

# Urological Complications of Radical Hysterectomy for Uterine Cervical Cancer

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## ABSTRACT

It is well known that radical hysterectomy produces a good survival rate for patients in the early stages of node-negative cervical cancer. The "radical" nature of the surgery may cause nerve injury and visceral damage due to extensive dissection. With improved technique, urinary tract injury is an increasingly rare intraoperative complication. However, dysfunctional changes to the urinary tract may persist in these women for a long period after surgery, impairing the quality of life. Partial or complete denervation of the urinary tract results in multifarious collocation of bladder and urethral dysfunctions. Clear understanding of the nature of the bladder and urethral dysfunction is necessary for appropriate management. As lower urinary tract dysfunction may keep progressing with time, regular follow-up is important to preserve renal function.

**Key words:** urological complication, low urinary tract dysfunction, radical hysterectomy

## INTRODUCTION

Radical hysterectomy with pelvic lymphadenectomy is a well established treatment for clinically localized cervical cancer. Werthein laid the foundation of modern, radical hysterectomy in 1911. With improvements in operative technique, the procedure has a very low immediate mortality with a good long-term survival rate. However, urinary tract dysfunction due to iatrogenic peripheral neuropathy is an inevitable consequence of surgical treatment for invasive cervical cancer. A better understanding of the pathophysiology of lower urinary tract denervation is essential for adequate intraoperative and postoperative management.

## INTRAOPERATIVE AND POSTOPERATIVE UROLOGICAL COMPLICATIONS

With meticulous surgery, intraoperative injury to the urinary tract during radical hysterectomy is rare. The incidence of the following complications depends on the stage of the disease and the radicality of the procedure [1].

1. Intra-operative injury of the bladder and ureters: Almost in all cases of bladder or ureteral injury, the disease was relatively more invasive, for example stage IIb with cancer reaching the bladder or ureter,

which are then sutured directly or require ureteral re-implantation [1].

2. Postoperative fistula formation: Radical hysterectomy requires the dissection of the entire pelvic course of the ureter, which may result in the interruption of several arterial branches that provide its blood supply [2]. Most fistulas result from postoperative ischemia, not from injury [1]. A wide range—from 0.6% to 6.6%—in the incidence of vesicovaginal and ureterovaginal fistula formation has been reported. The fistulas usually appear between twelfth and thirtieth postoperative days. Prominent signs and symptoms exhibited by patients who developed ureterovaginal fistula are fever, spontaneous leakage of urine from the vagina, and an enlarged pelvic mass. The ureterovaginal fistula is usually located in the lower third of the ureter. One must wait from two to six months to repair the fistula. Based on experience, waiting for at least six months after operation has resulted in not only spontaneous healing but also better more successful repair [2].
3. Ureteric stricture formation is also a potential hazard following radical hysterectomy, and should also be borne in mind when following-up patients treated by radical hysterectomy [2,3].

## THE FUNCTIONAL ALTERATION OF BLADDER AND URETHRA AFTER RADICAL HYSTERECTOMY

Postoperative lower urinary tract dysfunction is common among patients who undergo radical hysterectomy. Sensory loss and voiding disorders are the primary complaints. These complications relate to nerve damage to the pelvic plexus and pelvic organs. During radical hysterectomy, parasympathetic denervation may occur if the surgeon strips the sacral nerves bilaterally or excises a major portion of the paracervical and paravaginal webs of retroperitoneal tissue. The sympathetic nerves are also vulnerable to injury during dissection of bilateral lymph nodes [4].

The pelvic plexus is formed by the confluence of pelvic parasympathetic nerves with sympathetic hypogastric nerves, and also contains ganglia where parasympathetic and sympathetic nerves interact synchronously [5]. With nerve trunks emanating from S2-4, the pelvic plexus occupies the area of the inferior segment of the cardinal ligament. The urethra and bladder are connected to the terminal branches of the pelvic plexus [6,7].

Impaired micturition after a radical hysterectomy may result from altered modulation by the pelvic plexus and the resulting motor and sensory impairment of the detrusor [8]. Impaired detrusor contraction may be secondary to improper sensory input to the sacral and cortical micturition centers [9]. The combination of the failure to trigger the detrusor reflex and the urethral relaxation reflex results in detrusor un-

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deractivity and a nonrelaxing urethral sphincter, which manifests as a voiding dysfunction. Normal urinary sensation is lost, and such patients depend on substitute sensations (i.e., fullness in the abdomen, tension in the pelvic region, a vague feeling of discomfort), which they gradually learn to associate with a full bladder [10]. The patients have to void at regular intervals and learn to stimulate the intrinsic neuromuscular mechanism by straining and other manipulations that allow them to void by relaxing the voluntary sphincter [11]. However, voiding by straining is not a physiologic voiding method, and depends on the patient's effort. It may compensate incompletely for the detrusor acontractility and urethral resistance [10]. Dysuria, chronic urinary retention, overflow incontinence, and frequent urinary tract infection are the common symptoms accompanying a voiding dysfunction. Some of the patients also need clean, intermittent self-catheterization.

In addition to impaired bladder sensation and difficulty in micturition, urinary incontinence is also a common complaint of patients who undergo radical hysterectomy. A deficit in bladder neck support and the partial loss of alpha-adrenergic tone in the proximal urethra may result from the radical resection of the upper vagina and parametrium if there is damage to part of the pelvic plexus, resulting in a transection of urethral sympathetic innervation [6,11,12]. Axelsen et al recently reported that the urethral sphincter mechanism plays a role in the pathophysiology, rather than the mobility, of the bladder neck [13]. Bladder neck incompetence and low urethral closure pressure contribute to overflow incontinence or urinary stress incontinence, which are exacerbated when combined with poor bladder compliance. The reduction in bladder compliance on filling may be due to a loss of sympathetic beta-adrenergic innervation with its inhibition and relaxation of the detrusor muscle [11]. Chronic urinary tract infection may also cause decreased bladder compliance [14].

Functional changes to the bladder and urethra after radical hysterectomy are multi factorial. Anatomical changes and irreversible visceral damage after extensive dissection, as well as neurological alterations, may account for the resulting lower urinary tract dysfunction [15]. In other cases, pre-existing abnormal urinary tract function may worsen after radical hysterectomy [16]. Lin et al reported that up to 83% of patients with cervical cancer had abnormal urodynamic findings before radical hysterectomy [17]. Chen et al noted that the rate of detrusor instability in women with preoperative cervical carcinoma was higher than that of a control group with CIN 3 (37.5% vs. 14.8%,  $P < 0.05$ ) [18].

Urodynamic studies have made these functional disorders quantifiable. In 1949, Halter and Richter reported cystometric studies demonstrating a hypertonic bladder with reduced capacity in the early postoperative period. These findings have been confirmed by a number of authors [1,9,15]. Immediate postoperative hypertonic and poorly compliant bladder is believed to be related to perivesical adhesions and intrinsic myogenic tone change [19]. Overdistention in the early postoperative period should be avoided, for not only does it precipitate bladder atony but evidence also suggests that it may cause urinary fistulas [20].

Kuo et al performed urodynamic studies on 47 patients with cervical cancer who underwent radical hysterectomy and bilateral lymphadenectomy to assess the functional alteration of the bladder and urethra at different stages [15]. All patients developed hypertonic, poorly compliant bladders and reduction in urethral closure pressure before bladder training was begun. After 3 to 6 months, 3 different types of

cystometric change were noted. Twenty-five patients (53.2%) had hypotonic and acontractile bladders with enlarged capacity while 15 (31.9%) had better compliant bladders with normal tone but still had difficulty emptying the bladder. The remaining 7 patients (14.9%) maintained the immediate postoperative hypertonic state. Reduction of maximal urethral closure pressure was noted in 29 (61.8%) patients, remained unchanged in 13 (27.6%) and increased in 5 (10.6%). Forty-three patients had diminished or absent sensation of bladder fullness, and all except one complained of dysuria. The different urethral pressure changes and different cystometric changes documented in this study may reflect a more complicated mechanism after complete or incomplete denervation of autonomic nerves that control the lower urinary tract.

Generally, acute voiding symptoms disappeared within 6 to 12 months after radical hysterectomy [19,21]. However some authors have reported that 20% to 50% of similar patients have persistent urinary symptoms, mainly urinary incontinence, impaired bladder sensation, urinary tract infections, and straining to void [3,22]. Improvement of clinical symptoms alone was an unreliable indicator of improved function, since lower urinary tract dysfunction may be relieved by compensatory factors such as substitute sensations, abdominal straining, voiding technique, and the condition of the bladder outlet [19]. Such patients are permanently susceptible to decompensation, especially if placed in circumstances that promote bladder overdistention [9].

Dwyer et al investigated long-term symptomatic and urodynamic changes occurring in women with established urinary dysfunction after radical hysterectomy [23]. The only symptom that showed significant improvement over time was impaired sensation. There was no significant change in any of the urodynamic parameters between the initial and follow-up assessments. According to the study results, there was little improvement over time in urinary dysfunction following radical hysterectomy.

## UPPER URINARY TRACT DYSFUNCTION

Hydronephrosis is a sign of upper urinary tract deterioration. Later appearance of abnormalities on the intravenous pyelogram should first be investigated to exclude recurrent disease. Moreover, lower urinary tract dysfunction may affect the upper urinary tract, damaging the vesico-ureteric antireflux mechanism.

After radical hysterectomy, bladder and urethral dysfunction may keep progressing on long-term follow-up. Patients with acontractile detrusors void mainly by increasing abdominal pressure, with consequent high post-voiding residual urine (PVR). High intravesical pressure during the storage phase may occur if they have significant urethral resistance. Such increased intravesical pressure might cause vesicoureteral reflux, accelerating upper urinary tract deterioration [24]. Vesicoureteral reflux can also drive pathogenic bacteria into the upper urinary tract, causing pyelonephritis and renal scarring [25]. Decreased bladder compliance, increased detrusor leak-point pressure and acontractile detrusor are the main urodynamic risk factors that predict upper urinary tract dilatation [26].

For some patients, lowered urethral resistance results in severe stress or overflow incontinence but will protect the upper urinary tract. High urethral resistance causes no incontinence but endangers renal function in the long-term. Urodynamic tests with radiologic imaging can provide important prognostic clues to better plan follow-up and

management.

## NEW METHODS FOR MINIMIZING MORBIDITY

Radicality is closely related to postoperative morbidity. Zullo et al recently noted that the extent of vaginal resection was more strongly associated with bladder dysfunction than was the extent of the lateral parametrial resection [27]. Lower-risk patients, i.e., those with smaller-volume tumors and in the early stages might benefit from modified radical hysterectomy (class II) which have been shown to cause less voiding dysfunction without compromising disease-free survival [28].

Direct, nerve-sparing radical hysterectomy is a technique that spares the pelvic autonomic nerves without compromising radicality, providing another approach to improving quality of life and reducing bladder and bowel morbidity [29]. A number of studies have shown such surgical technique to be feasible with satisfactory recovery of voiding function [30,31]. Raspagliesi et al reported that the type III nerve-sparing radical hysterectomy seems to be comparable to type II radical hysterectomy and superior to type III radical hysterectomy in terms of reducing early bladder dysfunction [32]. Todo et al assessed postsurgical bladder function in 22 patients treated for cervical cancer with nerve-sparing radical hysterectomy by urodynamic study. There was no significant difference in compliance, maximal flow rate, and residual urine volume before the operation and at 12 months after the operation. This surgical technique is thought to be effective for preservation of bladder function [33].

A laparoscopic approach to reduce immediate postoperative morbidity has been an attractive prospect to surgeons in recent years. It may also become the preferred approach for surgical staging of the disease [34].

## CONCLUSIONS

Urinary tract dysfunction after radical hysterectomy is inevitable and related to the radicality of the parametrial and vaginal resection with its consequent partial or complete denervation of the pelvic viscera. Lower urinary tract dysfunction will persist in some patients after radical hysterectomy. Careful follow-up should be mandatory for patients undergoing radical hysterectomy, because compensating factors tend to mask their ongoing urological symptoms. Functional changes in the bladder and urethra after radical hysterectomy are multifarious, making it essential to understand the extent and causes of the dysfunction in order to manage symptoms. In addition to appropriate follow-up and management of the urological complications caused by radical hysterectomy, aggressive efforts should be directed to modifying the procedure to minimize functional consequences that affect quality of life.

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