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ORIGINAL STUDY

Cervical cancer survivors' attitudes and understanding of menopause and hormone therapy

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Abstract

Objective: We designed a survey study to assess the presence and severity of climacteric symptoms, in addition to better understand patients' knowledge and understanding of hormone therapy (HT).

Methods: We administered a 23-question survey during a patient's clinic visit or over the phone. Study enrollment spanned from March, 2019 to May, 2019. The primary outcomes were severity of menopausal symptoms and willingness to try HT, calculated as a summarized overall score. Chi-square and logistic regression were used for analysis.

Results: Our response rate was 38% (n = 34). Our participants were diverse—67% women were black and 21% women were Hispanic. Stage 1 and 2 disease was reported in 32% and 41% of women. Also, 82% and 94% of women reported ever receiving any chemotherapy or radiation therapy. There was no association between willingness to try HT for relief of menopausal symptoms and income (χ^2 [1, 29] = 0.56, $P = 0.81$) or education level (χ^2 [1, 29] = 2.78, $P = 0.10$). The most common climacteric symptoms experienced were hot flushes (85%) and decreased libido (77%). Neither symptom severity (odds ratio [OR] 1.31, 95% confidence interval [CI] 0.89-1.94) nor concern for side effects (OR 1.06, 95% CI 0.82-1.36) of HT significantly predicted willingness to try HT.

Conclusions: Menopausal symptoms were prevalent in this population. Our data indicate that women are experiencing climacteric symptoms, but are overall unmotivated to address symptoms using HT. Factors such as symptom severity, fear of side effects, income level, or education level were not associated with acceptability of HT for premature menopause.

Key Words: Cervical cancer – Hormone therapy – Menopause.

Cervical cancer is most frequently diagnosed in women aged 35 to 44 years, and will be diagnosed in 13,170 women in 2019.[1] Treatment typically involves hysterectomy with or without oophorectomy and/or chemoradiation depending on stage of disease. Premenopausal women undergoing oophorectomy will undergo premature menopause. Patients undergoing pelvic radiation will also inevitably undergo ovarian failure[2]. A radiation dose of 2 Gray (Gy) to the ovaries will lethally damage half of the oocyte population; 6 Gy or above can render patients menopausal.[2] Menopausal symptoms can begin within days of surgery or within 12 weeks after completion of radiation therapy.[3]

Premature menopause can affect quality of life and have long-term consequences. Women may experience dyspareunia, decreased libido, and mood changes.[3] There is also an increased risk for ischemic heart disease, osteoporosis, and cognitive disorders such as dementia and Parkinson's disease.[3] In fact, women who experience premature ovarian failure have a 50% higher risk of mortality from ischemic heart disease compared with women who undergo menopause at the age of 52 to 55 years.[3]

The use of hormone therapy (HT) in cervical cancer survivors has not been extensively studied, and there is no standard of care guiding the use of HT after iatrogenic menopause secondary to cervical cancer treatment. HT use in cervical cancer survivors has not been shown to increase risk of recurrence or affect overall survival.[4,5] However, due to results of the Women's Health Initiative, providers and patients alike may be fearful of prescribing or taking hormones.[6] Based on the health risks of premature menopause and because cervical cancer is primarily human papilloma virus-mediated, we believe HT is an integral component of survivorship care for these patients. There are no prior studies

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assessing cervical cancer patient attitudes and knowledge base regarding the use of hormones after premature ovarian failure. We designed a survey study to assess the presence and severity of climacteric symptoms, in addition to better understand patients' knowledge and understanding of HT.

METHODS

This survey study was approved by the institutional review board. We performed a retrospective chart review to identify premenopausal women treated for cervical cancer with surgery or chemoradiation at the University of Illinois, Chicago Cancer Center, between 2005 and 2016. Non-English speakers and women less than 18 years old were excluded. We designed a survey focusing on patient symptoms and attitudes towards menopause based off a study published by Biglia et al[7] and with the support from the Survey Research Laboratory at the University of Illinois, Chicago. The authors administered all surveys and performed all data entry, data management, and analysis. Our goal was to obtain a response rate of 60%.

Survey and data collection

We used our 23-question survey to collect information on the participants' self-reported presence and severity of menopausal symptoms and their opinions regarding HT, and also clinical and socioeconomic information (Tables 1-3). Survey response types included both dichotomous and Likert-type responses (eg, mild, moderate, or severe as subjectively experienced by the patient).

We administered the survey in-person during a patient's clinic visit or over the phone. Patients without follow-up visits within the next 6 months were informed of the study via mail, then invited to participate via phone. Study enrollment spanned from March, 2019 to May, 2019. We obtained verbal or written consent before survey initiation. Survey respondents were not asked to record their name to maintain anonymity. Two of the authors (K.C. and R.K.) administered and completed the surveys after reading the questions aloud. Due to limitations of the researchers, surveys were only conducted in English by the two authors. Survey answers were transferred to a REDCap database for data management.

Planned analysis

Using SPSS, we computed descriptive statistics to detail our sample population, and their reported menopausal symptoms and concerns regarding HT. We used chi-square analyses to determine if survey responses, particularly the participants' reported willingness to try HT, differed by various background factors. Logistic regression was used to predict the binary outcome of willingness to try HT from the participants' symptom severity and fear of side effects.

The primary outcomes measured were severity of menopausal symptoms and willingness to try HT, calculated as a summarized overall score, respectively. The secondary outcome measures were fear of HT side effects. We hypothesized that those with more severe symptoms would be more likely to initiate HT and that those with heightened concern for side effects of therapy would be less likely to initiate therapy for menopausal symptoms.

RESULTS

We identified 88 premenopausal women treated for cervical cancer at the University of Illinois Hospital between 2005 and 2016. We contacted 37 women; 51 women did not return our phone calls or had invalid contact information. Thirty one of these patients had disconnected phone numbers and were unable to be invited to participate in our survey. Our response rate was 38% ($n = 34$). Our participants were diverse—67% women were black and 21% women were Hispanic. Stage 1 and 2 disease was reported in 32% and 41% of women. Also, 82% and 94% of women reported ever receiving any chemotherapy or radiation therapy. The average age was 46 years. The average combined family income was less than $25,000 for 63% of respondents, and 44% of women reported having an education level of less than or equal to high school (Table 4).

There was no association between willingness to try HT for relief of menopausal symptoms and income ($\chi^2\,[1, 29] = 0.56$, $P = 0.81$) or education level ($\chi^2\,[1,\ 29] = 2.78$, $P = 0.10$) (Table 5). The most common climacteric symptoms experienced were hot flushes (85%) and decreased libido (77%). More than half of the women experiencing decreased libido reported severe symptoms (54%). Anxiety and depression were reported in 47% and 53% of women, respectively.

Fear of cervical cancer recurrence as a result of HT concerned 41% of women, whereas an additional 41% of women worried that HT might cause another form of cancer. Neither symptom severity (odds ratio [OR] 1.31, 95% confidence interval [CI] 0.89-1.94) nor concern for side effects (OR 1.06, 95% CI 0.82-1.36) of HT significantly predicted willingness to try HT. In total, 47% of women were unwilling to use HT under medical supervision.

DISCUSSION

The knowledge and attitudes towards HT in this population is currently unreported in the literature. We found that menopausal symptoms were prevalent in this population of cervical cancer survivors. Hot flushes, night sweats, decreased libido, insomnia, anxiety, and depression were commonly reported in these young women. Our survey study is unique and addresses the needs of young cervical cancer survivors. Our data indicate that women are experiencing climacteric symptoms, but are overall unmotivated to address symptoms using HT. In fact, we found that 47% of women were unwilling to use HT under medical supervision. Symptom severity did not significantly predict a patient's willingness to try HT for relief of menopausal symptoms. Although their concern for HT side effects had a nonsignificant but inverse association with their acceptance of HT, given a larger sample size, this effect may have reached significance. Perhaps, this finding can be attributed to the lack of education from the medical community regarding the benefits of HT in this unique population; further

TABLE 1. *Our 23-question survey collecting demographic and clinical information while assessing patient understanding and knowledge surrounding premature menopause and hormone therapy*

1. If I have your permission, let me begin by asking at what stage was your cancer first detected?	a. Stage 1 b. Stage 2 c. Stage 3 d. Stage 4 e. Other (please specify) _____
2. Can you tell me the month and year when you were first diagnosed?	Month _____ Year _____
3. And when did you complete treatment (including chemotherapy and radiation, if you had surgery)?	Month _____ Year _____
4. How was your cervical cancer treated? (Check all that apply)	a. Surgery b. Chemotherapy c. Radiation
5. Can you tell me – in your own words – about any medical problems that you now have?	
6. Have you ever had a blood clot in your leg or your lung?	a. Yes b. No c. Don't know
7. How long ago was your last menstrual period?	a. 0-6 mos b. 7-12 mos c. 1-3 y d. 4-5 y e. More than 5 y
8. I would also like to ask you about whether or not you have experienced any of the following symptoms.	Please refer to Table 2
9. Have you used hormone therapy since receiving treatment for your cervical cancer?	a. Yes b. No → (SKIP TO Q11)
10. Did you start hormone therapy for any of the following? (Please say yes or No)	a. Hot flash symptom relief: Y/N b. Osteoporosis prevention: Y/N c. Vaginal dryness reduction: Y/N d. Cardiovascular disease prevention: Y/N
11. Would you be willing to take hormone therapy under medical supervision?	a. Yes b. No → (SKIP TO Q13)
12. Are you interested in considering hormone therapy for any of the following? (Please say yes or no)	b. Osteoporosis prevention: Y/N c. Vaginal dryness reduction: Y/N d. Cardiovascular disease prevention: Y/N e. Other (please specify) _____
13. As you may be aware, there may be several risks associated with hormone therapy but also may be several benefits for hormone therapy I'm going to read you a short list of some of these. For each, please tell me if you are not at all concerned, slightly concerned, moderately concerned, or extremely concerned with each. Then please tell me how willing you would be to start hormone therapy for the improvement of several menopausal symptoms by telling me if you are not at all willing, slightly willing, moderately willing, or extremely willing.	Please refer to Table 3
14. Has a friend, family member, or relative ever had hormone therapy?	a. Yes b. No
15. Have you heard of other alternative non-hormonal therapies for the relief of menopausal symptoms?	a. Yes b. No → (SKIP TO Q16)
16. Please tell me if you have heard of any of the following alternative nonhormonal therapies (for the relief of menopausal symptoms). Please tell me yes or no	a. Paroxetine b. Gabapentin c. Anti-depressants d. Plant derived estrogens e. Herbal remedies (please specify if possible) _____ f. Cognitive behavioral and other treatments g. Progesterone h. Other (please specify)_____
17. What year were you born?	a. _____
18. What is your zip code?	a. _____
19. What is your race?	a. White b. Hispanic c. Black or African American d. Asian e. American Indian or Alaskan Native f. Native Hawaiian and Other Pacific Islander g. Other (Please specify): _____
20. What is the highest grade or year of school that you completed?	a. Less than high school b. Some high school c. High school graduate or GED d. Some college or vocational school e. Associate degree (junior college) or technical/vocational degree/license f. Bachelor's degree g. Some graduate school h. Graduate or professional degree
21. How many people are currently living in your household, including yourself?	_____
22. Of these people, how many are children under the age of 18	_____
23. Which of these categories best describes your total combined family income for your household for the past 12 months? This should include income (before taxes) from all sources, wages, rent from properties, social security, disability and/or veteran's benefits, unemployment benefits, workman's compensation, help from relatives (including child payments and alimony), and so on.	a. Less than $25,000 b. $25,000-<$50,000 c. $50,000-<$75,000 d. $75,000-<$100,000 e. $100,000-<$150,000 f. More than $150,000 g. Don't Know/Not sure h. Prefer not to answer

TABLE 2. *Question 8*

In the past 6 months, have you experienced . . .	Yes or no?	Mild symptoms	Moderate symptoms	Severe symptoms
Hot flashes	Y/N	1	2	3
Night sweats	Y/N	1	2	3
Insomnia	Y/N	1	2	3
Tiredness	Y/N	1	2	3
Anxiety	Y/N	1	2	3
Depression	Y/N	1	2	3
Irritability	Y/N	1	2	3
Vaginal dryness	Y/N	1	2	3
Painful intercourse	Y/N	1	2	3
Decreased sex drive	Y/N	1	2	3
Increased vaginal discharge	Y/N	1	2	3
Vaginal bleeding	Y/N	1	2	3

study is needed. Nevertheless, when asked if they feared any other side effects, patients volunteered a variety of answers including cardiac arrest, gastrointestinal upset, kidney damage, possibility of pregnancy, return of menses, hair growth, or weight gain. Many women feared that HT use might cause another form of cancer or cervical cancer recurrence. Perhaps, patient knowledge is low on these topics, discouraging their interest in clinical intervention.

There are several important limitations to consider when interpreting our findings. We had a small sample size and a low response rate. High-volume cervical cancer centers have been defined as 15 or more cervical cancer patients annually[8]—our sample was then limited to premenopausal women who received chemoradiation therapy. Nevertheless, the small sample size may increase variability in our statistical analysis making these findings less representative or replicable, given a larger sample size. Also, our response rate was low leaving the potential for response or recall bias. Unfortunately, our patient population has high clinic no-show rates and patients are often difficult to contact via phone or mail; the response rate was not unanticipated. In addition, the authors who designed the study also participated in data collection, possibly contributing to bias in administration or the responses elicited. To minimize these possible biases, no HT knowledge was provided to patients during their completion of the survey.

Given these limitations, our conclusions are limited. An additional strength of this study, however, is the inclusion of medically underserved, minority populations. Our survey study sheds light on their experiences and can prompt further investigation and research. There are data to suggest that only 46% of women experiencing iatrogenic menopause are prescribed HT—disproportionately affecting uninsured women.[7] Given that cervical cancer is often a disease diagnosed in underserved populations, our survey study identifies the importance of education in survivorship care particularly in urban settings. Patient perspectives regarding HT after cervical cancer treatment is unreported. This study highlights the importance of addressing climacteric symptoms in this population. Survivorship care is an important aspect of oncology, and addressing menopausal symptoms can help improve quality of life for our patients. Often, patients may be unaware that these symptoms are problematic or may be less inclined to disclose these symptoms to their provider. Clinical outcomes in women treated for cervical cancer can be improved when these quality of life issues are integrated into survivorship care.

CONCLUSIONS

Our survey study showed that menopausal symptoms were prevalent. Factors such as symptom severity, fear of side effects, income level, or education level were not associated

TABLE 3. *Question 13*

How concerned are you with the risk of . . .	Not at all concerned	Slightly concerned	Moderately concerned	Extremely concerned
Fear of cancer relapse?	1	2	3	4
Fear of HT side effects?	1	2	3	4
Developing breast cancer?	1	2	3	4
Developing some other form of cancer?	1	2	3	4
Other potential side effects? (Please specify) _____	1	2	3	4
How willing are you to start hormone therapy for the treatment of . . .	**Not at all willing**	**Slightly willing**	**Moderately willing**	**Extremely willing**
Vasomotor symptoms relief?	1	2	3	4
Osteoporosis prevention?	1	2	3	4
Vaginal dryness reduction?	1	2	3	4
Prevention of cardiovascular disease?	1	2	3	4
Other potential side benefits? (Please specify) _____	1	2	3	4

with acceptability of HT for premature menopause in our limited population. As treatment for cervical cancer evolves, discussing HT as a treatment for menopausal symptoms is an important area of concern and should be addressed in survivorship care. The benefits of estrogen as it relates to cardiovascular health, bone heatlh, and cognitive function after premature menopause should also be addressed.[9] Thorough counseling and shared decision is an important aspect of survivorship care.

TABLE 4. *Participant demographic, socioeconomic, and clinical background factors*

Characteristic	n (%)
Age (mean)	46
Race/ethnicity	
Black	23 (68)
White	4 (12)
Hispanic	7 (21)
Asian/Native American/Native Hawaiian/Pacific Islander/other	2 (6)
Education level	
High school degree or less	16 (47)
More than a high school degree	18 (53)
Yearly individual income level	
$25,000 or less	19 (56)
Greater than $25,000	15 (44)
Cancer stage	
1	11 (32)
2	14 (41)
3	6 (18)
4	3 (9)
Cancer treatment received	
Surgery	12 (35)
Chemotherapy	28 (82)
Radiation	32 (94)
Menopausal symptoms	
Hot flushes	29 (85)
Night sweats	21 (62)
Difficulty sleeping	23 (68)
Tiredness	26 (77)
Anxiety	16 (47)
Depression	18 (53)
Irritability	19 (56)
Vaginal dryness	18 (53)
Painful intercourse	21 (62)
Decreased libido	26 (77)
Increased vaginal discharge	8 (24)
Vaginal bleeding	4 (12)
Heard of alternatives to hormone therapy	7 (21)
Knows someone that has tried hormone therapy	7 (21)
Willingness to try hormone therapy	14 (41)

TABLE 5. *Results from chi-square and logistic regressions examining associations and predictions with participants' willingness to try hormone therapy*

	Outcome: willingness to try hormone therapy		
		OR (95% CI)	
Background or predictor variable	χ^2 (*P*)	Unadjusted	Adjusted
Income less than $25,000	0.56 (.81)		
Education high school degree or less	2.78 (.10)		
Symptom severity score	—	1.31 (0.89-1.94)	1.33 (0.88-2.00)
Concern for side effects	—	1.06 (0.82-1.36)	1.01 (0.77-1.33)
Cancer stage	—	1.32 (0.69-2.52)	1.25 (0.62-2.53)

Adjusted models were adjusted for income and education level.
CI, confidence interval; OR, odds ratio.

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