Maturitas 105 (2017) 126–131

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Review article

Sexual health after breast cancer: Recommendations from the Spanish Menopause Society, Federación Española de Sociedades de Sexología, Sociedad Española de Médicos de Atención Primaria and Sociedad Española de Oncología Médica

Nicolás Mendoza[a,*], Francisca Molero[b], Fermín Criado[c], Mª Jesús Cornellana[d], Encarna González[e], On behalf of the Sexuality In Breast Cancer Survivors Group[1]

[a] Departamento de Obstetricia y Ginecología, Universidad de Granada, Spain
[b] ASSIR Sant Andreu de la Barca, Barcelona, Spain
[c] Clinica Dr Criado Málaga, Spain
[d] Clínica Corachán, Barcelona, Spain
[e] Unidad de Oncología Médica, Hospital Virgen de las Nieves, Granada, Spain

ARTICLE INFO

Article history:
Received 28 December 2016
Received in revised form 10 January 2017
Accepted 14 February 2017

Keywords:
Breast cancer survivors
Sexual health
Sexual disorders
Sexual therapy

ABSTRACT

Breast cancer is the most common cancer in women. As survival rates are increasing, the long-term health problems of survivors now need attention. Many survivors develop sexual disorders as a consequence of either the side-effects of treatment or induced menopause. A panel of experts from various Spanish scientific societies (Spanish Menopause Society, SMS; Federación Española de Sociedades de Sexología, FESS; Sociedad Española de Médicos de Atención Primaria, SEMERGEN; and Sociedad Española de Oncología Médica) met to develop recommendations for the management of sexual health in breast cancer survivors based on the best evidence available. The main recommendation is that sexuality must be considered by a multidisciplinary team as an integral part of treatment, to improve the quality of life of breast cancer survivors.

Contents

* Correspondence to: Maestro Montero, 21, 18004, Granada, Spain.
E-mail address: nicomendoza@telefonica.net (N. Mendoza).

[1] Details of the Sexuality In Breast Cancer Survivors Group can be found in Supplementary file.

http://dx.doi.org/10.1016/j.maturitas.2017.02.010
0378-5122/

1. Introduction

More than 20,000 new cases of breast cancer are diagnosed annually in Spain. Breast cancer is the most common type of cancer in women (28.7% of all cancers) and is the leading cause of cancer death in Spanish women (15.5%) [1]. Nonetheless, mortality is decreasing because of early-detection programmes and advances in treatment. Consequently, the long-term health of survivors now needs to be addressed [2]. Although the definition of survival can vary considerably, the Spanish Menopause Society (SMS) has endorsed the very broad definition proposed by the National Cancer Institute, which considers survival to be any time after diagnosis [3].

All of the physical and emotional changes inherent to breast cancer can influence sexuality. Unfortunately, health professionals may not fully address these changes because they are focused on their patients' survival [4–6] and forget the psychosocial, cultural, emotional and relational dimensions of health, and the importance of sexual health [7,8]. This position paper aims to present recommendations for the management of sexual problems in breast cancer survivors.

A panel of experts from various Spanish scientific societies (Spanish Menopause Society, SMS; Federación Española de Sociedades de Sexología, FESS; Sociedad Española de Médicos de Atención Primaria, SEMERGEN; and Sociedad Española de Oncología Médica) met to develop recommendations for the management of sexual health of women with breast cancer based on the best evidence available. The recommendations are based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system [9]. The present article analyses the factors that impact the sexual health of women with breast cancer and presents the recommendations.

2. Epidemiology

The sexuality of breast cancer survivors has not been well studied. Sexual dysfunction is common among women with breast cancer (occurring in 25–66% of cases), particularly in those who are receiving chemotherapy in the immediate postoperative period and those who experience vaginal dryness. The most frequent problem is decreased sexual interest (49.3%), followed by dyspareunia (35–38%), concerns about body image, and problems with sexual desire (10–14%), arousal (5%) and orgasm (5%) [10,11]. However, most studies have not assessed sexuality before cancer diagnosis, making it difficult to identify the effects of breast cancer and its treatment *per se* [12–14].

3. Breast cancer's impact on sexuality

Most studies of the sexual health of women with breast cancer have focused on biomedical aspects such as the physiological and hormonal repercussions of cancer and its treatments in terms of sexual response; where the psychosocial and relational aspects have been studied, the focus has generally been on anxiety, stress or altered body image after breast cancer treatment, rather than sexuality. Studies of the experiential and cultural aspects of sexuality in breast cancer survivors would require the consideration of concepts such as sexual attractiveness, its plasticity in relation to body image, the internalization of gender role and self-demands regarding relationships, and would force more open, specialized and less prescriptive communication between professionals and patients [15].

Breast cancer and its treatments can produce physical sequelae that affect a woman's body image. However, relationship concerns, depression and increasing age are important influences in the development of sexual dysfunction in breast cancer survivors [16]. Thus, not surprisingly, some psychological interventions (mindfulness-based approaches, expression of positive emotions, spiritual interventions, hope therapy and meaning-making interventions) can improve quality of life (QoL) and well-being [17] and, *pari passu*, sexual health.

3.1. Impact of breast cancer treatments and concomitant treatments

Breast cancer treatments include surgery, radiotherapy, chemotherapy and adjuvant endocrine therapy. They often cause major physical changes (hair loss, breast or chest disfigurement, lymphedema, changes in skin texture, ovarian failure, vaginal irritation, hot flashes and weight gain or loss) which generate feelings of vulnerability and a loss of self-esteem and femininity [16].

The degree to which surgery affects sexual function depends on the type of intervention (breast-conserving surgery, mastectomy, axillary node removal). The impact of surgery is greater when the surgery is more radical and when a woman has had less involvement in treatment decisions [18]. A prospective study found that significantly more women reported sexual dysfunction and problems with sexual desire, arousal and orgasm after mastectomy than after breast-conserving surgery [19]. Lymphedema after axillary lymph node removal occurs in up to 30% of women and in 3% of patients undergoing sentinel node excisions it can be a long-term problem [9]. While breast reconstruction allows aesthetic restoration, sexuality may still be compromised because of loss of breast sensitivity [20–22].

Sexual health suffers after chemotherapy and adjuvant endocrine treatment, especially when aromatase inhibitors (AIs) are used, as these can cause hypoestrogenism and vaginal atrophy [23,24]. Radiotherapy can cause tiredness and skin erythema, as well as swelling and so breast asymmetry.

Breast cancer survivors are commonly prescribed antidepressants (typically serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors) and these may also impair sexual function [25,26].

3.2. Breast cancer and sexual and reproductive health in premenopausal women

Breast cancer in premenopausal women tends to be more aggressive and usually requires adjuvant treatment. Younger women also suffer more severe disruption of body image, anxiety, sleep disorders, dissatisfaction with relationships and fear of relapse. In this context, these women are more prone to worse sexual health than older women [27,28]. Furthermore, chemotherapy induces ovarian failure in more than 80% of women over 40 and in more than 20% of women over 30 [29]. It is therefore important to discuss oocyte cryopreservation, especially with younger women, before chemotherapy or prophylactic oophorectomy [30].

Most guidelines recommend postponing pregnancy for at least two years after the breast cancer is treated, depending on the stage and the treatment received [31,32], although for women with localised disease early conception is unlikely to worsen prognosis [33,34]. In addition, ovarian stimulation is not contraindicated, and women with breast cancer who are positive for hormone receptors may receive tamoxifen or AI during stimulation [35].

3.3. Alterations in sexuality and relationships

The impact of breast cancer on sexual health is higher in women with a history of psychological problems, with especially negative perceptions and expectations regarding their disease, low levels of social and family support and poor relationships [16]. Relationship quality can be considered the most important predictor of sexual satisfaction, function and desire after breast cancer, even greater than the degree of bodily damage caused by treatment [36].

Partners of breast cancer survivors also experience psychological and emotional stress. Apart from dealing with their partner's diagnosis and treatment, they may suddenly become carers, and this may have repercussions on their own quality of life and employment status, which in turn might affect their own sexual health [8,37]. It is therefore important that both partners are offered information and counselling and participate in decisions about treatment [38,39]. However, where breast cancer survivors do not wish to involve their partners, this must be respected.

4. Management strategies

The purpose of management is to minimize sexual and relationship problems. Discussing sexual health and the woman's personal future beyond breast cancer is a therapeutic act in itself and can increase confidence in surviving the disease. Management can be undertaken either in already planned visits for breast cancer treatment or at other times.

Semi-structured interviews and questionnaires can facilitate evaluation and management. We recommend the use of validated questionnaires such as the Female Sexual Function Index (FSFI), EVAS-M or SF-36 or the Cervantes Scale [40,41].

We also recommend assessment and the offering of help for sexual health at the three following time points [42–44], bearing in mind that breast cancer treatment in itself will take priority.

- before surgery or preoperative chemotherapy, to asses current sexual health and psychosocial support
- after surgery and after the postoperative radio-chemotherapy or adjuvant endocrine therapeutic strategies have been determined
- 6–9 months after surgery, to evaluate current problems, decide a management strategy and assess the need for subsequent visits.

5. Treatment

Few randomized controlled trials have evaluated treatments for sexual dysfunction in breast cancer survivors, and these are limited by small sample sizes and conflicting results [45]. We recommend that any advice should be given by a multidisciplinary team that includes oncologists, nurses, psychologists, psychiatrists and sex therapists, if possible.

5.1. Counselling

Health professionals can play a key role in managing sexual health problems in breast cancer survivors [46]. One method for identifying sexual problems is the PLISSIT model. This model centres on permission (to discuss the subject), limited information (not overwhelming the patient), specific advice (accurate and practical information) and intensive therapy (if referral to a specialist is needed) [47,48]. A non-judgemental approach and use of easily understandable language are advised [49]. It is best to refer women with severe sexual dysfunction to a specialist health professional.

Health professionals should ask open-ended questions and encourage women to ask questions. A good opening for the discussion could be as follows: "It's normal that at some point you worry about how breast cancer will affect your sex life and your relationships."

The information provided should be tailored to the needs of the woman, and misconceptions identified [50]. Points to cover include:

- Considering that sex is not important in a relationship.
- Maintaining a sexual relationship because of the patient's fear of being abandoned by the partner.
- Ignoring sexual problems and believing that they will solve themselves.
- Giving more importance to the pleasure of the partner than to that of the woman herself.
- Comparing current sex life with that previously achieved or with that of unaffected women (it may still be satisfactory even if it is not as good as it was).
- Living with sexuality but avoiding emotions (considered negative), and thereby reducing sex to a solely physical experience.

Specific tips for improving sexual activity and sex interaction [17,50]

- Exercises (Kegel) or sensory massage to regain confidence in the sexual response.
- Making time to improve the quality of emotional and erotic-sexual interaction with partner(s).
- Spending time with the partner and engaging in shared leisure activities.
- Renegotiating the type of sexual activity performed (vaginal intercourse is not imperative).
- Use of massage oils, lubricants or vibrators.

The inclusion of the partner in support or sex therapy programmes is considered to be essential, as most strategies to overcome sexual difficulties are based on couple relationships. This is especially important for younger women whose partners are less well prepared to cope with the woman's illness or with childcare [7,8,14].

Couple-based sex therapy appears to be an effective and accepted treatment for addressing sexual problems in breast cancer patients. These interventions were associated with improvements in sexual physiology, functioning, self-image and relationships, as

well as improved psychological well-being of both breast cancer survivors and their partners [51].

5.2. Symptomatic treatment

5.2.1. Vaginal lubricants and moisturizers

Non-hormonal vaginal lubricants and moisturiser creams are generally considered to be the treatment of choice in breast cancer survivors.

Women undergoing chemotherapy, particularly younger women, are more likely to suffer from vaginal dryness, dyspareunia, decreased libido and difficulty in reaching orgasm. Although there is limited evidence in breast cancer survivors, vaginal moisturizers and lubricants are effective in treating dyspareunia and vaginal dryness when used regularly (3–5 times per week). There are three types of vaginal moisturizers and lubricants: pectin-based, water-based and those containing polycarbophil gels [52].

One randomised controlled trial evaluating a lactic acid-spiked gel showed improvements in scores on both the Vaginal Health Index (mean 5.00 ± 0.816 vs 16.98 ± 3.875, $p < 0.001$) and the Vaginal Maturation Index (mean 51.18 ± 3.753 vs 47.87 ± 2.728, $p < 0.001$) at 12 weeks. The vaginal gel also reduced vaginal irritation, dryness and dyspareunia, although confirmatory studies are required [53].

The OVERcome study (Olive Oil, Vaginal Exercise and MoisturizeR) resulted in significant improvements in dyspareunia, sexual function and quality of life over time (all $P < 0.001$) in breast cancer survivors. Maximum benefits were observed at week 12 [54].

Furthermore, a randomized trial in 52 tamoxifen users who complained of vaginal dryness found that polyacrylic acid was superior to a lubricant in treating sexual dysfunction [55].

In some cases, vaginal dilators, vibrators, self-stimulation techniques and pelvic floor relaxation exercises may also be useful [56].

5.2.2. Vaginal estrogen therapy

The decision to use vaginal estrogen therapy (VET) should be made on an individual basis, considering the patient's tumour characteristics, symptoms, risk factors and other potential benefits. In the last ACOG Committee Opinion paper, the use of VET in breast cancer survivors was recommended only for patients who are unresponsive to non-hormonal remedies. There have been no clinical trials of VET in breast cancer survivors. Women with very pronounced vaginal symptoms may be treated with local, low-dose estrogens, which show minimal systemic absorption. However, such treatments should be avoided or used for only very short periods of time in women who are taking aromatase inhibitors [57].

VET, which is available as tablets, creams or rings, is very effective for the treatment of genital atrophy. Early systemic absorption when the vaginal epithelium is atrophic is a potential safety concern, though blood levels decline with continued use. A study of six women taking aromatase inhibitors, treated with vaginal estradiol 25 mcg tablets (a preparation no longer in use and now replaced with a 10mcg dose) found that serum estradiol levels rose from 5 pmol/l or less at baseline to a mean 72 pmol/l at 2 weeks. By 4 weeks this had decreased to <35 pmol/l in the majority (median 16 pmol/l) although significant further rises were seen in two women [58].

Although no breast recurrences have been documented with VET, estriol instead of estradiol has been proposed as a better option in breast cancer survivors because it has a faster clearance [59].

There are no data on interactions between VET and tamoxifen or aromatase inhibitors. Tamoxifen shows anti-estrogenic effects in premenopausal women but weak estrogenic effects on the vagina in postmenopausal women, although some also experience vaginal atrophy.

In our opinion, it is reasonable to use low doses of VET in tamoxifen users who suffer from vaginal dryness. The small amount that is absorbed is likely to be blocked by tamoxifen. However, we suggest not using VET in those taking aromatase inhibitors, as systemic estrogen levels should be minimised in this group.

5.2.3. Androgens

There are limited data on the use of topical testosterone in women with breast cancer, but no increases in estrogen levels in peripheral blood have been observed in women taking aromatase inhibitors [59]. Systemic testosterone has been used in various forms (oral, implant or transdermal patch or gel) for many decades to improve sexual desire but data in breast cancer survivors are limited [60].

The use of dehydroepiandrosterone (DHEA) has been proposed to treat vulvovaginal atrophy due to its intracellular transformation in estrogens. Clinical improvements in postmenopausal women have been observed with the use of vaginal DHEA, although there are no data in breast cancer survivors [61].

A 12-week randomized study of women taking aromatase inhibitors with early-stage breast cancer examined the use of intravaginal testosterone (IVT) cream and an estradiol-releasing vaginal ring (7.5 μg/day). Of the 75 who started the study, 69 completed treatment. The mean (range) baseline E2 level was 20 (<2–127) pg/mL. At baseline, E2 was above the postmenopausal range (>10 pg/mL) in 28 of the 75 women (37%). Persistent E2 elevation was observed in none of the 35 women who used a vaginal ring and in 4 of the 34 women (12%) using IVT cream. Transient E2 elevation was seen in 4 of the 35 (11%) using a vaginal ring and in 4 of the 34 (12%) using IVT. Vaginal atrophy and sexual interest and dysfunction improved for all patients [62]. Further data are required.

5.2.4. Tibolone

Tibolone improves sexual health in postmenopausal women. However, the LIBERATE study (Livial Intervention following Breast Cancer; Efficacy, Recurrence and Tolerability Endpoints) showed an increased risk of recurrence in tamoxifen users compared with placebo (15% vs 11.4%; HR 1.40, 95% CI 1.1–1.79). The study was therefore stopped early [63]. Consequently, tibolone is not recommended in breast cancer survivors.

5.2.5. Flibanserin

Flibanserin has been approved for use by premenopausal women with hypoactive sexual desire disorder that is not caused by a coexisting medical or psychiatric condition and that is not caused by other concomitant medication. However, there are no data on the use of flibanserin by breast cancer survivors and it is not approved for use by them.

5.2.6. Ospemifene

Approved in the USA and Europe, oral ospemifene is indicated for the treatment of moderate to severe symptomatic vulvovaginal atrophy in postmenopausal women who are not candidates for local vaginal estrogen therapy [64]. Ospemifene is a selective estrogen receptor modulator (SERM).

Although preclinical data and reports from animal experiments suggest that ospemifene has a neutral or inhibitory effect on mammary carcinogenesis, further studies are necessary to evaluate its safety in women with breast cancer [65].

6. Summary recommendations

- Sexuality must be approached as an integral part of treatment to improve quality of life in breast cancer survivors. If possible, sexual health should be addressed through a multidisciplinary team

that includes oncologists, nurses, psychologists, psychiatrists and sex therapists. If health professionals are unable to address this issue, referral to specialized professionals or sexologists is recommended (Grade 2B).
- Exercises to regain confidence in the sexual response and intervention techniques using positive psychology are improve sexual health (Grade 2B).
- Partners should be included in support programmes (Grade 2B).
- The use of vaginal moisturizers and lubricants is recommended for vaginal dryness (Grade 2B).
- Topical estrogen treatment for vaginal symptoms can be used but only after discussion with the treating oncologist, as clinical trials have not been undertaken in women with breast cancer (Grade 2B).

Contributors

NM and FM were responsible for the conception and design of these recommendations.

FC and MJC participated in the preparation of the statement recommendations.

NM, FM and EG were responsible for data interpretation and preparation of manuscript.

The Sexuality In Breast Cancer Survivors Group comprises R Castaño, MJ Cornellana, F Criado, MJ Cuerva, J Florido, E González, M González, M Honrado, AR Jurado, E Kartchenco, E Laforet, P Llaneza, D Lubian, N Mendoza, E Miguel, F Molero, E Ratia, M Ribes, R Sánchez Borrego, J Schneider, R Tulleuda. All members of the Group participated in the preparation of the recommendations.

All authors, including the members of the Sexuality In Breast Cancer Survivors Group, saw and approved the final version of the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

No funding was sought or secured for the preparation of these recommendations.

Provenance and peer review

This article has been peer reviewed.

Acknowledgements

This article has been translated and edited by American Journal Experts.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.maturitas.2017.02.010.

References

[1] R. De Angelis, M. Sant, M.P. Coleman, S. Francisci, P. Baili, D. Pierannunzio, EUROCARE-5 Working Group, et al., Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5-a population-based study, Lancet Oncol. 15 (1) (2014) 23–34.
[2] D. Hashim, P. Boffetta, C. La Vecchia, M. Rota, P. Bertuccio, M. Malvezzi, E. Negri, The global decrease in cancer mortality: trends and disparities, Ann. Oncol. 27 (5) (2016) 926–933.
[3] M.C. Delgado-Sanz, M.J. García-Mendizábal, M. Pollán, M.J. Forjaz, G. López-Abente, N. Aragonés, B. Pérez-Gómez, Heath-related quality of life in Spanish breast cancer patients: a systematic review, Health Qual. Life Outcomes 9 (2011) 3.
[4] R. Sánchez-Borrego, N. Mendoza, E. Beltrán, R. Comino, J. Allué, C. Castelo-Branco, M.J. Cornellana, M. Duran, J. Haya, M.D. Juliá, P. Llaneza, M.C. Navarro, F. Quereda, Position of the Spanish Menopause Society regarding the management of menopausal symptoms in breast cancer patients, Maturitas 75 (3) (2013) 294–300.
[5] B. Pestalozzi, M. Castiglione, Primary breast cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up, Ann. Oncol. 19 (Suppl. 2) (2008) 7–10.
[6] P. Ganz, Psychological and social aspects of breast cancer, Oncology 22 (2008) 642–653.
[7] A.J. Hordern, A.F. Street, Constructions of sexuality and intimacy after cancer: patient and health professional perspectives, Soc. Sci. Med. 64 (8) (2007) 1704–1718.
[8] A.J. Hordern, A.F. Street, Communicating about patient sexuality and intimacy after cancer: mismatched expectations and unmet needs, MJA 186 (5) (2007) 224–227.
[9] http://cebgrade.mcmaster.ca/.
[10] C.L. Paterson, C.A. Lengacher, K.A. Donovan, K.E. Kip, C.S. Tofthagen, Body image in younger breast cancer survivors: a systematic review, Cancer Nurs. 39 (1) (2016) E39–58.
[11] J. Lester, G. Pahouja, B. Andersen, M. Lustberg, Atrophic vaginitis in breast cancer survivors: a difficult survivorship issue, J. Pers. Med. 5 (2) (2015) 50–66.
[12] S. Pruthi, J.A. Simon, A.P. Early, Current overview of the management of urogenital atrophy in women with breast cancer, Breast 17 (4) (2011) 403–408.
[13] E. Gilbert, J.M. Ussher, J. Perz, Sexuality after breast cancer: a review, Maturitas 66 (4) (2010) 397–407.
[14] M. Jankowska, Sexual functioning in young women in the context of breast cancer treatment, Rep. Pract. Oncol. Radiother. 18 (4) (2013) 193–200.
[15] M.C. Halley, S.G. May, K.A. Rendle, D.L. Frosch, A.W. Kurian, Beyond barriers: fundamental disconnects underlying the treatment of breast cancer patientsí sexual health, Cutl. Health Sex. 16 (9) (2014) 1169–1180.
[16] J.J. Speer, B. Hillenberg, D.P. Sugrue, C. Blacker, C.L. Kresge, V.B. Decker, D. Zakalik, D.A. Decker, Study of sexual functioning determinants in breast cancer survivors, Breast J. 11 (6) (2005) 440–447.
[17] A. Casellas-Grau, A. Font, J. Vives, Positive psychology interventions in breast cancer. A systematic review, Psychooncology 23 (1) (2014) 9–19.
[18] Z.A. Alicikus, I.B. Gorken, R.C. Sen, S. Kentli, M. Kinay, H. Alanyali, O. Harmancioglu, Psychosexual and body image aspects of quality of life in Turkish breast cancer patients: a comparison of breast conserving treatment and mastectomy, Tumori 95 (2) (2009) 212–218.
[19] L. Aerts, M.R. Christiaens, P. Enzlin, P. Neven, F. Amant, Sexual functioning in women after mastectomy versus breast conserving therapy for early-stage breast cancer: a prospective controlled study, Breast 23 (5) (2014) 629–636.
[20] S.N. Razdan, V. Patel, S. Jewell, C.M. McCarthy, Quality of life among patients after bilateral prophylactic mastectomy: a systematic review of patient-reported outcomes, Qual. Life Res. 25 (6) (2016) 1409–1421.
[21] I.C. Aguiar, D.F. Veiga, T.F. Marques, N.F. Novo, M. Sabino Neto, L.M. Ferreira, Patient-reported outcomes measured by BREAST-Q after implant-based breast reconstruction: a cross-sectional controlled study in Brazilian patients, Breast 31 (2017) 22–25.
[22] V.L. Champion, L.I. Wagner, P.O. Monahan, J. Daggy, L. Smith, A. Cohee, K.W. Ziner, J.E. Haase, K.D. Miller, K. Pradhan, F.W. Unverzagt, D. Cella, B. Ansari, G.W. Sledge Jr., Comparison of younger and older breast cancer survivors and age-maches controls on specific and overall quality of life domains, Cancer 120 (15) (2014) 2237–2246.
[23] M. Panjari, R.J. Bell, S.R. Davis, Sexual function after breast cancer, J. Sex. Med. 8 (1) (2011) 294–302.
[24] J. Baumgart, K. Nilsson, A. Stavreus-Evers, K. Kask, K. Villman, H. Lindman, T. Kallak, I. Sundström-Poromaa, Urogenital disorders in women with adjuvant endocrine therapy after early breast cancer, Am. J. Obstet. Gynecol. 204 (26) (2011) e1.
[25] V.S. Williams, H.M. Edin, S.L. Hogue, S.E. Fehnel, D.S. Baldwin, Prevalence and impact of antidepressant-associated sexual dysfunction in three European countries: replication in a cross-sectional patient survey, J. Psychopharmacol. 24 (4) (2010) 489–496.
[26] P.L. Delgado, S.K. Brannan, C.H. Mallinckrodt, P.V. Tran, R.K. McNamara, F. Wang, J.G. Watkin, M.J. Detke, Sexual functioning assessed in 4 double-blind placebo- and paroxetine-controlled trials of duloxetine for major depressive disorder, J. Clin. Psychiatry 66 (6) (2005) 686–692.
[27] N.E. Avis, S. Crawford, J. Manuel, Psychosocial problems among young women with breast cancer, Psy.-Oncol. 13 (2004) 295–308.
[28] S.R. Burwell, L.D. Case, C. Kaelin, N.E. Avis, Sexual problems in younger women after breast cancer surgery, J. Clin. Oncol. 24 (18) (2006) 2815–2821.
[29] S. Archibald, S. Lemieux, E.S. Byers, K. Tamlyn, J. Worth, Chemically induced menopause and the sexual functioning of breast cancer survivors, Women Ther. 29 (1/2) (2006) 83–106.
[30] M.L. Greaney, K. Sprunck-Harrild, K.J. Ruddy, J. Ligibel, W.T. Barry, E. Baker, M. Meyer, K.M. Emmons, A.H. Partridge, Study protocol for young & strong: a cluster randomized design to increase attention to unique issues faced by

young women with newly diagnosed breast cancer, BMC Public Health 15 (2015) 37.
[31] A.L. Margulies, L. Selleret, S. Zilberman, I.T. Nagarra, J. Chopier, J. Gligorov, P. Berveiller, M. Ballester, E. Darai, N. Chabbert-Buffet, Pregnancy after cancer: for whom and when? Bull. Cancer 102 (5) (2015) 463–469.
[32] M. Haddadi, S. Muhammadnejad, F. Sadeghi-Fazel, Z. Zandieh, G. Rahimi, S. Sadighi, et al., Systematic review of available guidelines on fertility preservation of young patients with breast cancer, Asian Pacific J. Cancer Prev. 16 (3) (2015) 1057–1062.
[33] A. Ives, C. Saunders, M. Bulsara, J. Semmens, Pregnancy after breast cancer: population based study, BMJ 334 (7586) (2007) 194.
[34] N. Kroman, M.B. Jensen, J. Wohlfahrt, B. Ejlertsen, Danish Breast Cancer Cooperative Group, Pregnancy after treatment of breast cancer—a population-based study on behalf of danish Breast cancer cooperative group, Acta Oncol. 47 (4) (2008) 545–549.
[35] K.A. Reynolds, N.M. Grindler, J.S. Rhee, A.R. Cooper, V.S. Ratts, K.R. Carson, et al., Variability in the practice of fertility preservation for patients with cancer, PLoS One 10 (5) (2015) e0127335.
[36] E.M. Vieira, D.B. Santos, M.A. Santos, A. Giami, Experience of sexuality after breast cancer: a qualitative study with women in rehabitilation, Rev. Lat. Am. Enferm. 22 (3) (2014) 408–414.
[37] H. Moreira, M.C. Canavaro, Psychosocial adjustment and marital intimacy among partners of patienes with breast cancer: a comparison study with partners of healthy women, J. Psychosoc. Oncol. 31 (3) (2013) 282–304.
[38] A. Künzler, F.W. Nussbeck, M.T. Moser, G. Bodenmann, K. Kayser, Individual and dyadic development of personal growth in couples coping with cancer, Support. Care Cancer 22 (1) (2014) 53–62.
[39] K. Milbury, H. Badr, Sexual problems, communication patterns, and depressive symptoms in couples coping with metastatic breast cancer, Psychooncology 22 (4) (2013) 814–822.
[40] C. Castelo-Branco, S. Palacios, J. Ferrer-Barriendos, J.J. Parrilla, M. Manubens, X. Alberich, A. Martí, Cervantes Study Group, Understanding how personality factors may influence QOL of life: development and validation of the cervantes personality scale, Menopause 15 (5) (2008) 914–918.
[41] R. Rosen, C. Brown, J. Heiman, S. Leiblum, C. Meston, R. Shabsigh, D. Ferguson, R. D'Agostino Jr., The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function, J. Sex Marital Ther. 26 (2) (2000) 191–208.
[42] J. Lamont, Society of Obstetricians and gynaecologists of Canada: female sexual health consensus clinical guidelines, J. Obstet. Gynaecol. Can. 34 (8) (2012) 769–783.
[43] Sexuality and Cancer Treatment: Women Cancer.Net Editorial Board, 02/2016. Available at: http://www.cancer.net/navigating-cancer-care/dating-sex-and-reproduction/sexuality-and-cancer-treatment-women.
[44] J. Perz, J.M. Ussher, E. Gilbert, Constructions of sex and intimacy after cancer: Q methodology study of people with cancer, their partners, and health professionals, BMC Cancer 13 (2013) 270.
[45] B. Candy, L. Jones, V. Vickerstaff, A. Tookman, M. King, Interventions for sexual dysfunction following treatments for cancer in women, Cochrane Database Syst. Rev. 2 (2016), CD005540.
[46] E.M. Vieira, D.B. Santos, M.A. Santos, A. Giami, Experience of sexuality after breast cancer: a qualitative study with women in rehabilitation, Rev. Lat. Am. Enferm. 22 (3) (2014) 408–414.
[47] J. Perz, J.M. Ussher, Australian Cancer and Sexuality Study Team, A randomized trial of a minimal intervention for sexual concerns after cancer: a comparison of self-help and professionally delivered modalities, BMC Cancer 15 (2015) 629.
[48] S. Faghani, F. Ghaffari, Effects of sexual rehabilitation using the PLISSIT model on quality of sexual life and sexual functioning in post-mastectomy breast cancer survivors, Asian Pac. J. Cancer Prev. 17 (11) (2016) 4845–4851.
[49] A.C. Pinto, Sexuality and breast cancer: prime time for young patients, J. Thorac. Dis. 5 (Suppl. 1) (2013) S81–6.
[50] R. Sanchez-Borrego, F. Molero, R. Castaño, C. Castelo-Branco, M. Honrado, A.R. Jurado, E. Laforet, R. Prieto, F. Cabello, M. Larrazabal, F. Sánchez, J. Florido, N. Mendoza, Spanish consensus on sexual health in men and women over 50, Maturitas 78 (2) (2014) 138–145.
[51] A.J. Carroll, S.R. Baron, R.A. Carroll, Couple-based treatment for sexual problems following breast cancer: a review and synthesis of the literature, Support. Care Cancer 24 (8) (2016) 3651–3659.
[52] S. Mazzarello, B. Hutton, M.F. Ibrahim, C. Jacobs, R. Shorr, S. Smith, T. Ng, M. Clemons, Management of urogenital atrophy in breast cancer patients: a systematic review of available evidence from randomized trials, Breast Cancer Res. Treat. 152 (1) (2015) 1–8.
[53] Y.K. Lee, H.H. Chung, J.W. Kim, N.H. Park, Y.S. Song, S.B. Kang, Vaginal pH-balanced gel for the control of atrophic vaginitis among breast cancer survivors: a randomized controlled trial, Obstet. Gynecol. 117 (2011) 922.
[54] I. Juraskova, S. Jarvis, K. Mok, M. Peate, B. Meiser, Cheah breast cancer, S. Mireskandari, M. Friedlander, The acceptability, feasibility, and efficacy (phase I/II study) of the OVERcome (Olive Oil, Vaginal Exercise, and MoisturizeR) intervention to improve dyspareunia and alleviate sexual problems in women with breast cancer, J. Sex. Med. 10 (10) (2013) 2549–2558.
[55] P.T. Juliato, A.T. Rodrigues, R. Stahlschmidt, C.R. Juliato, P.G. Mazzola, Can polyacrylic acid treat sexual dysfunction in women with breast cancer receiving tamoxifen? Climacteric 23 (November) (2016) 1–5 [Epub ahead of print].
[56] R. Sánchez-Borrego, M. Manubens, M.C. Navarro, M.J. Cancelo, E. Beltrán, M. Duran, T. Orte, L. Baquedano, S. Palacios, N. Mendoza, Spanish Menopause Society: position of the Spanish Menopause Society regarding vaginal health care in postmenopausal women, Maturitas 78 (2) (2014) 146–150.
[57] American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice, Farrell R. ACOG Committee Opinion No. 659: The Use of Vaginal Estrogen in Women With a History of Estrogen-Dependent Breast Cancer, Obstet Gynecol 127(3) (2016) e93–e96.
[58] A. Kendall, M. Dowsett, E. Folkerd, I. Smith, Caution: vaginal estradiol appears to be contraindicated in postmenopausal women on adjuvant aromatase inhibitors, Ann. Oncol. 17 (4) (2006) 584–587.
[59] M.E. Melisko, M. Goldman, H.S. Rugo, Amelioration of sexual adverse effects in the early breast cancer patient, J. Cancer Surviv. 4 (3) (2010) 247–255.
[60] R. Tungmunsakulchai, S. Chaikittisilpa, T. Snabboon, K. Panyakhamlerd, U. Jaisamrarn, N. Taechakraichana, Effectiveness of a low dose testosterone undecanoate to improve sexual function in postmenopausal women, BMC Womens Health 15 (2015) 113.
[61] F. Labrie, D.F. Archer, W. Koltun, A. Vachon, D. Young, L. Frenette, D. Portman, M. Montesino, I. Côté, J. Parent, L. Lavoie, A. Beauregard, C. Martel, M. Vaillancourt, J. Balser, É. Moyneur, Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause, Menopause 23 (3) (2016) 243–256.
[62] M.E. Melisko, M.E. Goldman, J. Hwang, A. De Luca, S. Fang, L.J. Esserman, A.J. Chien, J.W. Park, H.S. Rugo, Vaginal testosterone cream vs estradiol vaginal ring for vaginal dryness or decreased libido in women receiving aromatase inhibitors for early-stage breast cancer: a randomized clinical trial, JAMA Oncol. (November) (2016) [Epub ahead of print].
[63] P. Kenemans, N.J. Bundred, J.M. Foidart, E. Kubista, B. von Schoultz, P. Sismondi, R. Vassilopoulou-Sellin, C.H. Yip, J. Egberts, M. Mol-Arts, R. Mulder, S. van Os, M.W. Beckmann, LIBERATE Study Group, Safety and efficacy of tibolone in breast-cancer patients with vasomotor symptoms: a double-blind, randomised, non-inferiority trial, Lancet Oncol. 10 (2) (2009) 135–146.
[64] Y. Cui, H. Zong, H. Yan, N. Li, Y. Zhang, The efficacy and safety of ospemifene in treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy: a systematic review and meta-analysis, J. Sex. Med. 11 (2) (2014) 487–497.
[65] G.T. Wurz, L.H. Soe, M.W. Degregorio, Ospemifene, vulvovaginal atrophy, and breast cancer, Maturitas 74 (2013) 220–225.