Pathology – Research and Practice 209 (2013) 433–440

Contents lists available at SciVerse ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.com/locate/prp

Original article

Breast cancer characteristics—Comparison of preoperative and postoperative values

Dusan Kolarik[a,*], Vaclav Pecha[b], Miroslava Skovajsova[c], Jozef Zahumensky[d], Marketa Trnkova[e], Lubos Petruzelka[f], Michael Halaska[g], Oldrich Sottner[g], Michal Otcenasek[g], Hana Kolarova[h]

[a] First Faculty of Medicine, Charles University in Prague, Czech Republic
[b] Department of Oncosurgery, Medicon s.r.o., Prague, Czech Republic
[c] Breast Unit Prague, Prague, Czech Republic
[d] Department of Gynecology and Obstetrics, Third Faculty of Medicine, Teaching Hospital Kralovske Vinohrady, Charles University in Prague, Czech Republic
[e] Biolab Praha s.r.o., Prague, Czech Republic
[f] Department of Oncology, First Faculty of Medicine, General Teaching Hospital, Charles University in Prague, Czech Republic
[g] Department of Gynecology and Obstetrics, First Faculty of Medicine, Hospital Na Bulovce, Charles University in Prague, Czech Republic
[h] Institute of Applied Mathematics and Information Technologies, Faculty of Natural Sciences, Charles University in Prague, Czech Republic

ARTICLE INFO

Article history:
Received 30 June 2012
Received in revised form 28 January 2013
Accepted 16 April 2013

Keywords:
Breast cancer
Characteristics
Preoperative diagnosis
Postoperative diagnosis
Biopsy

ABSTRACT

Breast cancer characteristics obtained at the time of diagnosis are important for setting the basic strategy of the treatment. Reliability of preoperative investigation differs for various features of the disease. The aim of this study was to ascertain the agreements and differences between preoperative and postoperative values.

This retrospective study analyzed the results of 617 women with primary surgery of the breast and axilla. Cohen's kappa coefficient has been employed to measure the degree of agreement between preoperative and postoperative values.

Substantial or "almost perfect" agreement has been documented for the histological type of the tumors, their histopathological grade, proliferation index Ki67, as well as for estrogen, progesterone, and HER-2/neu receptors. Substantial differences exist between preoperative and postoperative diagnoses of invasiveness of the tumor, determination of the size of the tumors, and the number of tumor foci. Preoperative imaging and clinical examination of lymph nodes exhibited unacceptably high false negative rates.

Heterogeneity of breast cancer cell population, methodology of histology examinations, and insufficient imaging of lymph nodes are the major limitations precluding satisfactory accuracy of preoperative diagnosis. Preoperatively diagnosed in situ carcinomas, as well as multifocal lesions, were the most often sources of diagnostic failures.

Introduction

Background

Breast cancer is the most frequent malignant disease in women responsible for 23% of all female malignancies. Its incidence of more than 120 cases per 100.000 women puts the Czech Republic among the countries with the highest rates of detection of this disease [32]. Prognostic and predictive markers are a key to understand the biologic characteristics, prognosis, and adequate treatment of breast cancer [23,33]. The independent prognostic value has been repeatedly proven for tumor size, histopathological grade, and lymph node status [11]; other studies also attribute this prognostic value to HER-2/neu [12,29]. Axillary lymph node status is the most important isolated prognostic factor for disease-free survival, as well as for overall survival of breast cancer patients [4,6]. The only reliable way to verify the lymph node status is by microscopic examination of dissected lymph nodes. Sentinel lymph node biopsy is a widely accepted alternative for complete axillary dissection in early breast cancer [22,24]. However, the average count of excised sentinel nodes should be 1.5–2.1 per patient [27], considering that the false negativity rate of sentinel lymph node biopsy decreases with each extra detected and excised sentinel node [25,26]. The size of the primary tumor reflected in its largest diameter correlates directly with the incidence of axillary metastatic involvement

* Corresponding author at: U vrbicek 168, 250 66 Zdiby, Czech Republic. Tel.: +420 736175858.
E-mail address: kolarikd@centrum.cz (D. Kolarik).

0344-0338/$ – see front matter © 2013 Elsevier GmbH. All rights reserved.
http://dx.doi.org/10.1016/j.prp.2013.04.011

[5,14,20]. Axillary lymph node status, together with tumor size and tumor grade, was in previous years widely used features for assigning a patient to systemic treatment [1,15,28]. At present, however, mainly the characteristics of the primary tumor itself are being used for indication of adjuvant therapy [8,16,17]. Hormonal receptor status, HER-2/neu status, and proliferation index Ki67 are the decisive features according to St. Gallen recommendations.

This study has two aims

First to describe the characteristics of early breast cancer in a population of Czech women. Second, to examine the reliability of preoperative investigations, i.e. to decide whether they are significantly different from features observed in postoperative histology specimens. These theoretical findings, thereafter, can be used for better individualization of the management of breast cancer patients, even at the time of diagnosis. Such findings can help to distinguish between primary surgery and neoadjuvant treatment, determine the type of neoadjuvant therapy, or establish if mastectomy or breast-conserving surgery is more appropriate.

Materials and methods

This trial presents a retrospective analysis of the data obtained from medical records of patients treated in a leading oncosurgical institution in Prague, Czech Republic; data collection and analysis were approved by an institutional ethical committee. The study population was composed of patients diagnosed with primary breast cancer between the years 2008 and 2010. Out of this group, 617 women underwent primary breast surgery (either breast conserving or mastectomy) followed by axillary sentinel lymph node biopsy in which at least one lymph node was obtained. In the case that one or more sentinel nodes contained tumor metastatic cells, standard axillary dissection was performed. The mean age of these patients was 57.9 years. Suspicion of malignancy was derived from imaging methods (mammography, ultrasonography, magnetic resonance) and clinical examination. Thereafter, the diagnosis was verified by core needle biopsy. All the patients also underwent necessary staging procedures to exclude distant metastases so that the exact clinical staging could be established according to the TNM system [3].

Clinical examination and imaging methods

Ultrasonography is more accurate for description of tumor extension than mammography. Magnetic resonance has been only used selectively, especially in cases in which ultrasound was hardly able to visualize and/or measure the lesion, or when the presence of more than one focus was suspected. Lymph node status (axillary and periclavicular) has also primarily been evaluated by ultrasound and physical examination.

Histopathological examination of the tumor and lymph nodes

The technique of processing and evaluating of samples is in accordance with the guidelines as summarized in the AJCC Cancer Staging Manual [2]. From the biopsy sample, the histological type of the tumor has been established (respecting the WHO classification 2003 [31]), its grade (according to Nottingham classification [13]), proliferative activity, and the presence of hormonal receptors and HER-2 receptors (following the ASCO and College of American Pathologists recommendations [21,35]). Definitive histology of surgical specimens, moreover, has taken into consideration the size of the lesion, its multifocality, and axillary lymph node status (these features have been preoperatively diagnosed by imaging methods) and also invasion of lymphovascular spaces (LVSI). This

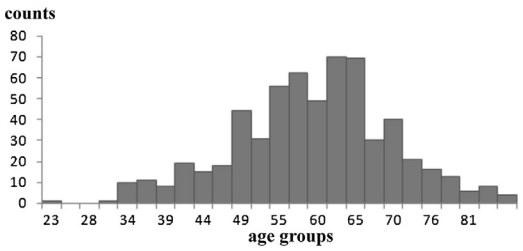

Fig. 1. Histogram of the distribution of the age of the patients.

LVSI cannot be reliably investigated preoperatively since the biopsy is directed to the center of the lesion, and LVSI must be obtained from the peripheral part of the tumor mass. The tumor is designated as "invasive" in the event that the spread of malignant cells through the basement membrane has been observed and/or myoepitelial cells were proved (using immunohistochemistry) inside tumorous lesion; otherwise, the tumor is considered as "carcinoma in situ" (CIS). The cases of preoperatively diagnosed CIS with invasion confirmed by postoperative histology are considered to be "invasive"; and in such cases, only the invasive component is taken into account when the size of the lesion is measured.

Cohen's kappa coefficient (κ) was used to measure the degree of correlation between preoperative and postoperative values; weighted kappa (κ_w) was used in characteristics with ordinal values. Kappa range $\kappa = 0.81–1$ indicates almost perfect congruence, $\kappa = 0.61–0.80$ substantial, $\kappa = 0.41–0.60$ moderate, $\kappa = 0.21–0.40$ fair and $\kappa = 0–0.20$ slight correlation [9]. In cases in which the value is missing for particular characteristics, the subject is then excluded from the analysis for that specific measurement. For this reason, the sum of all evaluated patients for specific characteristic will always be less than or equal to 617. Statistical software SPSS for Windows 10 has been used.

Results

The distribution of the study population according to age was not Gaussian (p-value = 0.002), with mean age reaching 57.9 years, range 23–86 and median 59 years (Fig. 1). The distribution according to body mass index (BMI) is shown in Fig. 2. It reflects usual body constitution of mostly postmenopausal women in the Czech population; the mean BMI was 26.7, range 14–50, median 26 (hypothesis of normal distribution was rejected on 5% level of statistical significance).

The following tables show a comparison between postoperative values (obtained from definitive histology) and preoperative results (those from biopsy and imaging methods).

For the invasiveness of the tumors (discrimination between benign histology, in situ carcinoma, and invasive cancer) $\kappa_w = 0.702$ proved substantial correlation of preoperative and postoperative values. However, a certain degree of disparity between the results

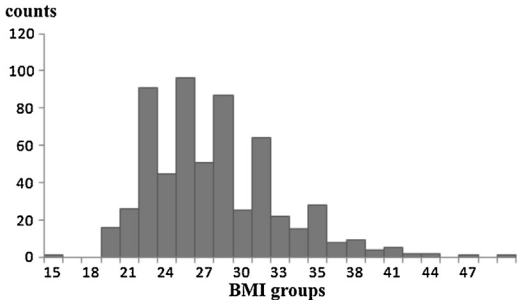

Fig. 2. Histogram of the distribution of the body mass index of the patients.