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Malignancies after renal transplantation: A single center retrospective study

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Abstract

A single center retrospective study Malignancies after renal transplantation are the third cause of graft loss. In this retrospective monocentric study, we analyzed the rates of malignancies in 750 patients who received a kidney transplant in our renal unit between 1981 and 2011 and the effects of the development of the malignancies in terms of graft outcomes. We also analyzed the influence of different immunosuppressive drug in the development of cancers. 12% of our transplanted patients developed a malignancy after transplantation. 51% of cases were non-melanocytic skin neoplasms. Other kind of tumors were less represented. 45.5% of patients lost their graft after the diagnosis of a neoplasm Vs 28% of transplanted patients without neoplasm. p <0.005. We observed no malignancies in patients receiving M-Tor based anti-rejection regimen.

Keywords: ISTDP; Eating disorders; Psychotherapy; Cost effectiveness

Introduction

Malignancies are the third cause of graft loss after kidney transplantation. According to the literature [1,2,3,4] the risk of cancer is 20 times higher than in the general population for non-melanocytic skin neoplasms and 15 times for tumors of the native kidney. Other types of neoplasms occur from 5 to 10 times more frequently than in non-transplanted patients. Malignancies have a negative effect on graft outcomes for both mortality and morbidity related to the tumor itself, and for the reduction of immunosuppression that may facilitate the development of acute or chronic rejection. In this study we wanted to investigate the rates of malignancies and their influence in terms of graft outcomes and if the different immunosuppressive regimens have influence on the development of malignancies in our cohort of transplanted patients.

Materials and methods

We conducted a retrospective observational cohort study to evaluate the occurrence of cancer in our population of kidney-transplanted patients. In our analysis, all transplanted patients in our nephrology unit were stratified in two groups (patients who developed a cancer after transplantation, and patients without cancer). Statistical analysis by means of χ^2, T test, odds Ratio when appropriate was performed to evaluate any difference between the two groups in terms of demographic characteristics, graft loss, renal function. Hence, patients with a diagnosis of malignancies after transplantation were stratified in groups according to immunosuppressive regimen to evaluate any difference in terms of rates of malignancies between different anti-rejection drugs. A Cox proportional hazard regression was performed to evaluate if age at transplantation, sex, being

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re-transplanted, induction therapy with Basiliximab or Thymoglobulin, use of mTOR achieved statistical significance as neoplastic risk factors at the multivariate analysis

Results

Of the 750 transplants of our center from 1991 to 2011, 90 patients (12%) developed a malignancy. The tumor was diagnosed after 3,6 ± 2,9 years after transplantation. Patients with neoplasm were male in 72% of cases and older (mean age at transplantation 51,1 ± 10,5 years Vs 47,1 ± 12,6 P <0.01 in non-neoplastic patients). 51% of tumors were of cutaneous origin, (22.2 % squamous cell, 18.8% basal cell, 12,2 Kaposi's sarcoma) 11 patients had carcinoma of native kidney (12.2%). Each of the other types of cancer were less frequent. (PTLD 5.5%, thyroid 4.4%, breast 3.3%, , bladder 3.3% and prostate 5.5 %). 41 kidneys were lost in patients with cancer (45.5%) compared to 186 of the 660 who did not develop tumors (28%) p <0.005 odds ratio: 2.1. In 28 of the 41 cases, graft loss was due to the death with a functioning kidney. The average time of loss of the kidney was 3.0 ± 2.6 years after diagnosis of cancer and 6.2 ± 3.3 years after transplantation. 22 of the 49 patients still in follow-up have chronic renal insufficiency defined as creatinine> 1.4 mg / dL. We observed no cases of malignancies in patients receiving immunosuppressive treatment with m-Tor, cyclosporine and steroids compared with 22% of patients on cyclosporine, azathioprine and steroids, 13% of those on cyclosporine, mycophenolate, and steroids and 14.2% of patients on cyclosporine and steroids (P <0.05) although the duration of follow up was different between treatment groups (tab 1) . The higher cancer incidence per patient-year was for patients receiving tacrolimus. At the multivariate analysis, only being re-transplanted resulted in an increased hazard ratio for developing a malignancy (14.2, p <0.05) while the use of m-TOR had a protective effect (hazard ratio 0,36, p <0,05).

Table 1: Type of Neoplasm and Immunosuppressive Regimens.

Immunosuppressive regimen	Number of patients starting treatment	Number of neoplasms for treatment	% of patients devolping cancers for each treatment	Cancer incidence per patient-year	Follow up (years)
Cya Aza Pred	117	27	22.2%	0.019	12 ±4,8
Cya Pred	84	13	14.2%	0.015	10,1 ± 5,9
FK Mmf Pred	33	7	16%	0.035	5,7± 3,5
Cya Mmf Pred	368	44	11.6%	0.019	5,9 ± 4,5
Cya m-TOR Pred	118	0	0	0	3,6 ± 2,9
Other various	30	0	0	0	-
Total	750	91	-		-

Abbreviations: CYA: Cyclosporine; Aza: Azathioprine; Pred: Prednisone; Mmf: Mycophenolate; FK: Tacrolimus; m-TOR: Sirolimus or Everolimus.

Discussion

The onset of cancer after kidney transplantation is a major cause of graft loss because of the higher mortality and morbidity related to the tumor itself. Furthermore, the reduction in immunosuppressive therapy usually made after the diagnosis of cancer can trigger the onset of acute or chronic rejection. Since skin and native kidney are more frequently involved, we strongly recommend following anti neoplastic screening measures (especially yearly dermatologic consulting and renal ultrasound) to recognize early lesions. In our series, the use of m-TOR appears to be protective against the development of malignancies. Since M-tor based protocols were started more recently in our institution, patients with m-tor based regimens have shorter follow up in our series. Nonetheless, since the development of neoplasms is an early event after transplantation the time of our observation can be considered sufficient to confirm an anti-neoplastic protection of m-TOR. Larger, metacentric, prospective studies are needed to confirm these results.

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