 1,492 65+: 161	The total number of deceased donors (7,761) does not add up to the total number of deceased donor transplants because many deceased donors are able to give both of their kidneys. <1: 100 1-5: 212 6-10: 103 11-17: 387 18-34: 2,328 35-49: 2,099 50-64: 2,110 65+: 422
Gender	Male: 2,052 Female: 3,486	Male: 4,647 Female: 3,114
Ethnicity	White/Caucasian: 3,895 Black: 592 Hispanic: 762 Asian: 221 American Indian/Alaska Native: 19 Pacific Islander: 10 Multiracial: 39	White/Caucasian: 5,266 Black: 1,101 Hispanic: 1,033 Asian: 196 American Indian/Alaska Native: 46 Pacific Islander: 28 Multiracial: 91

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Graft Survival: Short term

- A major improvement in renal allograft survival in the past 20 years has been the relative elimination of the early risk period.
- **1-Delayed allograft function;** The presence of delayed graft function has a major adverse impact upon both short- and long-term allograft survival.
  - In one single-center study of 518 patients, multivariate analysis found that delayed graft function was the principal factor underlying kidney survival at one year [Quiroga I. Nephrol Dial Transplant. 2006;21(6):1689.]
- **2-Human leukocyte antigen antibodies**; The risk of allograft failure at 1 year was significantly higher among those with HLA antibodies (6.6 vs. 3.3%), as well as among those who developed such antibodies de novo (8.6 vs. 3%). [Terasaki PI. Am J Transplant. 2004;4(3):438]
- **3-Type of kidney;** Allograft survival rates for living-donor transplants and deceased, non-expanded-criteria donors (ECDs) are 98 vs. 96 % at 3 months and 96 vs. 92 % at one year, respectively [US Transplant http://www.ustransplant.org]
- **4- Center effect, Donor age, Donor illness, Dialysis and preemptive transplantation**

Tissue Injury

Brain death

- Brain death resulting from trauma or catastrophic intracranial hemorrhage is associated with a variety of adverse effects upon donor organs prior to transplantation.

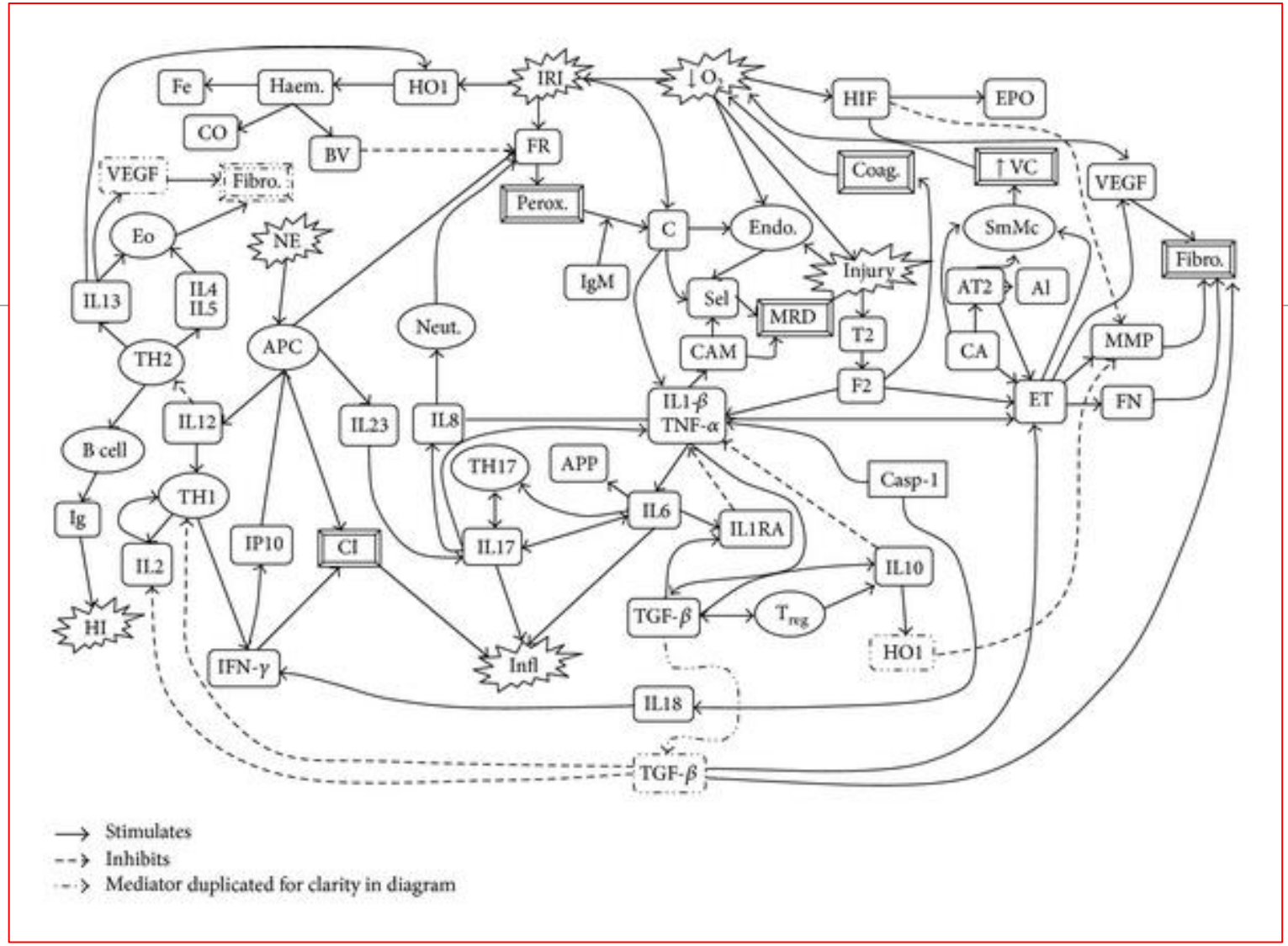


Figure 1: Primary mediators of peri-transplant related inflammation. Al: aldosterone, APC: antigen presenting cell, APP: acute phase proteins, AT2: angiotensin II, BV: biliverdin, C: complement, CA: catecholamines, CAM: cellular adhesion molecule, Casp-1: caspase 1, CI: cellular inflammation, CO: carbon monoxide, Coag: coagulation, Endo: endothelial cells, Eo: eosinophils, EPO: erythropoietin, ET: endothelin, F2: factor II (Thrombin), Fe: iron, Fibro: fibrosis, FN: fibronectin, FR: free radicals, HI: humoral immunity, HIF: hypoxia inducible factor, HO1: heme oxygenase 1, IFN: interferon, Ig: immunoglobulin, IL: interleukin, IL1RA: interleukin 1 receptor antagonist, Infl: inflammation, IP: interferon-γ-induced protein, IRI: ischaemia reperfusion injury, MMP: matrixmetalloproteinases, MRD: margination/rolling/diapedesis, NE: new antigens/neoepitopes, Neut: neutrophils, O_2: oxygen, Perox: peroxidation, Sel: selectin, SmMc: smooth muscle contraction, TF: tissue factor, TGF: transforming growth factor, TH1: type 1 helper T-cell, TH17: type 17 helper T-cell, TH2: type 2 helper T-cell, TNF: tumour necrosis factor, Treg: regulatory T-cell, VC: vasoconstriction, VEGF: vascular endothelial growth factor.

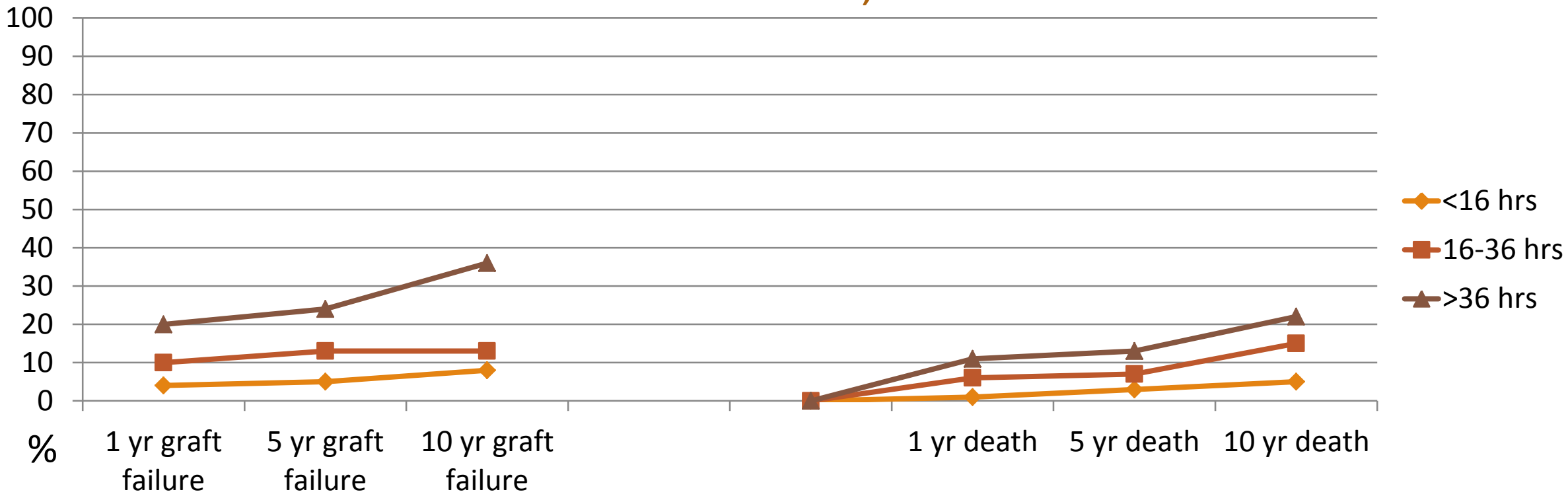
Ischemia and/or reperfusion injury

- Ischemia and/or reperfusion injury is critical risk factor for both early delayed graft function and late allograft dysfunction.
- It mainly depends on cold ischemia time.

Each additional hour of cold ischemia time significantly increases the risk of graft failure and mortality following renal transplantation.

3829 adult recipients of a first deceased-donor kidney

- They observed an increased risk of DGF with CIT (P<0.0001): from 22% for CIT between 6 and 16 h, to 40% for CIT above 24 h.



Debout A. Kidney International (2015) 87, 343–349;

Cold Ischemia Time

<16 hrs	1 yr	5 yr	10 yr
Graft failure	4%	10%	20%
Death	1%	6%	11%
16-24 hrs/ 24-36 hrs			
Graft failure	5%	13%	24%
Death	3%	7%	13%
>36 hrs			
Graft failure	8%	13%	36%
Death	5%	15%	22%

Debout A. Kidney International (2015) 87, 343–349;

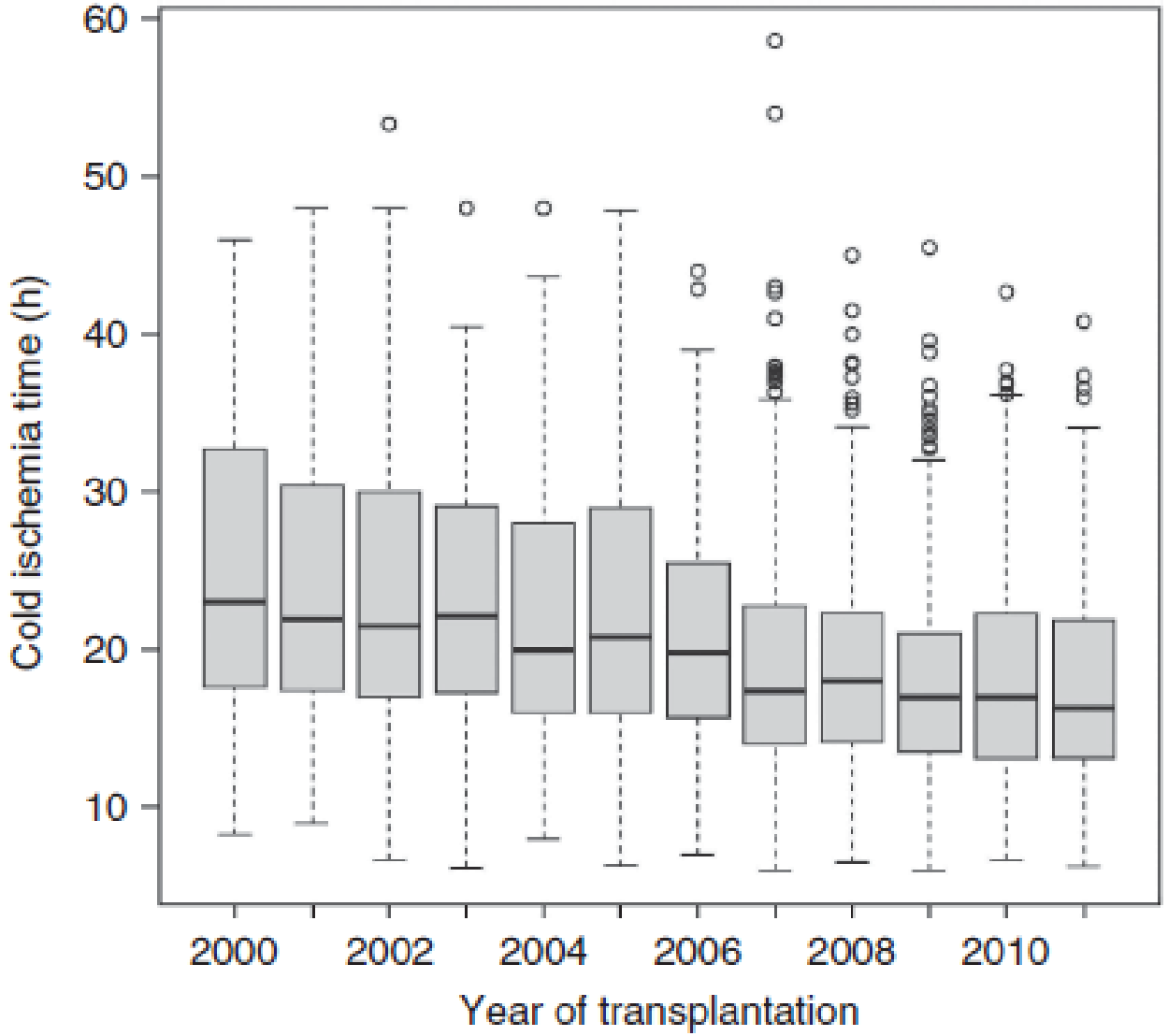


Figure 1 | Boxplots representing the minimum, the maximum, the first, second, and third quartiles of cold ischemia time duration for each year of transplantation.

Debout A. Kidney International (2015) 87, 343–349;

How long is our CIT considering the local Tx programs?

- Usually less than 6-7 hours and definitely less than 16 hours.
- This gives us a very good opportunity for achieving good results in deceased donor transplant if we imply appropriate harvesting techniques and organ care.

Graft Survival: Short term

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ORIGINAL ARTICLE

AJT

Long- and short-term outcomes in renal allografts with deceased donors: A large recipient and donor genome-wide association study

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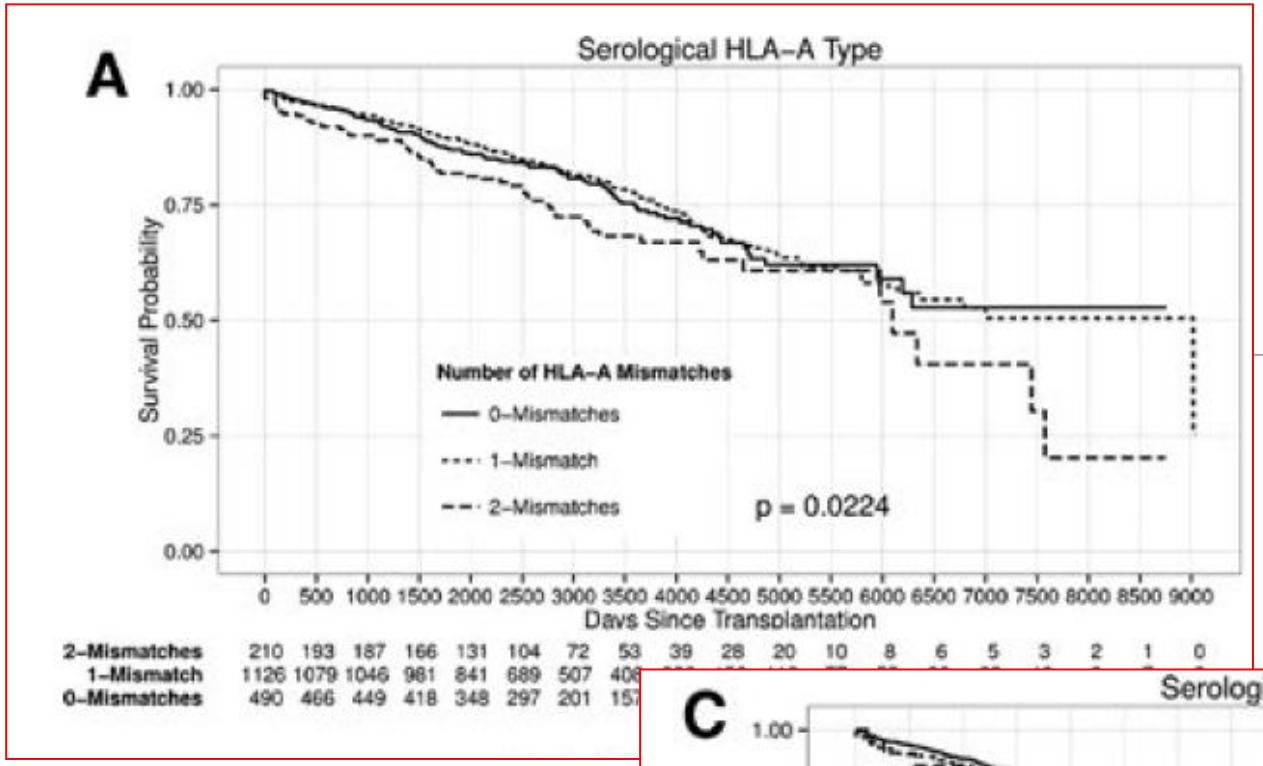

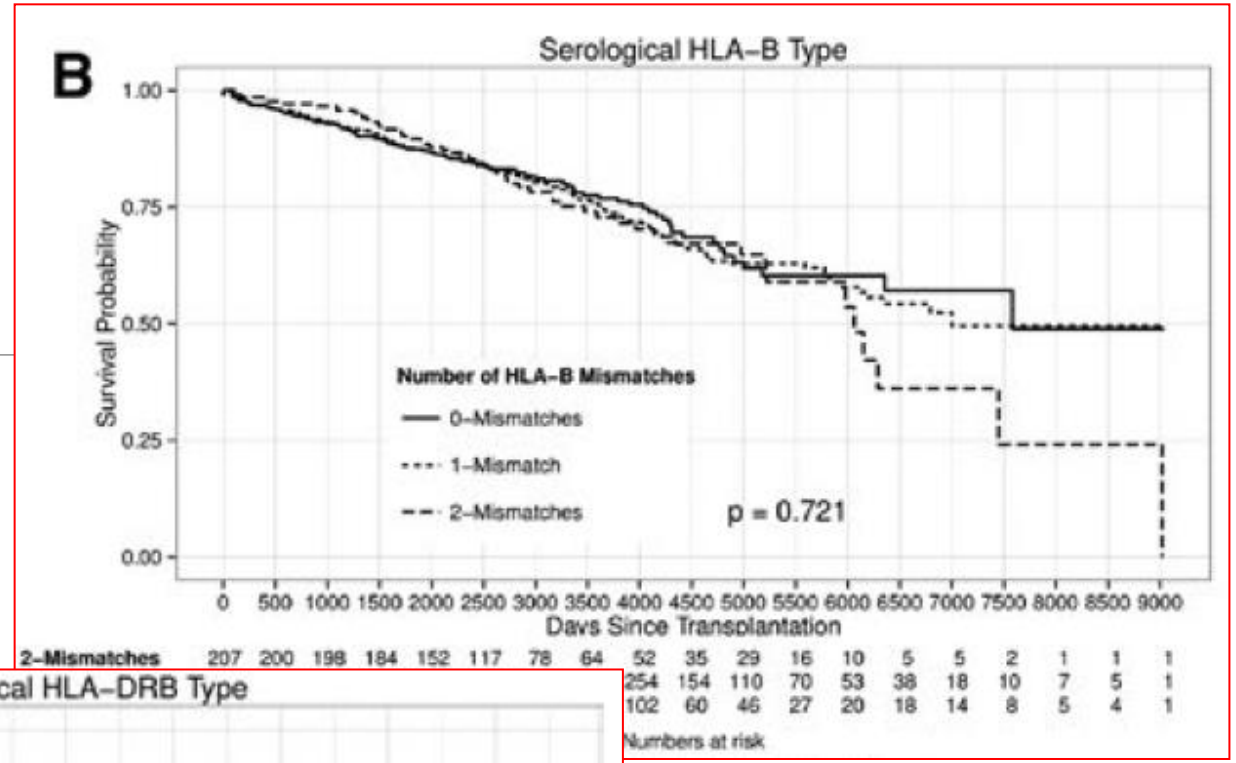

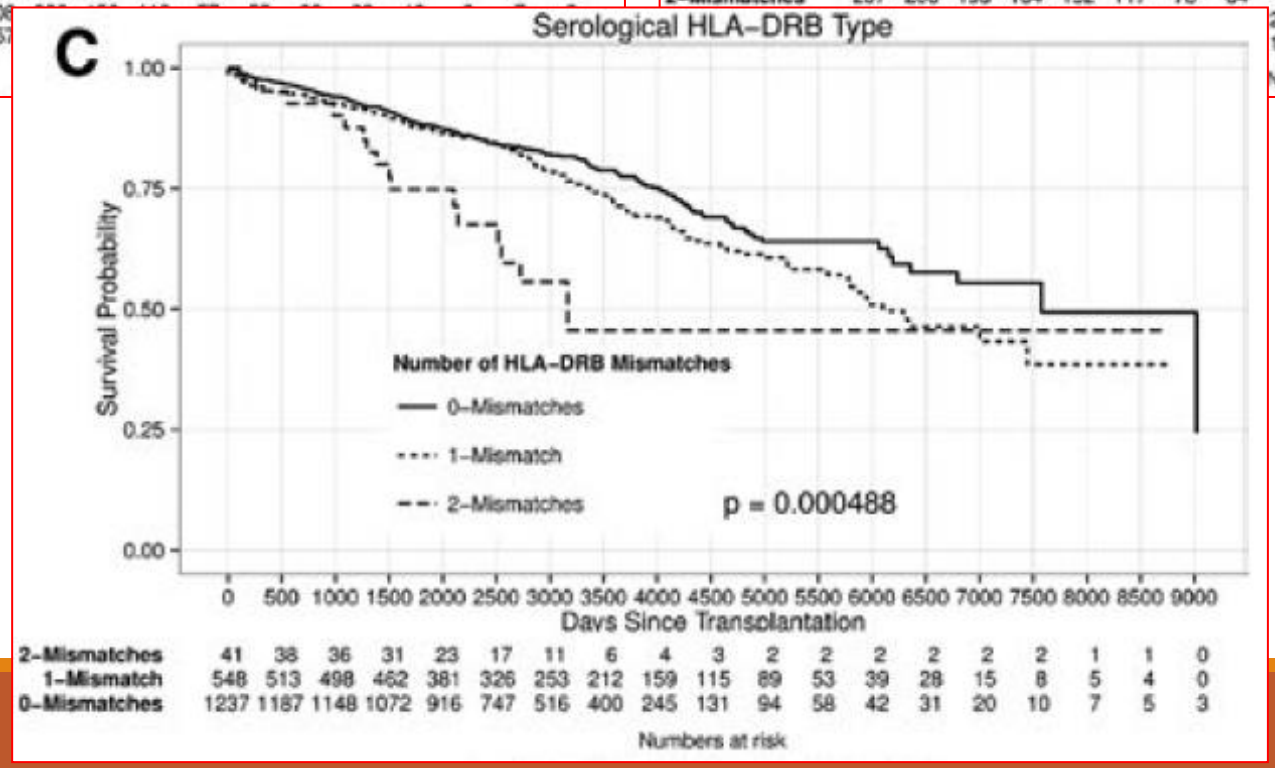

MP Fuentes. AJT. 2018 ;18: 1370

- For pediatric patients with end stage renal disease who require a kidney transplant, selection of an optimal donor is particularly important because these patients are young and hope to live with a functioning transplant well into adulthood, and indeed for the remainder of their lives.

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Graft Survival: Long-term

1-Alloantigen-dependent factors

- **Episodes of acute rejection** ; The risk of allograft failure at 1 year was significantly higher among those with HLA antibodies (6.6 vs. 3.3%), as well as among those who developed such antibodies de novo (8.6 vs. 3%). [PallardóMateu LM. NDT. 2004;19 Suppl 3:iii38.]
- **HLA matching;** An increased degree of HLA antigen mismatching is associated with a greater risk of chronic graft loss, presumably due to ongoing specific immunologic injury**.** [Opelz G. N Engl J Med. 1988;19:1289-92.]
  - **Prior Sensitization** [Cecka JM, Cho L. Sensitization. In: Clinical Transplants 1988, Terasaki PI (Ed), UCLA Tissue Typing Laboratory, Los Angeles 1989. p.365.]

2- Prior and ongoing tissue injury, cold ischemia time,

3-Inadequate renal mass, post-transplant hypertension, hyperlipidemia, a more marginal kidney, and recurrent or de novo glomerular disease, Gene polymorphisms,..

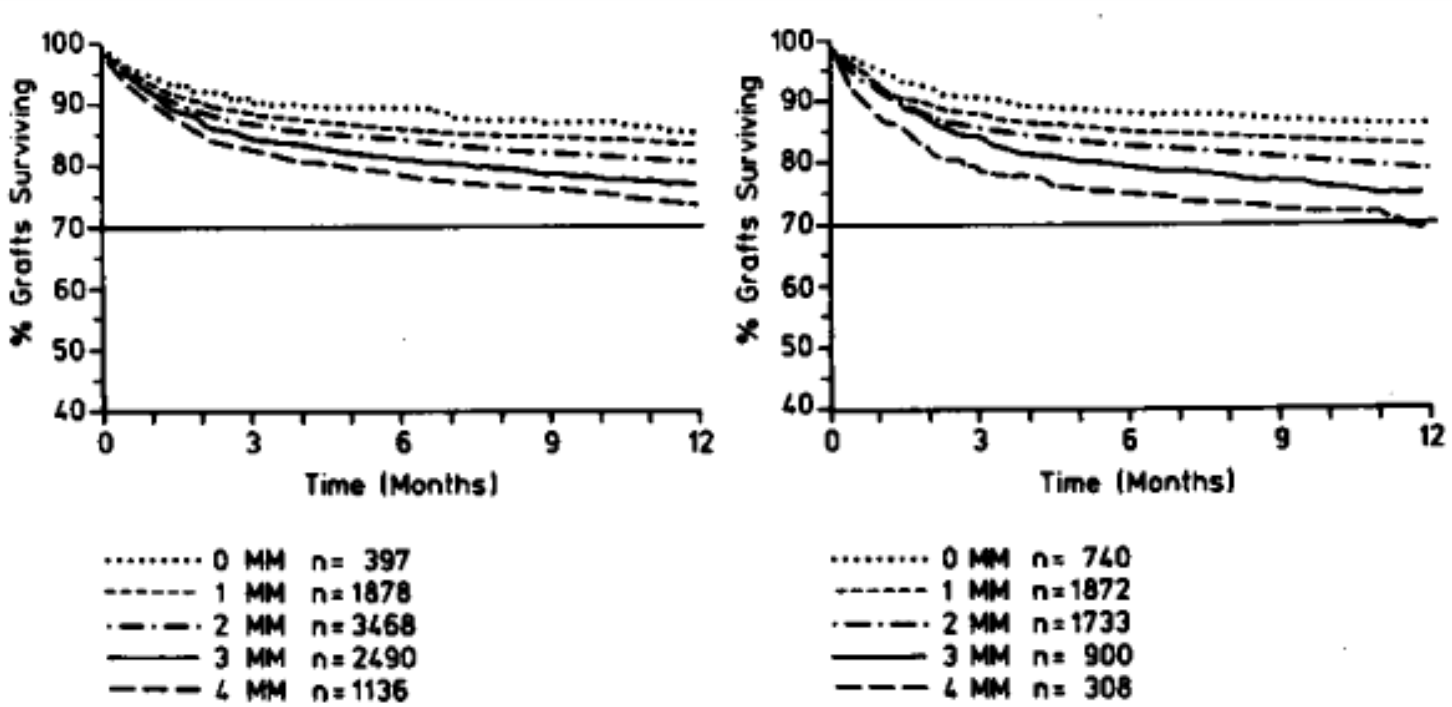


Figure 1. Effect of Matching for HLA-B and HLA-DR Antigens in First Cadaver-Donor Kidney Transplants.

Graft-survival rates for locally obtained kidneys (left) are compared with those for kidneys exchanged between centers (right). The effect of matching on graft outcome was statistically significant in both subgroups ($P<0.0001$). The number of patients studied is indicated according to the number of mismatched (MM) HLA antigens. The horizontal line at 70 percent was drawn to facilitate comparison. All patients underwent immunosuppression with cyclosporine.

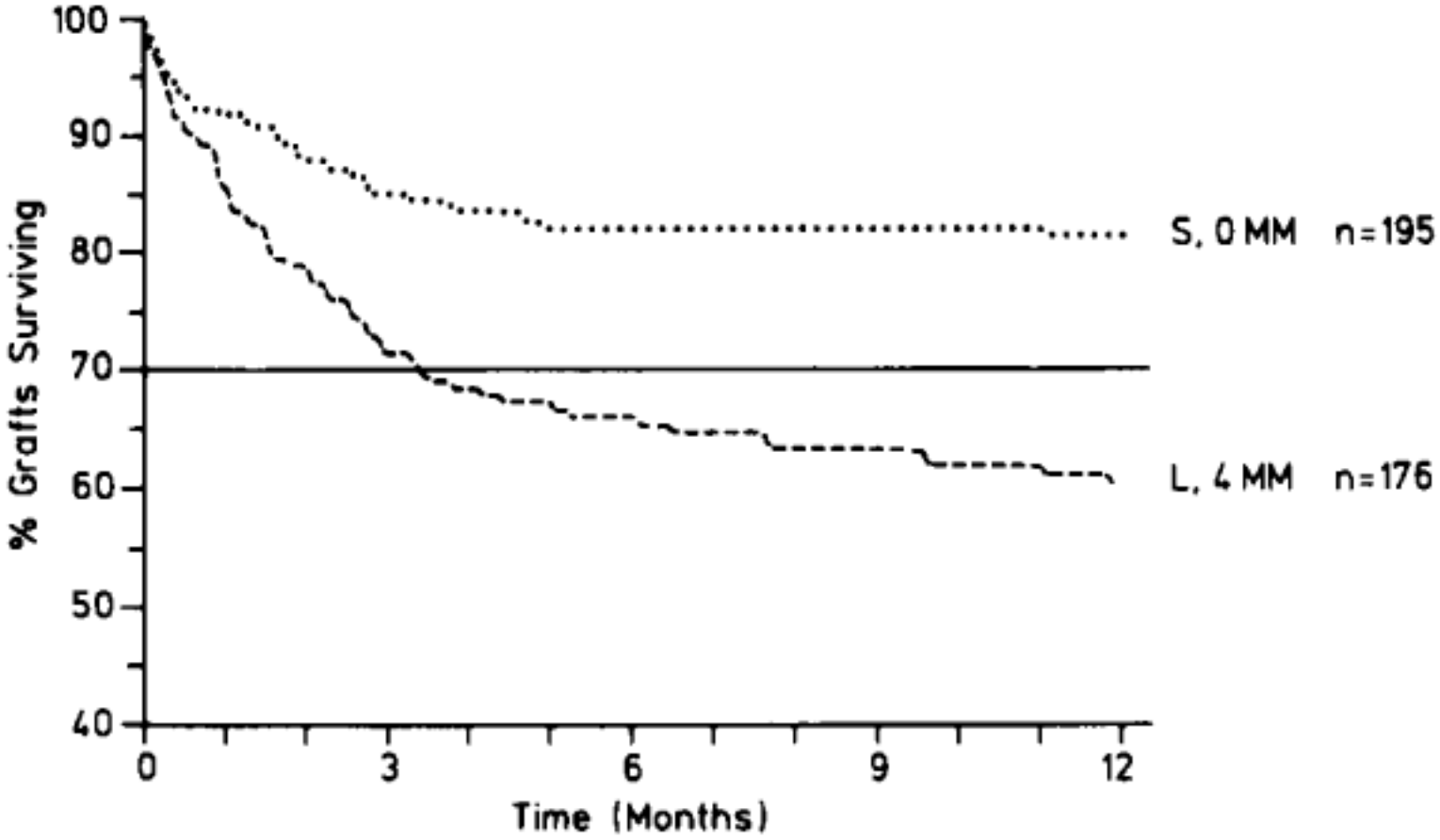


Figure 2. Graft Survival in Second Cadaver-Donor Transplants. Exchanged kidneys without a mismatch for HLA-B or HLA-DR (S, 0 MM) are compared with local kidneys with four mismatches (L, 4 MM) ($P<0.001$, log rank).

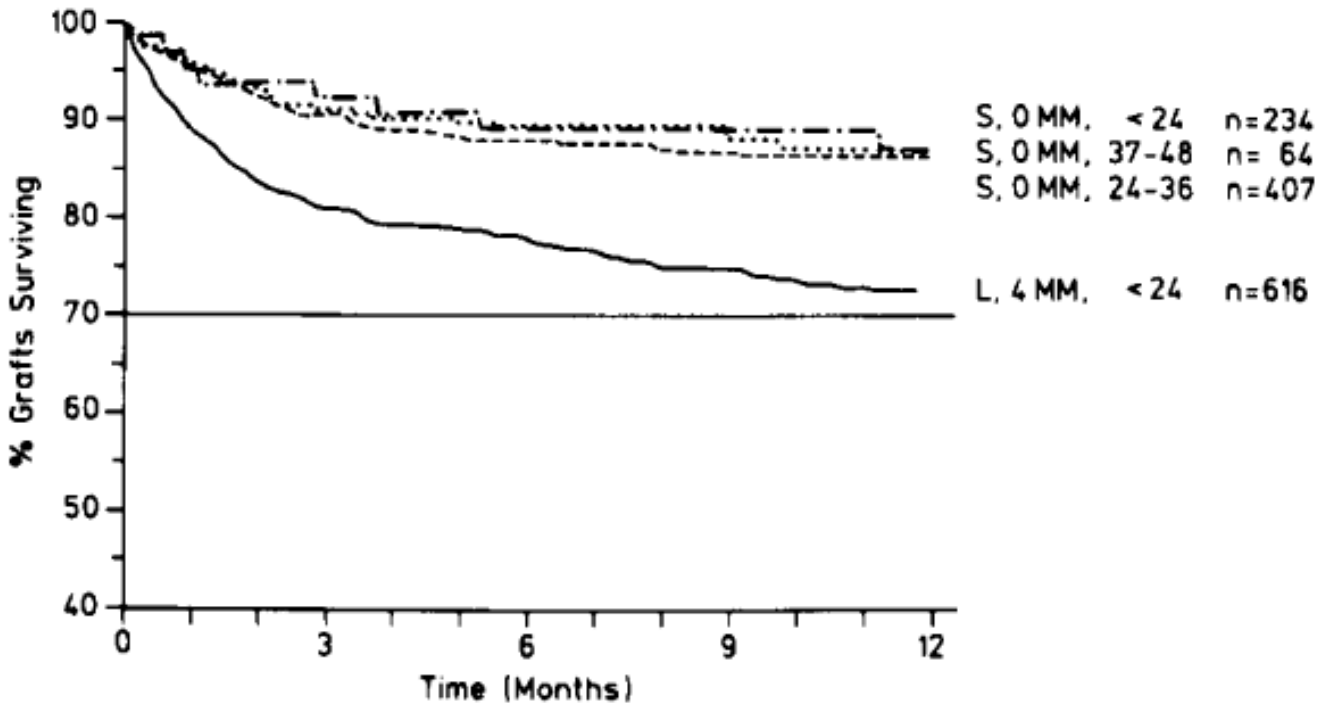


Figure 4. Comparison of First Cadaver Transplant-Survival Rates in Recipients of Exchanged Kidneys without Mismatches for HLA-B or HLA-DR (S, 0 MM) with Survival Rates in Recipients of Local Kidneys with Four Mismatches (L, 4 MM).

Recipients of exchanged kidneys were grouped according to the organs' cold-ischemia times (<24, 24 to 36, or 37 to 48 hours) and compared with recipients of local kidneys with less than 24 hours of ischemia. The difference in graft survival between local, poorly matched grafts and exchanged, well-matched grafts is statistically significant ($P<0.0001$, log rank).

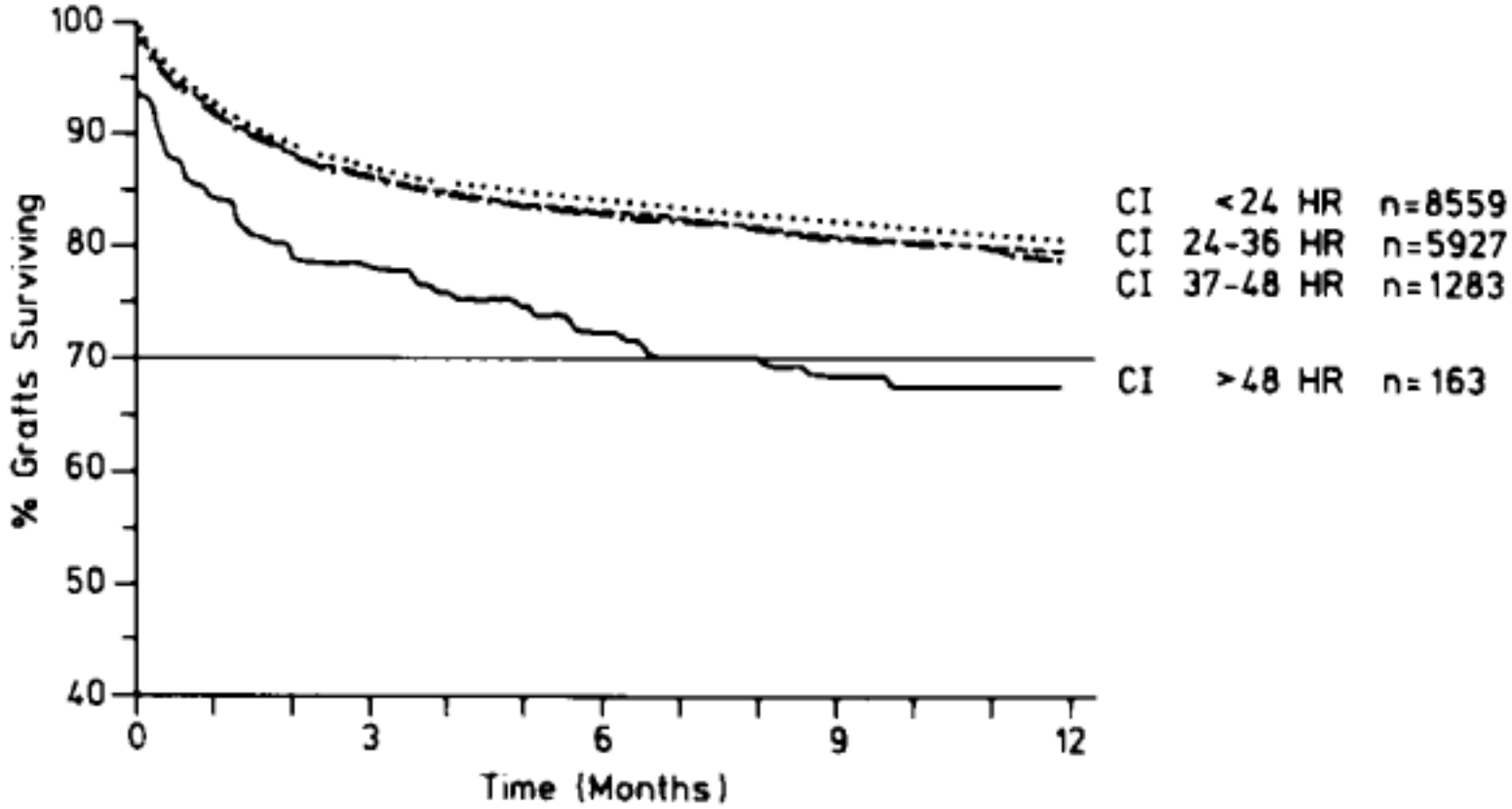


Figure 3. Influence of Period of Cold Ischemia for Kidney Preservation on Outcome of First Cadaver Transplants in Cyclosporine-Treated Patients.

Cold-ischemia time (CI) in hours is indicated for each curve. Kidneys with more than 48 hours had a significantly worse outcome than kidneys with 48 hours or less ($P<0.0001$).

- Early outcomes have steadily improved over the last 10 years, with risk-adjusted and death-censored, 1-year renal graft survival rates of 94% and 97% for deceased and living donor transplants, respectively.

Analyses of the short- and long-term graft survival after kidney transplantation in Europe between 1986 and 2015

see commentary on page 853

Maarten Coemans[1,2], Caner Süsal[3], Bernd Döhler[3], Dany Anglicheau[4], Magali Giral[5], Oriol Bestard[6], Christophe Legendre[4], Marie-Paule Emonds[1,7], Dirk Kuypers[1,8], Geert Molenberghs[2], Geert Verbeke[2] and Maarten Naesens[1,8]

[1]Department of Microbiology and Immunology, KU Leuven, University of Leuven, Leuven, Belgium; [2]Leuven Biostatistics and Statistical Bioinformatics Centre, Leuven, Belgium; [3]Institute of Immunology, University of Heidelberg, Heidelberg, Germany; [4]Service de Néphrologie-Transplantation Adulte, Hôpital Necker, Paris, Université Paris Descartes & INSERM U 1151, Hôpital Necker, Paris, France; [5]Centre de Recherche en Transplantation et Immunologie UMR1064, INSERM, Université de Nantes, Nantes, France; [6]Kidney Transplant Unit, Nephrology Department, Bellvitge University Hospital, Barcelona, Spain; [7]Histocompatibility and Immunogenetic Laboratory, Red Cross Flanders, Mechelen, Belgium; and [8]Department of Nephrology and Renal Transplantation, University Hospitals Leuven, Leuven, Belgium

The evolution of kidney allograft survival remains insufficiently studied in the context of the changing donor

Kidney International (2018) **94,** 964–973; https://doi.org/10.1016/j.kint.2018.05.018

Since European data are lacking a cohort study was performed (1986-2015) that, based on the Collaborative Transplant Study, included **108,787** recipients of brain-death kidney donors in 135 hospitals across 21 European countries (live donor and non heart beating excluded).

We noticed improvement from the first (1986–1995) to the second (1996–2005) decade, and to a somewhat lesser extent from the second to the last decade (2006–2015). The actual 1- and 5-year death-censored graft survival rates were, respectively, 86.8% and 74.6% in patients transplanted between 1986 and 1995, 91.1% and 82.5% in patients transplanted between 1996 and 2005, and 92.0% and 84.4% in patients transplanted between 2006 and 2015 (logrank test P < 0.001).

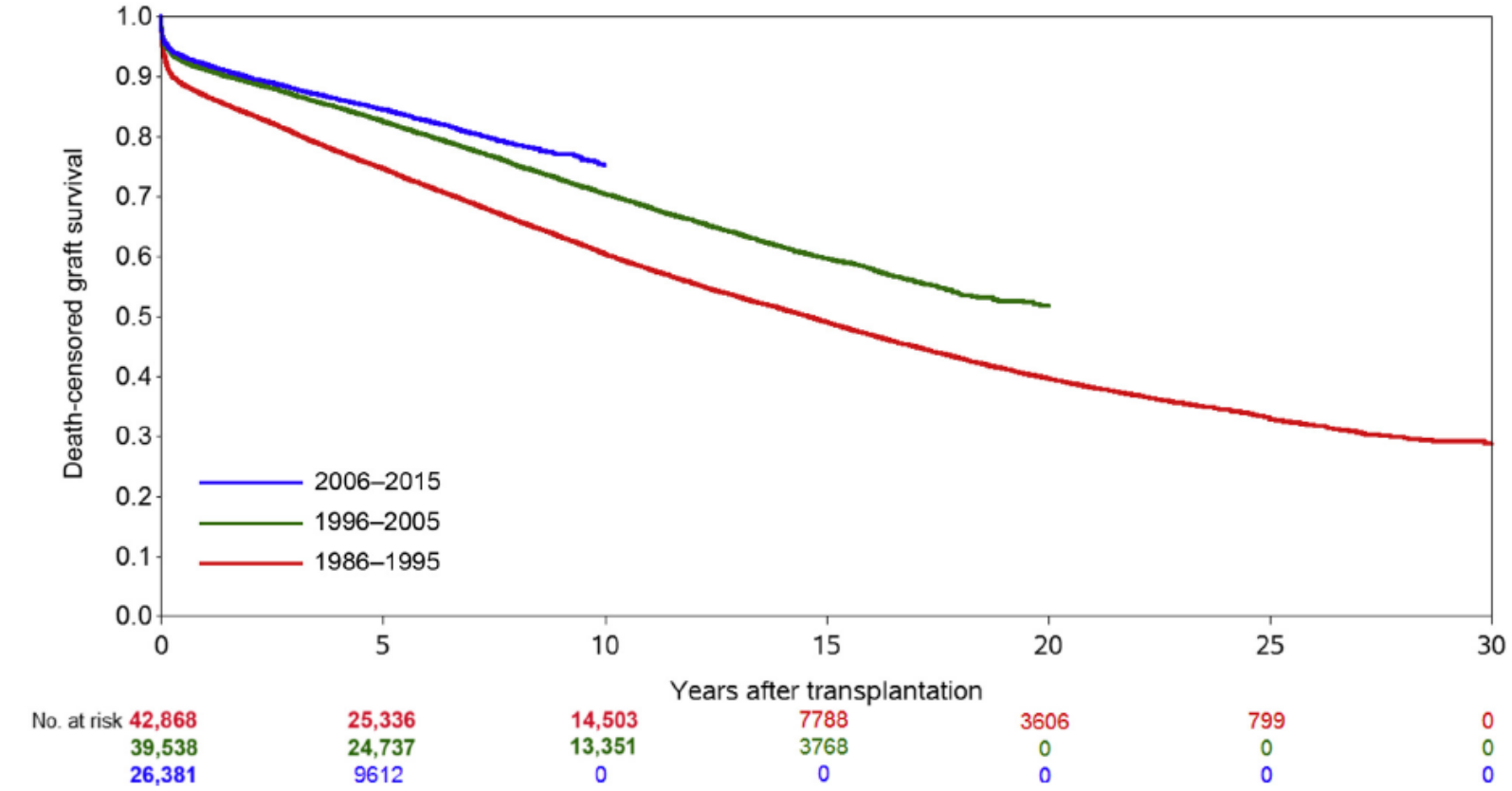
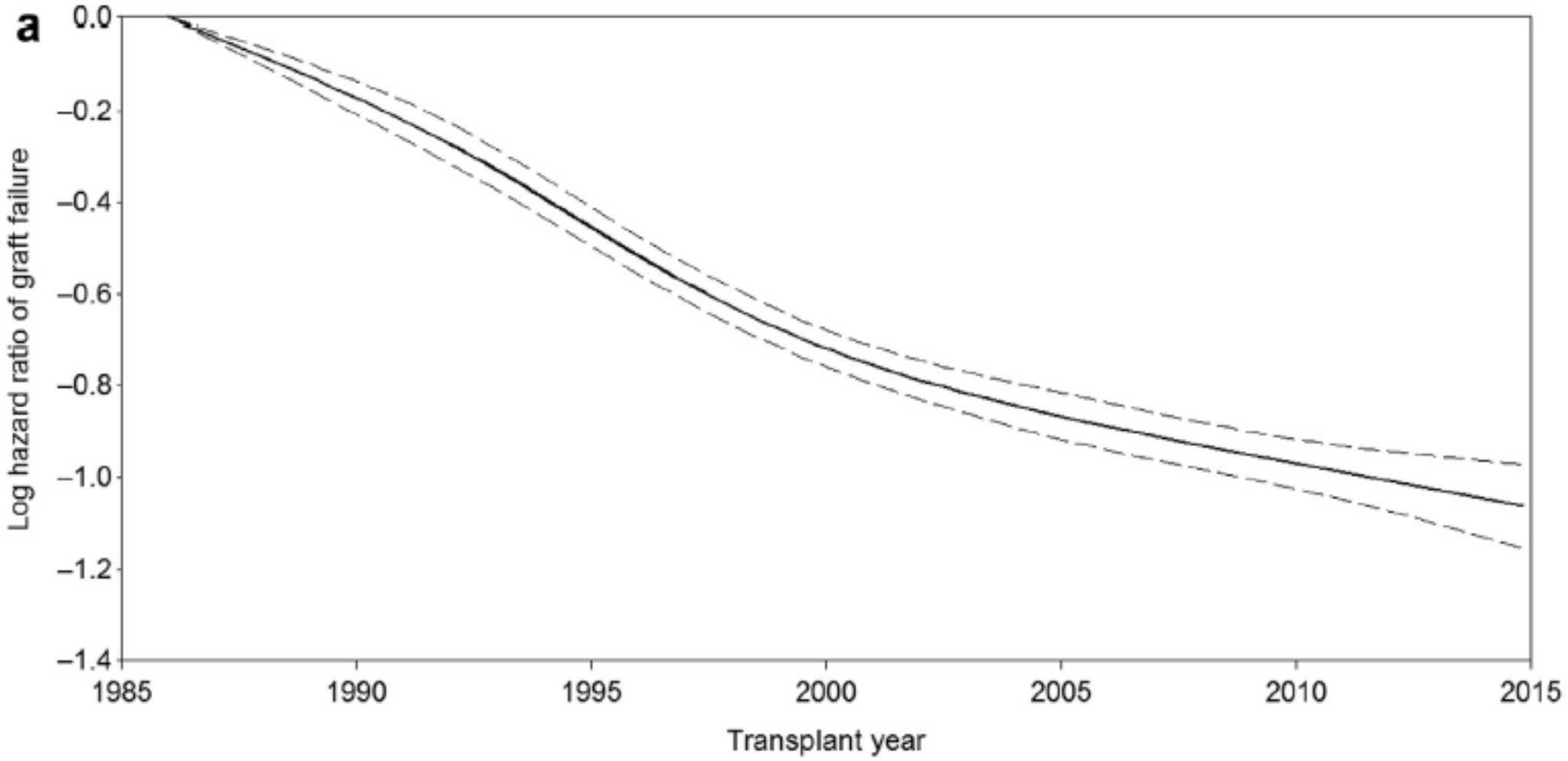
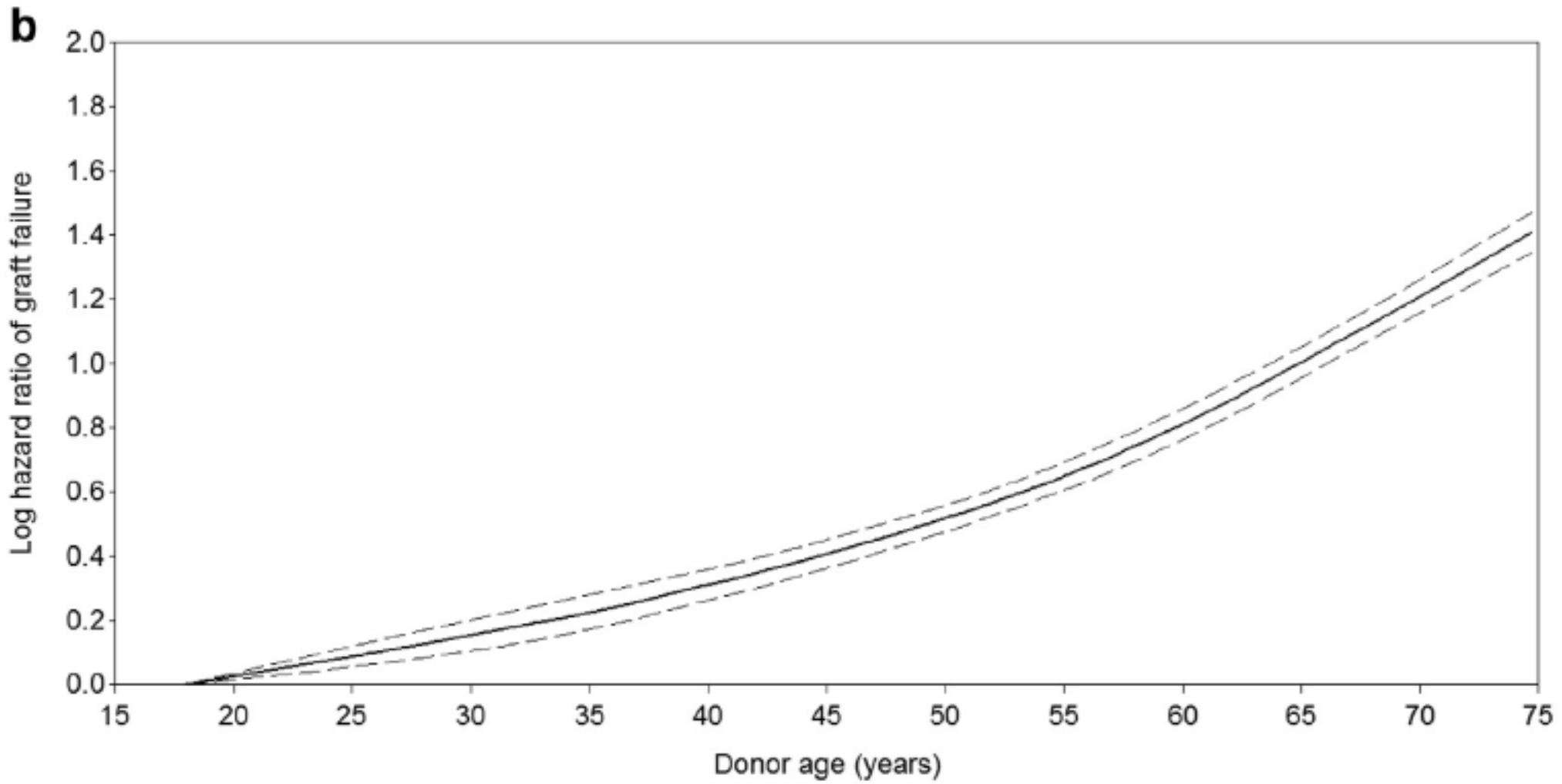
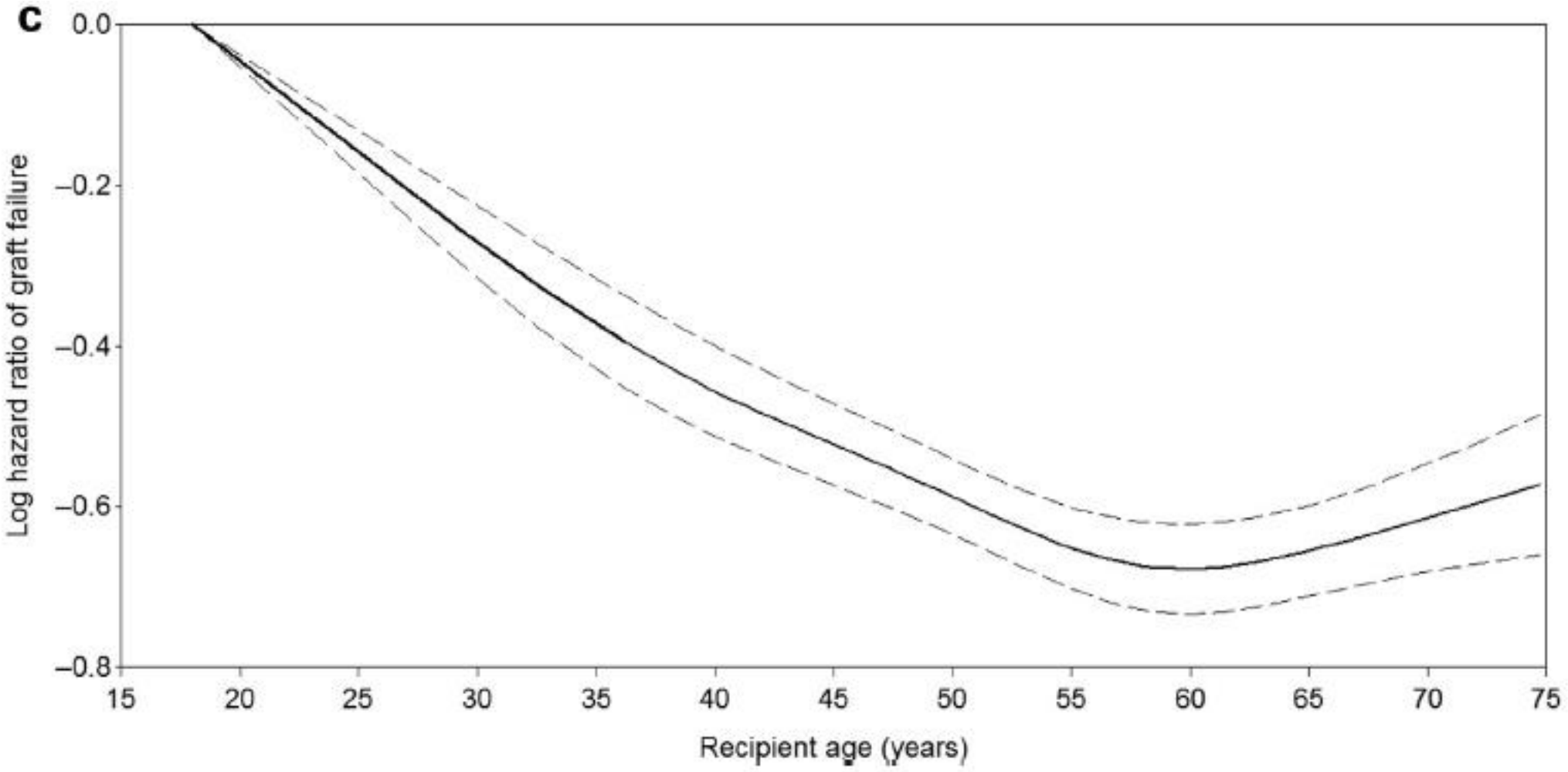


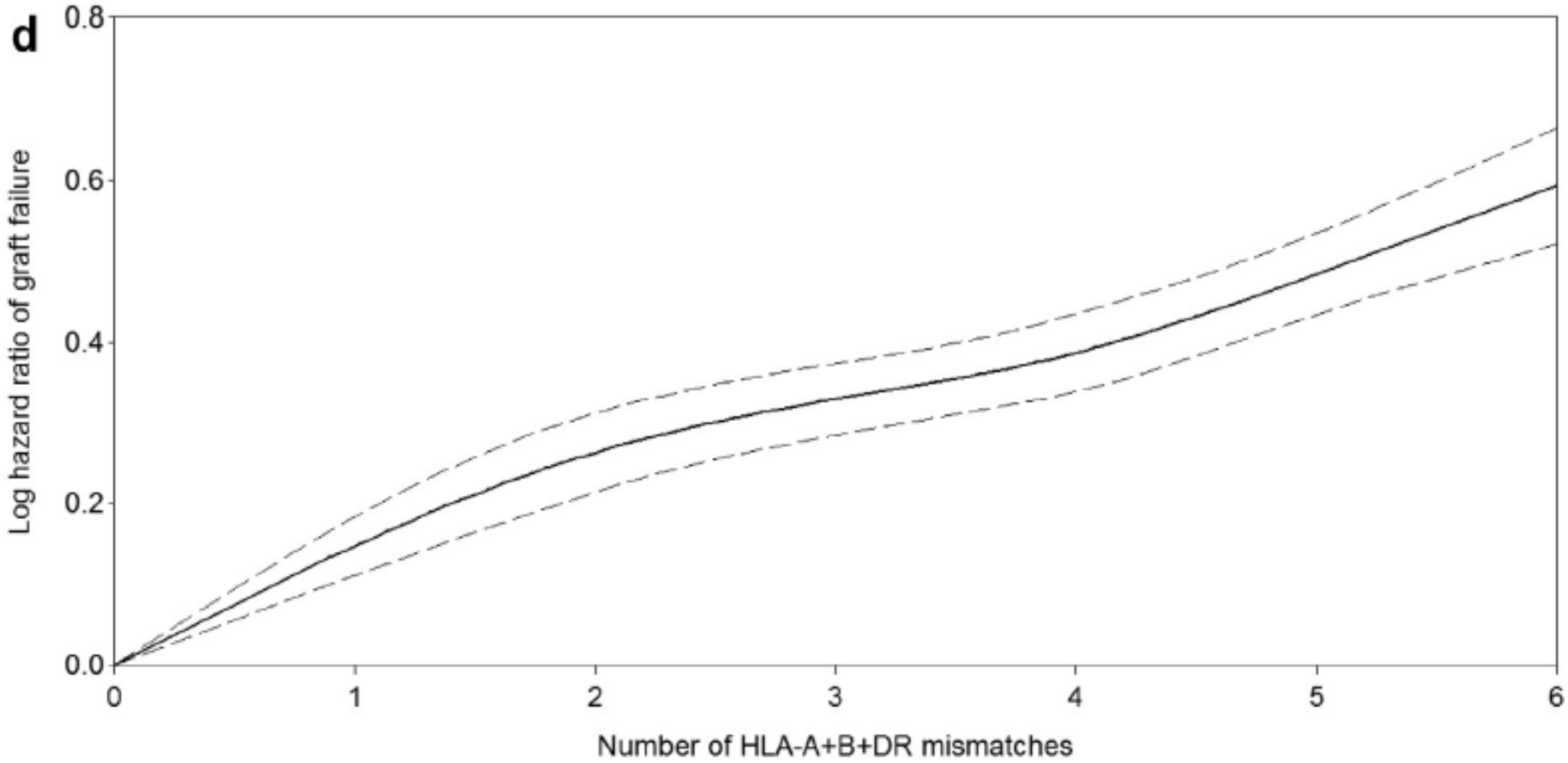
Figure 1 | Kaplan-Meier curve of kidney allograft survival (censored for recipient death), per decade of transplant year.

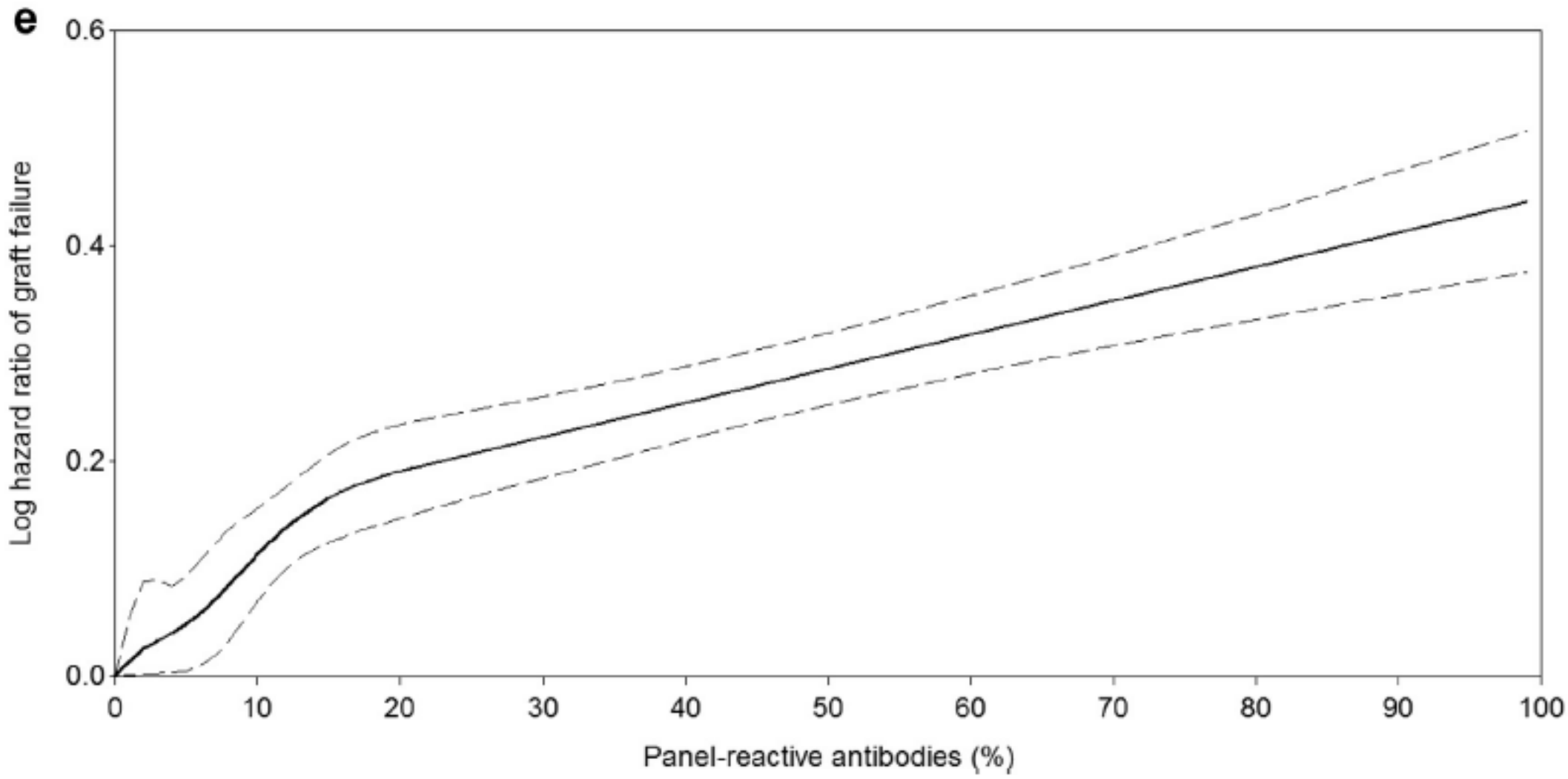
Coemans M. Kidney International 2018; 94:964–973


a
0.0
−0.2
−0.4
−0.6
−0.8
−1.0
−1.2
−1.4
Log hazard ratio of graft failure
1985
1990
1995
2000
2005
2010
2015
Transplant year


b
Log hazard ratio of graft failure
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
15
20
25
30
35
40
45
50
55
60
65
70
75
Donor age (years)


c
0.0
–0.2
–0.4
–0.6
–0.8
Log hazard ratio of graft failure
15
20
25
30
35
40
45
50
55
60
65
70
75
Recipient age (years)


d
0.8
0.6
0.4
0.2
0.0
Log hazard ratio of graft failure
0
1
2
3
4
5
6
Number of HLA-A+B+DR mismatches


e
0.6
0.4
0.2
0.0
Log hazard ratio of graft failure
0
10
20
30
40
50
60
70
80
90
100
Panel-reactive antibodies (%)

Why living-donor renal transplant yields better outcomes than cadaver renal transplant?

L. Guirado[1], E. Vela[2], M. Clèries[2], J. M. Díaz[1], C. Facundo[1] and R. García-Maset[1] and Catalonian Renal Patients Register (CRPR)[2]

[1]Kidney Transplant Unit. Fundación Puigvert. Barcelona. [2]Catalonian Renal Patients Register (CRPR). Servei Català de la Salut. Barcelona.

Nefrología 2008; 28 **(2)** 159-167

SUMMARY

Background: *According to literature, patient and graft survival is better in living donor renal transplants (LRT) than in cadaver renal transplants (CRT).*

Objective: *To study factors that determine the best results in LRT related to those of CRT, found in univariate studies.*

Patients and Methods: *Renal transplants (RT) done in Catalonia during the 1990-2004 period, performed in patients over 17 years (135 LRT and 3.831 CRT), have been analyzed (retransplants were not included). The data come from the Renal Patients Transplant Registry (RMRC). Student's t-test and χ^2 test were used to compare means and proportions, respectively. To analyze univariate and multivariate survival, actuarial method and Cox regression have been used, respectively. Estimated creatinine clearance has been studied and its data have been showed through Selwood modified Analysis.*

Results: *As it happens with other great RT patients series, the RMRC analysis, globally and without any adjustment, shows that patient and graft survival in LRT is better than that obtained with CRT. When we studied which variables explain these results, we found that main factors were smaller recipient age and the short time on dialysis. The great influence of both factors has been published in a large number of papers, explaining the differences obtained on the transplanted renal patient survival.*

Conclusions: *Once adjusted the analysis by the different factors that influence the survival of the patient and the graft, there are no differences in the obtained results, since the best outcomes of the TRV are due to factors like the smaller recipient age and the advanced TR.*

RESUMEN

Introducción: **Según la literatura hay una mejor supervivencia del paciente e injerto en los trasplantes renales (TR) realizados con órganos procedentes de donante vivo.**

Objetivos: **Estudiar los factores que determinan los mejores resultados en el trasplante de donante vivo (TRV) respecto al de donante cadáver (TRC), hallados en estudios univariados.**

Pacientes y métodos: **Se analizan los primeros TR realizados en Cataluña en el período 1990-2004 en mayores de 17 años (135 TRV y 3.831 TRC). Los datos proceden del Registro de enfermos renales de Cataluña (RMRC). Se ha utilizado la *t*-Student para la comparación de medias y el test de la χ^2 para la de proporciones. Para el análisis univariado de la supervivencia se ha utilizado el método actuarial y la regresión de Cox para el multivariado. Se ha estudiado la depuración estimada de la creatinina y sus datos se han representado con el análisis de Selwood modificado.**

Resultados: **Al igual que ocurre con las grandes series de trasplantados renales, el RMRC objetiva que, globalmente y sin ningún tipo de ajuste, el TRV presenta mejores resultados de supervivencia de paciente e injerto que el TRC. Cuando estudiamos los factores más relevantes para explicar estos resultados, obtenemos que los más determinantes son la menor edad del receptor y el menor tiempo en diálisis. Numerosas publicaciones han demostrado que ambos factores tienen una gran influencia sobre la supervivencia del paciente trasplantado renal, condicionando la diferencia en las supervivencias obtenidas.**

Conclusiones: Una vez ajustado el análisis por los diferen

Guirado L. Nefrolojia;2008; 28(20): 159-167

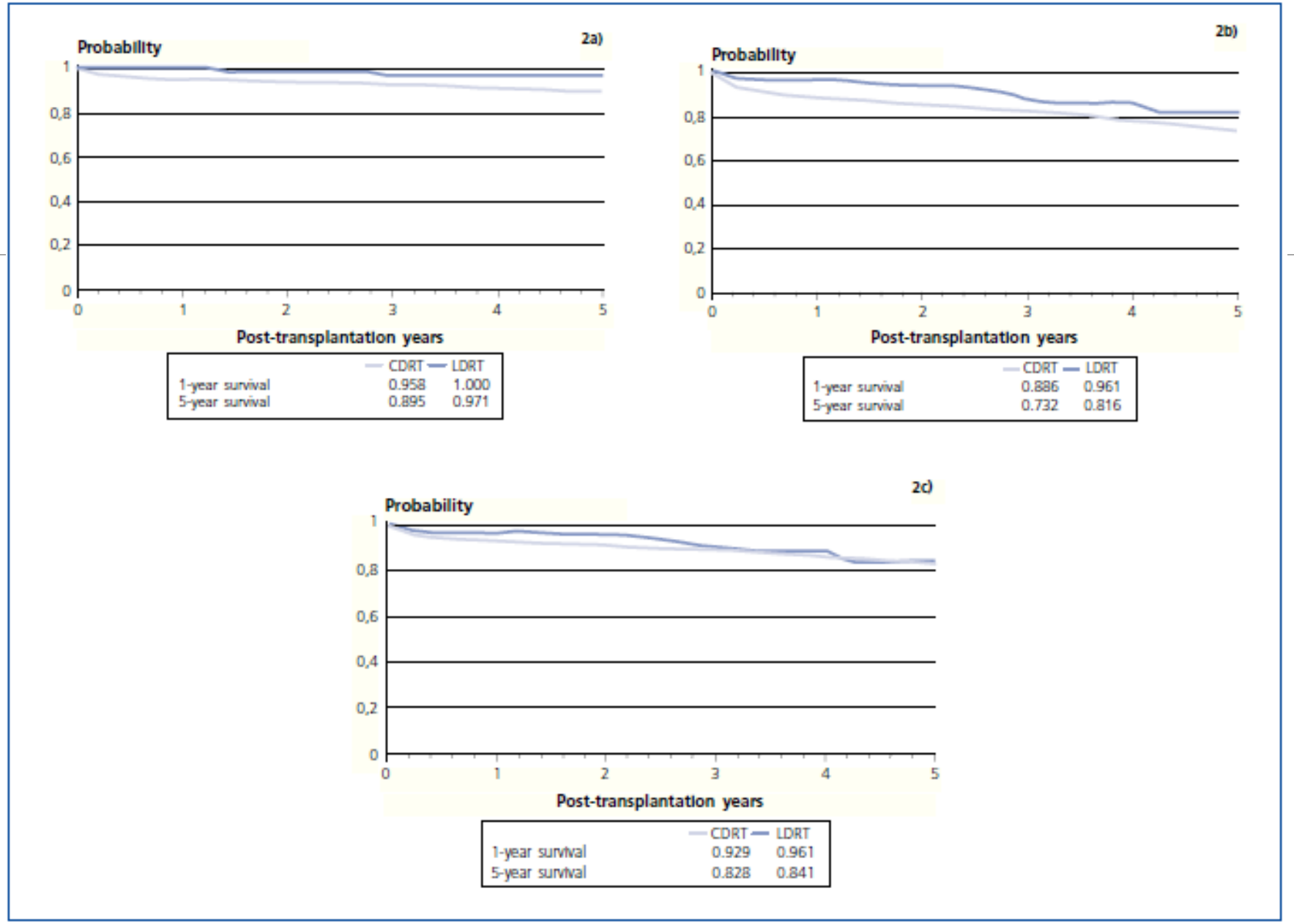


Figure 2. Actuarial survival analysis by type of transplant. Period 1990-2004: 2a) of the patient, 2b) of the graft, and 2c) of the graft with censored deaths.

Guirado L. Nefrolojia;2008; 28(20): 159-167

Table I. Demographics and characteristics of transplanted patients. Catalonia 1990-2004

	CDRT (n = 3,831) N	%	LDRT (n = 135) N	%	p	missing
Recipient's gender						
Males	2,385	62.3	89	65.9	0.4	0
Females	1,446	37.7	46	34.1		
Recipient's age						
Mean (years)	49.3 ± 13.6		37.9 ± 13.7		< 0.0001	0
18-44 years	1,294	33.8	92	68.1	< 0.00001	
45-64 years	2,038	53.2	38	28.1		
65-74 years	479	12.5	5	3.7		
> 74 years	20	0.5	0	0		
Primary kidney disease						
Standard	3,052	79.8	108	80.0	0.4	0
Diabetes	176	4.6	9	6.7		
Other	603	15.7	18	13.3		
Associated pathologies (personal history)						
Coronary heart disease	250	6.5	4	3.0	0.097	0
Cardiomyopathy	444	11.6	6	4.4	0.01	0
Disorder of heart conduction	203	5.3	1	0.7	0.02	0
COPD	256	6.7	2	1.5	0.02	0
Joint disease	625	16.3	9	6.7	0.003	0
Esophagus, stomach or duodenum disease	414	10.8	4	3.0	0.004	0

Guirado L. Nefrolojia;2008; 28(20): 159-167

	CDRT (n = 3,831) N	%	LDRT (n = 135) N	%	p	missing
Previous time on dialysis						
Mean (months)	37.0 ± 34.8		18.7 ± 33.1		< 0.0001	88 (2.2%)
0-6 months	223	5.9	60	46.5	< 0.0001	
7-24 months	1,502	40.1	39	30.2		
25-60 months	1,404	37.4	22	17.1		
> 60 months	620	16.5	8	6.2		
Period						
1990-1997	1,938	50.6	36	26.7	< 0.0001	0
1997-2004	1,893	49.4	99	73.3		
Maximum PRA						
0-10%	3,128	81.9	107	89.2	0.08	29 (0.7%)
11-50%	522	13.7	8	6.7		
51-100%	167	4.4	5	4.2		
Last PRA						
0-10%	3,621	94.8	113	95.0	0.3	28 (0.7%)
11-50%	174	4.6	4	3.4		
51-100%	24	0.6	2	1.7		
Number of HLA identities (mean)						
HLA-A	0.67 ± 0.60		1.01 ± 0.24		< 0.0001	28 (0.7%)
HLA-B	0.58 ± 0.58		1.00 ± 0.34		< 0.0001	28 (0.7%)
HLA-DR	1.05 ± 0.57		1.00 ± 0.32		0.4	27 (0.7%)
Time of cold ischemia (hours)	19.2 ± 6.42		1.81 ± 3.4		< 0.00001	713 (18.0%)
Donor's age						
Mean (years)	44.8 ± 18.0		50.3 ± 11.1		0.001	45 (1.1%)
0-49	2,065	54.4	56	42.7	< 0.0001	
50-59	832	22.0	49	37.4		
60-69	599	15.8	23	17.6		
> 69	294	7.8	3	2.3		
Donor's gender						
Male	2,403	63.3	43	32.6	< 0.00001	40 (1.0%)
Female	1,391	36.7	89	67.4		

Guirado L. Nefrolojia;2008; 28(20): 159-167

Time on dialysis before Tx

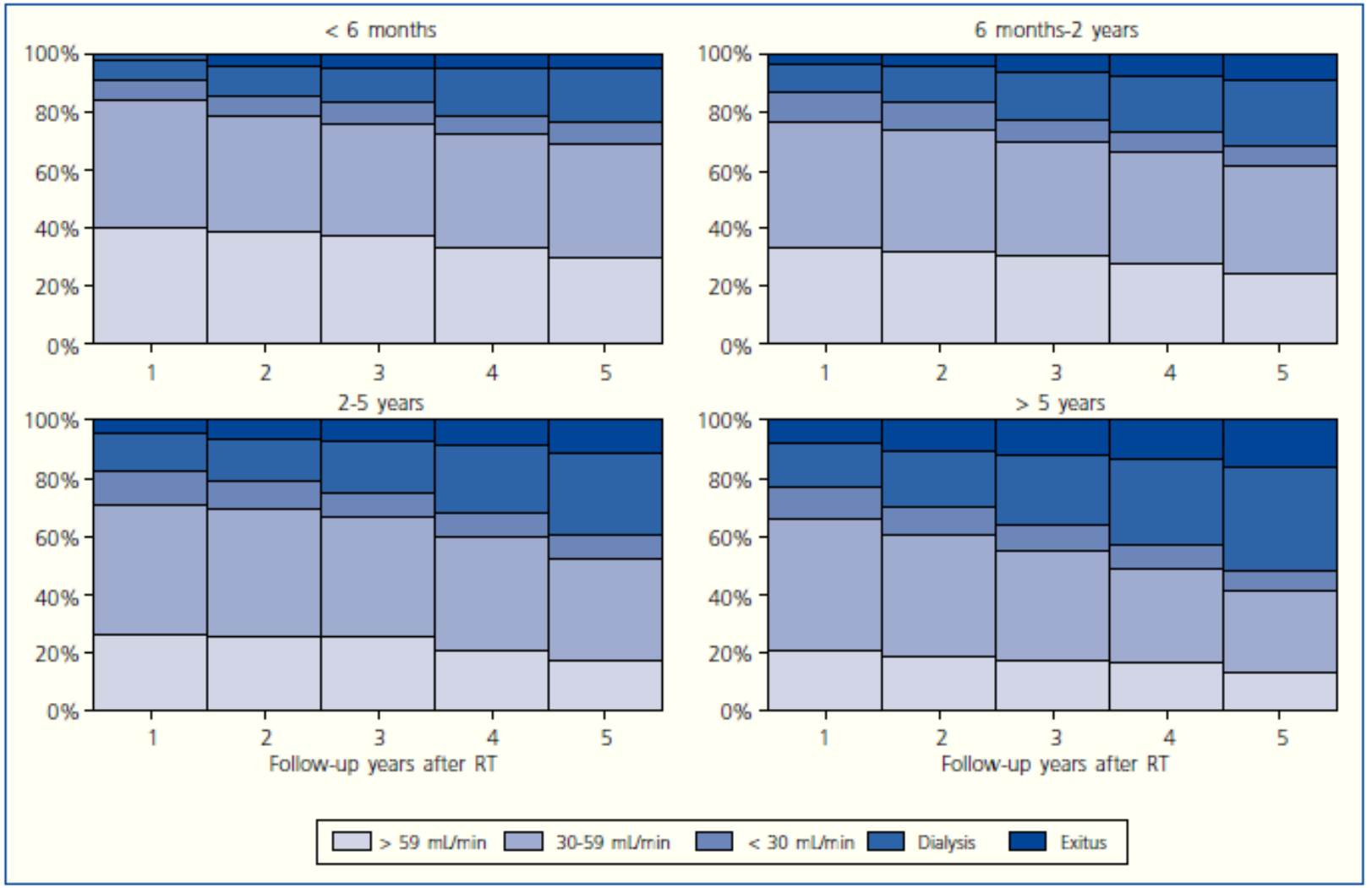


Figure 4. Estimation of glomerular filtration rate, patient's and graft's survival from the time of transplant, by previous time on dialysis. Period 1990-2004.

Guirado L. Nefrolojia;2008; 28(20): 159-167

They concluded that

- Globally and without any kind of adjustment, the living-donor renal transplant presents better survival outcomes for the patient and the graft than cadaver donor transplant.
- When studying the most relevant factors explaining the better results with LDRT, we obtained that the most determinant ones are the lower recipient's age and the lower time on dialysis.
- Both factors have shown in many publications to have a big influence on the survival of kidney transplant patients, conditioning the difference in the survival rates obtained.

ELSEVIER

Living Donor Kidney Transplantation in Catalonia: Comparison With Cadaveric Kidney Donors

R. Solà, E. Vela, M. Cleries, L.I. Guirado, J.M. Díaz, C. Facundo, and R. Deulofeu

ABSTRACT

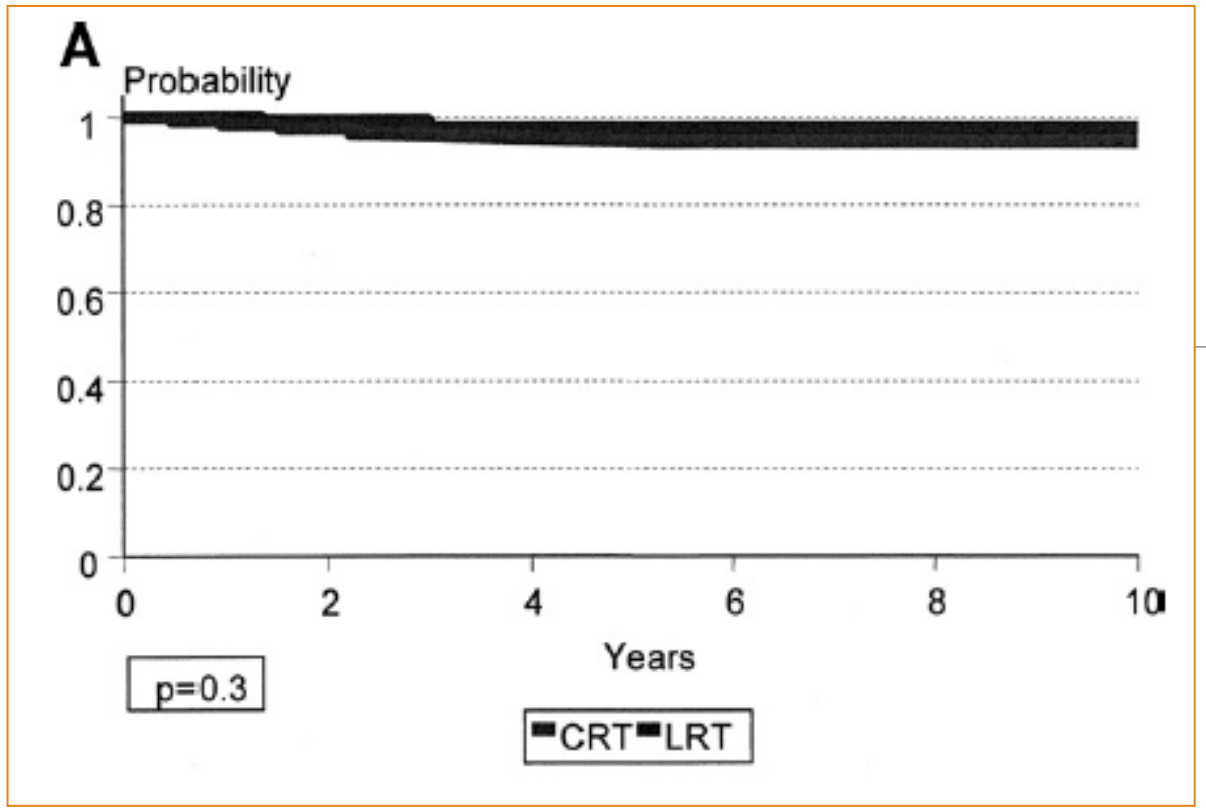
Introduction. We studied the renal transplantation results of living donor compared with cadaveric donor kidney transplantations.

Patients and Methods. One hundred thirty-six living donor transplantations performed during the period of 1990 to 2003 (group 1) were compared with a control group of 4304 cadaveric donor transplantations (group 2), paired 1:1 with group 1 patients, according to the period of transplantation, the primary renal disease, the transplant number, as well as the recipient and donor ages.

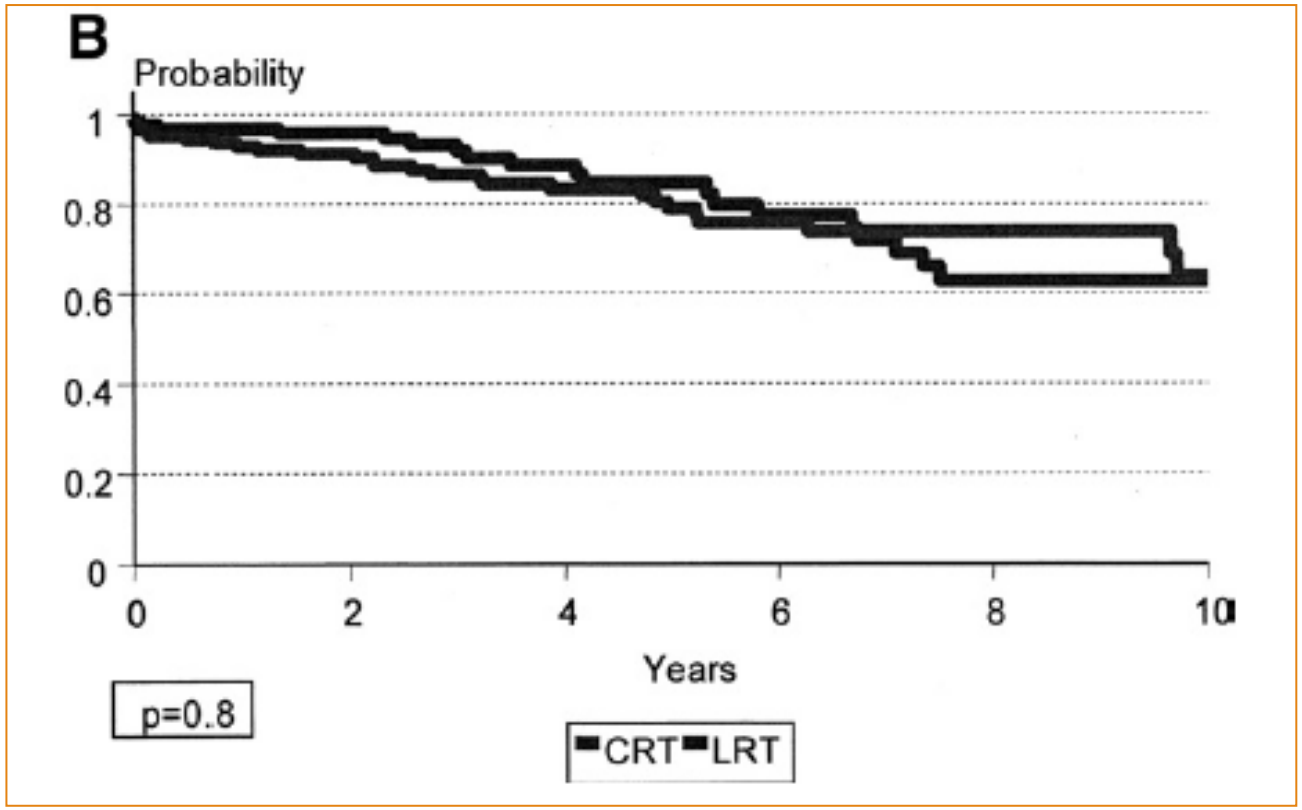
Results. There were no differences regarding patient or graft survival during a 10-year follow-up.

Conclusions. The benefit of performing living donor kidney transplantations is the possibility of having the donor available even before beginning dialysis treatment.

Transplantation Proceedings, 39, 2208–2209 (2007)



A) Patient survival according to type of transplantation.



(B) Graft survival according to type of transplantation.

They concluded that

- Knowing that prior renal replacement treatment influences transplantation results the only benefit of performing a transplantation from a living donor is the possibility of performing the procedure before treatment with dialysis.

Living Donation Has a Greater Impact on Renal Allograft Survival Than HLA Matching in Pediatric Renal Transplant Recipients

Matko Marlais, MRCPCH,[1] Alex Hudson, MSc,[2] Laura Pankhurst, MSc,[2] Susan V. Fuggle, D.Phil.,[2,3] and Stephen D. Marks, MD[1,4]

Background. Living donor (LD) kidney transplantation accounts for around half of all pediatric renal transplant recipients and results in improved renal allograft survival. The aim of this study was to determine the effect of HLA matching on deceased and LD renal allograft outcomes in pediatric recipients. **Methods.** Data were obtained from the UK Transplant Registry held by NHS Blood and Transplant on all children who received a donation after brain death (DBD) or LD kidney-only transplant between 2000 and 2011. HLA-A, HLA-B and HLA-DR mismatches were categorized into 4 levels and 2 groups. Data were fully anonymized. **Results.** One thousand three hundred seventy-eight pediatric renal transplant recipients were analyzed; 804 (58%) received a DBD donor kidney, 574 (42%) received an LD kidney. Five-year renal allograft survival was superior for children receiving a poorly HLA-matched LD kidney transplant (88%, 95% confidence interval [95% CI], 84-91%) compared with children receiving a well HLA-matched DBD kidney transplant (83%, 95% CI, 80-86%, log rank test $P = 0.03$). Five-year renal allograft survival was superior for children receiving an LD kidney with 1 or 2 HLA-DR mismatches (88%, 95% CI, 84-91%) compared with children receiving a DBD kidney with 0 HLA-DR mismatches (83%, 95% CI, 80-86%, log rank test $P = 0.03$). **Conclusions.** In children, poorly HLA-matched LD renal transplant outcomes are not inferior when compared with well HLA-matched DBD renal transplants. It is difficult to justify preferentially waiting for an improved HLA-matched DBD kidney when a poorer HLA-matched LD kidney transplant is available.

(*Transplantation* 2016;00: 00–00)

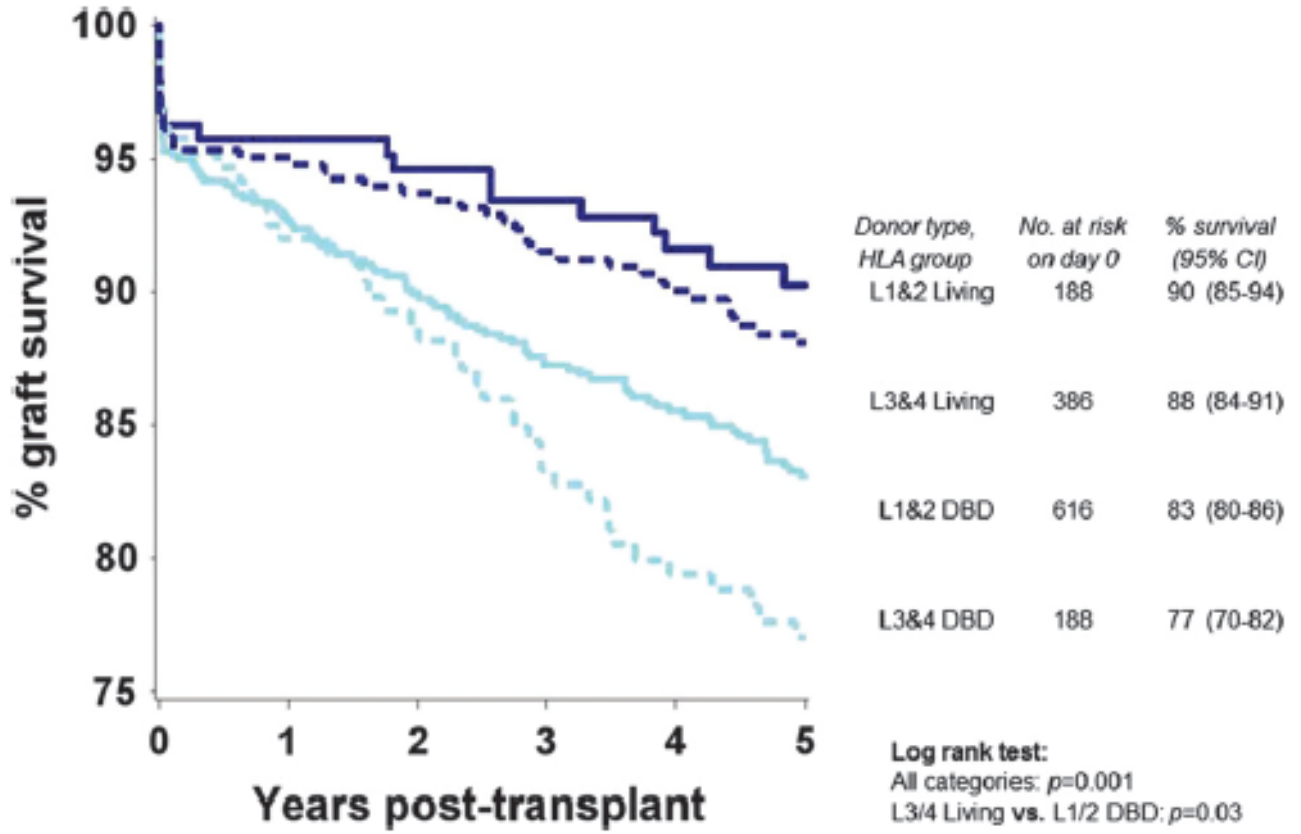


FIGURE 1. Kaplan-Meier curve showing 5-year renal allograft survival, by donor type and HLA group. L = HLA match level (levels correspond to HLA match level in Table 1).

Marlais M. Transplantation. 2016 100:2717-2722

TABLE 1.

HLA match groups and levels used in the analysis

HLA match group	HLA match level	HLA mismatch	HLA mismatch combinations
Good	Level 1	000	000
Good	Level 2	(0 HLA-DR and 0/1 HLA-B)	100, 010, 110, 200, 210
Poor	Level 3	(0 HLA-DR and 2 HLA-B] or [1 HLA-DR and 0/1 HLA-B)	020, 120, 220, 001, 101, 201, 011, 111, 211
Poor	Level 4	(1 HLA-DR and 2 HLA-B) or (2 HLA-DR)	021, 121, 221, 002, 102, 202, 012, 112, 212, 022, 122, 222

They concluded that

- In children, poorly HLA-matched LD renal transplant outcomes are not inferior when compared with well HLA-matched DBD renal transplants.
- It is difficult to justify preferentially waiting for an improved HLA-matched DBD kidney when a poorer HLA-matched LD kidney transplant is available.

HLA Matching in Pediatric Kidney Transplantation: HLA Poorly Matched Living Donor Transplants Versus HLA Well-Matched Deceased Donor Transplants

Gerhard Opelz, MD,[1] Bernd Döhler, PhD,[1] Derek Middleton, PhD,[2] and Caner Süsal, MD[1]
A Collaborative Transplant Study Report

Background. Based on an analysis of 542 pediatric kidney transplants recorded by the UK Transplant Registry from 2000 to 2012, it was concluded that the survival rate of HLA poorly matched living donor transplants is not inferior to that of HLA well-matched deceased donor transplants. **Methods.** We analyzed the impact of HLA matching on kidney graft survival in 3627 pediatric living donor transplants performed during 2000 to 2015 using the data of the Collaborative Transplant Study. The impact of HLA mismatches on graft survival was analyzed and survival rates of transplants from poorly matched living donors were compared with those from well-matched deceased donors. Multivariate Cox regression analysis was used to account for the influence of confounders. **Results.** HLA matching had a statistically significant impact on graft survival of pediatric kidney transplants ($P < 0.001$). Ten-year graft survival of pediatric transplants from living donors with 4 to 6 HLA-A+B+DR mismatches was significantly worse than that of transplants from well-matched deceased donors with 0 to 1 HLA mismatch (log rank, $P = 0.006$). **Conclusions.** In pediatric kidney transplantation, graft survival of kidneys from deceased donors with 0 to 1 HLA mismatches compares favorably with that of grafts from living donors with 4 to 6 HLA mismatches. If possible, living donor pediatric kidney transplants should be performed from donors with fewer than 4 HLA-A+B+DR mismatches.

(*Transplantation* 2017;101: 2789–2792)

Oplez G. Transplantation. 2017;101:2789-2792.

The important question whether HLA poorly matched living donor transplants do as well as HLA well matched grafts from deceased donors was analyzed

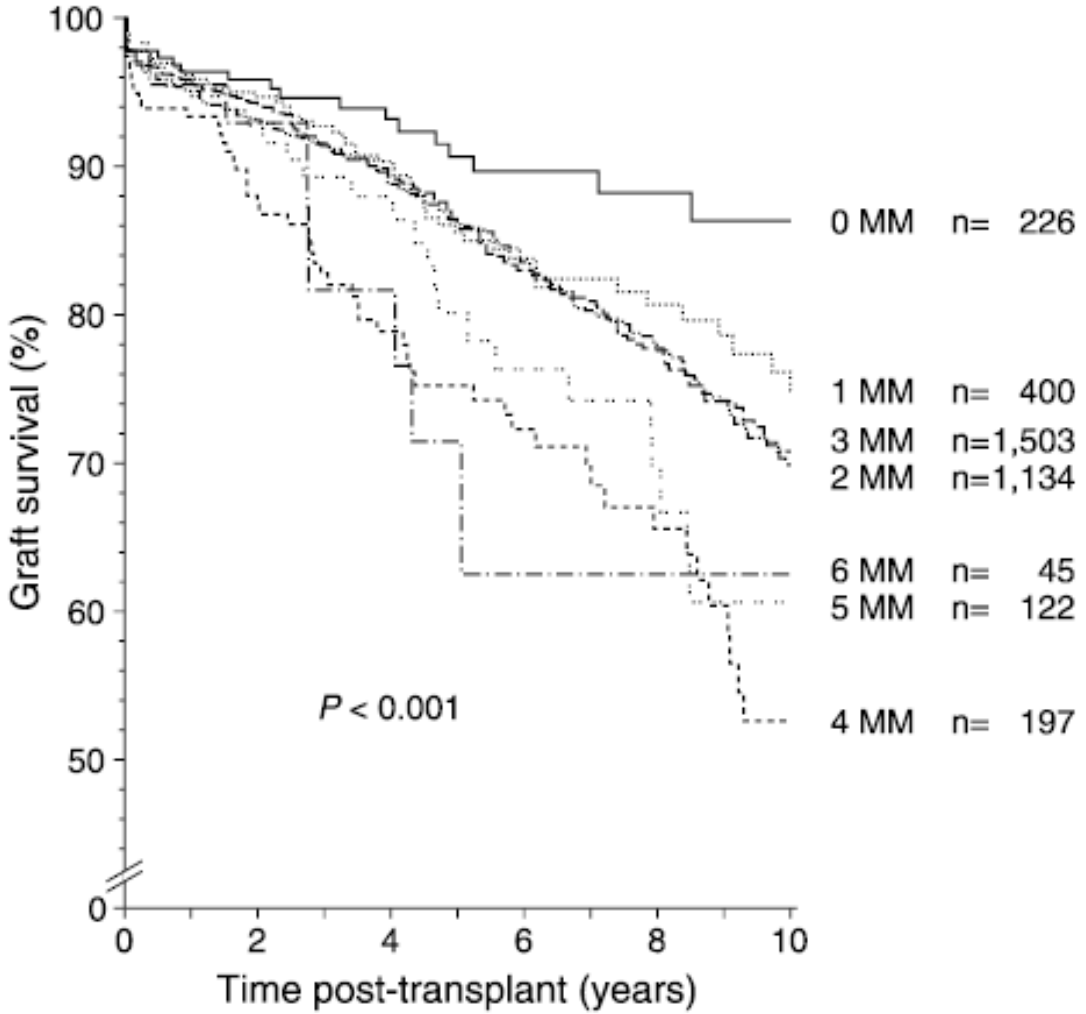


FIGURE 1. Influence of HLA-A+B+DR matching on graft survival of first pediatric kidney transplants from LDs performed 2000 to 2015 (log rank *P* value with trend). Sum of HLA-A, -B, -DR MMs between donor and recipient were added for analysis.

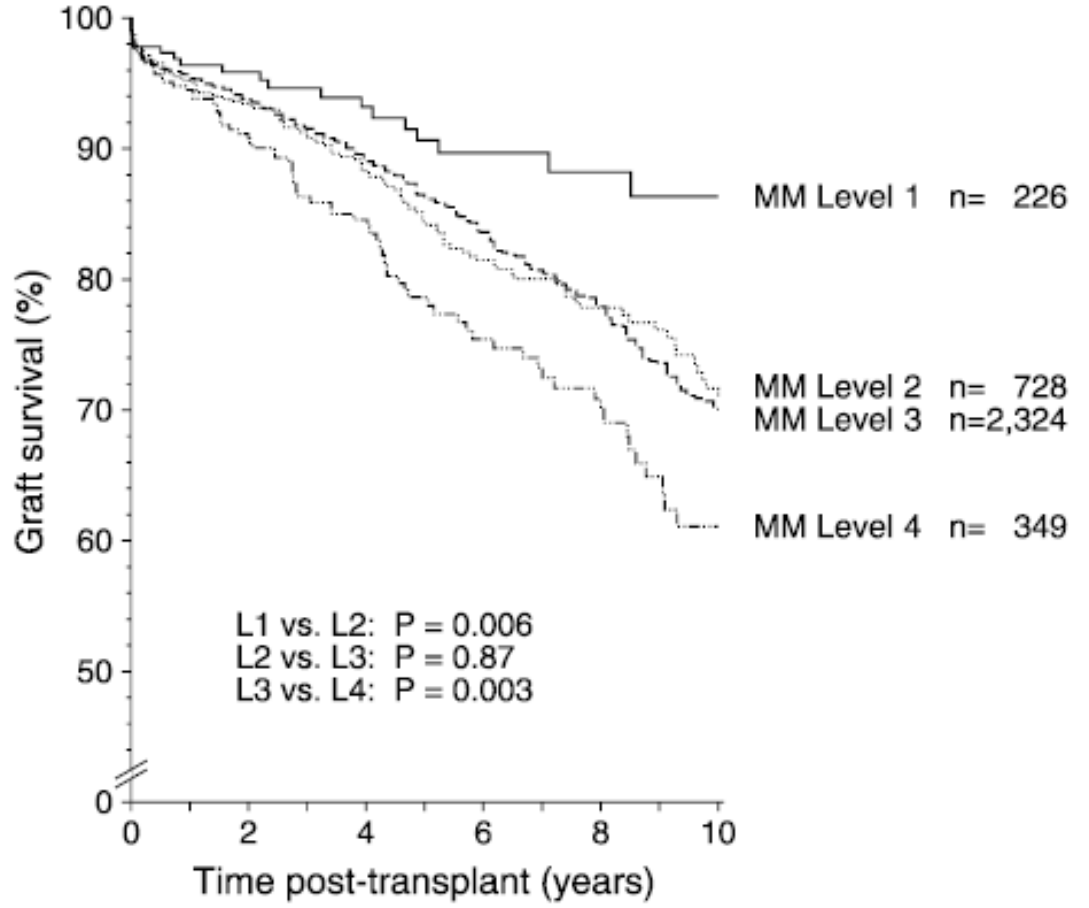


FIGURE 2. Influence of HLA-A, -B, -DR matching level on graft survival of first pediatric kidney transplants from LDs performed 2000 to 2015 (log rank *P* value with trend). Definition of MM levels per references 2 and 3: level 1, 0 MMs at all 3 HLA loci considered (HLA-DR, -A, -B). Level 2, 0 HLA-DR and 0 or 1 HLA-B MM. Level 3: 0 HLA-DR and 2 HLA-B, or 1 HLA-DR and 0 or 1 HLA-B. Level 4: 1 HLA-DR and 2 HLA-B, or 2 HLA-DR MMs.

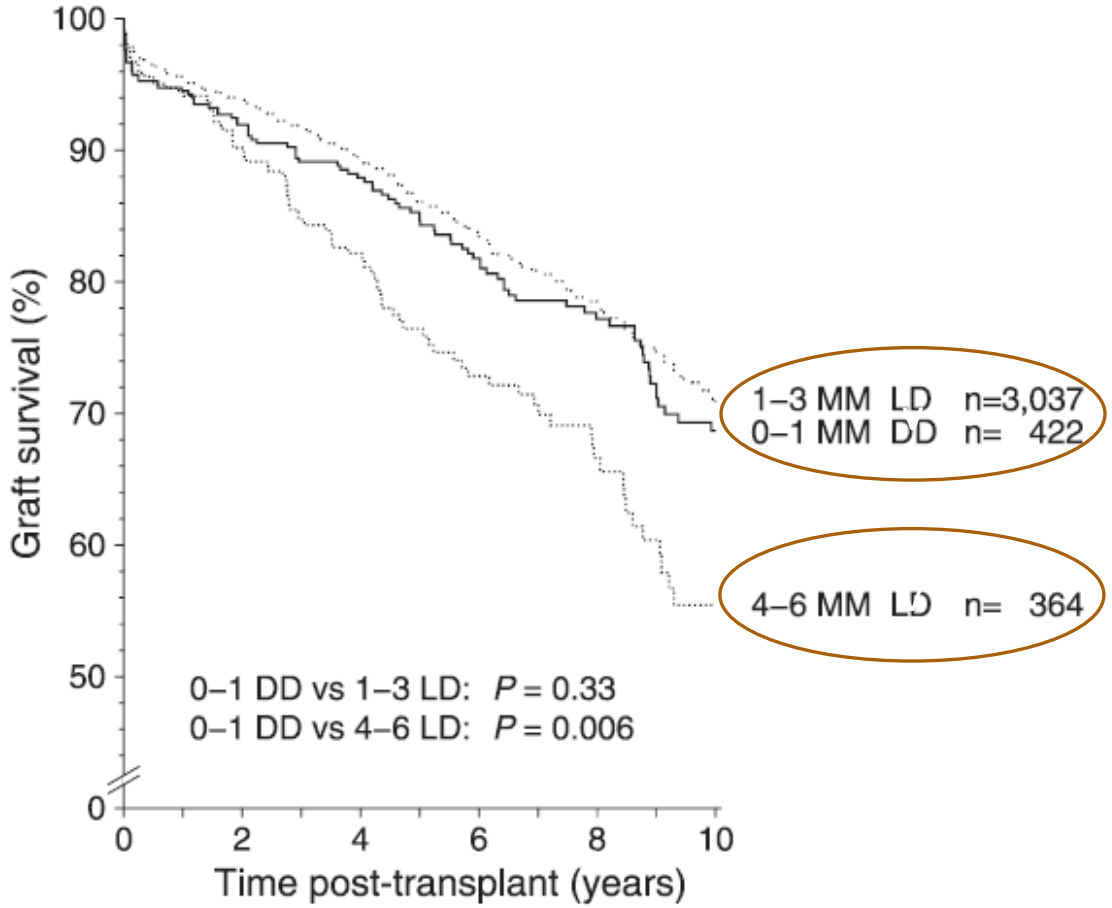
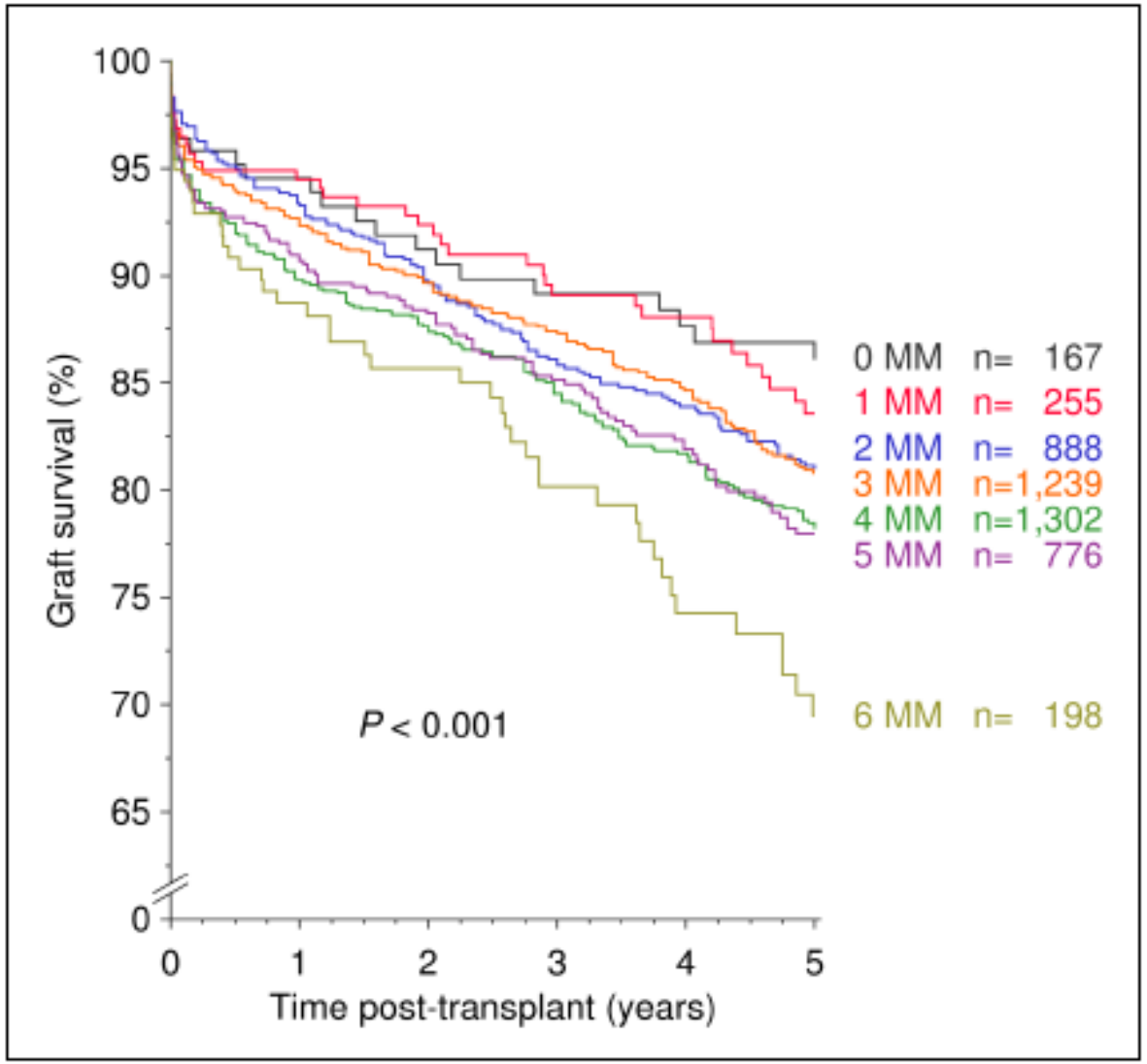


FIGURE 3. Graft survival of first pediatric kidney transplants. Comparison of well-matched DD grafts (0-1 MM DD) with good (1-3 MM LD) and poorly (4-6 MM LD) matched LD grafts. *P* values for log rank test of Kaplan-Meier analysis.

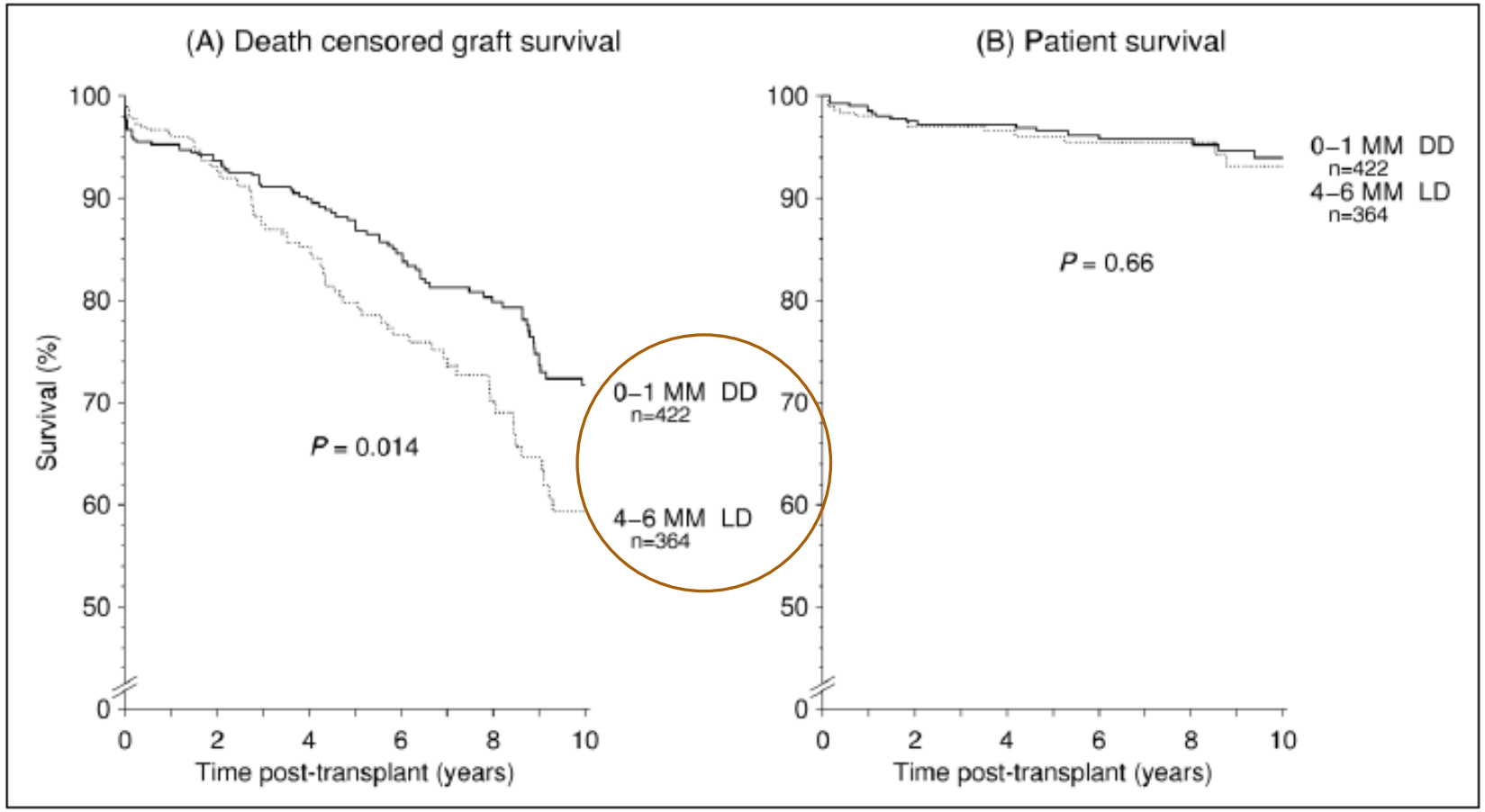
Of the 364 LD transplants with 4 to 6 HLA MMs, 149 were from blood-related donors, whereas 215 were from blood-unrelated donors

Figure S1. Influence of HLA-A+B+DR matching on graft survival of first pediatric kidney transplants from deceased donors performed 2000–2015 (log rank P value with trend)



Oplez G. Transplantation. 2017;101:2789-2792.

Figure S2. 10-year death censored graft survival (A) and patient survival (B) of first pediatric kidney transplants. Comparison of well-matched deceased donor grafts (0–1 MM DD) with poorly (4–6 MM LD) matched living donor grafts. P values for log rank test of Kaplan-Meier analysis.



Oplez G. Transplantation. 2017;101:2789-2792.

Analysis of the data contained in the CTS database yielded results that disagreed with the conclusion reached by Marlais et al.

- We found a strong and statistically significant impact of HLA-A+B+DR MMs on the survival of pediatric transplants from LDs and, furthermore, a significantly better transplant outcome with kidneys from DDs with 0 to 1 HLA MMs as compared to transplants from LDs with 4 to 6 MMs.

LD transplants with more than 3 HLA-A + B + DR MMs should be performed only under certain circumstances, for example, when the potential recipient possesses such a rare HLA phenotype that the likelihood of finding a well-matched (0-1 HLA MM) DD kidney is so small that the relatively low survival rate of a poor LD match is deemed acceptable.

Economic burden of deceased and living Tx on the community and recipients

Included all costs (outpatient care, diagnostic imaging, inpatient care, physician claims, laboratory tests and transplant medications) for 2 years after transplant for recipients and transplant-related costs prior to transplant (donor workup and management)

- Recipients of a deceased donor had a mean of 0.35 living donors evaluated, whereas recipients of a living donor had a mean of 1.8 donors evaluated.
- Excluding the cost of transplant surgery, the mean **workup cost for living donors** (including both potential and actual living donors) was $2261 and $209 for recipients who ultimately received a kidney from a living or deceased donor, respectively

Barnieh L. AJT. 2011; 11: 478–488

- For **living donors** proceeding to surgery, the mean cost of care for the donor, including physician and surgery costs, was **$18 129.**
- The mean cost of care for **deceased donors** was **$36 989**, and 95 (96.0%) had two kidneys recovered and transplanted.
- If the cost of care of the deceased donor was shared over four organs [the average number of organs recovered nationally]**, the total cost of transplantation for recipients of a deceased donor would decrease to $112 752.**
- Deceased donor kidney transplantation would then be significantly less expensive than living donation ($p = 0.03$).

- If comparing the cost of managing transplant eligible ESRD patients with a living donor transplant option, and transplant eligible ESRD patients who must wait on the deceased donor transplant wait list, while assuming an annual cost of dialysis of $73 618.82 (see Appendix A for details), the mean cost from the time of dialysis initiation to the end of the second year of follow-up posttransplant for recipients of living and deceased donor kidneys would increase to $189 412 and $306 216, respectively ($p = 0.0000$).

The concluded

- **Over a 2-year period, the cost of kidney transplantation did not differ for recipients of living and deceased donor transplant.**
- The results of this study can inform health care programs how best to allocate finite resources for funding strategies and initiatives to increase kidney donation rates.

Patients included adult recipients of a first kidney-only transplant between April 1, 1998, and March 31, 2006, as well as theirdonor information.

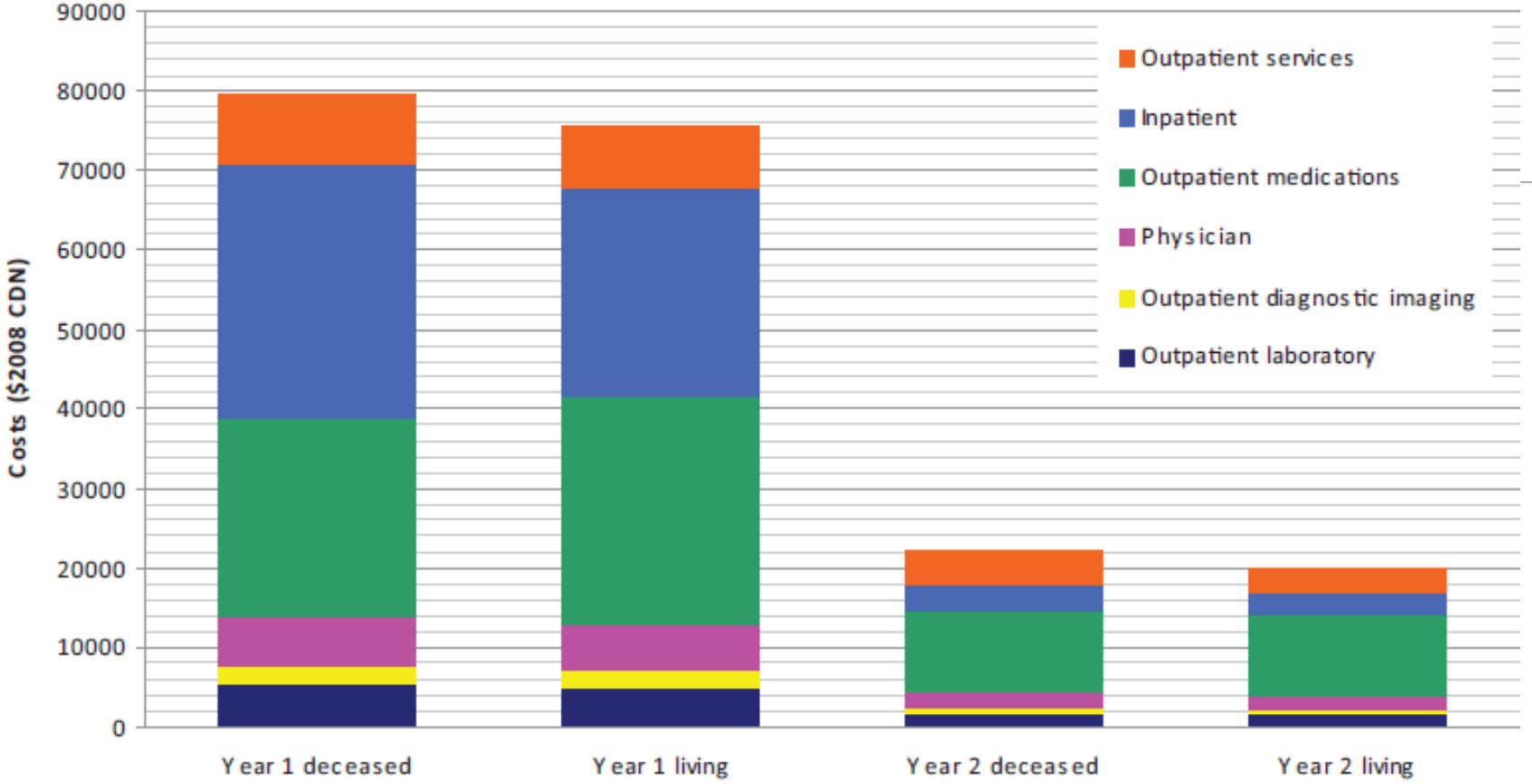


Figure 1: Mean recipient costs by type of resource utilization, time period and transplant type (2008 $CDN).

Recipient costs: There was no difference in the mean cost, including donor costs, for recipients of living and deceased donors ($118 347 and $121 121, respectively, p = 0.7) (Table 3). Excluding donor costs, there was still no difference in the mean cost for recipients of living and deceased donors (p = 0.5).

The differences with our country

- Donors are paid here (increases the costs)
- Donors are not followed here (In short-term reduces the costs). In long term?
- We have a cadaveric and love donor waiting list of about 1 year so approximately the same amount of waiting on dialysis for both types of donors

Influences of living and deceased donors on the recipient Immunology

Kidney International, Vol. 56 (1999), pp. 1551–1559

Cadaver versus living donor kidneys: Impact of donor factors on antigen induction before transplantation

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Cadaver versus living donor kidneys: Impact of donor factors on antigen induction before transplantation.

Background. It is widely recognized that living-related donor (LRD) renal allografts have a higher overall graft survival than cadaver donor transplants. We tested the hypothesis that part of this is attributable to LRD kidneys being obtained under optimal conditions from healthy donors, whereas cadaveric kidneys may have experienced injury as a result of inflammatory events around the time of brain death.

Methods. We have performed a comparative immunohistochemical analysis of pretransplant donor biopsies from cadaveric ($N = 65$) and LRD ($N = 29$) kidneys to determine any differences that may predispose them to subsequent damage.

uals who are genetically related to the recipient, whereas cadaver donor kidneys may undergo abnormal physiological changes associated with brain death, may experience prolonged cold storage times, and may be transplanted into unrelated recipients. In living-unrelated donor (LURD) transplantation, the immunological barriers are similar to those encountered with cadaveric allografts, but the clinical outcome of LURD allografts is significantly better than that of cadaveric transplantation and similar to one haplotype disparate LRD transplants [3–9].

The high success rates of LURD transplantation prob-

Coo DD. Kidney Int. 1999 Oct;56(4):1551-9.

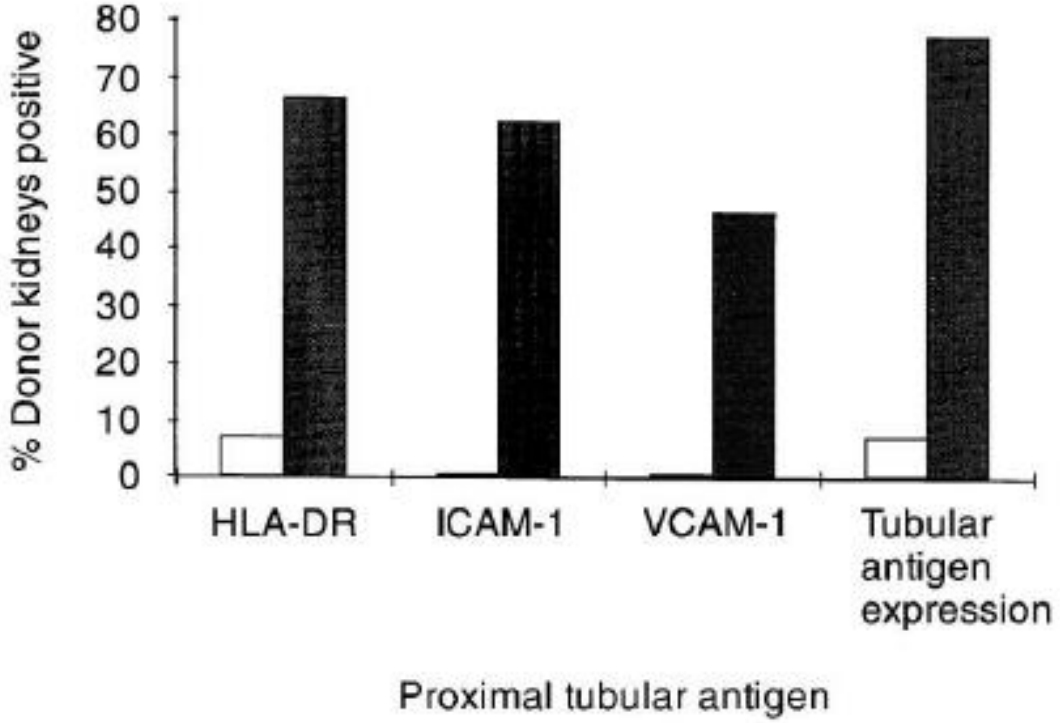

Fig. 3. Expression of HLA-DR antigens, intercellular adhesion molecular-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) on the proximal tubules of cadaveric (■; $N = 65$) and living-related donor (LRD; □; $N = 29$) kidneys. High levels of HLA-DR antigens were detected on the proximal tubules of 66% of cadaveric kidneys, whereas only 7% of LRD kidneys had elevated HLA-DR antigen expression ($P < 0.00001$). Elevated ICAM-1 and VCAM-1 expression was detected in 62 and 48% of cadaveric kidneys, respectively, whereas all 29 LRD kidneys were negative for tubular ICAM-1 and VCAM-1 expression ($P < 0.00001$). Elevated tubular antigen expression, defined as expression of either HLA-DR antigens, ICAM-1 or VCAM-1 either alone or in combination, was detected in 50 out of 65 (77%) cadaver kidneys, whereas only 2 out of 29 (7%) LRD kidneys had induced tubular antigen expression ($P < 0.00001$).

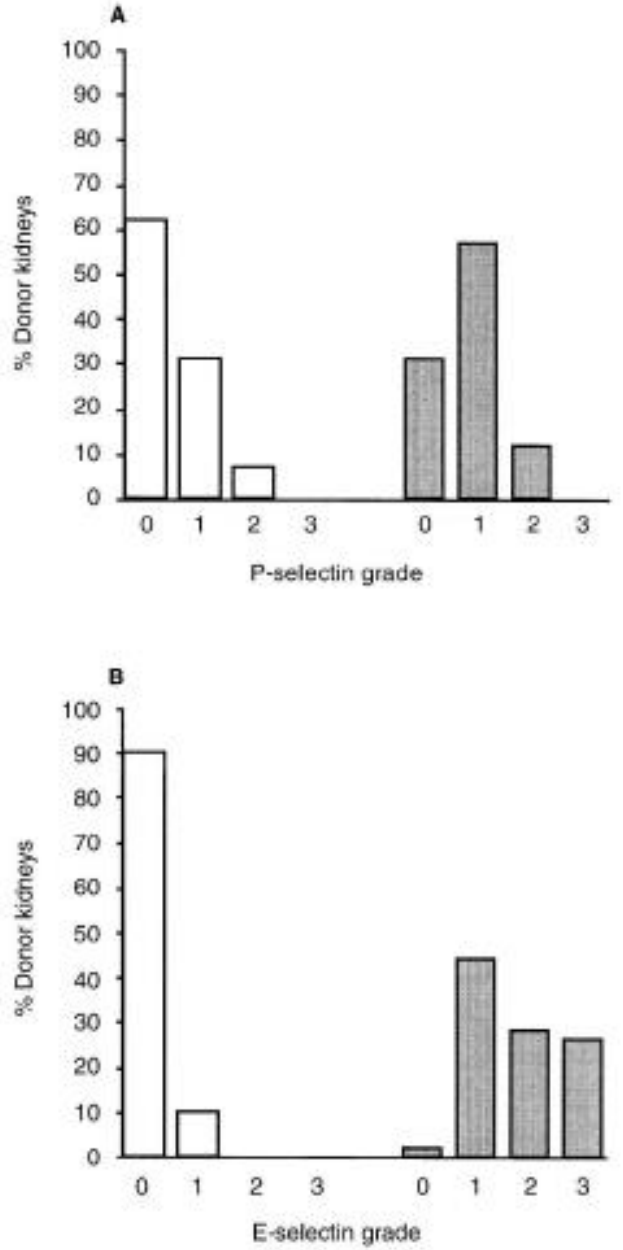

Fig. 1. Levels of P- and E-selectin expression in cadaveric and living-related donor (LRD) kidneys. (*A*) Similar patterns of low level P-selectin expression were detected in cadaveric (■; $N = 65$) and LRD (□; $N = 29$) kidneys. (*B*) High levels of E-selectin expression (≥ grade 2) were detected in 54% of cadaveric kidneys, whereas minimal expression was observed in LRD kidneys.

0041-1337/03/7512-2001/0
TRANSPLANTATION

Vol. 75, 2001–2007, No. 12, June 27, 2003
Printed in U.S.A.

LEUKOCYTE INFILTRATION AND INFLAMMATORY ANTIGEN EXPRESSION IN CADAVERIC AND LIVING-DONOR LIVERS BEFORE TRANSPLANT[1]

WAYEL JASSEM,[2] DICKEN D.H . KOO,[3] LUCIA CERUNDOLO,[3] MOHAMED RELA,[2] NIGEL D. HEATON,[2] AND SUSAN V. FUGGLE[3,4]

Background. **There is evidence to indicate that organs obtained from cadaveric donors may be injured as a result of inflammatory events occurring at around the time of brain death. The aim of this study was to investigate whether there are differences in the expression of proinflammatory molecules between cadaveric and living-donor livers before transplant and to determine whether there is any association with donor factors and posttransplant graft function.**

Methods. **A comparison of biopsies obtained before implantation from cadaveric (n=22) and living-related donor (LRD) (n=10) livers was performed. Cryostat tissue sections were stained with antibodies to leukocyte subpopulations, adhesion molecules, and human leukocyte antigen class II antigens.**

Results. **Significantly higher levels of CD3+ lymphocytes (1.5%±0.8% vs. 0.5%±0.3%; P=0.00004), CD68+ monocytes and macrophages (4.0%±1.2% vs. 2.7%±0.6%; P=0.0003), and Fas-ligand staining (4.2%±2.6% vs. 1.5%±1.1%; P=0.0003) were detected in cadaveric livers compared with LRD livers before transplantation. Furthermore, higher levels of intercellular adhesion molecule-1 expression were detected in cadaveric donor livers and found to be associated with longer periods of ventilation (P=0.01), infection in the donor (P=0.013), and administration of dopamine (P=0.03). Although there were no differences in neutrophil infiltration between cadaveric and LRD livers, significantly higher levels were found in cadaveric donors with infection (P=0.01).**

Conclusion. **This study demonstrates that inflammatory changes occur in cadaveric donor livers and are associated with events occurring during the period of intensive care. These proinflammatory changes did not seem to affect the short-term clinical outcome of cadaveric liver allografts but may contribute to alloimmune responses and impairment of graft function in the long term.**

[1] The results from this study were presented in 2001 at the 52nd Annual Meeting of the American Association of Studies of Liver Disease, Dallas, Texas.

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Jassem W. Transplantation.2003 ;27:2001-7

Although no significant associations with clinical outcome were found in this study, the inflammatory damage that occurs in cadaveric livers may contribute to a poor long-term prognosis.

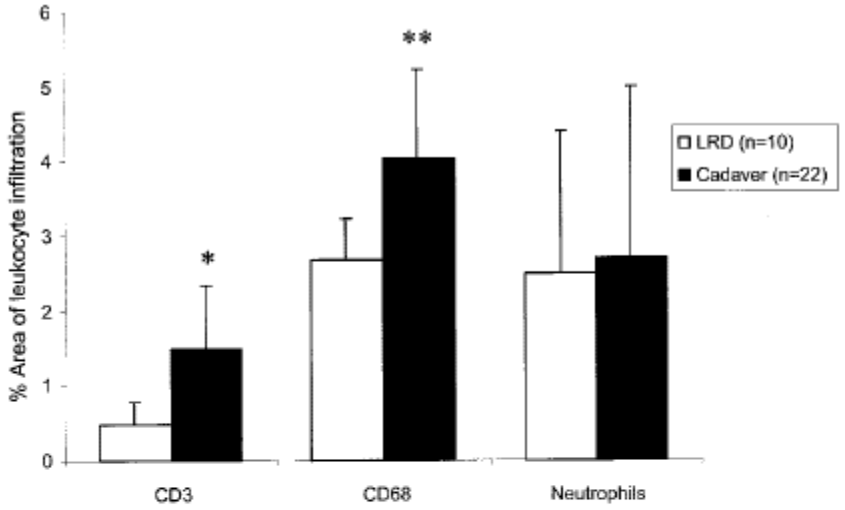

FIGURE 1. Leukocyte infiltration in cadaveric and living-related donor (LRD) livers before transplantation. Cadaveric and LRD liver biopsies were stained with monoclonal antibodies against CD3, CD68, and neutrophil elastase, and the percentage area of positivity was calculated by morphometric point counting. Significantly higher levels of CD3+ lymphocytes (*P=0.00004) and CD68+ Kupffer cells (P=0.0003) were detected in cadaveric livers compared with LRD livers. There were no significant differences in neutrophil infiltration between cadaveric and LRD livers before transplantation (P=0.8).**

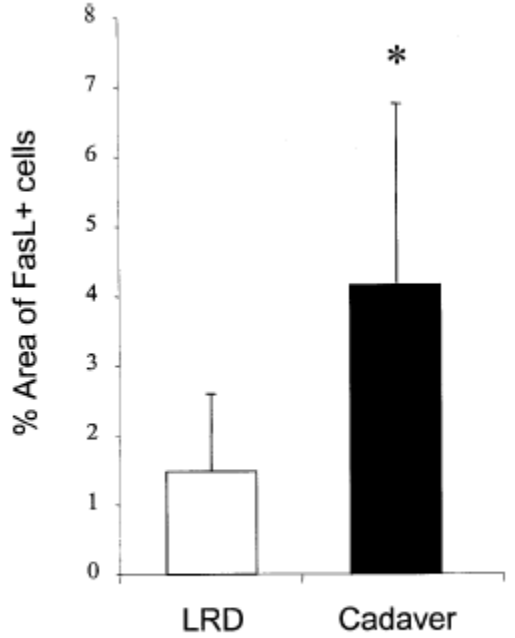

FIGURE 3. FasL expression in cadaveric and LRD livers before transplantation. Cadaveric livers contained a significantly greater percentage of cells expressing FasL than LRD livers before transplantation (*P=0.0003).

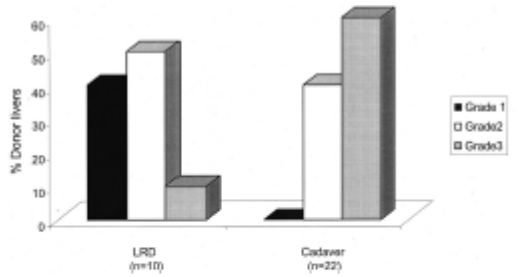

FIGURE 4. Expression of ICAM-1 on cadaveric and LRD livers before transplantation. Liver biopsies from cadaveric and LRD livers were stained with an anti-ICAM-1monoclonal antibody, and the staining was assessed semiquantitatively. Cadaveric livers expressed higher levels of ICAM-1 (grade 3) compared with LRD livers (P=0.02).

Jassem W. Transplantation.2003 ;27:2001-7

What factors affect the Cadaveric Kidney Tx Outcome?

Transplantation. 102(7):1188–1194, JUL 2018
DOI: 10.1097/TP.0000000000002106, PMID: 29346257
Issn Print: 0041-1337
Publication Date: 2018/07/01

Association of Cold Ischemia Time With Acute Renal Transplant Rejection

Merve Postalcioglu;Arnaud Kaze;Benjamin Byun;Andrew Siedlecki;Stefan Tullius;Edgar Milford;Julie Paik;Reza Abdi;

+ Author Information

In summary, we report the largest study on the association between CIT and ARTR among renal transplant recipients in the United States and found that longer CIT is associated with increased ARTR and death-censored graft loss. Older recipient age was associated with a decreased risk of ARTR.

Figure 1.

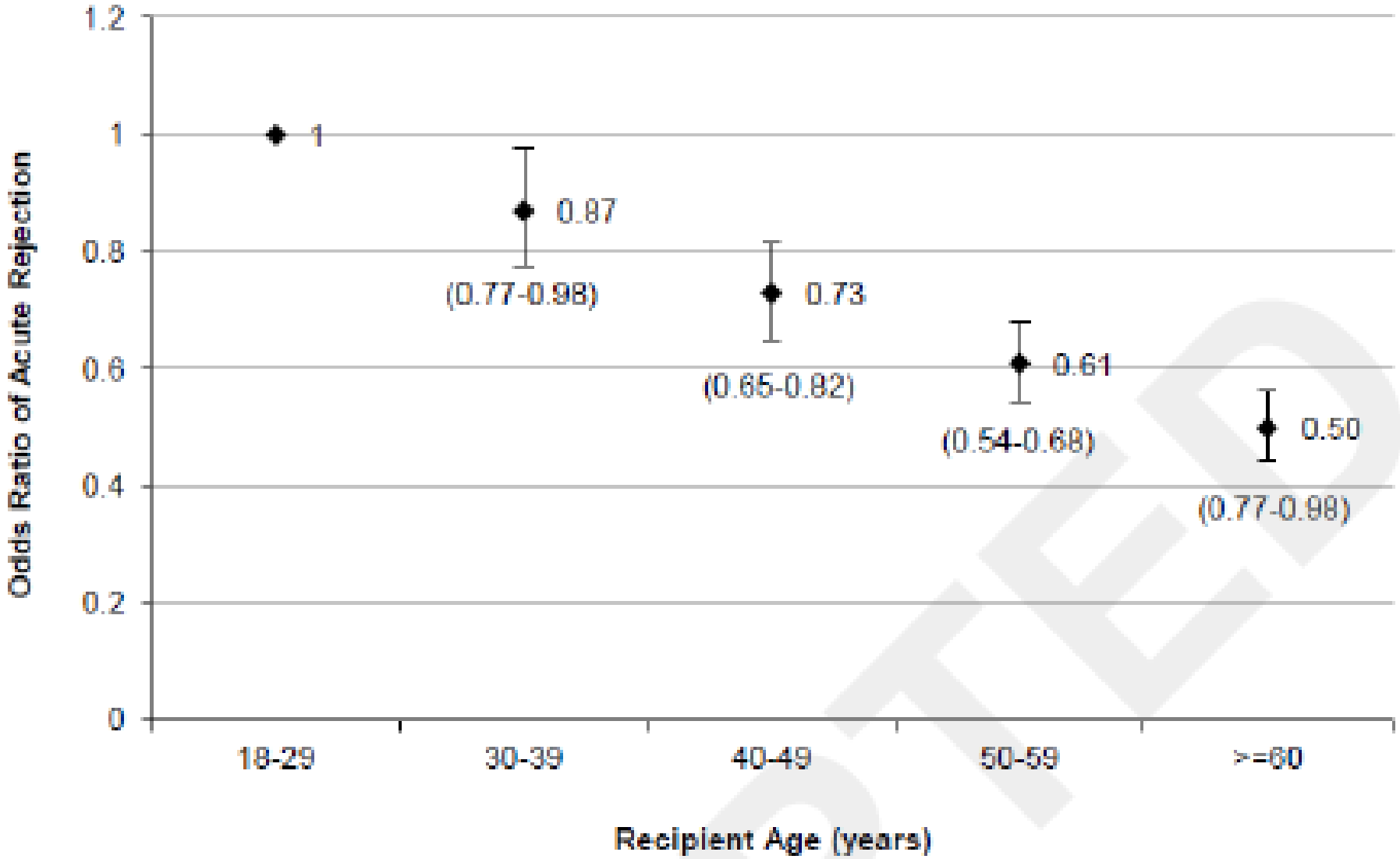
1.2
1
0.8
0.6
0.4
0.2
0
Odds Ratio of Acute Rejection
1
0.87
(0.77-0.98)
0.73
(0.65-0.82)
0.61
(0.54-0.68)
0.50
(0.77-0.98)
18-29
30-39
40-49
50-59
>=60
Recipient Age (years)

Table 2. Association of Cold Ischemia Time with Acute Renal Transplant Rejection in the OPTN Database between 2000-2010 (N= 6,802)

		Univariable Analysis			Multivariable Analysis*		
CIT	N	Odds Ratio (95% CI)	P-value	P_{trend}	Odds Ratio (95% CI)	P-value	P_{trend}
<12 h	1394	1.00			1.00		
12-17.9 h	1874	1.06 (0.99-1.14)	0.24		1.02 (0.95-1.11)	0.08	
18-23.9 h	1804	1.12 (1.05-1.22)	0.09		1.12 (1.03-1.21)	0.05	
≥24 h	1730	1.17 (1.09-1.26)	0.001		1.13 (1.04-1.23)	0.01	
				<0.001			<0.001

*The multivariable analysis adjusted for age of the recipients and donors, gender of the recipients and donors, ethnicity of the recipients and donors, recipient BMI, HLA mismatching, extended criteria donor, donation after cardiac death, calculated-panel reactive antibody, cause of death for the donor, dialysis vintage, re-transplantation and year of transplantation.

Table 4. Association of Recipient Age with Delayed Graft Function in the OPTN Database between 2000-2010 (N=14,992)

		Univariable Analysis		Multivariable Analysis[+]	
Recipient Age	N	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
18-29	735	1.00		1.00	
30-39	2056	1.27 (1.16-1.40)	<0.0001	1.11 (0.99-1.23)	0.06
40-49	3206	1.25 (1.14-1.37)	<0.0001	1.06 (0.96-1.17)	0.26
50-59	4498	1.36 (1.25-1.49)	<0.0001	1.09 (0.99-1.21)	0.08
≥60	4497	1.36 (1.24-1.48)	<0.0001	1.11 (1.01-1.23)	0.03

[+]The multivariable analysis adjusted for CIT, age of the donor, gender of the recipients

Table 5. Association of Cold Ischemia Time with Death-Censored Graft Loss in the OPTN Database between 2000-2010 (N=8,035)

		Univariable Analysis			Multivariable Analysis[+]		
CIT	N	Hazard Ratio (95% CI)	P-value	P_{trend}	Hazard Ratio (95% CI)	P-value	P_{trend}
<12 h	1478	1.00			1.00		
12-17.9 h	2259	1.09 (1.02-1.17)	0.08		1.09 (1.02-1.17)	0.01	
18-23.9 h	2136	1.11 (1.04-1.18)	0.02		1.17 (1.10-1.25)	<0.001	
≥24 h	2162	1.19 (1.12-1.27)	<0.001		1.22 (1.14-1.30)	<0.001	
				<0.001			<0.001

[+]The multivariable analysis adjusted for age of the recipients and donors, gender of the recipients and donors, ethnicity of the recipients and donors, diabetes history of the recipients and donors, hypertension history of the recipients and donors, recipient BMI, HLA mismatching, extended criteria donor, donation after cardiac death, CPRA, cause of death for the donor, dialysis vintage, re-transplantation and year of transplantation.

Effect of HLA matching

- The latest European Renal Best Practice Transplantation Guidelines still recommended that matching of HLA-A, -B, and -DR whenever possible, while gave more weight to HLA-DR locus.

Shi et al. BMC Nephrology (2018) 19:116
https://doi.org/10.1186/s12882-018-0908-3

BMC Nephrology

RESEARCH ARTICLE Open Access

What is the impact of human leukocyte antigen mismatching on graft survival and mortality in renal transplantation? A meta-analysis of 23 cohort studies involving 486,608 recipients

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Abstracts

Background: The magnitude effects of human leukocyte antigen (HLA) mismatching on post-transplant outcomes of kidney transplantation remain controversial. We aim to quantitatively assess the associations of HLA mismatching with graft survival and mortality in adult kidney transplantation.

Methods: We searched PubMed, EMBASE and the Cochrane Library from their inception to December, 2016. Priori clinical outcomes were overall graft failure, death-censored graft failure and all-cause mortality.

Results: A total of 23 cohort studies covering 486,608 recipients were selected. HLA per mismatch was significant associated with increased risks of overall graft failure (hazard ratio (HR), 1.06; 95% confidence interval (CI), 1.05–1.07), death-censored graft failure (HR: 1.09; 95% CI 1.06–1.12) and all-cause mortality (HR: 1.04; 95% CI: 1.02–1.07). Besides, HLA-DR mismatches were significant associated with worse overall graft survival (HR: 1.12, 95% CI: 1.05–1.21). For HLA-A locus, the association was insignificant (HR: 1.06; 95% CI: 0.98–1.14). We observed no significant association between HLA-B locus and overall graft failure (HR: 1.01; 95% CI: 0.90–1.15). In subgroup analyses, we found recipient sample size and ethnicity maybe the potential sources of heterogeneity.

Conclusions: HLA mismatching was still a critical prognostic factor that affects graft and recipient survival. HLA-DR mismatching has a substantial impact on recipient's graft survival. HLA-A mismatching has minor but insignificant impact on graft survival outcomes.

Keywords: Human leukocyte antigen, Kidney transplantation, Graft survival, Mortality, Meta-analysis

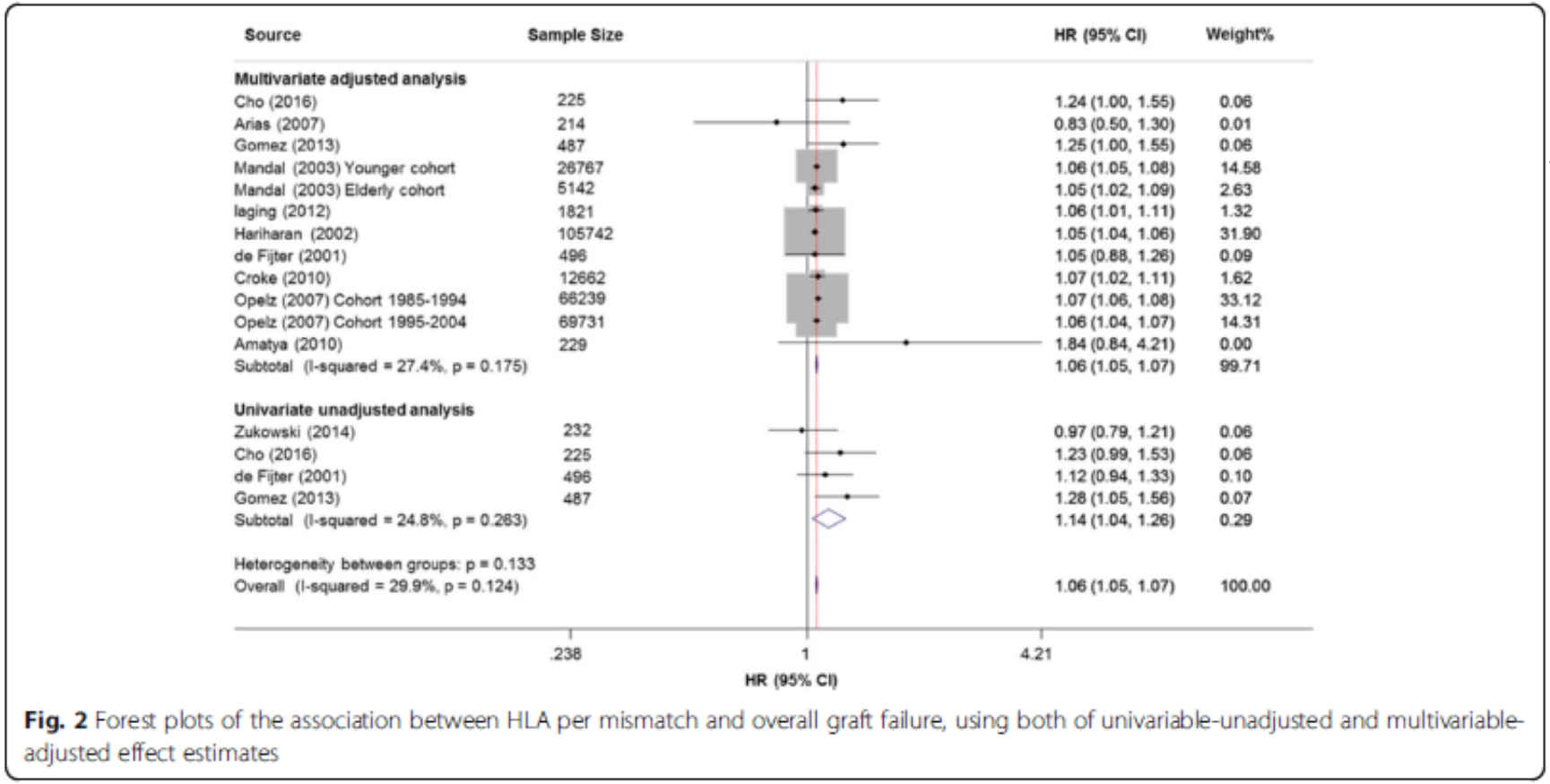

Fig. 2 Forest plots of the association between HLA per mismatch and overall graft failure, using both of univariable-unadjusted and multivariable-adjusted effect estimates

Each incremental increase of HLA mismatches was significant associated with a higher risk of overall graft failure, both in univariable-unadjusted summary estimates (HR: 1.14; 95% CI: 1.04–1.26; P = 0.008; Fig. 2) and multivariable-adjusted summary estimates (HR: 1.06; 95% CI: 1.05–1.07; P < 0.001.)

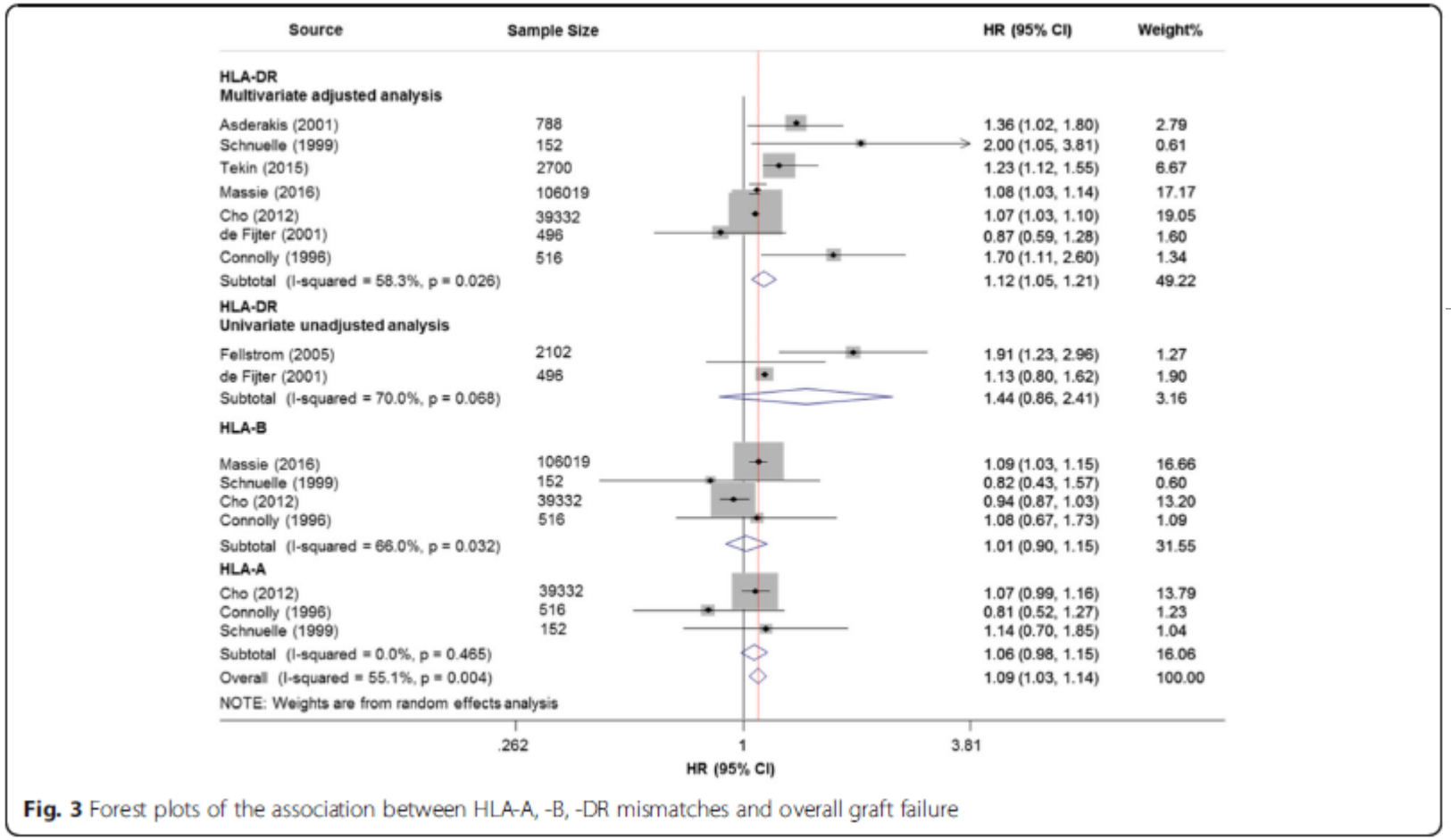

Fig. 3 Forest plots of the association between HLA-A, -B, -DR mismatches and overall graft failure

HLA-B mismatches was not associated with higher risk of overall graft failure.
Only 3 studies (40,000 recipients) reported data on the association of HLA-A epitope and overall graft failure.
1 or 2 HLA-DR mismatches were significantly associated with a 12% and 15% higher risk of overall graft failure.

- The pooled results were in favor of the kidney allocation guideline recommendations in almost all countries, such as the current US kidney allocation system, the revised United Kingdom kidney allocation scheme, and the latest European Renal Best Practice Transplantation Guidelines, which all highlighted the importance of HLA-DR testing.

-Ashby VB. Am J Transplant. 2011;11:1712–8.
-Johnson RJ. Transplantation. 2010;89:379–86 (UK)
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Pros and cons for a living donor

- Donating can be selfless and rewarding and studies have shown that living donors live just as long as people who never donated.
- However, living kidney donors face some medical, financial, and emotional risks. There is no way to know who will have a specific problem.

https://transplantliving.org/kidney/pros-and-cons-for-a-living-donor/

Medical pros

- General health is as good as the general population
- If you ever need a transplant, you will have a shorter wait on the UNOS transplant waitlist. People who have been kidney donors get priority.

Medical possible short-term cons

- Allergic reactions to anesthesia
- Heavy bleeding
- Pain
- Bloating from the air put into your belly for surgery
- Infection
- Bulging of stitches (hernia)
- Pneumonia
- Blood clots

- Less than 2% of donors need more surgery from problems such as:
  - Bleeding
  - Blocked bowel
  - Bowel injury
- Less than 2% of donors need to go back to the hospital because they have:
  - Feeling sick
  - Throwing up
  - Diarrhea (loose stool)
  - Infections
- Only 3 in 10,000 donors die in surgery.

Medical possible long-term cons

- Loss of 25-35% of kidney function
- Long term pain
- Adhesions (internal scars that connect tissues not usually connected)
- Scars, usually two small cuts and one longer one
- Blocked bowel, which may need surgery to correct
- Protein in urine, which may be a sign of diabetes
- Kidney problems or a need for a kidney transplant
- For women, higher chance of high blood pressure or preeclampsia if you become pregnant after donating
- Hernia
- People can get certain health problems after donating:
  - About 18% of donors (about 1 in 5) get high blood pressure
  - About 5% (1 in 20) get chronic kidney disease
  - 4% (less than 1 in 20) get diabetes within 5 years of donating

Emotional and social pros

- Feeling a sense of happiness, reward, satisfaction and relief because most transplant patients have much better health after their transplant
- Higher self-esteem than you had before donating
- In most cases, living donors report a better relationship with the transplant patient

Emotional and social possible short-term cons

- Worrying about the surgery before it happens
- Stress from recovery

Emotional and social possible long-term cons

- Sadness over loss of kidney
- Anger if the transplant patient's body rejects the donated kidney
- Feelings of guilt or regret
- Your mood may depend on your relationship with the transplant patient and what happens to them post-donation, such as if their body rejects the kidney or the transplant works well

Financial possible short-term cons

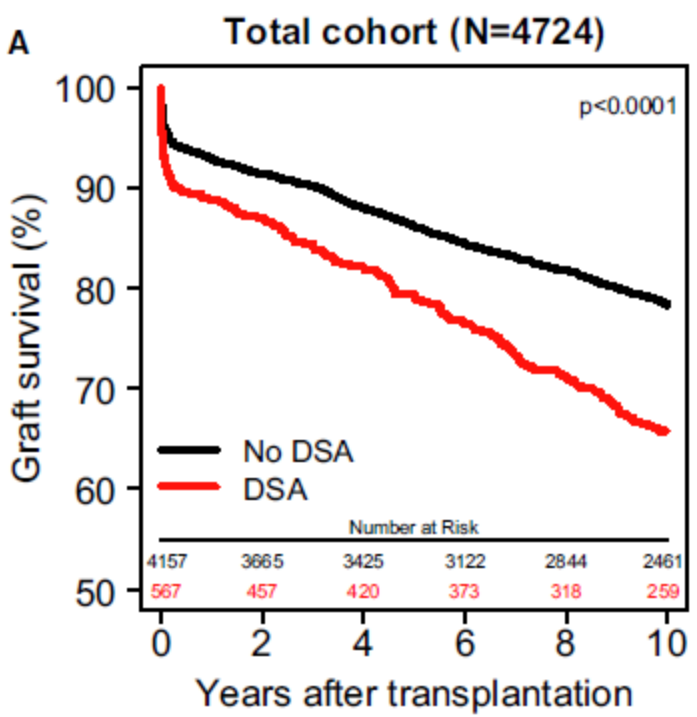
- Costs of travel to and from transplant center and hospital for testing and surgery, lodging, and child care if needed
- Money lost from time out of work for testing, surgery, and recovery

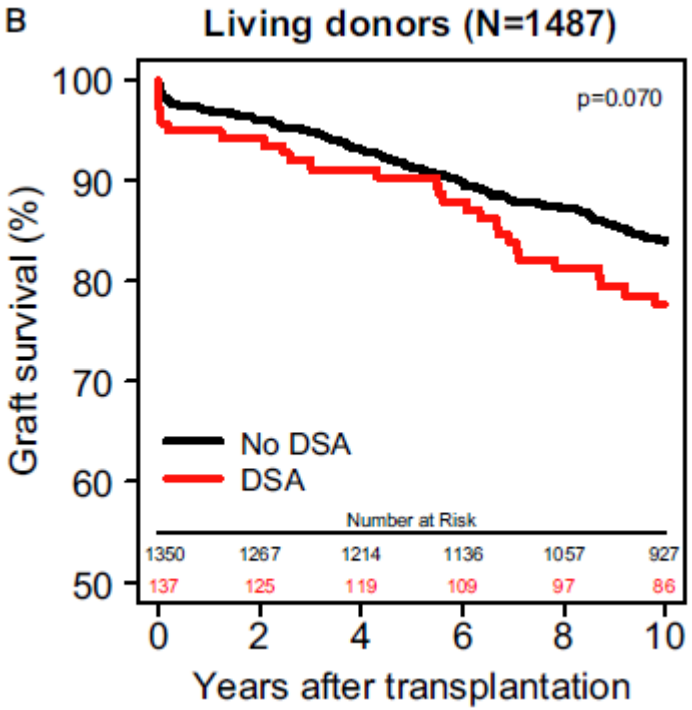
Conclusion

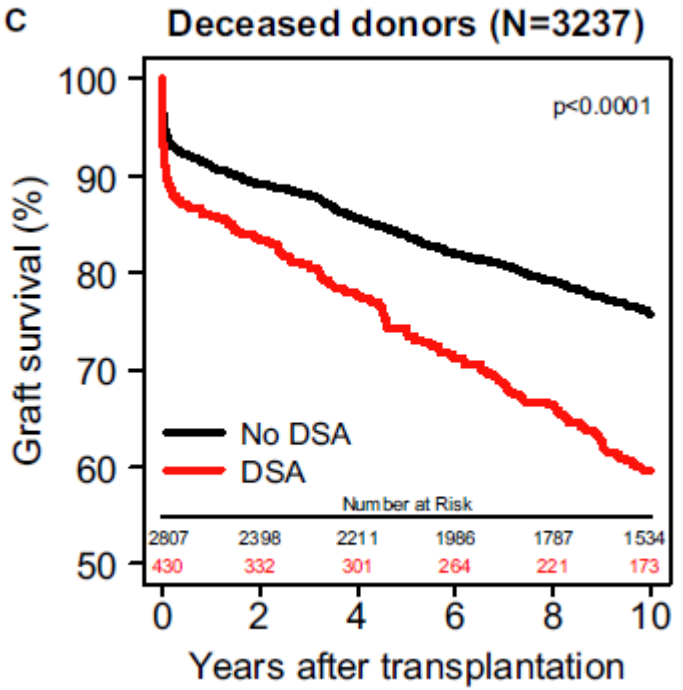
- Cadaveric Tx does not generally have an inferior outcome compared to living donor Tx, esp if CIT is minimized and a good HLA matching is considered.
- Costs of Cadaveric kidney Tx is comparable to live kidney Tx and may be much less in our country.
- Short CIT is an opportunity for getting very favorable results, if we treat the organ well.
- Emotional impact of live donation may not be as positive as mentioned in western countries considering the kidney for sale.
- Tx waiting list is almost the same for both methods in our country.
- We need well designed local researches to elucidate the many aspects of live donor and cadaveric idney Tx in our country.


Thank
you


Thank You!


A
Total cohort (N=4724)
p<0.0001
Graft survival (%)
100
90
80
70
60
50
No DSA
DSA
Number at Risk
4157 3665 3425 3122 2844 2461
567 457 420 373 318 259
0 2 4 6 8 10
Years after transplantation


B
Living donors (N=1487)
p=0.070
Graft survival (%)
100
90
80
70
60
50
No DSA
DSA
Number at Risk
1350 1267 1214 1136 1057 927
137 125 119 109 97 86
0 2 4 6 8 10
Years after transplantation


C
Deceased donors (N=3237)
p<0.0001
Graft survival (%)
100
90
80
70
60
50
No DSA
DSA
Number at Risk
2807 2398 2211 1986 1787 1534
430 332 301 264 221 173
0 2 4 6 8 10
Years after transplantation

They found

- A limited effect of pretransplant SAB assay–defined DSAs on graft failure in living donor transplants.
- In contrast, pretransplant SAB assay–defined DSAs are a clear risk factor for graft loss in deceased donor transplantations with a negative CDC-XM.
- DSAs against either class I or II did constitute a significant risk factor for graft loss and pretransplant DSAs against both HLA class I and class II resulted in the poorest death-censored graft survival.
- In living donor transplants, the combination of class I and II DSAs seem to be associated with an increased risk for graft failure, but this could not be assessed due to their low prevalence.

Characteristics	Deceased donor (N = 3237)	Living donor (N = 1487)	*P*-value	Total cohort (N = 4724)
Patient				
Age at transplant, y, mean ± SD	46.9 ± 14.1	42.3 ± 14.5	<.001[a]	45.4 ± 14.4
Female sex, n (%)	1309 (40.4)	585 (39.4)	.47[b]	1894 (40.1)
PRA at time of transplant, %, mean ± SD	7.0 ± 19.0	3.8 ± 13.4	<.001[a]	6.0 ±17.5
Highest PRA, %, mean ± SD	16.5 ± 28.3	8.0 ± 17.9	<.001[a]	13.8 ± 25.8
IL-2 receptor blocker	655 (20.2)	367 (24.7)	<.001[b]	1022 (21.6)
T cell–depleting antibody[c]	133 (4.1)	51 (3.4)	.26[b]	184 (3.9)
Initial immunosuppression				
Steroids, n (%)	3172 (98.0)	1444 (97.1)	.058[b]	4616 (97.7)
MMF/azathioprine	3163 (76.1)	442 (78)	<.001[b]	3605 (76.3)
Cyclosporine/ tacrolimus	3051 (94.3)	1383 (93.0)	.097[b]	4434 (93.9)
Sirolimus	176 (5.4)	110 (7.4)	<.001[b]	286 (6.1)
Other	436 (13.5)	172 (11.6)	.070[b]	608 (12.9)
Unknown	11 (0.3)	6 (0.4)	.73[b]	17 (0.4)

Table 2. Summary of statistically significant correlations between clinical parameters and high levels of endothelial E-selectin expression or induced tubular antigen expression in cadaveric kidneys

Clinical parameters	Endothelial E-selectin	Tubular antigen
Trauma at death	NS	$P<0.05$
Ventilator support >3 days	NS	$P<0.05$
Desmopressin (DDAVP) treatment	$P=0.015$	NS
Donor infection	NS	$P<0.05$
Rejection by day 7 post-transplantation	NS	$P<0.05$

Statistical analyses were performed using Fisher's exact or Student's *t*-test, and confirmed by multiple logistic regression analysis with respect to the large number of comparisons performed. NS is not significant.

Coo DD. Kidney Int. 1999 Oct;56(4):1551-9.

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ORIGINAL ARTICLE

AJT

Differential effects of donor-specific HLA antibodies in living versus deceased donor transplant

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- This multicenter study included all 6097 kidney transplants performed between January 1995 and December 2005 in all Dutch transplant centers.
- Patients were primarily white. In all cases, the T cell CDC-XM with current and historic highest sera was negative.
- Historic cytotoxic HLA antibodies were assigned as unacceptable for allocation in the Eurotransplant region.
- Bead assay–defined DSAs were not considered as risk factors in the matching procedure at that time and therefore had no influence in immunosuppressive treatment.
- The presence of HLA antibodies (HLA-Abs) in the pretransplant sera, used for pretransplant crossmatch, was assessed retrospectively in a central laboratory as described previously