

The Role of Retrograde Pyelography for Evaluation of Hematuria in Patients with Normal and Impaired Renal Function

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Purpose. Hematuria can be a sign of urinary tract disorders; therefore, it is necessary to arrange complete imaging studies to evaluate the entire urinary system. Our purpose is to elucidate the efficacy of retrograde pyelography (RP) for evaluating patients who present with hematuria.

Methods. From 2000 to 2002, a total of 634 patients underwent RP procedures because of hematuria. After excluding the 378 patients with urothelial carcinoma, stone disease, and urinary tract infection, 256 patients were included in this study. Patients were divided into two groups based on renal function: Group I: normal renal function ($n = 156$); Group II: poor renal function ($Cr > 2.0$) ($n = 100$). Patients in Group I were further classified into either group Ia: gross hematuria ($n = 104$) or Ib: microscopic hematuria ($n = 52$). Patients in Group II were further subdivided into either Group IIa uremia ($n = 39$) or IIb: chronic renal function impairment ($n = 61$).

Results. Patients in Group II (50.0%) were more likely to have malignancy (OR = 4.2, 95% CI = 2.5 to 7.0, $p < 0.001$) than those in Group I (19.2%). In Group II, uremia (74.3%) was most closely associated with urothelial carcinoma (OR = 5.5, 95% CI = 2.3 to 13.1, $p < 0.05$). The rate of stone disease was significantly higher for Group II (OR = 2.0, 95% CI = 1.1 to 3.8, $p < 0.005$).

Conclusions. Patients with impaired renal function are more likely to have urinary stone disease and urothelial cancer than those with normal renal function. Thus, RP is more valuable for evaluating hematuria in patients with impaired renal function than in those with normal renal function. Among the patients with impaired renal function, uremic patients are at highest risk of having urothelial cancer in Taiwan. Therefore, it is crucial to perform RP and cystoscopy for patients with impaired renal function, especially for those with uremia. (*Mid Taiwan J Med* 2007;12:14-9)

Key words

hematuria, retrograde pyelography, renal function impairment, urothelial carcinoma

INTRODUCTION

Hematuria can arise from disease in any part of the urinary tract. Both gross and microscopic hematuria are likely to be indicative

of clinically significant disease, such as stone, infection or malignant tumors [1,2]. If a patient is at risk for malignancy, such as having a history of smoking [3], analgesic abuse [4], residing in a arseniasis-endemic area in Taiwan [5-8], and exposure to chemicals agents [9,10], a complete urologic evaluation including intravenous pyelography (IVP), cystoscopy or urine cytology

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is necessary. However, the initial imaging studies might not provide a definitive diagnosis. Therefore, a second diagnostic procedure should be performed.

Retrograde pyelography (RP) has been used as an alternative imaging study in urology for many years, especially for patients with contrast medium allergy, or unsatisfactory image of IVP in the initial diagnosis of hematuria. RP is always performed in association with cystoscopic examination for providing complete urinary tract study. It has been questioned whether RP is useful for all patients with hematuria or just for patients with renal function impairment. We performed this study to evaluate the role for this relatively invasive procedure for patients with impaired renal function.

MATERIALS AND METHODS

From 2000 to 2002, a total of 634 patients who underwent RP procedures because of hematuria (either microscopic or gross hematuria) in this hospital were retrospectively reviewed. Patients with urothelial carcinoma, urolithiasis, urinary tract infection, or other urologic diseases were excluded from the study. A total of 256 patients with unknown causes of hematuria were enrolled in our study. The patients were divided into two groups according to their renal function: Group I: normal renal function ($n = 156$); Group II: poor renal function ($\text{Cr} > 2.0$) ($n = 100$). The patients in Group I who had undergone IVP (intravenous pyelography) before RP were further classified into group Ia: gross hematuria ($n = 104$); Ib: microscopic hematuria ($n = 52$). The patients in Group II who had undergone RP with

cystoscopy instead of IVP because of poor renal function were subdivided into: IIa uremia ($n = 39$) and IIb: chronic renal function impairment (CRI) ($n = 61$). Abnormal RP findings were further evaluated by ureteroscopy and computed tomography (CT). Suspicious upper urinary tract tumors were analyzed by pathologic examination of ureteroscopic biopsy or surgical specimens.

RP findings between the two groups were analyzed by the chi-square test with odds ratio evaluation. All p values < 0.05 were considered statistically significant. Calculations were performed using commercial statistical software (SPSS®).

RESULTS

The characteristics of patients are listed in Table 1. In Group I, there were normal findings in 66 patients (42.3%), ureteral stricture in 37 patients (23.7%), urothelial carcinoma in 27 patients (17.3%), urinary stones in 23 patients (14.8%), and renal cell carcinoma (RCC) in 3 patients (1.9%) (Table 2). In Group Ia, there were normal findings in 44 patients (42.3%), ureteral stricture in 23 patients (22.1%), urothelial carcinoma in 27 patients (26.0%), stones in 7 patients (6.7%), and 3 RCC (2.9%). In Group Ib, there were normal findings in 22 patients (42.3%), ureteral stricture in 14 patients (26.9%), and stones in 16 patients (30.7%). All of the tumors were found in Group Ia, and included urothelial cancers ($n = 27$) and RCC ($n = 3$).

In Group II, 13 patients had normal findings (13.0%); 7 patients had ureteral stricture (7.0%); 50 patients had positive findings of urothelial cancer (50.0%); 26 patients had urinary stones (26.0%), and 4 had cystitis (4.0%)

Table 1. Patient characteristics

Groups of patients	Age (yr)	Gender (male/female)
	Mean \pm SD (range)	
Group I, normal renal function ($n = 156$)	61.2 \pm 4.0 (38 to 83)	80/76
Ia: gross hematuria ($n = 104$)	60.3 \pm 3.2 (43 to 83)	55/49
Ib: microscopic hematuria ($n = 52$)	58.1 \pm 2.6 (38 to 77)	25/27
Group II, abnormal renal function ($n = 100$)	58.7 \pm 3.1 (46 to 80)	34/56
IIa: uremia ($n = 39$)	57.2 \pm 2.8 (48 to 80)	18/21
IIb: CRI ($n = 61$)	59.1 \pm 3.3 (46 to 75)	26/35

CRI = chronic renal function impairment.

Table 2. Results of the study by retrograde pyelography in patients in Group I and Group II

Findings of RP	n (%)		
Group I	Ia: Gross hematuria (n = 104)	Ib: Microscopic hematuria (n = 52)	
Normal	44 (42.3)	22 (42.3)	66 (42.3)
Ureteral stricture	23 (22.1)	14 (26.9)	37 (23.7)
Stone	7 (6.7)	16 (30.8)	23 (14.8)
Urothelial ca	27 (26.0)	0 (0.0)	27 (17.3)
RCC	3 (2.9)	0 (0.0)	3 (1.9)
Group II	IIa: Uremia (n = 39)	IIb: CRI (n = 61)	
Normal	0 (0.0)	13 (21.3)	13 (13.0)
Urothelia ca	29 (74.4)	21 (34.4)	50 (50.0)
Stones	10 (25.6)	16 (26.2)	26 (26.0)
Ureteral stricture	0 (0.0)	7 (11.5)	7 (7.0)
Cystitis	0 (0.0)	4 (6.6)	4 (4.0)

RCC = renal cell carcinoma. CRI = chronic renal function impairment.

Table 3. Comparisons of the percentages of tumors and urinary stones between group I and II from RP studies (chi-square test)

Groups of patients	RP findings			RP findings		
	Non-tumors n (%)	Tumors n (%)	OR	Non-stones n (%)	Stones n (%)	OR
I: normal renal function (n = 156)	126 (80.8)	30 (19.2)	1.0	133 (85.3)	23 (14.7)	1.0
II: abnormal renal function (n = 100)	50 (50.0)	50 (50.0)	4.2 [†]	74 (64.9)	26 (35.1)	2.0*
IIa: uremia (n = 39)	10 (25.7)	29 (74.3)	5.5 [†]	29 (74.4)	10 (25.6)	0.9
IIb: CRI (n = 61)	40 (65.6)	21 (34.4)	1.0	45 (73.8)	16 (26.2)	1.0

* $p < 0.05$, [†] $p < 0.01$.

(Table 2). In Group IIa, there were 29 patients with urothelial cancers (74.4%) and 10 patients with urinary stones (25.6%). In Group IIb, 13 patients had normal findings (21.3%); 7 had ureteral stricture (11.5%); 21 had urothelial cancers (34.4 %); 16 had urinary stones (26.2%), and 4 had cystitis (6.6%).

There was a higher percentage of malignancy in Group II than in Group I, (chi-square test, $p < 0.001$). The odds ratio (OR) was 4.2 in Group II (95% CI = 2.5 to 7.0) (Table 3). In comparing the rates of malignancy between subgroups IIa and IIb, the OR for subgroup IIa was 5.5 (95% CI = 2.3 to 13.1). Patients in Group II had a significantly higher rate of stone disease than patients in Group I (OR = 2.0, 95% CI = 1.1 to 3.8, $p < 0.05$) (Table 3). There was no significant difference in stone disease between subgroups IIa and IIb ($p = 0.947$). Patients with impaired renal function were more likely to have urinary stone disease and urothelial cancer than those with normal renal function.

DISCUSSION

The marked difference between gross and microscopic hematuria is that patients with gross hematuria are at higher risk for malignancy than those with microscopic hematuria [1-3]. For patients with impaired renal function, RP is helpful in diagnosing the cause of gross hematuria [12,13]. In Group I, RP showed that patients with gross hematuria were more likely to have malignancy (27 urothelial cancer, 3 RCC) compared with those with microscopic hematuria; no malignancies were diagnosed in patients with microscopic hematuria (Table 1). Our study is compatible with other series in which gross hematuria was shown to be a symptom of urinary tract malignancy [13-16]. Contrary to gross hematuria, RP has little diagnostic value in the evaluation of microscopic hematuria.

The results of RP revealed that gross hematuria in patients with impaired renal function was more closely related to malignancy than that in patients with normal renal function. There was a higher incidence of tumor in Group II (50.0%)

than in Group I (19.2%), (OR = 4.2, $p < 0.001$) (Table 3). Furthermore, uremic patients with gross hematuria were more likely to have malignancy than any other patients. RP revealed 29 urothelial cancers (74.3%) in 39 uremic patients in comparison with 21 urothelial cancers (34.4%) in 61 patients with impaired renal function (OR = 5.5, $p < 0.001$) indicating that uremic patients with hematuria are at high risk for urothelial cancer.

It has been reported that patients with chronic renal failure have a high incidence of malignant tumor [17]. According to many reports, gross hematuria in uremic patients in Taiwan is associated with urothelial cancer [12-14,18,19]. Our study confirmed the above findings. We strongly recommend that uremic patients undergo complete urologic imaging study including RP and cystoscopy because urothelial cancer tends to be multifocal and has a high rate of recurrence [13-15,20]. In contrast to ureteroscopy, RP and cystoscopy are less invasive and can be managed with regional urethral anesthesia, which is suitable for patients at high risk for anesthesia [11]. Furthermore, ureteroscopy can confirm the positive RP findings.

In addition to malignancy, hematuria can also be a sign of urolithiasis. Our study showed that urinary stones occur more frequently in patients with impaired renal function than in patients with normal renal function. RP showed that 26 (26.0%) in Group II had urolithiasis in comparison with 23 (14.8%) in Group I (OR = 2.0, $p = 0.025$). Stone formation in patients with renal failure may be due to metabolic factors such as high urinary oxalate and due to iatrogenic factors, namely vitamin D3 or calcium salt supplementation [21,22]. Therefore, RP is of diagnostic value for patients with impaired renal function whenever hematuria occurs. Once urinary stone has been confirmed, the following ureteroscopy can be arranged.

There was a high percentage of negative findings in Group I (42.3%), indicating that nearly half of the patients with normal renal function unnecessarily underwent the RP

procedure. It is important to improve the quality of IVP or, alternatively perform multi-detector CT urography (MDCTU) to detect urinary tract disease. To date, contrast-enhanced MDCTU performed with a combination of unenhanced, nephrogenic-phase, and excretory-phase can provide better visualization of urinary tract than IVP [23-26]. RP is a valuable diagnostic modality in patients with impaired renal function because more than half of them (61.0%) have urinary tract disease. All uremic patients with gross hematuria in our study had positive RP findings. Thus, RP is an essential and efficacious screening tool to evaluate upper urinary tract for patients with poor renal function.

Our study is limited because of selection bias; most of the patients were referred from local clinics or regional hospitals in central Taiwan. Our RP findings do not clarify the characteristic of hematuria in Taiwan. Therefore, a large and national multi-center study should be arranged to evaluate the efficacy of RP, especially for uremic patients.

In conclusion, our study indicated that gross hematuria is a cardinal sign of urinary tract disorders. For patients with poor renal function, RP and cystoscopy play an important role because disease is more frequently seen in those patients than in patients with normal renal function. Furthermore gross hematuria in uremic patients is more strongly related to urothelial cancer in Taiwan than in other countries. Therefore, it is crucial to perform RP and cystoscopy for patients with impaired renal function, especially for those with uremia.

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逆行性腎盂攝影對於腎功能正常及異常患者 在血尿評估上所扮演的角色

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目的 血尿可能是多種泌尿系統病變的一種表象。完整的泌尿系統影像學檢查有其必要性。此研究欲了解現今逆行性腎盂攝影在血尿診斷上的效用。

方法 從2000年到2002年，一共有634位患者因為血尿來本院接受逆行性腎盂攝影檢查。已知為尿路上皮癌、結石及尿道感染的患者378位經排除，一共有256位患者進行分析。患者依腎功能總共分為兩組：第一組為正常腎功能患者156位；第二組為腎功能異常患者100位。第一組患者又再分為Ia組：肉眼血尿104位；Ib組：顯微血尿52位。第二組患者又分為IIa組：尿毒症患者39位及IIb組：慢性腎功能不全61位。

結果 相較於第一組，第二組患者比較容易有惡性病變(OR = 4.2, 95% CI = 2.5 to 7.0, $p < 0.001$)。進一步比較第二組，尿症患者與尿路上皮癌有極大的關聯性(OR = 5.5, 95% CI = 2.3 to 13.1, $p < 0.05$)。除此之外，相較於第一大組，結石疾病發生率於第二組有明顯的統計學上的差異(OR = 2.0, 95% CI = 1.1 to 3.8, $p < 0.005$)。我們發現腎功能異常患者血尿比腎功能健全患者較易發生尿路上皮癌及結石。

結論 逆行性腎盂攝影在血尿診斷上，於腎功能異常患者的應用比腎功能正常患者有較高的診斷價值。特別值得一提的是，在台灣尿症患者與尿路上皮癌有十分明顯的關聯性。所以對於腎功能異常患者，尤其是尿毒症病患而言，安排逆行性腎盂攝影及膀胱鏡檢查是有其必要性。(中台灣醫誌 2007;12:14-9)

關鍵詞

血尿，逆行性腎盂攝影，腎功能異常，尿路上皮癌

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