

Sexuality, Menopausal Symptoms, and Quality of Life in Premenopausal Women in the First Year Following Hematopoietic Cell Transplantation

D. Kathryn Tierney, RN, PhD, Oxana Palesh, PhD, and Laura Johnston, MD

Hematopoietic cell transplantation (HCT) is an aggressive curative therapy for a number of malignant and nonmalignant diseases. The number of HCTs performed each year in the United States is about 18,000, and about 150,000 individuals are five or more years post-HCT (Horowitz, 2005; Pasquini & Zhu, 2014). In summarizing quality-of-life (QOL) research among recipients of HCT, Syrjala and Artherholt (2004) reported that the majority experience good to excellent QOL; however, about 5%–20% report ongoing problems, including alterations in sexual health. Sexual dissatisfaction and dysfunction were reported in QOL studies beginning in the 1990s (Baker et al., 1994; Wingard, Curbow, Baker, Zabora, & Piantadosi, 1992). The prevalence of altered sexuality in women following HCT has been reported to be as high as 80% (Syrjala, Kurland, Abrams, Sanders, & Heiman, 2008), and several studies have reported that sexual dysfunctions are more prevalent in female recipients of HCT (Humphreys, Tallman, Altmaier, & Barnette, 2007; Syrjala et al., 1998, 2008; Wong et al., 2013). Alterations in sexuality can persist for years, resulting in diminished QOL for the recipient of HCT, as well as for his or her sexual partner. A mandate from professional organizations, including the Oncology Nursing Society, the Institute of Medicine, and the National Comprehensive Cancer Network, addresses the QOL concerns of survivors (Brant & Wickham, 2013; Hewitt, Greenfield, & Stovall, 2006; Holland & Reznik, 2005).

Background

The World Health Organization (2002) has stated that sexuality is an integral component of the human experience. Sexuality is a multidimensional construct with physiologic, psychological, and social dimensions and complex interactions among these dimensions. The Diagnostic and Statistical Manual of Mental Disorders describes sexual dysfunction as a clinically significant disruption in an individual's ability to respond sexually

Purpose/Objectives: To describe sexuality, menopausal symptoms, and quality of life (QOL) in premenopausal women in the first year following hematopoietic cell transplantation (HCT).

Design: One-year prospective longitudinal study.

Setting: Stanford University Medical Center in California.

Sample: 63 premenopausal female recipients of HCT with a mean age of 34.5 years.

Methods: Three instruments were used: Female Sexual Function Index, Menopause-Specific QOL Questionnaire, and a visual analog scale to measure QOL.

Main Research Variables: Sexuality, menopausal symptoms, and QOL.

Findings: At one year post-HCT, women reported absent to low desire and arousal, adequate lubrication less than half of the time, absent or rare orgasm, pain during vaginal penetration more than half of the time, and dissatisfaction with overall sex life. Women also reported moderate to severe vasomotor symptoms, including hot flashes, night sweats, and sweating. Twenty-one women were avoiding sexual activity, and 25 women were not sexually active. Mean QOL scores significantly increased ($p = 0.028$) in the first year, signifying an improvement in QOL. Variables predictive of improved QOL at one year post-HCT include decreased psychosocial and physical symptoms, sexual satisfaction, and pre-HCT QOL score.

Conclusions: One year post-HCT, women reported sexual dysfunction, sexual dissatisfaction, and menopausal symptoms, which negatively affect QOL.

Implications for Nursing: Nurses and other healthcare providers working with recipients of HCT can provide anticipatory guidance on potential changes in sexuality and menopausal symptoms to facilitate adaptation by reducing discordance between expectations and new realities.

Key Words: hematopoietic cell transplantation; sexuality; menopause; quality of life

ONF, 42(5), 488–497. doi: 10.1188/15.ONF.488-497

or experience sexual pleasure (American Psychiatric Association, 2013). These disorders are characterized by physiologic or psychological changes that negatively

influence sexual functioning, resulting in psychological distress or stress within relationships.

Sexual Problems

Altered sexuality is the result of cumulative physiologic and psychosocial insults beginning with the cancer diagnosis. A review of the physiologic and psychosocial factors contributing to altered sexuality suggests that, for female recipients of HCT, therapy prior to HCT, the conditioning regimen, and complications of HCT, can cause physiologic changes that may directly alter sexuality, including menopause, chronic graft-versus-host disease (GVHD) affecting the vagina, and fatigue (Tierney, 2004). The review describes the psychological risks for sexual dysfunction, including altered body image, decreased self-esteem, and emotional distress, particularly depression and anxiety. In addition, the review describes alterations in the social dimension of sexuality, including an increased dependence on the partner(s), role changes, and relationship strain.

Although many QOL studies have identified alterations in the sexual health of recipients of HCT, few studies have focused specifically on exploring sexuality over time. An early longitudinal study to assess sexual health in long-term survivors was published in 1998 (Syrjala et al., 1998). At three years post-HCT, 52% of the 48 women studied reported problems with lubrication and arousal, 46% reported difficulties with orgasm, and 33% experienced pain with penetration. The number of women reporting problems with orgasm and lubrication significantly increased during the three years. A second longitudinal study assessing sexual health five years post-HCT found that 80% of female recipients of HCT experienced sexual problems compared to 61% of case-matched controls (Syrjala et al., 2008). Sexual dysfunction occurred 50% of the time and included loss of sexual desire, problems with orgasm, and dyspareunia. Compared to male recipients of HCT, sexual functioning for females significantly declined during the five years. A three-year longitudinal study that included 125 female recipients of HCT reported that sexual functioning was worse for women across all time points compared to men (Wong et al., 2013). Additional findings indicated that sexual satisfaction scores were lower for women with chronic GVHD, and lower rates of sexual activity were associated with older age, not being married, and poorer physical QOL. However, the number of sexually active women increased from 37% pre-HCT to 52% at three years post-HCT.

Menopausal Symptoms

Risk factors for ovarian failure include age, total body irradiation (TBI), alkylating agents, allogeneic transplantation, and chronic GVHD (Tauchmanová et al., 2003, 2007). Myeloablative preparative regimens for

HCT include combinations of high-dose chemotherapy with or without TBI. High-dose cyclophosphamide (Cytoxan[®], Neosar[®]) and busulfan (Busulfex[®], Myleran[®]) are agents commonly used in preparative regimens for HCT. The high risk of gonadal toxicity associated with alkylating agents is well established (Koyama, Wada, Nishizawa, Iwanaga, & Aoki, 1977; Warne, Fairley, Hobbs, & Martin, 1973). The risks of ovarian failure and infertility associated with radiation therapy are well documented, and the level of risk depends on the dose, field, and age, with older women at higher risk (Meirow, 1999; Sonmezer & Oktay, 2004). Almost all women experience ovarian failure following high-dose TBI (Majhail et al., 2012). The probability of ovarian failure and resulting transition into menopause following HCT approaches 90% (Tauchmanová et al., 2007).

The transition into menopause has physiologic and psychological consequences. Menopause is associated with a wide range of symptoms, including vasomotor symptoms, atrophic urogenital and vaginal changes, cognitive disorders, sleep problems, and sexual dysfunction (Graziottin, 2010; Wilson, 2003). Psychological sequelae of menopause may include mood swings, emotional distress, body image changes, and an altered sense of femininity and sexuality.

A paucity of studies explore the symptoms of menopause in recipients of HCT. An early study evaluating menopausal symptoms in recipients of HCT was published by Cust, Whitehead, Powles, Hunter, and Milliken in 1989. This cross-sectional study evaluated 36 women with an average age of 25.7 years (range = 14.3–42.6 years) who were a mean of 4.2 years (range = 8 months to 9 years) post-HCT. Results show that 61% experienced hot flashes, 81% reported vaginal dryness, and 82% of the sexually active women experienced dyspareunia. Findings from other earlier cross-sectional studies report similar results with 67%–83% of women experiencing vasomotor symptoms and 60%–94% describing dyspareunia (Chiodi et al., 1991; Schubert et al., 1990; Spinelli et al., 1994). Another study evaluated 31 premenopausal women with a median age of 36.6 years (range = 25–49 years) who were a median of 16.6 months (range = 6–36 months) following HCT (Piccioni et al., 2004). The incidence of menopausal symptoms reported by these women included the following: vasomotor symptoms (90%); vulvo-vaginal atrophy (54%); mood alterations (54%); urinary tract symptoms (42%); weight gain (26%); and sleep, memory, and concentration problems (16%). Fifteen of the women received hormone therapy (HT), resulting in a significant and rapid reduction in menopausal symptoms.

The published research consistently finds sexual dysfunction and dissatisfaction in a significant number of female recipients of HCT and that these changes are persistent and long-lasting. Menopausal symptoms,

particularly hot flashes, are also common in female transplantation survivors. Many of the published studies of sexuality following HCT are not longitudinal and do not include an assessment of menopausal symptoms, and the authors could not identify any longitudinal studies specifically addressing menopause in recipients of HCT; therefore, a prospective study was conducted to evaluate sexuality, menopausal symptoms, and QOL in female recipients of HCT.

Methods

Women were enrolled at a large academic medical center from December 2003 to September 2009. The final assessment of participants occurred one year post-HCT in September 2010. Eligibility for the study included (a) being premenopausal (defined as having a least one menstrual cycle in the past 12 months), (b) considering herself to be sexually active, (c) being able to read and write English, and (d) planning to receive a myeloablative conditioning regimen in preparation for transplantation. Women were approached regarding participation by one of the clinical nurse specialists who provided an explanation of the study and a study packet containing the consent form and study instruments. If women elected to participate, they could sign the consent form and complete the instruments, which were then collected at the time of admission to the hospital. The post-HCT assessments were mailed to participants along

with a stamped return envelope. If the surveys were not returned within one week, the participants received up to two reminder phone calls. The study was approved by the Stanford University Administrative Panels in Human Subjects Research in Palo Alto, California.

From December 2003 to September 2009, a total of 253 premenopausal women received a myeloablative conditioning regimen in preparation for HCT. Of these potential participants, 100 women agreed to participate and signed the consent form. The women were evaluated at four time points, pre-HCT (T1), as well as 2–3 (T2), 6 (T3), and 12 (T4) months post-HCT. The pre-HCT evaluation included a medical and demographic survey to record marital status, number of children, education background, ethnicity, and employment status. Details of the oncologic history and transplantation course were extracted from the medical record. At all four time points, women completed the Female Sexual Function Index (FSFI), the Menopause-Specific QOL questionnaire (MEN-QOL), and a visual analog scale rating their QOL.

The FSFI is a validated 19-item self-report questionnaire that addresses six domains of sexual functioning, including desire, arousal, lubrication, orgasm, satisfaction, and pain (Rosen et al., 2000). In cancer survivors, internal consistency reliability for the individual domains ranged from 0.85–0.94 and 0.94 for the FSFI total score (Baser, Li, & Carter, 2012). The authors report the instrument demonstrated convergent and discriminative validity consistent with the initial FSFI validation. The questions address sexual functioning for the past month. Some items address frequency, and responses include “no sexual activity” (score of 0) and a five-point scale, with responses ranging from “almost never or never” (score of 1) to “almost always or always” (score of 5). Other items assess intensity, and responses include “no sexual activity” (score of 0) and a five-point scale, with responses ranging from “very dissatisfied” (score of 1) to “very satisfied” (score of 5). Items assessing pain or discomfort during or after vaginal penetration are reverse coded so that higher scores indicate less pain or discomfort. Each domain score is obtained by summing the items and multiplying by the domain factor. The total instrument score is obtained by adding the six domain scores and is valid only in women who have been sexually active in the past month (Rosen et al., 2000); therefore, the total instrument score was not used in the statistical analyses. Higher scores indicate a greater degree of sexual functioning and satisfaction.

The MEN-QOL is a validated 29-item questionnaire covering four domains (i.e., vasomotor, psychosocial, physical, and sexual) of menopause-associated symptoms (Hilditch et al., 1996). The vasomotor domain has three items (i.e., hot flashes, night sweats, and sweating), the psychosocial domain has seven items (i.e., dissatisfaction with personal life, feeling anxious or nervous,

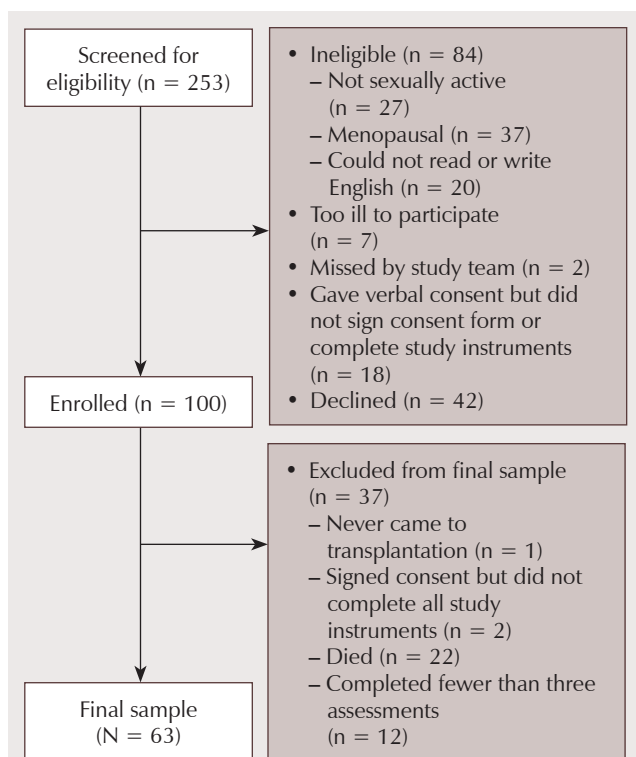


Figure 1. Final Sample Determination Flowchart

poor memory, accomplishing less, feeling depressed, impatience with others, and wanting to be alone), the physical domain has 16 items (i.e., flatulence; aching muscles and joints; feeling tired; difficulty sleeping; aches in neck or head; decreased physical strength; decreased stamina; feeling a lack of energy; dry skin; weight gain; increased facial hair; changes in appearance, texture, or tone of skin; feeling bloated; low backache; frequent urination; and involuntary urination when laughing or coughing). Respondents first respond “yes” or “no” to the presence of a symptom and then rank the severity of the symptom on a scale of “not at all bothersome” (score of 0) to “extremely bothersome” (score of 6). The mean of each domain is scored independently by dividing the sum by the number of items for each domain. No overall score for the instrument exists. Higher scores indicate a greater degree of symptoms. The psychometric properties of the MEN-QOL has been assessed in patients with breast cancer (Radtke, Terhorst, & Cohen, 2011). The reliability was reported as greater than 0.7 for each subscale. The convergent validity ranged from a correlation of 0.41–0.614, and the discriminant validity correlation was less than 0.176.

The QOL score was obtained using a visual analog scale that consisted of a 10 cm line. One end of the line was anchored with zero, representing a poor QOL and, on the other end, 100 indicated excellent QOL. Participants were asked to mark the line at the point representing their QOL. Two review articles have summarized the validity of using a visual analog scale to measure QOL and report it as a simple, reliable, and valid single-item measure of QOL (Donnelly, 2000; Donnelly & Walsh, 1996).

Data Analysis

Women (n = 63) who completed at least three of the four assessments were included in the final sample. Figure 1 shows how the final sample size was derived. Thirty-nine women completed all four assessments. For the 24 women who completed only three assessments, a mean change score was calculated using the two post-HCT assessments and substituted for the missing assessment. Sixty-three women completed the T1 assessment, 58 women completed the T2 and T3 assessments, and 49 women completed the T4 assessment. Descriptive statistics were calculated for the final sample. Analyses were conducted to assess for any differences in demographics and T1 outcome variables (QOL, MEN-QOL, and FSFI domains) between women included in the final sample and those not included.

Independent sample t tests were calculated to compare mean scores on the FSFI domains, MEN-QOL domains, and QOL scores based on age (40 years or younger or older than 40 years), marital status (single or married/cohabitating), ethnicity (Caucasian or non-

Table 1. Sample Characteristics (N = 63)

Characteristic	\bar{X}	SD	Range
Age (years)	34.5	8.7	21–51

Characteristic	n
Married	37
Heterosexual	62
Have children	34
Caucasian	45
Education	
High school	16
Two or more years of college	47
Income (\$)	
Less than 100,000	39
100,001 or greater	23
Unknown	1
Employment	
Employed	48
Student or unemployed	15
Diagnosis	
Hodgkin lymphoma	25
Acute or chronic leukemia	19
Non-Hodgkin lymphoma	8
Multiple myeloma	5
Nonmalignant diagnosis	3
Myelodysplastic or myeloproliferative syndromes	3
Type of transplantation	
Autologous	40
Allogeneic	20
Autologous followed by allogeneic	3
Received alkylating agents prior to transplantation	35

Caucasian), education (high school or two years or greater of college), type of transplantation (autologous or allogeneic), received alkylating agents pre-HCT (yes or no), antidepressant use (yes or no), having children (yes or no), income (less than \$100,00 or \$100,001 or greater), employed (yes or no), systemic HT (yes or no), and sexually active (yes or no). To assess for changes over time, repeated measures analysis of variance (ANOVA) were conducted for the domains of the FSFI, MEN-QOL, and QOL scores. Linear multiple regression analyses were performed to explore independent variables that predict sexual satisfaction, vasomotor symptoms, and QOL at T4.

Results

The characteristics of the women included in the final sample are shown in Table 1. Analyses indicated no significant differences between the women included in the final sample (n = 63) and those women not included (n = 37) on any of the demographic variables or prior alkylating therapy. Women included in the final sample were more likely to have undergone an autologous transplantation ($\chi^2 [1, n = 99] = 10.3, p = 0.001$) and have

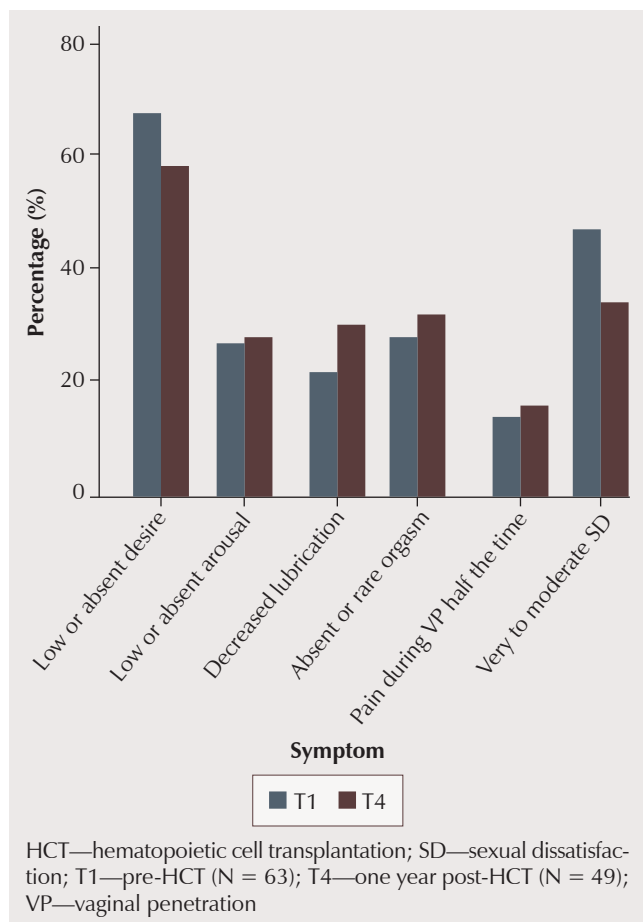


Figure 2. Sexual Dysfunction and Satisfaction From Pre-HCT to One Year Post-HCT

a significantly higher pre-HCT Karnofsky performance status ($t[98] = -2.93, p = 0.004$) than those who were not included. No significant differences were noted between the women included in the final sample and those not included on the outcome variables measured at T1, including QOL, MEN-QOL domains, and FSFI domains, with the exception of the pain domain. At T1, women included in the final sample had higher mean scores on the pain domain ($t[61] = 2.057, p = 0.042$), indicating less pain with vaginal penetration.

Participants in the final sample were aged a mean of 34.5 years (range = 21–51 years). The majority were Caucasian, married, had a least one child, had two years or greater of college education, were employed, and received an autologous transplantation. Eleven women received HT, and none of the women had documented chronic vaginal GVHD. The most common diagnosis was Hodgkin lymphoma, and 80% of these women received a preparative regimen consisting of gemcitabine (Gemzar[®]), vinorelbine (Navelbine[®]), carmustine (BiCNU[®]), etoposide (Toposar[®], VePesid[®], Etopophos[®]), and cyclophosphamide. The preparative regimens for those treated for leukemia included (a) busulfan and cyclophosphamide;

(b) busulfan and etoposide; (c) fractionated TBI (FTBI) and cyclophosphamide; (d) FTBI, etoposide, and cyclophosphamide; and (e) busulfan, etoposide, and cyclophosphamide. The women treated for non-Hodgkin lymphoma received a preparative regimen of carmustine, etoposide, and cyclophosphamide. All of the preparative regimens contained myeloablative doses of the agents used and contained at least one alkylating agent and/or TBI.

Female Sexual Function Index

The number of women sexually active in the month preceding assessment at T1, T2, T3, and T4, respectively, was 38, 28, 31, and 34. To examine the relationship between sexual activity and whether women had a partner or not, a chi-square test for independence (with Yates continuity correction) was conducted. Women with a partner were significantly more likely to be engaged in sexual activity at T2 ($\chi^2 [1, n = 58] = 9.1, p = 0.003$) and T3 ($\chi^2 [1, n = 58] = 9.7, p = 0.002$), but not pre-HCT or one year post-HCT. Figure 2 shows the prevalence of specific sexual dysfunctions at T1 and T4. At one year post-HCT, women reported absent to low desire ($n = 29$), absent or low arousal ($n = 14$), experiencing lubrication less than half the time ($n = 15$), absent or rare orgasm ($n = 16$), pain during vaginal penetration more than half the time ($n = 8$), and were moderately to very dissatisfied with overall sex life ($n = 17$). Mean scores for each domain are shown in Table 2. Independent samples *t* tests revealed no consistently significant differences on mean scores of the FSFI domains across the four time points based on demographic (i.e., age, marital status, ethnicity, education, having children, income, or employment status) or treatment (i.e., type of transplantation, receipt of alkylating agents pre-HCT, or use of antidepressants or HT) variables. One-way repeated measures ANOVA was conducted to compare mean scores on each domain (i.e., desire, arousal, lubrication, orgasm, pain, and sexual satisfaction) of the FSFI across the four time points. With the exception of the pain domain, no significant changes were noted in mean scores during the first year. Pain scores showed significant improvement in the first year ($p = 0.041$), indicating a decrease in pain with vaginal penetration. Bonferroni post-hoc analyses showed pain scores improved significantly from T2 to T4 ($p = 0.022$). Results of the multiple regression analysis are shown in Table 3, and the findings indicate that sexual satisfaction at one year post-HCT was explained by physical symptoms, sexual symptoms, desire, and pain. This model accounted for 68% of the variance in sexual satisfaction at T4 ($F[4, 58] = 34.62, p \leq 0.0001; R^2 = 0.705, \text{adjusted } R^2 = 0.684$). Pain measured at T4 uniquely explained 24% ($p \leq 0.0001$) of variance in sexual satisfaction at one year post-HCT.

Table 2. Mean Scores for Study Instruments From Pre-HCT to One Year Post-HCT and Results of One-Way Repeated Measures ANOVA

Domain	T1 (N = 63)			T2 (N = 58)			T3 (N = 58)			T4 (N = 49)			F	p
	\bar{X}	SD	Range	\bar{X}	SD	Range	\bar{X}	SD	Range	\bar{X}	SD	Range		
Female Sexual Function Index														
Desire	2.5	1.27	1.2–5.4	2.55	1.33	1.2–6	2.82	1.4	1.2–6	2.79	1.38	1.2–6	1.77	0.163
Arousal	2.3	2.25	0–6	2.06	2.03	0–6	2.47	2.12	0–6	2.68	2.19	0–6	1.78	0.161
Lubrication	2.57	2.42	0–6	2.03	2.26	0–6	2.52	2.31	0–6	2.64	2.34	0–6	2.15	0.103
Orgasm	2.37	2.38	0–6	2.19	2.49	0–6	2.41	2.37	0–6	2.64	2.35	0–6	0.71	0.551
Satisfaction	3.22	1.72	0–6	3.03	1.76	0–6	3.32	1.54	0.8–6	3.64	1.68	0.6–6	2.12	0.108
Pain	2.97	2.71	0–6	2.23	2.68	0–6	2.58	2.53	0–6	3.07	2.55	0–6	2.92	0.041
Menopause-Specific Quality-of-Life questionnaire														
Vasomotor	2.69	1.78	1–8	2.55	1.83	1–8	2.3	1.61	1–8	2.49	1.75	1–8	0.886	0.454
Psychosocial	3.56	1.5	1–6.29	3.32	1.31	1–6.71	2.88	1.25	1–5.71	2.94	1.43	1–7.14	5.98	0.001
Physical	3.47	1.18	1.13–6.56	3.28	1.1	1.16–6.94	2.98	1.21	1–8	2.97	1.34	1–7.13	4.28	0.008
Sexual	3.17	2.13	1–8	3.26	1.97	1–8	2.92	1.98	1–8	3.22	2.3	1–8	1.62	0.195
Quality-of-life visual analog scale														
Quality of life	73.41	19.24	24–100	77.77	19.16	30–100	81.93	16.5	22–100	80.98	19.51	7–100	3.661	0.017

ANOVA—analysis of variance; HCT—hematopoietic cell transplantation; T1—pre-HCT; T2—two to three months post-HCT; T3—six months post-HCT; T4—one year post-HCT

Note. Higher scores on the Female Sexual Function Index indicate a greater degree of sexual functioning and satisfaction, higher scores on the Menopause-Specific Quality-of-Life questionnaire indicate a greater degree of symptoms, and higher scores on the quality-of-life visual analog scale indicate better quality of life.

Menopause-Specific Quality-of-Life Questionnaire

The prevalence and severity of hot flashes and sexual symptoms are shown in Figure 3. At one year post-HCT, women experienced the following symptoms with an intensity ranging from moderate to severe: hot flashes (n = 13), changes in sexual desire (n = 21), vaginal dryness during intercourse (n = 17), and avoidance of intimacy (n = 12). Independent sample t tests did not reveal any consistently significant differences in mean scores of the MEN-QOL based on demographic (i.e., age, marital status, ethnicity, education, having children, income, employment status, or sexually active) or treatment (i.e., type of transplantation, receipt of alkylating agents pre-HCT, or use of antidepressants or HT) variables. Across all four time points, women who had received alkylating agents prior to HCT had higher mean scores on the sexual domain, and this difference was statistically significant at T1 (t[61] = 2.02, p = 0.048). Across all four time points, married women had higher mean scores (more severe

symptoms) on the sexual domain, and these differences were statistically significant at T1 (t[61] = 2.17, p = 0.034), T2 (t [61] = 2.3, p = 0.025) and T3 (t[61] = 2.39, p = 0.02). One-way repeated measures ANOVA were conducted to compare mean scores on each domain of the MEN-QOL across the four time points. During the first year, vasomotor and sexual symptoms remained stable; however, significant improvement was noted in psychosocial and physical symptoms. Bonferroni post-hoc analyses showed improvement in psychosocial symptoms from T1 to T3 (p = 0.003) and from T1 to T4 (p = 0.019). Bonferroni post-hoc analyses showed improvement in physical symptoms from T1 to T3 (p = 0.023) and from T1 to T4 (p = 0.011). At T4, women taking HT (n = 11) had significantly lower mean scores on the vasomotor domain than women not taking HT (t[58] = 2.8, p = 0.008). Results of the multiple regression analyses indicate that vasomotor symptoms at T4 were predicted by antidepressant use, physical, psychosocial, and sexual symptoms at one year post-HCT. This model accounted for 11% of the variance in vasomotor symptoms at T4 (F[4, 58] = 2.93, p = 0.028; R² = 0.168, adjusted R² = 0.111).

Table 3. One-Way Repeated Measures ANOVA for Study Instruments in Women From Pre- to Post-Hematopoietic Cell Transplantation

Instrument	Wilks' Lambda	F	p	Partial Eta Squared
Female Sexual Function Index				
Desire	0.919	1.77	0.163	0.081
Arousal	0.918	1.78	0.161	0.082
Lubrication	0.903	2.15	0.103	0.097
Orgasm	0.966	0.71	0.551	0.034
Satisfaction	0.904	2.12	0.108	0.096
Pain	0.873	2.92	0.041	0.127
Menopause-Specific Quality-of-Life questionnaire				
Vasomotor	0.958	0.886	0.454	0.042
Psychosocial	0.77	5.98	0.001	0.23
Physical	0.824	4.28	0.008	0.176
Sexual	0.925	1.62	0.195	0.075
Quality-of-Life visual analog scale				
Quality of life	0.838	3.661	0.017	0.162

ANOVA—analysis of variance

Note. Higher scores on the Female Sexual Function Index indicate a greater degree of sexual functioning and satisfaction, higher scores on the Menopause-Specific Quality-of-Life questionnaire indicate a greater degree of symptoms, and higher scores on the quality-of-life visual analog scale indicate better quality of life.

Quality of Life

Independent samples t test revealed no consistently significant differences in mean QOL scores based on any of the demographic (i.e., age, marital status, ethnicity, education, having children, income, employment status, or sexually active) or treatment (i.e., type of transplantation, receipt of alkylating agents pre-HCT, or use of antidepressants or HT) variables during the first year. One-way repeated measures ANOVA showed a significant effect of time, with improved QOL scores during the course of the year. Bonferroni post-hoc analysis showed significant improvement in QOL scores occurred between T1 and T3 ($p = 0.012$) and T1 to T4 ($p = 0.028$). Results of the multiple regression analyses show improved QOL scores at one year post-HCT were predicted by high school education, pre-HCT QOL score, and improvements in the first year in psychosocial symptoms, physical symptoms, and sexual satisfaction. This model accounted for almost 50% of the variance in QOL scores at T4 ($F[5, 56] = 12.81, p \leq 0.0001; R^2 = 0.533, \text{adjusted } R^2 = 0.492$). Psychosocial symptoms explained 22% ($p \leq 0.0001$) of variance, sexual satisfaction explained 5% ($p = 0.023$) of variance, and high school education explained 6% ($p = 0.01$) of variance in T4 QOL scores.

Discussion

The percentage of women reporting low or absent desire and very to moderate sexual dissatisfaction decreased from pre-HCT to one year post-HCT. This finding can be explained, in part, by the fact that many women were receiving chemotherapy right up to the time of transplantation, which can negatively affect sexuality and sexual activity. By one year post-HCT, these women had not received any cancer therapy for at least a year, and this may partially explain the improvement noted in desire and sexual satisfaction. Despite the improvement for some women, specific sexual dysfunctions reported by women at one year post-HCT include absent to low desire, absent to low arousal, decreased lubrication, absent or rare orgasm, and pain during vaginal penetration more than half of the time. More than one-third of women reported that they were moderately to very dissatisfied with their overall sex lives.

These findings are consistent with other studies describing sexual dysfunction in female recipients of HCT. The authors' data indicate that sexual health did not improve in the first year following transplantation, with the exception of a decrease in pain during vaginal penetration. Other studies have also reported that sexual dysfunction does not improve in the first year, and it continues to increase in incidence or severity after one year (Syrjala et al., 1998, 2008). The current study identified a modest improvement on the pain domain, with women reporting less pain with vaginal penetration. The study did not measure variables that may contribute to decreased pain, but one possible explanation is that women adapted by using lubricants or prolonging the arousal phase. Decreased pain with intercourse significantly predicted an improvement in sexual satisfaction at one year. This finding is encouraging because many interventions are available to improve vaginal lubrication and decrease dyspareunia (Tierney, 2004).

Menopausal symptoms reported by women in this study that did not improve with time include vasomotor (i.e., hot flashes, night sweats, and sweating) and sexual symptoms (i.e., changes in desire, dryness during intercourse, and avoiding intimacy). At one year post-HCT, 13 women were experiencing moderate to severe hot flashes. During the first year, women experienced a significant decline in psychosocial symptoms and physical symptoms. A decrease in psychosocial and physical symptoms significantly predicted improved QOL at one year post-HCT.

The authors had two assumptions regarding vasomotor symptoms. One assumption was that vasomotor symptoms would increase in the first year following the myeloablative conditioning regimen, and the second assumption was that younger women would experience a higher prevalence or severity of vasomotor symptoms.

The findings did not support these assumptions. One explanation for the lack of an increase in vasomotor symptoms is that more than half ($n = 35$) of the women in this study had received alkylating agents prior to HCT and were already experiencing vasomotor symptoms.

The average age for menopause in the United States is 51.3 years, with a range of 40–55 years (Wilson, 2003). The mean age of the women in this study was 34.5 years; therefore, these women are entering menopause an average of 16.8 years early. A review of the medical records indicates that 11 women had initiated HT. Although the number is small, the data indicated that, at one year post-HCT, women taking HT experienced fewer or less intense vasomotor symptoms. HT is recommended for women who experience premature menopause by the North American Menopause Society, the British Menopause Society, and the International Menopause Society (Pines et al., 2007; Pitkin et al., 2007; Utian et al., 2008). HT is recommended to minimize vasomotor symptoms, prevent alterations to vaginal and urogenital tissue, decrease the risk of osteoporosis, and decrease sexual dysfunction (Chatterjee & Kottaridis, 2002; Hilditch et al., 1996; King, Wynne, Assersohn, & Jones, 2011; Milroy & Jones, 2010; Piccioni et al., 2004; Tauchmanová et al., 2007). One group recommends that HT should be considered for female recipients of HCT younger than age 35 years in the absence of any medical contraindications (Shanis et al., 2012). Another group reports that, in the absence of medical contraindications, standard practice should be to initiate HT at the time of discharge from the transplantation center (Syrjala et al., 2008). The most appropriate type of HT in women with premature menopause following HCT is not known, and the safety of HT has not been studied in this population, necessitating very close follow-up of these women (Rebar, 2009). By minimizing alterations to vaginal tissue, HT can improve lubrication and decrease dyspareunia. Other investigators have reported that taking HT by one year post-HCT was predictive of less sexual dysfunction at three years (Syrjala et al., 1998).

QOL significantly improved in the first year in this group of women. The most significant improvement in QOL was attributed to a decrease in psychosocial symptoms. Other variables that predicted improved QOL included higher pre-HCT QOL, improved sexual satisfaction, decreased physical symptoms, and a high school education. These findings are also encouraging because interventions can be targeted to addressing psychosocial and physical symptoms post-HCT.

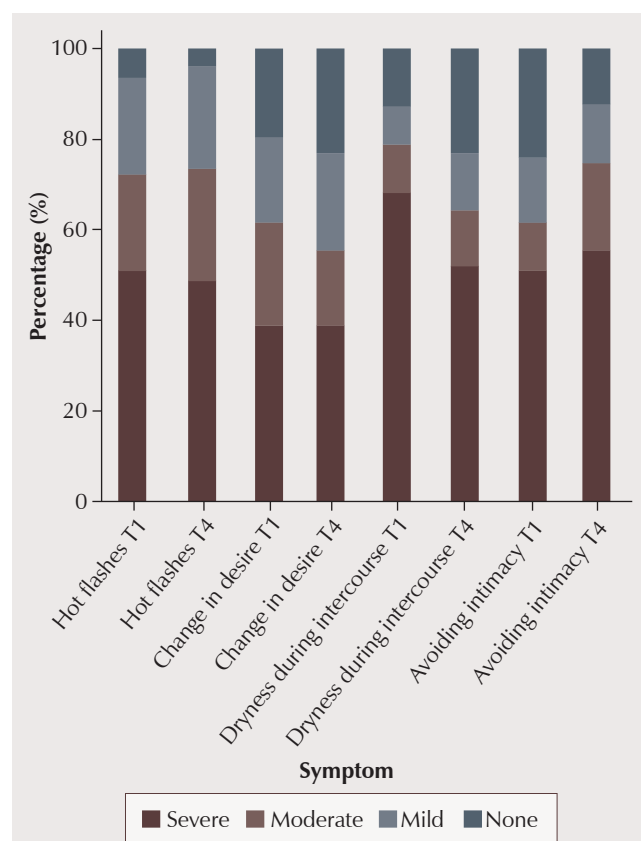
Limitations

One study limitation is that the sexual partner was not included. Understanding the response of the sexual partner to the HCT experience would provide additional information on the social dimension of altered sexuality. A second limitation is that the study followed

women for only one year. Alterations in sexuality and the symptoms associated with menopause may not be fully apparent at one year. The inclusion of a matched control group undergoing a natural menopause would provide an enriched understanding of the experience of premature menopause and provide a comparison on the symptom experience between women transitioning through menopause naturally versus recipients of HCT with early menopause. Therefore, the findings from this study are not generalizable beyond the population of female recipients of HCT experiencing early menopause. Another limitation is the symptoms measured on psychosocial and physical domains of the MEN-QOL are symptoms that commonly occur during the immediate recovery following HCT and may not be uniquely attributed to menopause. Finally, the pre-HCT assessment is not a true baseline of the main research variables because these women already carried a cancer diagnosis and the majority had received antineoplastic therapy.

Implications for Nursing

Nurses and other healthcare professionals working with recipients of HCT can provide anticipatory guidance



HCT—hematopoietic cell transplantation; T1—pre-HCT (N = 63); T4—one year post-HCT (N = 49)

Figure 3. Sexual Dysfunction and Satisfaction From Pre-HCT to One Year Post-HCT

on potential changes in sexuality and menopausal symptoms to facilitate adaptation by reducing discordance between expectations and new realities. Delivering anticipatory education creates an opportunity for nurses to improve the QOL of female recipients of HCT. Information provided pre-HCT should include potential alterations in sexual functioning and the symptoms associated with menopause. Including the sexual partner in this discussion may help the couple cope with changes and decrease the concerns of the sexual partner. Initiating a conversation pre-HCT on sexual health is an important intervention. By doing this, the nurse identifies himself or herself as a resource for the couple and validates that sexuality is an important aspect of recovery and QOL. In one study, the number of sexual dysfunctions experienced by HCT recipients was significantly lower in those who had discussions with their healthcare providers about sexual health (Humphreys et al., 2007). Readdressing sexual health at the time the individuals are returning from the transplantation center to their homes offers an opportunity to counsel the couple on any potential changes in sexual functioning and what symptoms should be reported. Nurses working in survivorship clinics should be competent performing an assessment of sexual health and suggesting interventions. A referral to a gynecologist or women's health nurse practitioner for a discussion of menopause and treatment or to a mental health professional for counseling may be required.

Implications for Research and Conclusions

Findings from this study add to a growing body of knowledge that one important QOL issue faced by female recipients of HCT is sexual health. Sexual dysfunction and sexual dissatisfaction negatively affect the QOL of the female recipient of HCT and, by extension, her sexual partner(s). Improvements in QOL at one year post-HCT were predicted by pre-HCT QOL scores, high school education, decreased psychosocial and physical symptoms, and improved sexual satisfaction. Decreased

Knowledge Translation

Sexual dysfunction and sexual dissatisfaction are common in female survivors of hematopoietic cell transplantation (HCT).

A decrease in psychosocial distress was associated with improved quality of life.

Nurses and other healthcare professionals working with recipients of HCT can play a key role in providing anticipatory guidance, assessing, and intervening to address sexual health.

pain during intercourse was the most significant predictor of improved sexual satisfaction at one year.

Research investigating interventions to address sexual dysfunction, particularly dyspareunia, offer an opportunity to improve the QOL of female recipients of HCT. In addition, interventions targeted at decreasing physical symptoms and psychosocial distress in the first year post-transplantation may lead to improved QOL. Although clinical trials investigating interventions targeted at improving the sexual health of women post-HCT are lacking, the literature offers guidance for nurses and other healthcare providers on interventions that may prove effective. One essential intervention is the provision of anticipatory guidance on potential alterations in sexual health and menopausal symptoms prior to transplantation.

The authors thankfully acknowledge the women who participated in this study, and the first author gratefully acknowledges her mentor, the late Karl G. Blume, MD.

D. Kathryn Tierney, RN, PhD, is an oncology clinical nurse specialist of blood and marrow transplantation, Oxana Palesh, PhD, is an assistant professor in the Psychiatry and Behavioral Sciences Department, and Laura Johnston, MD, is an associate professor of medicine, all at Stanford University in California. No financial relationships to disclose. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the *Oncology Nursing Forum* or the Oncology Nursing Society. Tierney can be reached at dtierney@stanfordhealthcare.org, with copy to editor at ONFEditor@ons.org. (Submitted September 2014. Accepted for publication March 6, 2015.)

References

- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: Author.
- Baker, F., Wingard, J.R., Curbow, B., Zabora, J., Jodrey, D., Fogarty, L., & Legro, M. (1994). Quality of life of bone marrow transplant long-term survivors. *Bone Marrow Transplantation*, *13*, 589–596.
- Baser, R.E., Li, Y., & Carter, J. (2012). Psychometric validation of the Female Sexual Function Index (FSFI) in cancer survivors. *Cancer*, *118*, 4606–4618. doi:10.1002/cncr.26739
- Brant, J., & Wickham, R. (Eds.). (2013). *Statement on the scope and standards of oncology nursing practice: Generalist and advanced practice*. Pittsburgh, PA: Oncology Nursing Society.
- Chatterjee, R., & Kottaridis, P.D. (2002). Treatment of gonadal damage in recipients of allogeneic or autologous transplantation for haematological malignancies. *Bone Marrow Transplantation*, *30*, 629–635. doi:10.1038/sj.bmt.1703721
- Chiodi, S., Spinelli, S., Cohen, A., Gualandi, F., Lamparelli, T., Lavagetto, A., . . . Romano, C. (1991). Cyclic sex hormone replacement therapy in women undergoing allogeneic bone marrow transplantation: Aims and results. *Bone Marrow Transplantation*, *8*(Suppl. 1), 47–49.
- Cust, M.P., Whitehead, M.I., Powles, R., Hunter, M., & Milliken, S. (1989). Consequences and treatment of ovarian failure after total body irradiation for leukaemia. *BMJ*, *299*, 1494–1497. doi:10.1136/bmj.299.6714.1494
- Donnelly, S. (2000). Quality-of-life assessment in advanced cancer. *Current Oncology Reports*, *2*, 338–342.

- Donnelly, S., & Walsh, D. (1996). Quality of life assessment in advanced cancer. *Palliative Medicine*, *10*, 275–283.
- Graziottin, A. (2010). Menopause and sexuality: Key issues in premature menopause and beyond. *Annals of the New York Academy of Sciences*, *1205*, 254–261. doi:10.1111/j.1749-6632.2010.05680.x
- Hewitt, M., Greenfield, S., & Stovall, E. (2006). *From cancer patient to cancer survivor: Lost in transition*. Washington, DC: National Academies Press.
- Hilditch, J.R., Lewis, J., Peter, A., van Maris, B., Ross, A., Franssen, E., . . . Dunn, E. (1996). A menopause-specific quality of life questionnaire: Development and psychometric properties. *Maturitas*, *24*, 161–175.
- Holland, J.C., & Reznik, I. (2005). Pathways for psychosocial care of cancer survivors. *Cancer*, *104*(Suppl.), 2624–2637.
- Horowitz, M.M. (2005). Use and growth of hematopoietic cell transplantation. In F.R. Appelbaum, S. Forman, R.S. Negrin, and K.G. Blume (Eds.), *Thomas' hematopoietic cell transplantation: Stem cell transplantation* (4th ed., pp. 15–21). West Sussex, UK: Blackwell Publishing.
- Humphreys, C.T., Tallman, B., Altmaier, E.M., & Barnette, V. (2007). Sexual functioning in patients undergoing bone marrow transplantation: A longitudinal study. *Bone Marrow Transplantation*, *39*, 491–496. doi:10.1038/sj.bmt.1705613
- King, J., Wynne, C.H., Assersohn, L., & Jones, A. (2011). Hormone replacement therapy and women with premature menopause—A cancer survivorship issue. *European Journal of Cancer*, *47*, 1623–1632. doi:10.1016/j.ejca.2011.04.007
- Koyama, H., Wada, T., Nishizawa, Y., Iwanaga, T., & Aoki, Y. (1977). Cyclophosphamide-induced ovarian failure and its therapeutic significance in patients with breast cancer. *Cancer*, *39*, 1403–1409. doi:10.1002/1097-0142(197704)39:4<1403::AID-CNCR2820390408>3.0.CO;2-8
- Majhail, N.S., Rizzo, J.D., Lee, S.J., Aljurf, M., Atsuta, Y., Bonfim, C., . . . Tichelli, A. (2012). Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Hematology/Oncology and Stem Cell Therapy*, *5*, 1–30. doi:10.5144/1658-3876.2012.1
- Meirow, D. (1999). Ovarian injury and modern options to preserve fertility in female cancer patients treated with high dose radiochemotherapy for hemato-oncological neoplasias and other cancers. *Leukemia and Lymphoma*, *33*, 65–76. doi:10.3109/10428199909093726
- Milroy, C.L., & Jones, K.P. (2010). Gynecological care in hematopoietic stem cell transplant patients: A review. *Obstetrical and Gynecological Survey*, *65*, 668–679. doi:10.1097/OGX.0b013e31820955be
- Pasquini, M.C., & Zhu, X. (2014). Current use and outcome of hematopoietic stem cell transplantation: 2014 CIBMTR summary slides. Retrieved from <http://www.cibmtr.org/referencecenter/slidesreports/summaryslides/pages/index.aspx>
- Piccioni, P., Scirpa, P., D'Emilio, I., Sora, F., Scarciglia, M., Laurenti, L., . . . Chiusolo, P. (2004). Hormonal replacement therapy after stem cell transplantation. *Maturitas*, *49*, 327–333. doi:10.1016/j.maturitas.2004.02.015
- Pines, A., Sturdee, D.W., Birkhäuser, M.H., Schneider, H.P., Gambacciani, M., & Panay, N. (2007). IMS updated recommendations on postmenopausal hormone therapy. *Climacteric*, *10*, 181–194. doi:10.1080/13697130701361657
- Pitkin, J., Rees, M.C., Gray, S., Lumsden, M.A., Marsden, J., Stevenson, J.C., & Williamson, J. (2007). Management of premature menopause. *Menopause International*, *13*, 44–45. doi:10.1258/175404507780456719
- Radtke, J.V., Terhorst, L., & Cohen, S.M. (2011). The Menopause-Specific Quality of Life Questionnaire: Psychometric evaluation among breast cancer survivors. *Menopause*, *18*, 289–295.
- Rebar, R.W. (2009). Premature ovarian failure. *Obstetrics and Gynecology*, *113*, 1355–1363.
- Rosen, R., Brown, C., Heiman, J., Leiblum, S., Meston, C., Shabsigh, R., . . . D'Agostino, R., Jr. (2000). The Female Sexual Function Index (FSFI): A multidimensional self-report instrument for the assessment of female sexual function. *Journal of Sex and Marital Therapy*, *26*, 191–208.
- Schubert, M.A., Sullivan, K.M., Schubert, M.M., Nims, J., Hansen, M., Sanders, J.E., . . . Storb, R. (1990). Gynecological abnormalities following allogeneic bone marrow transplantation. *Bone Marrow Transplantation*, *5*, 425–430.
- Shanis, D., Merideth, M., Pulanic, T.K., Savani, B.N., Battiwalla, M., & Stratton, P. (2012). Female long-term survivors after allogeneic hematopoietic stem cell transplantation: Evaluation and management. *Seminars in Hematology*, *49*, 83–93.
- Sonmezer, M., & Oktay, K. (2004). Fertility preservation in female patients. *Human Reproduction Update*, *10*, 251–266.
- Spinelli, S., Chiodi, S., Bacigalupo, A., Brasca, A., Menada, M.V., Petti, A.R., . . . Sessarego, M. (1994). Ovarian recovery after total body irradiation and allogeneic bone marrow transplantation: Long-term follow up of 79 females. *Bone Marrow Transplantation*, *14*, 373–380.
- Syrjala, K.L., & Artherholt, S.B. (2004). Assessment of quality of life in hematopoietic cell transplantation recipients. In F.R. Appelbaum, S. Forman, R.S. Negrin, and K.G. Blume (Eds.), *Thomas' hematopoietic cell transplantation: Stem cell transplantation* (4th ed., pp. 502–514). West Sussex, UK: Blackwell Publishing.
- Syrjala, K.L., Kurland, B.F., Abrams, J.R., Sanders, J.E., & Heiman, J.R. (2008). Sexual function changes during the 5 years after high-dose treatment and hematopoietic cell transplantation for malignancy, with case-matched controls at 5 years. *Blood*, *111*, 989–996.
- Syrjala, K.L., Roth-Roemer, S.L., Abrams, J.R., Scanlan, J.M., Chapko, M.K., Visser, S., & Sanders, J.E. (1998). Prevalence and predictors of sexual dysfunction in long-term survivors of marrow transplantation. *Journal of Clinical Oncology*, *16*, 3148–3157.
- Tauchmanová, L., Selleri, C., De Rosa, G., Esposito, M., Orio, F., Jr., Palomba, S., . . . Colao, A. (2003). Gonadal status in reproductive age women after haematopoietic stem cell transplantation for haematological malignancies. *Human Reproduction*, *18*, 1410–1416.
- Tauchmanová, L., Selleri, C., De Rosa, G., Sammartino, A., Di Carlo, C., Musella, T., . . . Colao, A. (2007). Estrogen-progestin therapy in women after stem cell transplant: Our experience and literature review. *Menopause*, *14*, 320–330.
- Tierney, D.K. (2004). Sexuality following hematopoietic cell transplantation: An important health-related quality of life issue. In F.R. Appelbaum, S. Forman, R.S. Negrin, and K.G. Blume (Eds.), *Thomas' hematopoietic cell transplantation: Stem cell transplantation* (4th ed., pp. 515–525). West Sussex, UK: Blackwell Publishing.
- Utian, W.H., Archer, D.F., Bachmann, G.A., Gallagher, C., Grodstein, F., Heiman, J.R., . . . Stuenkel, C.A. (2008). Estrogen and progestogen use in postmenopausal women: July 2008 position statement of the North American Menopause Society. *Menopause*, *15*, 584–602.
- Warne, G.L., Fairley, K.F., Hobbs, J.B., & Martin, F.I. (1973). Cyclophosphamide-induced ovarian failure. *New England Journal of Medicine*, *289*, 1159–1162. doi:10.1056/NEJM197311292892202
- Wilson, M.M. (2003). Menopause. *Clinics in Geriatric Medicine*, *19*, 483–506.
- Wingard, J.R., Curbow, B., Baker, F., Zabora, J., & Piantadosi, S. (1992). Sexual satisfaction in survivors of bone marrow transplantation. *Bone Marrow Transplantation*, *9*, 185–190.
- Wong, F.L., Francisco, L., Togawa, K., Kim, H., Bosworth, A., Atencio, L., . . . Bhatia, S. (2013). Longitudinal trajectory of sexual functioning after hematopoietic cell transplantation: Impact of chronic graft-versus-host disease and total body irradiation. *Blood*, *122*, 3973–3981.
- World Health Organization. (2002). *Defining sexual health: Report of a technical consultation on sexual health*. Geneva, Switzerland: Author.
- Yoo, C., Yun, M.R., Ahn, J.H., Jung, K.H., Kim, H.J., Kim, J.E., . . . Kim, S.B. (2013). Chemotherapy-induced amenorrhea, menopause-specific quality of life, and endocrine profiles in premenopausal women with breast cancer who received adjuvant anthracycline-based chemotherapy: A prospective cohort study. *Cancer Chemotherapy and Pharmacology*, *72*, 565–575. doi:10.1007/s00280-013-2227-5