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Renal graft survival in native and non-native European recipients

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Abstract Most studies on the influence of recipient race on kidney transplant survival have been performed in the United States. Generally, they show a lower survival in African-Americans than in Caucasians. Since Rotterdam has gradually become a multi-ethnic society, we were able to study the effect of origin on kidney survival. We restricted our study to recipients of a primary cadaveric kidney graft between July 1983 and July 1997 who received cyclosporin as primary immunosuppression. Patients were divided into two main groups according to origin: European (n = 399) and non-European (n = 110). No statistical differences were found for mean donor age, sex distribution, or the total number of HLA-A and DR mismatches. Non-Europeans had significantly more mismatches on their HLA-B locus (P = 0.01) and recipient age was lower (P = 0,003). The reason non-Europeans had lost their native kidneys was more often hypertension and less often congenital or hereditary diseases compared to Europeans. The causes of death and of transplant failure did not differ. A multivariate Cox proportional hazards analysis did not show European or non-European origin to be an independent predictor of graft survival (two categories, P = 0.25). The variable origin in five categories did show an independent influence on graft survival, with Arab en African recipients running higher risks than European and Asian recipients. We conclude that, in our center, the prognosis after kidney transplantation is comparable for Europeans and non-Europeans; however, in the subcategories, Arab and African recipients have a worse prognosis.

Key words Kidney transplantation, race · Graft survival, ethnic differences

Introduction

The impact of ethnic origin on graft and patient survival after kidney transplantation is quite controversial. Most studies have been done in the United States, analyzing the results in Black Americans versus Caucasians [2, 5, 12, 14, 17, 18, 20, 27, 29, 31–33]. Only a few studies have addressed the effect in other races, and no studies have evaluated the results in non-Europeans living in Europe [3, 6, 9, 21, 26, 33]. Contrary to the American situation, our medical health system assures equal care for all inhabitants, largely excluding economic circumstances as an important factor influencing graft survival.

Part of our non-native population has a poor command of the Dutch language. This often results in misunderstandings, for example with regard to medication, which could have a negative influence on graft survival. We studied the differences in patient characteristics and graft survival between European and non-European renal transplant recipients at our center in Rotterdam.

Materials and methods

Patients

At the University Hospital Rotterdam-Dijkzigt, 805 kidney transplantations were carried out between July 1983 and July 1997. At the moment of analysis, all patients had at least half a year of follow-up. Of these 805 transplantations, 509 were primary ones with a cadaveric donor. These were divided into two categories according to the origin of the recipient: European (n = 399) and non-European (n = 110). The non-European population included patients of African descent (Surinam-creoles, n = 15; Antillians, n = 9; and Cape Verdians, n = 13); of Asian descent (Surinam-Hindustani, n = 29; Surinam-Chinese, n = 2; Indonesian, n = 11; and Chinese, n = 2); of Arab descent (Moroccans, n = 11; and Middle Easterners n = 2); and of Turkish descent, n = 16. Two variables for origin were defined: origin 2 (European and non-European) and origin 5 (European, African, Asian, Arab, and Turkish).

Donor origin is not reported in Europe, but estimations are that almost all donors are Caucasian because of various (including religious) objections to postmortem organ donation in many of the non-European communities. In the Netherlands, the national health service assures that health care is equally accessible to the entire population.

Immunosuppression

Steroids were given starting the 1st day of transplantation, and they were slowly tapered to 10 mg of prednisone daily. Cyclosporine (CyA) was used as primary immunosuppression in all patients. CyA was started at a dose of 2 mg/kg i.v.; later, 4 mg/kg was given orally, while the same corticosteroid regimen was given. No patient received triple therapy on a routine basis.

Statistical analysis

Kidney transplant survival was defined as a patient's being alive with a functioning graft. There were no exclusions for technical or nonimmunological failures. Potential associations with graft survival were analyzed by means of the Cox proportional hazards regression analysis. Recipient and donor age, gender, and blood group, HLA mismatches on the A, B, and DR loci, recipient origin, original disease, and transplantation year were analyzed as independent variables. The difference in goodness-of-fit of the model, when origin 2 or origin 5 was introduced, was tested with the chi-square test. Patient characteristics were compared with an unpaired t-test when they were continuous. Discrete variables were tested with a chi-square test. A P value below 0.05 was considered significant. All data are presented as mean ± SD.

Table 1 Characteristics of the patient population

	Europeans	non-Europeans	P
n	399	110	
Age recipient (years)	49 ± 12	45 ± 13	0.003
Age donor (years)	38 ± 16	39 ± 17	NS
Gender recipient (m/f)	224/175	67/43	NS
Gender donor (m/f)	247/147	63/42	NS
Recipient blood group			
A	46%	34%	0.023
B	10%	20%	0.003
AB	5%	8%	NS
O	39%	38%	NS
Donor blood group			
A	44%	33%	0.030
B	8%	15%	0.024
AB	2%	4%	NS
O	46%	48%	NS
Observation time (months)	54 ± 45	44 ± 39	0.0433

Table 2 Comparison of HLA matching in the European and the non-European population

	Europeans	non-Europeans	P
Mean HLA mismatches			
A	0.71 ± 0.65	0.84 ± 0.70	NS
B	0.79 ± 0.61	0.95 ± 0.64	0.015
DR	0.48 ± 0.56	0.46 ± 0.54	NS

Table 3 Causes of renal failure in the European and non-European population

	Europeans	non-Europeans	P
Glomerulonephritis	27%	24%	NS
Interstitial disease	20%	13%	NS
Congenital or hereditary disease	17%	7%	0.009
Hypertension, renovascular disease	11%	22%	0.003
Diabetes mellitus	6%	9%	NS
Systemic disease	4%	7%	NS
Unknown	15%	18%	NS

Results

The characteristics of the two main groups are presented in Table 1. Donor age and donor and recipient gender did not differ between the groups. Recipient age was significantly lower in the non-European population. Blood group A was significantly less prevalent and blood group B more prevalent in the non-European compared to the European recipients. The same was true for the donor blood groups. Table 2 shows that the number of HLA mismatches on the A and DR loci did not differ between the groups, but non-Europeans had significantly more mismatches on HLA B. In non-European recipients, hypertension was more frequently observed as the cause of failure of their own kidneys (Table 3). This was caused by a higher incidence (though not significant) of hypertension in the African and Arab population. Congenital and hereditary diseases

Table 4 Numbers and causes of transplant failure in the European and non-European population

	Europeans	non-Europeans	*P*
N	399	110	
Number of failures	114	29	NS
Cause of failure			
Never functioning graft	9%	7%	NS
Surgical complications	25%	10%	NS
Acute rejection	30%	38%	NS
Recurring original disease	7%	0%	NS
Chronic rejection	13%	24%	NS
Infection	4%	7%	NS
Other	12%	14%	NS

Table 5 Number and causes of death in the European and non-European population

	Europeans	non-Europeans	*P*
N	399	110	
Number of deaths	124	24	NS
cause of death			
Cardiac	30%	25%	NS
Vascular	14%	9%	NS
Infectious	17%	25%	NS
Gastro-intestinal	4%	4%	NS
Treatment stopped	2%	0%	NS
Accidental	5%	4%	NS
Other causes	10%	8%	NS
Unknown	18%	25%	NS

were less frequently seen in the non-Europeans than in the Europeans. This was reflected in all non-European subgroups.

The causes of graft failure and the causes of death did not differ between the groups (Tables 4, 5). In the multivariate Cox analysis, recipient origin (two categories) was not a significant predictor of graft survival ($P = 0.25$). Figure 1 shows the survival curves of European and non-European recipients. Subdivision of the variable origin into five categories resulted in an improvement in goodness-of-fit of the model ($P < 0.05$). When the variable origin with five categories was introduced in the model, it turned out to be an independent variable influencing survival. Arab and African recipients had a significantly higher risk of either death or graft failure than Asian and European recipients (Fig. 2, Table 6). The other variables that were independent predictors of graft survival were recipient and donor age, original disease, recipient gender, and year of transplantation.

Discussion

Despite the early report by Opelz et al. in 1977 [25], showing a clear, negative impact of black race on kidney transplant outcome in the United States, the debate over the influence of race on kidney graft survival has not been settled. Several studies have demonstrated the existence of a racial disparity in transplant outcome, especially in long-term graft survival [4, 27]. Most of these studies have focused on the black race since they were performed in the United States. Some indicated

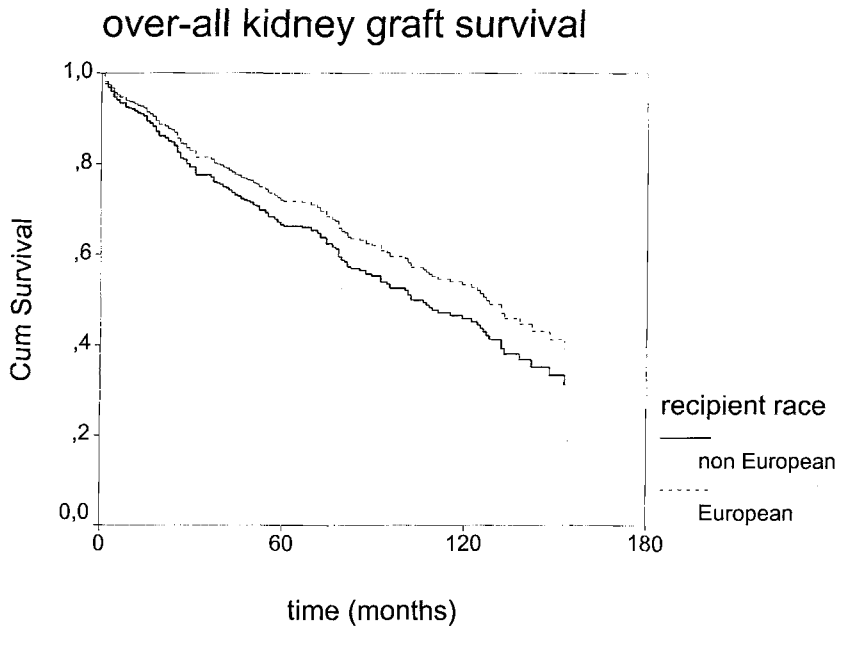

Fig. 1 Survival curves of Europeans ($n = 399$, - - -) and non-Europeans ($n = 110$, —). The difference was not significant ($P = 0.25$)

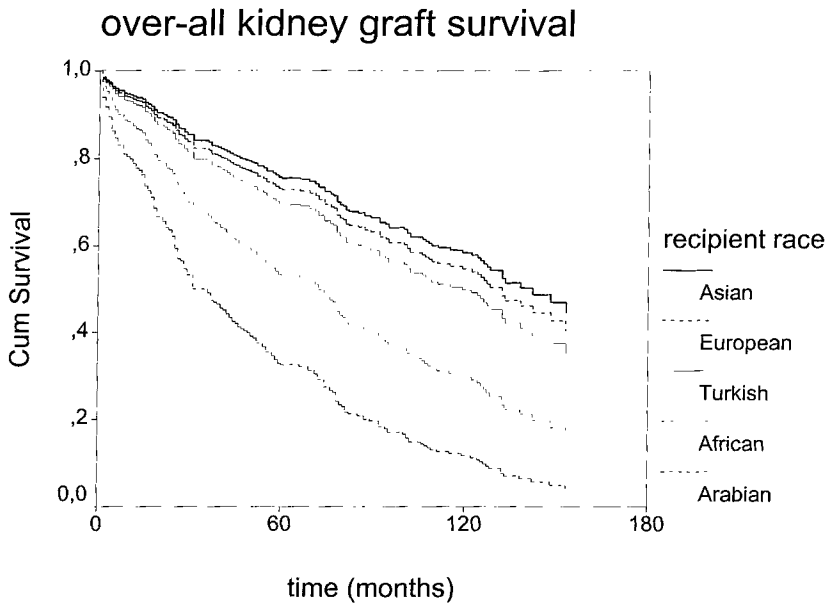

Fig. 2 Survival curves of the different racial categories. Asian (—), European (-----), Turkish (—), African (-----), Arabian (-----)

reduced transplant survival in blacks compared to whites [2, 9, 12, 14, 18, 20, 21, 26, 27, 29, 34], whereas others did not report any difference [3–5, 7, 17, 18, 31–33]. The results of kidney transplant survival in other non-black races compared to whites have appeared only sporadically in the literature [3, 6, 9, 21, 26, 33].

The issue of the effect of race is attracting increasing attention because it has been shown that it might influence long-term, rather than short-term, graft survival [4]. Several factors have been suggested to explain the results of kidney transplantation in the black population. These include: a higher prevalence of hypertension [4], poor compliance [2, 15, 21], stronger immunoresponsiveness [13], less living related kidney donation [22], and socio-economic variables [2, 8, 10, 16]. A higher degree of HLA polymorphism has also been demonstrated in blacks [19, 35]. This might cause a higher error rate in serological HLA-DR determinations [30]. Moreover, the most frequently occurring HLA haplotypes in blacks are different from those occurring in Caucasians [1, 11, 30]. This might explain why blacks have a smaller chance of getting equally HLA-matched kidneys from a predominantly Caucasian donor supply [19]. In many of the studies, HLA matching is relatively poor compared to European standards, and blacks often have worse matching than Caucasians [4, 9, 21, 23, 24]. Butkus et al. showed that although overall kidney graft survival in blacks was worse than in whites, there was no difference in graft survival between blacks and whites at any level of HLA mismatching [2].

In our patient population, graft survival was equal for European and non-European recipients. Except for a difference in recipient age and number of HLA-B mismatches, the risk variables for graft loss were comparable in both groups. As could be expected, blood group B was more prevalent in the non-European recipients. This was reflected in the donor population, indicating that non-Europeans with blood group B did not receive blood group O kidneys more often than Europeans.

Table 6 Results of the Cox proportional hazards analysis for over-all graft survival

	RR	95% CI	*P*
Variable race (5 groups)			0.037
European (reference category)	1		
Asian	1		NS
Turkish	1		NS
African	2.0	1.1–3.7	0.023
Arab	3.6	1.2–10.3	0.019

Hypertension and renovascular disease were more common causes of renal failure in non-Europeans. This could be expected because hypertension is more prevalent among originally African people. In addition, poor treatment of hypertension in the countries of origin leads to a higher incidence of terminal renal failure. However, hypertension in itself does not have an independent influence on renal graft survival [28]. In contrast, congenital and hereditary diseases were less frequently observed in the non-Europeans, possibly because they lead to death during childhood in less developed countries.

The number and causes of graft failure and of death did not differ. The possession of the European or non-European identity did not have an independent influence on graft survival (Fig. 1). In other words, European and non-European recipients of a first cadaveric kidney

graft have the same prospects. However, when studying the influence of the five racial categories, a significant influence on graft survival appeared, with the Arab recipients running the greatest risks, followed by the African recipients. The difference is significant when compared to Asian and European recipients. An explanation for the difference between the two racial variables could be that the opposite effects of the different races compensate each other. The difference between the five racial groups cannot be explained by socio-economic circumstances as they are equal for all inhabitants; however, the influence of cultural factors cannot be excluded. Of course, one must also consider the fact that there was a relatively small number of patients in each group. The other variables that showed an independent influence on graft survival are discussed elsewhere [28].

In conclusion, our single-center data do not support the concept that kidney graft survival is worse in non-European than in European recipients. Yet, Arab and African recipients do appear to have a higher relative risk of either death or transplant failure than European or Asian recipients.

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