MORBIDITIES AFTER BREAST CANCER TREATMENT

MORBIDADES APÓS TRATAMENTO DO CÂNCER DE MAMA

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ABSTRACT

Introduction: Breast cancer has a heterogeneous behavior of variable spectrum, presenting a global incidence that tends to increase. Today it is probably the most feared neoplastic disease by women due to its high frequency and its psychological effects and physical consequences, which, according to evidence, are related to morbidities associated with post treatment. **Objectives:** To describe the morbidity consequent to the treatment of breast cancer. **Methods:** This is a review that was performed through the PubMed, BIREME, Scielo and VHL databases using DeCS / MeSH descriptors. The search was carried out in English, Portuguese and Spanish. Regarding the diseases evaluated in the studies, those that evaluated the psychopathological entities were listed by their highest frequency the following: depression, fear of relapses, sleep disorders, cognitive problems, fatigue and sexual problems. **Comments:** The authors observed that the main symptom in the surgical procedure for breast cancer was paresthesia, caused by the injury of the intercostobrachial nerve. There has been research reporting that harmful effects are produced by systemic therapy. Chemotherapeutic agents may lead to amenorrhea and may play an important role in the development of brachial plexopathy. Studies analyzing the influence of radiotherapy have shown that it can lead to problems in the upper limb, such as: restrictions on the mobility of the arm and shoulder. Conclusion: Several morbid factors related to the treatment of breast cancer have been reported. It has been observed that any treatment can bring physical, psychological, social damages, among others.

Keywords: Breast cancer; Postoperative complications; Lymphatic vessels; Vascular system Injures; Dissection.

RESUMO

Introdução: O câncer de mama apresenta comportamento heterogêneo e variável e incidência global crescente, sendo a neoplasia mais temida pelas mulheres devido à alta frequência e aos efeitos físicos e psicológicos associados ao pós-tratamento. Objetivo: Descrever as morbidades pós-tratamento do câncer de mama. **Métodos:** Trata-se de revisão narrativa nas bases de dados PubMed, SciELO e BVS, utilizando descritores DeCS/MeSH na busca por artigos em inglês, português e espanhol que estivessem atualizados. Foram selecionados os estudos que avaliam as entidades psicopatológicas: depressão, medo de recidivas, distúrbios do sono, problemas cognitivos, fadiga e problemas sexuais. **Comentários:** Morbidades psicossomáticas, cirúrgicas associadas a plexos nervosos, restrição dos movimentos braquiais, efeitos da terapia sistêmica e da radioterapia, lesões dos sistemas linfático e hematológico, presença de infecção, dor, amenorreia, síndrome da rede axilar e a síndrome do ombro congelado foram mais frequentemente encontrados. **Conclusão:** Diversos fatores mórbidos estão vinculados ao tratamento do câncer de mama, e deve-se considerar a individualidade das respostas às terapêuticas propostas no manejo dessa condição.

Palavras-chave: Câncer de mama; Complicações pós-operatórias; Vasos linfáticos; Lesões do sistema vascular; Dissecação.

INTRODUCTION

Breast cancer has a heterogeneous pattern, with an increasing global incidence, being the most feared cancer by women due to its high frequency, psychological effects, and physical consequences, which are related to morbidities associated with post-treatment[1-8].

This review aimed to disclose the morbidity of cancer and its treatment, considering its growing economic, social, and humanistic burden.

METHODS

This narrative review was conducted in the PubMed, Scielo, and BVS databases with the following DeCS/MeSH descriptors: "*lesões do sistema vascular*", "*vasos linfáticos*", "*dissecação*", "*complicações pós-operatórias*"; encompassing recent studies published in English, Portuguese, and Spanish. Those evaluating depression, fear of recurrence, sleep disorders, cognitive problems, fatigue, and sexual problems were included.

RESULTS AND DISCUSSION

Among compiled studies, the main morbidities can be described as follows:

Psychosomatic: symptoms observed during diagnosis and treatment include depression, fear of recurrence, sleep disorders, cognitive problems, fatigue, sexual problems, higher risk of divorce, and changes in social and quality of life. Incentives for physical activity and social interaction may help alleviate the difficulties associated with these changes[9].

Surgery associated with nerve plexuses: paresthesia resulting from surgical injury to the intercostobrachial nerve. Chemotherapeutic agents and radiotherapy may lead to the development of superior brachial plexopathy, with mobility restrictions. Higher incidence after conservative surgeries (sectorectomies with axillary dissection), possibly by association with radiotherapy or by preservation of the small nerve bundles in techniques with small incisions. The injuries to brachial nerve bundles, after isolated or associated surgery, may lead to a greater involvement of the axilla, due to more aggressive axillary dissection and the use of radiotherapy and endocrine therapy[10,11].

Effects of systemic therapy: chemotherapeutic agents may lead to amenorrhea and, if post-left radiotherapy, may damage the heart. Endometrial thickening, weight gain, decreased bone calcium, marked bone loss in patients with premature or early menopause among postmenopausal women, and muscle and joint pain[8] are consequences of hormonal treatment. Peripheral neuropathies may coexist due to the use of microtubule-stabilizing agents, such as paclitaxel and docetaxel, although the mechanism remains uncertain. In the late phase, the findings include perineural fibrosis and vascular injury[12].

Related to radiotherapy: restriction of movement may be due to axillary web syndrome (AWS), the presence of pain in the scar, surgical wound, pectoral muscle, or axilla. The prevalence of this restriction may range between 10% and 70%, depending on the evaluation method (measurement or self-report), type and time elapsed after surgery, with more frequent associations in mastectomies and radiotherapy than in sectorectomies, and the absence of radiotherapy. Radio-induced cutaneous fibrosis is variable[12].

Restriction of movement: restricted flexion of the isolateral shoulder joint occurs after a sentinel lymph node biopsy. Regarding other movements, amplitudes were similar in these two groups[12].

Injury to the lymphatic system: injury to the axillary lymph nodes causes lymphostasis and lowers the threshold of the nociceptive impulse, causing pain, hypersensitivity, and allodynia. Lymphostasis may lead to regional or general accumulation of fluids in the interstitial space (i.e., acquired secondary lymphedema), a characteristic of lymphovascular incompetence. An ineffective response to stimuli caused by physical exercise could indicate a higher risk of developing lymphedema. However, lymphatic abnormalities seem to be a consequence of lymphedema per se, and not only to the treatment of breast cancer. Lymphedema after conservative surgery and sentinel lymph node biopsy is significantly less common than after more extensive axillary surgery[13].

Lymphedema: the chronicity of lymphedema leads to hypertrophy of the subcutaneous cellular tissue and the development of fibrosis. The postoperative and radiotherapy prevalence ranges from 9.4% to 25%, one to five years after diagnosis, depending on the evaluation method, laterality, number of lymph nodes removed, surgical site infection, postoperative drainage time, ipsilateral limb immobility, obesity, skinny skin flaps with removal of lymphatics from subcutaneous tissue, and extensive incisions. However, The prevalence of lymphedema may be

overestimated when self-reports are considered, as sensory disorders (e.g., paresis or paresthesias) may be mistaken for it[13].

Seromas, hematomas, and infection: women who are obese after a radical mastectomy are more susceptible to seroma formation than those who have undergone a simple mastectomy. Low fibrinogen levels, fibrinolytic network activity in lymphatic fluids, sectioning of lymphatic vessels, surgical scars, early removal of drains, and a cavity located between the anterior chest wall and the skin of the mastectomy site contribute to seroma formation. Recurrent and late episodes of breast cellulitis after quadrantectomy or radiotherapy have an incidence of around 5%. They may be associated with hematoma, seroma, lymphedema of the upper limb, and excision of a larger glandular volume, requiring the exclusion of inflammatory carcinoma of the breast[14,15].

Pain: pain in the region of surgery was reported by 47% of women one to three years after the end of treatment, and by 92% in 12 months after radiotherapy. Chronic pain seems to be higher in young women, with advanced primary stage, surgical technique, radiotherapy, chemotherapy, depression, immunodeficiency, and more evident pain in the immediate postoperative period. Pain complaints tend to decrease over time, persisting in around 20% patients for three years after surgery. A few patients experience chronic incisional pain, which may be debilitating, refractory to analgesics, lasting for months or years after surgery[16].

Axillary web syndrome, lymphedema cord, or cord: related to surgery with an armpit approach, with the formation of a cord network, mostly visible depending on the skin thickness, and may be broken with traction (Figure 1). It has variable incidence and extent, in younger and thinner women, diabetic, arterial hypertension, smokers, with upper limb volumes > 200 ml. Some cases are associated with lymphedema and exhibit variable appearances, both in the immediate postoperative period and months or years after surgery. Pathological and anatomical evidence support the angiolymphatic origin of the AWS through differential diagnosis with similar pathophysiological morbidities. The AWS is self-limiting, with therapeutic handling by non-steroidal anti-inflammatory drugs[17].

Figure 1. Axillary web syndrome (AWS).

Frozen shoulder syndrome: a rare condition that can be caused by surgical treatment and radiotherapy.

CONCLUSION

Treatment of breast cancer may lead to debilitating morbidities, detected even years after the therapeutic event. These morbidities, often adaptive, lead to physical, psychological, and social disorders. An analysis and search for the best scientific evidence is needed to identify preventive measures.

REFERENCES

1. Humphris G, Yang Y, Barracliffe L, Cameron J, Bedi C. Emotional talk of patients with breast cancer during review appointments with therapeutic radiographers: effects on fears of cancer recurrence. Support Care Cancer. 2018. doi: 10.1007/s00520-018-4484-7.
2. Ju J, Zhu AJ, Yuan P. Progress in targetd therapy for breast cancer. Chronic Dis Transl Med. 2018;4(3):164-175. doi: 10.1016/j.cdtm.2018.04.002.
3. Hopkinson J. Psychosocial support in cancer cachexia syndrome: the evidence for supported self-management of eating problems during radiotherapy or chemotherapy treatment. Asia Pac J Oncol Nurs. 2018; 5(4):358-368. doi: 10.4103/apjon.apjon_12_18..
4. Gee HE, Moses L, Stuart K, Nahar N, Tiver K, Wang T, Ward R, Ahern V. Contouring consensus guidelines in breast cancer radiotherapy: comparison and systematic review of patterns of failure. J Med Imaging Radiat Oncol. 2018. doi:10.1111/1754-9485.12804.
5. Yan M, Abdi MA, Falkson C. Axillary management in breast cancer patients: A Comprehensive review of the key rials. Clin Breast Cancer. 2018; pii: S1526-8209(18)30448-8. doi: 10.1016/j.clbc.2018.08.002.
6. Allahverdiyev AM, Parlar E, Dinparvar S, Bagirova M, Abamor EŞ. Current aspects intreatment of breast cancer based of nano drug delivery systems and future prospects. Artif Cells Nanomed Biotechnol. 2018: 1-8. doi: 10.1080/21691401.2018.1511573.
7. Samadi P, Saki S, Dermani FK, Pourjafar M, Saidijam M. Emerging ways to treatbreast cancer: will promises by met?. Cell Oncol (Dordr). 2018. doi: 10.1007/s13402-018-0409-1
8. Resnicow K, Patel MR, Mcleod MC, Katz SJ, Jagsi R. Physician attitudes about cost consciousness for breast cancer treatment: differences by cancer sub-specialty. Breast Cancer Res Treat. 2018; doi: 10.1007/s10549-018-4976-7.
9. Andersen KG, Aasvang EK, Kroman N, Kehlet H. Intercostobrachial nerve handling and pain after axillary lymph node dissection for breast cancer. Acta Anaesthesiol Scand. 2014; 58(10):1240-8. doi: 10.1111/aas.
10. Andersen KG, Kehlet H. Persistent pain aftereast cancer treatment: a critical review of risk factors and strategies for prevention. J Pain. 2011;12(7):725-46. doi: 10.1016/j.jpain.2010.12.005.
11. Harris SR. Axillary web sydrome in breast cancer: a prevalent but under-recognized postoperative complication. Breast Care (Basel).2018;13(2):132-135. doi:10.1159/000485023..
12. Seité S, Bensadoun RJ, Mazer JM. Prevention and treatment of acute and chronic radiodermatitis. Breast Cancer (Dove Med Press). 2017; 9:551-557. doi: 10.2147/BCTT.S149752.
13. Duyur Cakıt B, Pervane Vural S, Ayhan FF. Complex decongestive therapy in breast cancer-related lymphedema: does obesity affect the outcome negativevely. Lymphat Res Biol. 2018. doi: 10.1089/lrb.2017.0086.
14. Groen WG, van Harten WH, Vallance JK. Systematic review and meta-analysis of distance-based physical activity interventions for cancer survivors (2013-2018): we still havent found what we´re looking for Cancer Treat Rev.2018; 69:188-203. doi: 10.1016/j.ctrv.2018.07.012.
15. Ebner F, Friedl TWP, de Gregorio A, Lato K, Bekes I, Janni W, de Gregorio N. Seroma in breast surgery: all the surgeons fault?Arch Gynecol Obstet. 2018. doi: 10.1007/s00404-018-4880-8.
16. Chow E. Prevalence of pain in patients with breast cancer post-treatment: a systematic review. Breast. 2018; 42:113-27. doi: 10.1016/j.breast.2018.08.105.
17. Moskovitz AH, Anderson BO, Yeung RS, Byrd DR, Lawton TJ, Moe RE: Axillary web syndrome after axillary dissection. Am J Surg. Volume 181. 2001:434-439.