

Ninoslav IVANOVSKI<sup>1</sup>, Jelka MASIN<sup>2</sup>, Perko KOLEVSKI<sup>3</sup>,  
Olivera STOJCEVA-TANEVA<sup>4</sup>, Zivko POPOV<sup>5</sup>

## **USE OF ELDERLY LIVING KIDNEY DONORS – 20 YEARS OF EXPERIENCE IN THE BALKANS**

### **Abstract**

The Balkan region has changed dramatically over the past 20 years. Despite transplantation efforts, dialysis remains the standard way of treating end stage renal disease. Living renal transplantation is still the predominant transplant activity. Seeking to solve this problem, we decided to accept expanded criteria for living donors including the elderly, marginal, unrelated, and ABO incompatible individuals. We present our 20 years of experience with 230 living donor renal transplantations, using elderly individuals, including 90 individuals older than 65 years (mean age  $68 \pm 4.5$ ; range = 65 - 88; ED group). The predominantly haploidentical recipients had a mean age of  $45 \pm 6$  (range = 18 - 56 years). Sequential immunosuppressive protocols were used in all cases including induction with anti-thymocyte-globulin or interleukin-2 receptor antagonists. We analysed the

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<sup>1</sup> Clinical Hospital “Zan Mitrev” Skopje, Medical Faculty, University “SS Cyrill and Methodius, Skopje, North Macedonia (e-mail: nivanovski@yahoo.com)

<sup>2</sup> University Clinic of Nephrology, Medical Faculty, Skopje, North Macedonia

<sup>3</sup> Medical Faculty, University “SS Cyrill and Methodius”, Skopje, North Macedonia

<sup>4</sup> Centre for haemodialysis “Diaverum” Skopje, Medical Faculty, Skopje, North Macedonia

<sup>5</sup> Macedonian Academy of Sciences and Arts Skopje; Medical Faculty, University “SS Cyrill and Methodius, Skopje, North Macedonia  
(e-mail: zivkopopov2000@yahoo.com)

5-year Kaplan-Meier graft survival rate, rejection episodes, delayed graft function, and renal function for comparison with the outcomes of 110 kidneys from younger donors (mean age = 53.4 years; range 25 - 62; YD group) and haploidentical recipients (mean age 32.2; range = 16 - 42). This was performed within the same period. The 3- and 5-year cumulative graft survival rates in the ED group were 81% and 72% compared with 85% and 81% in the YD group, respectively ( $P > 0.9$ , NS). The incidences of acute rejection episodes were also comparable for both groups (19% and 17%, respectively). Delayed graft function occurred in 15% of the ED group but only in 8% in YD group. The serum creatinine value at the end of 60 months of follow up was 146.04  $\mu\text{mol/L}$  in the ED group versus 123.38  $\mu\text{mol/L}$  in the YG group ( $P < .001$ ). There were no major surgical complications in either group. We recommend the use of elderly living donors as a valuable source of kidneys, especially in countries where deceased donor transplantation has not yet been established.

**Keywords:** Kidney transplant, elderly donors, increased donor pool

## INTRODUCTION

In the last 30 years, the Balkan region in South Eastern Europe has changing dramatically. According to the EDTA – ERA registry data, the incidence and the prevalence of CKD patients in the Balkan countries is similar with those in Western Europe. However, transplant activity is still very low when compared with the developed countries, and dialysis remains the usual means of treatment. The shortage of available organs for kidney transplantation has led to several strategies in order to expand the donor pool. Our transplant centre promoted the strategy of acceptance of expanded criteria of living donors, including advanced age donors (over 65 years), marginal, unrelated, and ABO incompatible donors (1, 2).

Increased incidence of end-stage renal disease and an actual shortage of organs has led to the introduction of expanded criteria of organ donors including older donors. Thus, over the past decade older donors, (living or deceased) have become a relevant source of organs. Since 1999, the United Network for Organ Sharing reported an increase in kidney donors above age 65, an increase of 33% living donors and 26% for deceased donors. Initial

single centre reports of patient and graft survival of the recipients of kidneys from living donors 50 - 71 years old after 5 years are encouraging. Patient and graft survivals were comparable to those of recipients of younger living donor kidneys, and GFR appeared stable, though at a lower level (3, 4).

Our first experience of 28 older living donor recipients was published in the same journal 2001, but, despite the encouraging results, the significance was limited due to the limited number of transplant patients.

## **MATERIAL AND METHODS**

We performed a 5 year cumulative graft survival study in a total of 230 patients who underwent living donor renal transplantation in our Centre over the last 20 years. The living related (91.5%) and unrelated (8.5%) kidney donors were accepted according to our policy of widely acceptance of all potential donors. (1) Among the 230 subjects, 90 received kidneys from donors over 65 years of age (elderly donor group – EDG, mean age 68, range 66 - 86). The usual work-up for elderly donors was applied including the careful elimination of any potential risks associated with the donation process. Diabetic and nonregulated hypertensive elderly donors were excluded. The lower level of donor's GFR accepted for transplantation was 65 ml/min. Predominantly haploidentical children make up the recipient group (EDG) with a mean age of  $45 \pm 6$  (range 35 - 58) years. The usual preservation procedure with Euro-Collins solution was used. All recipients were treated with the Quadruple Sequential Immunosuppressive protocol including an induction therapy (ALG, ATG or IL-2R antagonists) and triple drug maintenance therapy with Micophenolat Mofetil or Azathioprin, Prednisolone and Cyclosporine A. Over the last 10 years (2000 to 2010), we used protocols with CyA minimisation corresponding to the Co trough level between 75 to 100 ng/m, full dose of MMF (2 gr/day) and induction with IL-2R antagonists or ATG for unrelated donors. The results were compared with the recipient's group of 140 patients (mean age 32.2, range 16 - 40 years) with the living donors younger than 65 years (YDG, mean age 53.4,

range 30 - 62). There was no statistical difference between the groups, warm and cold ischemia times, anastomosis time, HLA mismatches, racial distribution and number of unrelated donations.

## RESULTS

The 3 and 5 years Kaplan Meier cumulative death censored graft survival rate in the EDG was 81% and 72%, compared with 85% and 81% in the YDG without statistically significant differences (Log rank test:  $p = 0.6567$ ). Delayed graft function appeared in 15 patients in the EDG (16%) and 7 in the YDG (5%). Serum creatinine after 5 years of follow-up was  $146.04 \pm 33.9$  in the EDG compared with  $123.38 \pm 31.8$ . The rate of rejection episodes was low in both groups of patients: 16 (17%) and 17 (16%). The results are presented on Table 1 and Figure 1.

There were no significant surgical complications among the recipients and renal donors.

Table 1

Living donor recipient and transplant characteristics

	Age of the Donors		p
	>65 (68.3 years)	>65 (53.4 years)	< 0;01
N(%)	90 (40%)	140(60%)	<0;01
Age ( years)	45.6 (35-58)	32.2 (16-40)	<0,01
Male	55.4%	57.6%	ns
Related	85 (94%)	125 (89%)	ns
Nonrelated	5 (6%)	15 (11%)	ns
Cause of ESRD			
Glomerulonephritis	28%	29%	ns
Nephroangiosclerosis	20%	22%	ns
Lithiasis – Pyelonephritis	14%	16%	ns
Polycystic kidney disease	12%	13%	ns
Diabetes	7%	5%	ns
Others	19%	15%	ns
HLA mismatch	2.2	2.8	ns
WIT	3'	3'	ns
CIT	3.3 h	3.4 h	ns
Preservation	Euro-Colins	Euro-Collins	

Surgical complications			
Wound infections	8 (9%)	11 (8%)	ns
Lymphocells	6 (6.6%)	10 (7%)	ns
Ruptures	1	1	
Arterial kinking	3 (3.3%)	3 (2%)	ns
Renal artery stenosis	5 (5.5%)	7 (5%)	ns
Renal artery thrombosis	1	1	
DGF	15 (16%)	7 (5%)	0.001
Rejection episodes	16 (17%)	17 (15%)	ns
Serum creatinine	146 <sub>+33</sub>	123 <sub>+31</sub>	0.001

WIT – Warm Ischaemia Time

CIT – Cold Ischaemia Time

DGF – Delayed Graft Function

## DISCUSSION

Our findings confirmed the excellent clinical outcomes achieved with transplantation from older living donors, even over 65 years old. The excellent 5 graft survival rate in the EDG (74%) is not statistically different from those obtained with the younger donors (81%). Comparing our previous results regarding use of elderly living donors published in the same journal 10 years ago, it is clearly demonstrated that there are better short time outcomes regarding graft survival. The cumulative death censored graft survival rate of 74% after 5 years in the EDG is significantly better compared with 67% in the previous study. (5) The better graft survival rate is confirmed also in the YDG (74% vs. 81%, respectively). The introduction of new immunosuppressive protocols with ATG or IL-2R antagonists as an induction, a full dose of Micophenolat Mofetil as a part of a regular triple drug immunosuppression, and CNI minimisation protocols clearly contributed to better outcomes of living transplantation using elderly donors. Although the serum creatinine after 5 years of follow up was more among recipients of older living transplantation (146  $\mu$ mol compared with those with younger donors (123  $\mu$ mol/l), the results are still very satisfactory. Both values of serum creatinine are clearly superior when compared with

the graft function in deceased donor transplantation after 5 years (3, 6). DGF in our experience is still a clinically relevant problem when using elderly donors, but we strongly believe that the use of modern preservation solutions (HTC, Wisconsin, Celsior..) instead of Euro-Collins may contribute in minimising the problem. Regarding rejection episodes, we experienced a relatively low percentage (16 and 17% for both groups of the recipients), and this is also confirmed in daily clinical practice all over the world. The low percentage of rejection episodes may also contribute to better short and long term survival of renal transplantation.(7)

In summary, we confirm an excellent 5 years graft survival rate with living donors in our study cohort of 90 transplant recipients, even with those patients over 65 years of age. These results underline our policy to accept elderly donors as a valuable source of organs in the Balkans as well to recommend this practice to all regions where a deceased donor program is still underdeveloped. Thus, for further relevant conclusions regarding use of elderly living donors as a valuable source of organs, further additional long term survival studies are needed.

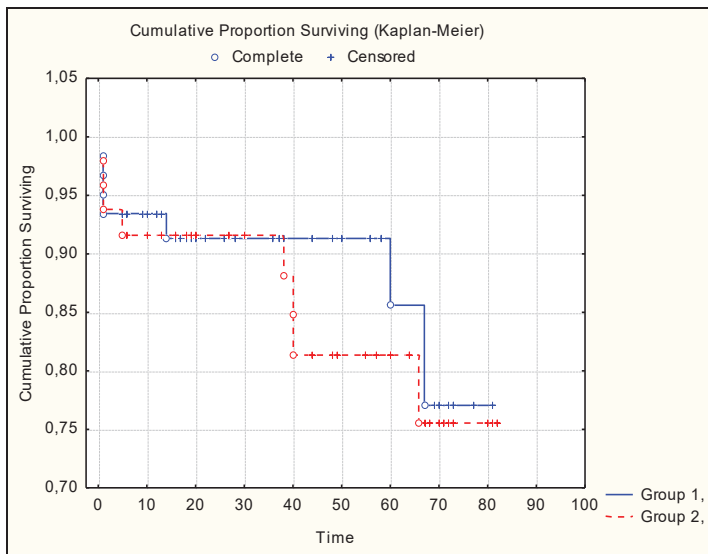


Figure 1 – Cumulative survival of kidney graft recipients regarding age N=219

Log rank test:  $p = 0.6757$

Group 1 – donor age < 65

Group 2 – donor age > 65

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