

Bladder and bowel symptoms in cervical and endometrial cancer survivors

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Abstract

Background: Previous studies likely underestimate the prevalence of bowel and bladder symptoms in gynecologic cancer survivors. We sought to estimate the prevalence of these symptoms in cervical and endometrial cancer survivors who had completed treatment 1 year previously compared with non-cancer controls, and to examine factors associated with more severe symptoms in survivors.

Methods: As part of a larger quality of life study, survivors who were 1-year posttreatment for cervical or endometrial cancer ($n = 104$) completed measures of bladder and bowel symptoms. An age-matched and race/ethnicity-matched sample of women with no history of cancer was recruited for comparison purposes.

Results: Survivors reported a higher prevalence of bladder symptoms, specifically storage and incontinence symptoms, than non-cancer controls. Prevalence rates for bowel symptoms in survivors were higher than those reported in previous studies. Greater symptom severity was associated with younger age, lower annual incomes, and less education. Other correlates included higher body mass index and history of smoking. As hypothesized, more severe symptoms were associated with radical hysterectomy and pelvic radiation.

Conclusions: Bladder and bowel symptoms are more prevalent in cervical and endometrial cancer survivors than non-cancer controls. Future research should replicate these findings in a larger, prospective study.

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Introduction

Symptoms such as dysuria, urinary incontinence, fecal incontinence, and constipation are commonly associated with radical pelvic surgeries and pelvic radiation for gynecologic cancer [1–5]. Although there is a relative paucity of research documenting bladder and bowel symptoms after gynecologic cancer, findings suggest symptoms are common among survivors [4,6–8], that they may persist long after treatment [9,10], and that they adversely affect quality of life in survivorship [5,11–13].

Reported prevalence rates for symptoms vary widely. For example, Vistad *et al.* [7] reported a prevalence rate of 19% for defecation urgency at least once a week among cervical cancer survivors treated with radiotherapy a median of 8 years previously, whereas Hazewinkel *et al.* [4] found a prevalence rate of 49% for defecation urgency in women who had completed surgery and radiation for cervical cancer a median of 6 years previously. The lack of consistency across studies can be attributed, in part, to methodological differences, including differences in the definition and assessment of bladder and bowel symptoms. Studies [5,6,8,11,14–16] have often assessed symptoms using

study-specific measures that may not have been validated or general quality of life measures rather than ecologically valid instruments designed specifically to assess bladder and bowel symptoms. Some studies [7,17] have included clinician-based symptom assessments; a recent study [7] found physicians underreport bladder and bowel symptoms associated with gynecologic cancer treatment. In general, differences in how these symptoms are defined and assessed make it challenging to compare results across studies.

Many studies also have methodological features that limit conclusions that can be drawn. Studies [14,17,18] have been marked by small sample sizes that yield inadequate statistical power. Others have had considerable variability within study samples [3,4,8,18,19] of time since treatment completion; one study [4], for example, included cervical cancer survivors who had been treated between 1 and 11 years previously. Most studies do not include groups that allow for comparisons with the general population (see, e.g., Lalos Kjellberg and Lalos [17] and Hsu *et al.* [5]). Among studies [3,4,6–8] with comparison samples, some have compared women with a history of gynecologic cancer to women with no history of cancer

who have undergone a hysterectomy for a benign condition [8] or to women with a diagnosed pelvic floor disorder [3]; others have included women from large population-based registries. When comparison samples are used, there often is a failure to match patients and comparison subjects on variables other than age that may influence bladder and bowel function (e.g., obesity and race/ethnicity). As a result, it is difficult to determine whether symptoms are more strongly associated with factors other than gynecologic cancer treatment. These methodological differences across studies suggest previous investigations underestimate the prevalence of bladder and bowel symptoms after cervical and endometrial cancer.

Present study

We sought to estimate the prevalence of bladder and bowel symptoms in women who had completed treatment for cervical or endometrial cancer 1 year previously and examine whether prevalence rates are higher in survivors than matched non-cancer controls. We hypothesized survivors would have higher prevalence rates. We also sought to explore whether symptom severity in survivors can be accounted for by demographic and clinical characteristics. Based on previous studies, we hypothesized that greater symptom severity would be associated with history of radical hysterectomy and radiation therapy.

Methods

Participant selection and recruitment

Women were eligible if they: (a) were 18 years of age or older; (b) had cervical or endometrial cancer; (c) had completed treatment 1 year previously; (d) had no other history of cancer besides nonmelanoma skin cancer; (e) had no documented or observable psychiatric or neurological disorders that would interfere with study participation; and (f) were able to speak and read standard English. As part of a larger quality of life study, women were screened for eligibility and asked to provide written informed consent prior to initiation of treatment. Assessments were conducted 1 year after treatment was completed. Every patient who completed the assessment was matched with a control using procedures described later. Of the 122 cervical and endometrial cancer patients enrolled in the larger study, 104 (85%) completed the 1-year posttreatment assessment and were included in the present analysis. There were no clinical or demographic differences between those who did and did not complete the 1-year posttreatment assessment.

Eligibility criteria for controls were they must (a) be female; (b) be within 3 years of the age of the survivor to whom they were being matched; (c) be the same race/ethnicity as the survivor to whom they were being

matched; (d) report no history of cancer other than nonmelanoma skin cancer (e) have not undergone a hysterectomy; (f) have no discernible psychiatric or neurological disorders that would interfere with study participation; (g) be able to speak and read standard English; and (h) reside within one of seven counties surrounding the cancer center where recruitment took place.

Potential controls were identified using a database maintained by Marketing Systems Group, Inc. (Fort Washington, PA) that draws from all listed telephone households in the USA and is estimated to include demographic and contact information for approximately two-thirds of the US population. For each survivor, up to 20 women who were within 3 years of the patient's age and who resided in one of seven counties surrounding the cancer center were selected randomly from the database. One of these women was selected at random and sent a letter of introduction describing the study. If this woman did not opt out by calling a toll-free telephone number, telephone contact was initiated to further determine eligibility. If she met all eligibility criteria and verbally agreed to participate, a study packet containing the study questionnaires and the informed consent was mailed to her. If the first woman selected could not be reached, was ineligible, refused to participate, or did not return the informed consent and completed study questionnaires, another woman on the list was selected randomly until a woman matched to the patient was recruited and data collection completed.

Measures

Demographic and clinical characteristics

Demographic and clinical characteristics were assessed via self-report. Tobacco use was assessed using validated items from the Behavioral Risk Factor Surveillance Survey [20]. Alcohol use was assessed with three items from the World Health Organization's Alcohol Use Disorders Identification Test [21]. Comorbid medical conditions were assessed via a self-report version of the Charlson Comorbidity Index [22]. Clinical variables assessed via medical record review for all survivors were the following: cancer type, disease stage, types of gynecologic surgery, chemotherapy agents, and types of radiation therapy received.

Bladder symptoms

The International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Module (FLUTS) [23] is a 12-item scale evaluating a range of urinary symptoms. Subscale scores for storage, voiding, and incontinence symptoms are calculated by adding relevant items. A total score is calculated by summing the three subscale scores; total scores range from 0 to 48 with higher scores indicating greater severity. Respondents also

are asked to indicate on 12 separate scales from 0 = not at all to 10 = a great deal the degree of bother associated with each symptom. Scores have been shown to have good construct and discriminant validity and good internal consistency and test-retest reliability in general and clinical populations [24]. The FLUTS [23] was used to determine prevalence (presence/absence) of bladder symptoms using definitions set forth by the standardization subcommittee of the International Continence Society [25] and to assess severity of storage, voiding and incontinence symptoms. We added an additional item assessing whether participants had experienced a urinary tract infection within the last year, and if so, how many. We did so because a number of symptoms (e.g., frequency and urgency) are associated with urinary tract infections.

Bowel symptoms

Memorial Symptom Assessment Scale (MSAS) [26] is a 32-item measure assessing symptom prevalence, symptom characteristics including severity, and distress associated with highly prevalent symptoms in cancer. Respondents indicate presence or absence of the symptom and if present, rate severity on a scale from 1 = slight to 4 = very severe. For the present study, we focused on items assessing diarrhea, constipation, and abdominal bloating. The larger quality of life study from which the current study is derived did not include administering the MSAS to non-cancer controls; thus, data from the MSAS are not available for comparison purposes from non-cancer controls.

Pelvic pain

We modified the MSAS [26] slightly by adding an item specific to pelvic pain. As noted, only cervical and endometrial cancer survivors completed the MSAS.

Statistical analysis

Chi-square tests for categorical variables and one-way analysis of variance for continuous variables were conducted to identify differences in demographic characteristics between survivors and controls. Variables for which there were significant ($p < .05$) differences were entered as covariates in the main analyses. Logistic regression was used to compare rates of symptoms as defined by the standardization subcommittee of the International Continence Society [25] between survivors and controls. Odds ratios and 95% confidence intervals were calculated. We then examined the relationship of symptom severity as indicated by survivors' responses on the FLUTS subscales and MSAS items to survivor demographic and clinical characteristics using univariate regression. Multivariate linear regression modeling was conducted to examine variability in symptom severity accounted for by these correlates. Only variables that were statistically significant ($p < .05$) in univariate analyses were entered in multivariate

models. Variables were entered by a forward selection method with significance level for entry set at $p < .15$. Separate models were tested for severity of each category of bladder symptom and bowel symptom, and for pelvic pain.

Results

Characteristics of survivors and non-cancer controls

A total of 208 women, aged 28 to 84 years old, were included. Demographic and clinical characteristics of survivors and controls are presented in Table 1. There were significant group differences in body mass index (BMI), alcohol use, marital status, annual income, and education. These variables were included as covariates in subsequent group comparisons.

Table 1. Sample characteristics

Variable	Survivors (n = 104; %(n))	Controls (n = 104; %(n))	p
Age (mean ± SD)	56.0 ± 12.6	56.4 ± 11.2	.85
Race/ethnicity			
Non-Hispanic white	88 (92)	88 (92)	1.00
Annual income			
≥\$40,000 per year	71 (74)	63 (66)	.004
Education			
Some college	69 (72)	82 (85)	.04
Marital status			
Married	62 (64)	80 (83)	.006
Menopausal status			
Perimenopausal or postmenopausal	64 (67)	72 (75)	.20
Smoking status			
At least 100 cigarettes in lifetime	50 (52)	50 (52)	.89
Alcohol			
Any in last month	46 (48)	73 (76)	< .0001
Body mass index (mean ± SD)	33.1 ± 9.1	27.9 ± 6.2	< .001
Comorbidities			
≥1	33 (34)	22 (23)	.12
Urinary tract infection (mean ± SD)			
In last 12 months	.19 ± .39	.30 ± .46	.06
Cancer type			
Cervical	30 (31)		
Endometrial	70 (73)		
Surgery			
Radical hysterectomy	23 (24)		
Total abdominal hysterectomy	70 (73)		
Stage			
I	71 (74)		
II	11 (11)		
III	15 (16)		
IV	3 (3)		
Chemotherapy	29 (30)		
Radiation			
External beam radiation	27 (28)		
High dose radiation	23 (24)		
Low dose radiation	4 (4)		

SD, standard deviation.

Bladder symptoms

In survivors and controls, prevalence rates for bladder symptoms varied widely across the full range of bladder symptoms (Table 2).

Storage symptoms

Survivors were significantly (p values from .04 to .0005) more likely to report storage symptoms. Survivors also reported significantly (p values < .002) more bother associated with each of the other storage symptoms (data not shown).

Several demographic and clinical characteristics were significantly (p < .05) associated with storage symptom severity in survivors: younger age ($r = -.23$), race/ethnicity other than non-Hispanic white ($r = -.20$), lower income ($r = -.30$), less education ($r = -.22$), being premenopausal at diagnosis ($r = -.23$), cervical cancer ($r = -.25$), radical hysterectomy ($r = .25$), external beam radiation ($r = .26$), and low dose radiation brachytherapy ($r = .26$). In multivariate linear regression, with severity of storage symptoms as the dependent variable, the model explained 27% of the variance. Age,

annual income, and low dose radiation brachytherapy remained significant predictors of severity (p values < .05).

Voiding symptoms

There were no significant group differences in prevalence of voiding symptoms. Approximately 60% of survivors and controls reported at least one voiding symptom. Survivors consistently reported more bother (p values < .04) associated with individual symptoms (data not shown).

Only younger age ($r = -.21$) was associated with more severe symptoms and accounted for 5% of the variability in voiding symptom severity.

Incontinence symptoms

Survivors were significantly (p values < .05) more likely to have symptoms of incontinence of every type. Survivors also reported significantly (p values < .0001) more bother associated with these symptoms (data not shown).

More severe symptoms were significantly (p values < .05) associated with higher BMI ($r = .21$), less education

Table 2. Prevalence of bladder and bowel symptoms

	Survivors	Controls	Odd ratio (95% confidence interval)	p
	% (n)	% (n)		
Bladder symptoms				
Storage symptoms				
Nocturia (2 or more times a night)	46.2 (48)	24.0 (25)	2.7 (1.5–4.9)	.001
Urinary urgency	82.7 (86)	51.9 (54)	3.5 (1.7–7.2)	.0005
Frequency of daytime urinary leakage:				
At least once per day	28.9 (30)	7.7 (8)	3.7 (1.5–9.2)	.006
Daytime frequency:				
9 or more times a day	14.4 (15)	16.4 (17)	0.8 (.3–1.9)	.59
Bladder pain	31.7 (33)	13.5 (14)	3.1 (1.4–6.6)	.005
Any storage symptom	96.2 (100)	83.7 (87)	3.7 (1.1–12.4)	.04
Voiding symptoms				
Hesitancy	38.5 (40)	34.6 (36)	1.2 (.6–2.2)	.64
Straining	19.2 (20)	13.5 (14)	1.3 (.6–3.1)	.50
Intermittent stream	52.9 (55)	48.1 (50)	1.1 (.6–2.0)	.80
Any voiding symptom	58.7 (61)	59.6 (60)	0.9 (.5–1.7)	.78
Incontinence symptoms				
Urge urinary incontinence	72.1 (75)	49.0 (51)	2.2 (1.2–4.2)	.01
Stress urinary incontinence	73.1 (76)	50.0 (52)	2.1 (1.1–4.0)	.02
Mixed urinary incontinence	64.4 (67)	32.7 (34)	2.9 (1.6–5.5)	.0008
Enuresis	40.4 (42)	9.6 (10)	5.7 (2.5–12.8)	.0001
Nocturnal enuresis	27.9 (29)	7.7 (8)	3.4 (1.3–8.6)	.01
Any incontinence symptom	82.7 (86)	66.4 (69)	2.1 (1.0–4.3)	.04
Bowel symptoms^a				
Diarrhea	29.8 (31)			
Constipation	36.5 (38)			
Both diarrhea and constipation	22.2 (14)			
Bloating	52.9 (55)			
Any bowel symptom	71.2 (74)			
Pelvic pain^a	35.6 (37)			

^aThe larger study quality of life study from which the current study is derived did not include administering the Memorial Symptom Assessment Scale to non-cancer controls; thus data on bowel symptoms and pelvic pain are not available for comparison purposes from non-cancer controls.

($r = -.27$), external beam radiation ($r = .23$) and low dose radiation brachytherapy ($r = .20$). In multivariate analysis, these variables explained 19% of the variance in incontinence severity. BMI ($p = .007$) and education ($p = .02$) remained significant predictors of severity.

Bowel symptoms

Prevalence rates for bowel symptoms are shown in Table 2. Seventy-one percent of survivors reported experiencing at least one bowel symptom.

Diarrhea

Greater severity of diarrhea was significantly ($p < .01$) associated with more comorbidities ($r = .28$) and a lifetime history of smoking at least 100 cigarettes ($r = .25$). In multivariate analysis, these variables accounted for 14% of the variance in severity. Both smoking status ($p = .01$) and comorbidities ($p = .006$) remained significant predictors of severity.

Constipation

Constipation severity was not significantly associated with any survivor characteristics. Based on results indicating that diarrhea and constipation were not associated with each other ($p = .22$) but that 22% of survivors reported both constipation and diarrhea, we considered the severity of this combination. Younger age ($r = -.28$) and greater number of comorbidities ($r = .30$) were significantly ($p < .005$) associated with mean severity of this symptom combination. In multivariate analysis, these variables accounted for 17% of the variability in mean severity; both age ($p = .003$) and comorbidities ($p = .001$) remained significant predictors of severity.

Bloating

Bloating severity was significantly ($p < .05$) associated with younger age ($r = -.32$), single status ($r = -.23$), lower income ($r = -.22$), being premenopausal at diagnosis ($r = -.29$), more comorbidities ($r = .21$), cervical cancer ($r = -.21$), a lifetime history of smoking at least 100 cigarettes ($r = .22$), and radical hysterectomy ($r = .23$). In multivariate analysis, these variables accounted for 29% of the variance in severity. Age ($p = .001$), comorbidities ($p = .02$), and smoking status ($p = .006$) remained significant predictors of bloating severity.

Pelvic pain

Pelvic pain severity was significantly ($p < .05$) associated with younger age ($r = -.20$), cervical cancer ($r = -.34$), radical hysterectomy ($r = .34$), and external beam radiation ($r = .23$). In multivariate analysis, these variables accounted for 12% of the variance in severity of pelvic

pain. Only type of cancer ($p = .0004$) remained a significant predictor of pain severity.

Discussion

The present study extends our knowledge of bladder and bowel symptoms in cervical and endometrial cancer survivors in three major ways. First, findings indicate that these symptoms are highly prevalent in these cancer survivors. Second, consistent with our hypothesis, bladder symptoms, specifically storage and incontinence symptoms, are more prevalent in survivors than non-cancer controls. There were no differences between survivors and non-cancer controls in voiding symptoms; this may reflect a degree of recovery and stabilization of bladder neck function over time or, more simply, a greater clarity in symptom delineation and assessment afforded by our use of the FLUTS. Survivors uniformly reported more bother associated with bladder symptoms, a finding that suggests that survivors may be more sensitive or less tolerant of bladder symptoms they perceive as being cancer-related. Third, in survivors, in addition to radical hysterectomy and pelvic radiation, a number of demographic and clinical characteristics are associated with more severe symptoms.

The diversity in symptom definition and assessment across studies makes direct comparisons of bladder and bowel symptom prevalence rates difficult. In general, however, compared with studies with similar patient samples and time since treatment, our rates are higher than those previously reported [4,6,11,14,19]. Our finding that 36% of women reported pelvic pain is consistent with a recent study [27] in which 38% of cervical cancer survivors met the criteria for chronic pelvic pain. Of these, 60 and 43% also reported severe bowel and bladder symptoms, respectively, leading researchers to suggest that one-third of survivors may be predisposed to experience both longer term symptoms and pain.

That symptoms, specifically bladder symptoms, are more prevalent in survivors is consistent with previous studies using population controls [4,6,19]. We did not assess bowel symptoms in our non-cancer controls and so were unable to compare prevalence rates. Previous controlled studies [3,4,6,8,19] suggest bowel symptoms are more prevalent in survivors. In the present study, prevalence rates for bowel symptoms were generally higher than those found previously.

Several survivor demographic and clinical characteristics were associated with symptom severity. Our findings relative to education and income are consistent with existing epidemiologic studies [28–30]. The finding that younger, not older, age was associated with greater severity of symptoms is inconsistent with the epidemiology of pelvic floor disorders, however [29–33]. It may be the case that younger women are more sensitive to the onset

of new or different symptoms, either alone or in the context of the abrupt menopause many young women experience as a result of cancer treatment. With respect to clinical characteristics, our findings are consistent with studies showing specific treatment modalities are associated with higher rates of bladder and bowel symptoms [1–5,12,34]. As well, reviews and epidemiologic studies of pelvic floor disorders in the general population have consistently cited obesity, smoking, and comorbidities as factors that promote bladder and bowel dysfunction [28–30,32,33].

Limitations

Whereas radical pelvic surgeries and radiation are typically associated with a range of bowel symptoms [3,6,11,14], the present study assessed only three bowel symptoms. Further, we did not assess bowel symptoms in controls, making it impossible to examine whether there were group differences in symptom prevalence. The cross-sectional design provides only data at 1-year posttreatment; without a pretreatment baseline and multiple follow-ups, we cannot know whether symptoms predate the diagnosis in some women and how symptoms may change. A more homogeneous sample would have enabled us to more definitively determine effects of surgeries and radiation on pelvic floor symptoms. Finally, the samples reflected little racial diversity. Accordingly, the present study may not be generalizable to the population of minority women with gynecologic cancer.

Strengths

The present study is one of the first to estimate prevalence of both bladder and bowel symptoms in survivors at the

same point: 1-year posttreatment. We included a relatively large sample compared with previous studies. We assessed and controlled for a number of known risk factors (e.g., smoking, BMI, and comorbidities). We used the FLUTS, a well-known and psychometrically sound measure widely recommended for use in pelvic floor research [35]. To our knowledge, the FLUTS has not been used to assess symptoms after gynecologic cancer. Finally, we included a matched comparison group of women with no history of cancer.

Conclusions

Bladder and bowel symptoms are highly prevalent after cervical or endometrial cancer treatment, and bladder symptoms are more prevalent in survivors than non-cancer controls matched for age and race/ethnicity. Future research should replicate these findings in a larger, prospective study. Research should also be designed to elucidate efforts to manage symptoms and identify barriers to seeking help. Clinicians should screen for symptoms and offer treatment recommendations or make referrals as appropriate.

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Conflict of interest

There are no financial disclosures to report.

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