Population-based study of breast cancer in older women: prognostic factors of relative survival and predictors of treatment

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Abstract

Background: A large proportion of women with breast cancer (BC) are elderly. However, there is a lack of information regarding BC prognostic factors and care in this population. The aims of this study were to assess the prognostic factors of relative survival (RS) among women with BC aged ≥ 75 years old and to identify the predictive factors of treatments administered to this population.

Methods: A population-based study was performed using data from the Cote d’Or breast and gynaecological cancer registry. Women aged 75 years and older with primary invasive BC and resident in Cote d’Or at the time of diagnosis made between January 1998 and December 2008 were retrospectively selected. Prognostic factors of RS were estimated in a generalized linear model with a Poisson error structure. RS rate for the whole population was given at 5 years. Logistic regression models were used to identify the predictors of the treatments administered.

Results: Six hundred and eighty-one women were included. Median age at diagnosis was 80. Comorbidities (p=0.02), pT stage (p=0.04), metastases (p=<0.001), having a family doctor (p=0.03) and hormone-receptor status (p=0.006) were independent prognostic factors of RS. The RS rate at 5 years for the whole population was 78.2%, 95%CI = [72.2-83.0]. Age, pT stage, metastases, histoprognostic SBR grade, hormone receptor status and comorbidities were frequently found to be predictors of treatment with surgery alone, hormone therapy alone, breast conserving surgery plus adjuvant therapy and mastectomy plus adjuvant therapy.

Conclusions: Comorbid conditions adversely affect survival in older women with breast cancer. Moreover the results of this study showed that there are numerous predictors of the type of treatment administered, and that the most important were age and comorbidities.

Keywords: Breast cancer, Elderly women, Predictors of treatment, Prognostic factors, Relative survival

Background

Breast cancer (BC) is the most common malignancy in women in France [1-4]. With the aging population and the increase in life expectancy, cancer in elderly people is increasing and this now constitutes a major public health concern.

Many studies have reported data about the prognostic factors of survival among women with BC [5,6]. Despite improved knowledge of these prognostic factors, there are no data about the prognostic factors of relative survival (RS) among older women with BC in a whole population. The treatment strategy for BC is based on the initial stage of the tumour, the patient’s age, general health, tumour histology and prognostic factors [7]. Progress made in the diagnosis and therapeutic management of BC [8-10] has led to improvements in prognosis and overall quality of survival [11]. However, elderly women with BC are currently undertreated in comparison with the youngest, and this leads to a considerable decrease
in specific survival [12-14]. Current therapeutic approaches in older women are most often empiric. Therapeutic decisions are based on wishful thinking on behalf of patients and their loved ones and on the clinician’s impressions [15-18]. Moreover, 12% of patients with BC aged ≥ 80 years old do not receive treatment and 44% do not undergo surgery. Older women are also less likely to receive treatment in compliance with guidelines [19]. In addition, comorbidities, which are particularly common among older women, complicated the management of cancer treatment [20].

Contrary to a long-standing belief, BC can be as aggressive in elderly patients as in younger women. Consequently, the management of older patients with BC should not differ from that in young patients. However, the predictors of treatment in the elderly have not yet been clearly assessed [13,14].

Cancer registries provide a unique opportunity to assess survival and to evaluate the predictors of treatments given in routine practice in this population on comprehensive population-based data.

The first aim of this study was to assess the prognostic factors of RS among women with BC aged ≥ 75 years. The secondary purpose was to identify the predictors of treatment in this population.

Methods

Population

A population-based study was undertaken using data from the Cote d’Or breast and gynaecological cancer registry. This registry is the only one in France that focuses on breast and gynaecological cancers. It has been collecting comprehensive population-based data since 1982. Women aged 75 years and older with primary invasive BC and residing in Cote d’Or at the time of diagnosis made between January 1998 and December 2008 were retrospectively selected. Women lost at the date of diagnosis were excluded. For patients with synchronous bilateral BC, the most advanced tumour according to the number of positive nodes, the tumour size, the Scarff, Bloom, and Richardson (SBR) grade, and the tumour histology was included.

Studied variables and end points

All patients were staged according to the TNM system [21]. We considered the pathologic TNM (pTNM) classification or, when absent, the clinical TNM (cTNM) classification. We used the cTNM for the predictors of treatments because the categories of treatments included surgery or other exclusive treatments without surgery; the pTNM could therefore not be used, and for the prognostic factors we used the pTNM, replaced by the cTNM when the patients were not treated with surgery.

Age at diagnosis was categorized into three classes: 75-79 years, 80-84 years and ≥ 85 years. Pathological tumour size and the number of removed and positive nodes were also recorded. Removed nodes were categorized into two classes: ≤ 10 nodes and > 10 nodes and positive nodes into three classes: 0, 1-3 and ≥ 4 nodes. Tumour characteristics, such as SBR grade classified as grades 1+2 or grade 3, and hormone receptor status, considered positive when oestrogen and/or progesterone were positive, were also collected. Clinical and demographic data, such as the circumstances of diagnosis (clinical diagnosis or individual screening), the matrimonial status (single or not), having a family doctor (yes or no), the vital status (dead or alive) and the place of residence (rural or urban) were recorded too. The comorbidities were collected at the diagnosis, as were all of the diseases associated with BC at the time of diagnosis: diabetes, high blood pressure, neurological disease (Alzheimer, Parkinson, epilepsy), psychiatric illness, tuberculosis, thyroid disorder, genetic abnormalities and previous history of disease affecting treatment administration. Comorbidities were classified in two categories: at least one comorbidity and no comorbidity. The period of diagnosis was split into two: 1998-2003 and 2004-2008 according to the median of distribution. Treatments were grouped into exclusive categories: surgery alone, hormone therapy alone, breast-conserving surgery plus adjuvant therapy (BCS plus adjuvant therapy) and mastectomy plus adjuvant therapy. Patients without treatment constituted the “no treatment” category, and the “others” category was used for the following exclusive treatments: chemotherapy alone, radiotherapy alone, chemotherapy plus hormone therapy, chemotherapy plus radiotherapy, radiotherapy plus hormone therapy, chemotherapy plus radiotherapy plus hormone therapy, neoadjuvant chemotherapy plus surgery plus adjuvant therapy and neoadjuvant chemotherapy plus surgery.

Survival was calculated from the date of diagnosis until the date of death or the date of last follow-up. The cut-off date for the survival analysis was set at 01 January 2010. Patients who were alive after the cut-off date were censored.

Statistical methods

Quantitative variables are given as means, standard deviations (SD), medians and ranges, while qualitative variables are given as percentages. The percentage of missing values is also provided.

Treatments categories were compared according to the follow-up periods using Chi2 tests. Cochran-Armitage trend tests were used to compare treatments according to the age classes.

RS rate with the 95% confidence interval (CI) for the whole population was given at 5 years. RS is an estimator of the excess mortality ratio (EMR) estimated from life tables as the ratio of the observed survival of the patients (where all deaths are considered events) to the expected survival (ES) [22]. The ES was estimated using Cote d’Or female life-expectancy tables stratified by age.
| Variables | N (681) | % | Mean (SD) | Median [min:max] |
|-----------|---------|---|-----------|------------------|
| Age at diagnosis (years) | 681 | 81.3 (5.2) | 80.0 [75;98] |
| Pathological tumor size (mm) | 546 | 27.0 (19.8) | 22.0 [2;160] |
| Nodes removed | 612 | 8.2 (6.3) | 8.0 [0;32] |
| Positive nodes | 519 | 2.0 (4.0) | 0.0 [0;32] |
| Age | | | |
| 75-79 | 310 | 45.5 |
| 80-84 | 208 | 30.5 |
| ≥ 85 | 163 | 23.9 |
| Unknown | 0 | 0.0 |
| T stage | | | |
| T0 | 8 | 1.2 |
| T1 | 214 | 31.4 |
| T2 | 186 | 27.3 |
| T3 | 19 | 2.8 |
| T4 | 108 | 15.9 |
| Unknown | 146 | 21.4 |
| N stage | | | |
| N0 | 451 | 66.2 |
| N1 | 112 | 16.4 |
| N2 | 10 | 1.5 |
| N3 | 2 | 0.3 |
| Unknown | 106 | 15.6 |
| M stage | | | |
| M0 | 579 | 85.0 |
| M1 | 64 | 9.4 |
| Unknown | 38 | 5.6 |
| pT stage | | | |
| p T1 | 259 | 38.0 |
| p T2 | 206 | 30.2 |
| p T3 | 20 | 2.9 |
| p T4 | 64 | 9.4 |
| p T* | 130 | 19.1 |
| Unknown | 2 | 0.3 |
| pN stage | | | |
| p N0 | 350 | 51.4 |
| p N+ | 269 | 39.5 |
| Unknown | 62 | 9.1 |
| pM stage | | | |
| p M0 | 576 | 84.6 |
| p M1 | 64 | 9.4 |
| Unknown | 41 | 6.0 |
| Nodes removed | | | |
| Nodes ≤10 | 389 | 57.1 |
| Nodes > 10 | 223 | 32.7 |
| Unknown | 69 | 10.1 |
| Positive nodes | | | |
| 0 | 290 | 42.6 |
| 1 - 3 | 136 | 20.0 |
| ≥ 4 | 93 | 13.7 |
| Unknown | 162 | 23.8 |
| Histoprog nostic SBR grade | | | |
| 1 | 132 | 19.4 |
| 2 | 350 | 51.4 |
| 3 | 160 | 23.5 |
| Unknown | 39 | 5.7 |
| Diagnosis circumstances | | | |
| Clinic | 471 | 69.2 |
| Individual screening | 109 | 16.0 |
| Unknown | 101 | 14.8 |
| Place of residence | | | |
| Urban | 474 | 69.6 |
| Rural | 203 | 29.8 |
| Unknown | 4 | 0.6 |
| Hormone receptors | | | |
| Positive | 590 | 86.6 |
| Negative | 80 | 11.7 |
| Unknown | 11 | 1.6 |
| Comorbidities | | | |
| Yes | 419 | 61.5 |
| No | 163 | 23.9 |
| Unknown | 99 | 14.5 |
and period-matched mortality rates. The EMR was estimated in a generalized linear model with a Poisson error structure [23]. Follow-up time was stratified in annual intervals. Prognostic factors of survival were assessed using univariate and multivariate analyses of RS.

Univariate and multivariate logistic regression models were performed to identify the predictive factors of the administration of the different type of exclusive treatments: surgery alone, hormone therapy alone, BCS plus adjuvant therapy alone and mastectomy plus adjuvant therapy alone. Odds Ratios (OR) and their 95% confidence intervals (CI) are given.

For RS and logistic regression, all variables with a univariate p-value ≤ 0.20 were eligible for multivariate analyses. Correlations and interactions were tested for eligible variables. To prevent co-linearity, when two variables were significantly correlated, one variable was retained according to its clinical relevance or to the value of the likelihood ratio. All reported p values are two sided. The statistical significance level was set at p<0.05. Analyses were done using SAS (Statistical Analysis system version 9.2) and or STATA (version 9.0).

**Ethics statement**

The Breast and Gynaecologic Cancer Registry of Cote d’Or was approved by the CNIL (National Commission on Informatics and Liberties) for the collection and recording data for research purposes (authorization number DR-2012-038).

### Results

**Patients’ characteristics**

Seven hundred and fifteen (715) women aged 75 years and older with invasive primary BC were registered from January 1998 to December 2008. Among them, 34 were lost to follow-up at the date of diagnosis. Finally, 681 patients were included in the study. The median age at diagnosis was 80 (range, 75 to 98 years). The clinical and pathological features of the studied population are summarized in Table 1.

Information on comorbidities was missing for 14.5% of the women. The comorbidities recorded were: high blood pressure (27%), diabetes (5.4%), neurological disease (3%), obesity (1.2%), psychiatric illness (1%), tuberculosis (1.5%), thyroid disorder (4%), previous history of stroke, heart failure or thrombosis (8%), and previous history of disease affecting treatment administration (10%).

**Treatment description**

Concerning treatment, 52 (7.6%) underwent surgery alone, and hormone therapy alone was given to 74 (10.9%). BCS plus adjuvant therapy was given to 238 (34.9) while 211 patients (31%) received mastectomy plus adjuvant therapy. Nineteen (2.8%) did not receive treatment and 26 patients (3.8%) were treated by other treatments: chemotherapy alone or radiotherapy alone or chemotherapy plus hormone therapy or radiotherapy plus hormone therapy or chemotherapy plus radiotherapy plus hormone therapy or chemotherapy plus neoadjuvant chemotherapy plus surgery plus adjuvant therapy or neoadjuvant chemotherapy plus surgery plus adjuvant therapy or neoadjuvant chemotherapy plus surgery. For 1998-2003 and 2004-2008, the use of BCS plus adjuvant therapy (p=0.63), mastectomy plus adjuvant therapy (p=0.52) and other treatments (p=0.43) was similar. In contrast, patients were less often treated by surgery alone in the second period (p<0.001): 11.2% and 4.4% for 1998-2003 and 2004-2008, respectively. The use of hormone therapy alone was more frequent in the second period (p=0.001): 6.5% and 14.7%, respectively (Table 2).

Older patients were more likely to be treated with surgery alone (p=0.02) and with hormone therapy alone (p<0.001) and were more likely to receive no treatment (p=0.006). BCS plus adjuvant therapy (p<0.001) and other treatments (p=0.03) were less likely to be given to older patients. In contrast, the use of mastectomy plus adjuvant therapy did not vary with age (p=0.40) (Table 3).

**Prognostic factors and analyses of RS**

The median follow-up was 3 years (min-max) = (0.01-11.96). At the cut-off, 305 deaths (45%) had occurred. RS rates decreased with follow-up. RS at 1 year for the whole population was 93.5%, 95% CI = [90.5-95.5] and at 5 years was 78.2%, 95% CI = [72.2-83.0].

In the multivariate analysis, the pathological tumor size correlated with the pT stage, and we therefore retained the pT stage for the analyses. Examined and
positive nodes correlated with clinical N stage and pN stage, respectively, and we retained the clinical N stage and pN stage for the analyses.

Multivariate RS analyses revealed an increased risk of death in patients with an advanced pT stage: Relative Excess Rates (RER) = 2.58, 95% CI = [1.23-5.42], in patients with metastasis at the time of diagnosis: RER = 6.86, 95% CI = [3.43-13.73] and in patients with comorbidities: RER = 2.35, 95% CI = [1.03-5.36]. In contrast, a decreased risk of death was observed in patients who had a family doctor: RER = 0.22, 95% CI = [0.07-0.68] and in patients with hormone-receptor positive tumours: RER = 0.33, 95% CI = [0.16-0.70] (Table 4).

Predictive factors of treatments administered
Predictors of the treatments are listed in Table 5. Patients with hormone-receptor positive tumours or patients diagnosed in the period from 2004 to 2008 were less likely to undergo surgery alone. OR were 0.29, 95% CI = [0.12-0.72], and 0.40, 95% CI = [0.20-0.78], respectively. Older patients with metastasis did not receive surgery alone. The oldest patients (≥85 years), patients with metastasis or with comorbidities were more often treated with hormone therapy alone. The oldest patients (80-84 and ≥85 years) or patients with advanced tumours (stages T2 and T3+T4) were less likely to receive BCS plus adjuvant therapy. In contrast, patients with advanced tumours (stages T2 and T3+T4) were more likely to be treated with mastectomy plus adjuvant therapy, OR were 5.57, 95% CI = [3.09-10.03] and 3.60, 95%CI = [1.78-7.29], respectively. Patients with histo-prognostic SBR grade 3 were more likely to be treated with mastectomy plus adjuvant therapy, OR= 2.18, 95% CI = [1.26-3.76]. Moreover, there were interactions between age and the circumstances of diagnosis for the predictors of mastectomy plus adjuvant therapy (p<0.001). Indeed, patients aged ≥85 years with a clinical diagnosis were 74% less likely to be treated with

| Table 2 Treatment description by period |
|----------------------------------------|
| Period | 1998-2003 (N=321) | 2004-2008 (N=360) | p value* | All cases (N=681) |
| Treatments | | | | |
| No treatment | 0.65 | | |
| Yes | 10 | 3.1 | 9 | 2.5 | 19 | 2.8 |
| No | 306 | 95.3 | 340 | 94.4 | 646 | 94.9 |
| Unknown | 5 | 1.6 | 11 | 3.1 | 16 | 2.3 |
| Surgery alone | <0.001 | | |
| Yes | 36 | 11.2 | 16 | 4.4 | 52 | 7.6 |
| No | 254 | 79.1 | 328 | 91.1 | 582 | 85.5 |
| Unknown | 31 | 9.7 | 16 | 4.4 | 47 | 6.9 |
| Hormone therapy | 0.001 | | |
| Yes | 21 | 6.5 | 53 | 14.7 | 74 | 10.9 |
| No | 264 | 82.2 | 282 | 78.3 | 546 | 80.2 |
| Unknown | 36 | 11.2 | 25 | 7.2 | 61 | 9.0 |
| Breast conserving surgery plus adjuvant therapy | 0.63 | | |
| Yes | 113 | 35.2 | 125 | 34.7 | 238 | 34.9 |
| No | 193 | 60.1 | 231 | 64.2 | 424 | 62.3 |
| Unknown | 15 | 4.7 | 4 | 1.1 | 19 | 2.8 |
| Mastectomy plus adjuvant therapy | 0.52 | | |
| Yes | 95 | 29.6 | 116 | 32.2 | 211 | 31.0 |
| No | 210 | 65.4 | 230 | 63.9 | 440 | 64.6 |
| Unknown | 16 | 5.0 | 14 | 3.9 | 30 | 4.4 |
| Others† | 0.43 | | |
| Yes | 10 | 3.1 | 16 | 4.4 | 26 | 3.8 |
| No | 275 | 85.7 | 319 | 88.6 | 594 | 87.2 |
| Unknown | 36 | 11.2 | 25 | 6.9 | 61 | 9.0 |

Abbreviations: N = number of patients.
*Chi 2 test.
†Others: chemotherapy alone, radiotherapy alone, chemotherapy plus hormone therapy, chemotherapy plus radiotherapy, radiotherapy plus hormone therapy, chemotherapy plus radiotherapy plus hormone therapy, neoadjuvant chemotherapy plus surgery plus adjuvant therapy, neoadjuvant chemotherapy plus surgery.
mastectomy plus adjuvant therapy than were those aged between 75 and 79 years old with a clinical diagnosis.

**Discussion**

The results of this study showed that tumours were discovered at an advanced stage in elderly patients. Nine per cent of patients had metastatic tumours and 9.4% had inflammatory tumours or tumours with extension to the skin or to the chest wall.

According to the follow-up period, older patients were less likely to be treated with surgery alone and more likely to receive hormone therapy alone in the more recent period. These results are in line with a study conducted by Bastiaannet et al, which showed that patients aged ≥ 75 years were less likely to undergo surgery and more likely to have hormone therapy [24]. One possible explanation could be that more recently surgery alone was not proposed to treat BC because with the improvement in breast cancer management other, more effective treatments like hormone therapy or treatment combinations have been preferred to surgery alone to treat older women with BC. Other explanations could be that elderly women with BC are too frail and have more advanced tumours associated with the presence of comorbidities.

Regarding the assessment of RS, the analyses were done on comprehensive data. Moreover, in this population-based study, the follow-up for vital status was complete for all included patients with no patients lost to follow-up at the cut-off date. Our multivariate analyses of RS showed that pT stage, metastasis, having a family doctor, hormone receptor status and comorbidities were independent predictors of the length of survival. pT stage, metastasis and hormone receptor status have already been shown to be prognostic factors of survival in BC patients [6]. Indeed, the influence of hormone receptors could be attributed to the efficacy of hormone therapy given to patients with

| Table 3 | Treatment description by age |
|---|---|---|---|---|---|
| Age | 75-79 (N=310) | 80-84 (N=208) | ≥85 (N=163) | p value* | All cases (N=681) |
| Treatments | 310 | % | 208 | % | 163 | % | 681 | % |
| No treatment | | | | | 0.006 | |
| Yes | 4 | 1.3 | 6 | 2.9 | 9 | 5.5 | 19 | 2.8 |
| No | 304 | 98.1 | 197 | 94.7 | 145 | 89.0 | 646 | 94.9 |
| Unknown | 2 | 0.6 | 5 | 2.4 | 9 | 5.5 | 16 | 2.3 |
| Surgery alone | | | | | 0.02 | |
| Yes | 19 | 6.1 | 13 | 6.3 | 20 | 12.3 | 52 | 7.6 |
| No | 272 | 87.7 | 184 | 88.5 | 126 | 77.3 | 582 | 85.5 |
| Unknown | 19 | 6.1 | 11 | 5.3 | 17 | 10.4 | 634 | 93.1 |
| Hormone therapy | | | | | <0.001 | |
| Yes | 12 | 3.9 | 18 | 8.7 | 44 | 27.0 | 74 | 10.9 |
| No | 277 | 89.4 | 176 | 84.6 | 93 | 57.1 | 546 | 80.2 |
| Unknown | 21 | 6.8 | 14 | 6.7 | 26 | 16.0 | 61 | 9.0 |
| Breast conserving surgery plus adjuvant therapy | | | | | <0.001 | |
| Yes | 144 | 46.5 | 69 | 33.2 | 25 | 15.3 | 238 | 34.9 |
| No | 157 | 50.6 | 135 | 64.9 | 132 | 81.0 | 424 | 62.3 |
| Unknown | 9 | 2.9 | 4 | 1.9 | 6 | 3.7 | 19 | 2.8 |
| Mastectomy plus adjuvant therapy | | | | | 0.40 | |
| Yes | 92 | 29.7 | 83 | 39.9 | 36 | 22.1 | 211 | 31.0 |
| No | 208 | 67.1 | 116 | 55.8 | 116 | 71.2 | 440 | 64.6 |
| Unknown | 10 | 3.2 | 9 | 4.3 | 11 | 6.7 | 30 | 4.4 |
| Others† | | | | | 0.03 | |
| Yes | 18 | 5.8 | 5 | 2.4 | 3 | 1.8 | 26 | 3.8 |
| No | 271 | 87.4 | 189 | 90.9 | 134 | 82.2 | 594 | 87.2 |
| Unknown | 21 | 6.8 | 14 | 6.7 | 26 | 16.0 | 61 | 9.0 |

Abbreviations: N = number of patients.

*Cochran-Armitage trend test.
†Others: chemotherapy alone, radiotherapy alone, chemotherapy plus hormone therapy, chemotherapy plus radiotherapy, radiotherapy plus hormone therapy, chemotherapy plus radiotherapy plus hormone therapy, neoadjuvant chemotherapy plus surgery plus adjuvant therapy, neoadjuvant chemotherapy plus surgery.
hormone-receptor positive tumours. A recent study showed that comorbidities had a significant impact on survival after BC with poorer survival among old patients with one or more comorbid conditions [25]. Patients who had a family doctor had a lower risk of death than those without a family doctor. This could be explained by the fact that patients who had a family doctor were more likely to be diagnosed with less advanced BC.

| Table 4 Prognostic factors for relative survival |
|------------------------------------------------|
| Factors                          | Univariate analysis | Multivariate analysis (N=495) |
|                                 | N=(681) | Number of deaths | RER | 95% CI | p value | RER | 95% CI | p value |
| Age                             | 681     | 0.001            | 0.18 |
| 75-79                           | 310     | 107              | 1    | 1      |
| 80-84                           | 208     | 88               | 0.99 | 0.52-1.88 | 1.01 | 0.47-2.16 |
| ≥85                             | 163     | 110              | 2.75 | 1.68-4.48 | 2.15 | 1.02-4.55 |
| pT stage                        | 658     | <0.001           | 0.04 |
| pT0+pT1                         | 283     | 91               | 0.53 | 0.24-1.17 | 1.77 | 0.72-4.36 |
| pT2                             | 245     | 109              | 1    | 1      |
| pT3+pT4                         | 130     | 89               | 3.89 | 2.20-6.82 | 2.58 | 1.23-5.42 |
| pN stage                        | 619     | <0.001           | 0.14 |
| pN0                             | 350     | 132              | 1    | 1      |
| pN+                             | 269     | 135              | 3.13 | 1.68-5.75 | 1.75 | 0.80-3.83 |
| pM stage                        | 640     | <0.001           | <0.001 |
| pM0                             | 576     | 227              | 1    | 1      |
| pM1                             | 64      | 47               | 10.18 | 6.11-16.95 | 6.86 | 3.43-13.73 |
| Having a family doctor          | 672     | <0.001           | 0.03 |
| No                              | 51      | 41               | 1    | 1      |
| Yes                             | 621     | 258              | 0.17 | 0.11-0.28 | 0.22 | 0.07-0.68 |
| Histoprognostic SBR grade       | 642     | <0.001           | 0.08 |
| 1+2                             | 482     | 185              | 1    | 1      |
| 3                               | 160     | 93               | 2.73 | 1.66-4.51 | 1.87 | 0.93-3.79 |
| Hormone receptors               | 670     | <0.001           | 0.006 |
| Negative                        | 80      | 46               | 1    | 1      |
| Positive                        | 590     | 255              | 0.38 | 0.23-0.63 | 0.33 | 0.16-0.70 |
| Comorbidities                   | 582     | 0.03             | 0.02 |
| No                              | 163     | 51               | 1    | 1      |
| Yes                             | 419     | 179              | 4.26 | 1.13-16.28 | 2.35 | 1.03-5.36 |
| Diagnosis circumstances         | 580     | 0.10             | 0.13 |
| Clinic                          | 471     | 209              | 1    | 1      |
| Individual screening            | 109     | 27               | 0.13 | 0.01-1.48 | 0.42 | 0.11-1.65 |
| Place of residence              | 677     | 0.43             |      |
| Rural                           | 203     | 92               | 1    |      |
| Urban                           | 474     | 211              | 0.82 | 0.50-1.35 |      |
| Period                          | 681     | 0.79             |      |
| 1998-2003                       | 321     | 190              | 1    |      |
| 2004-2008                       | 360     | 115              | 1.07 | 0.66-1.73 |      |
| Matrimonial status              | 471     | 0.89             |      |
| Single*                         | 288     | 131              | 1    |      |
| Not single                      | 183     | 73               | 0.96 | 0.53-1.75 |      |

Abbreviations: RER = relative excess rates; CI = confidence interval, N = number of patients.

* Patient single, divorced or widowed.
Table 5 Multivariate logistic regression analysis of predictive factors of treatments administered

| Variables                        | OR   | 95% CI       | p value |
|----------------------------------|------|--------------|---------|
| Predictive factors for surgery alone * (N=537) |      |              |         |
| Age                              | 0.06 |              |         |
| 75-79                            | 1    |              |         |
| 80-84                            | 1.28 | 0.57-2.88    |         |
| ≥85                              | 2.52 | 1.15-5.54    |         |
| N stage                          |      | 0.05         |         |
| N0                               | 1    |              |         |
| N+                               | 0.36 | 0.13-1.01    |         |
| Hormone receptors                |      |              |         |
| Negative                         | 1    |              |         |
| Positive                         | 0.29 | 0.12-0.72    |         |
| Period                           |      | 0.008        |         |
| 1998-2003                        | 1    |              |         |
| 2004-2008                        | 0.40 | 0.20-0.78    |         |
| Histoprognostic SBR grade        |      | 0.25         |         |
| 1+2                              | 1    |              |         |
| 3                                | 1.59 | 0.72-3.49    |         |
| Place of residence               |      | 0.16         |         |
| Rural                            | 1    |              |         |
| Urban                            | 1.84 | 0.78-4.33    |         |
| Predictive factors for hormone therapy alone (N=452) |      |              |         |
| Age                              | <0.001 |              |         |
| 75-79                            | 1    |              |         |
| 80-84                            | 2.07 | 0.80-5.35    |         |
| ≥85                              | 16.22 | 6.74-39.03  |         |
| T stage                          |      | 0.89         |         |
| T0+T1                            | 1    |              |         |
| T2                               | 1.21 | 0.53-2.74    |         |
| T3+T4                            | 1.22 | 0.42-3.52    |         |
| N stage                          |      | 0.52         |         |
| N0                               | 1    |              |         |
| N+                               | 1.32 | 0.57-3.07    |         |
| M stage                          |      | 0.02         |         |
| M0                               | 1    |              |         |
| M1                               | 3.67 | 1.25-10.74   |         |
| Comorbidities                    |      | <0.001       |         |
| No                               | 1    |              |         |
| Yes                              | 7.59 | 2.45-23.56   |         |
| Histoprognostic SBR grade        |      | 0.22         |         |
| 1+2                              | 1    |              |         |
| 3                                | 0.55 | 0.21-1.43    |         |
| Period                           |      | 0.23         |         |
| Predictive factors for BCS plus adjuvant therapy † (N=381) |      |              |         |
| Age                              | <0.001 |              |         |
| 75-79                            | 1    |              |         |
| 80-84                            | 0.53 | 0.30-0.95    |         |
| ≥85                              | 0.21 | 0.09-0.50    |         |
| T stage                          |      | <0.001       |         |
| T0+T1                            | 1    |              |         |
| T2                               | 0.17 | 0.09-0.31    |         |
| T3+T4                            | 0.13 | 0.05-0.30    |         |
| N stage                          |      | 0.23         |         |
| N0                               | 1    |              |         |
| N+                               | 0.64 | 0.31-1.33    |         |
| Diagnosis circumstances          |      | 0.11         |         |
| No                               | 1    |              |         |
| Yes                              | 0.62 | 0.34-1.12    |         |
| Diagnosis circumstances          |      |              |         |
| Clinic                           | 1    |              |         |
| Individual screening             | 1.71 | 0.90-3.24    |         |
| Histoprognostic SBR grade        |      | 0.30         |         |
| 1+2                              | 1    |              |         |
| 3                                | 0.7  | 0.36-1.37    |         |
| Matrimonial status               |      | 0.40         |         |
| Single†                          | 1    |              |         |
| Not single                       | 1.26 | 0.73-2.17    |         |
| Hormone receptors                |      | 0.78         |         |
| Negative                         | 1    |              |         |
| Positive                         | 1.14 | 0.46-2.83    |         |
| Predictive factors for mastectomy plus adjuvant therapy (N=381) |      |              |         |
| T stage                          | <0.001 |              |         |
| T0+T1                            | 1    |              |         |
| T2                               | 3.57 | 1.09-10.03   |         |
| T3+T4                            | 3.60 | 1.78-7.29    |         |
tumour at discovery and the presence of comorbidities. Adjuvant therapy, probably because of advanced stage of the tumour, was less frequent in the oldest age group with BC. This was not the case for hormone therapy, which was more likely to be administered in the oldest patients than in patients in the youngest age group.

According to the characteristics of the tumour, older patients with an advanced tumour (stage T2, T3+T4) were more likely to undergo mastectomy plus adjuvant therapy and less likely to have BCS plus adjuvant therapy. This could be due to large tumour size which precludes BCS. Treatment with mastectomy plus adjuvant therapy limits organ invasion and thus decreases the risk of disease recurrence in the breast or distant metastasis. Another explanation could be the choice of the physician to avoid adjuvant radiotherapy for extremely frail women. Nevertheless, patients with hormone-receptor positive tumours were less often treated with surgery alone because these patients were usually treated with hormone therapy in accordance with the guidelines of the French health authorities [29]. Patients with metastasis were also more likely to receive hormone therapy, but less often treated with surgery. Surgery is a local treatment and is thus inadequate for the treatment of metastatic disease. Patients with comorbidities were more often treated with hormone therapy. Older patients with comorbidity received less aggressive treatments as shown in another study [28]. Treatment are often modified according to age-related issues such as comorbidity and the general state of health. This highlights the importance of considering comorbidities in the management of BC.

The strength of this study is that the analyses were done in a heterogeneous and exhaustive group of patients, using data from the Cote d’Or breast and gynaecological cancer registry. Therefore, the results could be considered representative of elderly patients living in the department during this period. Cancer registries provide the unique opportunity to evaluate predictors of treatments given in routine practice and to assess survival using comprehensive population-based data. The use of RS makes it possible to correct for non-BC-related deaths while circumventing the problems associated with establishing the cause of death.

**Conclusions**

Comorbidity was associated with decreased survival in older women with breast cancer. Moreover, the results of this study showed that there are numerous predictors of the type of treatment administered, of which the most important were age and comorbidities.

**Abbreviations**

BC: Breast cancer; BCS: Breast conserving surgery; CI: Confidence intervals; EMR: Excess mortality ratio; ES: Expected survival; RER: Relative excess rates;
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