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Has breast cancer in the elderly remained the same over recent decades? A comparison of two groups of patients 70 years or older treated for breast cancer twenty years apart

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ABSTRACT

Objectives: Breast cancer (BC) in the elderly population is by far the most frequent malignancy in Western countries; however, little evidence is available regarding the specific management of this group. The purpose of this study was to identify how the biological and clinical characteristics of cancer have changed over the past 20 years by comparing two groups of elderly patients with breast cancer operated on 20 years apart. The secondary endpoint was to underline potential changes in surgical strategy over the past 20 years.

Materials and Methods: One group of consecutive elderly patients undergoing surgery for BC between January 1990 and December 1993 (Group A), and one group undergoing surgery between January 2008 and December 2011 (Group B) were identified and analyzed. Data regarding surgical treatment, stage, tumor grading, hormonal and HER2/neu receptors, and Ki-67 were collected and compared.

Results: A total of 422 elderly patients underwent surgical treatment, 142 in Group A and 280 in Group B. An earlier stage at presentation was detected in Group B, T1 (57.5% B vs. 31.6% A) and N0 (64.6% B vs. 54.2% A). Surgical treatment in the first group was more extensive while conservative procedures were more frequently performed in the second group. Despite the earlier presentation, tumor grade was higher in Group B (G3 10.6% A vs. 32.1% B, $p < 0.05$). Overexpression of Ki-67 was again more frequent in Group B (56.2% B vs. 32.5% A, $p < 0.05$). Hormonal and HER2/neu receptor expression was comparable.

Conclusions: Nowadays, elderly patients with BC are more likely to present at an early stage; therefore, conservative surgery is a feasible option. Despite potential bias related to changes of pathology and immunohistochemistry examination techniques over the decades, the biological characteristics of recent patients with BC seem to be consistent with more aggressive tumors. Tailored treatment should be offered with regard to biological age, the cancer-specific profile and active life expectancy.

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1. Introduction

Breast cancer is the most common type of cancer among women, and age is one of the most important risk factors for developing this disease.[1] It is estimated that 21% of cases occur in women over 70 years of age.[2] Despite the magnitude of the issue, there is little solid evidence regarding the management of this specific group of patients, leading to treatment based on incomplete knowledge. On the other hand, physicians are more likely to treat elderly patients with cancer following their own "gut feeling", overtreating in some cases and undertreating in others.

There were no specific guidelines for the management of elderly patients until 2007 when the International Society of Geriatric Oncology (SIOG) created, for the first time, a dedicated task force to provide precise recommendations for treating elderly women with breast cancer. Despite this effort, several issues still remain unresolved. For the treatment of breast cancer in elderly women, clinical practice is mostly based on clinical trials which have actually excluded these patients from the population studied; therefore, there are still many areas in which Level 1 evidence regarding the proper management of this specific category of patients is lacking.[3,4]

At the same time, the biological behavior of breast cancer is also not fully understood in this population. Patients are often treated with the idea that breast cancer in the elderly should have a favorable prognosis with no lymph node involvement, positive hormone receptors, a low proliferation rate and negative Her-2 receptor score.[2,4] However, in the past few years, it has been observed that there has been an increase in more aggressive cancers in this population, and a recent review of the United States population has estimated that 15% of breast cancers in older patients are triple negative.[2]

Yu et al. have also confirmed this statistic in the Asian population, reporting a study from the Shanghai Cancer Hospital where triple negative breast cancers represented 18.4% of all breast cancer cases in patients over 70 years of age.[5] Moreover, an increased rate of axillary lymph node involvement, even in small tumors, has been observed in older women, suggesting more aggressive cancers.[6]

The purpose of this study was to identify how the biological and clinical characteristics of cancer have changed over the past 20 years by comparing two groups of elderly patients with breast cancer operated on 20 years apart.

The secondary endpoint was to underline potential changes in surgical strategy over the past 20 years.

2. Materials and Methods

A retrospective analysis of the Breast Unit Database (including radiological, surgical and pathological data) was carried out in order to identify two groups of patients, 70 years and older, operated on for breast cancer between 1990 and 1993 (Group A) and between 2008 and 2011 (Group B). Invasive or in situ breast cancer was confirmed by pathological examination in all cases.

The Group A time frame (1990–1993) was chosen according to the date when complete immunohistochemical analysis was standardized in our Pathology Department. The Group B time frame was chosen in order to have the widest gap possible from the first group in order to be able to recognize changes as compared to the 1990s population.

The specific data set included: type of cancer (lobular vs. ductal vs. mixed ductal/lobular vs. other), stage at the moment of the surgical treatment (tumor-node-metastasis (TNM) classification) and tumor grading (G1, G2 and G3). When no axillary treatment was performed because of carcinoma in situ or in a few cases with invasive cancer but no palpable axillary lymph nodes, the stage was calculated using the size of the tumor (T) only. Immunohistochemical data included estrogen receptors (ERs) and progesterone receptors (PGRs), human epidermal growth factor receptor 2 (HER2/neu) and Ki-67 expression.

Cancer subtypes were obtained using immunohistochemical analysis and were classified following the St. Gallen 2011 Consensus Conference recommendations on Luminal A, Luminal B, HER-2 positive and Triple Negative (TN) breast cancers.[7]

The type of surgery was also noted: breast conserving surgery (BCS) vs. total mastectomy (TM), sentinel lymph node biopsy (SLNB) vs. axillary lymph node dissection (ALND).

The tumor was graded according to the Elston–Ellis classification[8] for patients operated after June 1991 and according to the Bloom and Richardson system[9] for those who underwent surgery before that time.

Cancer estrogen and progesterone receptors were considered to be positive when more than 10% of the cell population was stained.[10,11]

Evaluation of the HER2/neu membrane receptors was carried out according to international standards for immunohistochemical analysis[12]; in the case of an equivocal result, in situ hybridization was performed in order to evaluate potential gene amplification.

HER2/neu membrane receptors were considered as positive in case of a 3+ immunohistochemistry score or, in case of equivocal results, when HER2/neu protein was amplified with in situ hybridisation.[13,14]

The Ki-67 expression was defined as "high" (indicating a high proliferation rate) when detected in more than 14% of cancer cells.[7,15]

Over the course of years, the laboratory methodology for detecting Ki-67 expression has changed. For Group A (1990–1993), the mouse monoclonal antibody, clone MIB-1 (Dakopatts, Glostrup DK) was used; for Group B (2008–2011), instead, the rabbit monoclonal antibody, clone 30-9 (Ventana, Tucson USA), was utilized. In both groups, a computerized image analyzer was used to detect Ki-67 positivity. A minimum of 12 peripheral fields was selected (200×) for each tumor, evaluating the proportion of colored cells for not less than 1000 nuclei. The image analyzer automatically calculated the colored nuclear area as compared to the global nuclear area of the neoplastic population examined. Pathological and biomolecular examinations were carried out by the same pathologist (D.S.) and the same biologist (C.C.) in both groups.

The Statistical Package for the Social Sciences version 11 for Windows® (SPSS® Chicago, IL) was used to carry out the statistical analysis. The Fisher's exact test was carried out to compare the two study populations. A P-value of $p < 0.05$ was considered statistically significant.