Clinical Follow-Up of Children with Low Differential Function on Diuretic Renogram

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Objective: *One of the most challenging dilemmas in pediatric urology today is to determine the optimal management of children with hydronephrotic kidney secondary to suspected ureteropelvic junction obstruction. Some believe in early surgical management while others believe in conservative management. To better define these issues, the authors retrospectively reviewed 101 patients with hydronephrosis.*
Material and Method: *The present study was approved by The Children's Hospital of Philadelphia's institutional review board and waiver of informed consent for retrospective study. One hundred and one children (72 males and 29 females) of ages of 6 days to 19 years with hydronephrosis with suspected UPJ obstruction underwent diuretic renograms with ^{99m}Tc DTPA. The authors classified the differential renal function into three groups: Group I: 0-15%, Group II: 16-30%, and Group III: 31-46%.*
Results: *Forty-one patients with conservative management, 32% (5 in group I: 1 in group II and 7 in group III) showed improved differential renal function. Non-operative management patients from group I and II showed no deteriorating renal function and only one case from group III had deteriorating renal function. In operative management, 78% of group I, 41% of group II, and 25% of group III showed improvement in differential renal function. In the remaining operative cases, six showed deteriorated differential renal function [1(4%) group I: 3(18%) group II: 2 (10%) group III] whereas 24 remained stable or unchanged [Group I: 4(17%), Group II: 7(41%), Group III: 13 (65%)].*
Conclusion: *The authors recommended conservative management for children with differential renal function between 16-46%.*

Keywords: *Hydronephrosis, Diuretic renography, Differential renal function, Pelvic Ureterojunction Obstruction*

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With widespread use of ultrasonography in obstetrical and neonatal care, hydronephrosis, defined as renal pelvic dilatation, is being detected in as many as 1.4% of fetuses[1-3]. Half of these cases persist postnatally[4]. The most common etiology of hydronephrosis in infancy and children is ureteropelvic junction obstruction. Although hydronephrosis is now frequently diagnosed, the appropriate management remains controversial since the pathological mechanisms and the resolution are not well understood. The condition may progress over time and may result in damage to the renal parenchyma, which may lead to deterioration of renal function or may resolve spontaneously over time[5]. The urologist is confronted with the challenge of determining the existence, etiology and, most importantly, the management of upper urinary tract dilatation. The current debate centers on the indication

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for and optimal timing of surgical management in diagnosed cases of ureteropelvic junction obstruction[6,7].

However, many studies have advocated immediate reconstruction in the newborn with ureteropelvic junction obstruction and have shown this to be technically feasible on the basis that surgery will protect and prevent deterioration of renal function[8-11]. In one study, Bernstein et al[12] showed that early pyeloplasty is relatively safe and effective. In contrast, others believe that hydronephrosis will resolve over time and have thus suggested conservative treatment. Homsy et al[13] found that 47 percent of 17 renal studies with partial obstruction show spontaneous improvement in drainage during 3 to 6 months. In contrast, Koff[14] advocated observation alone and has found that renal function remains stable and improves in most cases.

In an attempt to clarify these issues, the authors retrospectively reviewed 101 cases of patients with hydronephrosis secondary to ureteropelvic junction obstruction based on serial assessment of renal function on diuretic renography.

Material and Method

The present study was approved by The Children's Hospital of Philadelphia's institutional review board and waiver of informed consent for retrospective study. There is no financial conflict of interest. This study was performed during one of our authors' (Chanisa Chotipanich) study, supported by International Atomic Energy Agency (IAEA) at Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

Patient population

Between January 1994 and September 2002, 101 children (72 Male, 29 Female), aged 6 days to 19 years with hydronephrosis suspected of ureteropelvic junction obstruction were retrospectively reviewed. Any patient who had previous surgery of the renal urinary tract, dilatation of the ureter due to ectopic ureter, ureteroceles, reflux, a solitary kidney, or anatomic or neurogenic abnormality of the lower urinary tract was excluded from this study.

Imaging procedures and data analysis

The syringe with the radioactive dose of ^{99m}Tc Diethylene-triaminepenta-acetic acid (DTPA) was counted by placing it in the center of the field of view exactly 30 centimeters below a large FoV gamma camera (ADAC-SKYLIGHT or ADAC-FORTE) fitted with a low energy high resolution collimator. Ten-second image acquisitions of the syringe were obtained pre and post injection. The syringe was counted to calculate the precise amount injected into the patient by the amount left in the syringe. The injection site was in the same location as the IV such as feet, hands, and arms.

Imaging Procedures

Diuretic renography augmented with intravenous furosemide was performed on a dual head gamma camera (ADAC-SKYLIGHT or ADAC-FORTE), using the posterior view, with a low energy high-resolution collimator, and a 20% window centered over the 140 keV photo peak of ^{99m}Tc.

Adequate hydration was attempted by providing a D5.3 NS or D5.25 NS solution intravenously over a 30-minute period before the present study. The bladder was then catheterized to assure adequate drainage throughout the present study. Following the intravenous injection of 74-185 MBq of ^{99m}Tc DTPA, the image data were collected in a 128x128 matrix at 1 sec per frame in the initial 1 minute to evaluate flow to the kidney and 30 seconds per frame for 50 minutes, which was combined renography and diuretic phase. Intravenous furosemide (1 mg/kg up to maximum of 40 mg) was administered after the renography phase (20 to 30 minutes) but not before the entire collecting system that was believed to be full.

Data Analysis

The regions of interest (RoIs) during the renography phase and diuretic phase were drawn to include the entire kidney and dilated renal pelvis, and a semiluminar area inferior and lateral to the lower pole of the kidney for background subtraction. Differential renal function for each kidney was determined from summation of all frames between 1 and 2 minutes. Drainage curves were generated from these ROIs using standard computer-generated curves. Patients were divided into three groups according to their initial differential renal function by diuretic renography as follow:

Group I: This group had differential renal function between 0% and 15%

Group II: This group had differential renal function between 16% and 30%

Group III: This group had differential renal function between 31% and 46%

Patients with differential renal function greater than 46% were considered to have normal renal

function and were not included in the present study. Improvement or deterioration in function in a renal unit was defined as a significant upward or downward change in function greater than 10%.

Indication for surgery

Given the retrospective nature of this review, the authors did not consult the urology department, so uniform and well defined indications for surgery were not ascertainable.

Statistic Analysis

Data was analyzed using StataCorp 2003 (Stata Statistical Software: Release 8.0. College Station, TX: Stata Corporation). Chi-square test was used for comparison of qualitative data. A p-value of less than 0.05 was considered to indicate statistical significance.

Results

Of the 101 patients, 36 (36%) had right sided obstruction and 61 (60%) had left sided. Four of 101 (4%) showed bilateral obstruction. The patients were grouped according to age and summarized in Tables 1 and 2. Table 1 shows comparison factors, which are sex, age, and differential renal function in between groups of patients with and without surgery. No significant differences in patient sex was evident between the two groups (p = 0.817). However, there was a statistically significant association between differential renal function in these groups (p = 0.002). The patients were subdivided according to initial differential renal function. There were 34 cases in Group I (0-15%), 22 cases in Group II (16-30%), and 45 cases in Group III (31-46%). Sixty of 101 patients (59%) underwent surgery while 41 (40%) were managed conservatively.

Patients treated with surgery

Twenty-three of sixty patients (38%) comprised group I, 17 patients (28%) in group II, and 20 patients (33%) in group III required surgery. The mean age for surgery was 18 months with 15% as neonates and 85% older. After surgery, 18 of 23 patients (78%) in group I, 7 of 17 (41%) in group II, and 5 of 20 (25%) in group III showed improvement in differential renal function. Thus, 50% (30 of 60) of all groups with impaired renal function (less than 45%) showed improved renal function. Post-operatively ten percent (1 in group I, 3 in group II and 2 in group III; of those, 16.66% were neonates, 83.33% were older) had deteriorated renal function. There were 24 (40%) patients of all groups that showed stable function post surgery.

Patients followed non-operatively

Of the 101 patients with suspected ureteropelvic junction obstruction, 41 (neonates 17%, older 83%) were managed conservatively. Of the 41 patients

Table 1. Comparison of factors in patient with operative and Non-operative groups

Factors	Operative	Non-operative	p-value
Sex			0.924
Male	43	29	
Female	17	12	
Age (month); median (min, max)	2.83 (0.16, 226.95)	1.86 (0.2, 209.46)	0.803
Differential renal function			0.002
Group I	23	11	
Group II	17	5	
Group III	20	25	

Table 2. Number of Patients, age for each subgroup in both operative and nonoperative groups

Variable	Group I		Group II		Group III	
	Non operative	Operative	Non operative	Operative	Non operative	Operative
No. (%) of patients	11 (10.8)	23 (22.7)	5 (4.9)	17 (16.8)	25 (24.7)	20 (19.8)
Age range, month	0.2-152.05	0.16-220.57	0.95-87.72	0.23-226.95	0.3-209.46	0.42-147.94

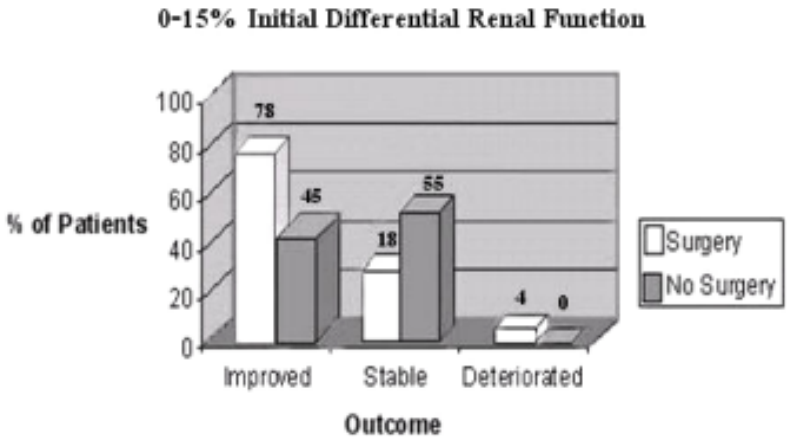

Fig. 1 Outcome of patients focused on group 1 (0-15%)

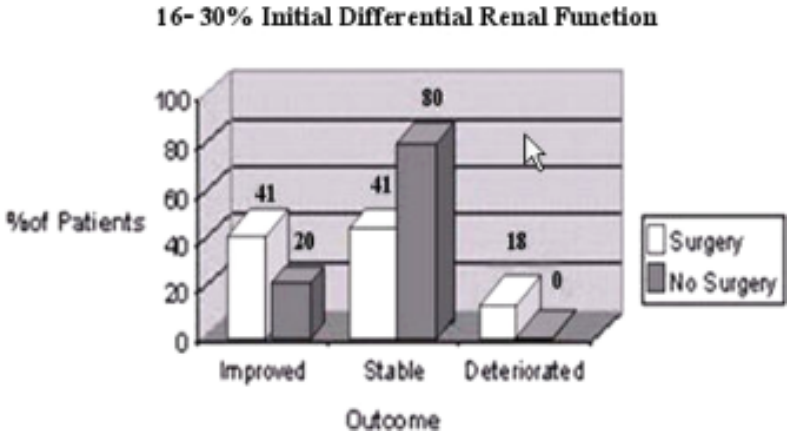

Fig. 2 Outcome of patients focused on group II (16-30%)

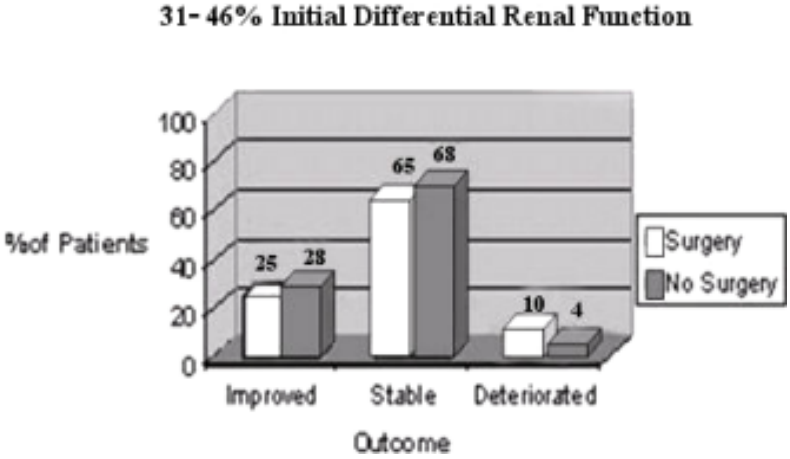

Fig. 3 Outcome of patients focused on group III (31-46%)

managed non-operatively, thirty-two percent (5 in group I, 1 in group II and 7 in group III) showed improved differential renal function (mean time was 7.44 months). Conservative management in Groups I and II showed no deteriorated renal function. The overall results of non-operative and operative management are summarized in Fig. 1-3.

Discussion

The management of children with hydronephrosis with suspected ureteropelvic junction obstruction has received considerable attention. A consensus on the optimal timing of surgical decompression and repair of obstruction uropathy has yet to be reached. The fundamental issue consistently debated is whether immediate surgical decompression and repair of obstructive uropathy result in greater improvement in function than delayed operation at an older age. As a result of several studies, Mayor et al[15] have demonstrated deterioration in the renal function of children who had surgical correction of urinary obstruction after they were a year old. A study by King[8] provided support for pyeloplasty, showing greater improvement in renal function in patients who underwent surgery before 3 months of age compared to patients who delayed surgery. Other investigators show that delayed pyeloplasty and late release of the obstruction result in the potential of functional recovery. These same investigators recommended the early correction of obstruction uropathy be within the first 2 years of life for possible improvement of renal function[6,16-18]. The logical conclusion is that surgery should be performed as soon as possible. Conversely, others have questioned the necessity for early surgery, showing that ureteropelvic junction obstruction presents a diagnostic but not a therapeutic dilemma[19-21]. Ureteropelvic junction obstruction may be a transitional period, which spontaneously improves, thus supporting conservative management. Samlem et al[22] reported the outcome of pediatric pyeloplasty in 108 children. Their results indicated that patient's age at pyeloplasty do not influence postoperative differential renal function and delayed surgery allows some renal units to mature, averting the need for pyeloplasty.

As evidenced in the present study, seven of 60 cases (12%) that underwent surgery after 2 years of age all improved in renal function. Koff[23] followed patients with ureteropelvic junction obstruction in whom function, drainage and hydronephrosis spontaneously improved, and recommended following patients with ultrasonography and diuretic renography, using operative intervention only if a change in renal function, or pelvic volume indicated obstruction.

The ideal time and the exact indication for surgical intervention are controversial. The determination of renal function by isotope imaging constitutes a major tool for the evaluation of relative renal function of the hydronephrotic kidney. In the present study, the authors classified the patients into three groups and the majority from group III, with mean age 18.99 months and 27.34 months in non-operative and operative groups, respectively. These classifications were made to distinguish marked (less than 15%), moderate (16%-30%), and mild (31%-46%) levels of differential renal function. The goal is to continue conservative management as long as possible without threatening renal function.

In Group III, most children showed improvement in renal function with conservative management. There was no clear benefit from surgery, as a high percentage remained stable in renal function but greater percentage risked deterioration. In Group II, seventeen had pyeloplasty, of these, only seven showed an improvement in renal function, seven remained stable, and three showed deterioration in renal function. Eighteen of the thirty-four in Group I had significant improvement in renal function post-operatively. Although surgery appeared to be optimal, one of the twenty-four operatively managed in Group I had postoperative deterioration in renal function and four remained stable. Furthermore, all patients managed conservatively in groups I and II either remained stable or improved, while none showed deterioration in renal function. Thus, the present study showed that conservative management was preferred over surgery, as the likelihood of renal function remaining stable was almost the same regardless of surgery and surgical intervention that might increase the risk of possible deterioration.

In all groups of improved renal function postoperatively, there was some debate that the kidney did in fact improve after surgery. It is well known that GFR is lower in newborns than in older children but the rate increases several times during the initial 6 months of life and levels off at age 2 years when adult values are reached[24]. From the data collected the kidney immaturity of children who underwent surgery at age 2 years and under could have been misinterpreted during the pre-and post-operative evaluations. One should keep in mind that apparent postoperative improvement in renal function in group I, II and III might be secondary to renal maturation during the first two

years of life and not to the results of surgery. Explanations of why six patients (1 in group I, 3 in group II, 2 in group III) had diminished function after surgery could be that the obstruction was not relieved, there was no initial obstruction, the decreased function reflected earlier transient obstruction, or there was dysmorphic development[25].

The present results demonstrate that conservative management of hydronephrosis, secondary to ureteropelvic junction obstruction is safe and effective when function is assessed carefully and serially with a lasix renogram. Chertin[26] followed 44 children with ureteropelvic junction obstruction and recommended conservative management. It spares the children of unnecessary surgery and although renal function may deteriorate, delayed pyeloplasty recovers to the initial function level. Ulman et al[27] reported that 81 of 104 patients with ureteropelvic junction obstruction, who were followed non-operatively, were resolved in 69% and improved in 31%. They recommended non-operative treatment with close follow up. Recent reports have suggested the safety and efficacy of a non-operative observation in most kidneys by 2 years[28,29].

Conservative management is desirable for several reasons. It has become apparent that the functional anatomy and physiology of ureteropelvic junction obstruction is dynamic in the first few months of life. Koff et al[30] showed the complex interaction between renal pelvic pressure, volume, and urinary flow rates in experimentally and clinically studied ureteropelvic junction obstruction in dogs and man. The labile ureteropelvic junction often declares itself within the first 6 months of life. Another advantage of delayed management of ureteropelvic junction obstruction is the enhanced technical ease with which surgical repair of either entity can be accomplished in the older neonate (3 to 6 months old). Thorup and associates[31] reported on nine infants who underwent immediate pyeloplasty in the neonate period and found an increased rate of complications when the procedures were performed in the immediate newborn period. The present study should not be misinterpreted as to imply that surgery for ureteropelvic junction obstruction is unnecessary or ineffective. On the contrary, surgery will markedly improve function and hydronephrosis and, if properly timed, will prevent permanent renal functional changes caused by obstruction.

Study Limitation

The current study was limited by the small numbers of the patients included. Therefore, it might have decreased the authors' powers to detect the true difference. Further study should be undertaken with a larger sample size.

Conclusion

The ideal management of ureteropelvic junction obstruction is still debated. The authors recommend conservative management for children with differential function between 16-46%. The risk of possible deterioration in renal function with surgery is greater than that of conservative management and there is the same likelihood of remaining stable in renal function. The authors recommend avoiding unnecessary surgery and allowing potential spontaneous improvement with careful follow up; the better alternative is to undergo surgery only when signs of deterioration are present.

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การเฝ้าติดตามผู้ป่วยเด็กที่มีค่า differential function ต่ำ จากการตรวจด้วย diuretic renogram

ชนิสา โชติพานิช, โจน รูบิน, โจเซฟ ลิน, มาร์ติน ชาล์รอน

วัตถุประสงค์: *เพื่อศึกษาการรักษาผู้ป่วยเด็กที่มีภาวะ hydronephrosis ที่สงสัยว่ามีสาเหตุจาก ureteropelvic junction obstruction ซึ่งเป็นข้อถกเถียงกันอยู่ในปัจจุบันถึงวิธีการรักษาที่ใช้ โดยบางกลุ่มใช้วิธีการรักษาโดยวิธีการผ่าตัด และบางกลุ่มใช้วิธีการรักษาแบบ ติดตามอาการของโรคอย่างต่อเนื่อง โดยการศึกษานี้มุ่งเน้นหาความชัดเจนของวิธีการรักษาผู้ป่วยเด็กที่มีภาวะดังกล่าว*

วัสดุและวิธีการ: *ศึกษาย้อนหลังผู้ป่วยเด็กที่มีภาวะ hydronephrosis ที่สงสัยว่ามีสาเหตุจาก ureteropelvic junction obstruction จำนวน 101 ราย ที่มารับการตรวจที่ The Children's Hospital of Philadelphia ในระหว่างเดือน มกราคม พ.ศ. 2537 ถึง เดือน กันยายน พ.ศ. 2545 โดยเป็นผู้ชาย 72 ราย ผู้หญิง 29 ราย อายุระหว่าง 6 วัน ถึง 19 ปี ศึกษาโดยวิธีการตรวจ diuretic renogram ด้วย ^{99m}Tc-DTPA และแบ่งกลุ่มผู้ป่วยตาม Differential renal function เป็น 3 กลุ่ม: กลุ่ม I: 0-15%, กลุ่ม II: 16-30% และกลุ่ม III: 31-46%*

ผลการศึกษา: *ในกลุ่มผู้ป่วยที่ไม่ได้รับการผ่าตัดพบว่า 12% จากกลุ่ม I, 2% จากกลุ่ม II และ 7% จากกลุ่ม III มีค่า differential renal function ดีขึ้น ส่วนในกลุ่มที่ได้รับการผ่าตัดพบว่า 30% จากกลุ่ม I, 12% จากกลุ่ม II และ 8% จากกลุ่ม III มีค่า differential renal function ดีขึ้น แต่มี 17% จากกลุ่ม I, 50% จากกลุ่ม II และ 33% จากกลุ่ม III มีค่า differential renal function แย่ลงจากการผ่าตัด*

สรุป: *จากการศึกษานี้แนะนำให้ติดตามอาการของโรคอย่างต่อเนื่อง ในผู้ป่วยเด็กที่มีค่า Differential renal function ระหว่าง 16-46%*