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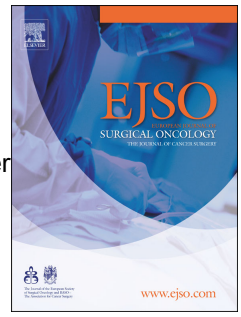

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EFFECTS ON RENAL FUNCTION OF OBSTRUCTIVE AND NONOBSTRUCTIVE DILATATION OF THE UPPER URINARY TRACT IN ILEAL NEOBLADDERS WITH REFLUXING URETEROENTERIC ANASTOMOSES

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KEYWORDS: orthotopic ileal neobbladder, urinary diversion, direct anastomosis, reflux, anastomotic stricture, renal function.

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ABSTRACT

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Aims. To investigate the incidence and long term effects on kidney function of obstructive and nonobstructive dilatation of the upper urinary tract in patients with ileal neobladder with refluxing ureterointestinal anastomoses.

Methods We retrospectively analyzed a prospectively derived database of 110 patients with bladder cancer and who were treated with an ileal neobladder between 1996 and 2007 using refluxing end-to-side ureterointestinal anastomoses on a short afferent limb. The mean follow up was 65 months. At every follow up visit the patients had an analysis of serum creatinine, urine culture, abdominal CT or ultrasonography, and, if there was dilatation of the upper urinary tract, ^{99m}Tc- DTPA renal scintigraphy was requested.

Results. In all, 206 renoureteral units were included in the study. Overall, seven had anastomotic stricture and of those, three were symptomatic and were corrected; while four were asymptomatic and of those, only two, with preserved split GFR, were surgically treated, while the remaining two, with a poor split GFR, were followed up. The last 99mTc-DTPA showed a preserved split GFR in the reimplanted units and further split renal function decrease in untreated units. Nonobstructive dilatation of the upper urinary tract, caused by reflux, was diagnosed in 13 units. The dilatation was bilateral in three patients with recurrent UTIs and urosepsis, and the split GFR was bilaterally reduced at diagnosis with a further reduction at the last 99mTc-DTPA. The remaining seven units with sterile urine, showed a preserved split GFR during follow up.

Conclusions. All strictures, regardless of their severity, should be immediately corrected. Reflux per se does not provoke renal impairment unless recurrent UTIs and urosepsis are present.

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EFFECTS ON RENAL FUNCTION OF OBSTRUCTIVE AND NONOBSTRUCTIVE DILATATION OF THE UPPER URINARY TRACT IN ILEAL NEOBLADDERS WITH REFLUXING URETEROENTERIC ANASTOMOSES

INTRODUCTION

Radical cystectomy is the treatment of choice for muscle-invasive bladder cancer[1] and even if recent reports have shown that patients with a neobladder enjoy marginal quality of life advantages over those with an ileal conduit [2-4], orthotopic bladder reconstruction remains the best option for patients undergoing cystectomy [5,6].

In patients with a neobladder, the preservation of renal function is the ultimate goal of successful treatment [7] and can be influenced by several factors including ureteral obstruction, urinary tract infection (UTI) and reflux [8-10].

Dilatation of the upper urinary tract is the major concern in ureteroileal anastomosis [11] and can be caused by strictures of the ureter and reflux [7].

The general question is whether a refluxing or nonrefluxing technique should be chosen. Proponents of nonrefluxing techniques cite the harmful effects on renal function of recurrent pyelonephritis caused by reflux [9,10] and bacteriuria [8] and the potential benefit in patients undergoing intermittent catheterization. Nevertheless, the danger to renal function caused by anastomotic stricture that occurs at a higher rate after an antirefluxing technique than after direct anastomosis is well documented [5,12,13] and it is reflected by the number of different antireflux mechanisms developed during the years, such as afferent nipple valves [14], the Le Duc technique [15], split-cuff ureteral nipples [16], the Abol-Enein and Ghoneim technique [17], the T pouch tecnique [18] and an afferent ileal tubular segment [19]; however, the multiplicity of these techniques suggests that an ideal solution has not yet been found.

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On the contrary, using a direct anastomosis, anastomotic strictures occur at a significantly lower rate than after an antireflux technique [5], but ureteral reflux might potentially endanger kidney function on the long term follow up [10].

In this study we investigated the incidence of obstructive and nonobstructive dilatation of the upper urinary tract, caused by ureterointestinal stricture and reflux, respectively, and their impact on split renal function in the long term in patients who had a low pressure ileal neobladder constructed using refluxing ureterointestinal anastomoses.

MATERIALS AND METHODS

Patients Population

A prospective derived database of patients undergoing ileal neobladder for bladder cancer was retrospectively analyzed. Between May 1996 and March 2007, 110 consecutive men (mean age 63.8 years, range 45–79) underwent radical cystectomy and orthotopic neobladder formation. Inclusion criteria for continent urinary diversion were normal renal function, absence of gastrointestinal disease and absence of tumor at the prostatic urethra. Preoperative evaluation included serum creatinine, ultrasonography and computerized tomography of the abdomen and pelvis. Mean (range) preoperative serum creatinine was 0.99 mg/dl (0.7-1.5, normal 0.7-1.4) (87.5 µmol/L, range 62-133, normal 62-124).

Surgical Technique

In all cases, the W-shaped ileal neobladder and ureteral anastomoses on a short afferent limb were done according to our previously described standard technique using 45 to 47 cm of ileum [7, 20]. The distal 40 cm were detubularized on a silicone tube and oriented into a “W” shape, the proximal 5 to 7 cm left intact for anastomosis with the ureters. The ureters were spatulated and implanted to the ileal chimney using the Nesbit nontunneled end- to- side ureteroileal anastomosis with 2 running 5-0 absorbable sutures.

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Evaluation of renal function during follow up

The patients were routinely examined every 6 months for the first 3 years and yearly thereafter. At every follow up visit the patients underwent serum creatinine, urine culture, abdominal CT scan or ultrasonography, and, in case of dilatation of the upper urinary tract at the imaging study, ^{99m}Tc-DTPA renal scintigraphy with a Foley catheter in the neobladder was requested to evaluate total and split GFR and to define the cause of the dilatation: obstructive, caused by anastomotic stricture or nonobstructive, caused by reflux.

The dilatation was considered obstructive if appearance of the radioisotope in the pelvicaliceal system was delayed, if there was retention of activity in the dilated collecting system over time and if T½ of the time-activity curve was greater than 20 minutes after intravenous administration of furosemide. Nonobstructive dilatation was assumed if the collecting system was dilated and the T½ of the time-activity curve was less than 10 minutes after furosemide injection.

Total and split renal function of patients with obstructive and nonobstructive dilatation was evaluated by measurements of plasma creatinine and GFR. Plasma creatinine was measured with the standard autoanalyzer technique. Standard ^{99m}Tc-DTPA renal scintigraphy and Gates' method were used to calculate GFR. GFR values measured as the renal clearance of ^{99m}Tc-DTPA are reported with reference to the standard body surface area of 1.73 m^2 [21,22] .

Clean catch urinalysis and urine cultures were done according to standard sterile procedures. UTI was defined as a urine culture showing greater than 10,000 cfu bacteria plus suprapubic pain or greater than 100,000 cfu bacteria with or without symptoms. Urosepsis was defined as greater than 100,000 cfu bacteria in the urine plus evidence of a positive blood culture [8] .

The final evaluation of patients status was in March 2008. The mean follow up was 65 months (range 12 to 141). A total of 40 patients died during follow up, 32 of bladder carcinoma and eight of causes independent from bladder tumor.

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RESULTS

Of the 110 patients, two died in the perioperative period and three were lost to follow-up. Of the 105 patients (210 renoureteral units), two had resection of the distal ureter and reimplantation for recurrent disease at 50 and 62 months after surgery and two had nephroureterectomy for upper urinary tract transitional cell carcinoma at 45 and 58 months after surgery. Therefore this study is based on a series of 206 renoureteral units (105 patients) and of those 20 units (17 patients) showed a dilatation detected during follow up and were further investigated.

Obstructive dilatation

Overall, in our series, seven renoureteral units had anastomotic stricture (Table 1) and of those, three had symptomatic anastomotic stricture detected at 2, 4 and 8 months after surgery (three renal units). These patients were treated with surgical reimplantation. Four patients had anastomotic stricture detected as asymptomatic dilatation of the upper urinary tract at 6, 12, 24 and 24 months after surgery (four renal units). The split GFR in these four patients was 45, 40, 21 and 26.3 ml/minute respectively and only patients with split GFR of 45 and 40 ml/minute were treated with surgical reimplantation. The nuclear renography at 6 months after diagnosis showed a GFR of 43.2 and 38.2 ml/minute, respectively, in patients treated with surgical reimplantation. The resolution of the anastomotic stricture was confirmed at the last follow up visit at 56 and 74 months after surgery with a split GFR of 39.2 and 34.8 ml/minute, respectively. There was a decrease to 14.2 and 16.3 ml/minute at the last nuclear renography performed 36 and 48 months after diagnosis in patients that were not treated.

Nonobstructive dilatation

The renal scan revealed nonobstructive dilatation of the upper urinary tract in ten patients (Table 2). The dilatation was bilateral in three patients with recurrent UTIs and urosepsis. The split GFR in these patients at diagnosis was 22/25, 31.2/33.2 and 27.6/28.3 ml/minute, and showed a further

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reduction to 15/17, 19/25.2 and 21.1/25.3 ml/ minute at the last nuclear renography performed at 17, 47 and 51 months after surgery.

The dilatation was unilateral and moderate in the remaining seven patients, with sterile urine or one positive urinalysis during follow up. These patients showed a preserved split GFR symmetrical with the nondilated renal unit, with a mean of 47.3 ml/minute at diagnosis that did not showed a significant reduction during follow up after a further mean (range) follow up of 44 (36-51) months (Table 2).

DISCUSSION

Reflux prevention in orthotopic bladder substitutes remains a controversial issue and although excellent long term results have been described using refluxing anastomoses, many surgeons continue to perform antireflux procedures [23].

The aim of the present study was to investigate the incidence of obstructive and nonobstructive dilatation of the upper urinary tract and their impact on split renal function on the long term in patients who had a low pressure ileal neobladder constructed using refluxing ureterointestinal anastomoses. Unfortunately our patients did not have a preoperative renal scan and this can be considered the main bias of this study but all patients had a thorough preoperative evaluation that included serum creatinine, ultrasonography and computerized tomography and all the 17 patient showing postoperative upper tract dilatation either due to stricture or reflux presented a normal morphology of the upper urinary tract before surgery associated with normal serum creatinine.

Anastomotic stricture: refluxing vs nonrefluxing techniques

All ureterointestinal anastomoses, whether antireflux or not, have an inherent risk of stricture with consequent ureteral obstruction and, thus, potential renal impairment. However, this risk appears, to be appreciatively higher after an antireflux technique than after direct anastomosis, irrespective of the anastomosis technique and the segment of bowel used [11, 24, 25] with a reported stricture rate of 1-4% for the direct anastomosis and of 9.5-20% for the different antireflux techniques described in

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the literature [5, 7, 12, 26, 27] . Better results were reported by Osman et al. with a 5.1% obstruction rate using the serous lined extramural tunnel technique [28] , and by Skinner with the ileal T pouch neobladder [18]. However, the T mechanism is not easy to construct, time-consuming and yet to be widely adopted.

Anastomotic stricture: long- term effects on renal function and treatment options

In our series, using a Nesbit nontunneled end- to- side ureteroileal anastomosis the stricture rate was 3.4% and in three over seven cases the strictures caused acute symptoms such as flank pain and fever. All symptomatic strictures occurred within the first 8 months after surgery and all were treated with open reimplantation. Others proposed the endourological treatment that consists in balloon dilatation or incision of the stricture due to its lower morbidity in comparison to the open surgical treatment [29], but we, and others consider the open surgical revision as the preferred method for its significantly higher success rate [12].

Another possible presentation of anastomotic strictures is in asymptomatic patients during follow up imaging showing unilateral hydronephrosis possibly associated with signs and symptoms of UTIs, pyelonephritis and increased serum creatinine. In our series, four anastomotic strictures were diagnosed during follow up in asymptomatic patients. We opted for open surgical treatment in two cases with a preserved split GFR at renal scintigraphy while decided for a close follow up in the other two patients due to the very poor split renal function of the obstructed unit with a preserved contralateral kidney function that in our view lowered the advantages of the surgical correction associated with all the possible complications of this type of surgery. Nevertheless, in these two patients, the last nuclear renography performed 3 and 4 years after diagnosis showed a further significant decrease of the split GFR. Therefore, we believe that all strictures, once detected, should be treated surgically with reimplantation because also asymptomatic strictures invariably lead to deterioration of kidney function during follow up.

Long-term effects of reflux on renal function

While the danger to renal function caused by anastomotic stricture is well documented in orthotopic

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neobladders, the benefits of reflux prevention are only clear for the continent cutaneous pouch requiring intermittent catheterization and for ureterosigmoidostomy, both usually showing high reservoir pressures and bacteriuria [30] . However, in the orthotopic neobladder, which is a low pressure reservoir with no major coordinated contractions and either with sterile urine or with asymptomatic bacterial colonization, the benefits related to reflux prevention are not well documented [25] .

All literature data suggest that even if present, reflux per se, does not provoke renal impairment unless infected urine is present. Indeed, most clinical and experimental studies show the important role of UTI together with reflux in the development of reflux nephropathy scars [9, 10, 25] . Moreover, asymptomatic bacterial colonization is not sufficient to cause renal damage but recurrent UTIs are; the latter occurring especially in women with hypercontinence and in men with severe voiding dysfunction [8] . In our series we confirm this assumption. Indeed, of the ten patients with nonobstructive dilatation caused by reflux, only three who had recurrent UTI and urosepsis had a severe reduction of parenchymal uptake during follow up, while the remaining seven patients, with sterile urine or one positive urinalysis during follow up, showed a preserved split GFR symmetrical with the not dilated renal units, that did not showed a significant reduction during follow up.

CONCLUSIONS

The direct, end-to-side Nesbit ureteroenteric anastomosis is a safe and acceptable technique for ureteral reimplatation in low pressure ileal neobladder, it provides excellent long-term results with a low stricture rate. All strictures, once detected, should be treated surgically with reimplatation because even asymptomatic strictures can lead to deterioration of kidney function during follow up. Reflux per se does not provoke renal impairment unless recurrent UTIs and urosepsis are present. In the latter, a progressive decrease in kidney function is awaited.

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CONFLICT OF INTEREST

We confirm that:

1. All authors have made a substantial contribution to the manuscript: "EFFECTS ON RENAL FUNCTION OF OBSTRUCTIVE AND NONOBSTRUCTIVE DILATATION OF THE UPPER URINARY TRACT IN ILEAL NEOBLADDERS WITH REFLUXING URETEROENTERIC ANASTOMOSES" submitted for publication.
2. All have read and approved the final manuscript.
3. All have no commercial relationship such as consultancies, stock ownership or other equity interests, patents received and/or pending, or any commercial relationship which might be in any way considered related to the abovementioned submitted article.
4. The manuscript or portions of it are not under consideration by another journal or electronic publication and have not been previously published elsewhere.
5. No financial support has been received for this research/study.

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Tab.1: GFR and characteristics of the 7 patients with obstructive dilatation of the upper urinary tract.

	Obstructive Dilatation	Diagnosis (months)	Creat (mg/dl) [µmol/L] at diagnosis	GFR at diagnosis (ml/minute)			GFR at last follow up (ml/minute)			Follow up (months)
				total	right	left	total	right	left	
1	Symptomatic	2	1.5 [133]	-	-	-	90.6	50.2	40.4	27
2	Symptomatic	4	1.35 [119]	-	-	-	96.4	51.3	45.1	62
3	Symptomatic	8	1.42 [125.5]	-	-	-	102.3	46	56.3	35
4	Asymptomatic	6	1.2 [106]	97	45	52	90.5	39.2	51.3	56
5	Asymptomatic	12	1.23 [109]	98	58	40	93.8	59	34.8	74
6	Asymptomatic	24	1.36 [120]	83	62	21	75.6	61.4	14.2	36
7	Asymptomatic	24	1.45 [128]	84.3	58	26.3	72.3	56	16.3	48

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Tab. 2: GFR and characteristics of the 10 patients with non-obstructive dilatation of the upper urinary tract.

	Unobstructive Dilatation	Diagnosis (months)	Creat (mg/dl) [µmol/L] at diagnosis	GFR at diagnosis (ml/minute)			GFR at last follow up (ml/minute)			Follow up (months)
				total	right	left	total	right	left	
1	bilateral Recurrent UTI	21	1.28 [113.5]	47	22	25	32	15	17	17
2	bilateral Recurrent UTI	22	0.8 [71]	64.4	31.2	33.2	44.2	19	25.2	47
3	bilateral Recurrent UTI	25	1.25 [110.5]	55.9	27.6	28.3	46.4	21.1	25.3	51
4	Monolateral No UTI	42	1.07 [95]	106.5	53.7	52.8	102.6	52	50.6	36
5	Monolateral No UTI	90	1.31 [116]	84.6	45	39.6	82.4	46	36.4	39
6	Monolateral No UTI	83	1.12 [99]	106.5	53.5	53	103.1	53	50.1	46
7	Monolateral No UTI	27	1.14 [101]	106.8	53	53.8	103.8	53	50.8	48
8	Monolateral No UTI	52	1.27 [112]	106.2	52.9	53.3	102.8	50.1	52.7	44
9	Monolateral No UTI	48	1.35 [119]	85.1	43.8	41.3	81.9	43.2	38.7	42
10	Monolateral No UTI	31	1.4 [124]	80.7	38.2	42.5	76.9	35.4	41.5	51

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