

Evaluation of the Effect of Serum Creatinine and Body Weight on Blood Pressure of Renal Transplant Recipients

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Introduction

Hypertension is a frequent complication of renal insufficiency¹. Unfortunately the incidence of hypertension does not decrease after transplantation^{1,2} and has been proposed that causes shortened graft survival^{2,3}. Also, its presence after transplantation has been considered an adverse prognostic factor for subsequent patient survival⁴.

Hypertension probably contributes not only to chronic allograft nephropathy but also to accelerated arteriosclerosis and arteriolosclerosis⁵. Blood pressure control is not always feasible and high rates of unsatisfactory blood pressure control have been reported⁶. Posttransplantation hypertension is multifactorial and immunologic and non-immunologic factors have been incriminated for this. Kasiske et al were unable to correlate hypertension and its treatment with subsequent graft loss to chronic rejection in a multivariate analysis of over 700 patients⁷. Obesity either at the time or after transplantation has been associated with shortened allograft and patient survival⁸, although the results are conflicting⁹ and there is no well-documented information concerning its influence on posttransplant hypertension.

We decided to investigate retrospectively the effect of renal function (serum creatinine levels) and body weight (Kg) on arterial blood pressure on a five year follow up basis after renal transplantation because of the contradictory information concerning the influence of these factors on posttransplant arterial blood pressure.

Patients and Methods

From 1.1.1987 to 31.12.1995, three hundred ninety five renal transplants took place in our center. We recorded retro-

spectively the blood pressure of 272 recipients (172 from LRD and 100 from cadaveric donor). In the study were not included pediatric transplants and patients with less than six months follow up. Hemodialysis was the replacement therapy for the 84.2% of the patients before transplantation and CAPD for the 15.8%. The immunosuppressive agents used were steroids; azathioprine (AZA) or mycophenolate mofetil (MMF), cyclosporine (CsA), antilymphocyte globulin (ALG) and the immunosuppressive protocols have already been described¹⁰. Blood pressure measurement was done in the morning, with the patient at sitting position. Each patient's blood pressure, serum creatinine (mg/dl) and body weight were recorded on the 7th, 15th, 30th posttransplant day, on the 3rd, 6th posttransplant month and on the 1st, 2nd, 3rd, 4th and 5th posttransplant year. Descriptive statistics was used to estimate means and standard deviations. Repeated measures analysis was used to estimate the changes of measured parameters during time. Multiple regression analysis was applied on the means of variables during time to evaluate the effect of body weight (kg) and serum creatinine levels on the recipient's blood pressure¹¹. A value of $p < 0.05$ was considered statistically significant. Quantitative results were expressed as Mean±SD. The Statistical Package for Social Sciences (SPSS for windows, version 11.0) was used.

Results

The mean SBP and DBP of the recorded patients from the 7th postoperative day to the end of the 5th year, as well as mean serum creatinine and body weight levels in the same time are shown in table 1.

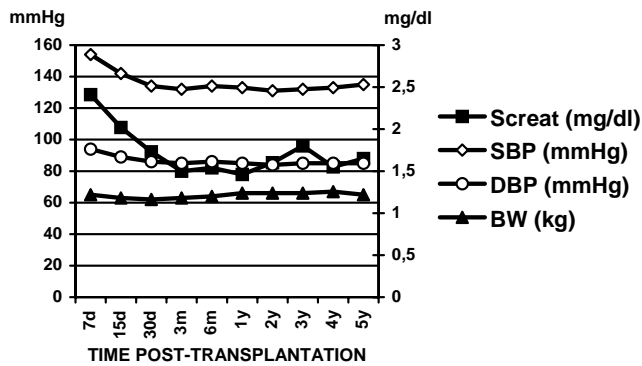
Table 1. Systolic/ diastolic blood pressure, serum creatinine and body weight during the 5 year follow up

Time	SBP (mmHg)	DBP (mmHg)	Serum creatinine (mg/dl)	Body weight (kg)
7 th pst/nt day	153.68±18.54	94.40±10.69	2.41±2.17	65.06±12.31
15 th pst/nt day	142.04±18.77	88.94±10.10	2.02±1.67	62.84±11.72
30 th pst/nt day	134.37±16.16	86.26±8.95	1.73±1.03	61.72±11.02
3 rd pst/nt month	132.48±15.81	84.72±9.63	1.50±0.61	62.93±10.51
6 th pst/nt month	134.12±15.86	86.16±9.65	1.54±0.75	64.57±10.57
1 st pst/nt year	133.58±17.35	85.50±10.00	1.46±0.46	65.79±11.40
2 nd pst/nt year	131.16±15.46	83.84±8.61	1.60±0.81	65.79±11.47
3 rd pst/nt year	131.64±18.2	84.72±10.20	1.80±1.39	65.60±11.33
4 th pst/nt year	133.24±16.20	85.22±8.59	1.55±0.79	66.50±11.69
5 th pst/nt year	134.72±14.22	84.62±8.50	1.65±1.04	65.56±11.41

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pst/nt: posttransplant



Repeated measures analysis showed that there was a significant reduction of SBP and DBP during the 1st year after transplantation (p: 0.000) while between 1st and 5th year there was no significant change. There was a significant body weight gain during the 1st posttransplant year (p: 0.000) while the next four years the body weight remained fairly stable (p: NS). Serum creatinine levels showed a significant fall during the 1st posttransplant year (p: 0.000) while there was a small but statistically significant raise of it during the next four years (p: 0.003).

Multiple regression analysis showed that serum creatinine had a significant impact on SBP (t: 7.00 and p: 0.0005) and DBP (t: 5.72 and p: 0.001) while body weight had no effect on systolic arterial blood pressure (t: 0.216 and p: 0.835) and diastolic blood pressure (t: -0.86 and p: 0.934) during the five year follow up.

Discussion

Atrial blood pressure after transplantation is influenced by intra – graft (rejection, donor hypertension, recurrence or de novo renal parenchymal disease development) and extra – graft (recipient hypertension before transplantation, immunosuppressive agents, renal graft artery stenosis, recipient age) factors^{10,12}. Often patients experience more than one of the identified causes and mechanisms. The graft dysfunction induced by rejection, acute or chronic, nephron underscoring, drug toxicity, de novo or recurrent glomerulonephritis or chronic atherosclerosis could result in hypertension. The routinely used marker for graft dysfunction is serum creatinine. In our study serum creatinine levels fell significantly during the 1st posttransplant year of follow up and this is in accordance with the reversal of acute rejection episodes, late recovery of grafts with delayed graft function (DGF) as well as with the lowering dose of cyclosporine that takes place in this time period. At the same time there was a significant reduction of systolic and diastolic blood pressure that fell to the lower levels at the end of the first year. We should say that the higher level of blood pressure during the first posttransplant month is possibly due to fluid overload during the transplant procedure, graft dysfunction, acute rejection episodes, steroid dose and higher cyclosporine levels. From the second to the fifth year of follow up we noticed a significant raise of serum creatinine. At the same time the

blood pressure remained at about the same levels with those measured at the end of the first year. In spite of this, multiple regression analysis showed that the blood pressure, systolic and diastolic, as dependent variable, was significantly affected by the serum creatinine changes during the five year follow up and this in agreement with the findings of Fernandez – Fresnedo et al¹³.

It has been reported that post-transplant hypertension negatively impacts long-term allograft survival^{3,14,15}. The analysis by Opelz et al, suggests a causal relationship between hypertension and chronic renal damage but already has been proposed that, even in these cases, hypertension activates inflammatory effector mechanism^{3,16}. The complex nature of post-transplant hypertension has made it difficult to discern if its occurrence is the cause or the consequence of chronic allograft dysfunction. The possibility remains that the two processes coexist. Hypertension is a known risk factor for atherosclerotic vascular disease, which is the leading cause of long – term patient mortality in kidney transplantation. Therefore irrelevant if hypertension were a consequence or a cause of renal allograft dysfunction it should still require careful therapy because of therapy's known benefit on the cardiac and cerebral vascular systems. Nevertheless, our results suggest that renal allograft function expressed by serum creatinine levels is an independent variable affecting significantly systolic and diastolic blood pressure during the five-year period after transplantation.

Obesity is a significant risk factor for cardiovascular disease (CVD) in the general population mainly because of induction of hypertension, insulin resistance and lipid abnormalities¹⁷ and has been proposed that weight reduction may help to reduce blood pressure¹⁸. The majority of renal transplant recipients presents 10% weight gain after transplantation¹⁹. Our finding of significant body weight gain during the 1st posttransplant year is in accordance with the findings of Johnson et al¹⁹. At the same time (1st year) there was a significant reduction of SBP and DBP and multiple regression analysis showed that there was no significant effect of body weight on the blood pressure, systolic or diastolic. The last finding combined with the knowledge that obesity causes hypertension in common people suggests that there are factors affecting blood pressure which are removed during the first year after transplantation so that the influence of weight gain on blood pressure is counterbalanced. Obesity is among the reasons end stage renal disease patients are not placed on the renal transplant waiting list²⁰. Recently the influence of obesity on posttransplant survival has been disputed and has been shown that obese patients with ESRD have improved survival after renal transplantation compared with remaining on the renal transplant waiting list with the exception of those with BMI ≥41 Kg/m²²¹.

In spite the negative result of our study the influence of obesity on posttransplant blood pressure remains open. Given that almost 90% of transplant recipients are hypertensives or prehypertensives according to the JNC 7th Re-

port²² most of our patients were taking antihypertensive treatment. Further studies must take into account the number of drugs used to regulate high blood pressure after transplantation and the body weight before renal transplantation (overweighed and underweighed patients before transplantation).

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