

RESEARCH COMMUNICATION

Long-term Lower Urinary Tract Dysfunction in Gynecologic Cancer Survivors

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Abstract

Objective: To determine the prevalence of lower urinary tract dysfunction (LUTD) in gynecologic cancer survivors after radical hysterectomy (RH) as compared to total abdominal hysterectomy (TAH). The impact on quality of life (QOL) was also evaluated. **Materials and Methods:** From January to April 2010, 108 gynecologic cancer survivors (52 cervical, 28 ovarian and 28 endometrial cancer patients) who underwent primary surgery at King Chulalongkorn Memorial Hospital completed the Urogenital Distress Inventory and Incontinence Impact Questionnaire (UDI and IIQ). The UDI has 3 subscales for 19 items of symptoms associated with LUTD. The IIQ is a QOL questionnaire which has 4 subscales for 30 items referring to degree of urinary incontinence affecting various activities and emotions. A higher score indicates a greater impairment of QOL. **Results:** The RH group was younger (52.3 ± 8.0 years) than TAH group (56.2 ± 9.1 years), with a lower nulliparous rate (13.2% and 55.4%) but more sexual activity (56.6% and 21.4%). Median time from primary surgery was the same in both groups (5 years, range 3-20). Seventy gynecologic cancer survivors (64.8%) had LUTD, without significant variation between the two groups (68.6% and 61.4%, respectively). However, the RH group had significantly more stress urinary incontinence (45.1% as compared to 21% for the TAH group) and voiding dysfunction (31.4% and 1.8%). The total scores and scores from most UDI subscales except irritative symptoms were significantly higher in the RH group. In contrast, there were no differences in total and all IIQ subscale scores. **Conclusion:** Stress urinary incontinence and voiding dysfunction were prevalent in gynecologic cancer survivors after RH. However, there was no impact on QOL when compared to survivors undergoing TAH.

Keywords: Gynecologic cancer survivors - lower urinary tract dysfunction - QoL - urinary incontinence

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Introduction

Gynecologic cancer is one of the most common malignancies in women. Because of the improvement in treatment modalities has influenced an increased cure rates and prolonged survival. Survivors may experience any morbidity related to cancer treatments. Specific sequelae may be more prevalent in specific gynecologic cancer. Hysterectomy with bilateral salpingo-oophorectomy and surgical staging are mainstay treatment in the majority of gynecologic cancer patients including ovarian cancer and endometrial cancer patients. While, radical hysterectomy is used for early stage of cervical cancer and some endometrial cancer patients with cervical involvement.

Lower urinary tract dysfunctions (LUTD) are common complication after hysterectomy. Hysterectomy has been reported 40% increased in the odds of developing urinary incontinence (UI) in long-term and twice likely to undergo subsequent incontinence surgery (Brown et al., 2000; Altman et al., 2007). More radicality may disrupt autonomic nerve innervations of lower urinary tract causing more LUTD after radical hysterectomy (Zullo et al., 2003). These dysfunctions can persist in long-term and

may affect the quality of life (QOL) of the survivors. The definition of long-term survivor is indefinite and ranges between at least 1 to 3 years after diagnosis (Goncalves, 2010). Most gynecologic cancer patients had recurrence of disease within 3 years after their primary treatment. Therefore, a 3-year criterion is used in this study. Recently, QOL has become an increasingly interesting issue and has been studies worldwide. Questionnaires include symptom and QOL questionnaires. The symptom questionnaires assess the presence, severity, and degree of bothersome. The QOL questionnaires include generic and condition-specific quality of life (QOL) questionnaires. Generic questionnaires are widely used but they lack of specificity to the particular diseases. In contrast, condition-specific QOL questionnaires are designed to assess the impact of specific diseases on health related QOL (Barber, 2007). Among these questionnaires, the Urogenital Distress Inventory and Incontinence Impact Questionnaire (UDI and IIQ) are the most widely used for urinary incontinence (Shumaker et al., 1994)

The primary aim of this study was to evaluate the prevalence of LUTD in gynecologic cancer survivors after radical hysterectomy (RH) compared to total abdominal

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hysterectomy (TAH). The secondary aim was to evaluate the impact of LUTD on quality of life.

Materials and Methods

Cross sectional study was performed on 108 gynecologic cancer survivors who received primary surgery at King Chulalongkorn Memorial Hospital and had surveillance visit at gynecologic oncology clinic from January to April 2010. They included 52 patients with early stage cervical cancer, 28 ovarian cancer, and 28 endometrial cancer patients. Radical hysterectomy (RH) group included 51 early stage cervical cancer patients. The standard type III radical hysterectomy and bilateral pelvic lymphadenectomy was performed in this study. Bilateral salpingo-oophorectomy (BSO) was performed on selected patients. All patients with ovarian and endometrial cancer performed TAH with BSO, other surgical staging procedures were performed on indicated patients. In total, 57 patients including one stage IA cervical cancer patient were in the TAH group.

The LUTD was evaluated using validated Thai version of the Urogenital Distress Inventory and Incontinence Impact Questionnaire (UDI and IIQ). The UDI is symptom questionnaire which has 3 subscales consisting of 19 items of symptoms associated with LUTD (Table 1). The IIQ is quality of life (QOL) questionnaire which has 4 subscales consisting of 24 items; they refer to the degree of UI affects to various activities such as household chores, recreation, entertainment, travel, social activity, sexual

activity. The other 6 items are related to the degree of UI on various emotions such as anxiety, fear, frustration, anger, depression, embarrassment (Table 2). A higher score represents a greater impairment on the QOL; a lower score a better QOL (Shumaker et al., 1994).

Demographic data are shown as means, medians, and percentages. Chi-squared test or Fisher exact test was used to compare categorical data between the two groups. Comparison of nonparametric data between the two groups was analyzed by Mann-Whitney U test. A *P* value of less than 0.05 was considered statistically significant.

Results

RH group were younger (52.3 ± 8.0 years) than TAH group (56.2 ± 9.1 years); they had lower number of nulliparous (13.2% and 55.4%), but they were more sexually active (56.6% and 21.4%). No significant difference in menopause status at the initial treatment, hormone treatment, and body mass index (BMI) between both groups (Table 3). Median time from primary surgery was equal in both groups (5, range 3–20 years). There was no significant difference in postoperative radiotherapy between the two groups. Seventy gynecologic cancer survivors (64.8%) had LUTD. There was no significant difference of the prevalence of overall LUTD between the two groups: 68.6% and 61.4%, respectively ($p=0.54$). Forty-seven survivors (43.5%) had UI. The prevalence of stress urinary incontinence (SUI), urgency urinary

Table 2. Items in the Incontinence Impact Questionnaire

Has urine leakage and/or prolapse affected	
Physical activity (6 items)	- Household chores - Maintenance or repair work - Shopping activities - Hobbies and parttime activities - Physical recreational activities - Physical health
Social relationships (10 items)	- Church or temple attendance - Volunteer activities - Having friends visit in home - Participating in social activities outside home - Relationship with friends - Relationship with family excluding husband/companion - Sexual relations - Way you dress - Fear of odor restrict activities - Fear of embarrassment restrict activities
Travel (6 items)	- Entertainment activities - Travel for distance less than 20 min from home - Travel for distance more than 20 min from home - Going to place if not sure about restrooms - Going on vacation - Employment outside the home
Emotional health (8 items)	- Emotional health - Sleep - Nervousness or anxiety - Fear - Frustration - Anger - Depression - Embarrassment

Table 1. Items in the Urogenital Distress Inventory (UDI)

Do you experience, and, if so, how much are you bothered by:

Irritative symptoms (6 items)	- Frequent urination - Feeling of urgency - Urine leakage related to the feeling of urgency - Large amounts of urine leakage - Nighttime urination - Bedwetting
Obstructive/discomfort or activity (11 items)	- Urine leakage not related to urgency - Difficulty emptying bladder - Feeling of incomplete bladder emptying - Lower abdominal pressure - Pain when urinating - Pain in the lower abdominal or genital area - Heaviness or dullness in the pelvic area - Feeling of bulging or protrusion in the vaginal area - Bulging or protrusion that can see in the vaginal area - Pelvic discomfort when standing or physically exerting - Have to push on the vaginal walls to have a bowel movement
Stress symptoms (2 items)	- Urine leakage related to physical activity, coughing or sneezing - Small amounts of urine leakage

Table 3. Baseline Characteristics

	RH group (N=51)	TAH group (N=57)	P value
Mean age, years $\pm$ SD	52.3 $\pm$ 8.0	56.2 $\pm$ 9.1	0.02
Nulliparous, n(%)	6 (11.8)	32 (56.1)	< 0.001
Menopause, n(%)	22 (43.1)	26 (45.6)	0.85
Hormone treatment, n(%)	2 (3.9)	6 (10.5)	0.28
Sexually active, n(%)	29 (56.9)	12 (21.1)	< 0.001
Mean body mass index, kilograms $\pm$ SD	25.3 $\pm$ 3.8	26.1 $\pm$ 4.7	0.33
Median time from primary treatment, years (range)	5 (3-20)	5 (3-20)	0.41
Postoperative radiotherapy, n (%)	5 (9.8)	7 (12.3)	0.74

Table 4. Lower Urinary Tract Dysfunction

	RH group (N=51)	TAH group (N=57)	P value
Increase daytime frequency	9 (17.6)	15 (26.3)	0.36
Nocturia	13 (25.5)	22 (38.6)	0.16
Urgency	8 (15.7)	11 (19.3)	0.80
Any type of urinary incontinence	29 (56.9)	18 (31.6)	0.01
Urgency urinary incontinence	1 (2.0)	4 (7.0)	0.37
Stress urinary incontinence	23 (45.1)	12 (21.0)	0.01
Mixed urinary incontinence	5 (9.8)	2 (3.5)	0.25
Voiding difficulty	16 (31.4)	1 (1.8)	< 0.001

Table 5. Comparison of Total and Subscale Scores of the Urogenital Distress Inventory (UDI) and Incontinence Impact Questionnaire (IIQ)

	RH group (N=51)	TAH group (N=57)	P value
Total UDI	6 (0, 18)	2 (0, 6.5)	0.018
Irritative symptoms	0 (0, 18)	0 (0, 6)	0.38
Obstructive/discomfort	3 (0, 9)	0 (0, 3)	0.004
Stress symptoms	0 (0, 33)	0 (0, 0)	0.023
Total IIQ	0 (0, 8)	0 (0, 2.5)	0.088
Physical activity	0 (0, 6)	0 (0, 0)	0.255
Social relationships	0 (0, 7)	0 (0, 0)	0.071
Travel	0 (0, 11)	0 (0, 0)	0.115
Emotional health	0 (0, 8)	0 (0, 0)	0.06

incontinence (UII), mixed urinary incontinence (MUI), and voiding dysfunction was 32.4%, 4.6%, 6.5%, and 15.7%, respectively. However, RH group had significantly more SUI (45.1% and 21%) and voiding dysfunction (31.4% and 1.8%) The other LUTD were not different (Table 4). The total scores and scores from most UDI subscale except irritative symptoms subscale were significantly higher in RH group. In contrast, there was no difference in the total and all IIQ subscale scores between the two groups (Table 5).

Discussion

Improvement in treatment modalities in gynecologic cancers causes increased cure rates. However, each cancer treatments have the potential to cause different long-term morbidities. Hysterectomy is a mainstay treatment in most gynecologic cancers. It has been reported as a risk factor for urinary incontinence in a previous systematic review (Brown et al., 2000). However, more recent studies have contradicted the assumption that hysterectomy causes

urinary incontinence or other LUTD (Engh et al., 2006; Miller et al., 2008). From one population-based, cross-sectional study reported no difference of UI between women with and without previous gynecologic cancer (34.4% and 34.3%, respectively). They suggested that long-term gynecologic cancer survivors did not increase the risk for UI (Skjeldestad et al., 2008). However, types of surgical treatments were not mentioned in this study. More radical surgery may cause more prevalence of LUTD. Radical hysterectomy comprises excision of the uterus and cervix including parametrial tissue and upper vagina which disrupt pelvic autonomic nerve innervation causing pelvic floor dysfunction (Jackson et al., 2006). This includes the dysfunction in at least one of these three systems: urinary, anorectal, and genital system. However, this study focuses only the dysfunction in urinary system because it is the most common long-term morbidity after RH. Our previous study reported up to two-third of cervical cancer survivors after RH showed urodynamic abnormalities. One-third of them had storage dysfunction and half of them had voiding dysfunction (Manchana et al., 2010). Although, the prevalence of LUTD was not diagnosed by urodynamic studies, validated condition-specific questionnaires were used in this study. Up to 68% of gynecologic cancer survivors had LUTD which is comparable to our previous study.

This study was initiated to further evaluate the difference of LUTD between gynecologic cancer survivors who received different types of surgical treatment. Although, overall LUTD showed no difference between the two groups, significantly higher prevalence of SUI (45% and 21%), and voiding dysfunction (31% and 2%) were reported in RH group. This result was contradictory to a previous study reported by Brook et al (Brook et al., 2009). They suggested that RH does not associated with more long-term bladder dysfunction than simple hysterectomy. They reported 83% of cervical cancer survivors who underwent type III radical hysterectomy and 78% of patients who underwent hysterectomy for benign conditions developed UI. There was no difference in the degree of LUT symptom in women who underwent radical versus simple extrafascial hysterectomy. Different controls might be a plausible explanation. Furthermore, various factors such as age, parity, obesity, hormone replacement therapy (HRT), and previous pelvic surgery were reported to have an association with UI (Irwin et al., 2006). Furthermore, pelvic radiation is another factor associated with increased risk of UI. Endometrial cancer survivors who received adjuvant radiation therapy had more severe UI and a higher impact on QOL (Erekson et al., 2009). Combination of risk factors for both cancers and UI may influence the prevalence of UI. Each type of cancer has a different profile in terms of demographic data. Although, endometrial and ovarian cancers were more common in the elderly but they usually occur in nulliparous. In contrast, cervical cancer patients were younger but more multiparous. As age is the most important risk factor for UI, endometrial and ovarian cancer survivors in TAH group should have more UI (Irwin et al., 2006). In fact, RH group had more UI in this study. As there was no significant difference in term of obesity, menopause, HRT,

and adjuvant pelvic radiotherapy between the two groups, therefore, radical surgery may have negative correlation with UI.

Significantly more prevalence of SUI and voiding dysfunction in RH group were reported in this study. SUI is the most common type of UI (Hannestad et al., 2000). It is more prevalent in women after radical hysterectomy. The exact pathophysiology of SUI is uncertain. Over excision of the upper vagina and parametrium may result in disruption of the bladder neck support. Moreover, loss of control from alpha adrenergic receptors and pudendal nerve denervation will relax the internal and external urethral sphincter, respectively, causing SUI (Zullo et al., 2003). Voiding dysfunction is also common after radical hysterectomy. Our previous study showed low maximal flow rate, high post-void residual urine and void with abdominal straining in patients after radical hysterectomy (Manchana et al., 2010). However, these patients will cope by adapting their urination habit to minimize LUTD. As a result, LUTD had no impact on QOL.

Most studies reported that gynecologic cancer survivors had similar general QOL to healthy control (Goncalves, 2010). Limited studies reported the impact of specific conditions especially LUTD on QOL. Our findings reveal that LUTD is relatively common in gynecologic cancer survivors. However, it has no impact on QOL which is agreeable with previous studies (Brook et al., 2009; Skjeldestad et al., 2009). Although, long-term bladder dysfunction is relatively common after RH, majority of survivors had mild symptoms and did not have markedly impact on their QOL. It is hypothesized that cancer patients may cope with LUTD better than non-cancer patients. Cancer patients are usually more concerned over their underlying malignant disease than the other symptoms (Brook et al., 2009). Only one-third of patients complained about their symptoms to their health care-providers and sought for treatments (Skjeldestad et al., 2008). Patients with UII have more often consultation than those with SUI and had worse impact on QOL (Hägglund et al., 2001). Because of this result, most survivors in this study who had SUI might not recognize these symptoms as problems that affected their QOL.

In conclusion, high prevalence of LUTD was demonstrated in gynecologic cancer survivors. UI especially SUI and voiding dysfunction were more common in survivors after radical hysterectomy. Although, these dysfunctions had no impact on their QOL, healthcare provider should be encouraged to ask these cancer survivors about these symptoms and offer proper treatments.

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