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Original article

Prognostic features of breast cancer differ between women in the Democratic Republic of Congo and Belgium



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ABSTRACT

Objectives: Compared to European women, breast cancers in African women present at a younger age, with a higher tumor grade and are more often estrogen receptor (ER)/progesterone receptor (PR) negative. We here investigate the histopathological and immunohistochemical characteristics (ER, PR and human epidermal growth receptor 2 (HER2)) and the proportion of triple negative (Tneg) invasive breast cancers from an unselected series of patients diagnosed in Kinshasa, and compare them to a population of Caucasian women with a palpable breast cancer.

Materials and methods: From 2010 till 2013, during the first breast cancer awareness campaign, organized in Kinshasa, 87 patients were diagnosed with invasive breast cancer. Diagnose was based on core biopsy. The control group consisted of Caucasian women (University Hospitals of Leuven, Belgium) with a palpable mass, diagnosed between 2000 till 2009, treated with surgery of which the histopathological and immunohistochemical characteristics were collected on excision specimens. Each patient in the Kinshasa group was matched based on age and tumor size to one or more patients of the Leuven database. Differences between both groups with respect to hormone receptors (ER, PR, HER2, Tneg) or grade are presented as relative risks (RR). The analysis is based on a log-binomial model accounting for clustering through matching by a random intercept for cluster. Differences between both groups with respect to hormone receptors correcting for grade is performed by the inclusion of grade as a covariate in the model.

Results: After adjusting for age, tumor volume and tumor grade, ER was more frequently negative (RR = 0.71, p < 0.001), with a trend in the same direction for PR (RR = 0.87, p = 0.057), and HER2 more often positive (RR = 1.60, p = 0.015) compared to the group from the University Hospitals of Leuven. There was no difference in the proportion of breast cancers being triple negative. Sub-analysis showed that the higher HER2 positive rate was only observed in older patients (\geq 50y: RR = 2.07, p = 0.037) whereas no difference in HER2 positive rate was found in younger patients (\leq 50y: RR = 1.30, p = 0.358). A higher ER negative rate was observed in both age groups, however more pronounced in older patients (\geq 50y: RR = 0.64, p = 0.001; <50y: RR = 0.79, p = 0.018).

Conclusion: Breast cancer in women of Kinshasa presents at younger age and is more aggressive (more frequently ER negative and HER2 positive) compared to Caucasian women and this is more pronounced in older women (>50y). Only the ER results were concordant with the results of two similar studies

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(comparing an African with a European group), but were different when compared to studies on African-American women with breast cancer. This information is very important considering the treatment option: as more tumors are ER negative, endocrine therapy cannot be given while chemotherapy is often too expensive.

Introduction

Worldwide, breast cancer remains the most frequently diagnosed malignancy in women. In developed countries, improvements in screening and adjuvant treatments have resulted in declining mortality rates, but breast cancer remains the leading cause of cancer death worldwide. In contrast with Europe the incidence rate in Sub-Saharan Africa is 25.5 per 100,000 and the mortality rate 19.3 per 100,000; for the Democratic Republic of Congo (DRC) the incidence rate is 23.5 per 100,000 and the mortality rate 14.2 per 100,000, showing a 4 times lower incidence but slightly lower mortality rate [1]. Due to demographic evolutions in Africa, incidence rates for breast cancer are increasing, even in the absence of screening. For example, in Uganda, population growth and aging have led to an increased breast cancer incidence from 11/ 100.000 in 1961 to 22/100.000 in 1995 [2,3]. A further increase in breast cancer incidence in Africa is anticipated, but the continent is one of the least prepared to face this unprecedented growth in cancer burden [4].

Retrospective studies have reported that 70-90% of African women present with advanced stage (stage III and IV) disease, which can be related to the lack of proper diagnostic facilities, but also to a more aggressive tumor biology among African women [5–7].

Previous studies on racial differences in breast cancer characteristics comparing African-American and African-British women with Caucasian women reveal not only breast cancer at younger age but also that African-American women were more likely to be diagnosed with higher grade and estrogen receptor (ER) negative breast cancer and triple negative (Tneg) tumors [5,7–13].

Studies on Sub-Saharan women i.e. of Nigeria, Central Sudan and Sub-Saharan Africa, showed similar results: presentation at younger age, larger tumor sizes at diagnosis, higher grade and more frequently ER and progesterone receptor (PR) negative breast cancers [5,7,13–15].

Comparing the biomarkers of breast cancer of indigenous women in Africa to black women in Europe and America suggest that genetics play an important role in breast cancer which can have an impact on the treatment of breast cancer in African women [16,17].

In Kinshasa (DRC), a breast cancer awareness program was started in 2010, since governmental bodies were not yet willing to invest in an organized screening program. The awareness program was initiated by the team of dr. G Luyeye in the General Hospital of Kinshasa (GHK) and was based on breast selfexamination (BSE) and clinical breast examination (CBE). The strategy of this program is described in Biomed Health Services [18]. During this program data on diagnosed breast cancers were collected.

The aim of the study is to investigate histopathological and immunohistochemical differences between breast cancers from an unselected series of patients diagnosed during the set-up of an awareness campaign in Kinshasa and compare them to a group of palpable (non-screen detected) breast cancers in a group of European women (Leuven, Belgium).

Materials and methods

Kinshasa patients

All women filled in a questionnaire and signed an informed consent to be included in this study. The study was approved by the ethical board of the General Hospital of Kinshasa. From 2010 till 2013 an awareness campaign on breast cancer was set up in Kinshasa: when a lump was palpated by BSE or during CBE, women were advised to present at the GHK. The involved radiologists and radiographers of the GHK received at least 3 months training in the University Hospital of Leuven, Belgium.

All palpable breast lumps were investigated with mammography, ultrasound and, in case of BIRADS 3, 4, 5 lesions, an additional needle biopsy or fine needle aspiration [19]. Only patients with invasive malignant breast lesions diagnosed on core biopsy were included while patients with in situ lesions were excluded. One patient underwent a fine needle aspiration cytology only and was excluded from the study.

For each of the invasive tumors, diameter, tumor grade, ER status, PR status and human epidermal growth factor receptor 2 (HER2) status were listed. These tumor characteristics were determined on the core needle biopsy specimen only, since not all women received surgical treatment and since no pathologist was available locally in case surgery was performed. For all patients, weight, length, body mass index (BMI) and age at diagnosis, number of pregnancies, number of children, age of menarche, menopausal status and 1-year follow-up were registered. The following subgroups were defined: ER/PR positive HER2 negative, ER/PR/HER2 positive, ER positive PR/HER2 negative, ER negative PR negative PR positive PR negative PR positive PR negative PR positive, ER negative PR positive HER2 negative PR PR/HER2 positive, ER positive HER2 negative ACM PR negative HER2 positive.

Pathology

Due to the lack of pathologists in the region of Kinshasa, the specimens were immersed in 4% formaldehyde for fixation and sent to the department of pathology of the University Hospital of Ghent (Belgium). No funding was received for these evaluations. Of each tumor, at least 3 samples of an 18 G needle biopsy were sent for evaluation.

The histologic subtype of invasive breast carcinoma and Nottingham histologic grade were defined [20]. Immunohistochemistry was done for ER, PR and HER2 using a Ventana Benchmark immuno stainer (Tucson, Arizona), with the manufacturer's supplied antibodies (clones 6F11 for anti-ER, 1A6 for anti-PR, and 4B5 for HER2). ER and PR were considered positive even if only focal nuclear staining was observed and negative if nuclear staining was completely absent. All ER and PR receptor evaluations were then rescored according to the Allred score: a score 0–1 was considered as negative, a score 2–8 as positive (ASCO-CAP Guideline Recommendations for Immunohistochemical Testing of Estrogen and Progesterone Receptors in Breast Cancer June 1, 2010 - See more at: http://www.instituteforquality.org/practice-guidelines#sthash. fTzpaGZL.dpuf). Because the ER/PR receptor status did not change Download English Version:

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