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.

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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.*

Key words: *Living donor renal transplant. Survival. Outcomes comparison. Registries.*

Correspondence: *Emili Vela Vallespín*
Servei Catalá de la Salut
Travessera de les Corts, 131-159
08028 Barcelona
evela@catsalut.net

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 diferentes factores que intervienen en la supervivencia del paciente y del injerto, no existen diferencias en los resultados obtenidos por los dos tratamientos, ya que los mejores resultados del TRV son debidos a factores como la menor edad del receptor y el TR anticipado.**

Palabras clave: Trasplante renal de donante vivo. Supervivencia. Comparación de resultados. Registros.

INTRODUCTION

Living-donor renal transplant yields better outcomes than cadaver-donor transplantation. This statement has been widely reported in the medical literature, particularly in that based on large patient registers. In the European Study (Collaborative Transplant Study), Opelz et al.[1] reached the conclusion that

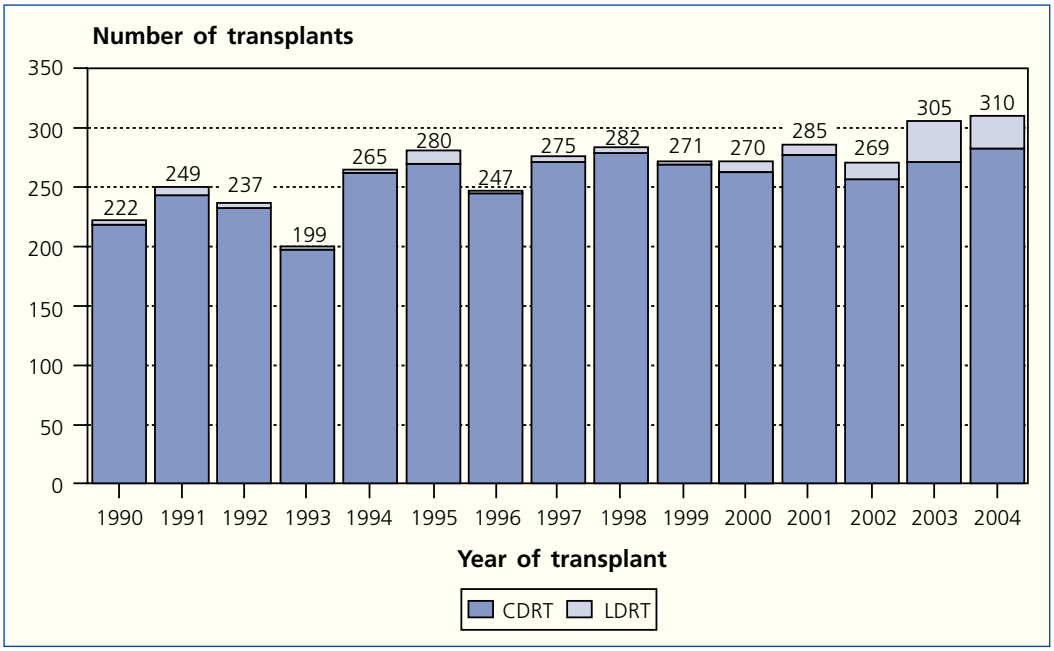

Figure 1. Number otr transplants performed per year by type of donor. Period 1990-2004.

the longest kidney graft survival is achieved with identical twins, followed by kidney grafts from haplo-identical living donors, and finally, the worst survival rate is obtained when cadaver donors are used for renal transplantation.

The UNOS Register also shows similar results, the patient's and graft's survival at 5 years being 80.7% and 65.7% for cadaver-donor renal transplant, and 90.1% and 78.6% for living-donor renal transplant.[2] Previous studies[3] carried out, using data from the CRPR and the same univariate methodology, obtained similar results.

In spite of the fact that the mentioned studies are based on large series, it remains unclear whether the differences found may be attributed to the better quality of the living-donor graft. In fact, in a previous study[4] carried out with a different methodology, we found out that the survival rates for the patient and the graft became even when adjusting for several factors.

The aim of our work is to study which are the factors determining the best outcomes from living-donor transplant as compared with cadaver-donor by means of univariate analyses.

PATIENTS AND METHODS

We analyzed all first renal transplantations performed in Catalonia during the period 1990-2004 to patients older than 17 years, of whom 135 patients received a living-donor renal transplant (LDRT) and 3,831 a cadaver-donor renal transplant (CDRT). One hundred and seventy-one cases (4.3% of the whole) have been excluded due to information missing at any of the variables. The data were gathered from the Catalonian Renal Patients Register (CRPR), which is a population-based register with mandatory fulfillment, gathering information on all end-stage renal failure (ESRF) patients managed with dialysis or renal transplant at both public and private health care centers in Catalonia.

The variables analyzed included the recipient's and donor's age and gender, primary kidney disease, previous comorbidity history (diabetes, coronary heart disease, cardiomyopathy, arrhythmia, cerebrovascular disease, peripheral vascular disease, COPD, malignant tumors, joint disease, chronic liver disease, esophageal, gastric and duodenal diseases, intestinal diseases), previous time on dialysis, transplantation year, the maximal and last antibodies percentage (maximal and last PRA), HLA A, B and DR identities, number of hours of cold ischemia, and acute tubular necrosis.

The primary kidney disease (PKD) was grouped in three categories by using the codifying system of the European Renal Association Register-European Dialysis and Transplant Association (ERA-EDTA)[5] (see appendix 1).

The CRPR gathers comorbidity information of all patients by means of the usual questionnaires for notification and yearly follow-up that, among other, contain the following specific questions regarding 13 pathologies grouped according to the International Classification of Diseases (ICD-9) (see appendix 2).

For the descriptive analysis, the data from the quantitative variables are presented as the mean and standard deviation (M ± SD) and as percentages for categorical variables. The Student's t test has been used for means comparisons, and the chi-squared test for proportions comparison. The actuarial method has been used for the survival analysis. The statistical significance level between the different curves has been assessed by using the Gehan's test. The Cox regression model was used for the multivariate analysis. The statistical significance for the estimated relative risks has been determined by using the maximum verosimility method and the chi-squared test. For the construction of the multivariate analysis, all variables not showing statistical significance were excluded one after the other, except for those variables having shown differences in its distribution between LDRT and CDRT.

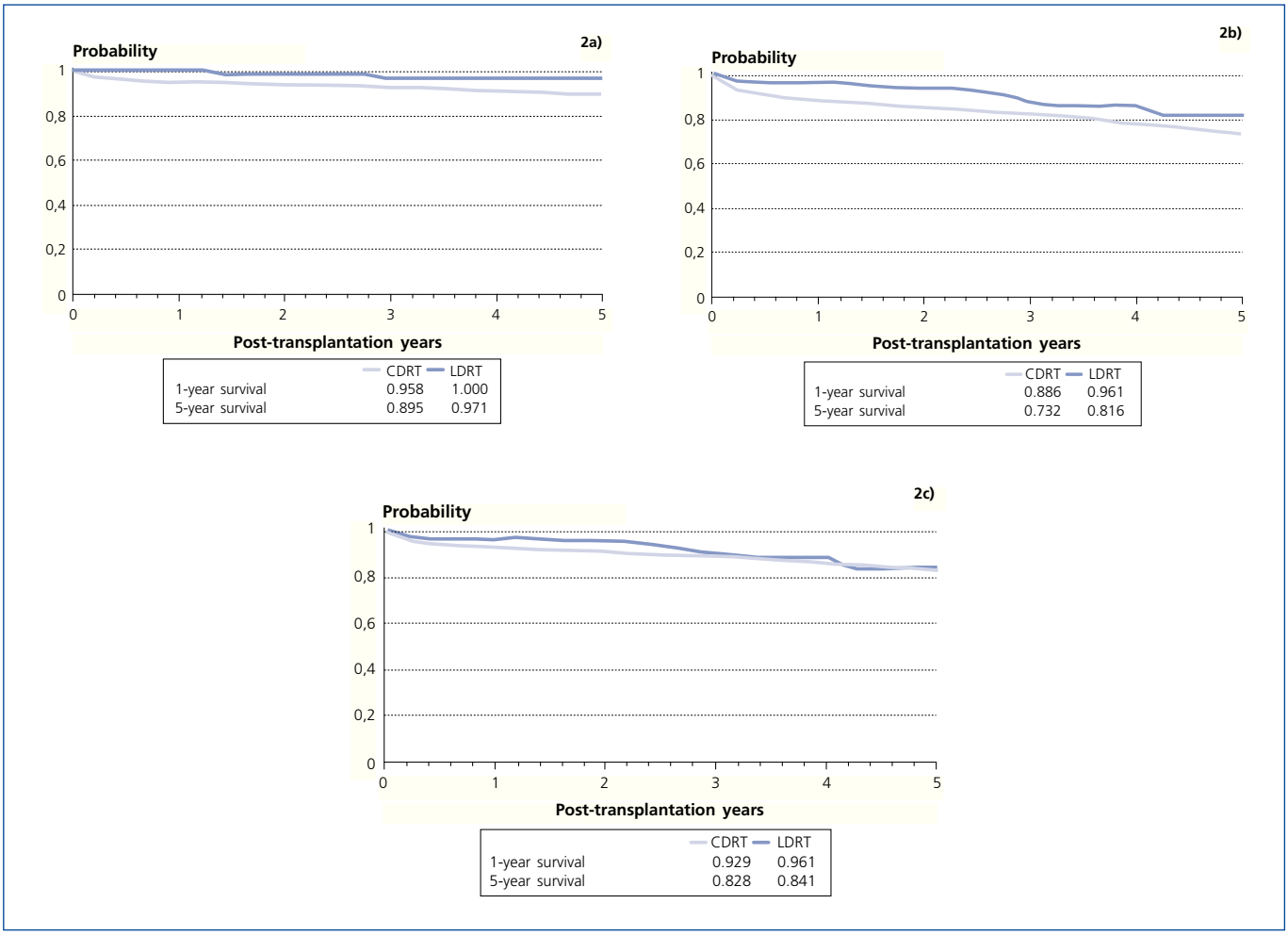

Figure 2. Actuarial survival analysis by type of transplant. Period 1990-2004: 2a) of the patient, 2b) of the graft, and 2c) of the graft with censored deaths.

Another indicator studied to assess the graft functional status was the estimated creatinine clearance. The problem with analyzing this indicator lies on the fact it changes with time and that, in the event of graft loss and lack of determinations, a selection bias will occur. Thus, with whatever longitudinal analysis using this indicator we should take into account, on the one hand, its progression through time, and on the other hand, the impact that cases with graft loss or patient's dead will have on it.

The CRPR yearly gathers information on creatinine and weight of all patients with functioning graft. With these data available, the Cockcroft-Gault's formula has been applied[6], which allows obtaining the yearly estimated creatinine clearance for each patient. The modified Selwood Analysis[7] has been used, where time zero corresponds to the time of renal transplant, and the percentage distribution of the different aggregates of estimated glomerular filtration rates for patients with functional renal graft, patients with graft loss, and deceased patients, is shown for each time interval. Given the characteristics of this type of methodology and the low number of cases with LDRT, the analyses have to be bivariate.

The SPSS, 12.01 statistical package has been used for all the analyses.

RESULTS

Figure 1 shows the progression in the number of renal transplants performed according to the type of donor during the study period.

Table I shows the differences found between CDRT and LDRT patients. Patients receiving an LDRT are younger (11 years on average) suffer less from cardiomyopathy, heart conduction disorders, COPD, joint disease, and digestive diseases than those receiving a CDRT. There are no differences by gender, PKD, or any of the following pathological conditions: CVA, peripheral vascular disease, malignant tumors, diabetes (not PKD), chronic liver disease, or intestinal diseases. Patients receiving an LDRT have been for shorter time on renal replacement therapy (RRT) (half of them on average). LDRT patients have higher HLA identities between the donor and the recipient than CDRT patients, although they are limited to HLA-A and HLA-B, and no differences are found in the number of HLA-DR identities. There are no significant differences either in the proportion of hypersensitized patients, independently of looking at the maximum or last PRA. There is a higher proportion of women among LDRT, as well as a higher proportion of donors aged 50-59 years. The time of cold ischemia is substantially different between both types of trans-

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

	CDRT (n = 3,831)		LDRT (n = 135)		p	missing
	N	%	N	%		
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
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		

plants, the average being of around 20 hours in CDRT and less than 2 hours in LDRT. Half of the donors died from CVA.

We have studied the outcomes indicators: the graft survival and the estimation of the glomerular filtration rate. Univariate and multivariate analyses have been carried out for graft survival analysis.

Firstly, a univariate survival analysis for the patient, for the graft, and for the graft with censored deaths has been done. The results are shown in figure 2. Taking into account only the type of transplant received, these data show that LDRT patients have better survival and the graft outcomes are better as well, as compared with CDRT patients (p = 0.016 and p = 0.047, respectively). When analyzing the graft survival with censored deaths, the differences are no longer significant (p = 0.67).

Table II shows the results obtained by using the Cox' regression analysis, by which the graft survival is compared by type of donor (LDRT or CDRT) and is adjusted for all the variables that may have an impact on it. When adjusting for all these factors, the differences observed in the previous analysis disappear. The Cox' regression shows as factors increasing the risk for graft loss the increasing recipient's and donor's age, diabetes as the primary kidney disease, certain comorbidity conditions (heart conduction disorders, COPD, diabetes,

Table II. Graft's survival analysis (Cox' regression). First transplantations 1990-2004

	p	OR	95,0% CI for OR Lower	Upper
Type of RT:				
Cadaver		1	–	–
Living	0.722	0.917	0.570	1.476
Recipient's age:				
18-44 años		1	–	–
45-64 años	0.505	0.955	0.833	1.094
65-74 años	0.001	1.415	1.146	1.748
> 74 años	0.018	2.419	1.165	5.023
PKD:				
Standard		1	–	–
Diabetes	0.053	1.157	0.998	1.341
Other	0.000	1.644	1.261	2.144
Heart conduction disorder:				
Heart conduction disorder	0.008	1.370	1.086	1.728
COPD	0.000	1.473	1.200	1.809
Diabetes	0.012	1.678	1.120	2.515
Chronic liver disease	0.067	1.237	0.985	1.551
Tiempo previo en diálisis:				
< 6 months on dialysis		1	–	–
6 months-2 years on dialysis	0.034	1.400	1.025	1.913
2-5 years on dialysis	0.004	1.585	1.160	2.166
> 5 years on dialysis	0.000	1.896	1.363	2.637
Period:				
1990-1997		1	–	–
1998-2004	0.000	0.528	0.455	0.612
Number of HLA DR identities:				
0 HLA-DR identities		1	–	–
1 HLA-DR identity	0.007	0.796	0.673	0.940
2 HLA-DR identities	0.001	0.720	0.588	0.882
Maximum Abs:				
0%-10%		1	–	–
11%-50%	0.289	1.089	0.930	1.276
> 50%	0.001	1.479	1.166	1.875
Donor's age:				
< 20 years		1		
20-29 years	0.619	1.063	0.835	1.352
30-39 years	0.078	1.255	0.975	1.616
40-49 years	0.000	1.573	1.256	1.971
50-59 years	0.000	1.903	1.535	2.361
60-69 years	0.000	2.355	1.879	2.952
> 69 years	0.000	2.430	1.819	3.246
Not significant adjusting variables				
Donor's gender:				
Males		1	–	–
Females	0.592	0.968	0.859	1.090
Concurrent pathologies (personal history)				
Coronary heart disease	0.706	0.956	0.759	1.206
Cardiomyiopathy or heart failure	0.243	1.114	0.929	1.336
Artropathy	0.909	0.991	0.844	1.163
Esophagus, stomach. or duodenum disease	0.891	0.987	0.818	1.191
Number of HLA A identities:				
0 HLA-A identities		1	–	–
1 HLA-A identity	0.265	1.070	0.950	1.206
2 HLA-A identities	0.222	0.856	0.668	1.098
Number of HLA B identities:				
0 HLA-B identities		1	–	–
1 HLA-B identity	0.114	0.910	0.811	1.023
2 HLA-B identities	0.221	0.835	0.625	1.115

and chronic liver disease), the increasing time on dialysis, and hypersensitized patients (maximum percentage of antibodies > 50%). The risk decreases with higher number of HLA-DR identities and having received the transplant within the most recent period. Other adjusting variables have been included into the model (donor's gender, number of HLA-A and HLA-B identities, and certain comorbidity) that, although not being statistically significant, have been maintained because they showed differences between the different populations of transplanted patients, as shown in table I.

The data regarding the glomerular filtration rate estimate, according the modified Selwood's analysis,[5] are presented graphically (figs. 3 and 4). Figure 3 shows the time evolution for the different levels of glomerular filtration rate and the

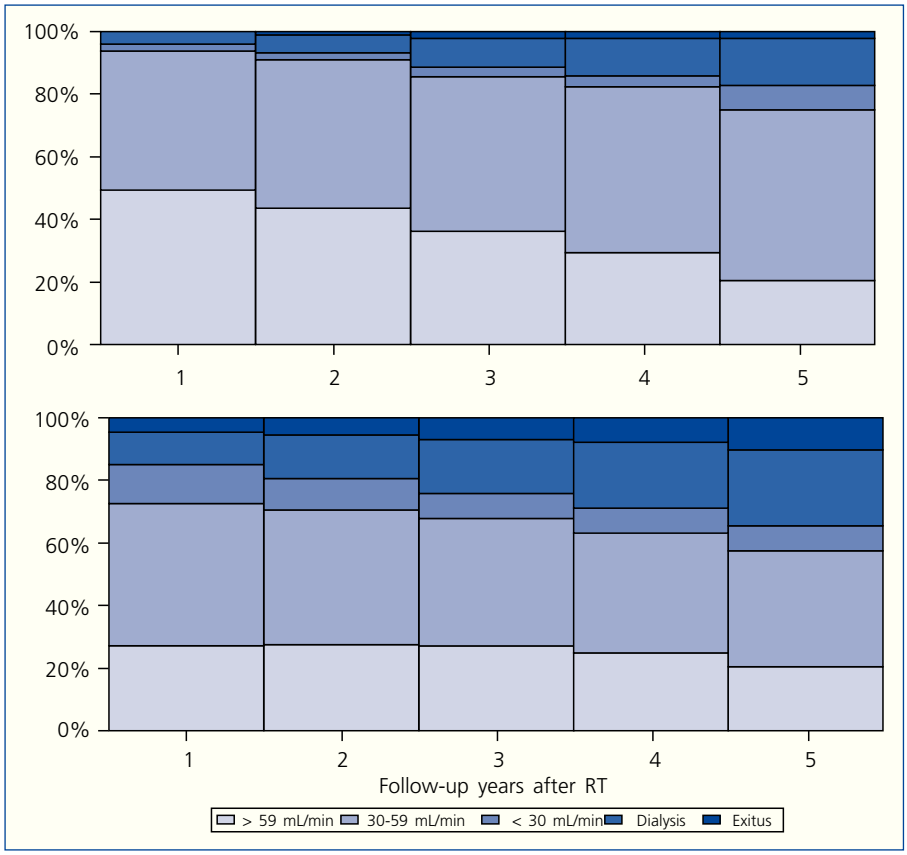

Figure 3. Estimation of glomerular filtration rate, patient's and graft's survival with time by type of transplant. Period 1990-2004.

proportion of patients that have died or returned to dialysis, for both LDRT and CDRT patients. LDRT patients have better patient and graft survival, with an almost null patient mortality. The glomerular filtration rates are generally also better. Also presented (fig. 4) are the data on glomerular filtration rate by previous time on RRT. As previous time on RRT increases, the glomerular filtration rates and patient's survival get worse, as do the percentage of patients returning to dialysis. The 5-year mortality rate for the patients with less than 6 months on previous dialysis is one third of that of patients with therapy durations longer than 5 years, whereas in the patients with a good glomerular filtration rate (> 59 mL/min) it is three times higher (29% *vs.* 12.5%); the differences are not so big between other glomerular filtration categories: for a glomerular filtration rate of 30-59 mL/min the values are 40% *vs.* 28%, and for the percentage of patients returning to dialysis the values are 18% *vs.* 35%; the most stable percentage at 5 years in all study groups is for those patients having a poor glomerular filtration rate, being of about 7%.

DISCUSSION

The data presented come from the CRPR, which is a mandatory population-based register gathering information on all patients receiving RRT in Catalonia. In 1988, an external validation was carried out, showing comprehensive notification of the relevant variables as well as excellent concordance. These results verified the validity of the data to be used in clinical and epidemiological studies. In 1990, the CRPR became the local EDTA register, and from 1998 a collaborator of the Collaborative Transplant Study (CTS).

We have not observed differences in the results obtained with CDRT and LDRT by adjusting for all factors affecting graft survival, in spite of the fact of observing better results with univariate analysis of LDRT.

According to different studies,[8,9] there are several factors that may contribute to explain the better survival and glomerular filtration rate with LDRT. Some of these factors have shown to be relevant also in our analysis, as it is for better HLA compatibility, lower recipient's age, and lower time on dialysis for LDRT.

About the HLA compatibility, we can obtain a higher number of HLA identities with LDRT since most of the donors are selected within the recipient's family, and sometimes we may even obtain grafts from identical brothers, which are the ones having the best outcome.[2,10] However, this trend may change in the future since transplantation between couples is becoming more common.

Without a doubt, the recipient's age is a paramount factor affecting transplant outcomes.[2] Despite having selected only adult patients (> 17 years), the age difference between the donor and the recipient is remarkable in LDRT because usually the donors are the parents of the recipient. In our study, the recipients' average age in LDRT was 11 years younger than in CDRT, and that of LDRT donors' was 5 years older than that for CDRT donors. When the recipient reached certain age, it became more difficult to find an appropriate living donor within the biological family. Again, this may

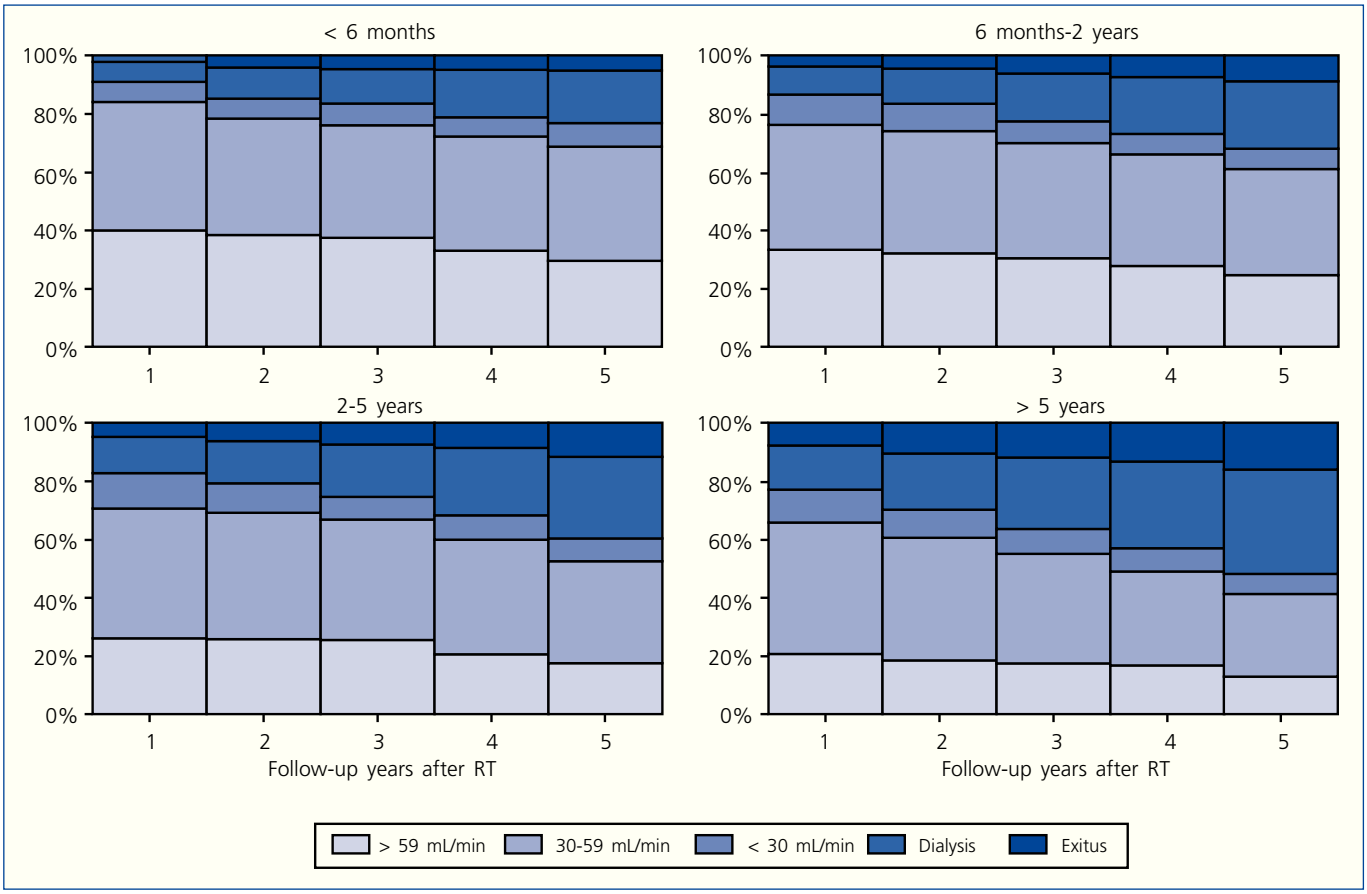

Figure 4. Estimation of glomerular filtration rate, patient's and graft's survival from the time of transplant, by previous time on dialysis. Period 1990-2004.

change with donation between couples. In addition, we should take into account that age increase (of both the donor and the recipient) is associated to increased comorbidity, which is also a risk factor for transplant survival.

Transplantation previous to dialysis yields better outcomes, as it has been shown by Meier-Kriesche in many publications.[11-14] The increase in graft and patient survival has been verified in recipients of both LDRT and CDRT. Given the low number of cases, we have not been able to establish in our study a group of analysis including patients with transplant previous to dialysis; even so, our results also confirm that the outcomes are poorer as the time on dialysis prior to transplantation increases, for both the graft survival (adjusted for all relevant factors) and the estimated glomerular filtration rate. The great advantage from LDRT is that it allows decreasing (and even getting rid of) the previous time on dialysis in ESRF patients susceptible to renal transplant. In our study, CDRT showed an average time on dialysis before having access to transplant of 37 months, although the average time on dialysis until the first transplantation has been reduced by one year (from 50 to 33 months) during the 15-year span of our study, thanks to the high donation rates in our community.[15] The access to LDRT in certain patients not only improves their own results but also contributes to decrease the number of patients on the waiting list,[16] and thus the time that they spend on dialysis, leading to a whole improvement of the outcomes from all transplants performed.

Other factors related to better outcomes from LDRT have also been reported in the literature, including the more extent study of the living donor, anticipated immunosuppression in LDRT, absence of brain dead-associated phenomena in the dead donor (ischemia-reperfusion damage), or lower time of cold ischemia. Due to several reasons, we have not been able to validate these factors.

LDRT allows grafting the kidney with a much lower time of cold ischemia than with CDRT. In our series, we have not been able to introduce this variable into the model due to the high number cases not reporting it (18% of all transplants); even so, considering the cases reporting it, the average times of cold ischemia were 1.5 hours for LDRT and 18 hours for CDRT. Cold ischemia has also been related with poorer outcomes of renal transplantation in many publications.[17] Another advantage of LDRT is that it offers the possibility of having the recipient immunosuppressed from several days before the transplant because the latter is scheduled. This might contribute to decrease the likelihood of acute graft rejection.[18,19]

Grafts from a living donor are not submitted to brain dead and its intrinsic phenomena.[20] A number of studies[21,22] show that brain dead is an independent risk factor for a poor graft's evolution. During brain dead, cytokines with an effect on leukocytes adhesion and migration are released. This promotes ischemia-reperfusion damage and acute rejection. On the other hand, cerebral edema leads to venous compression, and

the latter to the release of catecholamines causing vasoconstriction and endothelial lesion. In turn, endothelial damage increases the expression of class II antigens and cytokines release accelerating the processes of graft rejection. In parallel, brain dead causes hypophyseal necrosis and diabetes insipidus (75%), it may cause volume depletion and damage secondary to the brain dead itself. Hypothalamic damage causes thermal dysfunction (coagulopathy, hypoxia, liver and heart dysfunction).

By contrast with cadaver donor, the living donor may be extensively studied through months in order to determine his/her suitability in detail. At the same time, the living donor is commonly chosen among several members of a same family (the best donor possible among those available), so that the selection process is different from that with a cadaver donor (is he/she appropriate or not?). In this case, once the strict process determining whether or not the kidney is appropriate for transplantation is concluded, the best recipient possible is found among those on the waiting list. When a cadaver donor with associated pathology (arterial hypertension, diabetes, etc.) is accepted, there is an assessment on the minimal or absent involvement of the renal graft in order to prevent transmitting important damage to the recipient, which would condition the graft's survival; by contrast, with a living donor, before minor graft damage, donation is excluded to avoid that the donor's baseline pathology may cause irreversible lesions in the residual kidney that may lead in the future to needing dialysis and/or kidney transplant.[23]

These latter factors, which are intrinsic to living donation and that we have not been able to introduce as variables into the model, ought to be reflected in the multivariate analysis, showing a better outcome with LDRT as compared with CDRT; however, we have not observed significant differences between both treatment types.

The limitations of this work are those of studies performed with data coming from a population-based register in which the variable used are scant and with a low clinical specificity, although robust.

Another limitation related with the data source is the absence of certain variables that might have been relevant as prognostic factors for graft's survival, such as the time of cold ischemia or ATN, which we have not been able to analyze because of the high number of cases with absent data.

The low number of LDRT performed as well as their time distribution (only 26% of LDRT were carried out during the period 1990-97) causes different follow-up times and immunosuppressive regimens. To solve this problem, we introduced the variable «period» into the multivariate analysis. In the same way, we tried to solve the problem of the different age distribution between CDRT and LDRT recipients.

CONCLUSIONS

Similarly to what happens with large series of kidney-transplanted patients, it is observed from the CRPR 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. We conclude that after adjusting for the different factors affecting the survival of both the patient and the graft, there are no differences in the results obtained for both types of treatments since the better outcomes from LDRT are due to factors such as the lower recipient's age and scheduled renal transplant, which allow improving the survival expectancies and renal transplant functioning. Besides, performing LDRT allows reducing the global waiting lists of renal transplant with the subsequent improvement of the global outcomes.

APPENDIX 1. GROUPING OF THE PKD CODES

Standard PKD: codes 00-66.
Diabetic Nephropathy: codes 80-81.
Other PKD: codes 70-79 and 82-99.

APPENDIX 2. MORBIDITY GROUPED BY ICD-9 CODES

Heart disease: codes 410-414.
Cardiomyopathy or heart failure: codes 425 and 428.
Heart conduction disorders: codes 426-427.
Cerebrovascular disease: codes 430-438 and 342.
Vascular disease: codes 440, 441 and 443.
Chronic obstructive pulmonary disease (COPD): codes 491-496.
Tuberculosis: codes 10-18.
Malignant neoplasms: codes 140-208.
Cirrhosis and other chronic liver diseases: code 571.
Arthropathy: codes 712, 714 and 715.
Disease of the esophagus, stomach, and duodenum: codess 530-537.
Intestinal diseases: codess 562-569.

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