Indications for Ureteropyeloscopy Based on Radiographic Findings and Urine Cytology in Detection of Upper Urinary Tract Carcinoma

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Objective: To verify the indication of diagnostic ureteropyeloscopy based on clinical features for upper urinary tract urothelial cancer with over 100 patients and over a 10-year series.

Methods: From January 1997 to December 2008, consecutive 129 units in 124 patients underwent ureteropyeloscopy to obtain a definitive diagnosis of upper urinary tract cancer or to rule out a malignancy. Patients were divided into four subgroups based on voided urine cytology and preoperative radiographic findings: group A (n = 8), positive urine cytology and positive radiographic findings; group B (n = 4), positive cytology and negative radiographic findings; group C (n = 55), negative cytology and positive radiographic findings and group D (n = 62), gross hematuria originating from the upper urinary tract with negative cytology and negative radiographic findings. Ureteropyeloscopic findings were compared with radiographic and cytological results. Adverse effects were also investigated.

Results: In group A, all patients had confirmed cancer. In group B, one revealed small cancer and the remaining three confirmed carcinoma in situ by biopsy with ureteropyeloscopy. In groups C and D, 33 patients (60%) and four (6.5%) revealed cancer. Seventy-eight patients out of 80 (97.5%) in groups C and D were confirmed to have benign disease. No patient was found with malignancy during follow up after negative finding of ureteropyeloscopy.

Conclusions: Ureteropyeloscopy can help in detecting upper urinary tract cancer or to rule out malignancy for patients with negative voiding cytology. However, ureteropyeloscopy is redundant for patients with positive radiographic findings and positive voiding cytology.

Key words: upper urinary tract carcinoma – ureteropyeloscopy – urothelial carcinoma – diagnosis – indication

INTRODUCTION

Upper urinary tract urothelial carcinoma (UUT-UC) represents 5–6% of all urothelial carcinomas. Macroscopic hematuria is the most common symptom. The diagnostic algorithm includes the patient’s medical history, clinical investigation, cystoscopy, urinary cytology, ultrasound and intravenous urography (IVU). In addition, a complementary retrograde ureteropyelography with collecting selective urinary cytology has been conducted. However, recent advances in ureteropyeloscopy have revolutionized the diagnosis of upper urinary tract diseases. Rigid and flexible small-caliber ureteroscopes have permitted direct optical examination and biopsy for the upper urinary tract. The accuracy and importance of ureteropyeloscopy procedures in the diagnosis of UUT-UC have already been reported (1–8), leading to the procedure becoming a widespread diagnostic and therapeutic tool. However, several limitations and potential adverse effects have been suggested, such as the dissemination of malignant cells, perforation of the ureteral wall and ureteral stricture (9,10). Thus, we have performed diagnostic ureteropyeloscopy for UUT-UC under indication which is described in text-book (11) based on
prior series; (i) cases with ureteral or intrarenal filling defect in excretory urography, (ii) case with gross hematuria originating from the upper urinary tract and (iii) neither necessary nor prudent in case with positive urine cytology associated with a filling defect.

For a practical use of diagnostic ureteropyeloscopy in the modern era, results of a longer term and a larger sample should be evaluated. The aim of the present study is to verify the indication for ureteropyeloscopy based on radiographic findings and urine cytology in patients with possibility of UUT-UC in our over 100 cases and over a 10-year series.

**PATIENTS AND METHODS**

From January 1997 to December 2008, 124 consecutive patients (70 men and 54 women) with a mean age of 57.5 years (range, 14–87 years) underwent ureteropyeloscopy for 129 units (bilateral examination in 5 patients) to obtain a definitive diagnosis of UUT-UC or to rule out a malignancy. Before the ureteropyeloscopy, all patients who were considered possible candidates underwent IVU, CT, cystoscopy and cytology of voided urine. The site of disease was predicted according to radiographic and cystoscopic findings. Patients with positive urine cytology and without radiographic finding underwent random biopsy of bladder at first. Patients with bladder tumors diagnosed on cystoscopy or bladder biopsy were excluded. No patient underwent retrograde pyelography before ureteropyeloscopy. We believe that a retrograde pyelography before ureteropyeloscopy does not provide useful or additional information that would preclude an ureteropyeloscopy.

Indications for diagnostic ureteropyeloscopy in the present study were described in the text (11). Briefly, patients with radiographic findings suspicious of upper urinary tract (UUT) malignancy and/or with gross hematuria originating from the upper urinary tract, and with could not be ruled out malignancy by conventional diagnostic modalities or other etiologies were primary indication for the ureteropyeloscopy. In principle, patients with positive urine cytology associated with a filling defect were excluded from the ureteropyeloscopy. However, some of the patients underwent the ureteropyeloscopy due to reasons described as below.

Voided urine cytology of Class IV or V was considered positive. Defect and/or stenosis on ureteropyelography, hydronephrosis, ureteral wall thickening and ischemia of the renal parenchyma on CT were considered positive radiological findings.

### Procedure Description

The procedure started with cystoscopy under general anesthesia. The distal to middle portion of the ureter was inspected using a 6.9 Fr semi-rigid ureteroscope without a guide wire. An initial guide wire was then placed. Special caution was taken not to advance the guide wire beyond the middle ureter in order to avoid any inadvertent injury to the collecting system. The semi-rigid ureteroscope was removed and a flexible ureteroscope (AUR-7, size: 7.2 Fr, working channel: 3.6 Fr) or URF-P3 (6.9, 3.6 Fr)) was passed over the guide wire into the ureter under fluoroscopic guidance, again with caution so as not to advance the guide wire beyond the middle ureter. The guide wire was then removed. The proximal ureter and collecting system were inspected with a flexible ureteroscope. The entire upper collecting system was evaluated systematically from the upper to lower calyx. A biopsy was performed if any suspicious lesion was observed. Continuous irrigation was maintained at the lowest flow pressure (40 mmHg) with Uromat™ (Karl Storz). An irrigant containing iodinated contrast material (17%) was used to outline the collecting system for radiographic monitoring.

Patients were selected by voided urine cytology and preoperative radiographic findings and divided into four subgroups. Group characteristics were as follows: group A (n = 8, 6.2%), positive voided urine cytology and positive preoperative radiographic findings, and need to definitive diagnosis before radical treatment since those with single kidney or with low renal functions; group B (n = 4, 3.1%), positive cytology and negative radiographic findings, and the need to confirm a lesion of malignancy; group C (n = 55, 42.6%), frank hematuria originating from the upper urinary tract but negative cytology and negative radiographic findings, and the need to rule out malignancy. Patient background in each group is summarized in Table 1. We compared the findings of ureteropyeloscopic examination with the results of radiographic examination and cytology and any adverse effect of ureteropyeloscopy.

The diagnostic value of each examination was assessed by calculating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. Statistical analysis was performed using McNemar’s test.

### RESULTS

The diagnostic value of preoperative examinations is as below. For voided urine cytology, sensitivity was 20%, specificity 100%, PPV 100% and NPV 68%. For

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**Table 1. Patient background in each group**

<table>
<thead>
<tr>
<th>Group</th>
<th>Urine cytology</th>
<th>Radiographic findings</th>
<th>Number of patients</th>
<th>No. male/female</th>
<th>Mean age</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>+</td>
<td>+</td>
<td>8</td>
<td>8/0</td>
<td>67.8</td>
</tr>
<tr>
<td>B</td>
<td>+</td>
<td>−</td>
<td>4</td>
<td>3/1</td>
<td>70.3</td>
</tr>
<tr>
<td>C</td>
<td>−</td>
<td>+</td>
<td>55</td>
<td>32/23</td>
<td>67.9</td>
</tr>
<tr>
<td>D</td>
<td>−</td>
<td>−</td>
<td>62</td>
<td>31/31</td>
<td>46.5</td>
</tr>
</tbody>
</table>
Table 2. Ureteropyeloscopic findings

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 8)</th>
<th>Group B (n = 4)</th>
<th>Group C (n = 55)</th>
<th>Group D (n = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal pelvic cancer</td>
<td>5</td>
<td>1</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>Ureteral tumor cancer</td>
<td>3</td>
<td>0</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoma in situ</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (%)</td>
<td>8 (100%)</td>
<td>4 (100%)</td>
<td>33 (60%)</td>
<td>4 (6.5%)</td>
</tr>
<tr>
<td>Benign disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic unilateral hematuria</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>58</td>
</tr>
<tr>
<td>Urinary stricture</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Urolithiasis</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Other abnormalities*</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Normal finding</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>22 (40%)</td>
<td>58 (93.5%)</td>
</tr>
</tbody>
</table>

*Other abnormalities: inflammation 4, tuberculosis 1, retroperitoneal fibrosis 1, cystic polyp 1.

radiographic examination, sensitivity was 69%, specificity 82%, PPV 65% and NPV 88%.

These findings indicate that many UUT-UC cases were associated with positive voided cytology and abnormal radiographic findings. However, many patients would have been over diagnosed using only radiographic findings and some incompletely even if combined cytology/radiography results were considered. Distribution of ureteropyeloscopic findings were shown in Table 2. In group A, all 8 patients had confirmed UUT-UC by ureteropyeloscopy. In group B, all patients underwent bilateral ureteropyeloscopy. One revealed small UUT-UC and the remaining three confirmed carcinoma in situ (CIS) by biopsy with ureteropyeloscopy. These CIS lesions were observed as rough and erythematic mucosa by ureteropyeloscopy. In group C, 33 patients (60%) revealed UUT-UC. And in group D, 4 patients (6.5%) were found to have UUT-UC. Thirty-four patients with diagnosed UUT-UC by ureteropyeloscopy underwent nephroureterectomy, eight underwent nephron-sparing surgical treatment and the remaining seven underwent non-surgical treatment, e.g. bacillus Calmette-Guérin instillation therapy after biopsy. All patients were confirmed urothelial carcinoma in their pathological specimens. Benign conditions were diagnosed in 78 of 80 patients (97.5%) in groups C and D. Among patients without UUT-UC in group C, treatment delivery was immediate during the diagnostic procedure according to the underlying disease. For those in group D, those patients without UUT-UC underwent hemostatic treatments with cauterization under ureteropyeloscopy immediately. Patients with negative ureteropyeloscopy for UUT-UC remained tumor-free during the follow-up period. All patients with benign disease were cured.

Complications

Two complications occurred in 4 patients who were cured within a few days: minor ureteral extravasation in 2 was resolved uneventfully after insertion of an indwelling ureteral catheter, and acute bacterial pyelonephritis in 2 which was cured with antibiotics.

DISCUSSION

Ureteropyeloscopy procedures have become a valuable asset in the diagnosis and treatment of the upper urinary tract. Ureteropyeloscopy performed to evaluate a filling defect can greatly enhance diagnostic accuracy. In addition to visualization values, it offers the opportunity for a biopsy of any lesion encountered, allowing histopathological confirmation. Using a flexible ureteropyeloscopy and biopsy forceps, the sensitivity and accuracy of a biopsy in detecting malignant lesions has been reported to range from 82 to 100% and from 83 to 100%, respectively (3–8). These results are superior when compared with those obtained from conventional analyses of urine cytology and radiological examinations. In our series, we have neither patients with false-positive findings in ureteropyeloscopic examination nor patients found with UUT-UC during follow up after negative findings during ureteropyeloscopy. In addition, benign conditions or abnormalities were confirmed in almost all patients without UUT-UC. This high accuracy for diagnosis is based on the refined technical procedure as described. Modern ureteropyeloscopy has been greatly aided by new and smaller optical devices and instruments, a development that has enabled urologists to evaluate the entire urinary tract with high accuracy and precision. Ureteropyeloscopy today must be considered a reliable and robust diagnostic modality for a definitive diagnosis of UUT-UC. However, ureteropyeloscopy includes a certain risk for the dissemination of malignant cells and post-examined ureteral stricture due to mucosal injury and the need for general anesthesia or spinal anesthesia even though easy to examine upper urinary tract, therefore, its indication is still controversial. No guidelines have been published concerning ureteroscopy for detecting UUT-UC and, as previously reported (10–13), the accuracy of ureteropyeloscopic examination appears to depend on patient selection.

The aim of the present study was, therefore, to verify the indication for ureteropyeloscopy based on a comparative evaluation of categories with voided urine cytology and preoperative radiographic findings in patients with the possibility of UUT-UC by the relative large volume and long-term series.

In group A, all 8 patients were confirmed to have UUT-UC, results suggesting that ureteropyeloscopy can be omitted during the diagnosis process of UUT-UC. However, ureteropyeloscopy may be valuable in providing anatomical and histopathological information when considering the
possibility of nephron-sparing surgery in patients with a single kidney or bilateral disease.

In group B, CIS of the upper urinary tract was the most likely diagnosis and was confirmed in all 4 patients in our series. Although voiding urine cytology appears useful in these patients, ureteropyeloscopy and biopsy should be mandatory for a definitive diagnosis of CIS.

Ureteropyeloscopy was the most useful in group C. In the present series, 42.6% of patients who underwent ureteropyeloscopy were assigned to this group and UUT-UC found in 60%. As Matsumoto et al. (13) concluded in similar categorizations, the role of ureteropyeloscopy in group C patients is to obtain a definitive diagnosis when malignancy is unidentified by other examinations and to provide histopathological information when considering therapeutic strategies, such as nephron-sparing management including endoscopic therapy. In addition, all remaining patients without UUT-UC were confirmed with benign disease and some were treated with ureteropyeloscopy immediately. Therefore, ureteropyeloscopy can benefit most patients in this group.

In group D, ureteropyeloscopy was performed to evaluate unilateral hematuria. In the present series, the largest number (48.1%) of patients was assigned to this group and UUT-UC was found in 6.5%. Although the percentage of UUT-UC here was small, non-detection of a malignant disease is a serious issue. In addition, bleeding points were identified and treated endoscopically in all chronic unilateral hematuria patients without UUT-UC (14–17). Treatment provided a definitive cure for all patients. The role of ureteropyeloscopic examination in this group would be to detect or exclude a malignant disease and provide immediate management of chronic unilateral hematuria.

Although additional modalities for imaging-based diagnosis, including retrograde pyelography and MR urography, in patients without significant findings in excretory urography can bring some information, definitive diagnosis for such patients should be achieved by ureteropyeloscopy. On the other hand, retrograde pyelography and/or MR urography before ureteropyeloscopy can have certain value in patients who cannot use the contrast medium.

On the basis of these points, Fig. 1 shows a proposed algorithm for diagnosis of upper urinary tract urothelial carcinoma.

CONCLUSIONS

Ureteropyeloscopy can help in the detection of UUT-UC or to rule out a malignancy for patients with negative voiding cytology. However, ureteropyeloscopy is redundant for patients with positive radiographic findings and positive voiding cytology.

Conflict of interest statement
None declared.

References

Figure 1. Proposed algorithm for diagnosis of upper urinary tract urothelial carcinoma.


