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Original article

The use of adjuvant endocrine breast cancer therapy in the oldest old

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ABSTRACT

In order to report specifically on the use of adjuvant endocrine therapy (ET) in the oldest old breast cancer (BC) patients, we compared treatment patterns including drug compliance and persistence in a cohort of patients who were ≥80 years at diagnosis ($n = 79$) with those of "younger elderly" patients who were 60–79 years old ($n = 358$). The geriatric cohort more commonly declined the recommended ET (non-compliance: 13.0% vs. 4.5%, $p = 0.011$). Of the patients who initiated ET, only a minority of the older patients completed the planned therapy duration of five years (39.6% vs. 71.3%, $p < 0.001$). However, when applying strict criteria for non-persistence, this was found in comparable frequency (17.0% vs. 12.0%, $p = 0.370$). In older patients, medication was more often discontinued by the physician due to serious medical reasons independent of BC (17.0% vs. 4.7%, $p = 0.003$). Older women were treated by a general practitioner more often and not by an oncologist (54.4% vs. 23.9%, $p < 0.001$). Studies on compliance/persistence on cancer therapy in the oldest old demand a detailed follow-up of the patients and the consideration of principles of geriatric medicine. Efforts should be made to make sure that all physicians, but above all general practitioners, who are predominantly involved in the treatment of elderly BC patients, are provided with current knowledge and skills, as to ensure optimal patient management.

Introduction

In recent years, the issue of "breast cancer in the elderly" has increasingly become a focus of interest.[1–6] However, when reviewing the literature, which explicitly reports on breast cancer (BC) therapy in older women, it quickly becomes apparent that most studies analyzed patients in their 60s and 70s (in a disease where the median patients' age at initial diagnosis lies in the early 60's, thus the 65-year-old or the 70-year-old patient represent the standard BC patient). Women who are ≥80 years of age, representing the oldest 10% of the entire BC cohort, were often not included or comprised a negligible minority of the cohorts analyzed.[1–7]

Underreporting of patients who form the peak of the age pyramid of a BC cohort is also common in studies evaluating the issue of "compliance/adherence/persistence" to adjuvant endocrine therapy (ET). Studies which exclusively analyzed "elderly patients" and did not define an upper age limit, the percentage of women ≥80 years of age ranges from 12.6% to 19%.[8–15] In geriatrics, the medical sub-discipline that concerns itself chiefly with elderly patients, the percentage of individuals ≥80 years of age is quite the opposite and the vast majority of patients are ≥80 years. Studies on endocrine BC therapy focusing on this particular geriatric cohort are scarce.[16–19]

For three decades, a 5-year treatment has been the standard adjuvant ET for women with hormone receptor (HR)-positive BC. This highly effective therapy is usually applicable up until an advanced age. Thus, principles of geriatric care in cancer patients can be demonstrated effectively by ET. In order to report specifically on the use of adjuvant ET in the group of the oldest old BC patients, we compared treatment patterns including drug compliance and persistence in a cohort of patients who were ≥80 years at initial diagnosis with those of "younger elderly" patients who were 60–79 years old.

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Patients and methods

Data pertaining to all patients who had HR-positive non-metastatic invasive BC and who received surgical therapy between 1997 and 2009 at the University Hospital Basel (Basel, Switzerland) form the basis of the current analysis; this data was collected in the institutional prospective relational web-based Basel Breast Cancer Database. We restricted the analysis to elderly women who were ≥60 years at initial BC diagnosis. In total, 437 patients met these inclusion criteria. This entire study cohort was divided into two age-defined subgroups; Group A: ≥80 years ($n = 79$), and Group B: 60–79 years ($n = 358$).

The following clinicopathological and treatment data was available for all patients: histological subtype, grading, HR status, TNM stage,[20,21] surgery type and receipt of adjuvant chemotherapy and/or radiation. Furthermore, we recorded the location of treatment and follow-up of the patients (oncology unit or general practitioner).

The treatment recommendations for all patients were based on decisions from the interdisciplinary tumor board of the University Hospital Basel. Since 1997, adjuvant ET has been the standard recommendation for all HR-positive patients, with few exceptions. All patients received a comprehensive consultation at the departmental oncology unit, during which the treatment rationale and duration, as well as the potential adverse effects, were extensively discussed.

During follow-up, information concerning the prescribed endocrine agent given and duration of the medication was obtained from the medical record. In doing this, we recorded any change of endocrine agents and the indication for the change ((a) sequential therapy: receiving tamoxifen for 2–3 years, followed by an aromatase inhibitor for 2–3 years to complete a total of five years of therapy; (b) extended therapy beyond the standard five years of tamoxifen-containing treatment; or (c) change due to adverse effects). For the patients who stopped therapy, particular attention was paid to precise recording of the reasons for modifications and discontinuations. Patients who had no follow-up at our institution were monitored via telephone. Afterwards, contact was made with the treating physician to confirm the patients' statements.

We had complete follow-up for 434 patients of our study cohort (99.3%). Three patients (0.7%) who were lost to follow-up (median observation time: 13 months) were not considered in the analysis of therapy persistence.

Definition of compliance and persistence

In this study, we defined "compliance" as the readiness to accept a proposed drug, i.e. to accept starting the ET. When the patients started the treatment, we used the term "persistence" and not "adherence" for the further intake of the drug regimen. Persistence is defined as the length of time from initiation to discontinuation of treatment; it is a specific aspect of adherence, which is defined as the extent to which patients take medications as prescribed.[22–24] As it was the intention of this study to evaluate patients' non-persistence, which in most cases occurs within the first two years of therapy,[25–27] we also included patients with an ongoing therapy who took their medication for at least 36 months ($n = 79$; 18.1%) and considered these patients as being persistent with therapy.

In this study, the following situations where the discontinuation of the ET was not chosen but was mandatory were not defined as being "non-persistent":

- Patients who had to stop therapy due to local or systemic BC recurrence
- Cases where a physician decided to stop the therapy for serious medical reasons other than BC (e.g. in palliative situation of malignant diseases, dependence on nursing care, severe dementia) and independent from therapy-related adverse effects.
- Patients who died within the planned five years of treatment from intercurrent illness and took the medication shortly before death.

Data collection methods and study design were approved by the institutional review board.

Results

The clinicopathological, treatment and follow-up characteristics of the 437 patients in the study are summarized in Tables 1–4.

In a first step, we excluded the patients for whom ET was not recommended by the institutional interdisciplinary tumor board (Group A: $n = 10$; median age: 90 years, range 86–95 years) from further analysis; the reasons therapy was not recommended included a low-risk constellation (pT1a/b N0, favorable grading) and/or advanced age with considerable comorbidity.

Compliance

Compared with the patients who were 60–79 years old at initial diagnosis, older patients (≥80 years) more commonly declined the

Table 1
Clinicopathologic and treatment characteristics of 437 women with hormonal receptor-positive breast cancer.

Variable	Group A: ≥80 years[a] $n = 79$	Group B: 60–79 years[a] $n = 358$
Median age (range)	84 (80–95)	69 (60–79)
AJCC/UICC TNM stage[b]		
I	24 (30.4)	178 (49.7)
II	39 (49.4)	132 (36.9)
III	16 (20.2)	48 (13.4)
Histologic subtype		
Ductal invasive	61 (77.2)	240 (67.0)
Lobular invasive	11 (13.9)	82 (22.9)
Rare types	7 (8.9)	36 (10.1)
Grading		
G1/G2	56 (70.9)	271 (75.7)
HER-2 neu status[c]		
Positive	13 (17.6)	32 (9.9)
Negative	61 (82.4)	291 (90.1)
Unknown	5 (6.3)	35 (9.8)
Types of surgery		
Breast conserving therapy	31 (39.2)	220 (61.5)
Mastectomy	48 (60.8)	138 (38.5)
Surgical axillary staging (SLND/ALND)	57 (72.2)	345 (96.4)
Adjuvant radiotherapy	23 (29.1)	245 (68.4)
Systemic therapy		
Previous chemotherapy	1 (1.3)	50 (14.0)
Adjuvant treatment with trastuzumab	–	10 (2.8)

ER, estrogen receptor; PR, progesterone receptor; AJCC, American Joint Committee on Cancer; UICC, International Union Against Cancer; SLND, sentinel lymph node dissection; ALND, axillary lymph node dissection.

[a] Age at initial breast cancer diagnosis.

[b] In 13 patients (Group A: $n = 7$; B: $n = 6$), where neoadjuvant therapy was performed, the ypT and ypN status were used for stage grouping.

[c] HER-2/neu status has been routinely assessed for all patients since 2002 and was available for 397 patients (90.8%).