Follow-Up After Breast Cancer

BBSG – Brazilian Breast Study Group

Introduction

The number of breast cancer survivors has increased steadily due to early diagnosis and advances in treatment. It is estimated that there are 3,000,000 women with a history of breast cancer in the United States, which corresponds to 41% of all women with cancer in that country. These patients are exposed to the appearance of a new tumor, local recurrence, other types of cancer, and adverse effects of the treatment received. There are differences in the literature on the best way to follow up such patients, which contributes to a variation of conduct among entities that guide daily practice.

Definition and Objectives

Follow-up can be defined as the period from the time of diagnosis/treatment to the occurrence of a relapse or death. The objectives of the follow-up are to diagnose a local or contralateral relapse early, to evaluate and resolve possible treatment-related complications, and to provide psychological support and information necessary to restore a normal life.

BBSG – Brazilian Breast Study Group (✉)
BBSG, Sao Paulo, SP, Brazil

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Table 1 Frequency of physical exam follow-up

Physical exam	ASCO	ESMO	NCCN
First year	3–6 months	3–4 appointments/year	1–4 appointments/year
Second year	3–6 months	3–4 appointments/year	1–4 appointments/year
Third year	3–6 months	Annually	1–4 appointments/year
Fourth year	6 months	Annually	1 to appointments /year
Fifth year	6 months	Annually	1–4 appointments/year
Sixth year on	Annually	Annually	Annually

Clinical Follow-Up

There is no evidence from randomized studies regarding the periodicity and time of patients follow-up. The recommendations of the American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN), and European Society of Surgical Oncology (ESMO) are summarized in Table 1.

During the appointment, anamnesis must be targeted at the symptoms and signs of local recurrence or distant metastasis.

- Pain or breast lumps
- Headache, altered visual acuity, and behavioral changes
- Coughing and dyspnea
- Nausea, vomiting, and change in appetite
- Genital bleeding and hematuria
- Osteoarticular pain

During physical examination and skeletal muscle, lung, cardiac, genital and abdominal evaluation should be performed

Complementary Exams

Mammography

Post-treatment mammography for breast cancer shows a decrease in mortality in all age groups. This practice is aimed at the detection of ipsilateral cancer after conservative surgery and contralateral breast disease. In patients undergoing conservative surgery, the first mammogram should be performed between 6 months and 1 year after radiotherapy is completed and continued annually.

Ultrasonography

The indication of mammary ultrasonography at follow-up is restricted to the mammography complement. There is no evidence to justify its routine use in the follow-up of patients with breast cancer. A study comparing mammography and

ultrasonography versus isolated mammography showed an increase in the diagnosis of local recurrence from 8 to 12 cases per 1000 but with a false-positive increase from 4.4% to 10.4%.

Magnetic Resonance Imaging (MRI)

The use of MRI in post-treatment follow-up deserves prospective studies. Evidence shows an increase in unnecessary procedures due to high sensitivity and low specificity. However, in women at high risk of local recurrence, genetic mutation carriers or high risk family history, they benefit from the MRI at follow-up.

Systemic Follow-Up

In the follow-up of asymptomatic patients, there is no evidence that routine radiological examinations and early diagnosis of metastases result in improved survival. Routine use of these tests will result in high rates of false-positive and false-negative results, with a significant financial impact.

For patients using aromatase inhibitors, attention should be given to bone density, indicating bone densitometry.

Regarding the use of tamoxifen, especially in extended therapy, evaluation of the endometrium with transvaginal ultrasound should be performed only in cases of abnormal bleeding. This routine examination should not be used because of the increase in false-positive results, which will result in unnecessary invasive exams (hysteroscopy or uterine curettage).

Genetic Counseling

The NCCN suggests that patients diagnosed with invasive carcinomas, triple-negative tumors and who are younger than 60 years be investigated for mutation of Brca1 and Brca2 genes. Especially in young patients with a suggestive family history, one should consider the genetic tests.

Treatment Complications

Patients with childbearing potential should be advised of the possible reproductive consequences of adjuvant treatment. An evaluation with a reproduction specialist is recommended to evaluate the best way to preserve fertility before starting chemotherapy.

The possible side effects resulting from systemic treatment are usually managed in a multidisciplinary team, but we must remember specially the cardiac effects of some drugs, especially anthracycline and trastuzumab.

The most common complaints following treatment are due to the early menopause caused by chemotherapy drugs and treatment with prolonged hormone therapy.

Among patients who use tamoxifen, hot flushes represent one of the most common complaints. Venlafaxine and desvenlaflaxine are the drugs of choice, with about 50% efficacy. In refractory cases, the use of gabapentin and clonidine is described in the literature but with a high incidence of side effects.

Osteopenia should be managed in association with lifestyle guidelines (exercises, adequate diet, exposure to sun) and with calcium and vitamin D replacement. In patients at risk for osteoporosis development and with AI, bisphosphonates can be used.

Currently, there is a growing use of denosumab, a monoclonal antibody that inhibits osteoclast activity with a subcutaneous half-yearly application. The drug most commonly used in our environment is zoledronic acid, intravenously every 6 months. It acts on the inhibition of osteoclast action. Its main side effects are increased risk of osteonecrosis of the jaw, hypocalcemia, and renal failure.

Other symptoms that deserve attention are the following:

- Sexual dysfunction (loss of libido, dyspareunia, genital atrophy)
- Depression and anxiety
- Cognitive dysfunctions
- Fatigue
- Symptoms resulting from surgical treatment (lymphedema, paresthesia, movement limitations) and radiotherapy (radiodermity, edema, actinic pneumonitis, cardiopathy)

Physical Activity and Life-Style Habits

Recently, more attention has been given to regular physical activity and life style habits in the prevention of recurrence of breast cancer. It is up to the mastologist to recommend and supervise that the patients follow these recommendations.

A 2005 study published in JAMA showed that those who walked for at least 30 min, on average five times a week at speeds of 5–6 km/h (or performed equivalent exercises), had about 60% reduction in the risk of disease recurrence, as well as lower mortality from breast cancer and lower probability to die from other causes.

Potential risk reduction is associated with physical exercise, reduced levels of insulin-like growth factor (IGLF), as well as other factors associated with carcinogenesis.

Overall Guidelines

In premenopausal patients, contraception with hormone contraceptives is contraindicated, regardless of the receptors; so non-medicated intrauterine devices, barrier methods, or tubal ligation/vasectomy are recommended.

It is strongly advised that smoking, alcohol consumption, and sedentary life style habits be avoided, while keeping the body mass index below 25 is recommended.

Recommended Reading

1. Ellegaard MB, Grau C, Zachariae R, Jensen AB. Women with breast cancer report substantially more disease- and treatment-related side or late effects than registered by clinical oncologists: a cross-sectional study of a standard follow-up program in an oncological department. Breast Cancer Res Treat. 2017;164(3):727–36. *A prospective study showing that intensive post-treatment investigation does not diagnose early-stage metastases. More important than research is the management of complications of long-term treatment, according to questionnaires answered by patients.*
2. Khatcheressian JL, Hurley P, Bantug E, et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013;31(7):961–5. *Recommendations of the American Society of Clinical Oncology, not indicating complementary radiological and biochemical exams in asymptomatic women. However, it concludes that patients with tumors of worse prognosis (triple negative) need better studies to evaluate the impact of intensive follow-up.*
3. Lash TL, Fox MP, Buist DS, et al. Mammography surveillance and mortality in older breast cancer survivors. J Clin Oncol. 2007;25(21):3001. *Prospective study with over 1800 women above 65 y-o, with breast cancer at stages I and II, showing that continuation of tracking after treatment led to lower rate of specific death cases.*
4. Quinn EM, Coveney AP, Redmond HP. Use of magnetic resonance imaging in detection of breast cancer recurrence: a systematic review. Ann Surg Oncol. 2012;19(9):3035. *Meta-analysis including 10 studies and 494 patients, aiming to evaluate the impact on magnetic resonance imaging in recurrence of breast cancer. It showed the high sensitivity, but low specificity of this test, determining a greater number of interventions.*
5. Senkus E, Kyriakides S, Ohno S, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015;26(Suppl 5):v8–30. *Recommendations of the European Society of Oncology as to post-treatment follow-up.*