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Long-term Outcomes of Kidney Function in Living Kidney Donors – The Gothenburgh Experience

Background: It is important to increase knowledge about and devote more attention to long-term living kidney donors. Although we have used living donors for over 40 years, they have not, until recently, undergone regular check-ups.
Material and methods: A total of 1100 living donor nephrectomies were performed at our hospital from 1965-2005. We located the donors, assessed their general health and focused on renal function with measurement of the glomerular filtration rate and urinary albumin excretion.
Results: Eight of the 1100 had developed ESRD with male dominance ($p<0.05$). Of 823 donors who were still living and eligible, 668 responded to a questionnaire and 573 provided a sample of p-creatinine for estimated GFR (eGFR). The mean time since donation was 15 (9) years and the mean age was 62 (12) years. Using MDRD for estimates of eGFR, 10% of donors belonged to CKD stage I, 66% to stage II, 23% to stage III, 0% to stage IV and 1% to stage V. The last group included one donor in dialysis and two who had received a transplant due to ESRD.
Conclusions: Long-term renal function after living kidney donation is excellent with the majority having eGFR between 60-90 ml/min.

Key words: kidney donors, long-term evaluation, renal function, eGFR, CKD stage, ESRD

Langzeitergebnisse der Nierenfunktion bei Lebendnierenspendern – Erfahrungen aus Gothenburg

Hintergrund: *Es ist wichtig, das Wissen über die Langzeitergebnisse von Lebendnierenspendern zu erweitern und sich mehr mit diesem Thema zu befassen. Wir transplantieren zwar schon seit über 40 Jahren Organe von lebenden Spendern, jedoch gibt es für diese Spender erst seit kurzem regelmäßige Kontrolluntersuchungen.*
Material und Methoden: *An unserem Krankenhaus wurden von 1965 bis 2006 insgesamt 1100 Lebendspende-Nephrektomien durchgeführt. Wir haben die Spender ausfindig gemacht, ihren allgemeinen Gesundheitszustand beurteilt und uns auf die Nierenfunktion konzentriert, indem wir die glomeruläre Filtrationsrate und die Albuminexkretion im Urin gemessen haben.*
Ergebnisse: *Acht der 1100 Spender, vorwiegend männliche Spender, hatten eine terminale Nierenerkrankung (ESRD) entwickelt ($p<0.05$). Von den 823 Spendern, die noch am Leben waren und in*

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unsere Auswertungen eingeschlossen werden konnten, antworteten 668 auf unseren Fragebogen und von 573 Spendern konnten wir eine p-Kreatinin-Probe zur Schätzung der GFR (eGFR) erhalten. Die mittlere Dauer seit der Organspende betrug 15 (9) Jahre und das mittlere Alter der Personen lag bei 62 (12) Jahren. Wenn MDRD zur Schätzung der eGFR verwendet wurde, dann fielen 10% der Spender in die Gruppe I der chronischen Nierenerkrankung (CNV), 66% in Gruppe II, 23% in Gruppe III, 0% in Gruppe IV und 1% in Gruppe V. In der letzten Gruppe befinden sich ein Spender, der Dialyse erhält, sowie zwei Spender, die aufgrund von ESRD ein Transplantat erhalten hatten.

Schlussfolgerungen: *Die Langzeit-Nierenfunktion nach Lebendnierenspende ist hervorragend, die Mehrzahl der Spender weist eine geschätzte GFR zwischen 60-90 ml/min auf.*

Schlüsselwörter: *Nierenspender, Langzeit-Untersuchungen, Nierenfunktion, eGFR, CNV-Stadium, ESRD*

Abbreviations

CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
ESRD	end stage renal disease
mGFR	measured glomerular filtration rate

Introduction

With more living kidney donors worldwide, knowledge regarding the long-term outcome and risks for these altruistic people is of great importance. We have previously demonstrated that kidney donors live longer (1). In this follow-up study, we focused on measurement of kidney function and our intention was to allow as many donors as possible to participate. We do not have a tradition of carrying out long-term check-ups of donors. In addition, there is no Swedish donor registry from earlier years. Previous studies from centres with long experience revealed that in large donor populations ESRD exists in 0.2 to 0.6 % of individuals who underwent living donor nephrectomies (2,3,4).

Subjects and Methods

The subjects consist of all living donors who underwent a nephrectomy at Sahlgrenska University Hospital from 1965 to 2005, in total 1110 persons. Of the 1100 donors 13% had died, 6% were not possible to identify and 4% were living abroad. Out of these, 823 persons, i.e. 77 % were available. The donors were invited to participate in this follow-up study by letter. The Regional Ethics Committee in Gothenburg, Sweden, approved the study to cover all donors in Sweden in 2006.

The tests could be performed in their local hospitals. This was important, as the donors are from different parts of Sweden and many of them live far away from the Transplant centre.

The medical examination included measurement of blood pressure, height, weight, s-creatinine and urine albumin/creatinine ratio. GRF measured using iohexol or Cr-EDTA clearance was optional. GFR was estimated using MDRD (creatinine based, four factors). MDRD 4 Study equation (5).

Previous studies have shown that GFR in healthy Swedish people decreases annually by 1 mL/min from the age of 50 (6,7,8).

Results

ESRD among all 1110 donors

We found that 8 / 1110 donors had developed chronic renal failure. Today, three were alive. Seven of these 8 donors were males, 4 being fathers of the recipients. The gender difference was significant ($p<0.05$). The diagnosis behind the ESRD was nephrosclerosis in 6 cases, verified by kidney biopsy in 2 cases. One had postrenal failure. The youngest donor had his remaining kidney removed due to renal carcinoma.

Time from donation to development of ESRD was 14-27 years (median 19) and the donor age at time of ESRD was 45-89 years (median 75).

Participation rate among the available donors

Of 823 donors, 668 responded to a questionnaire and 573 provided at least a p-creatinine for eGFR. Of 573, 183 underwent iohexol or CrEDTA clearance for measured GFR. The current mean age of the donors was 62 (12) years, range 24-92 and 59 % were female. Time since donation was 15 (9) years, range 1.8- 43 years.

Renal function in the study group

The mean s-creatinine of the 573 donors at follow-up was 94 (25), range 48-383 µmol/L. The eGFR was 71 (16), range 14-145 mL/min/1.73 m^2 body surface. Using CKD staging to characterize the group, the majority, 66%, was in stage II (Fig 1). Only 1% belonged to CKD stage V, comprising one donor in dialysis and two who received a kidney graft (both functioning very well).

The mGFR showed a mean value of 68 (15), range 25-111 mL/min/1.73m^2 body surface.

Microalbuminuria in donors

Microalbuminuria defined as the albumin/creatinine ratio in urine above 3 mmol albumin/mol creatinine was found in 19 %. The mean value of 6.5 and median value of 0.7 indicates that microalbuminuria was found in very few donors but that these had high amounts.

Discussion

This single centre cross-sectional study of kidney donors demonstrates that the majority of our donors were in CKD stage II. The staging is built on estimates of GFR. Thus, the majority of donors had eGFR between 60-90 ml/min which is excellent having one kidney. Although the CKD staging has been questioned, this gives an easy survey (9). In the normal population the results

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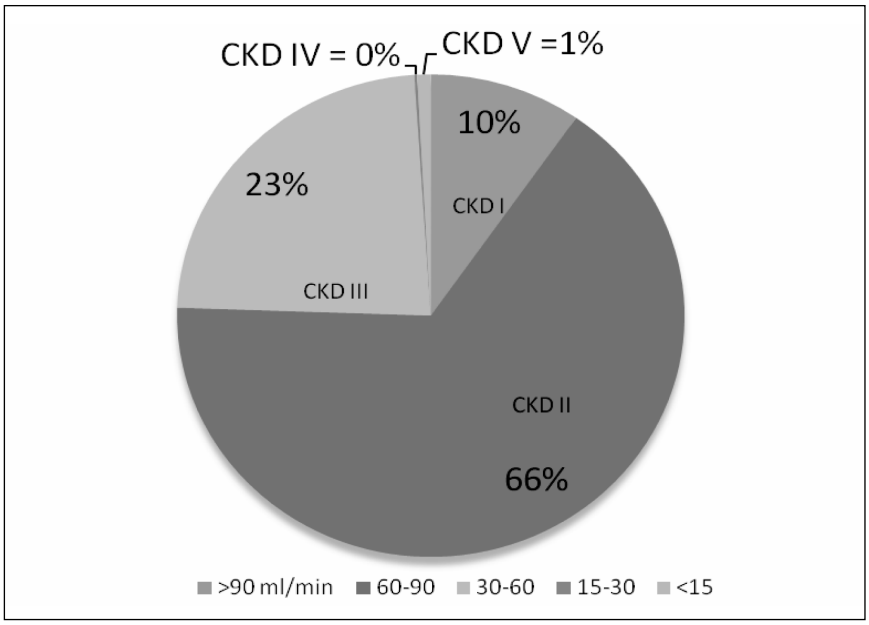

Fig. 1: CKD stages in 573 kidney donors based on eGFR. Median time since donation 13.3 years and median age at donation 48.3 years.

are different. The proportion of CKD stages in a large Norwegian population study showed 57% belonging to stage I, 39% to stage II, 4.5% stage III and 0.2% to stage IV and this did not differ much from American figures (10). The donors thus have inferior stages but it is unclear what relevance this has.

The remaining kidney in a donor does not seem to age in a normal way but maintains a hyperfiltration capacity that negates the ageing process for several years. Such data have recently been published by the Minneapolis group, but the mean age of their donors was 10 year younger compared to ours (11). Increasing kidney function in donors has been observed by Thiel et al. in a prospective study from Switzerland (12).

Hyperfiltration damage with micro-albuminuria was only found in 19 % of the donors. The first to report microalbuminuria post donation in kidney donors were Eberhard et al., who revealed that 25% of donors had microalbuminuria approximately 10 years after donation (13). The Swiss donor-registry listed 9 % of the donors as having microalbuminuria, but this figure includes donors treated with ACE inhibitors or AII antagonists. That microalbuminuria is a risk factor for cardiosvascular disease has been established (14), but is this also true for kidney donors? Why does the kidney hyperfiltrate? Is it due to increased blood supply or hormonal effects? To date no one knows. We measured the IGF1 factor in donors and found a large variation (unpublished data).

The strengths of this study are that the observation time is long and the material is large. A limitation is that local laboratories were used and only one measurement of creatinine to enable old donors and those who lived far away to participate.

In conclusion, our study demonstrates that kidney donors left with one kidney have well preserved renal function. The majority had eGFR of between 60-90 mL/min. We believe studies on long term consequences are important in order to keep the donors under observation and increase their safety. It would be interesting to study the prevalence of cardiovascular diseases among the donors.

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