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# MRU Imaging after Infection of Furosemide for the Accuracy Diagnosis of Symptomatic Hydronephrosis

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## Abstract

**Objectives: To explore the feasibility of MRU (Magnetic Resonance Urography) under the intravenous injection of furosemide (FRS) in the diagnosis of abnormal hydronephrosis caused by renal pelvis and ureteral junctions during the intermittent period, though a 1.5T magnetic resonance scanner.**

**Study Design: Clinical research.**

**Place and Duration of Study: Department of Radiology and Urology, Children's Hospital of Zhejiang University School of Medicine, Hangzhou, China, from April to September 2019.**

**Methods: Twenty-four children, with symptomatic hydronephrosis caused by abnormal pelvic ureteral junctions during the intermittent period, were scanned by MRU after the first static hydration and the second intravenous injection of FRS, and contrast with ultrasound (US) results. Then comparison with the pathological results for who undergoing surgical treatment. The US and MRU image development was evaluated on a 4-point scale for renal pelvis and ureter development, and the overall situation was evaluated on a 5-point scale.**

**Results: BUS had 70.8% sensitivity of hydronephrosis, 16.7% sensitivity of ureteral dilatation, and overall sensitivity of 70.8%. The sensitivity of the three indexes in the hydraulic group was 87.5%, 95.8% and 100%, respectively. For the FRS group, the sensitivity increased to 100%, and when comparison with the pathological results from the 13 out of 24 cases underwent surgical treatment, the positive rate of coincidence was 77%.**

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**Conclusion: The rate of positive detection of MRU imaging after FRS injection in the intermittent period of symptomatic hydronephrosis caused by abnormal Pelviureteric junctions was higher than that in the hydration and US group. The 77% pathological coincidence rate of surgical treatment indicated that the method had certain application for the early diagnosis of children with symptomatic hydronephrosis.**

**Keywords:** ***Abnormal pelvic ureteral junction; Hydronephrosis; Children; MRU; Furosemide***

## 1. Introduction

Congenital hydronephrosis is a common urinary tract disease in children, which can be detected by Ultrasound (US), while some children have no symptoms until childhood. Its clinical manifestations contain abdominal pain, hematuria, urinary tract infection, or hypertension, which is also named as symptomatic hydronephrosis. Such children may show persistent stability or progressive exacerbations, as well as intermittent episodes [1], with pelvic ureteral obstructive hydronephrosis during the acute episode, but no obvious obstruction signs during the intermittent period [2]. The disease is mainly because of the abnormalities of the junctions between the pelvic and ureteral, which lead to the chronic and incomplete obstruction, with the symbol of renal function declines for surgery [3]. However, the early diagnosis is often delayed due to the negative result.

Several methods could be applied for the clinical diagnosis of hydronephrosis, of which the US is routinely used. When the hydronephrosis is found without ureteral dilatation, it could be diagnosed as pelvic ureteral junction obstruction [4], however, the narrow segments cannot be displayed, and multiple review and comparison are required. Intravenous urography (IVU) can display anatomical variations of the urinary tract and morphological changes of various diseases, but the injection of contrast agents is required, which may lead to iodine allergy and impaired renal excretion, and the display of kidney relies on the renal function [5].

Although retrograde angiography can provide the shape and obstruction of the renal ureter, the pain and high failure rate because of its invasion, as well as the radiation damage limit its clinical application [6]. MRU, as a safety and radiation-free inspection method, has been discovered and extremely suitable for children, since urine, as a natural contrast agent, can clearly display the shape of the pelvic ureteral junction obstruction, the length of the narrow segment, and develop well even if the renal function is significantly impaired. However, the amount of urinary fluid secretion directly affects the efficiency of MRU. When there is no urine in the urinary tract or less urine accumulation, the efficiency of conventional MRU is not ideal. Furosemide (FRS), as a diuretic, can dilate blood vessels and increase glomerular blood flow, besides, it inhibits the renal tubular concentrating function and causes urine increase through inhibiting the reabsorption of NaCl by the renal tubules.

All above lead us to explore the value of MRU combined with FRS injection in the diagnosis of symptomatic hydronephrosis of children in the non-seizure phase, which could guide the clinicians make early diagnosis and avoid renal impairment of children.

## 2. Materials and Methods

Twenty-four children were collected with symptomatic hydronephrosis during six months, including 20 males and 4 females, aged from 3.83 to 15.17 years old, with a median age of 8.17. All had clear history of acute attacks with different clinical symptoms, including abdominal pain (n=13), hematuria (n=3), urinary infections (n=2), vomiting (n=4), and hematuria (n=3). All examinations and details of the study received informed consent from the parents of children.

All children were in the intermittent period of symptomatic hydronephrosis. Two control groups were set, group 1 were examined by US in the previous day, then fasted for 6 hours on the day for the MRU examination; group 2 (hydration group) were injected with 0.9% sodium chloride at a volume of 10 ml per kilogram of body weight. After the first round of MRU examination, the children were instructed to urinate, and then FRS (fast urine group) was injected intravenously at a dose of 1 mg/kg with second round of MRU scans 5 minutes later.

The situations of the renal pelvis and ureter were compared to evaluate the sensitively and differences between the three methods. For children undergoing surgical treatment, the results of diuresis group were compared with the surgical pathological results to evaluate the positive detection rate.

### 2.1 MRU techniques

MRU inspections were performed on a Siemens 1.5T superconducting magnetic resonance scanner (Siemens Avanto). The children were placed in the supine position with phased body coils, breathing navigation was used to monitor breathing, and all children cooperated with scanning in the awake state. Scan sequence: transversal position IR-T1WI, TR 7494 ms, TE 2.3 ms, layer thickness 6 mm, trig breath trigger; transversal position FSE-T2WI, TR 4670 ms, TE 101 ms, layer thickness 6 mm, trig breath trigger, blade inhibition Motion artifacts; MRU-FSE sequence, TR 5347 ms, TE 687 ms, layer thickness 1 mm, no interval, trig breath trigger. The maximum signal intensity projection technology was applied in the post-processing of MRU to perform three-dimensional rotation observation on the region of interest, and rotates 18º to reconstruct 19 frames of images.

### 2.2 Statistical analysis

Statistical Note: The 24 data collected in this study did not conform to the normal distribution, so it was expressed as the median (IQR) and expressed as a frequency and percentage. Statistical processing: Based on SPSS 21.0, chi-square test was performed on a single sample, and the signed-sum rank test on sensitivity was performed on each group of samples. $P < 0.05$ was considered statistically significant.

### 2.3 Image analysis

According to the UTD classification proposed by the American Association of Fetal Urology, Pediatric Kidney Association, Pediatric Radiology Association and Ultrasound Society in 2014 [7], the scoring criteria was set for the renal pelvis, ureters and comprehensive conditions in this study. If there are inconsistencies on both sides, the higher score will prevail (TABLE 1-3).

TABLE 1. **The scoring criteria of renal pelvis.**

| **Anteroposterior diameter of renal pelvis** | **Grade (4-point scale)** |
|---|---|
| <10 mm | 1 |
| 10 mm ≤ maximum diameter<20 mm | 2 |
| 20 mm ≤ maximum diameter<30 mm | 3 |
| ≥ 30 | 4 |

TABLE 2. **The scoring criteria of ureter.**

| **Display situation of ureter** | **Grade (4-point scale)** |
|---|---|
| No | 1 |
| In the upper | 2 |
| In the middle and upper | 3 |
| All | 4 |

TABLE 3. **The scoring criteria of comprehensive.**

| **Display situation of comprehensive image** | **Grade (5-point scale)** |
|---|---|
| Unacceptable, without pelvic dilation | 1 |
| Pelvic dilation, without ureter displayed | 2 |
| Pelvic dilation, with upper ureter displayed | 3 |
| Pelvic dilation, with middle and upper ureter displayed | 4 |
| Pelvic dilation, with entire ureter displayed | 5 |

## 3. Results

Among the 24 cases with 20 (83.3%) males and 4 (16.7%) females, the incidence of males was higher than that of females and the incidence of hydronephrosis in the left was higher than others, with 19 (79.2%) cases of left hydronephrosis, 4 (16.7%) cases of right hydronephrosis and 1 (4.2%) case of bilateral hydronephrosis, the P=0.001 and P<0.001. In the BUS group (control group 1), the sensitivities of hydronephrosis, ureteral dilatation and comprehensive were 70.8%, 16.7% and 70.8%, while that of in the hydration group were 87.5%, 95.8% and 100%, respectively. The sensitivities of that in the FRS group could be further enhanced to 100% (TABLE 4.1-4). Thirteen of the 24 children underwent surgical treatment were diagnosed with 7 (29%) cases of chronic mucositis, 1 (4%) case of ectopic vascular compression, 3 (12.5%) cases of polyp, and 2 (8.3%) cases of concretion in the pelvic ureteropelvic junction. Compared with the results of the FRS group, 5 (20.8%) cases with filling defect and 5 (20.8%) cases with twist and narrow in the pelvic ureteral junction, the positive coincidence rate reached 77%. (TABLE 5, FIG.1-2).

TABLE 4.1. **The sensitivity of different groups.**

| | | **BUS** | | | | **FRS** | | | | **Hydration** | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Renal Pelvis Ratings** | **Ureter Ratings** | **Comprehensive Ratings** | | **Renal Pelvis Ratings** | **Ureter Ratings** | **Comprehensive Ratings** | | **Renal Pelvis Ratings** | **Ureter Ratings** | **Comprehensive Ratings** |
| **Median (IQR)** | 2(1.25-2) | 1(1-1) | 2(1.25-2) | Median (IQR) | 3(2-4) | 4(4-4) | 5(5-5) | Median (IQR) | 2(2-3) | 2(2-3) | 3(3-4) |

TABLE 4.2. **The sensitivity of different groups.**

| **Group** | **US** | | | **Hydration** | | | **FRS** | | |
|---|---|---|---|---|---|---|---|---|---|
| **Grade** | **renal pelvis** | **Ureter** | **Comprehensive** | **renal pelvis** | **Ureter** | **Comprehensive** | **renal pelvis** | **Ureter** | **Comprehensive** |
| 1 | 2 | 2 | 3 | 2 | 2 | 3 | 3 | 4 | 5 |
| 2 | 1 | 1 | 1 | 1 | 2 | 3 | 2 | 4 | 5 |
| 3 | 2 | 1 | 2 | 2 | 1 | 2 | 3 | 3 | 4 |
| 4 | 2 | 2 | 3 | 2 | 3 | 4 | 2 | 4 | 5 |
| 5 | 2 | 1 | 2 | 2 | 3 | 4 | 2 | 4 | 5 |
| 6 | 3 | 1 | 2 | 3 | 3 | 4 | 4 | 4 | 5 |
| 7 | 4 | 1 | 2 | 4 | 3 | 4 | 5 | 4 | 5 |
| 8 | 1 | 1 | 1 | 1 | 3 | 4 | 2 | 4 | 5 |
| 9 | 3 | 1 | 2 | 3 | 3 | 4 | 4 | 4 | 5 |
| 10 | 3 | 1 | 2 | 4 | 3 | 4 | 5 | 4 | 5 |
| 11 | 1 | 1 | 1 | 2 | 3 | 4 | 3 | 4 | 5 |
| 12 | 3 | 1 | 2 | 3 | 3 | 4 | 4 | 4 | 5 |
| 13 | 2 | 2 | 3 | 3 | 2 | 3 | 3 | 4 | 5 |
| 14 | 2 | 1 | 2 | 2 | 2 | 3 | 3 | 4 | 5 |
| 15 | 1 | 1 | 1 | 2 | 2 | 3 | 2 | 4 | 5 |
| 16 | 2 | 1 | 2 | 2 | 2 | 3 | 3 | 3 | 4 |
| 17 | 1 | 1 | 1 | 2 | 2 | 3 | 4 | 4 | 5 |
| 18 | 2 | 1 | 2 | 3 | 2 | 4 | 4 | 4 | 5 |
| 19 | 2 | 1 | 1 | 2 | 2 | 3 | 4 | 4 | 5 |
| 20 | 1 | 1 | 2 | 3 | 2 | 3 | 4 | 3 | 5 |
| 21 | 2 | 1 | 2 | 2 | 2 | 4 | 3 | 3 | 5 |
| 22 | 2 | 2 | 1 | 2 | 2 | 3 | 3 | 4 | 5 |
| 23 | 1 | 1 | 2 | 1 | 2 | 2 | 3 | 3 | 5 |
| 24 | 2 | 1 | 2 | 3 | 2 | 3 | 4 | 3 | 5 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Sensitivity (Positive/Total)×100% | 70.8% | 16.7% | 70.8% | 87.5% | 95.8% | 100.0% | 100.0% | 100.0% | 100.0% |

Grade Score=1: Negative

Grade Score≥2: Positive

TABLE 4.3. **The sensitivity of different groups.**

| **Z\P** | renal pelvis Hydration | renal pelvis FRS | Ureter Hydration | Ureter FRS | Comprehensive Hydration | Comprehensive FRS |
|---|---|---|---|---|---|---|
| **BUS** | -2.646 | -4.233 | -4.053 | -4.428 | -4.008 | -4.371 |
| | 0.008 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

TABLE 4.4. **The sensitivity of different groups.**

| **Z\P** | renal pelvis Comprehensive FRS | Ureter FRS |
|---|---|---|
| **Hydration** | -3.900 | -4.428 -4.428 |
| | <0.001 | <0.001 <0.001 |

TABLE 5**. The comparison of pathological diagnosis after surgical treatment with MRU of FRS group in the pelvic ureteral junction.**

| **Case** | **Pathological diagnosis** | **MRU (FRS group)** |
|---|---|---|
| 1 | Chronic active inflammation | (-) |
| 2 | Ectopic small vessel compression | Narrow and twisted |
| 3 | Chronic active inflammation | Distorted |
| 4 | Chronic active inflammation | Narrow and twisted |
| 5 | Polyp with 1.2 cm narrow section | Narrow with filling defect |
| 6 | Chronic active inflammation | (-) |
| 7 | Small crystals | Distorted with filling defect |
| 8 | Chronic active inflammation | Distorted |
| 9 | Polyp with 1.5 cm narrow section | Narrow with filling defect |
| 10 | Small stones | Pelvic with filling defect |
| 11 | Chronic active inflammation | (-) |
| 12 | Chronic active inflammation | Narrow and twisted |
| 13 | Polyp with 1.3 cm narrow section | Pelvic with filling defect |
| Positive coincidence rate: 77% | | |

**Fig. 1**

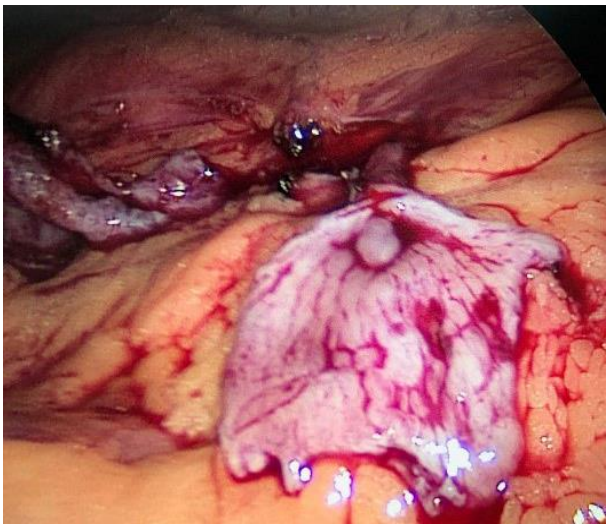

**Fig. 2**

FIG. 1 & 2. **MRU FSR group showed filling defect at left ureteropelvic junction.**

## 4. Discussion

Although the screening standard of the US for the obstruction of the pelvic and ureteral junction is the dilation of the pelvis and non-dilatation of the ureter in the onset of symptomatic hydronephrosis in children, the hydronephrosis is significantly reduced during the intermittent period [8], which is hard to be found out and requires multiple rechecks and comparisons, resulting in misdiagnosis or missed diagnosis. MRU combined with the principle of water imaging to visualize the dilated urinary tract has the characteristics of high soft tissue resolution, multi-directional image sectioning, and high image reconstruction. It does not require contrast agents and rely on renal function, and its diagnostic effects have been widely confirmed [9,10]. However, the fasting needed before examination lead to the absence and less amount of urine accumulation, which directly affect the quality, especially during the intermittent period of symptomatic hydronephrosis. Considering the similar grades of hydronephrosis between the BUS and MRU, they were set as control group. The study revealed that during the intermittent period of symptomatic hydronephrosis, the BUS had a sensitivity of 70.8% for the renal pelvis dilation, but most of the ureters failed to show dilation, with the sensitivity of only 16.7%; the sensitivity of the renal pelvic dilatation in the hydration group increased to 87.5%, and the ureter dilation increased to 95.8%, but, 2/3 cases still only showed the upper and middle ureters, the imaging effect for the narrow and distorted pelvic ureteral junction was still not ideal, and the imaging quality could be affected by the motion artifacts due to children hold urine. The FRS had quick effect and can significantly improve the urethral filling and expansion, compared with the other groups, the imaging sensitivity in FRS group increased to 100% during the same examination time. FRS is normally effective after 5 min of intravenous administration, which could avoid the artifact caused by the intestinal fluid filling surface after hydration, and can also be conducive to rapid hydration and full expansion of the urinary tract to form artificial urinary system flow and expansion. All above lead to the clear development of normal non-dilated or mildly to moderately dilated urinary tract [11]. Alok Sharma et al. [5] chose to inject furosemide 15

minutes after the injection of contrast agent in MRU to enhance the development effect. Our research confirmed that the sensitivity of FRS in 5 minutes after hydration reached 100%, which was not consistent with previous report.

Besides, we also found that there are statistical differences in gender and location of the disease, which may be related to chromosomal abnormalities, the sensitivity of gender embryos to teratogenic factors, and the exposure of their father to high-risk factors [12], the phenomenon was consistent with previous related reports, such as the female endogenous estrogen had a protective effect on the kidney [13]. However, the reasons for the differences in the incidence sites have not been well explained, and the mechanism needs to be further explored.

Abnormal pelvic ureteral junctions in children are related to inflammatory stenosis, valvular, polyp, or abnormal small blood vessel compression, which lead to the obstruction of urine excretion to the ureter in the renal pelvis, accompanied by the continuous expansion of the renal collecting system and secondary renal damage [14]. Confirmed by the results of surgical treatment of 13 patients, the positive coincidence rate of FRS group was 77%. When chronic mucosal chronic inflammation occurs, the MRU is mostly the distortion of the pelvic ureteral junction with long twisted section. During the abnormal small blood vessels compression, it presents the narrow and distorted pelvic ureteral junctions with short stenosed segments. When the polyp or small crystal is obstructed, it appears as filling defect in the pelvic ureteral junction, with narrow stenosis and no distortion. As a conclusion, the potential of a static MRU combined with FRS in suggestion of etiology has been confirmed.

The shortcomings of our study are that the sample size is small, and the study subjects are older children, which may not suitable for the young children with chloral hydrate to sedate. At the same time, the urine flow rate could not be quantitatively measured, the assessment of urine dynamics is lacking, and the rapid urinary flow is still invasive. Finally, surgical intervention is required while the total renal function decline of more than 10% or sub-renal function decline to less than 40% [15,16], and the degree of disease damage to renal function is increased and even irreversible. The renal function of some children, who still undergo surgery after a long follow-up period, is difficult to return to the ideal state [17]. However, because of no standard reference for the thickness of the renal cortex changes with the growth and development of children, the thickness of the renal cortex could not be scientifically judged.

## 5. Conclusions

MRU imaging combined with intravenous injection of FRS to diagnose the abnormal hydronephrosis, resulting from the abnormal Pelviureteric during the intermittent period, had high sensitivity, and the positive rate of coincidence with surgical cases reached 77%. The results indicate that the method established in this study has certain clinical value for the early diagnosis of such children.

## 6. Ethical Approval

All the children were examined in the intermittent stage, and all the examinations were given informed consent from the parents of the children, and approved by the Ethics Committee of Children's Hospital Affiliated to Medical College of Zhejiang University (2019-IRB-101).

## 7. Conflicts of Interest

The authors report no conflicts of interest. The authors are solely responsible for the content and writing of this article.

## 8. Conflict of Interest Disclosures

None.

## 9. Author Contributions

Jia Xuan and Chen Zhongyu designed the study, Jia Xuan wrote the first draft of the manuscript. Director Chen Guangjie provided patient information. Chu Linfeng performed the literature search and analysis. Zhao Yijun conducted the statistical analysis. All authors participated in and approved the final manuscript.

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