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# Quantitative analysis of infantile ureteropelvic junction obstruction by diuretic renography

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Infantile hydronephrosis detected by ultrasonography poses a clinical dilemma on how to treat the condition. This article reports a retrospective study to evaluate infantile hydronephrosis due to suspected ureteropelvic junction (UPJ) obstruction by means of standardized diuretic renography and to speculate its usefulness for quantitative assessment and management of this condition. Between November 1992 and July 1999, 43 patients who had the disease detected in their fetal or infantile period were submitted to this study. Standardized diuretic renograms were obtained with $^{99m}$Tc-labeled diethylene-triaminepenta-acetate (Tc-99m-DTPA) or $^{99m}$Tc-labeled mercaptoacetyl triglycine (Tc-99m-MAG3) as radiopharmaceuticals. Drainage half-time clearance (T 1/2) of the activity at each region of interest set to encompass the entire kidney and the dilated pelvis was used as an index of quantitative analysis of UPJ obstruction. Initial T 1/2s of 32 kidneys with suspected UPJ obstruction were significantly longer than those of 37 without obstruction. T 1/2s of kidneys which had undergone pyeloplasty decreased promptly after surgery whereas those of units followed up without surgery decreased more sluggishly. These findings demonstrate that a standardized diuretic renographic analysis with T 1/2 can reliably assess infantile hydronephrosis with UPJ obstruction and be helpful in making a decision on surgical intervention.

**Key words:** hydronephrosis, diuretic renography, quantitative analysis, infant, pyeloplasty

## INTRODUCTION

GREATER AVAILABILITY of prenatal and infantile ultrasonography for routine check-ups resulted in an increased number of cases of fetal and infantile hydronephrosis.[1–3] The most frequent cause of detected hydronephroses is ureteropelvic junction (UPJ) obstruction,[4] which often requires surgical intervention because it may cause pyelonephritis and impaired renal function but most cases detected by screening are known to subside spontaneously,[5,6] and immediate surgery is indicated for only a limited number of cases.

Assessment of patients with suspected UPJ obstruction is needed to differentiate obstructed from non-obstructed hydronephrosis and to justify surgical intervention. Grading systems by means of intravenous pyelography and ultrasonography have been utilized to express the degree of UPJ obstruction,[7–9] but they are essentially morphologic studies of the dilated pelvis, assuming that the pelvic shape reflects the degree of obstruction. The pressure flow study proposed by Whitakar et al.[10] is a direct approach to assess obstruction by puncturing the dilated pelvis but its invasiveness deters one to apply it for an apparently normal kidney and for serial studies in infants.

Radionuclide renography has been utilized for assessment of UPJ obstruction. Initially the renogram pattern was demonstrated to be an indicator of obstruction and later diuretic renography with intravenous furosemide has been reported and a standardized method was proposed for pediatric patients.[11–13] This article reports a retrospective study which reviews infants with suspected UPJ obstruction evaluated by this standardized diuretic

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renography to document its validity in assessing that condition in infancy.

## MATERIALS AND METHODS

*Patients and kidneys*

Between November 1992 and July 1999, 43 pediatric patients who had their disease detected in their fetal or infantile period were submitted to diuretic renography at Tokai University Hospital and 162 renograms of 86 kidneys were obtained to evaluate their urologic condition at various ages ranging from 1 to 53 months.

Thirty-two kidneys were hydronephrotic due to suspected UPJ obstruction, which is defined as a dilated pelvis demonstrated by ultrasonography but without dilated ureter or marked vesicoureteral reflux shown by contrast studies. Twenty-eight kidneys with other diseases included 18 with vesicoureteral reflux (VUR), 6 with ureterovesical junction (UVJ) obstruction, and 4 others. Two kidneys with both UPJ obstruction and repaired VUR and one with UPJ obstruction and mild VUR were categorized into those with UPJ obstruction. Twenty-six kidneys were examined because of an associated urologic condition in contralateral kidneys and were considered to have no apparent disease (Table 1).

Eight out of 32 kidneys with suspected UPJ obstruction were treated with pyeloplasty and 3 of them were associated with significant urinary tract infection(s). The UTI episode occurred after renography in 2 cases and prior to the examination in one, all of which underwent pyeloplasty. Five other units also underwent pyeloplasty without any symptom. Postoperative renograms were obtained from 6 operated kidneys more than 6 months after pyeloplasty. Twenty-four kidneys with suspected UPJ obstruction were followed up without surgery and 10 of them were evaluated with serial renograms during follow-up (Table 2).

In summary, 74 renograms were of kidneys with UPJ obstruction including 25 for surgically treated kidneys 49 for kidneys treated without surgery. Seventy-four diuretic renograms were obtained from 46 kidneys without either renal disease or obstructive uropathy including 34 of those with VUR. These 148 renograms were analyzed for the purpose of this study, and excluded from the analysis were 10 of kidneys with UVJ obstruction and 4 for kidneys with other renal diseases.

**Table 1** Patient and unit profile

| Diagnosis | Units (cases) |
|---|---|
| Hydronephrosis with suspected UPJ obstruction | 32* (25) |
| Vesicoureteral reflux (VUR) | 18 (11) |
| Hydronephrosis with UVJ obstruction | 6 (5) |
| Other diseases | 4 (3) |
| Contralateral unit | 26 (26) |
| Total | 86 (43) |

*includes two units with repaired VUR and one with mild VUR

**Table 2** Treatment of units with suspected UPJ obstruction

| Treatment | Units |
|---|---|
| Pyeloplasty | 8 |
| (with UTI episode | 3) |
| (without UTI episode | 5) |
| Followed without pyeloplasty | 24 |

*Patient preparation and data acquisition*

A standardized diuretic renography suggested by The Society for Fetal Urology[12] was adopted and modified as follows for the specific need in our institution. (1) The patient was hydrated prior to the exam for 2 hours with 10 ml/kg/hr of intravenous fluid. (2) The patient was sedated if necessary with oral triclofos sodium and diazepam supplemented sometimes with 2–3 mg/kg of intravenous ketamine. (3) The bladder was emptied by urethral catheterization prior to renography. (4) A radiopharmaceutical was given intravenously with an age appropriate dose of radioactivity (18.5–74 MBq). Either Tc-99m-labeled diethylene-triaminepenta-acetate (Tc-99m-DTPA) or Tc-99m-labeled mercaptoacetyl triglycine (Tc-99m-MAG3) was used as a radiopharmaceutical. (5) Intravenous 0.5 mg/kg of furosemide was administered exactly 20 minutes after the radiopharmaceutical injection. (6) Data were collected by means of a large-field of view gamma camera from the back of the patient in the supine position. The field of view of the camera was set to cover the body area from the upper abdomen to the bladder. (7) $64 \times 64$ pixels of digital data were accumulated at 10 second/frame for 40 minutes. (8) Regions of interest (ROIs) were set to encompass the entire kidney and the dilated pelvis as well as the background rectangular ROIs set beneath both kidneys to obtain a renogram. (9) Background subtracted renal time-activity curves were obtained.

*Data analysis of the renography*

On a diuretic renogram, a renal activity curve usually declines more rapidly after furosemide injection, which is defined as the diuretic phase. Quantitative analysis of the UPJ obstruction is made by measuring drainage half-time clearance (T 1/2) of the activity at each ROI during the diuretic phase. To measure T 1/2, the start and end point of declining activity on each curve were determined manually and fitted by an exponential curve. Then the parameter of the equation was defined as T 1/2 and this was considered to be the index of the UPJ obstruction. An example of a renographic curve and the method to determine T 1/2 are shown in Figure 1 and the method to determine each point is shown Figure 2 in detail.

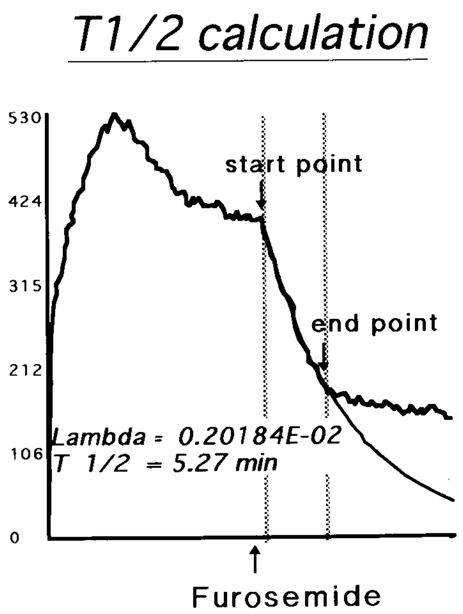


**Fig. 1** Representative time-activity curve and measurement of drainage half-time clearance (T 1/2) of the activity. Start and end points of declining curve during the diuretic phase were determined and fitted by an exponential curve. Parameter of the equation was defined as T 1/2 at each ROI.

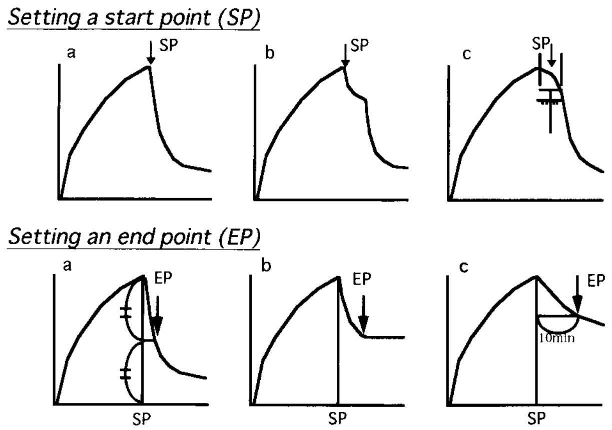


**Fig. 2** Methods to determine start and end points on an activity curve. A start point is set either at the edge of the monophasic declining curve (a), at the initial edge when the decline is biphasic (b) or at the midpoint between two points when the edge is dull (c). An end point is set either at the point of the half of the peak activity (a), at the point where the activity becomes plateau (b) or at 10 min from the start point when the decline is slow (c).

### *Statistical analysis*

Values are expressed as the mean ± SD. Data were evaluated by an analysis of variance. Data that appeared statistically different were further compared by unpaired t-test and the difference was considered significant if the p-value was less than 0.05. Regression analysis was done to see if T 1/2 length of the specific condition correlated with the patient's age. Two parameters were considered correlated if the regression coefficient was larger than 0.6.

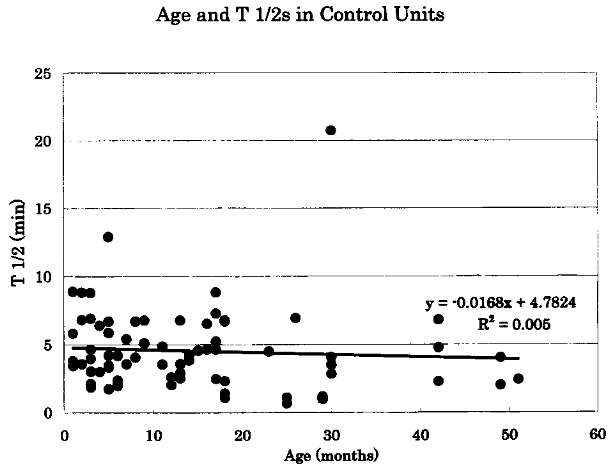


**Fig. 3** Age distribution and T 1/2 length in 74 renograms either without renal disease or obstructive uropathy. Average T 1/2 can be considered to express the urinary flow at UPJ of the infantile kidney.

**Table 3** Initial T 1/2s of units with UPJ obstruction and controls

| Category | No. of units | mean ± SD (min) |
|---|---|---|
| UPJ obstruction* | 32 | 19.58 ± 23.24 |
| (with pyeloplasty**,*** | 8 | 45.85 ± 32.26) |
| (without pyeloplasty***,† | 24 | 10.85 ± 9.65) |
| (with UTI | 3 | 80.20 ± 23.40) |
| (without UTI | 29 | 13.30 ± 11.14) |
| Controls*,**,† | 74 | 4.54 ± 2.99 |

Units categorized as controls are those without either renal disease or obstructive uropathy. Statistically, T 1/2s of units with UPJ obstruction and of those undertaken pyeloplasty were significantly longer than those of controls ($p < 0.05$*,**) and T 1/2s of the operated units were significantly longer than those of units treated without surgery ($p = 0.01$***). But the difference between T 1/2s of units with UPJ obstruction treated without surgery and those of controls were not significant ($p = 0.06$†).

## RESULTS

### *T 1/2s of kidneys without obstructive disease*

In 74 diuretic renograms obtained from 46 kidneys without renal disease or obstructive uropathy, their T 1/2s ranged from 0.68 to 20.73 (4.54 ± 2.99) min. Age distribution and T 1/2 length in 74 renograms either without renal disease or obstructive uropathy are shown in Figure 3. Regression analysis indicated that there is no significant correlation between age and T 1/2 length ($y = -0.0168x + 4.782$ ($R = 0.07$)).

As a radiopharmaceutical, Tc-99m-DTPA was used in 66 renograms and Tc-99m-MAG3 in 8 renograms for

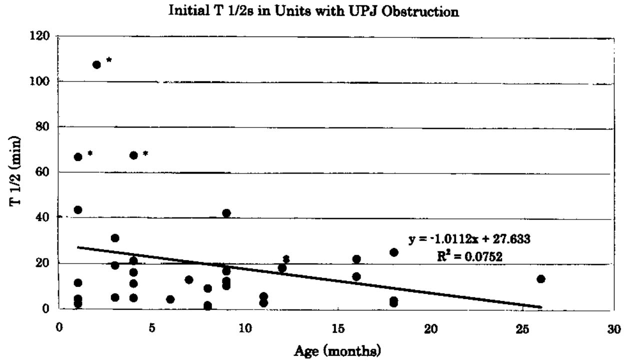


**Fig. 4** Initial T 1/2s of units with suspected UPJ obstruction. Distribution of patient's age and T 1/2 in 32 units with UPJ obstruction is demonstrated. Three units associated with significant urinary tract infection(s) are marked with * and one which developed renal caliculi is shown with $.

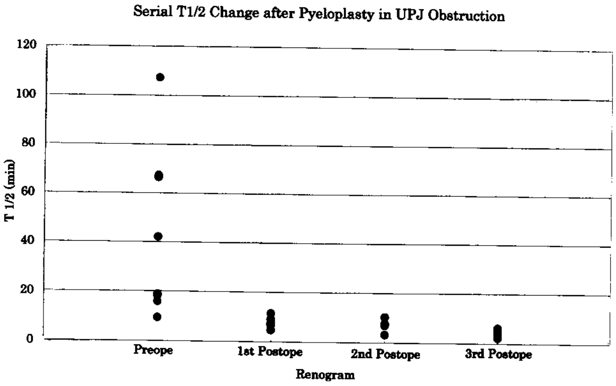


**Fig. 5** Serial T 1/2 change after pyeloplasty in UPJ obstruction. Eight preoperative renograms were obtained from 7 units and their average T 1/2 was 43.08 ± 12.19 min. Average T 1/2s of serial postoperative renograms were 8.10 (1st, n = 6), 7.02 (2nd, n = 5) and 4.29 (3rd, n = 5) respectively and they were significantly shorter than average T 1/2 of preoperative renograms.

units without obstructive disease. Mean T 1/2s were 4.55 ± 3.04 min and 4.51 ± 2.88 min from Tc-99m-DTPA and Tc-99m-MAG3 renograms respectively, which were not statistically different ($p = 0.48$). Therefore, the above-mentioned mean T 1/2 of 4.54 min was used as the control for T 1/2 in this age group and other renograms were analyzed regardless of the radiopharmaceutical nature.

*T 1/2s of kidneys with UPJ obstruction*

Of 32 kidneys with suspected UPJ obstruction, the initial diuretic renograms were obtained at various ages ranging from 1 to 26 months (mean 7 ± 6.4) and their T 1/2s ranged from 1.15 to 107.2 min (mean 19.58 ± 23.24). Patient's age and T 1/2 length were shown to be not correlated with each other by regression analysis ($y = -1.0112x + 27.633$ ($R = 0.28$)) (Fig. 4). When T 1/2s were compared with those of kidneys without either renal disease or obstructive uropathy, they were significantly different (19.58 ± 23.24 vs. 4.54 ± 2.99) ($p = 0.001$) (Table 3).

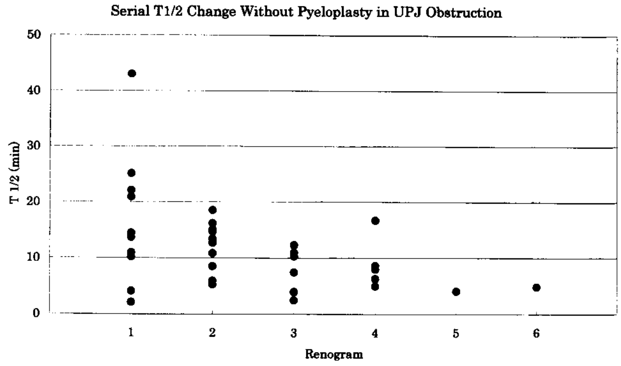


**Fig. 6** Serial T 1/2 change without pyeloplasty in UPJ obstruction. Serial renograms were obtained from 10 units which were treated without surgical intervention. Average T 1/2s of each renograms were 16.65 (initial, n = 10), 12.09 (2nd , n = 10), 7.97 (3rd, n = 8), 7.64 (4th and later, n = 7). When average T 1/2s of follow-up renograms were compared with that of initial ones, only T 1/2 of 4th and later renograms was significantly shorter than the initial T 1/2 ($p = 0.048$).

Among 32 kidneys, 3 associated with significant urinary tract infection(s) had extraordinarily long T 1/2s (66, 67, 107 min) and were treated with pyeloplasty. Five kidneys also underwent pyeloplasty without any symptom. One kidney with T 1/2 of 18.03 min at its initial renography had been followed without surgery yet developed renal caliculi despite decreased T 1/2, which necessitated pyeloplasty at three years of age (Fig. 4).

T 1/2s of the 8 operated kidneys were significantly longer than those of 24 kidneys treated without surgical intervention (45.85 ± 32.26 vs. 10.85 ± 9.65) ($p = 0.02$). But the latter were not statistically different from those of kidneys without either renal disease or obstructive uropathy (10.85 ± 9.65 vs. 4.54 ± 2.99) ($p = 0.06$) (Table 3).

*T 1/2 change during the treatment course*

Serial renograms were obtained from 17 kidneys with UPJ obstruction including 7 kidneys operated on and 10 without surgical intervention. Whereas the T 1/2s of 8 preoperative renograms obtained from 7 kidneys were 43.08 ± 12.19 min, the average T 1/2s of serial postoperative renograms were 8.10 (n = 6), 7.02 (n = 5) and 4.29 (n = 5), respectively, and they were significantly shorter than the T 1/2s of preoperative renograms. Perioperative change in T 1/2s in the operated kidneys is shown in Figure 5.

Ten kidneys which had been considered equivocal on initial renography were followed up by serial renograms without surgical intervention. T 1/2s were 16.65 ± 11.90 (initial, n = 10), 12.09 ± 4.41 (2nd , n = 10), 7.97 ± 4.04 (3rd, n = 8) and 7.64 ± 4.33 (4th and later, n = 7) at each renogram respectively. When the T 1/2s of follow-up renograms were compared with those of the initial ones, only the T 1/2 of the 4th and later renograms was significantly shorter than the initial one ($p = 0.048$) (Fig. 6).

## DISCUSSION

*Diuretic renography for quantitative analysis of UPJ obstruction*

Most babies with hydronephrosis due to suspected UPJ obstruction detected by ultrasonography are usually asymptomatic but some need surgical intervention to relieve severe obstruction. The degree of obstruction cannot be quantitatively assessed by the morphological change alone and direct pressure flow study is too invasive to apply to an apparently normal kidney.

Diuretic renography has been used to evaluate UPJ obstruction and the criteria initially proposed were to classify the renogram by the pattern,[11] but later the more sophisticated "well-tempered" diuretic renogram protocol adopted in this series was proposed to evaluate the degree of obstruction more precisely.[10,11,14]

In this series the protocol was modified from the practical standpoint. Furosemide was injected at a fixed timing set to 20 minutes after the radiopharmaceutical injection instead of injecting when the renal pelvis looks fully distended, considering it more objective. To determine the clearance half-time quantitatively by calculating or analyzing the curve, the response curve was fitted to an exponential curve after manually setting the start and end points of the declining activity curve, and this is considered to be a clinically reasonable method. Two different radiopharmaceuticals, Tc-99m-DTPA and Tc-99m-MAG3, were used but the renograms obtained had similar T 1/2s in kidneys without obstruction, so the data were analyzed regardless of the radiopharmaceuticals.

*T 1/2 as a quantitative index of UPJ obstruction*

The aim of this study was to demonstrate whether the adopted quantitative analysis of T 1/2 should reflect the obstructive state at UPJ in infancy. As for the control value of T 1/2 at this age, T 1/2s of 46 kidneys without either renal disease or obstructive uropathy were independent of age and without much variation, which implies that their average 4.54 min could be considered as a standard value.

When T 1/2s of 32 kidneys with suspected UPJ obstruction were compared with those of the kidneys without any obstruction, T 1/2s of the affected kidneys were significantly longer than the control. And T 1/2s decreased significantly after successful pyeloplasty for operatively confirmed UPJ obstructions (Table 3). We can therefore assume that the renographic analysis by means of the T 1/2 could evaluate the degree of UPJ obstruction quantitatively.

The fact that T 1/2s of kidneys with suspected UPJ obstruction were widely distributed suggests that the degree of UPJ obstruction would vary (Fig. 4). This observation reflects the fact that patients were submitted to this study regardless of the ultrasonographic degree of hydronephrosis, so that they are a mixed population in terms of UPJ obstruction. Further study comparing the degree of ultrasonographic hydronephrosis with the T 1/2 assessment would demonstrate its quantitative aspect more clearly.

T 1/2s of the serially assessed hydronephrotic kidneys without surgery decreased gradually. This supports other reported observations by serial ultrasonograms or diuretic renograms[4,5,15,16] showing that in many cases UPJ obstruction can resolve without surgical intervention, but serial observation of T 1/2s of the non-operated units suggested that T 1/2s declined sluggishly and shortened significantly only after a long period (Fig. 6). This suggests that successful operations should resolve the obstruction more efficiently than conservative management although the number of patient is too small to reach a conclusion on this issue.

*How to decide the treatment strategy by predicting the adverse outcome of UPJ obstruction*

The results of this study suggest that the severity of UPJ obstruction varies widely in infantile hydronephrosis. In this context, distinguishing obstructed from non-obstructed UPJ means to predict an adverse outcome of an affected kidney if UPJ obstruction is left uncorrected. Comparing the T 1/2s of 32 units with UPJ obstruction and prognosis in terms of urinary tract infection, it is noteworthy that all three kidneys with an infection episode had extraordinarily long T 1/2s ($80.20 \pm 23.40$ min ($n = 3$)) whereas ones without any complication had relatively short T 1/2s ($13.30 \pm 11.14$ min ($n = 29$)) (Table 3). This suggests that the longer the T 1/2 of the affected kidney is the more susceptible the patient is to urinary tract infection. When the T 1/2 is noticeably prolonged, early surgical intervention is indicated to prevent urinary tract infection.

Nevertheless, it is rather difficult to draw a line where intervention is mandatory since T 1/2s varies within the population with suspected UPJ obstruction. A T 1/2 greater than 20 min, which was suggested in the protocol guideline by SNM to be interpreted as an obstruction, seems to be in agreement with our observations[14] but 20 min is an arbitrary number without enough data concerning whether renal function is maintained with a T 1/2 which is longer but still less than 20 min. In our series, one patient who had had a kidney with an initial T 1/2 of 18 min but which decreased, yet developed renal caliculi necessitating lithotomy and still had definite UPJ obstruction (Fig. 4). Even if the T 1/2 decreased gradually without surgery, when it is moderately prolonged, it may be beneficial to do surgical correction to obtain more rapid and complete relief from the obstruction. A T 1/2 between 10 and 20 min is considered equivocal according to the SNM guidelines, but surgical intervention could be justified with this range of T 1/2.

It is clear that quantitative analysis of the standardized diuretic renography for kidneys with suspected UPJ is of great benefit for their management. More experience and analysis are needed to draw a conclusion about the surgical intervention for UPJ obstruction in order to achieve the best prognosis for the affected kidney.

## REFERENCES


1. Scott JE, Renwick M. Urological anomalies in the Northern Region Fetal Abnormality Survey. *Arch Dis Child* 1993; 68: 22–26.
2. Arger PH, Coleman BG, Mintz MC, Snyder HP, Camardese T, Arenson RL, et al. Routine fetal genitourinary tract screening. *Radiology* 1985; 156: 485–489.
3. Hirakawa H, Yokoyama S, Ueno S, Tajima T, Makuuchi H, Hamazaki Y, et al. Infantile abdominal ultrasound screening. *Proceedings of 32nd Annul Meeting of Pacific Association of Pediatric Surgeons* 1999: 55.
4. Tam JC, Hodson EM, Choong KK, Cass DT, Cohen RC, Gruenewald SM, et al. Postnatal diagnosis and outcome of urinary tract abnormalities detected by antenatal ultrasound. *Med J Aust* 1994; 160: 633–637.
5. Kitagawa H, Pringle KC, Stone P, Flower J, Murakami N, Robinson R. Postnatal follow-up of hydronephrosis detected by prenatal ultrasound: the natural history. *Fetal Diagn Ther* 1998; 13: 19–25.
6. Morin L, Cendron M, Crombleholme TM, Garmel SH, Klauber GT, D'Alton ME. Minimal hydronephrosis in the fetus: clinical significance and implications for management. *J Urol* 1996; 155: 2047–2049.
7. Terashima K, Nakaigawa N, Sano K, Asakura T. Long-term follow-up of mild hydronephrosis. *J Jpn Soc Pediatr Surg* 1995; 31: 748–753. (in Japanese)
8. Stocks A, Richards D, Frentzen B, Richard G. Correlation of prenatal renal pelvic anteroposterior diameter with outcome in infancy. *J Urol* 1996; 155: 1050–1052.
9. Cost GA, Merguerian PA, Cheerasarn SP, Shortliffe LM. Sonographic renal parenchymal and pelvicaliceal areas: new quantitative parameters for renal sonographic followup. *J Urol* 1996; 156: 725–729.
10. Whitaker RH. Methods of assessing obstruction in dilated ureters. *Br J Urol* 1973; 45: 15–22.
11. Thrall JH, Koff SA, Keyes JW Jr. Diuretic radionuclide renography and scintigraphy in the differential diagnosis of hydroureteronephrosis. *Semin Nucl Med* 1981; 11: 89–104.
12. Conway JJ, Maizels M. The "well tempered" diuretic renogram: a standard methods to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis. A report from combined meetings of The Society for Fetal Urology and members of The Pediatric Nuclear Medicine Council—The Society of Nuclear Medicine. *J Nucl Med* 1992; 33: 2047–2051.
13. O'Reilly P, Aurell M, Britton K, Kletter K, Rosenthal L, Testa T. Consensus on diuresis renography for investigating the dilated upper urinary tract. Radionuclides in Nephrourology Group Consensus Committee on Diuretic Renography. *J Nucl Med* 1996; 37: 1872–1876.
14. Mandell GA, Cooper JA, Leonard JC, Majd M, Miller JH, Parisi MT. Procedure guideline for diuretic renography in children. Society of Nuclear Medicine. *J Nucl Med* 1997; 38: 1647–1650.
15. Arnold AJ, Rickwood AM. Natural history of pelviureteric obstruction detected by prenatal sonography. *Br J Urol* 1990; 65: 91–96.
16. Madden NP, Thomas DFM, Gordon AC, Arthur RJ, Irving HC, Smith SEW. Antenatally detected pelviureteric junction obstruction. Is non-operation safe? *Br J Urol* 1991; 68: 305–310.