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## Clinical Risk Factors on Patient and Graft Survival After First Kidney Transplantation

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### Introduction

Survival after renal transplantation is the most important outcome measure when transplantation results are analyzed. The determinators of patient and graft survival after renal transplantation are incompletely known and conflicting results have been reported. Also it is universally accepted that there are various factors that may influence graft and patient survival. There are differences between centers that can result in 10% higher or lower graft survival. This may have been influenced by time related changes in patient selection, post – transplantation management and immunosuppressive regimens. In a previous study we found that grafts from living related donors are related with significantly better graft survival when compared with those from cadaveric donors and that donor hypertension, acute rejection and DGF affect negatively graft survival. Donor and recipient hypertension before transplantation negatively affect patient survival while recipients of a graft from LRD have better survival than those who had cadaveric donors<sup>1</sup>. Extending our survey we decided to estimate the influence of recipient hypertension after renal transplantation, donor and recipient age, cold ischemia time and waiting - list dialysis time on patient and graft survival.

### Material and Methods

From January 1, 1987 through December 31, 1996 four hundred forty two renal transplantations took place at Hippokratio General Hospital of Thessaloniki. The study cohort consisted of three hundred sixty three patients (363) that had their first kidney transplantation. There were 235 men and 128 women. Mean recipient age was 38.83±11.86 years (range 16.38 to 68.86 years). On hemodialysis were 297 and CAPD 54 patients. In twelve cases we were not able to define the mode of dialysis in our records. During this period 54 deaths were recorded.

There were 232 living related and 131 cadaveric donors. There were 163 male and 200 female donors the mean donor age was 51.00±16.94 years (range 1.7 to 84.46 years). The mean waiting – list time (time from starting dialysis to transplantation) was 2.29±2.48 years (range 0.08 to 16.65 years) and the mean cold ischemia time was 333.49±440.74 min (range 10 to 2940 min).

The influence of blood pressure on patient and graft survival was evaluated in 223 patients. From them, 157 were hypertensives and 66 normotensives. Patients who had not hypertension during the whole period of observation (early

or late hypertension) or had not full time follow up were excluded. The statistical analysis in this case was extended to three years because after this time the sample of normotensives was too small. We considered that there was hypertension when systolic blood pressure was more than 140 mmHg or diastolic blood pressure more than 90 mmHg in two or more different readings or the patient was taking antihypertensive treatment. Blood pressure was always measured in the morning with the patient in sitting position.

Descriptive statistics were used for the demographic data. The cumulative survival was estimated with the product limit method (Kaplan Meier) and the differences between group survivals were estimated by the methods log rank, Breslow and Tarone - Ware. The relative risk of patient death and graft loss was estimated with Cox Regression Analysis (Forward stepwise). Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for windows, version 10.1).

### Results

One and 5 year patient (pt) and graft (gr) survival of the whole sample was 96.14% (pts) / 87.33% (gr) and 90.63% (pts) / 68.60% (gr) respectively.

The relative risk of patient death was affected significantly by recipient age (rr: 1.043, p: 0.001) and waiting - list dialysis time (rr: 1.195, p< 0.0001 respectively). Donor age and cold ischemia time had no significant impact on patient death.

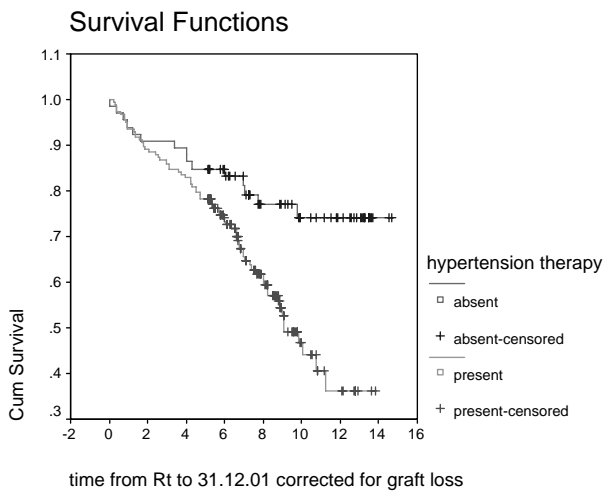
Donor age (rr: 1.018, p: 0.001) and cold ischemia time (rr: 1.000 p: 0.031 respectively) proved to be significant predictors of graft loss. Recipient age and waiting – list time had no significant impact on graft loss.

Hypertensive patient grafts presented significantly lower survival rates compared to grafts of normotensive patients (Log Rank: 0.001, Breslow: 0.022, Tarone – Ware: 0.007). Patient survival was not influenced by recipient hypertension after transplantation and the one and three year graft survival was 93.63 % / 78.34 % and 93.94 % / 84.85 % respectively, in hypertensives and normotensives.

**Table 1. The significant predictors of patient and graft survival**

Predictors	Patient survival		Graft survival	
	RR	p	RR	p
Recipient age (years)	1.043	0.001		NS
Donor age (years)		NS	1.018	0.001
Cold ischemia time (min)		NS	1.000	0.031
Waiting – list time (years)	1.195	0.0001		NS

**Fig 1. Graft Cum Survival of normotensive (red line) and hypertensive patients (green line).**



**Discussion**

Although long term survival following renal transplantation remains considerably below that of general population, it is much superior to that experienced by dialysis patients. Recently it was reported that the mortality risk of dialysis patients placed on a transplantation waiting – list was 68% lower among those receiving a transplant when compared with the patients remaining on the waiting list<sup>2</sup>. The overall patient and graft survival in our sample is in agreement with the results published recently in the Guidelines for Renal Transplantation by the EDTA<sup>3</sup>.

Several pretransplant variables may influence patient survival after transplantation. Patient and donor factors are strong determinants of renal transplant outcomes<sup>4</sup>. Faced with a perennial shortage of transplantable organs, donor acceptability criteria are being relaxed cautiously to include marginal donors as a means of expanding the potential donor pool<sup>5</sup>. The marginal donor pool includes non-heart beating donors and donors at the extremes of age. Adequacy of renal function is a major factor used to determine the viability of cadaver kidneys. Therefore conditions associated with diminished functional renal reserve (for example, advanced age, systemic illnesses leading to renal parenchyma damage, preexisting renal disease or hyperten-

sion) are often used as exclusion criteria for donor acceptability.

The incidence of deaths per year per 1000 transplant recipients, as reported to the UNOS Scientific Registry, revealed 25 deaths among pediatric recipients, 10 among adults under the age 75 years and 80 among adults at or above age 75 years<sup>6</sup>. A multivariate analysis suggested that reduced survival of cadaveric renal transplant recipients correlated with older patient age, longer duration of pre-transplant dialysis treatments, diabetes, and /or smoking, but not with any specific posttransplant variables<sup>7</sup>. Our sample contained a mixed population of 232 LRD transplants and 131 cadaveric. In spite of this, the relative risk (rr) for patient death was significantly higher in patients with older age and longer duration on dialysis (waiting – list time), in agreement with the previous observations, while cold ischemia time, donor age and hypertension after renal transplantation did not present any impact on patient survival (table 1).

It is already known that pretransplant donor hypertension is associated with reduced graft survival<sup>1</sup> and donor and recipient hypertension before transplantation affect negatively patient survival<sup>1</sup>. In this study, in agreement with others<sup>8</sup>, we have confirmed a significant negative association between posttransplant hypertension and graft outcome<sup>9</sup>. The hypertensive patients presented significantly lower graft survival compared to non – hypertensives (fig 1). Several authors have proposed that graft dysfunction rather than the presence of hypertension is the major determinant of graft prognosis<sup>10</sup> but this is a matter of debate. Kidney grafts with extended cold ischemia time (> 36 hours), as well as grafts coming from older donors (age > 55 years) have been characterized as marginal<sup>11</sup>. There is a controversy regarding the influence of prolonged graft ischemia and delayed graft function<sup>12-14</sup>. Our Cox regression model, in agreement with others, showed that donor age<sup>14</sup> and cold ischemia time<sup>12,13</sup> are the predictors of significant risk for graft loss. In spite of this, transplantation of marginal kidneys is associated with a significant survival benefit when compared with maintenance dialysis<sup>11</sup>. In our analysis the predictors patient age and waiting – list time had no impact on graft survival.

In summary our findings suggest that the older patient age and the accumulation of risk factors during dialysis<sup>15</sup>, influence negatively patient survival after transplantation<sup>15</sup>. The better patient survival after transplantation compared with patient survival on dialysis, shows that there is at least partial reversal of these factors<sup>16</sup>. Cold ischemia time, donor age and hypertension are significant adverse risk factors for graft loss. These factors must be taken into account seriously in the procedure of allograft allocation.

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