12. Mann DV, Lam WW, Hjelm NM, et al. Metabolic control patterns in acute phase and regenerating human liver determined in vivo by 31-phosphorus magnetic resonance spectroscopy. Ann Surg 2002; 235: 408–416.
13. Pomposelli JJ, Pomfret EA, Burns DL, et al. Life-threatening hypophosphatemia after right hepatic lobectomy for live donor adult liver transplantation. Liver Transpl 2001; 7: 637–642.
14. George R, Shiu MH. Hypophosphatemia after major hepatic resection. Surgery 1992; 111: 281–286.
15. Fisher B, Szuch P, Fisher ER. Evaluation of a humoral factor in liver regeneration utilizing liver transplants. Cancer Res 1971; 31: 322–331.
16. Pomfret EA, Pomposelli JJ, Lewis WD, et al. Live donor adult liver transplantation using right lobe grafts: donor evaluation and surgical outcome. Arch Surg 2001; 136: 425–433.
17. Bernuau J, Goudeau A, Poynard T, et al. Multivariate analysis of prognostic factors in fulminant hepatitis B. Hepatology 1986; 6: 648–651.
18. Castells A, Salmeron JM, Navasa M, et al. Liver transplantation for acute liver failure: analysis of applicability. Gastroenterology 1993; 105: 532–538.
19. Harrison PM, O'Grady JG, Keays RT, et al. Serial prothrombin time as prognostic indicator in paracetamol induced fulminant hepatic failure. BMJ 1990; 301: 964–966.
20. Van Thiel DH, Udani M, Schade RR, et al. Prognostic value of thyroid hormone levels in patients evaluated for liver transplantation. Hepatology 1985; 5: 862–866.
21. Pereira LM, Langley PG, Hayllar KM, et al. Coagulation factor V and VIII/V ratio as predictors of outcome in paracetamol induced fulminant hepatic failure: relation to other prognostic indicators. Gut 1992; 33: 98–102.
22. Dawson DJ, Babbs C, Warnes TW, et al. Hypophosphataemia in acute liver failure. BMJ (Clin Res Ed) 1987; 295: 1312–1313.
23. Davenport A, Will EJ. Hypophosphataemia in acute liver failure. BMJ (Clin Res Ed) 1988; 296: 131.
24. Nanji AA, Anderson FH. Acute liver failure: a possible consequence of severe hypophosphatemia. J Clin Gastroenterol 1985; 7: 338–340.
25. Trey C, Davidson CS. The management of fulminant hepatic failure. Prog Liver Dis 1970; 3: 282–298.
26. Segal MR. Regression trees for censored data. Biometrics 1988; 44: 35–47.
27. Forsstrom JJ, Dalton KJ. Artificial neural networks for decision support in clinical medicine. Ann Med 1995; 27: 509–517.
28. Subramanian R, Khardori R. Severe hypophosphatemia. Pathophysiologic implications, clinical presentations, and treatment. Medicine (Baltimore) 2000; 79: 1–8.
29. Lee WM, Galbraith RM, Watt GH, et al. Predicting survival in fulminant hepatic failure using serum Gc protein concentrations. Hepatology 1995; 21: 101–105.
30. Shakil AO, Kramer D, Mazariegos GV, et al. Acute liver failure: clinical features, outcome analysis, and applicability of prognostic criteria. Liver Transpl 2000; 6: 163–169.
31. O'Grady JG, Gimson AE, O'Brien CJ, et al. Controlled trials of charcoal hemoperfusion and prognostic factors in fulminant hepatic failure. Gastroenterology 1988; 94: 1186–1192.

0041-1337/03/7512-2014/0
TRANSPLANTATION Vol. 75, 2014–2018, No. 12, June 27, 2003

THE SUPERIOR RESULTS OF LIVING-DONOR RENAL TRANSPLANTATION ARE NOT COMPLETELY CAUSED BY SELECTION OR SHORT COLD ISCHEMIA TIME: A SINGLE-CENTER, MULTIVARIATE ANALYSIS

J. I. ROODNAT,[1,5] I. C. VAN RIEMSDIJK,[1] P. G. H. MULDER,[2] I. DOXIADIS,[4] F. H. J. CLAAS,[4] J. N. M. IJZERMANS,[3] T. VAN GELDER,[1] AND W. WEIMAR[1]

Background. **The results of living-donor (LD) renal transplantations are better than those of postmortem-donor (PMD) transplantations. To investigate whether this can be explained by a more favorable patient selection procedure in the LD population, we performed a Cox proportional hazards analysis including variables with a known influence on graft survival.**

Methods. **All patients who underwent transplantations between January 1981 and July 2000 were included in the analysis (n=1,124, 2.6% missing values). There were 243 LD transplantations (including 30 unrelated) and 881 PMD transplantations. The other variables included were the following: donor and recipient age and gender, recipient original disease, race, current smoking habit, cardiovascular disease, body weight, peak and current panel reactive antibody, number of preceding transplants and type and duration of renal replacement therapy, and time since failure of native kidneys. In addition, the number of human leukocyte antigen identical combinations, first and second warm and cold ischemia periods, left or right kidney and fossa, donor kidney anatomy, donor serum creatinine and proteinuria, and transplantation year were included.**

Results. **In a multivariate model, donor origin (PMD vs. LD) significantly influenced the graft failure risk censored for death independently of any of the other risk factors (P=0.0303, relative risk=1.75). There was no time interaction. When the variable cold ischemia time was excluded in the same model, the significance**

[1] Department of Internal Medicine, University Hospital Rotterdam-Dijkzigt, The Netherlands.
[2] Department of Epidemiology and Biostatistics, Erasmus University Rotterdam, The Netherlands.
[3] Department of General Surgery, University Hospital Rotterdam-Dijkzigt, The Netherlands.
[4] Department of Immunohaematology, University Hospital Leiden, The Netherlands.
[5] Address correspondence to: J. I. Roodnat, Room CA305, University Hospital Rotterdam-Dijkzigt, Dr. Molewaterplein 40, 3015GD Rotterdam, The Netherlands. E-mail: jroodnat@erasmusmc.nl.

Received 6 March 2002. Revised 27 June 2002 and 29 October 2002. Accepted 8 January 2003.
DOI: 10.1097/01.TP.0000065176.06275.42

of the influence of donor origin on the graft failure risk increased considerably, whereas the magnitude of the influence was comparable (P=0.0004, relative risk=1.92). The influence of all other variables on the graft failure risk was unaffected when the cold ischemia period was excluded. The exclusion of none of the other variables resulted in a comparable effect. Donor origin did not influence the death risk.

Conclusion. **The superior results of LD versus PMD transplantations can be partly explained by the dichotomy in the cold ischemia period in these populations (selection). However, after adjustment for cold ischemia periods, the influence of donor origin still remained significant, independent of any of the variables introduced. This superiority is possibly caused by factors inherent to the transplanted organ itself, for example, the absence of brain death and cardiovascular instability of the donor before nephrectomy.**

The dire need of kidneys for transplantation has led to increasing numbers of living (un)related donor transplantations. In univariate analyses, living-donor (LD) kidney transplantations have been shown to have better results compared with postmortem donor (PMD) transplantations (*1–5*).

Figure 1 shows the results of a univariate analysis regarding survival with a functioning graft (overall graft survival) of LD versus PMD transplantations performed at our center. At 5 years, the graft survival is 80% in those who received an organ from an LD versus 58% in those who received an organ from a PMD. We speculated whether this difference could be attributed completely to organ origin or whether other differences between the LD and the PMD populations play a role. We investigated whether the difference in graft survival between the two populations can be explained on the basis of differences in the prevalence of variables with a known influence on graft survival. We performed a multivariate analysis to correct for other variables with a known influence on the graft failure risk censored for death.

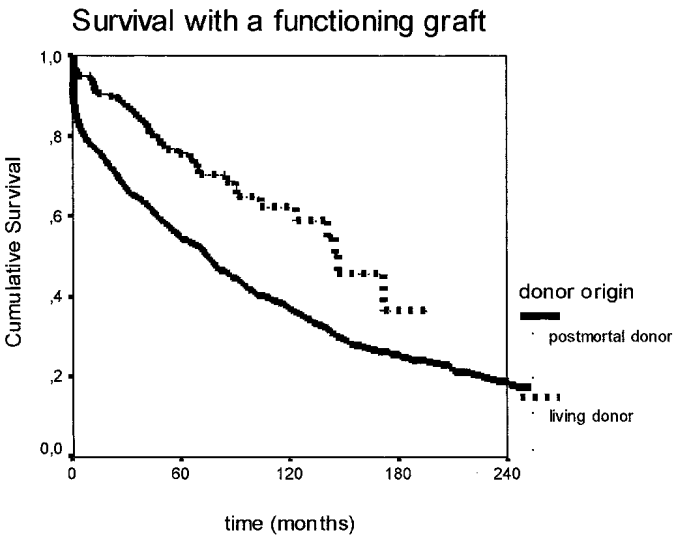

FIGURE 1. Kaplan Meier curve comparing survival after living-donor (LD) versus postmortem donor (PMD) transplantation.

MATERIALS AND METHODS

Patients

The first living (un)related renal transplant performed at the University Hospital Rotterdam "Dijkzigt" was in 1981. Between January 1981 and July 2000, 1,124 kidney transplantations were performed. The analysis was performed in June 2001, and all patients had at least 1 year of follow-up. One or more variables were missing in 29 patients (2.6%).

Immunosuppression

Initially, azathioprine was the primary immunosuppressant, administered in a dose of 2 to 3 mg/kg body weight. From July 1983 onward, cyclosporine has been the primary immunosuppressant, administered on the basis of 12-hr trough levels. Steroids were started on the day of transplantation and were gradually tapered to a maintenance dose of 10 mg of prednisone daily 6 months after transplantation. Throughout the study period, patients were included in several immunosuppressive treatment protocols. Although some of these treatments resulted in a significant reduction in the number of acute rejection episodes, none of them resulted in a significant increase in 1-year graft or patient survival.

Statistical Analysis

Two separate analyses were performed: Graft survival censored for death was the endpoint of observation in the first analysis, and patient survival censored for graft failure was the endpoint of observation in the second analysis. The observation included a 3-month period after graft failure. There were no exclusions for technical or nonimmunologic failures. Potential associations with survival were analyzed with the Cox proportional hazards regression model. Apart from donor origin (LD or PMD), the 23 variables mentioned in Table 1, transplantation year, and native kidney disease were candidate explanatory variables (26 variables).

Because the number of variables was large compared with the number of events (n=362), a univariate analysis was performed on all variables separately. The nine variables with the highest P values (P>0.23) were excluded, and the model was run with the 17 other variables. Variables were selected by backward elimination using likelihood ratio tests. When no more variables met the criteria for exclusion, the nine variables that were excluded previously were included simultaneously in the model and tested again using backward elimination.

Linearity of the influence of all variables was checked by the introduction of high-order variables (e.g., squares). To investigate the time dependency of the effect of all remaining variables on the risk for graft failure censored for death, we performed an analysis according to Smits et al. (*6*). First, an attempt was made to estimate and test time dependency by one coefficient for the interaction between the linear predictor as a whole and the logarithm of time (one mutual time interaction term). Next, a comparison was made with a model in which each explanatory variable had its own interaction with the logarithm of time, irrespective of its coefficient in the linear predictor of main effects. In case the latter model seemed superior in terms of goodness-of-fit, backward elimination was used to further try to take out time dependencies to obtain the final model.

Because the influence of azathioprine and cyclosporine on survival seemed to not satisfy the proportional hazards assumption, we chose to stratify for immunosuppressive medication. The analyses were performed with SPSS for Windows version 9.0 (SPSS Inc., Chicago, IL). P values 0.05 or less were considered significant.

RESULTS

Similar to the trend observed in many centers worldwide, the number of LD transplantations performed in our center has increased, and the number of PMD transplantations has

TABLE 1. Transplantation characteristics

	All	LD	PMD	*P*
Number	1,124	243	881	
Recipient age (mean±SD)	44.8±13.5	39.5±13.7	46.3±13.0	<0.0001
Male recipients (%)	58.5	58.4	58.5	NS
Recipient race (% white)	80.1	81.9	79.6	NS
Recipient weight (kg)	68.9±14.0	70.0	68.6	NS
Current smoking (%)	38.4	39.9	38.0	NS
Cardiovascular disease (%)	11.4	10.3	11.7	NS
Peak PRA (mean±SD)	27.6±30.0	18.9±25.8	30.0±30.7	<0.0001
Current PRA (mean±SD)	10.9±21.0	8.4±19.1	11.6±21.5	0.035
First transplant (%)	79.4	87.7	77.2	0.001
No preceding RRT (%)	9.7	24.7	5.6	<0.0001
Time since failure native kidneys (mo)	41.2±50.9	28.1	44.8	<0.0001
Time on RRT before present transplantation (mo)	30.3±31.4	16.6±23.8	34.0±32.2	<0.0001
Donor age (mean±SD)	39.8±16.3	45.6±12.7	38.2±16.8	<0.0001
Male donors (%)	58.9	49.4	61.5	<0.0001
Donor creatinine (umol/L)	86.4±36.7	74.2±14.9	89.9±40.1	<0.0001
Donor proteinuria (%)	19.1	0	25.8	<0.0001
Normal anatomy kidney (%)	78.7	84.4	77.2	0.013
Left kidney (%)	45.6	48.1	44.9	NS
Left fossa (%)	47.4	48.6	47.1	NS
First warm ischemia period (min)	1.4±3.5	2.7±4.2	1.1±3.2	<0.0001
Second warm ischemia period (min)	30.5±11.0	28.4±10.4	31.1±11.1	<0.0001
Cold ischemia period (hr)	21.6±12.0	2.5±0.8	27.3±7.3	<0.0001
HLA identical (%)	16.0	23.0	14.1	0.001

LD, living donor; PMD, postmortem donor; PRA, panel reactive antibody; SD, standard deviation; RRT, renal replacement therapy; HLA, human leukocyte antigen; NS, not significant.

decreased. The percentage of LD transplantations represents more than one-third of the total number of transplantations performed in the last 5 years. Most LDs were siblings (who more often donated to brothers than to sisters), and parents were the next most frequent donors. Partner donation has increased during the last 2 years.

The LD and PMD recipient populations differed in many respects. Transplantation characteristics are shown in Table 1. Recipients were significantly younger and donors were significantly older in the LD population compared with the PMD population. Peak and current panel reactive antibody were lower in those who received an LD organ. Recipients of an LD organ waited a shorter time for the transplantation, and hemodialysis was used less often. This is because more patients received an LD organ without preceding renal replacement therapy. Warm ischemia time was significantly longer in the LD population because of the introduction of laparoscopic donor nephrectomy in 1999. As would be expected, cold ischemia time was significantly shorter in the LD population. Donor serum creatinine was significantly lower in the LD population. Although the mean number of human leukocyte antigen (HLA) mismatches was not different between the groups, there were significantly more HLA identical transplantations in the LD population. In addition, there were more first transplants, more female donors, and more frequent normal anatomy in the LD population (Table 1). The prevalence of the various native kidney diseases was not different between the populations.

There were 362 failures and 244 deaths in the period studied. In the method by Smits et al., (*6*) the interaction of each variable with the logarithm of time is proportional to the main effect of that variable, with the same proportionality parameter for all variables. This constant proportionality parameter was tested for significance, and the model was not significantly better compared with the model without time-interaction variables ($P=0.6974$). However, this model is a simplification of the model in which the interaction with the logarithm of time is left completely free (i.e., independent of the main effect). Subsequently, this complete model was tested, and here we did find an amelioration of the fit of the model with all variables having their own interaction with time ($P=0.008$ likelihood ratio test). Because not all time-interaction variables significantly influenced the risk, we decided to eliminate those according to the backward elimination method. Finally, only two time-interaction variables were left that exerted a significant effect on the risk of failure. These were cold ischemia time ($P=0.0126$) and donor serum creatinine ($P=0.0393$). This final model did not fit significantly worse with the data than the model with all time interactions ($P=0.099$ likelihood ratio test).

Donor origin significantly influenced the graft failure risk censored for death without interaction with any of the other variables or time. To find out which variables were most influential for the success of LD renal transplantation and its superior results, each variable (one at a time) was eliminated from the model. Thus, the model was run nine times, each time omitting another variable. When the model was run without cold ischemia time, the same variables turned out to influence the risk for graft failure with comparable significance and magnitude in both models (Table 2). However, the influence of donor origin became more significant with a comparable magnitude (Table 2). The exclusion of none of the other variables resulted in such a large shift in significance of the influence of donor origin (data not shown). The other variables with a significant influence on the graft failure risk are shown in Table 2.

Donor origin was not found to influence the death risk in a separate analysis.

TABLE 2. Results of the Cox proportional hazards analysis

	Multivariate Cox proportional hazards analysis					
	Model with cold ischemia time			Model without cold ischemia time		
Graft failure censored for death	Exp (B)	95% CI for Exp (B)	*P*	Exp (B)	95% CI for Exp (B)	*P*
Cold ischemia period (hr)	1.0102	0.9939–1.0267	<0.0001			
Cold ischemia period*ln (time) time in months	0.9999	0.9999–1.0000				
Donor creatinine	1.0035	1.0005–1.0065	<0.0001	1.0039	1.0009–1.0068	<0.0001
Donor creatinine*ln (time) time in months	1.0009	1.0000–1.0017		1.0007	0.9999–1.0016	
Recipient age (yr)	0.9829	0.9744–0.9914	0.0001	0.9829	0.9745–0.9914	0.0001
Donor gender (female)	1.3985	1.1220–1.7433	0.0028	1.4029	1.1260–1.7478	0.0025
Donor age (yr)	0.9764	0.9496–1.0041	0.0030	0.9751	0.9483–1.0027	0.0029
Donor age squared (yr)	1.0004	1.0001–1.0008		1.0005	1.0001–1.0008	
HLA matching (nonidentical)	1.6262	1.1433–2.3131	0.0068	1.5992	1.1249–2.2734	0.0089
Number of previous transplants			0.0106			0.0272
One	1.4637	1.1291–1.8973	0.0040	1.4468	1.1166–1.8745	0.0052
More			NS			NS
Transplantation year (yr)	0.9653	0.9383–0.9931	0.0147	0.9612	0.9352–0.9879	0.0046
Donor origin (cadaveric)	1.7523	1.0548–2.9111	0.0303	1.9157	1.3359–2.7472	0.0004
Peak PRA	1.0037	1.0003–1.0072	0.0338	1.0039	1.0004–1.0073	0.0288

DISCUSSION

There have been few studies comparing the influence of donor origin (LD or PMD) with the risk of graft failure in a multivariate analysis (*7–9*). There were two multicenter studies with large numbers of patients (*7*, *8*) and one small single-center study (*9*). All of the studies investigated the graft failure risk uncensored for death and showed a better prognosis for the LD population. This means that death was included in the analysis as an endpoint of observation. Including death as an endpoint of observation will influence and obscure the results, because the risk factors that determine death are unlikely to be the same as those that determine graft failure (*10*). Even worse, a variable that favorably affects the risk for graft failure may have a negative effect on the risk for death. This has been shown in the present study and other studies for recipient age; increasing recipient age is associated with increasing risk of death but with a decreasing risk of graft failure censored for death (*11–13*). Cold ischemia time was included in all three studies; the effect on the risk was not mentioned (*7*), not significant (*8*), and respectively significant (*9*).

The population studied in the present analysis consisted of patients who received an LD or a PMD transplantation. Most donors are siblings and parents, but the number of partners is increasing. Table 1 shows the characteristics, and it is striking that there are remarkable differences between the two populations concerning variables that are known from other studies to influence graft survival. In fact, the differences between the populations could explain the differences in graft survival between the LD and PMD populations. In the LD population, we more often see a lower number of previous transplants, lower peak and current panel reactive antibody, shorter cold ischemia period, lower donor serum creatinine, shorter period of renal replacement therapy before the present transplantation, normal anatomy of the kidney graft, and more HLA identical combinations. These have all been associated with a better prognosis (*5*, *7–9*, *13–23*). Conversely, lower recipient and higher donor age are associated with a worse prognosis concerning graft survival, and they are also dominate in the LD population (*11*, *12*, *24*). In the Cox proportional hazard analysis, all these influences are weighed, and the influence of one variable can be expressed adjusted for the influences of all other variables in the analysis. We found that the relative risk for graft failure censored for death is significantly influenced by donor origin, independently of any of the other variables (Table 2, $P=0.0303$). However, after exclusion of cold ischemia time and its time-dependent effect, the influence of donor origin is more significant ($P=0.0004$, relative risk=1.92), whereas the influence of the remaining variables is unaffected (Table 2). In the complete model, no interaction is found between cold ischemia period (and its time interaction) and donor origin. There is a dichotomy in cold ischemia time on the basis of donor origin, because 95% of the recipients of an LD organ have cold ischemia times between 77 and 255 min, whereas recipients of a PMD organ have cold ischemia times between 821 and 2,536 min. All this indicates that the superior results after LD transplantation are partly, but not completely, the result of the shorter cold ischemia periods in this population. An increased sharing of unknown immunologic variables (e.g., minor antigens) in the LD population that beneficially influences graft survival cannot be excluded. The rest of the difference in graft survival between LD and PMD populations seems to be the quality of the donor organ itself. It is possible that donor-related factors preceding and during nephrectomy, for example, brain death, use of vasopressins, cardiovascular instability, and differences in anesthetics during LD and PMD kidney procurement, could explain this difference (*25–29*).

REFERENCES

1. Terasaki P, Cecka JM, Gjerdson DWJ, et al. High survival rates of kidney transplants from spousal and living unrelated donors. N Engl J Med 1995; 333: 333–336.
2. Hariharan S, Johnson CP, Bresnahan BA, et al. Improved graft survival after renal transplantation in the United States, 1988 to 1996. N Engl J Med 2000; 342: 605–612.
3. Jones JW, Gillingham KJ, Sutherland DER. Successful long-term outcome with zero-haplotype-matched living related kidney donors. Transplantation 1994; 57: 512.
4. Foss A, Leivestad T, Brekke IB, et al. Unrelated living donors in 141 kidney transplantations. A one center study. Transplantation 1998; 66: 49–52.
5. D'Allesandro AM, Solinger HW, Knechtle SJ, et al. Living related and

unrelated donors for kidney transplantation: a 28 year experience. Ann Surg 1995; 222: 353.
6. Smits JMA, Houwelingen van HC, Meester de J, et al. Permanent detrimental effect of nonimmunological factors on long-term renal graft survival. Transplantation 2000; 70: 317–323.
7. Gjertson JW, Cecka JM. Living unrelated donor kidney transplantation. Kidney Int 2000; 58: 491–499.
8. Sesso R, Klag MJ, Meide S, et al. Kidney transplantation from living unrelated donors. Ann Intern Med 1992; 117: 983–989.
9. Madrenas J, Newman S, McGregor JR, et al. An alternative approach for statistical analysis of kidney transplant data: multivariate analysis of single center experience. Am J Kidney Dis 1988; 12: 524–530.
10. Matas AJ, Gillingham KJ, Sutherland DER. Half-life and risk factors for kidney transplant outcome. Importance of death with function. Transplantation 1993; 55: 757–761.
11. Roodnat JI, Zietse R, Mulder PGH, et al. The impact of donor age on renal graft survival. Transplant Proc 2000; 32: 136–138.
12. Roodnat JI, Zietse R, Mulder PG, et al. The vanishing importance of age in renal transplantation. Transplantation 1999; 67(4): 576–580.
13. Chertow GM, Milford EL, MacKenzie HF, et al. Antigen independent determinants of cadaveric kidney transplant failure. JAMA 1996; 276: 1732–1736.
14. Chertow GM, Brenner BM, Mori M, et al. Antigen independent determinants of graft survival in living related kidney transplantation. Kidney Int 1997; 63: S84-S86.
15. Opelz G. Impact of HLA compatibility on survival of kidney transplants from living unrelated live donors. Transplantation 1997; 27: 1473–1475.
16. Barama A, Oza U, Panek R, et al. Effect of recipient sensitization (peak PRA) on graft outcome in haploidentical living related kidney transplants. Clin Transplant 2000; 14: 212–217.
17. Bryan CF, Shield CF, Pierce GE, et al. Successful cadaveric renal transplantation of patients highly sensitized to HLA class I antigens. Clin Transplant 2000; 14: 79–84.
18. Cecka JM. The UNOS scientific renal transplant registry. Clin Transplant 1992; 1–16.
19. Connolly JK, Dyer PA, Martin S, et al. Importance of minimizing HLA-DR mismatch and cold preservation time in cadaveric renal transplantation. Transplantation 1996; 61: 709–14.
20. Gjertson JW. A multifactor analysis of kidney graft outcomes at one and five years post transpantation: 1996 UNOS update. Clin Transplant 1996; 343.
21. Karpinski J, Lajoie G, Cattran D, et al. Outcome of kidney transplantation from high-risk donors is determined by both structure and function. Transplantation 1999; 67: 1162–1167.
22. Thorogood J, Houwelingen JC, Persijn GG, et al. Prognostic indices to predict survival of first and second renal allografts. Transplantation 1991; 52: 831–6.
23. Thorogood J, Houwelingen JC, van Rood JJ, et al. Factors contributing to long-term kidney graft survival in Eurotransplant. Transplantation 1992; 54: 152–158.
24. Kerr SR, Gillingham KJ, Johnson EM, et al. Living donors > 55 years. To use or not to use. Transplantation 1999; 67: 999–1004.
25. Guesde R, Benoit B, Leblanc I, et al. Administration of desmopressin in brain-dead donors and renal function in kidney recipients. Lancet 1998; 352: 1178–1181.
26. Jawang B, Cheung HK, Yang LC, et al. Comparison of anesthesia for kidney procurement in living related donor and brain dead donor. Transplant Proc 1994; 26: 2375–2376.
27. Koo DDK, Welsh KI, McLaren AJ, et al. Cadaver versus living donor kidneys: impact of donor factors on antigen induction before transplantation. Kidney Int 1999; 56: 1551–1559.
28. Pratschke J, Wilhelm MJ, Kusaka M, et al. Brain death and its influence on donor organ quality and outcome after transplantation. Transplantation 1999; 67: 343–348.
29. Schnuelle P, Lorenz D, Mueller A, et al. Donor catecholamine use reduces acute allograft rejection and improves graft survival after cadaveric renal transplantation. Kidney Int 1999; 56: 738–746.

0041-1337/03/7512-2018/0
TRANSPLANTATION
Vol. 75, 2018–2023, No. 12, June 27, 2003
Printed in U.S.A.

METABOLIC EFFECTS OF A CORTICOSTEROID-FREE IMMUNOSUPPRESSIVE REGIMEN IN RECIPIENTS OF PANCREATIC TRANSPLANT

LIVIO LUZI,[1,4] LUCIA PICENI SERENI,[1] ALBERTO BATTEZZATI,[1] ATTILIO ELLI,[2] JEAN-PAUL SOULILLOU,[3] AND DIEGO CANTAROVICH[3]

Background. **A corticosteroid (CS)-free immunosuppressive regimen may be considered less diabetogenic than treatments including CSs principally after pancreas transplantation.**

Methods. **To test whether a CS-free immunosuppressive treatment is metabolically superior to a regimen including CSs, we prospectively studied 19 CS-free simultaneous pancreas and kidney (SPK) transplant recipients (body mass index=22±1 kg/m^2; cyclosporine dose=400±19 mg/kg/day; azathioprine dose=77±8 mg/day; basal plasma C-peptide=1.3±0.12 ng/mL) and 12 matched CS-treated SPK transplant recipients (prednisone dose=9±1 mg/day; basal C-peptide=2.2±0.2 ng/mL) by means of the 6,6-$^2H_2$-glucose infusion and the euglycemic insulin clamp (1 mU/kg/min, insulin infusion rate). In addition, six renal transplant recipients receiving a CS-free regimen were also studied as a control group.**

Results. **In the postabsorptive state, CS-treated SPK transplant recipients demonstrated comparable plasma glucose levels but higher plasma insulin levels**

[1] Department of Medicine, San Raffaele Scientific Institute, Milano, Italy.
[2] Ospedale Maggiore Policlinico, Milano, Italy.
[3] Division of Nephrology and Clinical Immunology, ITERT, Centre Hopitalier Universitaire, Nantes, France.
[4] Address correspondence to: Livio Luzi, M.D., Head, Amino Acid and Stable Isotopes Laboratory, San Raffaele Scientific Institute, Via Olgettina n. 60, 20132 Milano, Italy. E-mail: luzi.livio@hsr.it.

Received 5 March 2002. Revised 23 May 2002. Accepted 29 October 2002.

DOI: 10.1097/01.TP.0000065177.18714.2E