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Original Article

Prevalence and Risk Factor of Chronic Kidney Disease after Unilateral Nephrectomy in Patients with Renal Calculi

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Abstract

Objective: **To study risk factor affecting changes in glomerular filtration rate (GFR) and a prevalence of chronic kidney disease (CKD) after unilateral nephrectomy in patients with renal calculi.**

Methods: **We retrospectively studied 65 patients who underwent unilateral nephrectomy at least 12 months before study between March 2006 and September 2014. The GFR of the individual patients was estimated by using CKD-EPI formula before and after nephrectomy. By performing univariate and multivariate regression analysis, we evaluated the risk factors that affect changes in GFR, such as age, sex, body mass index (BMI), preoperative GFR, presence of diabetes mellitus (DM), presence of hypertension (HTN), presence of dyslipidemia (DLP) and duration of follow up after nephrectomy.**

Results: **Prevalence of CKD was 22.64%. We found that male was the only risk factor that statistically significantly associated with CKD by univariate and multivariate regression analysis (Odds ratio 7.619 [1.516-38.303], p = 0.006; Odds ratio 7.347 [1.419-38.049, p = 0.017, respectively). The change of GFR was not significantly influenced by age, BMI, preoperative GFR, DM, HTN, DLP and duration of follow up after nephrectomy.**

Conclusions: **A prevalence of CKD was 22.64% and significant risk factor for CKD in our study was male gender.**

Keywords: **CKD, glomerular filtration rate, unilateral nephrectomy, renal calculi**

INTRODUCTION

Nephrectomy is a surgical procedure for the removal of a kidney. The first successful nephrectomy was performed by the German surgeon Gustav Simon on August 2, 1869 in Heidelberg. There are various indications for this procedure, such as renal cell carcinoma, a non functioning kidney and a congenital small kidney. Nephrectomy is also performed for the purpose of living donor kidney transplantation[1].

Urologic management should focus on optimizing renal function and avoiding chronic kidney disease (CKD) whenever possible. Protection of renal function is a primary concern of urologist who manages surgical diseases of the kidney.

Living kidney donation is safe, and development of renal failure after donation is caused by the same cause as in general population[2]. But, in 2012, Tsai et al. reported that a significant proportion of living donors may develop CKD upon long-term follow-up. The factors affecting donor risk of CKD were baseline renal function, older age, and duration after kidney donation[3].

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Radical nephrectomy is a significant risk factor for CKD[4,5]. In 2011, Cho et al. reported that acute kidney injury (AKI) after radical nephrectomy in patients with renal cell cancer (RCC) is a potent risk factor for new-onset CKD. Prevention of post-operative AKI is essential for reducing the incidence of CKD after nephrectomy[6].

Since the first description of the association between CKD and heart disease, many epidemiological studies have confirmed and extended this finding. As CKD progresses, kidney-specific risk factors for cardiovascular events and disease come into play. As a result, the risk for cardiovascular disease (CVD) is notably increased in individuals with CKD. When adjusted for traditional cardiovascular risk factors, impaired kidney function and raised concentrations of albumin in urine increase the risk of CVD by two to four times[7-10].

The purpose of this study was to evaluate the factors affecting glomerular filtration rate (GFR) and a prevalence of CKD after unilateral nephrectomy in patients with renal calculi.

METHODS

1. Patients

We retrospectively reviewed 65 patients who underwent unilateral nephrectomy at least 12 months before study between March 2006 and September 2014 at Warinchamrab General Hospital in Ubon Ratchathani. Patients' characteristic including age, gender, body mass index (BMI), preoperative GFR, presence of hypertension (HTN), presence of diabetes mellitus (DM), presence of dyslipidemia (DLP) and duration of follow up after nephrectomy were recorded before admission. GFR levels were measured before and yearly after surgery. The GFR was estimated using the CKD-EPI equation, expressed as a single equation, is $GFR=141*\min(Scr/k,1)^{\alpha}*\max(Scr/k,1)^{-1.209}*0.993^{Age}*1.018$ female$*1.159$ [if black]

- All individuals with CKD-EPI of less than 60 ml/min/1.73 m^2 at least 12 months after nephrectomy were classified as having CKD.
- We excluded those patients whose GFR was less than 60 ml/min/1.73 m^2 before surgery, and the presence of morphologic abnormality in the remaining kidney (chronic pyelonephritis with scar, renal calculi and obstructive uropathy, etc.).
- An intravenous pyelogram (IVP) was performed in every case.
- We categorized patients into 2 groups on the basis of GFR at least one year after nephrectomy, GFR $\geq$ 60 ml/min/1.73 m^2 (Group A) and GFR < 60 ml/min/1.73 m^2 (Group B).

2. Statistical analysis

The group A and group B GFR values were compared using a paired *t*-test, and the subjects' characteristics of two groups were compared using the unpaired student *t*-test. Categorical variables were examined using a Chi-square analysis. To determine

Table 1 Patient characteristics

Parameter	Patients who maintained normal renal function, GFR ≥ 60 (Group A, N = 53)	Patients who later developed CKD , GFR < 60 (Group B, N = 12)	*p*-value
Age (years)	58.11± (10.40) (22-74)	59.58 ± 11.11(45-76)	0.077
Sex			
Male	21 (39.62%)	10 (83.33%)	0.112
Female	32 (60.38%)	2 (16.67%)	
BMI (kg/m^2)	22.89 ± 3.90 (16.71-34.13)	23.03 ± 4.29 (17.58-32.87)	0.921
Pre-operative GFR (ml/min/1.73 m^2)	83.55 ± 15.70 (62.07-123.38)	74.57 (61.81-95.98)	0.032*
Diabetes mellitus	7 (13.21%)	1 (8.33%)	0.995
Dyslipidemia	6 (16.81%)	3(25%)	0.822
Hypertension	16 (30.19%)	2 (16.67%)	0.925
Duration of follow up after nephrectomy (years)	3.49 ± 2.03 (1-8)	2.77 ± 1.76 (1-7)	0.218

*Statistically significant

Table 2 Factors for GFR<60 ml/mim/1.73m^2 1 year after nephrectomy (univariate and multivariate regression analysis)

Variable	Univariate analysis			Multivariate analysis		
	ODDS Ratio	95%CI	p-value	ODDS Ratio	95%CI	*p*-value
Age (years)	3.077	0.844-11.212	0.080	NS	NS	NS
Sex						
Male	7.619	1.516-38.303	0.006*	7.347	1.419-38.049	0.017*
Female	7.619	1.516-38.303		7.347	1.419-38.049	
BMI (kg/m^2)	1.278	0.356-4.586	0.706	NS	NS	NS
Preoperative & GFR (ml/min/1.73 m^2)	3.360	0.817-13.812	0.081	NS	NS	NS
Diabetes mellitus	0.579	0.066-5.371	0.643	NS	NS	NS
Dyslipidemia	1.875	0.415-8.467	0.412	NS	NS	NS
Hypertension	0.507	0.660-2.590	0.408	NS	NS	NS
Duration of follow up After mephrectomy (years)	0.720	0.200-2.591	0.614	NS	NS	NS

*Statistically significant

the factors that were most predictive of the post-nephrectomy change in GFR, we performed univariate and multivariate regression analysis. The values are expressed as mean ± SD. Two tailed *p*-values were used, and $p < 0.05$ was considered to be statistically significant.

Results

Prevalence of CKD was accounted for 22.64% (N=65) of the patients. Clinical characteristics of the 65 patients included in the present study are expressed in Table 1. On the basis of the GFR at 1 year after nephrectomy, 53 patients with an GFR of 60 ml/min/ 1.73 m^2 or higher (Group A) and 12 patients with an GFR of less than 60 ml/min/ 1.73 m^2 (Group B) were compared. Of these patients, 31 were men and 34 were women. The median age of the patients was 58.11 years (range 22-74 years) in Group A and 59.58 years (range 45-76 years) in Group B. The median BMI of the patients in Group A was 22.89 kg/m^2 (range 16.71-34.13 kg/m^2) and 23.03 kg/m^2 (range 17.58-32.87 kg/m2) in Group B. The median pre-operative GFR was 83.55 ml/min/1.73 m^2 (range 62.07-123.38) in Group A and 74.57 ml/min/1.73 m^2 (range 61.81-95.58) in Group B. The median duration of follow up after nephrectomy was 3.49 years (range 1-8) in Group A and 2.77 years (range 1-7) in Group B. Diabetes mellitus, dyslipidemia, and hypertension were 13.21%, 16.81%, and 30.19% in Group A and 8.33%, 25%, and 16.67% in Group B, respectively.

From Table 1, we found that median pre-operative GFR (83.55 vs 74.57, $p = 0.032$) was statistically significantly different between group A and group B. There was no significant difference between the two groups regarding age, sex, BMI, diabetes mellitus, dyslipidemia, hypertension, or duration of follow after nephrectomy. We performed univariate and multivariate regression analysis to evaluate the factors for CKD (GFR < 60 ml/min/1.73 m^2) 1 year after nephrectomy (Table 2), adjusted for age, sex, BMI, pre-operative GFR, diabetes mellitus, dyslipidemia, hypertension and duration of follow up after nephrectomy. We found that male gender was the only factor that was statistically significant associated with CKD, Odds ratio (OR) 7.619, 95% confidence interval (CI) 1.516-38.303, $p = 0.006$ in univariate regression analysis, and OR 7.347, 95%CI 1.419-38.049, $p = 0.017$ in multivariate regression analysis. The univariate and multivariate

Table 3 Comparison of prevalence of CKD after unilateral nephrectomy

Series	Prevalence of CKD number (%)
Our study (N = 65)	22.64
Manuel Praga *et al*[11]. (N = 73)	27
Tan L *et al*[12]. (N = 86)	24.4

regression analysis showed that age, BMI, preoperative GFR, diabetes mellitus, dyslipidemia, hypertension, and duration of follow up after nephrectomy had no influence on CKD.

Discussion

In our study, we found that prevalence of CKD was 22.64%. This was similar to the reports by Manuel Praga et al.[11] and Tan L et al.[12] (27% and 24.4%, respectively) (Table 3) but risk factors in the 3 series were different.

Our study showed that male was the only risk factor for post-unilateral nephrectomy CKD. That was similar to the report by Him SH et al.[13]. They found that, between the non-CKD and CKD patients, male gender and age at diagnosis were significantly distinctive common risk factors for CKD. However, we studied in patients with renal calculi disease, but Kim SH et al. studied in patients with renal cell carcinoma.

In the study by Manuel Praga et al., they found that obese patients are at risk for developing CKD, but in the study by Tan L et al., preoperative estimated GFR of less than 82 ml/min/1.73 m^2 was an independent risk factor for CKD.

We are interested in CKD after unilateral nephrectomy because Mark J Marnak et al.[14] reported in 2003 that CVD is also frequently associated with CKD which is important because individuals with CKD are more likely to die of CVD than develop kidney failure, CVD in CKD is treatable and CKD appears to be a risk factor for CVD. The mortality due to CVD was 10-30 times higher in dialysis patients than in the general population.

Gansevoort RT et al[7]. reported that as CKD progresses, kidney-specific risk factors for CVD events and disease come into play. As a result, the risk for CVD is notably increased in individual with CKD. When adjusted for traditional CVD risk factors, impaired kidney function and raised concentrations of albumin in urine increase the risk of CVD by two to four times.

Why male was at greater risk for CKD than females; Silbiger SR et al.[15] reported in 1995 that deterioration of renal function in patients with CKD is more rapid in men than in women, independently of differences in blood pressure or serum cholesterol levels. In addition to genetically determined difference between the sex in renal structure and function, sex hormones may directly influence many process implicated in pathogenesis of renal disease progression. Potential mechanisms include receptor-mediated effect of sex hormones on glomerular hemodynamics and mesangial cell proliferation and matrix accumulation as well as effects on the synthesis and release of cytokines, vasoactive agents, and growth factors. In addition, estrogens may exert potent antioxidant action in mesangial microenvironment, which may contribute to the protective effect of female gender.

Later, Gandolfo NT et al.[16] reported that, with aging, men exhibit greater decrements in renal function and increased glomerular sclerosis than women. Data from meta-analysis indicated that women with several non-diabetic renal diseases such as membranous nephropathy, IgA nephropathy and polycystic kidney disease present a slower progression, but in diabetic renal disease, this is not yet established. Thus, men appear at greater risk for renal injury than women, but the underlying mechanisms are unknown. Sex hormones may mediate the effects of gender on chronic renal disease through the interaction with renin-angiotensin system, the modulation of nitric oxide synthesis and the down regulation of collagen degradation. New observations indicate that androgens may contribute to continuous loss of kidney cells through the stimulation of apoptotic pathways. Apoptosis is a unique type of programmed cell death which is activated in several CKD. In vitro studies indicated that androgens prime a FAS/FASL dependent apoptotic pathway in kidney tubular cells. This apoptotic cell death pathway is receptor-link and interacts with the mitochondrial pathway, which may be activated by other mechanisms, such as toxins and ischemia. Therefore, the mechanisms of cell death which are primed by androgens may interact with others occurring in several conditions leading to the loss of renal cells. These findings are consistent with the role of androgens in promotion of chronic renal injury in men. In 2011, Grzegorczyk K et al.[17], reported that the main female hormone, 17B estradiol, is capable of inhibiting inflammatory and pro-apoptotic process and protects the renal tissue. In contrast, the male hormones, testosterone and dehydroepian-drosterone, have the opposite effect. Hormonal manipulation by male or female castration changes the course of renal disease and confirms the influence of the sex hormones.

Further studies assessing the factors involved in

the gender disparity in renal diseases progression and effect of sex hormones are warranted.

Conclusions

In conclusion, a prevalence of CKD was 22.64% and male gender was a significant risk factor for CKD in our study. Recent epidemiological studies have demonstrated that CKD is a significant risk for CVD, so prevention recommendations based on CVD risk stratification should take into account the highest-risk status of patient with CKD.

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บทคัดย่อ **ความชุกของโรคและปัจจัยเสี่ยงของโรคไตเรื้อรังในผู้ป่วยโรคนิ่วไตที่รักษาโดยการผ่าตัดไตข้างใด ข้างหนึ่งออกทั้งหมด**

บรรจง สืบสังข์, พ.บ.

แผนกศัลยกรรมระบบปัสสาวะ กลุ่มงานศัลยกรรม โรงพยาบาลวารินชำราบ จังหวัดอุบลราชธานี

วัตถุประสงค์: เพื่อศึกษาปัจจัยเสี่ยงที่มีผลต่อการเปลี่ยนแปลงอัตราการกรองของไต (GFR) และความชุกของโรคไตเรื้อรังในการรักษาผู้ป่วยโรคนิ่วไต โดยการผ่าตัดไตข้างใดข้างหนึ่งออกทั้งหมด (Nephrectomy)

ผู้ป่วยและวิธีการ: การศึกษาวิจัยครั้งนี้ได้ทำการศึกษาวิจัยแบบย้อนหลัง (Retrospective study) ในผู้ป่วยจำนวน 65 คน ที่ได้รับการวินิจฉัยว่าเป็นโรคนิ่วไต และได้รับการรักษาโดยการผ่าตัดไตข้างใดข้างหนึ่งออกทั้งหมดอย่างน้อยเป็นระยะเวลา 1 ปีก่อนทำการศึกษาวิจัย ได้ทำการศึกษาวิจัยตั้งแต่เดือนมีนาคม 2549 ถึงเดือนกันยายน 2557 การประเมินค่าอัตราการกรองของไตใช้สูตร CKD-EPI (Chronic kidney disease epidemiology collaboration) ทั้งก่อนและหลังการผ่าตัดไตออก ส่วนการวิเคราะห์ทางสถิติเกี่ยวกับปัจจัยเสี่ยงที่มีผลต่ออัตราการกรองของไตใช้การวิเคราะห์ถดถอยเอกนาม (Univariate regression analysis) และการวิเคราะห์ถดถอยพหุนาม (multivariate regression analysis) ปัจจัยที่ใช้ในการศึกษาวิจัยครั้งนี้ ได้แก่ อายุของผู้ป่วย เพศของผู้ป่วย ดัชนีมวลกาย (BMI) ของผู้ป่วย ค่าอัตราการกรองของไตก่อนการผ่าตัด ระยะเวลาในการติดตามผลการรักษาหลังจากผ่าตัดไตออก และโรคประจำตัวของผู้ป่วย (เบาหวาน, ความดันโลหิตสูง, ภาวะไขมันในกระแสโลหิต)

ผลการศึกษา: พบว่าผู้ป่วยมีความชุกของโรคไตเรื้อรัง 22.64% และพบว่าเพศชายเป็นปัจจัยเสี่ยงต่อการเป็นโรคไตเรื้อรังหลังจากการรักษาโรคนิ่วไตโดยการผ่าตัดไตข้างใดข้างหนึ่งออกทั้งหมดอย่างมีนัยสำคัญทางสถิติโดยการวิเคราะห์ทางสถิติโดยใช้วิธีวิเคราะห์การถดถอยเอกนาม และวิเคราะห์การถดถอยพหุนาม ง(Odds ratio, 7.619 [1.516 - 38.303], $P = 0.006$; Odds ratio, 7.347 [1.419 - 38.049], $P = 0.017$, ตามลำดับ) การเปลี่ยนแปลงอัตราการกรองของไตไม่มีนัยสำคัญทางสถิติเกี่ยวกับ อายุของผู้ป่วย ดัชนีมวลการของผู้ป่วย ค่าอัตราการกรองของไตก่อนการผ่าตัด ระยะเวลาในการติดตามผลการรักษาหลังจากผ่าตัดไตออก และโรคประจำตัวของผู้ป่วย (เบาหวาน, ความดันโลหิตสูง, ภาวะไขมันในกระแสโลหิต)

สรุปผลการศึกษา: ในการศึกษาวิจัยในครั้งนี้ พบว่าความชุกของโรคไตเรื้อรัง 22.64% และพบว่าเพศชายเป็นปัจจัยเสี่ยงที่มีนัยสำคัญ ในการเกิดโรคไตเรื้อรังในผู้ป่วยโรคนิ่วไตที่ทำการรักษาโดยการผ่าตัดไตข้างใดข้างหนึ่งออกทั้งหมด