The Urological Complications of Renal Transplantation : An 11-Year-Experience at Ramathibodi Hospital

SOMBOON LEUNGWATTANAKIJ, M.D.*,
WACHIRA KOCHAKARN, M.D.*,
SUCHART CHAIMUANGRAT, M.D.*,
SOPON JIRASIRITHAM, M.D.**,
PONGSAKORN EAMTANAPORN, M.D.**,
PHAITON GOJASENI, M.B., B.S., F.R.C.S.*,
CHAROEN LEENANUPUNTH, M.D.*,
VERASING MUANGMAN, M.D.*

Abstract

From February 1986 to December 1996, renal transplantation was performed on 344 patients at Ramathibodi Hospital. The urological complications were retrospectively analyzed in 335 patients (338 renal transplants), 9 patients were lost to follow-up. There were 227 males and 108 females with age ranging from 15 to 62 years (mean age 40.28 years). There were 207 cadaveric and 131 living-related graft donors. The ureteroneocystostomy was performed either by modified Politano-Leadbetter (93 cases) or extravesical technique (245 cases).

There were 23 cases of urological complications : ureterovesical anastomotic leakage 6, ureteric obstruction 6, vesicoureteric reflux 4, significant bleeding from ureterovesical anastomosis 3, renal infarction with fistulas 2, hydronephrosis due to blood clot retention and swelling of the anastomosis, requiring temporary double J stenting 2. The analysis was done by dividing the patients into 3 groups, the first and second groups consisted of 100 cases each and the third group consisted of 138 cases. The urological complications in the groups were 10 per cent, 9 per cent and 2.89 per cent respectively. There was a statistically significant difference between the first two groups combined and the third group in terms of complications ($p<0.025$). The urological complications of living-related cases were 9 (6.87%), and of cadaveric cases were 14 (6.76%). There was no significant difference of the complications between living-related and cadaveric transplants ($p>0.05$). The comparative results of the ureteric complications of the extravesical technique were significantly less than the modified Politano-Leadbetter technique (4.49% *vs* 10.75%), ($p<0.05$). In conclusion, the extravesical technique of ureterovesical anastomosis was superior than the modified Leadbetter-Politano technique in terms of post-operative ureteral complications.

Key word : Renal Transplantation, Complication

LEUNGWATTANAKIJ S, et al
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* Division of Urology,
** Division of General Surgery, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Bangkok 10400, Thailand.

The results of renal transplantation have improved significantly after the introduction of cyclosporine by Calne et al in 1978[1]. At present, renal transplantation has become the conventional treatment of nearly all end stage renal diseased patients.

At Ramathibodi Hospital Medical School, we have performed renal transplantation on 344 patients since beginning in February 1986 until December 1996. The overall 2 year-graft survival for cadaveric donors and living related donors was 81 per cent and 96 per cent respectively. Ureteroneocystostomy was performed using both the modified Politano-Leadbetter technique and extravesical technique resulting in some urological complications. The purposes of this study were 1, to review the urological complications and factors that might influence their outcome; 2, to compare the urological complications, patient and graft survival rates between cadaveric and living-related renal transplantations; 3, to compare the results of ureteroneocystostomy between modified Politano-Leadbetter and extravesical techniques in terms of complications.

MATERIAL AND METHOD

The records of 335 patients (338 renal transplantations) from 344 patients who had renal transplantations performed at Ramathibodi Hospital from February 1986 to December 1996 were retrospectively analyzed. Nine patients were excluded from the study because the data were lost. There were 5 second transplantations and 1 third transplantation. The recipients were 227 males and 108 females with age ranging from 15 to 62 years (mean 40.28 years).

All living-related donors were either HLA identical siblings or shared one haplotype with the recipients. All of the cadaveric donor grafts were obtained from irreversible brain damaged patients. All recipients had ABO blood group identical with the donors and had negative crossmatch against donor T and B lymphocytes.

The kidney grafts were implanted mainly by a standard vascular technique[2], end-to-side anastomosis of the renal artery and vein to external iliac vessels.

The immunosuppressive regimen was cyclosporine and low dose steriod[3]. The surgical complications including urological complications herein were defined as complications related to the transplantation procedures, either immediate or late development, and needed further surgical procedures.

Of 338 renal transplantations, 131 grafts were living-related (mean age 38.40 years) and 207 grafts were cadaveric donors (mean age 41.03 years). In cadaveric transplantation, 3 grafts were newborn cadaveric donors. In data analysis, firstly, the urological complications were compared between the cadaveric and living-related groups. The graft and patient survival curves were calculated by Kaplan-Meier method and Log-rank statistic, and were also compared between both groups to identify whether or not it might be influenced by the urological complications.

Secondly, the ureteroneocystostomy techniques were evaluated. Modified Politano-Leadbetter technique was performed in 93 cases (mean age 41.28 years) and extravesical technique as described by Lich and Gregoir[4] in 245 cases (mean age 39.43 years). Mainly, modified Politano-Leadbetter technique was performed in the first period (91 in the first 200 cases and 2 were done in the remaining 138 cases). The urological complications associated with the implantation techniques were compared between both groups. In all cases, 160 mg of gentamycin mixed with 500 ml of 0.9 per cent normal saline solution was partially instilled into the bladder *via* a urethral catheter before the ureteroneocystostomy.

Finally, the urological complications were analyzed by dividing the patients into 3 groups; group 1: the first 100 cases, group 2 :the second 100 cases and group 3 : the remaining 138 cases. The urological complications were compared between each group to follow-up our results and to identify the factors that might influence the outcome of urological results.

Graft loss included both post-transplant nephrectomy and retained failure graft, requiring dialysis. It also included death of a patient from any cause. The early graft loss meant graft loss within 3 months after transplantation. The perioperative mortality meant death within 3 months after transplantation.

RESULTS

Among 338 renal transplantations, there were 83 overall complications (24.56%) divided into vascular 28 (8.28%), lymphatic 18 (5.33%),

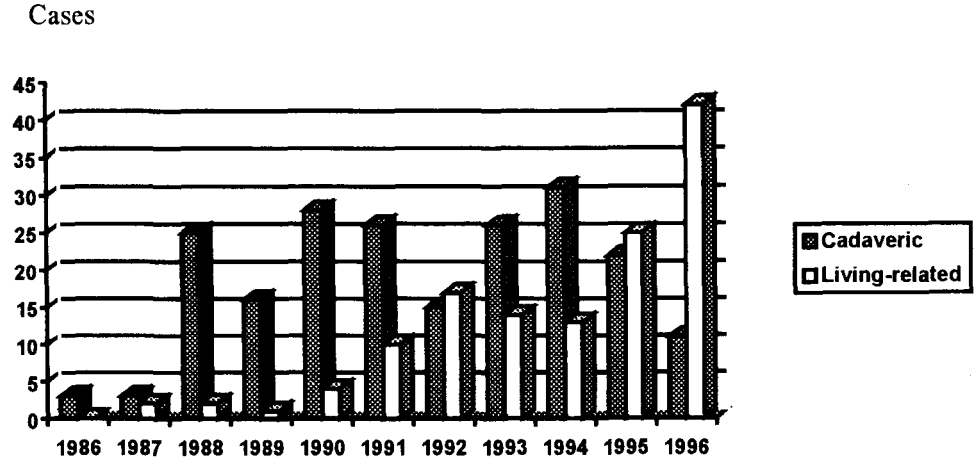

Fig. 1. Bar chart showing the ratio of cadaveric and living-related donors between 1986-1996.

Table 1. The 1 to 5 year graft and patient survival of the cadaveric and living-related transplantations in Ramathibodi Hospital from 1986 through 1996.

Year	% Graft survival		% Patient survival	
	Cadaveric	Living-related	Cadaveric	Living-related
1st	85	96	90	98
2nd	81	96	88	98
3rd	75	95	83	98
4th	69	95	80	98
5th	61	95	73	98

general 11 (3.28%) and urological 23 (6.80%) complications. Eight cases developed multiple complications.

There were 26 cases (7.69%) of early graft loss. The major cause was due to acute rejection in 10 cases (38.46%). Until May 1997, there were 50 deaths among 335 patients with perioperative mortality occurring in 14 (4.18 %). The other causes of death were as follows : graft failures 9, diverse causes not related to transplantation 17, and from unknown causes outside the hospital 10.

From the beginning of the renal transplantation programme until the last 2 years, cadaveric transplantation had been more numerous than living-related transplantation (Fig. 1). Among the 285 patients who were alive, the graft survival of the living-related and cadeveric kidneys at 1 and 5 years were 85 per cent *vs* 61 per cent and 96 per cent *vs* 95 per cent respectively. The patient survival of both groups at 1 and 5 years were 90 per cent *vs* 73 per cent and 98 per cent *vs* 97 per cent respectively (Table 1).

There were 23 cases of urological complications : ureterovesical anastomotic leakage 6, ureteric obstruction 6, vesico-ureteral reflux 4, significant bleeding from ureterovesical anastomosis 4, renal infarction with fistulas 2, and hydronephrosis due to blood clot and swelling of the anastomosis requiring temporary double J stenting 2, (Table 2).

Of 338 transplants, there were 131 (38.76%) living-related (mean age 38.40 years) and 207 (61.24%) cadaveric donors (mean age 41.03 years). The urological complications occurring in both groups were 9 (6.87%) and 14 (6.76%) cases respectively, and were not statistically different ($p > 0.05$), (Table 3).

Table 2. Twenty three urological complications in 335 patients (338 kidneys).

	Case no.	Ureteroneocysto-stomy technique*	Donor **	Treatment
Anastomtic leakage 6 cases				
1. Distal ureteric necrosis	17	Pol.	CD	Reimplantation
2. Anastomotic leakage	22	Pol.	CD	Reimplantation
3. Anastomotic leakage	61	Pol.	LRD	Reimplantation
4. Anastomotic leakage	131	Ext.	CD	Reimplantation
5. Distal ureteric necrosis	176	Ext.	CD	Nephrectomy (Infected kidney)
6. Anastomotic leakage	261	Pol.	CD	Reimplantation
Ureteric obstruction 6 cases				
7. Stenosis of middle ureter	4	Pol.	CD	Ureteropyelostomy
8. Stenosis of middle ureter	34	Pol.	CD	Segmental resection with end to end anastomosis
9. UVJ obstruction	102	Ext.	LRD	Reimplantation
10. Ureteric obstruction from silastic drain compression	103	Ext.	LRD	Exploration with silastic drain relocation
11. UVJ obstruction	182	Ext.	CD	Reimplantation
12. UVJ obstruction	280	Ext.	CD	Reimplantation
Vesicoureteric reflux 4 cases				
13. VUR	66	Pol.	CD	Conservative treatment
14. VUR	133	Pol.	LRD	Reimplantation
15. VUR	147	Ext.	CD	Reimplantation
16. VUR	186	Ext.	CD	Conservative treatment
Temporary hydronephrosis 2 cases				
17. From blood clot	134	Ext.	LRD	Double J stent indwelling
18. From orifice swelling	289	Ext.	CD	Double J stent indwelling
Significant hematuria 3 cases				
19. Bleeding from anastomosis	99	Pol.	LRD	Transurethral fulguration
20. Bleeding from anastomosis	136	Pol.	LRD	Transurethral fulguration
21. Bleeding from anastomosis	202	Ext.	LRD	Transurethral fulguration
Renal infarction 2 cases				
22. Cortical infarction	45	Pol.	CD	Nephrectomy
23. Cortical infarction	303	Ext.	CD	Nephrectomy

* Pol. = Modified Politano-Leadbetter technique, Ext = Extravesical technique (Lich-Gregoir)
** CD = Cadaveric, LRD = Living-related donor
UVJ = Uretero-vesical junction, VUR = Vesicoureteral reflux

Modified Politano-Leadbetter was performed in 93 cases (27.51%), the mean age was 41.28 years. Extravesical technique was performed in 245 cases (62.49%), the mean age was 39.43 years. The urological complications associated with modified Politano-Leadbetter and extravesical technique of ureteroneocystostomy (ureteric problems) occurred in 10 (10.75%) and 11 (4.49%) cases respectively (Table 4). The difference was statistically significant ($p<0.05$). Noteworthy, all cases of the modified Politano-Leadbetter technique were done in the first 200 cases and only 2 cases were done in the remaining 138 cases.

By dividing the patients into 3 groups, the urological complications among the first 100 cases, the second 100 cases and the remaining 138 cases were 10 (10%), 9 (9%) and 4 (2.89%) respectively (Table 5). The complications of the first and the second 100 cases were not significantly different ($p>0.05$). However, the complications of the last group were significantly less than the first two groups ($p<0.025$).

Furthermore, there was a case of squamous cell cancer of the skin in a 59 year-old male which occurred 4 years after transplantation, a case of bladder cancer in a 38 year old female, 4 years after transplantation, 3 cases of stones in transplant kidneys occurred 3 years after transplantation, two of them were successfully treated by extracoporeal shock wave lithotripsy and a 36 year old woman died from fulminating systemic infection after transplantation with a kidney containing a small calculus.

Table 3. Comparative results of the urological complications between living-related and cadaveric transplants.

	Numbers		Mean age	Urological	complications
	Cases	Per cent	Years	Cases	Per cent
Living-related transplant	131	38.76	38.40	9	6.87
Cadaveric transplant	207	61.24	41.03	14	6.76
Total	338	100	40.28	23	6.80

Table 4. Comparative results of the 21 ureteric problems between modified Politano-Leadbetter and extravesical techniques (*2 cases of renal infarction with fistulas were excluded from all 23 urological complications).

	Numbers		Mean age	Ureteric	problems
	Cases	Per cent	Years	Cases	Per cent
Modified Politano-Leadbetter	93	27.51	41.28	10	10.75
Extravesical	245	62.49	39.43	11	4.49
Total	338	100	40.28	21*	6.21

Table 5. Comparative results of the urological complications in the first 100, second 100 and the last 138 cases.

	Urological complications	
	Cases	Per cent
The first 100 cases	10	10
The second 100 cases	9	9
The last 138 cases	4	2.89

Table 6. Comparative results of the surgical complications between the literature' s series and Ramathibodi's series.

	Literature	Ramathibodi
Overall perioperative complication[6]	20%	25.15%
Vascular complication[6-13]	1.1-12.4%	8.28%
Urological complication[14,15]	0.9-29.6%	6.80%
Lymphocele[16-20]	0.6-22%	5.33%
General complication	-	3.25%

A 35 year-old female became pregnant 1 year after transplantation and had a subsequently normal delivery.

DISCUSSION

Since the beginning of the transplantation program in 1986, the cadaveric donors have been exceeding the living-related donors (61% *vs* 39%), although the number of the cadaveric transplantations has dropped dramatically over the last 2 years. Suffice it here to state that the low procurement rate of cadaveric kidney is due to familiarization of the transplantation concepts and traditional convention. Over a 10 year period we have had 126 cadaveric transplantations from 95 per cent of road traffic accidents, countrywide[5].

The incidence of the surgical complications in the literature ranged from 0.9 per cent[14] to 29.6 per cent[15] compared to 5.3 per cent to 8.2 per cent in our series (Table 6). Urological complications occurred in 23 cases (6.80%) in our series mainly associated with ureterovesical anastomosis ; i.e. : anastomotic leakage, ureterovesical obstruction, vesicoureteral reflux and significant hematuria, in only 2 cases the urinary leakage was secondary to renal cortical infarction and regarded as a non-ureteric problem (Table 2).

In 1994, Cranston[21] reported 2.5 per cent of ureteric leakage and 3.6 per cent of ureteric obstruction in 1,000 transplant patients in Oxford. In our series, we had 6 (1.78%) ureteric leakages and 8 (2.37%) ureteric obstructions resulting in temporary hydronephrosis.

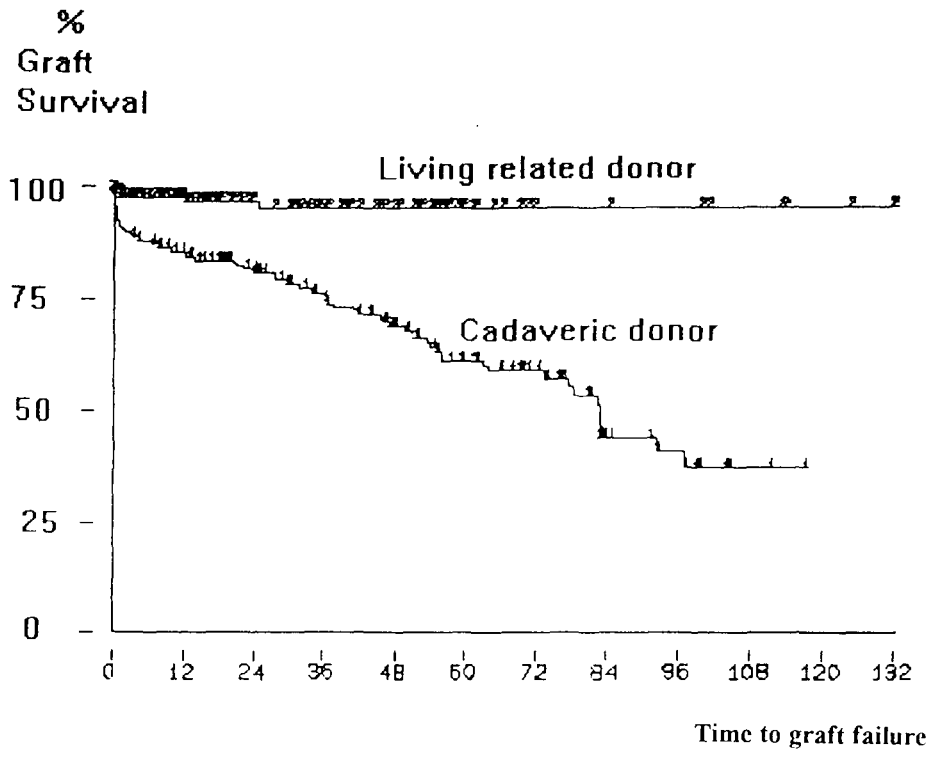

Fig. 2. Graft survival of cadaveric and living-related kidney transplants in Ramathibodi Hospital from 1986 to 1996.

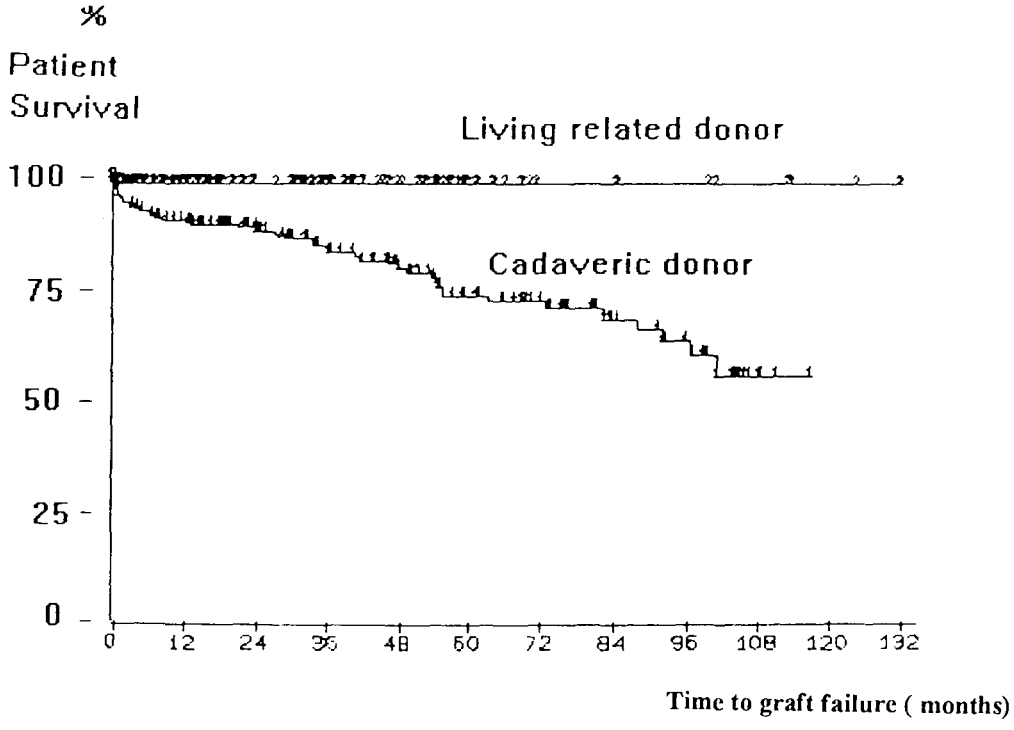

Fig. 3. Patient survival of cadaveric and living-related kidney transplants in Ramathibodi Hospital from 1986 to 1996.

The comparative results of graft and patient survival curve showed that the living-related transplants were significantly better than that of the cadaveric cases when calculated by Log-rank test and Kaplan-Meier method (Fig. 2 and 3). However, the urological complications of the living-related and the cadaveric transplants remained the same (6.87% and 6.76% respectively), $p>0.05$ (Table 3). The results showed that the causes of graft and patient survival were not correlated with the urological complications, but probably depended on immunological difference, ischemic time and post-transplantation management.

However, the comparative results of urological complications of the extravesical technique were significantly better than the modified Politano-Leadbetter technique (4.49% *vs* 10.75%) in terms of ureteric problems ($p<0.05$), (Table 4). Interestingly, in 1978 Mehta et al reported that the urological complications of the conventional Politano-Leadbetter and the extravesical technique were 9.2 per cent and 21.8 per cent respectively in 119 patients. But in 1990 Thrasher reversibly reported that the urological complications of the modified Politano-Leadbetter and the extravesical technique were 9.4 per cent and 3.7 per cent respectively in 320 transplants. It was difficult, however, to conclude the comparative results of the complications of both techniques because the modified Politano-Leadbetter technique was performed mainly in the early years while the extravesical technique was performed in recent years with more or less healthier donors and recipients. In the last 138 cases, the modified Politano-Leadbetter technique was performed in only 2 cases.

Starzl et al (1970)[22] and Loughlin et al (1984)[23] reported that the urological complications were 10 per cent to 25 per cent. Over the past two decades, the complication rates have dropped to 5 per cent[23,24]. In our series, the urological complication rate decreased slightly from 10 per cent to 9 per cent in the first 100 cases and the second 100 cases, with no statistical difference ($p>0.05$). However, the urological complication rate has decreased dramatically to 2.89 per cent in the last 138 cases ($p<0.025$). This might be due to increasing surgical experience and modifications of our surgical technique of ureteroneocystostomy such as double J stent indwelling. However, in the last 138 cases, the follow-up period was shorter than the former 200 cases. This may have given rise to the lower complication rate, while last case had only a 4 month follow-up period.

Cho et al (1988) reported a 1.7 per cent incidence of stones in transplanted kidneys in 544 transplant patients[25]. Cranston (1994) reported a 0.2 per cent incidence of stones in the first 1,000 transplants[21]. The risks are higher than in the general population due to hypercalcemia, recurrent urinary tract infection, decreased fluid intake and increased incidence of urinary tract obstruction. Our series also had 3 cases or 0.9 per cent incidence of stones in the transplant kidneys.

The incidence of cancer in transplant recipients varies considerably in different geographic areas. A great deal of the variation is due to a high incidence of skin cancer in some areas. Sheil (1994) reported that if malignancies of the skin are excluded, a cancer incidence of 4-7 per cent in transplant recipients is usual[26]. The incidence of cancer in our series was 0.6 per cent among 335 patients, one case of skin cancer and another case of bladder cancer, all cancers occurred about 4 years after transplantation.

SUMMARY

A retrospective analysis of 344 renal transplant patients or 338 kidneys during the period of 11 years from February 1986 to December 1996 was done. There were 23 cases of urological complications, 21 of which were related to ureteral anastomosis (stricture, fistulas, temporary obstruction) and 2 cases due to renal infarction resulting in renocutaneous fistula. The living related transplants and the cadaveric transplants consisted of 38.8 per cent and 61.2 per cent of kidneys respectively. Two ureteric anastomotic techniques were employed, modified Politano-Leadbetter and extravesical. Comparative results of ureteric problems between the cases undergoing the two techniques revealed that the former technique resulted in greater ureteric problems than the latter (10.75% *vs* 4.49%), the total ureteric problem among our series of 338 cases was 6.21 per cent and has lead to the conclusion that the ureteric complication rate in our series is comparable to others and the extravesical technique of ureteroneocystostomy is superior than the modified Politano-Leadbetter technique.

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ภาวะแทรกซ้อนของระบบทางเดินปัสสาวะในผู้ป่วยเปลี่ยนไตในโรงพยาบาลรามาธิบดี

สมบุญ เหลืองวัฒนากิจ, พ.บ., พงศกร เอี่ยมธนาภรณ์, พ.บ.**, วชิร คชการ, พ.บ.*, ไพฑูรย์ คชเสนีย์, เอฟ.อาร์.ซี.เอส.*, สุชาติ ไชยเมืองราช, พ.บ.*, เจริญ ลีนานุพันธุ์, พ.บ.*, โสภณ จิรสิริธรรม, พ.บ.**, วีระสิงห์ เมืองมั่น, พ.บ.**

ระหว่างเดือนกุมภาพันธ์ พ.ศ. 2529 ถึง ธันวาคม พ.ศ. 2539 โรงพยาบาลรามาธิบดีได้ทำการผ่าตัดเปลี่ยนไต รวม 344 ราย ผู้เขียนได้ทำการศึกษาย้อนหลังเพื่อศึกษาภาวะแทรกซ้อนของระบบทางเดินปัสสาวะในผู้ป่วย 335 ราย (ไม่สามารถติดตามการรักษาได้จำนวน 9 ราย) เป็นชาย 227 ราย และหญิง 108 ราย อายุระหว่าง 15–62 ปี (เฉลี่ย 40.28 ปี) เนื่องจากผู้ป่วยบางรายผ่าตัดเปลี่ยนไตมากกว่าหนึ่งครั้ง การศึกษาครั้งนี้ จึงมีการผ่าตัดเปลี่ยนไตทั้งสิ้น 338 ไต จากผู้ป่วยรวม 335 ราย โดย 207 ไต ได้จากผู้บริจาคที่มีสมองตาย และ 131 ไตได้จากญาติ 93 ราย ใช้ ureteroneocystostomy technique ด้วยวิธี modified Politano–Leadbetter technique และ 245 ราย ใช้วิธี extravesical technique

ภาวะแทรกซ้อนของระบบทางเดินปัสสาวะมีทั้งหมด 23 ราย แบ่งเป็น ureterovesical anastomotic leakage 6 ราย, Ureteric obstruction 6 ราย, esicoureteric reflux 4 ราย, significant bleeding from ureterovesical anastomosis 3 ราย, renal infarction with fistulas 2 ราย, hydronephrosis due to blood clot retention and swelling of the anastomosis, requiring temporary double J stenting 2 ราย

เมื่อเปรียบเทียบกลุ่มที่หนึ่งในผู้ป่วย 100 รายแรก กลุ่มที่ 2 ในผู้ป่วยรายที่ 101–200 และกลุ่มที่ 3 ในผู้ป่วย 138 รายสุดท้าย พบว่าภาวะแทรกซ้อนของระบบทางเดินปัสสาวะลดลงจากร้อยละ 10, 9 และ 2.89 ตามลำดับ โดยภาวะแทรกซ้อนในกลุ่มที่ 3 จะต่ำกว่ากลุ่มที่ 1 และ 2 อย่างมีนัยสำคัญทางสถิติ ($p<0.025$)

การเปรียบเทียบระหว่างกลุ่มที่ได้รับไตจากผู้บริจาคที่มีสมองตายและไตจากญาติ พบว่ามีภาวะแทรกซ้อนของระบบทางเดินปัสสาวะเท่ากับ ร้อยละ 6.76 และ 6.87 ตามลำดับ และไม่มีนัยสำคัญทางสถิติ ($p>0.05$)

ส่วนการเปรียบเทียบวิธี ureteroneocystostomy technique ระหว่าง modified Politano–Leadbetter technique และ extravesical technique พบว่ามีภาวะแทรกซ้อนของระบบทางเดินปัสสาวะร้อยละ 4.49 และ 10.75 ตามลำดับ โดยวิธี extravesical technique จะดีกว่าวิธี modified Politano–Leadbetter technique อย่างมีนัยสำคัญทางสถิติ ($p<0.05$)

คำสำคัญ : เปลี่ยนไต, ภาวะแทรกซ้อน

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* หน่วยศัลยศาสตร์ ระบบทางเดินปัสสาวะ,

** หน่วยศัลยศาสตร์ทั่วไป, ภาควิชาศัลยศาสตร์, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, กรุงเทพ ฯ 10400