Management of Lower Urinary Tract Dysfunction After Radical Hysterectomy With or Without Radiotherapy for Uterine Cervical Cancer

Fei-Chi Chuang¹, Hann-Chorng Kuo²*

Background/Purpose: Urinary dysfunction is a common long-term sequela after radical hysterectomy (RH). The aims of this study were to investigate the characteristics and treatment response of lower urinary tract dysfunction (LUTD) after RH with or without adjuvant radiotherapy (RT) for uterine cervical cancer.

Methods: We analyzed retrospectively 49 patients who developed LUTD after RH with (n = 16) or without (n = 33) RT for stage IB or IIA uterine cervical cancer.

Results: The mean interval between RH and first visit for urological management of LUTD was significantly shorter in the RH+RT (5.9 ± 4.5 years) than the RH (11.3 ± 9.5; p < 0.05) group. Combined therapy also resulted in a smaller bladder capacity and poorer bladder compliance. Further urological management was given to 29 patients, including a pubovaginal sling procedure in seven, urethral injection of botulinum toxin A in 13, transurethral incision of the bladder neck in three, and augmentation enterocystoplasty in six. Among the patients who received active urological management, 88.9% were satisfied with the outcome.

Conclusion: Patients treated with RH+RT are likely to have a worse bladder condition and require urological intervention sooner than those who receive RH alone. Active urological management of LUTD in these patients leads to satisfactory improvements in symptoms of difficult urination and urinary incontinence. [J Formos Med Assoc 2009;108(8):619–626]

Key Words: adjuvant radiotherapy, hysterectomy, lower urinary tract dysfunction, urological management, uterine cervical neoplasms, videourodynamic study

The treatment of cervical cancer by radical hysterectomy (RH) with or without pelvic radiotherapy (RT) is well established, and results in an excellent long-term survival rate. However, urinary dysfunction is a common long-term sequela after RH. Several studies of preoperative and postoperative urodynamic data have demonstrated the adverse effects of RH on urinary tract function.¹⁻⁴ Nevertheless, the long-term morbidity of lower urinary tract dysfunction (LUTD) after RH remains difficult to determine from the available data. Most patients with cervical cancer treated with RH receive postoperative bladder care at gynecology departments for the inability to empty the bladder or urinary incontinence by bladder training, clean intermittent self-catheterization (CISC),...
urecholine, or prolonged catheter drainage. However, initial urological complications may become chronic or worsen, and new symptoms may also develop in patients who are managed in these ways. Close monitoring of lower urinary tract function and adequate urological management of LUTD are mandatory to prevent upper urinary tract dysfunction, and to improve the quality of life of these patients.

The aims of the present study were to investigate the characteristics of LUTD after RH with or without RT for uterine cervical cancer and the results of active management of these conditions in patients from Eastern Taiwan.

Materials and Methods

This was a retrospective study of 49 patients who were treated for LUTD after RH with or without adjuvant RT for stage IB or IIA cervical cancer from 1997 to 2006. These patients had received voiding training after RH, which was provided by the department of obstetrics and gynecology in several hospitals, and were referred for further management to improve quality of life with regard to urination or for the treatment of urological complications. After detailed physical examination, voiding history taking, urinalysis, urine bacterial culture, and diagnostic imaging, a complete urodynamic or videourodynamic study was performed to identify the underlying pathophysiology of LUTD.

A videourodynamic study was performed according to the recommendations of the International Continence Society.5 We reviewed patient chart records and collected data including the presenting symptoms at the initial urological visit and videourodynamic findings. Storage dysfunction was detected by the presence of detrusor overactivity or intrinsic sphincter deficiency (ISD). Voiding dysfunction was detected by the presence of detrusor underactivity, acontractile detrusor, non-relaxing urethral sphincter, or bladder neck dysfunction. Detrusor overactivity is a urodynamic observation that is characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked. ISD denotes an intrinsic malfunction of the urethral sphincter itself, and we used abdominal leak point pressure < 60 cmH2O as the objective measure.6 Detrusor underactivity is defined as contraction of reduced strength and/or duration, which results in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span. Acontractile detrusor cannot be demonstrated to contract during urodynamic studies. Non-relaxing urethral sphincter obstruction usually occurs in individuals with a neurological lesion and is characterized by a non-relaxing, obstructing urethra that results in reduced urine flow. A tight bladder neck that shows on fluoroscopy during the voiding phase signifies bladder neck dysfunction.

In this study, the results of management of LUTD according to bladder or urethral dysfunction were also analyzed. A satisfactory rate was defined as subjective improvements in symptoms of difficult urination or urinary incontinence.

The interval between RH and the patient’s first visit to the urology department for management of LUTD, urodynamic findings including cystometric capacity, bladder compliance and postvoid residual urine (PVR), as well as various voiding dysfunctions and resultant complications, were compared between patients who received RH alone and those who received RH+RT. Student’s t tests and χ² tests were used for statistical analysis. Statistical significance was assumed when p < 0.05.

Results

Patient characteristics

Forty-nine women who were treated for LUTD after RH were included in this study. The interval between RH and initial assessment at the urology department ranged from 6 months to 30 years. The interval between RH and initial assessment was > 1 year and < 10 years in 38.8% of patients, and 10–30 years in 36.6%. Difficulty in urination...
(69.4%) and urinary incontinence (55.1%) were the most common urinary symptoms, followed by frequent urinary tract infection (UTI) (30.6%) and urinary frequency and urgency (30.6%). Table 1 shows the characteristics of the patients in the RH and RH+RT groups. There were 33 women treated with RH alone and 16 with RH+RT. The mean age at the time of RH was 48.9 ± 11.3 years in the RH group and 51.2 ± 8.4 years in the RH+RT group (p = 0.473). The mean interval between RH and first visit to the urology department for treatment of LUTD was 11.3 ± 9.5 years and 5.9 ± 4.5 years in the RH and RH+RT groups, respectively (p < 0.05).

### Urodynamic findings

The RH group had significantly larger cystometric capacity than the RH+RT group (mean, 331 ± 139 mL vs. 238 ± 111 mL; p = 0.024). The difference in bladder compliance between the two groups was not significant, but the incidence of low and poorly compliant bladder (< 10 mL/cmH₂O) was significantly higher in the RH+RT group (7/16, 43.8%) than in the RH group (5/33, 15.2%; p < 0.05). There was no significant difference between the two groups for the incidence of a large PVR (> 100 mL), incontinence, dysuria, hydronephrosis, vesicoureteral reflux, or frequent UTI (Table 1).

The results of the videourodynamic study are shown in Table 2. There was no significant difference in the incidence of bladder dysfunction between patients in the RH and RH+RT groups. Patients with detrusor underactivity or acontractile detrusor comprised 85.7% of all the patients in the study. Detrusor overactivity was found in 10.2% of patients, while normal detrusor function was found in only 4.1%. The incidence of urethral dysfunction, ISD and non-relaxing urethral sphincter were not significantly different between the RH and RH+RT groups. Only 14.3% of patients had normal urethral function.

### Urological management of LUTD

The patients were treated according to their bladder and urethral dysfunctions. Previously, LUTD was managed conservatively with self-voiding by the clock, Crede maneuver or abdominal straining, medication, pelvic floor muscle training, CISC, or indwelling catheterization. When these conservative treatments failed to relieve their LUTD, active urological management was undertaken, including pubovaginal sling procedure for ISD in seven patients (5 with RH, 2 with RH+RT), urethral sphincter injection of botulinum toxin A (BTX-A) for non-relaxing urethral sphincter in 13 (11 with RH, 2 with RH+RT), transurethral incision of the bladder neck (TUI-BN) for a tight

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### Table 1. Comparison of characteristics of patients treated with RH and RH+RT*

<table>
<thead>
<tr>
<th></th>
<th>RH (n = 33)</th>
<th>RH+RT (n = 16)</th>
<th>p</th>
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<tbody>
<tr>
<td>Age at RH (yr)</td>
<td>48.9 ± 11.3</td>
<td>51.2 ± 8.4</td>
<td>0.473</td>
</tr>
<tr>
<td>Interval between RH and first visit to urology department (yr)</td>
<td>11.3 ± 9.5</td>
<td>5.9 ± 4.5</td>
<td>0.039</td>
</tr>
<tr>
<td>Cystometric capacity (mL)†</td>
<td>331 ± 139</td>
<td>238 ± 111</td>
<td>0.024</td>
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<tr>
<td>Bladder compliance†</td>
<td>70 ± 108</td>
<td>18 ± 14</td>
<td>0.063</td>
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<tr>
<td>Large PVR (≥ 100 mL)†</td>
<td>17 (51.5)</td>
<td>4 (25)</td>
<td>0.078</td>
</tr>
<tr>
<td>Incontinence</td>
<td>18 (54.5)</td>
<td>9 (56.3)</td>
<td>0.912</td>
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<tr>
<td>Difficult urination</td>
<td>23 (69.7)</td>
<td>11 (68.8)</td>
<td>0.947</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>9 (27.3)</td>
<td>7 (43.8)</td>
<td>0.247</td>
</tr>
<tr>
<td>Vesicoureteral reflux</td>
<td>5 (15.2)</td>
<td>1 (6.3)</td>
<td>0.372</td>
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<tr>
<td>Frequent UTI</td>
<td>10 (30.3)</td>
<td>5 (31.3)</td>
<td>0.947</td>
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*Data presented as mean ± standard deviation or n (%); †urodynamic parameters. RH = radical hysterectomy; RH+RT = radical hysterectomy plus adjuvant radiotherapy; PVR = postvoid residual urine; UTI = urinary tract infection.
bladder neck in three (2 with RH, 1 with RH + RT), and augmentation enterocystoplasty for a contracted bladder, with or without vesicoureteral reflux in six (3 with RH, 3 with RH + RT) (Table 3).

All seven patients who received the pubovaginal sling procedure had urinary continence for at least 3 months, but five needed CISC because of chronic urinary retention during the initial postoperative period. One patient treated with pubovaginal sling required two repeats of the same procedure because of failure to achieve continence, at intervals of 3 months and 3 years. Four patients, including two with RH and two with RH + RT, had recurrent mild stress urinary incontinence at > 6 months after the pubovaginal sling procedure. All of these conditions were attributed to poor bladder compliance with low urethral resistance that led to overflow incontinence. Despite these problems, the overall satisfaction rate of the pubovaginal sling procedure was 85.7% (6/7 continent for > 3 months).

Among the 13 patients who received periurethral injection of BTX-A, five showed smooth voiding with less abdominal straining and minimal PVR. However, two of these patients experienced exacerbated stress urinary incontinence and nocturnal enuresis after the procedure. Nevertheless, they were not dissatisfied with this outcome because of the overall improvement in voiding symptoms. One patient treated with RH + RT had six repeat injections of BTX-A at 6-month intervals. She was satisfied with the easier voiding that resulted from the procedure, despite an episode of postoperative urethral edema and initially

<table>
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<th>Table 2.</th>
<th>Pathophysiology of voiding dysfunction disclosed by videourodynamic study*</th>
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<tr>
<td>RH (n = 33)</td>
<td>RH + RT (n = 16)</td>
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<tr>
<td>Bladder function</td>
<td></td>
</tr>
<tr>
<td>DU</td>
<td>30 (90.9)</td>
</tr>
<tr>
<td>DO</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>ND</td>
<td>1 (3.0)</td>
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<tr>
<td>Urethral function</td>
<td></td>
</tr>
<tr>
<td>ISD</td>
<td>12 (36.4)</td>
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<tr>
<td>Non-relaxing urethral sphincter</td>
<td>16 (48.5)</td>
</tr>
<tr>
<td>NU</td>
<td>5 (15.2)</td>
</tr>
</tbody>
</table>

*Data presented as n (%). RH = radical hysterectomy; RH + RT = radical hysterectomy plus adjuvant radiotherapy; DU = detrusor underactivity; DO = detrusor overactivity; ND = normal detrusor function; ISD = intrinsic sphincter deficiency; NU = normal urethral function.

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<th>Table 3.</th>
<th>Active urological management for lower urinary tract dysfunction after RH with or without RT for uterine cervical cancer</th>
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<tr>
<td>Urological management</td>
<td>Indication</td>
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<tr>
<td>Pubovaginal sling procedure</td>
<td>ISD</td>
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<tr>
<td>Urethral sphincter injection of botulinum toxin A</td>
<td>Non-relaxing urethral sphincter</td>
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<tr>
<td>Transurethral incision of the bladder neck</td>
<td>Tight bladder neck</td>
</tr>
<tr>
<td>Augmentation enterocystoplasty</td>
<td>Contracted bladder with or without vesicoureteral reflux</td>
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*Two patients were lost to follow-up. RH = radical hysterectomy; RH + RT = radical hysterectomy plus adjuvant radiotherapy; Satisfaction rate = improvements in symptoms of difficult urination or urinary incontinence; ISD = intrinsic sphincter deficiency.
difficult urination. CISC was still needed in four patients with significantly improved lower urinary tract symptoms and voiding efficiency after BTX-A injection. Further examination revealed that two of these patients had bladder neck dysfunction, and subsequent TUI-BN resulted in improvement in lower urinary tract symptoms and voiding efficiency. The first BTX-A injection did not lead to improvements in two patients treated with RH, one of whom reported fair improvement after a second injection 3 weeks later. The other two patients were lost to follow-up after the initial BTX-A injection. Excluding the two patients who were lost to follow-up, the satisfaction rate with BTX-A injection was 81.8% (9/11, subjective improvements in symptoms of difficult urination).

Augmentation enterocystoplasty was performed for contracted bladder with upper urinary tract deterioration in six women, including three in the RH group, and three in the RH+RT group. The interval between RH and enterocystoplasty ranged from 1 to 11 years. All of these patients had good resolution of hydronephrosis and increased bladder capacity after enterocystoplasty. CISC was a necessary adjuvant management after enterocystoplasty in all of these patients because of acontractile detrusor and non-relaxing urethral sphincter. Two patients received periurethral injection of BTX-A and TUI-BN for urination difficulties, and no longer needed CISC after these further treatments. One patient in the RH+RT group required repeat enterocystoplasty as a result of contracture of the previous augmented bladder 4 years after the initial procedure. After the second enterocystoplasty, her condition remained stable for >4 years. All patients who underwent enterocystoplasty had a successful result, as defined by reported satisfaction. In this study, 84.2% of patients treated with RH, and all those treated with RH+RT who received active urological management, were satisfied with their outcome, mainly because of improved quality of life. The overall satisfaction rate of active urological management of LUTD after RH with or without RT for uterine cervical cancer was 88.9%.

Discussion

This retrospective analysis included 49 patients who underwent RH with or without RT for cervical cancer and subsequent treatment for LUTD. The interval between RH and the urological intervention was 1–30 years. The urological evaluation and intervention in this study were relatively late after RH, and the urological symptoms could therefore be considered as long-term complications of RH or RH+RT. Woodside and McGuire reported that 92% of patients who underwent RH had normal voiding at 1 year after surgery.7 Other studies have reported that urinary symptoms persisted in 20–50% of patients after RH, and consisted mainly of urinary incontinence, impaired bladder sensation, UTI, and straining on voiding.8,9 A small fraction of patients who undergo RH or RH+RT for cervical cancer might develop long-term LUTD, which may be caused by neurological insult sustained during radical pelvic surgery and compounded by adjuvant irradiation or poor postoperative bladder care. Lin et al demonstrated that abnormal urodynamic findings exist in some patients with cervical cancer before treatment, and that these findings may worsen, and/or additional abnormal states may arise subsequent to RH.10,11

In the present study, patients who received RH+RT compared with RH alone had a shorter interval between RH and urological evaluation for LUTD, and had a smaller cystometric capacity and higher incidence of low and poor bladder compliance. These findings are similar to those of previous studies12,13 and suggest that RT can have a significant impact on lower urinary tract function. Patients who undergo RH with adjuvant RT need careful surveillance for LUTD, and early urological intervention may be necessary to improve quality of life.

Fraser reported that a significant amount of PVR was present in 50% of patients at 5–15 years after RH, and was correlated significantly with impaired bladder sensation, difficult urination, and UTI.14 In our study, PVR > 100 mL was noted in 21 of 49 (42.9%) patients, with a similar
prevalence in the two treatment groups. Large PVR can result in many complications such as frequent UTI, urinary incontinence, increased frequency and urgency of urination, and upper urinary tract deterioration.

The functional changes in the bladder and urethra after RH are multifarious. The final changes in lower urinary tract function may also vary among patients. In general, bladder dysfunction immediately after RH consists of a hypertonic and poorly compliant bladder, reduced bladder capacity, and diminished bladder sensation.\(^2,^3\) Anatomical factors such as perivesical adhesion and intrinsic myogenic tonic change are thought to play a major role in early postoperative bladder dysfunction.\(^3,^15\) In the present study, 85.7% of patients presented with either detrusor underactivity or an acontractile detrusor, while only 10.2% had detrusor overactivity, and 4.1% had normal detrusor function. Detrusor hypotonicity was thought to be caused by parasympathetic and sympathetic denervation in the pelvic plexus. The most likely etiology of late detrusor hypertonicity after RH is an alteration of bladder innervation. A relatively normal detrusor function reflects partial denervation of the peripheral autonomic nerves, with intact autoregulation and coordination of the autonomic system.\(^3\) Different kinds of neurological insult sustained during RH and dissection of bilateral lymph nodes can result in complete or incomplete denervation of the autonomic nerves that supply the lower urinary tract.\(^3,^16\)

In the present study, the prevalence of isolated sphincter obstruction and ISD was about equal in the RH and RH+RT groups. Non-relaxing urethral sphincter may result from altered modulation by the pelvic plexus and the resulting motor and sensory impairment of the detrusor.\(^17–^20\) ISD may be the result of a deficit in bladder neck support, partial loss of alpha-adrenergic tone in the proximal urethra, complete autonomic denervation, aging, or weakened pelvic-floor musculature.\(^19–^21\) The multifarious combination of detrusor and urethral dysfunction needs precise classification because of its clinical importance for the treatment and prevention of late urological complications.

After RH, patients have to learn a new method of voiding and have to use the bathroom at regular intervals. Voiding dysfunction that is characterized by straining to void without detrusor contraction and a non-relaxing urethral sphincter can result in difficulty in urination, large PVR, and subsequent UTI. CISC has been used widely to manage this LUTD, but it is not a convenient method for all patients. Medication with alpha-adrenergic blockers and skeletal muscle relaxants to relieve bladder neck dysfunction and external sphincter tone may be helpful in some cases, but the side effects of these drugs may not be tolerable.\(^22\) Urethral injection of BTX-A to treat patients with voiding dysfunction caused by detrusor underactivity and non-relaxing urethral sphincter after RH is a new therapy to reduce urethral resistance. Kuo reported that this treatment had an 80% success rate in facilitating efficient voiding, with few adverse effects.\(^23\) Poor response to urethral BTX-A injection might be caused by high urethral sphincter tone, and repeat injections in the early stage might be necessary. Bladder neck dysfunction may be another site of functional obstruction in addition to the urethral sphincter. Careful interpretation of cystourethrography during the voiding phase is important.\(^23,^24\)

Urinary incontinence may be a protective method for the upper urinary tract because a high leak-point pressure can produce vesico-urethral reflux and subsequent hydronephrosis. However, urinary incontinence is associated with a worse quality of life. Thus, the need for preservation of renal function and improved quality of life requires careful balancing when selecting treatment. The obstructive effect of a suburethral sling may become prominent in patients with detrusor underactivity or an acontractile detrusor, and may lead to the complication of chronic urinary retention. Patients with detrusor underactivity or an acontractile detrusor usually void with the aid of abdominal straining, and low urethral resistance is often necessary for voiding by abdominal straining. Before surgery, it is necessary to make sure that the patient has sufficient energy to produce abdominal pressure to overcome
urethral resistance. Kuo reported that patients with detrusor underactivity or an acontractile detrusor had a higher rate of recurrent stress incontinence (36%) and difficulty with urination (36%) after a suburethral sling procedure. In the present study, four patients, including two in the RH+RT group, developed overflow incontinence after the sling procedure because of poor bladder compliance and low urethral resistance. In addition to detrusor and urethral dysfunction, bladder compliance and capacity should be considered when developing a treatment strategy for LUTD. As LUTD may change with time in such patients, careful follow-up is mandatory.

When RH leads to the complications of low bladder compliance and contraction, high intravesical pressure, vesicoureteral reflux, and hydronephrosis, an aggressive therapeutic strategy to rescue the patient from impending renal insufficiency is necessary. Enterocystoplasty is effective for the treatment of neuropathic contracted bladder if the patient has the ability to perform CISC for the likely difficulty in emptying the bladder after surgery. Difficult urination, UTI and stone formation are possible complications that may be encountered after enterocystoplasty. Nevertheless, this treatment provides the chance to preserve renal function and improve quality of life. The present study shows that enterocystoplasty is a feasible method for the treatment of contracted bladder in patients who have undergone RH with or without RT.

Patients treated with RH+RT are likely to have a worse bladder condition and require urological intervention sooner than those who receive RH alone. Active urological management for LUTD after RH with or without RT for uterine cervical cancer had a satisfactory success rate with regard to improvements in symptoms of difficult urination and urinary incontinence.

References


