The Breast 34 (2017) 53–57

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Follow-up of patients with localized breast cancer and first indicators of advanced breast cancer recurrence: A retrospective study

Julien Viot [a], Martin Bachour [b], Aurélia Meurisse [c], Xavier Pivot [a], Frédéric Fiteni [a, c, *]

[a] University Hospital of Besançon, Department of Medical Oncology, France
[b] Bregille Reeducation Center, Besançon, France
[c] University Hospital of Besançon, Methodology and Quality of Life in Oncology Unit, France

ARTICLE INFO

Article history:
Received 20 January 2017
Received in revised form
9 May 2017
Accepted 10 May 2017

Keywords:
Breast cancer
Diagnosis
Follow-up
Recurrence

ABSTRACT

We conducted a retrospective study to assess the follow-up of patients with localized breast cancer and the first indicators of advanced breast cancer recurrence.

All patients with advanced breast cancer recurrence treated between January 2010 and June 2016 in our institution were registered. Among these patients, 303 patients initially treated for early breast cancer with curative intent were identified.

After initial curative treatment, follow-up involved the oncologist, the general practitioner and the gynecologist in 68.0%, 48.9% and 19.1% of cases, respectively. The median DFI was 4 years for luminal A, 3.8 years for luminal B, 3.7 years for HER2-positive and 1.5 years for TNBC ($p = 0.07$). Breast cancer tumor marker was prescribed for 164 patients (54.1%). No difference in terms of follow-up was observed according to the molecular subtype. Symptoms were the primary indicator of relapse for 143 patients (47.2%). Breast cancer recurrence was discovered by CA 15.3 elevation in 57 patients (18.8%) and by CAE elevation in 3 patients (1%). The rate of relapse diagnosed by elevation of CA 15.3 or CAE was not statistically associated with the molecular subtype ($p = 0.65$). Luminal A cases showed a significantly higher rate of bone metastases ($p = 0.0003$). TNBC cases showed a significantly higher rate of local recurrence ($p = 0.002$) and a borderline statistical significant higher rate of lung/pleural metastases ($p = 0.07$).

Follow-up recommendations could be adapted in clinical practice according to the molecular subtype. General practitioners should be more involved by the specialists in breast cancer follow-up.

1. Introduction

Ten-year survival of breast cancer exceeds 70% in most European regions, with 89% survival for local and 62% for regional disease [1]. The aims of follow-up are to detect early recurrences and to evaluate and treat therapy-related complications. International or national organizations (American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), Haute Autorité de Santé) have published evidence-based clinical practice guidelines on breast cancer follow-up and management in asymptomatic patients after primary, curative therapy [2–4]. Nevertheless, variations in practice exist and have different cost implications. In the follow-up of patients with localized breast cancer, a large difference in costs has been observed between different regimens, with no change in health outcomes expected. De Bock et al. conducted a meta-analysis of 12 studies which assessed the proportion of isolated locoregional recurrences diagnosed during routine visits or routine tests in asymptomatic patients compared with the proportion of isolated locoregional recurrences in symptomatic patients. In these 12 studies, 40% of patients had been diagnosed as having no symptoms and 18% as having symptoms [5]. In a retrospective study conducted by Pivot et al. of 1145 patients with metastatic breast cancer, symptoms were the primary indicator of relapse in 57.6% of patients [6]. Moreover, the annual hazard of recurrence peaks in the second year after diagnosis, but remains at 2%–5% in years 5–20 and many studies have demonstrated that the time and the sites of recurrence depend on the breast cancer molecular subtype [7–10].

In this retrospective study, we describe the follow-up of patients with localized breast cancer and the first indicators of advanced recurrence.

* Corresponding author. University Hospital of Besançon, Department of Medical Oncology, 3 boulevard Fleming, 25000, Besançon, France.
E-mail address: fredericfiteni@gmail.com (F. Fiteni).

http://dx.doi.org/10.1016/j.breast.2017.05.005
0960-9776/

2. Methods

2.1. Study population

Patients were identified using a computerized software for chemotherapy prescriptions that transfers prescriptions from the medical office to the centralized pharmaceutical unit in charge of antineoplastic drugs preparation BPC (acronym for Bonne Pratique de Chimiothérapie). Through this database, all patients with advanced breast cancer (ABC) (i.e. with any unresectable recurrence) treated between January 2010 and June 2016 in the university hospital of Besançon were registered. Among these patients, only those who were initially treated for early breast cancer with curative intent were identified for follow-up screening. Our study population was divided into four subtypes: luminal A (estrogen receptor (ER) + and/or progesterone receptor (PR) > 20%, human epidermal growth factor receptor type 2 (HER2) - and Ki-67 < 10%); luminal B (ER + and/or PR ≤ 20%, HER2 - and Ki-67 ≥ 10%; HER2-enriched (HER2 +); and triple-negative breast cancer (TNBC) (ER -, PR - and HER2 -) [2].

2.2. Statistical analysis

We used the mean and range to analyze continuous variables, and proportions for categorical variables. We compared proportions using a chi-squared test, or Fisher's exact test where appropriate. A p-value of 0.05 or lower was considered statistically significant. Disease-free interval (DFI) was defined as the time between the primary breast cancer and the local or distant recurrence. An ANOVA regression was performed to analyze the association between the DFI and the breast cancer subtype. All analyses were performed using SAS software, Version 9.3 (SAS Institute).

3. Results

3.1. Clinicopathological features

Among 574 patients with ABC, 303 patients were initially treated for localized breast cancer with curative intent. Mean age at diagnosis of localized breast cancer was 52 (range, 27–87). Among the 303 patients, 95 (31.4%) were luminal A, 32 (9.9%) luminal B, 34 (11.2%) were HER2 +, 35 (11.6%) were TNBC and 107 (35.3%) were unknown. The characteristics of patients are presented in Table 1.

3.2. Follow-up

After initial curative treatment, follow-up involved the

Table 1
Patients' characteristics.

Characteristics	All patients (n = 303)	Luminal A (n = 95)	Luminal B (n = 32)	HER2 + (n = 34)	TNBC (n = 35)
Age at diagnosis, years [mean (range)]	52 (27–87)	52 (27–79)	56 (34–87)	52 (32–87)	51 (31–82)
Type, n (%)					
Ductual	199 (65.7)	66 (69.4)	23 (71.9)	30 (88.2)	28 (80)
Lobular	55 (18.2)	23 (24.2)	6 (18.8)	2 (5.9)	3 (8.6)
Unknown	49 (16.2)	6 (6.3)	3 (9.4)	2 (5.9)	4 (11.4)
Tumor size, n (%)					
T1	85 (28.1)	31 (32.6)	10 (31.3)	15 (44.1)	8 (22.9)
T2	105 (34.7)	43 (45.3)	15 (46.9)	11 (32.4)	16 (45.7)
T3-T4	26 (8.6)	12 (12.6)	4 (12.5)	1 (2.9)	3 (8.6)
Unknown	87 (28.7)	9 (9.5)	3 (9.4)	7 (20.6)	8 (22.9)
N stage, n (%)					
N0	57 (18.8)	13 (13.7)	9 (28.1)	4 (11.8)	10 (28.6)
N1	77 (25.4)	22 (23.2)	6 (18.8)	14 (41.2)	10 (28.6)
N2	46 (15.2)	22 (23.2)	5 (15.6)	6 (17.7)	4 (11.4)
N3	27 (8.9)	11 (11.6)	4 (12.5)	8 (8.8)	5 (14.3)
Unknown	96 (31.7)	27 (28.4)	8 (25)	7 (20.6)	6 (17.1)
Histologic grade, n (%)					
I	27 (8.9)	9 (9.5)	1 (3.1)	0 (0)	1 (2.9)
II	124 (40.9)	53 (55.8)	15 (4.7)	13 (38.2)	6 (17.2)
III	67 (22.1)	21 (22.1)	12 (37.5)	16 (47.1)	22 (62.9)
Unknown	85 (28)	12 (12.6)	4 (12.5)	5 (14.7)	6 (17.2)
Local treatment, n (%)					
breast conservation	131 (43.2)	29 (30.5)	14 (43.8)	16 (47.1)	24 (68.6)
Mastectomy	153 (50.5)	60 (63.2)	18 (56.3)	13 (38.2)	10 (28.6)
Unknown	19 (6.3)	6 (6.3)	0	5 (14.7)	1 (2.9)
Neoadjuvant chemotherapy, n (%)					
Done	65 (21.5)	28 (29.5)	11 (3.6)	9 (26.5)	16 (45.7)
Not done	238 (78.6)	67 (70.5)	21 (65.6)	25 (73.5)	21 (54.3)
Adjuvant chemotherapy, n (%)					
Done	168 (55.4)	53 (55.8)	17 (53.1)	23 (67.6)	17 (48.6)
Not done	125 (41.3)	39 (12.9)	14 (43.8)	10 (29.4)	18 (51.4)
Unknown	10 (33)	3 (3.2)	1 (3.1)	1 (2.9)	0
Endocrine therapy, n (%)					
Done	209 (69.0)	87 (91.6)	25 (78.1)	17 (50)	0
Not done	83 (27.4)	6 (6.3)	6 (18.8)	16 (47.0)	35 (100)
Radiotherapy, n (%)	11 (3.6)	2 (2.1)	1 (3.1)	1 (2.9)	0
Done	266 (87.8)	85 (89.5)	27 (28.4)	32 (94.1)	33 (94.3)
Not done	25 (8.3)	7 (7.4)	3 (3.2)	1 (2.9)	1 (2.9)
Unknown	12 (4.0)	3 (3.2)	2 (2.1)	1 (2.9)	1 (2.9)
Anti-HER2 therapy, n (%)					
Done	0	0	0	26 (76.5)	0
Not done	0	0	0	8 (23.5)	0