JOURNAL OF ADOLESCENT AND YOUNG ADULT ONCOLOGY
Volume 5, Number 1, 2016

DOI: 10.1089/jayao.2015.0051

Original Article

Perceptions, Attributions, and Emotions Toward Endocrine Therapy in Young Women with Breast Cancer

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Purpose: The aims of this study were to describe symptoms attributed to endocrine therapy (ET) and perceptions of ET in a sample of young women with breast cancer and to explore whether these factors are associated with adherence to ET.
Methods: An online questionnaire was completed by 106 young women taking ET for hormone receptor-positive breast cancer. In addition to demographic and medical characteristics, the survey assessed symptom attribution, emotions, and perceptions related to ET. A supplemental survey measuring adherence to ET was completed by 82/106 women. Means, medians, and frequency distributions were calculated for continuous and categorical covariates, respectively. An exploratory analysis evaluated whether adherence was associated with patient characteristics and views.
Results: The mean age of respondents was 39 years (range 22–45 years). Two-thirds of women had stage 1 or 2 breast cancer. Women attributed an average of nine symptoms to ET; hot flashes, night sweats, and decreased libido were the most frequently attributed symptoms. Positive emotions toward ET were more common than negative emotions were, although only 48% of respondents believed that ET was essential. Women of higher financial status and those who reported more positive emotions toward ET reported greater adherence with ET. A significant difference in symptom attribution was not detected between less and more adherent respondents.
Conclusions: Young women's views regarding ET may play an important role in determining adherence behavior. Given that young women have a higher risk of recurrence, some of which may be attributable to ET non-adherence, further work is needed to confirm these findings and determine whether interventions designed to modify young women's perceptions of ET could promote adherence.

Keywords: breast cancer, survivorship, psychosocial

Five years of adjuvant endocrine therapy (ET) with tamoxifen or an aromatase inhibitor reduces recurrence and improves survival in women with hormone receptor positive (HR+) breast cancer.[1] The ATLAS and aTTom trials recently demonstrated that 10 years of tamoxifen further reduces the risk of breast cancer recurrence and mortality compared to 5 years of treatment.[2,3] Non-adherence to ET (i.e., failure to take ET as prescribed) has been associated with increased mortality, as has non-persistence (i.e., early discontinuation).[4–6] Despite the efficacy of ET, non-adherence is relatively common. A meta-regression analysis using data from 26 studies estimated non-adherence (e.g., using medication possession ratio [MPR] <80%) to range from 20% at 1 year to 32% at 5 years, although even higher rates of non-adherence have been reported.[7,8]

Adherence to ET may be critically important for young women given their increased risk of breast cancer recurrence and decreased survival. Young women are also less likely than older premenopausal women are to experience long-term ovarian dysfunction from chemotherapy alone, and are therefore less likely to benefit from this chemo-endocrine effect.[9] In this context, it is concerning that young age is associated with non-adherence with ET.[5,8,10–13] Hershmann et al. reported women younger than 40 years of age were 40% more likely to be non-adherent (i.e., MPR <80%) than those 50–65 years old ($p < 0.001$).[11] Studies including breast cancer patients of all ages have reported several additional demographic and medical characteristics associated with higher ET adherence such as higher income and being married[10,14,15]; conversely, non-white race

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and prior mastectomy have been identified as predictors of non-adherence.[10,11]

Importantly, patients' beliefs about their medications also predict adherence and may influence behavior to a greater extent than demographic and medical characteristics.[16] For example, adherence has been associated with perceived necessity of ET and views about long-term adverse effects of tamoxifen.[17,18] Patient attribution of unpleasant symptoms to a medication is a common contributor to medication non-adherence.[19] In women being treated with ET, the number of symptoms attributed to the treatment seems to be a critical factor in predicting discontinuation, but few studies have examined which symptoms are attributed to ET.[18]

This study examined young women's beliefs, perceptions, and attitudes regarding ET with the aim of identifying possible reasons for suboptimal ET adherence in this population. Specifically, the study focused on symptom attribution, beliefs about ET necessity, and emotions related to ET. As a secondary aim, the study explored whether the above factors differed between young women classified as either more or less adherent to ET. Better understanding of the factors that impact on young women's adherence to ET may suggest ways to improve outcomes in this population.

Methods

Study design

Helping Ourselves, Helping Others: The Young Women's Breast Cancer Study (YWS) is an ongoing prospective cohort study examining biological, medical, and quality of life issues specific to women diagnosed with breast cancer at 40 years of age or younger. Study participants are mailed a baseline survey, followed by surveys twice a year for the initial 3 years following diagnosis and then annually. In October 2011, women who: (1) provided an email address upon study enrollment and (2) had hormone (estrogen and/or progesterone) receptor positivity ascertained by pathology or medical record review were emailed an invitation to complete a survey if they had taken ET in the prior year. Women currently taking ET were subsequently emailed supplemental questions in March 2012 regarding adherence to ET. The YWS is approved by the Institutional Review Board at the Dana–Farber/Harvard Cancer Center and other participating sites.

Participants

Of 257 women invited to participate, 54 had not been on ET in the prior 12 months. Of the remaining 203 women, 113 responded and completed the survey (response rate: 56%). Seven of these 113 women had discontinued ET within the prior 12 months and were excluded from analyses because of their small number. A total of 82 women on ET completed the adherence supplement (Fig. 1).

Measures

The questionnaire was composed of measures used in a recent study of contributors to non-adherence that included more than 1400 women with an average age of 56 years.[15]

Demographic and medical characteristics. Demographic characteristics included age, ethnicity, number of children, marital status, and educational background. Respondents were also asked to describe their household's financial situation.[20,21] Clinical information including stage and treatment history was also self-reported. Specific survey items related to ET included type (tamoxifen or aromatase inhibitor) and duration of ET use.

Symptom attribution. Attribution of symptoms to ET was assessed using the Breast Cancer Prevention Trial Symptom Checklist.[22] Several symptoms (e.g., bone pain) were added to account for aromatase inhibitor side effects. Women were asked if they had been bothered by each of 47 symptoms in the past 4 weeks, and whether each symptom was attributed to ET. The total number of symptoms attributed to ET was calculated for each patient.

Perceptions of ET necessity and risk. Perceived necessity of ET was measured on a 0–10 scale with two items: (1) ''How much do you feel that your current ET can help reduce

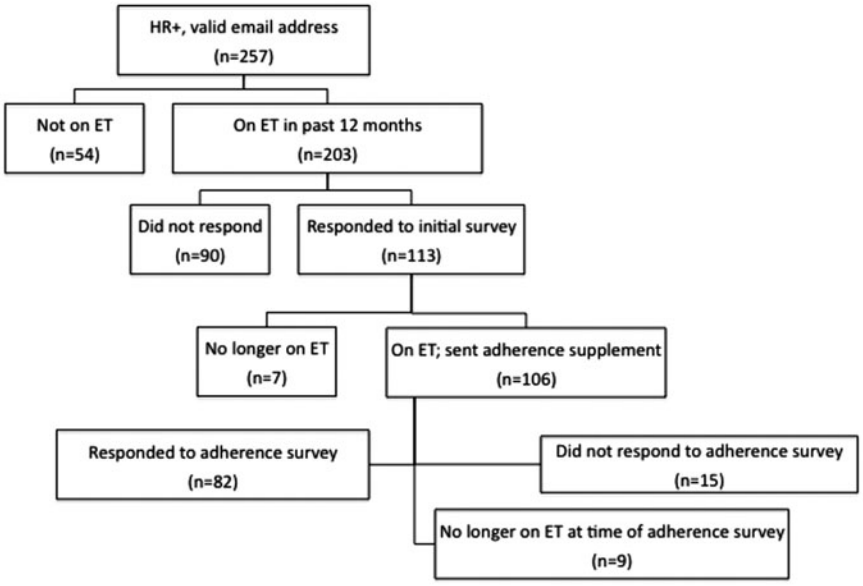

FIG. 1. Study flow diagram. ET, endocrine therapy; HR+, hormone receptor-positive.

Table 1. Sociodemographic and Medical Characteristics

	N	M *(SD)*
Age (years)	106	38.5 (4.1)
Months on current ET	102	24.7 (15.9)
Missing	4	
	N	**%**
Ethnic background		
Non-white	10	9
White	94	90
Missing	2	
Children pre-diagnosis		
No	41	39
Yes	64	61
Missing	1	
Marital status		
Married	80	78
Not married	23	22
Missing	3	
Financial situation		
After paying bills, I have extra money for special things (Most affluent)	60	58
All others responses (Less affluent)	43	42
Missing	3	
College education		
No	11	11
Yes	93	89
Missing	2	
Which ET are you currently taking?		
Tamoxifen	94	89
Aromatase inhibitor	12	11
Bilateral mastectomy		
Yes	38	37
No	65	63
Missing	3	
Any radiation therapy		
Yes	72	70
No	31	30
Missing	3	
Chemotherapy		
Yes	73	70
No	31	30
Missing	2	
Ovaries suppressed/removed		
Yes	38	37
No	64	63
Missing	4	
Stage		
0	3	3
1	32	31
2	37	36
3	21	20
4	8	8
Unsure	2	2
Missing	3	

SD, standard deviation.

your risk of your breast cancer recurring?'' (0 = not at all, 10 = a great deal), and (2) ''How much do you feel that you need your current ET for your breast cancer?'' (0 = not at all, 10 = absolutely essential).[15,16] Patients' understanding of their illness and treatment was assessed similarly (''How well do you feel you understand the current status of your diagnosis and treatment?'' 0 = not at all, 10 = very well). A single question addressed concern (0 = not at all concerned, 10 = extremely concerned) about the long-term adverse effects of ET. Perceived control over recurrence was assessed on a scale of 0 (no control) to 10 (extreme control).

Emotions toward ET. Emotions toward ET were evaluated using adapted items for affective properties of attitudes and included five positive (happy, calm, enthusiastic, comforted, accepting) and five negative (sad, annoyed, tense, reluctant, angry) emotions.[23] Participants indicated the degree to which each emotion described their feelings regarding ET (does not, slightly, definitely describes).

Concern about cancer recurrence. Fear of recurrence was evaluated with two questions: (1) ''Overall, how worried are you about your breast cancer recurring?'' (0 = not at all, 10 = extremely), and (2) ''How long do you think your breast cancer will continue to be in remission/cured?'' (0 = very short time, 10 = forever).

Adherence. Adherence to ET was assessed using an adaptation of the Morisky Medication Adherence scale, which has previously been used to evaluate adherence among breast cancer survivors.[15,24] One question (''When you feel better, do you sometimes stop taking your medication?'') from the original Morisky Medication Adherence scale was not relevant to ET and so was removed and replaced with two items regarding intentional non-adherence: (1) ''I alter the dose of my current ET from what has been prescribed,'' and (2) ''I decide to miss a dose of my current ET.'' Responses for each item ranged from 1 (never) to 5 (always); scores from the five items were added to create a composite score ranging from 5 to 25, with a score of 5 considered ''most adherent.'' Patients were also asked how many doses of endocrine therapy they had missed in the past week and month.

Analysis

Means, medians, and frequency distributions were calculated for continuous and categorical outcomes, respectively. For items not answered by all participants, the number of respondents who answered the question is specified. Response scales for the items measuring perceived need for ET, long-term risk, and fear of recurrence (i.e., Likert scales that ranged from 0 to 10) were grouped as follows: ratings of 0–6 were categorized as low to moderate levels of endorsement, ratings of 7–9 were classified as high levels of endorsement, and a rating of 10 represented the highest level of endorsement. Positive and negative emotions were evaluated both categorically and continuously, with scores calculated by summing the endorsed items (each item scored as follows: 1 = does not describe; 2 = slightly describes; 3 = definitely describes). Pearson correlation coefficients were calculated to evaluate the relationship between positive/negative emotions and perceptions toward ET and breast cancer recurrence risk.

Table 2. Emotions and Perceptions Toward ET and Breast Cancer Recurrence Risk

	All women		*More adherent*[a]		*Less adherent*[a]		
	n	%	n	%	n	%	p-*Value*[b]
How much do you feel you need your current ET for your breast cancer?							0.10
Little to moderate need (0–6)	17	16	2	4	6	17	
Strong need (7–9)	38	36	17	37	15	42	
Absolutely essential (10)	51	48	27	59	15	42	
How much can your current ET reduce your risk of recurrence?							0.82
Low to moderate amount (0–6)	19	18	6	13	6	17	
Considerable amount (7–9)	59	56	26	57	20	57	
A great deal (10)	27	26	14	30	9	26	
Missing	1		0		1		
How much control do you feel you have over your breast cancer recurring?							0.27
Low to moderate level (0–6)	79	77	33	75	31	86	
High level (7–9)	24	23	11	25	5	14	
Extreme control (10)	0	0	0	0	0	0	
Missing	3		2		0		
How well do you understand the current status of your diagnosis and treatment?							0.23
Not well/somewhat (0–6)	11	11	3	7	5	14	
Well (7–9)	52	50	20	44	19	54	
Very clearly (10)	42	40	23	50	11	31	
Missing	1		0		1		
How concerned are you about long-term use of your ET?							0.29
Minimally to moderately concerned (0–6)	60	57	31	67	18	50	
Considerably concerned (7–9)	37	35	13	28	15	42	
Extremely concerned (10)	9	9	2	4	3	8	
Overall, how worried are you about your breast cancer recurring?							0.25
A little to moderately worried (0–6)	44	42	16	35	19	53	
Considerably worried (7–9)	38	36	21	46	11	31	
Extremely worried (10)	24	23	9	20	6	17	
How long do you think your cancer will continue to be in remission/cured?							0.48
Short to moderate length of time (0–6)	31	30	15	34	10	28	
Long time (7–9)	51	50	23	52	17	47	
Forever (10)	21	20	6	14	9	25	
Missing	3		2		0		
To what extent does each of the following emotions describe your feelings toward ET?							
Negative emotions:							
Sad							0.83
Does not describe	61	60	29	63	24	69	
Slightly describes	30	30	12	26	8	23	
Definitely describes	10	10	5	11	3	9	
Missing	5		0		1		
Annoyed							0.01
Does not describe	45	46	26	57	14	40	
Slightly describes	42	42	19	41	13	37	
Definitely describes	12	12	1	2	8	23	
Missing	7		0		1		
Tense							0.93
Does not describe	60	60	28	61	22	63	
Slightly describes	33	33	16	35	11	31	
Definitely describes	7	7	2	4	2	6	
Missing	6		0		1		

(*continued*)

Table 2. (Continued)

	All women		*More adherent*[a]		*Less adherent*[a]		
	n	%	n	%	n	%	p-*Value*[b]
Reluctant							0.001
Does not describe	65	64	39	85	17	49	
Slightly describes	28	28	5	11	15	43	
Definitely describes	9	9	2	4	3	9	
Missing	4		0		1		
Angry							0.15
Does not describe	64	65	35	76	19	56	
Slightly describes	25	25	8	17	10	29	
Definitely describes	10	10	3	7	5	15	
Missing	7		0		1		
Positive emotions:							
Happy							0.009
Does not describe	54	54	23	50	22	63	
Slightly describes	34	34	13	28	13	37	
Definitely describes	13	13	10	22	0	0	
Missing	5		0		1		
Calm							0.74
Does not describe	49	50	20	44	15	46	
Slightly describes	29	29	14	30	12	36	
Definitely describes	21	21	12	26	6	18	
Missing	7		0		3		
Enthusiastic							0.05
Does not describe	67	67	27	59	27	77	
Slightly describes	26	26	13	28	8	23	
Definitely describes	7	7	6	13	0	0	
Missing	6		0		1		
Comforted							0.23
Does not describe	31	30	15	33	13	37	
Slightly describes	46	45	17	37	17	49	
Definitely describes	25	25	14	30	5	14	
Missing	4		0		1		
Accepting							0.053
Does not describe	6	6	0	0	3	8	
Slightly describes	34	32	10	22	12	33	
Definitely describes	66	62	36	78	21	58	

[a]82 women responded to the adherence supplement and were categorized as either more adherent (Morisky score 5–6) or less adherent (Morisky score 7 and above).
[b]*p*-Value compares more and less adherent women.
ET, endocrine therapy.

As a secondary analysis, differences in patient characteristics, perceptions, and attitudes toward ET were explored between women who were categorized as more adherent or less adherent using the modified Morisky scale. Respondents were dichotomized using the median cutoff (score of 6) on the Morisky scale; those scoring 5–6 were designated as more adherent ($n=46$), and those scoring 7 or above were designated less adherent ($n=36$). Additionally, symptom attribution (dichotomized as ''bothered by symptoms over the past 4 weeks and attributed to ET'' versus ''no symptoms'' or ''bothered by symptoms but not attributed to ET'') was compared between women taking tamoxifen and those taking an aromatase inhibitor. Two-tailed Fisher's exact test was used to compare proportional differences, and *t*-tests were used to compare means between more and less adherent women and between women on tamoxifen and aromatase inhibitors. All analyses were conducted in JMP Pro 10 and SAS v9.4.

Results

Demographic and medical characteristics

The mean age of participants was 38.5 years (range 22–45 years). Most participants were white and financially comfortable (Table 1). At the time of the initial survey, 89% (93/105) were taking tamoxifen, and 11% (12/105) were taking an aromatase inhibitor. The average duration of ET use was 25 months (range 0.3–56 months).

Symptom attribution

On average, respondents ($n=104$) attributed nine (range 0–28) symptoms experienced over the preceding month to ET. Hot flashes (75/104), night sweats (62/105), and decreased libido (55/104) were each attributed to ET by more than 50% of respondents. Nine other symptoms were attributed

Table 3. Correlations Between Emotions and Perceptions Toward ET and Breast Cancer Recurrence Risk

	Positive emotions			*Negative emotions*		
	n	r	p-*Value*	n	r	p-*Value*
Need for current ET	98	0.17	0.09	99	–0.19	0.07
ET reduces breast cancer recurrence risk	97	0.24	0.02	98	–0.23	0.02
Concern about long-term ET use	98	–0.22	0.03	99	0.37	0.0002
Understanding of diagnosis/treatment	97	0.24	0.02	98	–0.34	0.0007
Control over breast cancer recurrence	95	–0.06	0.55	96	–0.06	0.56
Belief that cancer will continue to be in remission/cured	95	0.23	0.02	96	–0.09	0.37
Worry about recurrence	98	–0.23	0.03	99	0.15	0.13

to ET by more than 30% of respondents: joint pain (37/104), general aches and pains (34/104), tiredness (35/104), lack of sexual enjoyment (46/104), vaginal dryness (52/105), forgetfulness (33/102), irritability (33/103), weight gain (44/103), and unhappiness with appearance (35/105). Bone pain was attributed to ET in 16% (16/103) of respondents. Patients taking aromatase inhibitors more often attributed muscle stiffness ($p = 0.04$), hot flashes ($p = 0.02$), joint pain ($p < 0.0001$), and bone pain ($p = 0.003$) to ET than those taking tamoxifen did. Among all 106 women, those taking tamoxifen were more likely to attribute vaginal discharge to ET than those taking aromatase inhibitors were ($p = 0.02$).

Perceptions and emotions toward ET and breast cancer recurrence

Table 2 describes various perceptions and emotions related to ET. Overall, 48% of participants viewed ET as absolutely essential for the treatment of their breast cancer, and 36% believed they had a strong need for ET. Eighteen percent (19/105) believed ET could reduce their risk of recurrence by only a low to moderate amount; conversely, 56% (59/105) thought it would reduce the risk by a considerable amount, and 26% (27/105) thought it could greatly reduce their risk. Regarding fear of recurrence, 36% were considerably worried, and 23% endorsed extreme worry about recurrence. Forty percent (42/105) felt they had a very clear understanding of their illness and treatment. While 57% reported low to moderate levels of concern about long-term ET use, 43% reported either considerable or extreme concern. Thirty percent (31/103) believed their cancer would be in remission for only a short to moderate length of time.

More than 20% of women said the following emotions ''definitely describe'' their attitude toward ET: calm, comforted, and accepting. The most common negative emotion toward ET was annoyance, with 12% (12/99) and 42% (42/99) endorsing feeling ''definitely'' and ''slightly'' annoyed, respectively. Higher perceived recurrence risk reduction, less concern about long-term ET use, a better understanding of diagnosis and treatment, less worry about recurrence, and a greater belief the cancer would stay in remission or be cured were significantly ($p \leq 0.05$) correlated to endorsement of positive emotions; negative emotions were significantly ($p \leq 0.05$) correlated to lower perceived recurrence risk reduction, more concern about long-term ET use, and less understanding of diagnosis and treatment (Table 3).

Adherence

Women reported relatively high rates of adherence to ET, with 84% (69/82) reporting no doses missed in the last week, and 59% (48/82) reporting no doses missed in the last month. Approximately one-quarter of respondents (20/82) indicated they had missed two or more doses of ET in the last month. Thirty-eight percent (31/82) had a Morisky scale score of 5 (a score of 5 indicates the highest level of adherence); the median Morisky score was 6 (range 5–13). Correlation of Morisky scale scores with self-reported doses missed over the past week and month were $r = 0.40$ and $r = 0.58$, respectively ($p < 0.0001$).

An exploratory analysis was performed in which patients' perceptions, attributions, and emotions were stratified by adherence status (Table 2). Compared with less adherent respondents, more adherent women were significantly more likely to report positive emotions toward ET, including happiness ($p = 0.009$) and enthusiasm ($p = 0.05$); more adherent women were less likely to report negative emotions such as annoyance ($p = 0.01$) and reluctance ($p = 0.001$). Of examined medical and sociodemographic characteristics, only financial status differed significantly between the more and less adherent group, with a greater percentage of more adherent women reporting they had enough money remaining for luxury purchases after paying bills (72% [31/43] of more adherent vs. 47% [17/36] of less adherent women, $p = 0.04$). With regard to symptom attribution, the more ($n = 45$) and less adherent ($n = 36$) groups attributed a mean of 9.6 and 8.0 symptoms to ET, respectively ($p = 0.20$). When individual symptoms were analyzed by adherence status, only night sweats were significantly different ($p = 0.03$) between adherent (67% [31/46]) and non-adherent (42% [15/36]) women.

Discussion

Young women are at increased risk of recurrence and death after a diagnosis of breast cancer compared with older women with breast cancer. While there are a number of reasons for this disparity, one likely contributor is that young women are less adherent and persistent with adjuvant ET.[4,10,11] Thus, understanding and optimizing adherence with ET in younger women may improve their outcomes. Due to their life stage at the time of diagnosis, younger women with breast cancer may experience various aspects of illness and therapy differently from older women. Patients' perceptions and emotions regarding ET are potentially modifiable, providing opportunities for future intervention.

In support of the need to focus research on psychosocial factors, prior work has demonstrated that patients' beliefs about medications are powerful predictors of adherence and possibly more important than clinical and sociodemographic factors.[16] The present finding that more adherent women were more likely to report feeling happy and enthusiastic toward ET and less likely to report feeling annoyed or reluctant is consistent with prior research, and suggests that assessing women's self-reported emotions toward ET may help physicians to identify those at greatest risk for non-adherence.[15] Further, both positive and negative emotions were correlated to perceptions of risk reduction, concerns about long-term ET, and understanding of one's diagnosis and treatment, supporting these domains as potential targets for modification.[15]

While side-effect burden has been repeatedly associated with non-adherence in older breast cancer patients,[8,18,25–27] a significant difference in symptom attribution was not detected between more and less adherent women. Of note, this survey did not measure symptom severity or how disruptive symptoms were in the context of women's lives, and less adherent women may experience more severe or disruptive symptoms. Further, more financially secure women may be more likely to pursue interventions to improve symptom burden, and such intervention was not evaluated in this analysis. Regardless, this study population experienced a substantial burden of symptoms. Importantly, on average, women attributed nine of their symptoms to ET. It has been suggested that younger women report more side effects from ET than older women do.[27] Menopausal symptoms may be more dramatic for young women. Prior work has shown an association between treatment-associated transition to menopause and worsened hot flash severity.[28] When examining reasons for non-adherence in young women on ET, continued attention to their experience of adverse effects is clearly warranted.

It is important to recognize that self-reported adherence, as assessed in this study, often overestimates more objective measures of adherence (e.g., as measured by medication possession ratios).[29,30] The majority of respondents described themselves as adherent. However, 24.4% indicated they missed two or more doses in the last month. Importantly, even missing a few doses per month may place women at risk for future non-compliance and worse outcomes. Huiart et al. found that self-reported non-adherence (i.e., missing at least three pills in 10 months) was a significant risk factor for future tamoxifen discontinuation,[31] which in turn has implications for survival.[4–6] Despite the limitations of self-reported adherence, such metrics are valuable, as they can be used in clinical practice to identify patients in need of additional support.

While we did not find significant differences in beliefs endorsed by more and less adherent women, 52% of all respondents did not believe ET was essential, and 18% indicated ET would reduce their risk of recurrence by only a low to moderate amount. These findings highlight a need to educate young women with HR+ disease better about ET, especially given that greater perceived need for ET has been associated with improved adherence.[15,17,18] Forty-three percent of women also reported considerable or extreme concern about the long-term adverse effects of ET. Such concerns have been associated with increased risk of tamoxifen discontinuation.[17] The relatively high prevalence of concern among both more and less adherent women suggests value in emphasizing to patients that the potential benefits of ET usually far outweigh the risks of dangerous side effects. Of examined sociodemographic characteristics, only financial comfort level was significantly different between the more and less adherent groups. Other studies have similarly found an association between affluence and improved adherence.[10,14,15]

There are several limitations to this study. The sample size was small, and response bias likely exists. Additionally, there are multiple variables potentially related to adherence behavior that were not examined in the present study, such as symptom severity, perceived social support, and concerns about fertility, which warrant further exploration.

This study provides important information regarding perceptions and attitudes related to ET and adherence behavior in a sample of young breast cancer survivors. Interventions designed to improve their perceptions and attitudes toward ET may represent an effective strategy for improving both ET adherence and associated morbidity and mortality outcomes in young women with breast cancer.

Acknowledgments

Research support was provided by the following: NIH 5 R25 CA057711 (to S.M.R.), Breast Cancer Research Foundation (to A.L.S.), and Susan G. Komen (to A.H.P.).

Disclaimer

The findings of this study were presented at the 7th Biennial Cancer Survivorship Research Conference, June 18–20, 2014, Atlanta, GA.

Author Disclosure Statement

No competing financial interests exist.

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