Breast cancer in elderly women – perspective of geriatricians
Câncer de mama na mulher idosa – a visão do geriatra

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ABSTRACT
Breast cancer is one of the neoplasms with highest incidence and prevalence among women. Elderly women are frequently excluded from clinical trials and very few prospective data on this age group are collected. In this article, we reviewed some aspects of this type of cancer in the elderly population. Although elderly women are frequently spared of full doses of toxic treatments, some data suggest that there is significantly higher benefit when normal-dose therapy is well tolerated. The current review suggests that chronological age by itself should not be a criterion to withhold chemotherapy. Due to heterogeneity in the geriatric population, prospective studies are necessary to address global geriatric assessment.

Keywords: Breast neoplasms; Aged; Female; Drug toxicity

INTRODUCTION
Breast cancer is one of the neoplasms with highest incidence and prevalence among women in most of the world. Despite major progress achieved thanks to modern treatment in past decades, older women are frequently excluded from clinical trials and few prospective data are collected regarding these individuals. We reviewed epidemiological data on this population and approached aspects related to tolerance to treatment.

EPIDEMIOLOGY
Breast cancer is the most prevalent neoplasm in women in industrialized countries and represents, at least, one third of all cases of cancer. The incidence is closely related to aging, although it is also a relatively frequent neoplasm in younger women.

In 2005, in the United States, a total of 21,2930 new cases were diagnosed, with 40,870 deaths due to the disease in the same period. Half of the patients diagnosed were over 65 years and this proportion is estimated to grow 30% in the next ten years⁽¹⁾. Older populations, such as in Switzerland, have the highest rates of breast cancer in Europe. Life expectancy of Swiss women is particularly high (around 82.5 years), and women aged over 80 years represent 5% of the female population of the country. Over 500 new cases of breast cancer are diagnosed per year in this population group, and represent 12% of all cases of breast cancer⁽²⁾, showing a high incidence in women of very advanced age.
In Brazil, breast cancer also ranks first among women (with the exception to non-melanoma skin cancer), with an estimated total of 48,930 new cases, in 2006, representing an estimated risk of 52 cases per 100,000 women(3).

LACK OF GERIATRIC DATA

Despite the increased incidence of cancer with aging, medical society faces a certain nonsense: the inclusion of patients over 70 years in major clinical trials is negligible. The results of these studies are eventually extrapolated from young individuals to geriatric patients, despite the influence that age at diagnosis has in the natural history of the disease(4-5) and in tolerance to treatment. In this fashion, adjuvant treatments (postoperative) that have proven to be beneficial to young women, may have only marginal benefits in elderly patients(6). On the other hand, heterogeneity of the elderly population makes the clinician frequently establish less aggressive treatments, based on some prerogatives, such as low functional reserves, theoretical more indolent course of disease, low survival consequent to multiple comorbidities and questions as to effectiveness and toxicity of chemotherapy. Several smaller studies show more conservative management by oncologists(1-2,6-7).

Mortality due to breast cancer decreases year after year, and this information is well defined for women aged under 70 years. Still, this statement is not true for more elderly patients. In the 70 to 79 year-old group, the specific mortality rate has remained stable and it has grown for women over 81 years(7). In the United States, specific breast cancer mortality was 27% for women over 80 years in 2001, although this group contributed only with 13% of cases of this type of cancer(7).

According to a recent retrospective study(8), specific breast cancer mortality would depend on the presence of hormone receptors and age at diagnosis. The authors reviewed 234,828 patients diagnosed between 1990 and 2003, and 77% of the sample comprised patients with hormone receptor expression. They verified that mortality in women with hormone-sensitive tumors declined 38% and 19% for women with non hormone-sensitive tumors. For women in the same conditions, but above this age, the decrease was 14% for those with hormone-sensitive tumors and without statistic significance for patients with non hormone-sensitive tumors.

The efficacy and toxicity of adjuvant chemotherapy for patients over 70 years are very much discussed in Oncology, given prospective studies have not answered this question. In order to fill this gap and access preliminary data, several authors have been carrying out retrospective analyses.

Bouchard et al.(2) published a retrospective study on 407 women with breast cancer and aged over 80 years from 1989 to 1999. The sample comprised 48 (12%) non treated patients; 132 (32%) patients that received only treatment with tamoxifen; 28 (7%) were submitted to conserving surgery; 133 (33%) were submitted to mastectomy; in 57 (14%) patients conserving surgery was associated to adjuvant chemotherapy; and nine patients (2%) received various treatments. Specific survival for breast cancer in five years was respectively 46, 51, 82 and 90% for women without treatment, women receiving only hormones, only mastectomy, and conserving surgery associated to adjuvant therapy. The authors concluded that half of these patients were insufficiently treats but had expressive decrease in survival as a consequence. The current challenge is to establish treatment protocols adjusted to the population group and health status that provide the best likelihood of cure, regardless of age.

Elkin et al.(9) performed a study aimed at patients aged over 66 years, with hormone receptor negative breast cancer but with lymph node involvement, from 1992 to 1999, using the Medicare database (public healthcare system offered to the geriatric population and used by most of this population in the United States). A total of 45,701 women with breast cancer were identified – in that, 5,081 with hormone receptor negative tumors and 1,711 (34%) of them received chemotherapy in the first six months after diagnosis. Adjusting for potential confounding factors, chemotherapy reduced general mortality by 16%. According to the bivariate analysis, chemotherapy was associated with the presence of large tumors, extensive nodal involvement, metastatic disease, poorly differentiated tumors and the presence of little co-morbidity. This study, therefore, showed a significant benefit on survival for this sample. Analyzing subgroups, the 70 to 74-year group was 44% less likely to receive chemotherapy in comparison to the 66 to 69-year group. Indication for chemotherapy increased throughout the years, representing 25% for cases diagnosed in 1992 and 45% in 1999.

A meta-analysis study, published in 1998(10) on women aged 50 to 69 years with nodal involvement and hormone receptor expression, showed that the absolute reduction in general mortality was 2.3% within ten years when they were submitted to chemotherapy (in addition to hormone therapy). Comparatively, the utilization of acetylsalicylic acid in order to prevent cardiovascular events yields a 2 to 5% drop in mortality(11). Hence, the absolute reduction in mortality by 1 to 3% in elderly women treated by chemotherapy fits into the expected average in secondary prevention(6).

Patients with advanced age referred to chemotherapy are known to frequently not receive ideal treatment,
whether because of choice of drugs, or due to a dose below that standardized for young patients. Efficacy may be reduced exactly due to more conservative management in these cases(12).

**TOXICITY IN THE ELDERLY POPULATION**

Regarding treatment toxicity in the geriatric population, Hurria et al.(13) studied 1,405 women submitted to chemotherapy according to three classical regimens (CMF = cyclophosphamide, methotrexate and fluorouracil; AC = cyclophosphamide, doxorubicin; ACT = cyclophosphamide, doxorubicin and paclitaxel). The authors verified that the incidence of toxicity depends more on the type of drug used than age or presence of concomitant chronic conditions. Patients who received regimens with doxorubicin developed with a higher incidence of grade 3 and 4 toxicity and required more hospitalizations.

In a prospective study carried out between 2001 and 2003, the primary goal of Hurria et al.(14) was to verify the toxicity of adjuvant chemotherapy and detect the impact on functionality and quality of life of patients aged over 65 years. The variables analyzed were: Functional Assessment Cancer Therapy (FACT, quality of life scale applied to oncology patients), mini mental state examination (MMSE), Geriatric Depression Scale (GDS), Katz (functionality scale), Charlson (comorbidity scale) and nutritional status. Forty-nine patients participated, and approximately half had toxicity grade 3 and 4. Thrombotic complications occurred in 9% of patients who received CMF. Despite these complications, patients kept their ability to carry out instrumental activities of daily living (IADL) and basic daily life activities (BDLA), maintained the same psychological standard, with no increased incidence of depressive symptoms and did not change quality of life scores. The authors concluded that it is possible to reduce toxicity rates even further in this population, but emphasized tolerance that these patients demonstrated to treatment, since no decrease in functionality after chemotherapy was shown. Therefore, age analyzed alone should not be a barrier to indicate chemotherapy(15).

**CONCLUSIONS**

Due to the heterogeneity inherent to the elderly population, it is necessary to perform oriented prospective studies, including aspects of global geriatric assessment, in order to offer the best treatment to these patients and, at the same time, respect their limitations. Otherwise, there is a risk of transforming the best intent to treat in subtreatments or iatrogeny.

**REFERENCES**