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NEÜ YAYINEVİ

Evaluation of Kidney Functions After Nephrectomy: Single Center Experience

Nefrektomi Sonrası Böbrek Fonksiyonunun Değerlendirilmesi: Tek Merkez Deneyimi

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Öz

Amaç: Bu çalışmada tek böbreği kalan bireylerde böbrek fonksiyonu, hipertansiyon gelişimi ve proteinüriyi araştırmak amaçlanmıştır.
Hastalar ve Yöntem: Çalışmaya Ocak 2016-Aralık 2019 tarihleri arasında çeşitli nedenlerle Siirt Devlet Hastanesi Nefroloji ve Üroloji polikliniklerine başvuran 17800 hasta arasından daha önce nefrolitiyazis ve kronik piyelonefrite bağlı nonfonksiyone böbrek, RCC (Renal Cell Karsinom), travma ve donör nefrektomi nedeniyle nefrektomi yapılmış 96 hasta dahil edildi. Hastaların verileri retrospektif olarak hasta dosyalarından elde edildi.
Bulgular: Çalışmaya 45'i kadın 51'i erkek olmak üzere toplam 96 hasta dahil edildi. Hastaların 23'üne (% 24) donör nefrektomi (DN) yapılmış, 73'üne (%76) nefrolitiyazis, kronik piyelonefrit, travma ve Renal Cell Hücreli Kanser (RCC) nedeniyle nefrektomi yapılmıştı. Hastalar DN yapılanlar ve diğer etyolojiler nedeniyle nefrektomi (DE) yapılan hastalar olarak iki gruba ayrıldı. DN grubu ile DE grubu arasında sırasıyla; yaş ortalamaları, kadın erkek dağılımı, nefrektomi öncesi HT varlığı, DM, hematüri ve yeni başlangıçlı proteinüri varlığı yönünden karşılaştırıldığında istatistiksel olarak anlamlı farklılık görülmedi (P>0.05). DN grubuna göre DE grubunda yeni başlangıçlı KBH ve HT gelişme sıklığı istatistiksel anlamlı olarak daha yüksek idi (P<0.05).
Sonuç: Nefrektomi KBH, proteinüri ve HT gelişimi için risk faktörüdür. Bu nedenle benign hastalıklar nedeniyle yapılan nefrektomilerin prevalansını azaltmak için zamanında önleyici tedbirler alınmalıdır.

Anahtar Kelimeler: Kronik böbrek hastalığı, proteinüri, nefrektomi

Abstract

Aim: In this study, it was aimed to investigate the kidney function, hypertension development and proteinuria in individuals with only one kidney.
Patients and Methods: The study included 96 patients who had previously undergone nephrectomy with the causes of nephrolithiasis and chronic pyelonephritis-induced nonfunctional kidney, RCC (Renal Cell carcinoma), trauma, and donor nephrectomy among 17800 patients who applied to the Siirt State Hospital Nephrology and Urology outpatient clinics between January 2016 and December 2019. The data of the patients were obtained from patient files database retrospectively.
Results: A total of 96 patients, 45 female and 51 male, were included in the study. 23 (24%) of the patients had donor nephrectomy (DN), and 73 (76%) had nephrectomy (DE) due to nephrolithiasis, chronic pyelonephritis, trauma, and renal cell cancer (RCC). The patients were divided into two groups as those who underwent DN and DE due to other etiologies. Between DN and DE group, there was no statistically significant difference in terms of mean age, distribution of gender, presence of HT before nephrectomy, DM, presence of hematuria and new onset proteinuria (P> 0.05). Compared to the DN group, the frequency of new onset in CKD and HT development was significantly higher DE group.
Conclusion: Nephrectomy is a risk factor for the development of CKD, proteinuria and hypertension. Therefore, preventive measures should be taken in a timely manner to reduce the prevalence of nephrectomies due to benign diseases.

Key words: Chronic kidney disease, proteinuria, nephrectomy

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INTRODUCTION

Chronic kidney disease (CKD) is a health problem that is increasing worldwide and poses a significant burden on the economy of countries (1). In addition, CKD is found to be a strong risk factor for cardiovascular mortality(2). The solitary kidney is mostly caused by; unilateral kidney agenesis; congenital hypoplasia and dysplasia, and surgical removal of the kidney due to disease, injury, tumor or kidney donation. Decreased nephron count with nephrectomy causes hypertension, proteinuria, and a decrease in long-term glomerular filtration rate (GFR) (3). CKD may develop in people with solitary kidneys and in addition to its extraordinary healthcare costs it can lead to end-stage kidney disease (ESRD). In the past, nephrectomy for live kidney donation has been considered safe without the possibility of developing CKD, while new data suggest that there is an 8-11 times greater relative risk of ESRD after unilateral nephrectomy (3-7). Nephrectomy increases the risk of cardiovascular events and death by causing CKD(8, 9).

Decreased kidney capacity in individuals with nephrectomy may contribute to metabolic acidosis (MA) by leading to endogenous and dietary kidney acid burden(10). Pathogenesis of CKD and ESRD in kidney donors with solitary kidney may differ from those of CKD without nephrectomy. Physiological adaptation in the solitary kidney causes higher glomerular filtration rates (GFR) compared to the nephron units. It initially increases GFR but may lead to a gradual decrease in kidney function in the long term (11). Kidney stones and kidney stone-related CKD are common and affect 5 and 13% of the adult population, respectively (12). Although clinical outcomes such as renal failure, development of hypertension, coronary artery disease in patients with solitary kidney have been extensively investigated in previous studies, clinical problems caused by a solitary kidney are still controversial(1, 3, 9, 13). There are a lot of evidences suggesting that a congenital or acquired reduction in kidney mass predisposes the patient to HT, proteinuria, and, in the long term, a decrease in the GFR rate(3, 14, 15). The aim of this study is to investigate the development of CKD, proteinuria and hypertension in the post-nephrectomy follow-up of individuals who have had a single kidney after donor nephrectomy or other reasons.

PATIENTS AND METHODS

The study included 96 patients who had undergone nephrolithiasis and chronic pyelonephritis-induced nonfunctional kidney, RCC, trauma, and donor nephrectomy among the 17800 patients who applied to the Siirt State Hospital Nephrology and Urology outpatient clinics between January 2016 and December 2019. The data of the patients were obtained from patient files retrospectively. Ethical approval for this study was obtained from the Non-Interventional Clinical Research Ethics Committee. (Decision number 31.12.2020, 2020 / 13.11). The study was carried out in accordance with the Helsinki Declaration.

Statistical analysis

The Kolmogorov-Smirnov test was used to investigate whether the distribution of continuous numerical variables is distributed close to normal or not, and the assumption of homogeneity was verified with the Levene test. Descriptive statistics: While mean ± standard deviation or median (25th - 75th) percentages were used for continuous numerical variables, categorical variables were shown as number of cases and (%) percentages. Student's t test was used to determine the significance of the difference in terms of continuous numerical variables in which parametric test statistic assumptions are provided between the groups, while Mann Whitney U test was used to determine the significance of the difference in terms of continuous numerical variables in which sortable variables and parametric test statistic assumptions were not provided. Categorical variables were analyzed by continuity corrected Chi-Square or Fisher's exact probability test.

Analysis of the data was done in IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA) package program. Results with $p < 0.05$ were considered statistically significant.

RESULTS

A total of 96 patients with normal GFR values, 45 female and 51 male, were included in the study. 23 (24%) of the patients had donor nephrectomy, 73 (76%) had nephrectomy due to nephrolithiasis, chronic pyelonephritis, trauma and Renal Cell Cancer (RCC). There were 7 patients in total who underwent nephrectomy for RCC. 3 of the patients were stage 2a and 4 of them were stage 2b. The patients were divided into two groups as those who underwent donor nephrectomy (DN) and those who underwent nephrectomy (DE) due to other etiologies. Creatinine, uric acid, PTH, pH, Chronic Kidney Disease Epidemiology Collaborative equation (CKD-

Table 1. Frequency distributions of cases according to nephrectomy cause

Nephrectomy cause	Number of cases	Percentage
Nephrolithiasis	57	59.4
Donor nephrectomy	23	24.0
Renal cell carcinoma	7	7.3
Chronic pyelonephritis	8	8.3
Trauma	1	1.0
Total	96	100.0

EPI) GFR, complete urine test, protein and creatinin spot urinalysis and vitamin D levels examined in both groups. Proteinuria was accepted in patients with Protein / Creatinine> 150 mg / g in spot urine. CKD was defined as the presence of predicted GFR <60 ml / min / 1.73 m^2 and / or proteinuria in two or more biochemical and spot urinalysis of the patient. The estimated glomerular filtration rate (eGFR) CKD-EPI equation. Urinary system ultrasonographies performed before in outpatient follow-ups for nephrectomy were examined. Table 1 shows the frequency distributions of the cases according to the causes of nephrectomy. Table 2 shows the comparisons made in terms of demographic and clinical features of the cases according to the causes of nephrectomy.

Between DN group and DE group, respectively; there was no statistically significant difference in terms of mean age, distribution of gender, presence of HT before nephrectomy, history of DM, presence of hematuria and proteinuria (p> 0.05). However, the time elapsed after nephrectomy in the DE group was statistically significantly shorter than the DN group (P <0.001). For both group's patients with GFR below 60 ml / min / 1.73m^2 according to CKD-EPI were considered as developing new CKD. In the DE group, the development of new CKD was detected in 54.8% patients and in the DN group, 39% of the patients. Compared to the DN group (median CKD stage: 2, min: 1 - max: 3b), CKD stage was also statistically significantly higher in the DE group (median CKD stage: 3a, min: 1 - max: 5) (P= 0.030). In DE group, 67% of men and 45% of women developed CKD. In Table 3, comparisons made in terms of biochemical measurements of the cases according to the causes of nephrectomy were given.

Between DN group and DE group, respectively; there was no statistically significant difference in terms of Na+, K+, uric acid, PTH, pH, proteinuria and CKD-EPI GFR levels (p> 0.05). However, compared to the DN group, urea, creatinine, phosphorus and vitamin D levels were statistically higher in the DE group (p <0.05). Also, compared to the DN group, calcium, albumin, HCO3- and hemoglobin levels were statistically lower in the DE group (p <0.05).

Table 2. Demographic and clinical features of cases according to nephrectomy cause

	Donor nephrectomy (DN) (n=23)	Other etiologies (DE) (n=73)	P-value
Age	48.9±15.1	50.2±18.6	0.762†
Sex			0.068‡
Male	9 (39.2%)	42 (57.5%)	
Female	14 (60.8%)	31 (42.5%)	
HT before nephrectomy	1 (5.0%)	7 (12.3%)	0.672$
Time after nephrectomy (Year)	1.0 (1.0-12.0)	10.0 (1.0-40.0)	< 0.001¶
After nephrectomy			
HT	8 (40.0%)	36 (63.2%)	0.124‡
DM	1 (5.0%)	9 (15.8%)	0.439$
HD	0 (0.0%)	9 (12.3%)	0.077$
Proteinuria	3 (13.0%)	24 (32.9%)	0.065‡
CKD stage			
1	2 (10.0%)	6 (10.5%)	
2	10 (50.0%)	17 (29.8%)	
3a	7 (35.0%)	15 (26.3%)	
3b	1 (5.0%)	7 (12.3%)	
4	0 (0.0%)	10 (17.5%)	
5	0 (0.0%)	2 (3.5%)	

† Student's t-test, ‡ Continuity corrected Chi-square test, ¶ Mann-Whitney U test, $ Fisher's exact test, HT: hypertension, DM: diabetes mellitus, HD: hemodialysis, CKD: chronic kidney disease

Table 3. Biochemical measurements of cases according to nephrectomy cause

	Donor nephrectomy (DN) (n=23)	Other etiologies(DE) (n=73)	P-value
Creatinine (mg/dl)	1.1 (1.0-1.3)	1.3 (1.1-1.8)	0.004†
Ca++ (mg/dl)	9.42±0.28	9.19±0.47	0.011‡
Phosphorus (mg/dl)	3.3 (2.9-3.7)	3.6 (3.2-4.1)	0.007†
Albumin (g/L)	4.3 (4.2-4.5)	4.2 (4.0-4.3)	0.018†
Uric acid (mg/dl)	5.9 (4.6-6.5)	6.6 (5.5-7.5)	0.016†
PTH (pg/mL)	94.0(77.2-27.2)	84.0(55.0-131.5)	0.601†
Vitamin D (IU)	7.4 (5.0-13.8)	17.9(10.9-5.5)	<0.001†
pH	7.38 (7.37-7.38)	7.37(7.36-7.38)	0.051†
HCO3-	25.7±0.8	24.9±1.8	0.016‡
Proteinuria (mg/gr)	80.0(62.0-20.0)	96.0(56.0-350.0)	0.257†
CKD-EPI GFR (ml/min/per/1.73m^2)	67.0±18.0	54.6±26.7	0.024‡
Hemoglobin (g/dl)	13.9±1.3	13.1±1.7	0.063‡

† Mann-Whitney U test, ‡ Student's t-test, Ca++: calcium, PTH: parathyroid hormone HCO3-: bicarbonate, CKD-EPI: chronic kidney disease epidemiology, GFR: glomerular filtration rate

DISCUSSION

Recent advances in the early diagnosis and treatment of kidney disease have significantly reduced the number of nephrectomies, especially for benign kidney diseases(16). Clinically important renal endpoints after nephrectomy include development of CKD, proteinuria, and ESRD (17). In recent studies, the risk of ESRD after DN has been shown to increase relatively 3-5 times (1, 4-6). There is an increasing acceptance that CKD is found to be a strong risk factor for cardiovascular mortality(2). In addition, other important complications of CKD include HT, anemia, malnutrition, neuropathy, poor quality of life, and mortality risk(18, 19). In the literature, there are geographical differences in terms of nephrectomy rates according to etiology. Nephrectomy rates due to malignant diseases were 67.7% in Norvay (20) and 68% in Nigeria (21), whereas nephrectomy rates due to benign diseases were 76.6% in Pakistan (22) and 70% in Jordan (23). In our study, the rate of nephrectomy due to benign diseases was 68.7%. More than half of the group (78%) had stones in etiology similar to the study made in Pakistan (22). In our study, the high rate of simple nephrectomy due to stone disease may be related to warm climatic conditions, feeding habits, hydro mineralogy and dehydration (24). Advances in the early diagnosis, minimally invasive treatment, and adequate prophylactic measures in urinary stone disease have led to a decrease in the incidence of nephrectomies (12).

In previous studies, it was emphasized that the relationship between male gender and CKD development is stronger among patients with solitary kidneys(3, 5). Similarly, in our study, 67% of males and 45% of females developed CKD in the DE group. However, it does not seem to be possible to explain the relationship between male gender and CKD development with our study. More comprehensive studies are needed to explain this relationship. Compensatory glomerular hyperfiltration due to a reduction in kidney mass can damage the solitary kidney in the long term, especially if there are other factors that exacerbate glomerular hyperfiltration, such as high protein and salt intake with diet(1, 25). The reduction in kidney mass leads to progressive glomerular damage associated with glomerular hypertrophy, hyperfiltration, and systemic hypertension(3). HT development in the follow-up of solitary kidney patients was reported as 28% in the study of Imen Abdellaoui et al.(26), 36% in the study of A.J. Haugen et al. (27) and 50.6 % in the study of J.A. Campos-Sanudo et al.(28). In our study, in the long-term follow-up in the postoperative period, HT developed in 43.5% of patients in the DN group and in 46.5% in the DE group.

A population-based analysis suggested that proteinuria is a risk factor independent of the glomerular filtration rate for the development of ESRD or cardiovascular disease(29). It has been previously shown that a reduction in nephron mass causes an increase in proteinuria in animal models (30). In studies in solitary kidney patients, proteinuria development rates were reported as 12.5 % (26) and 25% (31). In our study, similarly the proteinuria was observed in 24% of patients in the DE group in postoperative period. Whereas proteinuria was detected in 3% of the patients in the DN group. The lower rate of proteinuria in the DN group may be related to the selection of healthy individuals for donor nephrectomy. In our study, the CKD stage was also significantly higher in

the DE group (median CKD stage: 3a, min: 1 - max: 5) compared to the DN group (median CKD stage: 3a, min: 1 - max: 5) (P<0.05). This situation was thought to be related to the selection of candidates for DN from the normal and healthy adults. Zhang et al. (9) reported that new-onset CKD developed in 52.9% of patients who underwent unilateral nephrectomy. Eymen G. et al.(32) reported the rate of CKD development as 25.7% in the donor nephrectomy group and 50.8% in the radical nephrectomy group. In our study, new onset CKD was found in 54.8% of patients in the DE group which supports the previous studies. In our study, the development rate of new-onset CKD in the DN group was 39%. This rate is lower than that of the DE group and the absence of stage 4-5 KBH may be associated with more preserved kidney function in individuals with DN.

CKD can lead to metabolic acidosis as a result of inadequate renal tubular bicarbonate reabsorption or abnormal bicarbonate production (33). In previous studies, metabolic acidosis and CKD have been observed with a higher rate in patients undergoing radical nephrectomy (34, 35). In our study, compared to the DN group, urea, creatinine, phosphorus, and vitamin D levels were statistically higher in the DE group (p <0.05). Also, according to the DN group, in the DE group, respectively; Calcium, albumin, HCO3- and hemoglobin levels were statistically lower (p <0.05). These results can be explained by the higher rate of CKD development in the DE group compared to the DN group, and that the CKD stage was more advanced. One of the important factors affecting the results of nephrectomy is the time elapsed after nephrectomy. Renal parenchymal loss is a risk factor for worsening kidney function over time. The time elapsed after nephrectomy is inversely related to GFR(9). In our study, it was observed that the loss of GFR increased with the prolongation of the time after nephrectomy. The limitations of our study are that it was a single-center and retrospective study, the number of patients was low, the follow-up period was short in the DN group, and the subgroup analysis was not performed due to the small number of patients in the DE group.

Nephrectomy is a risk factor for the development of CKD, proteinuria and hypertension. Therefore, preventive measures should be selected in a timely manner to reduce the prevalence of nephrectomies due to benign diseases. Patients need systematic nephrological care after nephrectomy to prevent the progression of CKD. More research is needed to better understand the risk of CKD after nephrectomy and to optimize patient management. Nephron-sparing surgery should be preferred if possible in patients who will undergo nephrectomy for RCC.

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