Urology Journal
UNRC/IUA

Vol. 2, No. 1, 36-39 Winter 2005
Printed in IRAN

The Role of Pretransplant Smoking on Allograft Survival in Kidney Recipients

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ABSTRACT

Purpose: Cigarette smoking contributes to a number of health-related problems, but its impact on allograft survival in kidney recipients is not clear. This study was performed to evaluate the relationship between smoking and graft survival.

Materials and Methods: A total of 199 adult kidney recipients were enrolled in this study. All transplantations had been done in our center and all grafts had been taken from living donors. The patients were asked about their cigarette smoking behavior before transplantation and assessed for diabetes mellitus, hypertension, and hyperlipidemia, pre- and post-operatively.

Results: Of 199 recipients, 142 (71.4%) were male and 57 (28.6%) were female. They were 40.45 (range 18 to 65) years old. Forty-one recipients (20.6%) were smokers before kidney transplantation that 87.7% of them continued smoking after transplantation. Mean pack-year smoking was 13.2. Of the patients, 32.7% and 33.7% had hypertension, 19.3% and 23.1% had diabetes mellitus, and 46.2% and 42.2% had hyperlipidemia, before and after transplantation, respectively, showing no significant difference. Pretransplant smoking was significantly associated with reduced overall graft survival (P = 0.01), but no correlation between smoking cessation after transplantation with survival graft was found.

Conclusion: Cigarette smoking before kidney transplantation contributes significantly to allograft loss. However, smoking is not associated with increase in rejection episodes. Although we could not prove it, smoking cessation after renal transplantation may have beneficial effects on graft survival. These effects should be emphasized for patients with end-stage renal disease who are candidates for kidney transplantation.

KEY WORDS: smoking, kidney transplantation, graft survival

Introduction

Kidney transplantation is one of the recommended treatment modalities for young patients with chronic renal failure.[1] However, kidney transplant patients have an increased risk of atherosclerosis and neoplasm due to their chronic immunosuppressed state.[2,3] On the other hand, cigarette consumption is one of the well known causes of many systemic diseases and factors increasing mortality,[4] and considering the above-mentioned factors, renal transplant patients who smoke increase the risk of cardiac and pulmonary diseases, in comparison with those who do not smoke. However, does cigarette smoking affect the survival rate of kidney allograft? There are few studies pertaining to this topic[5,6,7]; some point to the positive outcome in those patients who quit smoking. Based on our review of the literature, there have not been such studies in our country. In this study, we reviewed the effect of pretransplant cigarette smoking on the survival of the

Received December 2002
Accepted June 2004
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transplant kidney in our center.

Materials and Methods

From 1989 to 2002, 360 patients underwent renal transplant from live donors at Golestan hospital of Ahwaz (affiliated with Ahwaz Medical School). All of the above-mentioned cases had complete records from the onset of their evaluation. These records had been updated upon each readmission. In addition, all of the patients had been under the care of the nephrologists in the area.

The inclusion criteria were age greater than 18, transplant at the above-mentioned center, receiving a first transplant, having at least one year post-transplant follow-up, being alive at the time of the study, and having the last evaluation record within the 6 months before the study. Given the above considerations, 199 patients were eligible for this study.

Reviewing the hospital records, the following data were collected: age, sex, age at time of transplant, history of diabetes, hypertension, and hyperlipidemia prior to transplant, rejection history, and history of smoking. The completed forms were reviewed by the authors and the most recent status of the patient (with regard to condition of the transplanted kidney, smoking status, diabetes, hypertension, and hyperlipidemia) were recorded.

After transplantation, all patients had been started on immunosuppressive agents including cyclosporine, azathioprine, and corticosteroids. In cases of rejection, patients had been treated with pulse steroid therapy or anti-thymus antibodies or anti-lymphocyte antibodies.

All collected data were analysed with SPSS 9.0 software package. The survival of the transplanted kidney was cumulatively calculated using Kaplan-Meier method. The subjects were divided into two groups of smokers and non-smokers prior to transplantation. Differences between groups were examined, using *t* test for continuous variables and Chi-square test for differences for categorical data. The cumulative survival of graft in the two groups were calculated and compared with Kaplan-Meier method and log-rank test. P value less than 0.05 was considered statistically significant.

Results

One hundred and forty-two (71.4%) of 199 recipients were male and 57(28%) were female. Female to male ratio was 2 to 5. Mean age was 40.45 (range 19 to 65) years. Characteristics of smokers prior to transplantation are shown in table 1. Forty-one recipients were smokers prior to transplantation (20.6%). The smokers had a mean 13.2 pack-year smoking history. Of this group, 87.7% continued to smoke after transplant and only 5 patients stopped smoking after receiving a renal transplant (12.2%), and 4 cases started smoking after transplant (all of them smoked less than half a pack per day.

There was not any significant age difference between smokers and non-smokers (47.9 ± 12.5 years vs. 42.6 ± 14.5 years) at transplantation time. However, smoking was more prevalent among males: 36 of 142 male recipients (25.4%) versus 5 of 57 female recipients (8.8%).

Mean 1- and 5-year cumulative graft survival were 78% and 67% in smokers and 84% and 73% in non-smokers (P = 0.01). Yet, this reduction of graft survival was not associated with acute rejection. In addition, gender had no major role in the effect of smoking on survival of transplanted kidney.

Thirty-eight recipients (19.9%) had suffered from diabetes before transplant and after transplant this number increased to 46 cases (21.61%). Hypertension increased from 32.7% to 33.7% after transplant and hyperlipidemia increased from 42.2% to 46.2% (table 2).

TABLE 1. *Smoking behaviors in kidney recipients*

	Number of patients (%)
Smoking history	41 (20.6)
<5 pack-year	8 (19.5)
5-10 pack-year	8 (19.5)
11-15 pack-year	5 (12.2)
16-20 pack-year	11 (26.8)
>20 pack-year	9 (22)
Smoking after transplant (continued)	36 (87.7)
Smoking after transplant (start)	4 (2)

TABLE 2. *Diabetes, hypertension, and hyperlipidemia in smokers and non-smokers*

	Smokers		Non-smokers	
	Pre-transplant	Post-transplant	Pre-transplant	Post-transplant
Diabetes mellitus	8	10	30	36
Hypertension	14	14	51	54
Hyperlipidemia	20	20	72	67

Five recipients quit smoking after transplant, yet in comparison to those who continued to smoke, there was no increase in survival of the allograft (P = 0.3)

Discussion

Kidney transplant recipients are susceptible to many illnesses, some of which are due to immunosuppressants.[7] Cigarette smoking increases risk of many diseases such as cancer and cardiac or pulmonary disorders. Combination of smoking and renal transplant may increase the risk of complications, resulted from either of these factors.[2,8] Renal transplant patients are at increased risk for atherosclerosis after transplant which may be the result of hypertension, hyperlipidemia, and hyperglycemia, all of which may be exacerbated with smoking.[9,10] Smoking alone increases the risk of coronary disease and vascular disorders.[5,11] In addition, smoking accelerates atherosclerosis in transplant recipients, which can lead to decreased survival of the allograft. This may be due to microvascular changes in the allograft, decreased plasma flow, elevation of endothelin-1, increased platelet aggregation, and increased thickness of renal artery.[12-14]

In our review, we have shown that smoking leads to a decrease in allograft survival. However, acute rejection rate in smokers was the same as that in non-smokers; therefore, smoking may not decrease survival via rejection. But, smoking can lead to microvascular injury, subacute rejection, and other unknown disorders relating to allograft rejection.[7]

Although the amount of smoking (pack-year) did not correlate significantly with the allograft survival rate, there has been a relative correlation with allograft survival in other studies.[6,7,15] In addition, it has been shown in some studies that cessation of smoking increases graft survival. Thus, it is not possible to know whether the decrease in graft survival is a result of smoking before transplantation or keeping on smoking after the transplantation.[7,15,16] In our study, we could not show a clear association of improvement in allograft survival with smoking cessation. However, this may be due to the small number of cases who quit smoking in our series. In this study, there was not a significant difference in the rate of hypertension, hyperlipidemia, and diabetes between smokers and non-smokers before and after transplantation. Therefore, it does not appear that smoking decreases allograft survival via the above-mentioned disorders. Another point mentioned in the literature is the social, economic, and educational differences between smokers and non-smokers, which makes them different in their cooperation and compliance.[17,18] For example, the majority of our smoker patients failed to follow the recommendation of their physicians to quit smoking. This may be a representation of non-compliance which can be seen in other areas of their health care. In our study, the number of recipients who started smoking after transplant surgery was very small and the quantity of smoking in this group was also very low. Yet, the effect of smoking after transplantation was not studied.

Conclusion

Cigarette smoking prior to receiving a renal transplant is associated with a decrease in graft survival, which seems not to be due to acute rejection. Cessation of smoking after receiving a transplant appears to have positive impact. However, this conclusion should be considered more in renal transplant candidates.

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