

## Original Research Article

# Association between the histopathologic findings of a zero-time biopsy and the donor kidney function 24 hours and a year after nephrectomy

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### ABSTRACT

**Background:** The living-donor transplantation (LDT) is essential to provide patients with chronic kidney disease (CKD) a superior quality of life and improve their lifespan. Recent investigations prove that the living donors (LD) have a risk of developing CKD, without there being a way to anticipate it. The zero-time biopsies provide valuable information that may contribute to this objective since they report histopathologic findings of subclinical chronic damage.

**Methods:** Retrospective, observational and analytical study. The information from the medical files and pathology department of LD attended at “Dr. Miguel Silva” general hospital from January 2006 to January 2018 was analyzed. The glomerular filtrate rate was obtained 24 hours and a year after nephrectomy and was estimated based on CDK-EPI. The comparison among groups was made through Mann-Whitney testing for continuous numeric. A value of  $p < 0.05$  was considered statistically significant.

**Results:** A total of 56 medical files were studied, 29 of which had a report of biopsy, the general prevalence of histologic anomalies was 65%. We found that those patients that showed a lower value in the GFR after 24 hours also showed lower GFR the next year, likewise a narrow and statistically significant correlation between the creatinine levels in the immediate post-operative period and the following year was found. In the same way, we found that the higher the dropping rate of GFR after 24 hours of nephrectomy, the lower the GFR a year after donation being statistically significant. It was decided to divide the sample into two groups (with and without histological alterations), it was found that a year later the GFR in the group with histological damage was less ( $75.6 \pm 21.7$  ml/min/1.73 m<sup>2</sup>) compared to the group without damage ( $85.2 \pm 11.6$  ml/min/1.73 m<sup>2</sup>) with a  $p < 0.05$  (Figure 4) and finally, there is association between the age group and the GFR the year after donation.

**Conclusions:** Among the candidates for LDT, the zero-time biopsy alterations, the age  $> 36$  years, the dropping of the GFR  $> 43\%$ , the GFR and the creatinine levels after 24 hours of nephrectomy were associated with a reduction of the GFR the year after nephrectomy.

**Keywords:** CKD, Kidney transplant, Zero biopsy

## INTRODUCTION

Living donor transplantation has been a necessity and an essential part of providing patients with CKD with a superior quality of life and increasing survival.<sup>1</sup> Recent research shows that donors are at risk of developing CKD, with no way to predict it so far.<sup>2</sup>

Living kidney donor selection practices aim to quantify the risk of kidney disease throughout life based on the demographic and health characteristics of a candidate. For a long time, donation was considered a relatively safe practice, however in recent years there has been a renewed interest in studying the effects of donors caused by nephrectomy.<sup>3,4</sup>

Zero-time biopsies are a diagnostic element that is performed just before or just after kidney implantation, they are evaluated in permanent sections and used to determine the baseline histological characteristics or subclinical disease of living or deceased kidney donors, in order to detect opportunely new alterations in the recipient; however, until today, it has not been taken as a starting point to analyse and correlate these results with the renal function of the donor after the loss of 50% of the renal mass.<sup>5</sup>

## METHODS

Retrospective, observational and analytical study, without anticipated risk. The clinical and pathology records of the living donors treated at the general hospital "Dr. Miguel Silva". The inclusion criteria were: Records of living donor patients who underwent nephrectomy for kidney donation in the period from January 2006 to January 2018 was analyzed, aged 18 to 60 and seen in the nephrology consultation at the general hospital "Dr. Miguel Silva" with a minimum follow-up time of 1 year.

### Exclusion criteria

Incomplete donor patient records. Records of patients who have presented hypotension 24 hours after nephrectomy and this explains the drop in GFR and patients with inadequate biopsy sample record were excluded from the study.

Descriptive statistics analysis was performed, measures of central tendency and dispersion were evaluated according to the distribution of variables. The comparison between groups was carried out using the Mann Whitney U test for numerical continuous variables. The statistically significant value was taken with a  $p < 0.05$ . The results will be presented in tables and graphs.

## RESULTS

This study included a total of 56 kidney donor patients who underwent left nephrectomy in 98.15%, whose mean

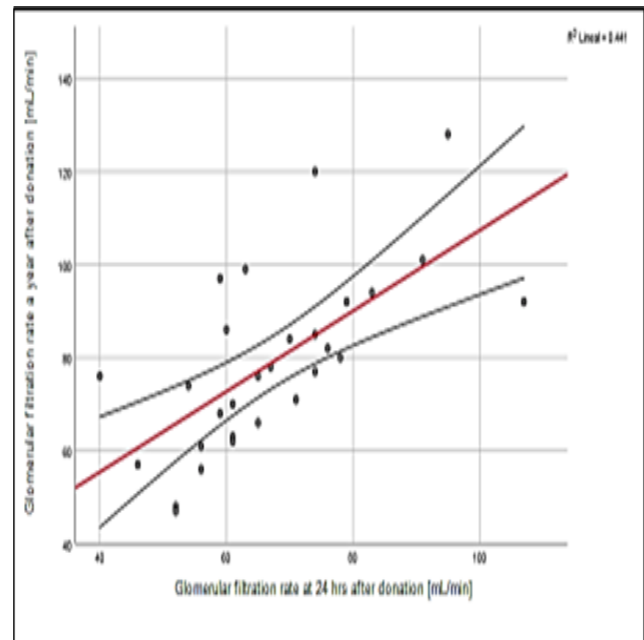
age was  $36.4 \pm 11$  years, the general prevalence of histological abnormalities was 65% (Table 1).

**Table 1: Baseline characteristics of the studied population.**

Variables	Mean	Standard deviation
Systolic pressure (mmHg)	117.38	13.56
Diastolic pressure (mmHg)	72.06	8.44
Size (M)	1.63	0.087
Age (years)	36.43	11.00
Weight (kg)	69.49	11.31
Glucose (mg/dl)	120.3	69.4
Creatinine (mg/dl)	0.69	0.12
Urea (mg/dl)	23.42	7.72
BMI (kg/m <sup>2</sup> )	26.00	3.57
Glomerular filtration rate (ml/min/ 1.73 m <sup>2</sup> )	115.50	12.96

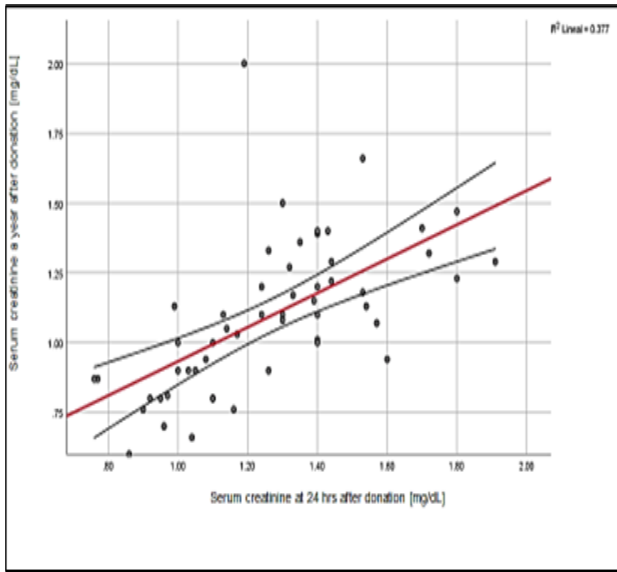
Of the total of the subjects, 50% were women, with a mean GFR before donation of  $115.5 \pm 12.9$  ml/min/ 1.73 m<sup>2</sup> and a mean serum creatinine of  $0.6 \pm 0.1$  mg/dl. The rest of the baseline characteristics are reported in Table 1.

When analysing the correlation between GFR at 24 hours and GFR at one-year post nephrectomy, a value of  $r = 0.66$  with a  $p < 0.001$  was found (Figure 1). showing to be significant at different points of time.



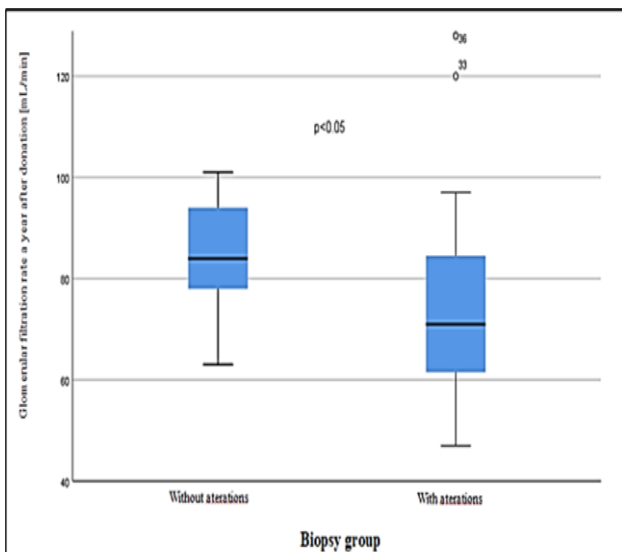
**Figure 1: Correlation between glomerular filtration rate at 24 hours and one year after donation.**

Performing the analysis by means of Pearson's correlation between serum creatinine at 24 hours and serum creatinine at one-year post nephrectomy, a value of  $r = 0.61$  with a  $p < 0.001$  was found (Figure 2), being a significant correlation at different points of time.



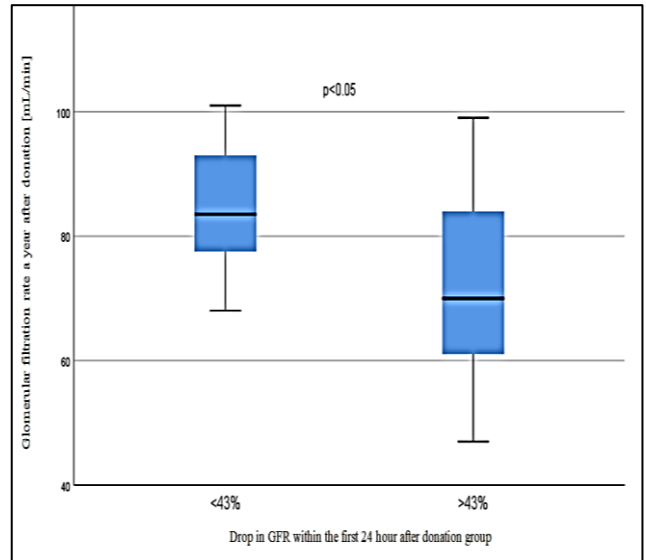
**Figure 2: Correlation between creatinine at 24 hours and one year after donation.**

Figure 3 shows the association between the histopathological findings of the zero time biopsy and the GFR one year after nephrectomy, for which it was decided to divide the sample of 29 patients into two groups, those who did not show documented histological damage with a damage index chronic damage by biopsy of 0 points and those who presented histological damage demonstrated by a chronic damage score greater than 1 in the preimplantation biopsy, finding that the GFR at one year in the group with histological alterations was lower compared to the group without histological alterations, for In the group without histological alterations, the mean GFR was  $85.2 \pm 11.6$  ml/min, while for the group with histological alterations, the mean GFR was  $75.6 \pm 21.7$  ml/min with a  $p < 0.05$  (Figure 3).



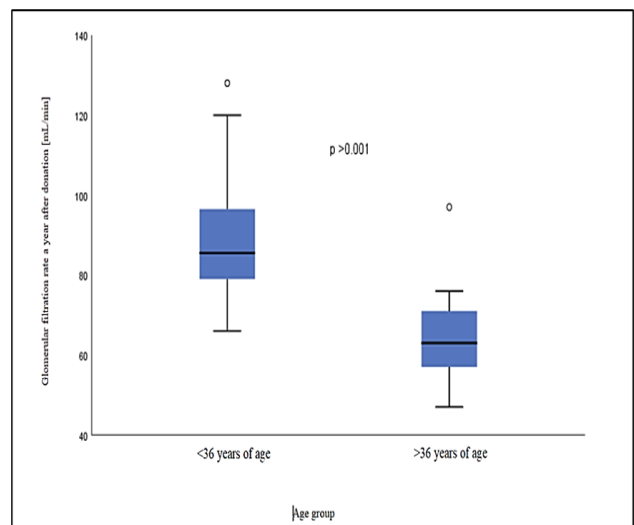
**Figure 3: Box and whisker plot between the groups with and without histological alterations in the zero biopsy.**

This box-and-whisker plot shows the association between the drop-in glomerular filtration rate expressed as a percentage at 24 hours and the GFR one year after nephrectomy, for which it was decided to divide the sample into two groups according to the mean drop, which was  $43 \pm 10.4\%$ ; We found a lower GFR at one year in the group with a drop  $< 43\%$  ( $87 \pm 16$  ml/min) and in the group with a drop  $> 43\%$  ( $73 \pm 19.4$  ml/min) significantly different with a  $p < 0.05$  (Figure 4).



**Figure 4: Comparison of the drop in GFR within the first 24 hours with the GFR a year after donation.**

This box and whisker graph shows the association between the age of the population and the GFR one year after donation, for which it was decided to divide the sample into two groups according to the mean age, which was  $36 \pm 11$  years; We found a significantly lower GFR at one year in the group aged  $> 36$  years with a  $p < 0.001$  (Figure 5).



**Figure 5: Comparison between age groups and TFG per year after donation.**

When analysing the correlation between GFR at 24 hours and GFR at one-year post-nephrectomy, a value of  $r=0.66$  with a  $p<0.001$  was found (Figure 1), showing to be significant at different points of time.

Performing the analysis by means of Pearson's correlation between serum creatinine at 24 hours and serum creatinine at one-year post nephrectomy, a value of  $r=0.61$  with a  $p<0.001$  was found (Figure 2), being a significant correlation at different points of time.

## DISCUSSION

In this research project, the association between GFR at 24 hours and one year after nephrectomy was evaluated, as well as the correlation of these figures and serum creatinine with the histopathological data shown in the zero-time biopsy. A total of 80 clinical records were analyzed, 20 being discarded for lack of follow-up at 1 year and 4 for presenting post-surgical hypotension. Of the 56 files used, only 29 included a biopsy report.

One of the outstanding findings was that those patients who presented higher GFR at 24 hours showed higher GFR the following year, in the same way a close and statistically significant correlation was found between creatinine levels in the immediate postoperative period and a year after nephrectomy being directly proportional.

All of this disagreeing with the result obtained in a study published in 2018 by Burballa et al called factors associated with compensation of kidney function after kidney donor nephrectomy, which was a retrospective observational study of a cohort of kidney donors who consecutively underwent a kidney donor nephrectomy between January 2001 and December 2015 in at the hospital del Mar de Barcelona in this, baseline renal function was analysed and one year after nephrectomy of 66 donors, the evaluation of the renal compensation rate revealed that donors with higher creatinine and, therefore, a baseline GFR lower, they compensated more than those with a higher GFR.<sup>6,7</sup>

However, it is important to recognize that in Spain hypertensive patients under treatment are taken as candidates for donation, who were included in the study, who under continuous and close medical surveillance.<sup>8</sup>

In our study, the comparison in age groups showed that the older the donor's age, the lower the GFR the subsequent year, according to the analysis carried out in the United Kingdom published in 2019 by Bellini et al where a total of 889 consecutive living kidney donors were analysed in which the difference in renal function after donation was studied according to the characteristics of age, genetic relationship with the recipient, sex, ethnic origin and body mass index (BMI).<sup>9</sup>

The mean eGFR of the different groups was compared at 6 months and during the 60-month follow-up, the average

age was  $46\pm 13$  years, showing that the lowest eGFR is within 6 months after follow-up and is related significantly with the age over 60 years and the male sex, regarding the distribution by sex in our study, lower GFR was found in men, however this was not significant when analysing the data with the limitation of having a smaller population being studied.<sup>9</sup>

In this research, the association between histopathological findings reported in the zero biopsy and GFR at 24 hrs and one year after nephrectomy was evaluated in a total of 29 files, finding histological alterations of chronic damage in 65% of the reports, patients with A score  $>1$  presented a lower GFR both at 24 hrs and a year later. Among the histological characteristics evaluated were glomerular sclerosis, hyaline arteriosclerosis and tubular atrophy. We found an article published in 2016 by Fahmy et al and collaborators conducted at the department of surgery at the Johns Hopkins university school of medicine, Baltimore, where 310 donors were studied between 1997 and 2012, the mean follow-up it was 6.2 (2.5-8.7; maximum 14.0) years. In this cohort, the overall prevalence of histological abnormalities was 65.8% (19.7% abnormal glomerulosclerosis, 23.9% abnormal interstitial fibrosis and tubular atrophy (IFTA), 4.8% increase in mesangial matrix abnormal, 32.0% of abnormal arteriolar hyalinosis and 32.9% of abnormal vascular intima thickening), the analysis concluded that IFTA was associated with a decrease of 5 ml/min/ 1.73 m<sup>2</sup> in eGFR after donation.<sup>10</sup>

Our study is limited by the size of the sample, the retrospective nature of the data, and the use of eGFR to quantify kidney function; however, despite being a small sample, the results obtained were statistically significant and are consistent with research conducted with older populations. At the Dr. Miguel Silva hospital, zero-time biopsies are routinely performed on all kidneys prior to organ implantation, this research demonstrates the importance of considering this valuable information as a tool to modify the follow-up scheme in patients who show histological alterations in order to avoid the deterioration of the GFR in the most susceptible patients and incorporate the reports of these biopsies into the clinical records of the donors, since in most centers around the world these reports are used to evaluate allograft pathology in recipient patients.

These results may help guide the direction of future research on post-donor kidney function in living kidney donors.

## CONCLUSION

Among the candidates for LDT, the zero-time biopsy alterations, the age  $>36$  years, the dropping of the GFR  $>43\%$ , the GFR and the creatinine levels after 24 hours of nephrectomy were associated with a reduction of the GFR the year after nephrectomy. It is necessary to

implement this valuable tool in the follow-up of donors and to identify those who have histopathological alterations in order to offer timely medical interventions that delay or limit the development of CKD, specify the risks in informed consent and monitor the short and long term the glomerular filtration rate of these patients.

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