RESEARCH COMMUNICATION

Prevalence and Characteristics of Late Postoperative Voiding Dysfunction in Early-Stage Cervical Cancer Patients Treated with Radical Hysterectomy

Kittipat Charoenkwan*, Savitree Pranpanas

Abstract

Background: Although effective as a primary treatment for early-stage cervical cancer, radical hysterectomy is associated with significant long-term morbidities, most commonly, voiding dysfunction. Objective: To examine prevalence and characteristics of voiding dysfunction following radical hysterectomy for early-stage cervical cancer. Methods: One hundred-eighty seven patients with FIGO stage IA2-IIA cervical cancer who underwent class II-III radical hysterectomy with systematic pelvic lymphadenectomy between January 1, 2002 and June 31, 2005 were interviewed with questionnaire on voiding function. Medical records were also reviewed for operative and pathologic data. Results: The prevalence of symptomatic bladder dysfunction was 25.1%. There was no statistically significant association between rates of bladder dysfunction and all examined clinical/operative factors. The most common pattern of bladder dysfunction were incomplete emptying in 25 (13.4%) and urgency and nocturia in 21 (11.2%) each. Conclusion: Voiding dysfunction is a common and clinically significant long-term complication following radical hysterectomy. The pattern of dysfunction reflects combined surgical disruption of both parasympathetic and sympathetic innervations of the pelvis.

Key Words: Bladder dysfunction - cervical cancer - radical hysterectomy - vesical dysfunction - voiding dysfunction

Asian Pacific J Cancer Prev, **8**, 387-389

Introduction

Cervical cancer is the most common female cancer in Thailand and comprises 80% of gynecologic cancer diagnosed in the country (Deerasamee and Srivatanakul, 1999; Srisomboon, 2004). For early-stage disease, treatment either with radical surgery or radiotherapy has appeared equally effective with a 5-year survival rate approaching 70-90% (Newton, 1975; Landoni et al., 1997). The surgical treatment, radical (class III) hysterectomy and pelvic lymphadenectomy, provides advantages of ovarian and vaginal function preservation that are particularly beneficial for young patients. However, the operation is associated with significant postoperative morbidities including bladder dysfunction, colorectal motility disorder, and sexual dysfunction (Barnes et al., 1991; Bergmark et al., 1999; Zullo et al., 2003). Bladder dysfunction is the most common long-term complication with the incidence of 8-80% depending on institution (Zullo et al., 2003).

The aim of this study was to examine the prevalence and pattern of patient-reported symptomatic bladder dysfunction following radical hysterectomy for early-stage cervical cancer at our institution.

Patients and Methods

From March to July 2006, 187 patients with FIGO stage IA2-IIA cervical cancer who underwent class II-III radical hysterectomy with systematic pelvic lymphadenectomy between January 2002 and June 2005 were interviewed at oncology clinic with questionnaire on bladder function by one interviewer. The questionnaire consisted of questions on basic demographic information and long-term bladder function. In addition, the medical record review on operative and pathologic data of all recruited patients was conducted. To examine association between clinico-pathologic factors and prevalence of symptomatic bladder dysfunction, statistical analysis with chi-square and student's t-test were used for categorical and continuous data, respectively. The Faculty of Medicine Ethic Committee approval and informed consent were obtained.

Results

Mean age of the patients was 44.6 years (range 19-75). The average parity of the patients was 2.25 (0-10). The number of pelvic lymph node obtained was 27.34 nodes on average (range 10-67). The basic clinical and

*For Correspondence: Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang, Mai University, Chiang Mai 50200, Thailand Fax: +66-53-946112 E-mail: kicharoe@mail.med.cmu.ac.th

Table 1. Association between Clinico-Pathologic Characteristics and Prevalence of Voiding Dysfunction

Characteristics	Number of patients	Number of patients with bladder dysfunction (%)	P-value
Age (years)			
<50	144	35 (24.3)	0.63
≥50	43	12 (27.9)	
Stage			
IA2	20	4 (20.0)	0.31
IB1	136	37 (27.2)	
IB2	16	5 (31.3)	
IIA	15	1 (6.7)	
Histology			
Squamous	123	31 (25.2)	0.43
Adeno	51	12 (23.5)	
Adenosquamous	10	3 (30.0)	
Neuroendocrine	2	0 (0.0)	
Others	1	1 (100)	
Grade			
1	54	9 (16.7)	0.19
2	84	24 (28.6)	
3	39	11 (28.2)	
Procedure*			
RH	181	46 (25.4)	0.63
MRH	6	1 (16.7)	
Adjuvant treatment#			
None	116	29 (25.0)	0.81
WPRT+Chemo	47	11 (23.4)	
Chemo alone	17	6 (35.3)	
WPRT alone	6	1 (16.7)	
HDR+Chemo	1	0 (0.0)	

* Procedure RH: Radical (class III) hysterectomy MRH: Modified radical (class II) hysterectomy # Adjuvant treatment WPRT: Whole pelvic radiotherapy (teletherapy)HDR: High-dose rate radiotherapy (brachytherapy)

pathologic characteristics were demonstrated in Table 1.

The prevalence of symptomatic bladder dysfunction was 25.1% (95% CI 20.1-33.1). All symptoms had readily developed since the time of urinary catheter removal after surgery and had continued to the time of interview. There was no statistically significant association between rates of bladder dysfunction and all examined clinico-pathological factors (Table1). Mean number of dissected lymph nodes in the patient with and without symptomatic bladder dysfunction were 27.09 ±10.65 and 27.43±11.15 nodes, respectively (p=0.86).

The patterns of bladder dysfunction were incomplete emptying in 25 (13.4%), urgency and nocturia in 21 (11.2%) each, incontinence in 16 (8.6%), loss of bladder sensation (decreased desire to void) in 15 (8.0%), terminal dribbling in 13 (7.0%), and frequency and pain on voiding in 12 (6.4%) each.

Discussion

Lower urinary tract dysfunction is a most common long-term complication of radical hysterectomy. Several anatomical and clinical studies have shown that this disturbance result from disruption of pelvic autonomic nerve during dissection of the parametrium (Butler-Manuel et al., 2002; Ercoli et al., 2003; Maas et al., 2005; Yabuki et al., 2005). The pelvic autonomic nerves are essential for a normal physiologic function of the pelvic organs. The pelvic nerves system is composed of the superior hypogastric plexus, the hypogastric nerve, the splanchnic nerves, the inferior hypogastric plexus and its visceral branches that supply each side of the pelvis. The two hypogastric nerves (one on each side) which contain predominantly sympathetic fibers originate from the superior hypogastric plexus located over the surface of the sacral promontory. They run parallel to and on the dorsomedial side of the ureter into the pelvis. Then, they fuse with the pelvic splanchnic nerves which carry mainly parasympathetic innervation from the sacral roots S2 to S4 to form the inferior hypogastric plexus on each side just lateral to the lower uterine segment and cervix. This plexus is a triangular shape structure in a sagittal plane that stretches from an area anterolateral of the rectum, courses through the cervix and the vaginal fornix laterally, and extends to the lateral vaginal wall and the bladder base.(Maas et al., 2003) Important anatomic landmarks for radical hysterectomy where the pelvic autonomic nerves are at risk for disruption are the uterosacral ligament and rectovaginal septum posteriorly, lateral parametrium laterally, and vesicouterine ligament anteriorly.(Maas et al., 2005)

The prevalence of long-term bladder dysfunction varies widely between 8-80% depending on institution (Zullo et al., 2003). This reflects the varying degrees of surgical radicality and various measurement methods used to diagnose bladder dysfunction. The prevalence of approximately 25% in this study confirms the significance of this condition. Because this data is based on patients' view of bladder dysfunction, the authors believe that it reflects the clinically significant concern. Although other instrumental methods, such as the urodynamic study, are more accurate and sensitive for bladder dysfunction diagnosis, clinical significance of their findings frequently appears minimal. In one study, most of the patients who had abnormal urodynamic findings were satisfied with their voiding habits. The disagreement between urinary symptoms and urodynamic diagnosis could be explained by the mild intensity of the urodynamic findings and by the adjustable bladder habits at home (Zullo et al., 2003). Also, in the other study, only 17% of patients with cervical cancer had normal urodynamic findings before radical hysterectomy (Lin et al., 2001).

The authors have found no statistically significant association between all examined clinico-pathologic factors and the rate of bladder dysfunction. This is somewhat expected because the only consistent predicting factor for post radical hysterectomy bladder dysfunction in literature is extent of parametrial resection (Maas et al., 2003; Zullo et al., 2003), which was not reflected in most of the examined factors in this study. Of note, however, the factors that directly and indirectly represent radicality such as procedure (class II versus class III hysterectomy) and FIGO stage have shown a trend toward association with bladder dysfunction. Statistically significant association between hysterectomy class (extent of resection) and symptomatic bladder dysfunction could

possibly be demonstrated if the sample size in the modified (class II) radical hysterectomy group was larger.

For pattern of urinary dysfunction, parasympathetic nerve disruption results in a hypocontractile or acontractile bladder with decreased sensation. Sympathetic denervation causes a bladder with decreased compliance and high storage pressure. In addition, sympathetic nerve damage could result in bladder neck incompetence that leads to incontinence (Maas et al., 2003). The equally common findings of incomplete emptying and decreased bladder sensation (hypocontractile dysfunction), and urgency and incontinence (decreased compliance and bladder neck incompetence) in this study suggests the combined surgical disruption of both pelvic parasympathetic and sympathetic innervations.

Measures have been proposed to reduce bladder dysfunction following radical hysterectomy. Because of the apparent relation between bladder dysfunction and extent of radicality, a reduced radicality has been proposed to decrease the rate of the dysfunction (Tamussino et al., 1997; Landoni et al., 2001). Some authors have described a surgical technique to preserve the pelvic nerve bundle during radical hysterectomy (Yabuki et al., 2000; Kato et al., 2003; Trimbos et al., 2001; Raspagliesi et al., 2004; Raspagliesi et al., 2006). Long-term outcome on therapeutic efficacy must be demonstrated before these measures could be accepted as standard of patient care.

In conclusion, voiding dysfunction is a common and clinically significant long-term complication following radical hysterectomy. The pattern of dysfunction reflects combined surgical disruption of both parasympathetic and sympathetic innervations of the pelvis.

Acknowledgments

The authors would like to thank Associate Professor Sangwal Rakpao, M.D. for her help with statistical analysis.

References

Barnes W, Waggoner S, Delgado G, et al (1991). Manometric characterization of rectal dysfunction following radical hysterectomy. *Gynecol Oncol*, **42**, 116-9.

Bergmark K, Avall-Lundqvist E, Dickman PW, et al (1999). Vaginal changes and sexuality in women with a history of cervical cancer. *N Engl J Med*, **340**, 1383-9.

Butler-Manuel SA, Buttery LD, A'Hern RP, et al (2002). Pelvic nerve plexus trauma at radical and simple hysterectomy: a quantitative study of nerve types in the uterine supporting ligaments. *J Soc Gynecol Investig*, **9**, 47-56.

Deerasamee S, Srivatanakul P (1999). Cervix Uteri. In: Deerasamee S, Martin N, Sontipong S, Sriamporn S, Sriplung H, Srivatanakul P, editors. Cancer in Thailand, 1992-1994. Lyon: International Agency for Research on Cancer, pp 56-9.

Ercoli A, Delmas V, Gadonneix P, et al (2003). Classical and nerve-sparing radical hysterectomy: an evaluation of the risk of injury to the autonomous pelvic nerves. *Surg Radiol Anat*, **25**, 200-6.

Kato T, Murakami G, Yabuki Y (2003). A new perspective on nerve-sparing radical hysterectomy: nerve topography and over-preservation of the cardinal ligament. *Jpn J Clin Oncol*, **33**, 589-91.

Landoni F, Maneo A, Colombo A, et al (1997). Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. *Lancet*, **350**, 535-40.

Landoni F, Maneo A, Cormio G, et al (2001). Class II versus class III radical hysterectomy in stage IB-IIA cervical cancer: a prospective randomized study. *Gynecol Oncol*, **80**, 3-12.

Lin HH, Yu HJ, Sheu BC, et al (2001). Importance of urodynamic study before radical hysterectomy for cervical cancer. *Gynecol Oncol*, **81**, 270-2.

Maas CP, Trimbos JB, DeRuiter MC, et al (2003). Nerve sparing radical hysterectomy: latest developments and historical perspective. *Crit Rev Oncol Hematol*, **48**, 271-9.

Maas CP, Kenter GG, Trimbos JB, et al (2005). Anatomical basis for nerve-sparing radical hysterectomy: immunohistochemical study of the pelvic autonomic nerves. *Acta Obstet Gynecol Scand*, **84**, 868-74.

Newton M (1975). Radical hysterectomy or radiotherapy for stage I cervical cancer. A prospective comparison with 5 and 10 years follow-up. *Am J Obstet Gynecol*, **123**, 535-42.

Raspagliesi F, Ditto A, Fontanelli R, et al (2004). Nerve-sparing radical hysterectomy: a surgical technique for preserving the autonomic hypogastric nerve. *Gynecol Oncol*, **93**, 307-14.

Raspagliesi F, Ditto A, Fontanelli R, et al (2006). Type II versus Type III nerve-sparing radical hysterectomy: comparison of lower urinary tract dysfunctions. *Gynecol Oncol*, **102**, 256-62.

Srisomboon J (2004). Epidemiology. Cervical cancer: diagnosis and management. 1st ed. Bangkok: P.B. Foreign Books Center, pp 1-12.

Tamussino K, Winter R, Lang PFJ (1997). The cardinal ligament: surgical anatomy and resection. *CME J Gynecol Oncol*, **6**, 265-71.

Trimbos JB, Maas CP, Deruiter MC, et al (2001). A nerve-sparing radical hysterectomy: guidelines and feasibility in Western patients. *Int J Gynecol Cancer*, **11**, 180-6.

Yabuki Y, Asamoto A, Hoshiba T, et al (2000). Radical hysterectomy: An anatomic evaluation of parametrial dissection. *Gynecol Oncol*, **77**, 155-63.

Yabuki Y, Sasaki H, Hatakeyama N, et al (2005). Discrepancies between classic anatomy and modern gynecologic surgery on pelvic connective tissue structure: harmonization of those concepts by collaborative cadaver dissection. *Am J Obstet Gynecol*, **193**, 7-15.

Zullo MA, Manci N, Angioli R, et al (2003). Vesical dysfunctions after radical hysterectomy for cervical cancer: a critical review. *Crit Rev Oncol Hematol*, **48**, 287-93.