

Breast cancer in elderly women: a different reality? Results from the NORA study

G. Mustacchi^{1*}, M. E. Cazzaniga², P. Pronzato³, A. De Matteis⁴, F. Di Costanzo⁵ & I. Floriani⁶
On behalf of the NORA Study Group

¹Medical Oncology, University of Trieste, Trieste; ²Medical Oncology, Treviglio Hospital, Treviglio; ³Medical Oncology, La Spezia Hospital, La Spezia; ⁴Medical Oncology, Pascale Institute, Napoli; ⁵Medical Oncology, Careggi Hospital, Firenze; ⁶Oncology Department, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy

Received 28 October 2006; revised 22 January 2007; accepted 23 January 2007

Background: The incidence of breast cancer increases with age, and the disease affects many older women; however, attitudes about prevention and treatment of breast cancer vary based on the patient's age. Older women have less access to clinical trials and fewer opportunities for treatment with innovative therapies. The National Oncological Research observatory on Adjuvant therapy in breast cancer (NORA) study was a cohort study designed to obtain information about adjuvant strategies for treatment of breast cancer after surgery, patterns of recurrence, and possible correlations between cancer-related events and biological factors.

Patients and methods: This report describes patient characteristics, disease status, and local and systemic adjuvant treatments in a population of breast cancer patients aged ≥ 65 years. The NORA study consecutively enrolled >3500 patients from 2000 through 2002 at 77 Italian hospitals; of these, 1085 were aged ≥ 65 years. Data on patient characteristics, cancer presentation, and treatments were analyzed to identify possible relationships between these factors and age.

Results: The findings indicate that age is significantly related to later diagnosis and different patterns of treatment. Choice of adjuvant systemic treatment was primarily related to hormone receptor status and tumor stage but was strongly influenced by the patient's age; there was a proportional relationship between endocrine treatment and increasing age. Cyclophosphamide, methotrexate, and 5-fluorouracil as well as anthracyclines were widely used, but the use of taxanes was limited to a very small percentage of patients.

Conclusions: The findings of the NORA study may help to change attitudes that currently exclude a significant proportion of breast cancer patients from secondary prevention policies, more active treatment strategies, and clinical research trials based on age.

Key words: adjuvant therapy, breast cancer, elderly

introduction

The incidence of breast cancer increases with age. While only one in 225 women aged <40 years develops breast cancer, the rate increases to one in 24 for women aged 40–59 years and to one in 14 for women aged 60–79 years [1]. As the population ages and chronic disease survival rates improve, it is expected that the number of older women with breast cancer will increase. During the late 1990s in northeastern Italy, breast cancer incidence and mortality rates in women aged ≥ 65 years were >289/100 000 and 134/100 000 per year, respectively [2, 3].

In women aged >70 years, the disease is often diagnosed at a later stage. No screening guidelines are available for older patients, and the majority of screening mammography trials did not include women in this age group. Because of the higher

incidence of comorbid diseases, breast cancer management in the elderly often differs from the management of younger women [4]. Women aged >70 years are usually excluded from randomized clinical trials, thus making the therapeutic impact of new approaches difficult to assess in this population [5, 6]. Consequently, there are no consensus guidelines on treatment, and data are often conflicting. In Italy, in particular, there is a lack of information about patterns of care, including diagnostic level, surgical approach, and adjuvant treatment for older breast cancer patients [7].

The National Oncological Research observatory on Adjuvant therapy in breast cancer (NORA) study was designed to collect information regarding adjuvant treatment strategies after surgery, patterns of recurrence, and possible correlations between cancer-related events and biological factors.

This report describes patient characteristics, disease status, and local and systemic adjuvant treatments provided to the subgroup of breast cancer patients aged ≥ 65 years.

*Correspondence to: Prof. G. Mustacchi, Medical Oncology, University of Trieste, Via Pietà 19, 34100 Trieste, Italy. Tel: +39-040-3992232; Fax: +39-040-7606111; E-mail: g.mustacchi@fmc.units.it

materials and methods

NORA is a multicenter, observational cohort study whose design and methods have previously been described in detail [8]. Participating oncological centers included academic and nonacademic institutions that were well distributed throughout Italian territory. Academic institutions comprise 21.2% of the centers; 42.3% are located in northern Italy, 28.2% in central Italy, and 29.6% in southern Italy and the islands. Therefore, both the type and geographical distribution of the institutions are well distributed and representative of the national situation.

Each center was asked to record data for the first 10 consecutive patients treated in the years 2000, 2001, and 2002 (the retrospective cohort), as well as for the first 20 consecutive patients who reached the oncology unit in 2003 (the prospective cohort), for a total of at least 50 patients at each center. Patients with a first diagnosis of invasive breast cancer and absence of metastatic disease were included; women whose sole diagnosis was *in situ* carcinoma or those who underwent surgery with palliative intent (macroscopic residual disease) were considered ineligible.

The study design assumed that 77 centers would enroll a minimum of 50 patients each, and that a planned total enrollment of ~3500 women would be required to obtain an estimate of the distribution of adjuvant treatment strategies with a 95% confidence interval range that was, at most, $\leq 3\%$.

The study complied with the requirements of Italian law regarding observational studies. The nature and purposes of the survey were explained in detail to all participants, and consent to data handling according to Italian regulations on privacy was obtained from each participant.

statistical analysis

To study the influence of age on patterns of care in breast cancer, the distributions of selected factors related to patient characteristics, disease status, and treatment were assessed across three age groups: (i) <70 years (up to 69), (ii) 70–75 years, and (iii) >75 years. These categories have been predefined and chosen due to different reasons: up to 65 years, screening programs are active in the national territory, but, as described in other reports, older age is frequently associated with delayed diagnosis. Furthermore, the increase in age is often associated with other diseases, such as cardiovascular and gynecologic ones, which could affect the treatment. We assume that these three categories could well describe the old population. The characteristics of selected factors across age groups were described by relative and absolute frequencies. Analyses were carried out using the Mantel–Haenszel test for trend and the χ^2 test for heterogeneity. Unless otherwise specified, all tests are with 1 *df*.

results

A total of 3515 breast cancer patients were enrolled by 77 Italian centers. Of these, 1085 patients (30.8%) were aged ≥ 65 years.

In this older subgroup, the median age was 71.4 years; 435 patients (40.1%) were aged 65–69+ years, 336 (31.0%) were aged 70–75+ years, and 314 (28.9%) were aged >75 years.

comorbidities

In all, 35% of patients in the old population did not have comorbid disease but the percentage of women without comorbid disease significantly decreased with age from 61.7% in women aged 65–69 years to 34.3% in women aged 70–75 years and 29.6% in women aged >75 years (χ^2 test for trend = 5.94; $P = 0.0148$). Cardiovascular diseases, predefined as thromboembolic, recurrent phlebitis, pulmonary embolism,

previous myocardial infarction, and previous ictus, were present in 465 women (43.2%), the distribution significantly increased with age, accounting for 37.9% of patients aged 65–69 years, 42.2% of those aged 70–75 years, and 51.6% of those aged >75 years (χ^2 test for trend = 14.35; $P = 0.0002$). Skeletal problems affected 85 women (7.9%) and were also significantly age related, affecting 5.3% of patients aged 65–69 years, 8.4% of patients aged 70–75 years, and 10.8% of patients aged >75 years (χ^2 test for trend = 7.89; $P = 0.005$).

There is no detailed information on the grade of comorbidities.

diagnosis

Overall, heterogeneity was found when assessing the relationship between age groups and modalities of breast cancer detection (χ^2 test for heterogeneity = 42.37; 6 *df*; $P < 0.0001$). In all, 447 patients of 926 patients with available records (48.3%) discovered a lump in the breast by self-examination. This modality of diagnosis was directly correlated with age: 40.5% were up to 70, 49.3% were aged 70–75 years, and 57.7% were aged >75 years. Conversely, diagnosis through periodic screening occurred in 22% of patients and showed an inverse correlation with age (31.2% in the group aged up to 70 years, 21.1% in group aged 70–75 years, and 10.6% in the group aged >75 years). Occasional diagnosis, predefined as diagnosis done during medical procedures for different reasons, occurred in 28.8% of cases, irrespective of age.

local treatments

Of the 597 patients (55.1%) who underwent breast-conserving surgery (BCS) in this subgroup, 82.6% had axillary clearance and 13.2% had sentinel node (SN) biopsy. Radiotherapy after BCS was done in 83.1% of cases. BCS significantly decreased with increasing age, from 60.2% in the group aged 65–69 years to 55.6% in the group aged 70–75 years and 47.1% of cases in the group aged >75 years (χ^2 for trend = 12.34; $P = 0.0004$). Data on surgery and radiotherapy are shown in Table 1.

Table 1. Local treatments

	All (N = 1085)	65–69 years (n = 435)	70–75 years (n = 336)	>75 years (n = 314)
BCS				
Total	597 (55.1)	262 (60.2)	187 (55.6)	148 (47.1)
+ Axilla	493 (82.6)	230 (87.8)	161 (86.1)	102 (68.9)
+ SN	79 (13.2)	36 (13.7)	22 (11.8)	21 (14.2)
+ Radiotherapy	496 (83.1)	236 (90.1)	163 (87.2)	97 (65.5)
Mastectomy				
Total	487 (44.9)	172 (39.6)	149 (44.3)	166 (52.9)
+ Axilla	470 (96.5)	167 (97.1)	144 (96.6)	159 (95.8)
+ SN	11 (2.2)	5 (2.9)	5 (3.4)	1 (0.6)
+ Radiotherapy	69 (14.2)	31 (18.0)	23 (15.4)	15 (9.0)

Surgery: χ^2 for trend = 12.344; 1 *df*; $P = 0.0004$.

Axillary clearance: χ^2 for trend, stratified for surgery = 19.316; 1 *df*; $P < 0.0001$.

Radiotherapy: χ^2 for trend, stratified for surgery = 41.761; 2 *df*; $P < 0.0001$.

BCS, breast-conserving surgery; SN, sentinel node.

Mastectomy was carried out in 44.9% of patients; 96.5% of these patients were given axillary clearance, while SN was chosen as axillary nodes evaluation in 2.2% of patients, and radiotherapy was given to 14.2% of the patients.

Age was significantly related to decrease in postoperative radiotherapy in both the BCS and mastectomy subgroups (χ^2 for trend, stratified for surgery = 41.761; 2 *df*; $P < 0.0001$), as well as of axillary clearance (χ^2 for trend, stratified for surgery = 19.316; 2 *df*; $P < 0.0001$).

histotype

A total of 76.3% of tumors were ductal and 12.5% were lobular, without evidence of age-related differences (χ^2 for heterogeneity 9.64; 6 *df*; $P = 0.140$).

hormone receptor status

Hormone receptor status data were available for 1042 patients (96.0%). Overall, 85.5% of patients had at least one positive receptor; 67.9% were positive for both, 16.0% for estrogen receptor (ER) alone and 1.6% for progesterone receptor (PgR) alone. Receptor positivity increases with age, with ER⁺/PgR⁺ patients ranging from 63.6% to 68.6% to 73.1% for groups aged 65–69 years, 70–75 years, and >75 years, respectively, and the difference was highly significant (χ^2 for trend = 7.886; $P = 0.005$). ER and PgR receptor status distributions are shown in Table 2.

proliferation index

The proliferation index, evaluated by Ki67/MB1, was known in 870 (80.1%) cases. According to different published reports, we choose the cut-off at 10% to differentiate low versus high proliferation rate. In 65.5% of the patients the proliferation rate was high (>10%), without statistical evidence of age-related differences (χ^2 for trend = 0.349; $P = 0.555$).

HER-2-neu/c-erbB2 status

HER-2 status, evaluated by immunohistochemistry, was known in 492 cases (45.3%). HER2++ cases totaled 17.7% and HER2+++ cases, 16.0%. No statistical evidence of age-related variation (χ^2 for trend = 0.261; $P = 0.610$) was found.

pathological tumor size

Pathological tumor size was available in 99.4% of cases. Overall, 52.0% of tumors were <2 cm in diameter (T0–T1), 38.9%

were T2 (2–5 cm), 3.7% were T3 (>5 cm), and 5.4 were T4. Tumor size was related to age (χ^2 for trend = 12.430; $P = 0.0004$). The number of T1 tumors (561 patients) decreased from 57.4% to 50.8% to 46.0% for the groups aged 65–69 years, 70–75 years, and >75 years, respectively. The number of T2 tumors (469 patients) increased from 35.5% to 39.6% to 42.8% for the groups aged 65–69 years, 70–75 years, and >75 years, respectively. T3 tumors decreased from 4.1% to 3.6% to 3.2% (40 patients), while T4 tumors increased from 3.0% to 6.0% to 8.0% (58 patients) for the groups aged 65–69 years, 70–75 years, and >75 years, respectively.

pathological nodal status

Pathological nodal status was known in 1037 cases (95.5%). Overall, 56.7% of patients had negative nodes, 23.9% had one to three positive nodes, 12.3% had 4–10 positive nodes, and 7.1% had >10 positive nodes, without any age-related difference (χ^2 for trend = 0.007; $P = 0.933$).

The median number of examined nodes was 14 (25th–75th percentile, 10–20). This number is slightly reduced with age: 65- to 69-year age group, 15 (25th–75th percentile, 11–20); 70- to 75-year age group, 14.5 (25th–75th percentile, 11–20); and >75-year age group, 14 (25th–75th percentile, 9–19) (χ^2 for trend = 10.856; $P = 0.001$).

adjuvant systemic treatments

Both age and stage seemed to affect the choice of adjuvant systemic treatments. Only 45 patients (4.1%) did not receive any systemic adjuvant treatment.

Overall, 52.4% of patients received endocrine therapy alone, 13% chemotherapy alone, and 30.4% both. The use of endocrine treatment alone significantly increased with age (from 37.1% to 51.9% to 74.8% for the groups aged 65–69 years, 70–75 years, and >75 years, respectively) and conversely chemotherapy (alone or followed by endocrine treatment) decreased from 62.2% to 44.7% to 17.2% for the groups aged 65–69 years, 70–75 years, and >75 years, respectively (χ^2 test for heterogeneity = 146.51; 6 *df*; $P < 0.001$). Data are shown in Table 3.

Adjuvant systemic treatment choice was strongly related to hormone receptor status (Table 4), but the general trend observed for any given receptor status was that of increasing endocrine treatment and decreasing chemotherapy with age. In ER⁺/PgR⁺ patients, endocrine treatment alone was given in 44.5%, 65.9%, and 86.8% of cases for the groups aged 65–69

Table 2. Receptor status

	All (N = 1042)	65–70+ years (n = 426)	70–75+ years (n = 319)	>75 years (n = 297)
ER ⁺ /PgR ⁺	707 (67.9)	271 (63.6)	219 (68.6)	217 (73.1)
ER ⁺ /PgR [−]	167 (16.0)	74 (17.4)	50 (15.7)	43 (14.5)
ER [−] /PgR ⁺	17 (1.6)	8 (1.9)	5 (1.6)	4 (1.3)
ER [−] /PgR [−]	151 (14.5)	73 (17.1)	45 (14.1)	33 (11.1)

Data available for 1042 of 1085 patients.

χ^2 for trend = 7.886; $P = 0.005$.

ER, estrogen receptor; PgR, progesterone receptor.

Table 3. Systemic adjuvant treatments

	All (N = 1042)	65–70+ years (n = 426)	70–75+ years (n = 319)	>75 years (n = 297)
None	45 (4.1)	9 (2.1)	11 (3.3)	25 (8.0)
Endocrine alone	567 (52.4)	158 (37.1)	174 (51.9)	235 (74.8)
Chemotherapy alone	140 (13.0)	75 (17.6)	43 (12.8)	22 (7.0)
Chemotherapy + endocrine	329 (30.4)	190 (44.6)	107 (31.9)	32 (10.2)

Data available for 1042 of 1085 patients.

χ^2 for heterogeneity = 146.51; 6 *df*; $P < 0.001$.

years, 70–75 years, and >75 years, respectively. In the same receptor grouping, chemotherapy (alone or followed by endocrine therapy) was given to 55.5%, 34.1%, and 13.2% of patients in the groups aged 65–69 years, 70–75 years, and >75 years, respectively. In patients with both negative receptors, chemotherapy was given in 97% of cases to patients aged <75 years and to 76% of patients aged >75.

The choice of systemic adjuvant treatment is related also to tumor stage but always according to age (Table 5). Patients with T0–T1 tumors and negative nodes received chemotherapy (plus or minus endocrine therapy) in 27.8%, 13.4, and 5.9% of cases, while patients with T0–T1 tumors and positive nodes received chemotherapy (plus or minus endocrine therapy) in 92.9%, 67.7%, and 25.7%, in the groups aged 65–69 years, 70–75 years, and >75 years, respectively. Similarly, patients with T2 tumors and negative nodes received chemotherapy in 60.4%, 36.1%, and 12.5% of cases, while patients with T2 tumors and positive nodes received chemotherapy in 92.4%, 76.5%, and 30.3% of cases in the groups aged 65–69 years, 70–75 years, and >75 years, respectively.

Table 4. Systemic treatments and receptor status

	65–70+ years (n = 414)	70–75+ years (n = 309)	>75 years (n = 276)
ER⁺/PgR⁺			
Endocrine	118 (44.5)	141 (65.9)	178 (86.8)
Chemotherapy	6 (2.3)	1 (0.5)	2 (1.0)
Both	141 (53.2)	72 (33.6)	25 (12.2)
ER⁺/PgR⁻			
Endocrine	33 (45.8)	23 (46.9)	38 (88.4)
Chemotherapy	2 (2.8)	2 (4.1)	– (0)
Both	37 (51.4)	24 (49.0)	5 (11.6)
ER⁻/PgR⁺			
Endocrine	2 (28.6)	2 (40.0)	2 (66.7)
Chemotherapy	1 (14.3)	1 (20.0)	1 (33.3)
Both	4 (57.1)	2 (40.0)	– (0)
ER⁻/PgR⁻			
Endocrine	2 (2.9)	1 (2.4)	6 (24.0)
Chemotherapy	64 (91.4)	35 (85.4)	17 (68.0)
Both	4 (5.7)	5 (12.2)	2 (8.0)

ER, estrogen receptor; PgR, progesterone receptor.

The presence of cardiovascular comorbidities did not affect the choice of systemic adjuvant treatment in the older population subgroup (χ^2 test for heterogeneity = 1.96; 2 *df*; *P* = 0.580), even if no correlation is available with the grade of these diseases. (Table 6)

chemotherapy regimens

Overall, 43.4% of women received chemotherapy. Chemotherapy alone was given to 140 patients (13%) and with endocrine treatment to 329 patients (30.4%). The pattern of chemotherapy regimens varied with age (χ^2 for heterogeneity = 15.66; 6 *df*; *P* = 0.016).

Taking into account the population receiving chemotherapy, cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) in its different types was utilized in 57.1% of older patients, while anthracycline-containing regimens were used in 37.8%, with a preference for three-drug regimens (20.7% versus 15.7% for two-drug regimens). CMF use did not vary with increasing age (from 57.5% to 62.8% to 50.0% for the groups aged 65–69 years, 70–75 years, and >75 years, respectively). Three-drug anthracycline regimen use decreased with age (28.8% to 16.3% to 4.5% in the groups aged 65–69 years, 70–75 years, and >75 years, respectively), while two-drug regimens were preferentially used in patients aged >75 years (9.6% to 14.0% to 40.9 for the groups aged 65–69 years, 70–75 years, and >75 years, respectively). Taxanes were used in one patient (0.7%).

discussion

The results of studies concerning patterns of care for older breast cancer patients in Italy are controversial. Recently, a retrospective study of long-term follow-up of breast cancer patients receiving locoregional treatment alone showed that age is not an independent prognostic factor and that there is no difference in the biological behavior of the disease in women aged >70 years and younger women [9]. This finding, however, has been debated [10], and it is reasonable to believe that a breast cancer patient’s life expectancy varies according to tumor characteristics and to general health status and age as well [11]. Some authors believe that undertreatment appears to be related to a worse prognosis for older (≥80 years) breast cancer patients [12], although the Italian, randomized, phase III group

Table 5. Adjuvant systemic treatment and pathological findings (T1–T2) (%)

	65–70+ years		70–75+ years		>75 years	
T0–T1	N– (n = 162)		N+ (n = 70)		N– (n = 85)	
Endocrine	72.2	7.1	86.6	31.1	94.1	74.3
Chemotherapy	10.5	20.0	5.4	20.0	1.2	11.4
Both	17.3	72.9	8.0	47.7	4.7	14.3
T2	N– (n = 58)		N+ (n = 92)		N– (n = 47)	
Endocrine	39.7	7.6	63.9	23.4	87.2	69.7
Chemotherapy	20.7	23.9	13.1	15.6	10.4	12.1
Both	39.7	68.5	23.0	60.9	2.1	18.2

Stages T3 and T4 not shown due to the small number of patients.

Table 6. Adjuvant systemic treatment and cardiovascular comorbidities (%)

	65–70+ years (n = 163)	70–75+ years (n = 140)	>75 years (n = 162)
Endocrine	35 (34.3)	46 (51.7)	57 (77.0)
Chemotherapy	24 (23.5)	10 (11.2)	7 (9.5)
Both	43 (42.2)	33 (37.1)	10 (13.5)

χ^2 test for heterogeneity = 1.96; 2 df; $P = 0.580$.

for research on endocrine therapy in the elderly (GRETA) study showed no difference in 13-year overall survival in 474 patients >70 years old who were treated with tamoxifen alone or surgery plus tamoxifen [13].

According to different authors, older women are less likely to undergo optimal surgery, radiotherapy, and chemotherapy [9, 12, 14]; this variability is also related to different policies at treating institutions [10, 14]. The NORA study provides an important contribution to the knowledge base about recent patterns of care in breast cancer in Italy.

Our data indicate that conservative surgery is used less frequently in older women, but the proportion of patients treated in a radical manner (i.e. axillary clearance) is not particularly different among age groups. The data actually indicate that in patients aged >75 years who are treated with BCS, axillary clearance is carried out in ~20% of cases; however, when axillary clearance is done, the median number of examined nodes is >10, so there is no particular risk of understaging. This probably reflects the idea of limiting surgery to lumpectomy in older patients with receptor-rich tumors. The same explanation may account for the reduced frequency of radiotherapy after BCS or mastectomy in women aged >75 years in comparison with younger women.

Women >70 years old are usually excluded from periodic screening procedures, and in almost 60% of their cases, diagnoses were made by self-examination. It is also important, however, to note that patients younger than age 70 were diagnosed through periodic screening in only 31% of cases, and one-third of diagnoses, regardless of age, were occasional. This could explain why increasing tumor size according to increasing age is statistically significant and why BCS, axillary clearance, and radiotherapy decrease in older women.

This finding does not seem to be related to an age-oriented policy, because tumors suitable *ab initio* for BCS were 57.4%, 50.8%, and 46.0% in the groups aged 65–69 years, 70–75 years, and >75 years, respectively, and BCS was done in the same proportions as in the study population.

The patterns of pathological nodal status show, as expected, a strong relationship with tumor size but not with age. The biological patterns are not surprising because the older the patient, the higher the probability of hormone-sensitive disease.

A recent survey of 277 oncologists in 28 countries worldwide disclosed that they would exclude 28% of patients >70 years old, 21% of patients >75 years old, and 8% of patients >80 years old from adjuvant chemotherapy [15], although the median life expectancy in Western countries for a 70-year-old woman is 15.5 years and for an 80-year-old woman is 9.2 years [16].

In addition, functional domains, even the physical, were less impaired in older women during adjuvant chemotherapy for breast cancer compared with younger patients [17]. In a recent survey of 768 Italian patients [most of whom ($n = 400$) were aged 50–69 years and 54 patients >70 years], 40 of 51 patients were treated with CMF, and only 10 with anthracycline-containing regimens [18].

According to our data, only 4.1% of the 1085 patients did not receive any systemic adjuvant treatment. We have no direct explanation for this choice regarding a very small number of patients.

The use of endocrine treatment alone is significantly increasing with age from one-third to more than two-thirds of patients; conversely, chemotherapy (alone or followed by endocrine treatment) is decreasing from two-thirds to one-third of patients. Treatment choice is strongly related to age, hormone receptor status, and tumor stage. Since receptor status is quite similar among age groups (Table 2) and older patients had significantly more advanced tumors, probably the strongest determinant for the decreased use of chemotherapy in older patients is age itself.

The presence of cardiovascular comorbidities does not modify the choice of systemic adjuvant treatment, when older patients with such comorbidities are compared with the older population as a whole. Unfortunately, there is no specific information about the grade of these diseases.

CMF, in its different types, is used in more than one-half of older patients. In patients receiving anthracycline, three-drug regimens were preferred in younger women, while a two-drug regimen was more widely chosen for those aged >75 years. Taxanes were used in <1% of patients.

Another recent survey that included 260 breast cancer patients aged >70 years in Northeastern Italy [19] reported similar findings when treatments were analyzed according to tumor size, but high-risk patients were considered for adjuvant chemotherapy in only 51% of cases. In our survey of 1085 women, high-risk patients aged >70 were treated with chemotherapy in 76.5% of cases (30% of those aged >75 received chemotherapy).

conclusions

Our data confirm that age is significantly related to later stage breast cancer diagnosis and to different patterns of treatment. Although surgical and radiotherapy protocols are largely related to tumor size rather than to age, this is not completely true for patients who are aged >75 years. The choice of adjuvant systemic treatment is primarily related to hormone receptor status and tumor stage; however, it is strongly influenced by age, with an inversely proportional relationship between endocrine treatment and chemotherapy according to increasing age. While CMF and anthracyclines are widely used, the use of taxanes is limited to a very small percentage of patients. We believe that the findings of the NORA study, which to our knowledge is the largest published study of breast cancer in older patients, may help to change current attitudes that exclude an important population of patients from secondary prevention policies, more active treatment strategies, and clinical research trials, on the basis of misconceptions about aging.

contributors

G. Nastasi, G. Rodà (Alzano Lombardo—BG); C. Massacesi, F. Marcucci (Ancona); M. Barduagni, M. Rosselli (Anzio—RM); F. Schittulli, R. Altieri (Bari); N. Marzano, M. Altieri (Bari); G. Paladini, A. Fini (Bologna); A. Huscher, S. Magrini (Brescia); M. C. Chetrl̃, P. Rizzo (Brindisi); C. Floris, M. C. Cherch̃ (Cagliari); B. Massidda, M. T. Ionta (Cagliari); F. Artioli, K. Cagossi (Carpi—MO); M. Botta, D. Degiovanni (Casale Monferrato—AL); G. Tansini, G. Sbalzarini (Casalpusterleno—LO); P. Manente, G. Sgarbossa (Castelfranco Veneto—TV); M. Caruso, R. Aiello (Catania); G. Lavenia (Catania), P. Pugliese, G. Gini (Como); S. Conforti, V. Liguori (Cosenza); O. Garrone, M. Ocelli (Cuneo); L. Giustini, R. Bisogni (Fermo—AP); C. Modonesi, G. Lelli (Ferrara); F. Mazzoni (Firenze); A. Contillo (Foggia); S. Calpona, M. Dall'Agata (Forlì); M. D'Amico, A. Decensi (Genova); A. Tognoni (La Spezia); M. D'Aprile, S. Busco (Latina—RM); A. Bonetti, M. Zaninelli (Legnago—VR); A. Falcone, R. Di Marsico (Livorno); B. Pistilli, L. Latini (Macerata); P. Spadaro, G. Dottore (Messina); D. Tabiaddon, S. Masseroni (Milano); A. Scanni, K. Borgonovo (Milano); V. De Pangher Manzini (Monfalcone—GO); G. Landi (Napoli); R. Thomas, G. R. Cortino (Napoli); E. Procaccini, F. Procaccini (Napoli); G. Borea, M. Trunfio (Napoli); G. Barberis, A. Salzano (Napoli); D. Sartori, S. Coccato (Noale—VE); L. Mesi (Palermo); G. Bernardo, R. Palumbo (Pavia); M. Danova, E. Collovà (Pavia); S. Gori, F. Ciacci (Perugia); G. Pandoli, D. Natale (Pescara); C. Naso, A. Gozza (Pietra Ligure—SA); B. Salvadori, S. Donati (Pisa); M. Di Lieto, A. Chiavacci (Pistola); F. Tropea (Reggio Calabria); M. Nardi, D. Azzarello (Reggio Calabria); A. Ravaioli, B. Rudnas (Rimini); R. Tonachella, E. Colella (Roma); P. Carlini, N. Salesi (Roma); E. Cortesi, R. Ferraldeschi (Roma); F. Scinto, V. Zagonel (Roma); M. Roselli, G. Del Monte (Roma); A. Pancotti (S. Omero—TE); C. Florillo, G. Di Giulio (Salerno); C. Verusio, E. Bossi (Saronno—VA); G. Sanna, M. A. Pinna (Sassari); A. Lavarello, O. Sanguineti (Sestri Levante—GE); T. Gamucci, T. Trapasso (Sora—FR); S. Pisconti, G. Pezzella (Taranto); M. Brugia, M. Tagliaventi (Terni); M. Porpiglia, P. Sozzani (Torino); S. Danese, E. Bertone (Torino); S. Barni (Treviglio—BG); C. Dellach (Trieste); M. Mansutti, G. Fasola (Udine); V. Fossier, M. Magazù (Vicenza); C. F. Pollera, C. Signorelli (Viterbo).

acknowledgements

We thank LINK Italia for data entry. We also thank I. Floriani, E. Rulli, and L. Porcu of the Clinical Trial Unit, Oncology Department, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, for statistical analysis.

references

- Singh R, Hellman S, Heimann R. The natural history of breast carcinoma in the elderly: implications for screening and treatment. *Cancer* 2004; 100: 1807–1813.
- University of Padua. Venetian Tumor Registry. <http://www.unipd.it/regtumve/altro/age.pdf> (February 2007).
- Basso U, Brunello A, Pogliani C, Monfardini S. Treatment options for early breast cancer in elderly women. *Expert Rev Anticancer Ther* 2004; 4: 197–211.
- Yancik R, Wesley MN, Ries LA et al. Effect of age and comorbidity in postmenopausal breast cancer patients aged 55 years and older. *JAMA* 2001; 285: 885–892.
- Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005; 365: 1687–1717.
- Townsend CA, Selby R, Siu LL. Systematic review of barriers to the recruitment of older patients with cancer onto clinical trials. *J Clin Oncol* 2005; 23: 3112–3124.
- Inghelmann R, Grande E, Francisci S et al. National estimates of cancer patients' survival in Italy: a model-based method. *Tumori* 2005; 91: 109–115.
- Cazzaniga ME, Mustacchi G, Pronzato P et al. Adjuvant systemic treatment of early breast cancer: the NORA study. *Ann Oncol* 2006; 17(9): 1386–1392.
- Wylid L, Garg DK, Kumar ID et al. Stage and treatment variation with age in postmenopausal women with breast cancer: compliance with guidelines. *Br J Cancer* 2004; 90: 1486–1491.
- Gennari R, Curigliano G, Rotmensz N et al. Breast carcinoma in elderly women: features of disease presentation, choice of local and systemic treatments compared with younger postmenopausal patients. *Cancer* 2004; 101: 1302–1310.
- Extermann M, Balducci L, Lyman GH. What threshold for adjuvant therapy in older breast cancer patients? *J Clin Oncol* 2000; 18: 1709–1717.
- Bouchardy C, Rapioti E, Fioretta G et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. *J Clin Oncol* 2003; 21: 3580–3587.
- Mustacchi G, Ceccherini R, Milani S et al. Tamoxifen alone versus adjuvant tamoxifen for operable breast cancer of the elderly: long-term results of the phase III randomized controlled multicenter GRETA trial. *Ann Oncol* 2003; 14: 414–420.
- Giordano SH, Hortobagyi GN, Kau SW et al. Breast cancer treatment guidelines in older women. *J Clin Oncol* 2005; 23: 783–791.
- Biganzoli L, Goldhirsch A, Straehle C et al. Adjuvant chemotherapy in elderly patients with breast cancer: a survey of the Breast International Group (BIG). *Ann Oncol* 2004; 15: 207–210.
- Kimmick GG, Balducci L. Breast cancer and aging. *Clinical interactions. Hematol Oncol Clin North Am* 2000; 14: 213–234.
- Watters JM, Yau JC, O'Rourke K et al. Functional status is well maintained in older women during adjuvant chemotherapy for breast cancer. *Ann Oncol* 2003; 14: 1744–1750.
- Roila F, Ballatori E, Patoia L et al. Adjuvant systemic therapies in women with breast cancer: an audit of clinical practice in Italy. *Ann Oncol* 2003; 14: 843–848.
- Brunello A, Basso U, Pogliani C et al. Adjuvant chemotherapy for elderly patients (> or = 70 years) with early high-risk breast cancer: a retrospective analysis of 260 patients. *Ann Oncol* 2005; 16: 1276–1282.