

Breast cancer in elderly women. Optimizing the treatment

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Abstract The elderly population is on the rise. Breast cancer is the most common cancer in western women and its incidence increases with age. Despite the epidemiological burden of this condition, there is a lack of knowledge regarding the management of older patients, as treatment planning is mainly based on personal preferences rather than hard data. Older women are often offered sub-optimal treatment when compared to their younger counterpart at any particular stage. This is due to various reasons, including the lack of scientific evidence from well-conducted clinical trials. Reluctance to prescribe systemic treatments may be explained by the complexity of cost-benefit evaluations in such patients. It is also an ethical dilemma to decide how aggressive one should be when it comes to treat cancer in the elderly in view of the higher rate of cognitive impairment and specific patients' expectations. This paper reviews the currently available evidence and attempts presenting and discussing chemoprevention of breast cancer, risk and benefit of hormone replacement therapy and the various treatment options for older women with breast cancer.

Keywords Breast cancer · Breast conserving surgery · Chemoprevention · Chemotherapy · Elderly patients · Hormone replacement therapy · Radiotherapy · Treatment

Introduction

Breast cancer is the most common form of malignant disease among women in the developed world and aging remains one of the single greatest risk factors for the development of new breast cancer. Approximately 50% of breast cancers occur in women 65 years of age or older and more than 30% occur after age of 70 [1]. Older women are the fastest growing segment of the United States and European population [2, 3]. Therefore, during the coming decades, older women will represent an increasing cohort of patients with newly diagnosed breast cancer as well as cancer survivors [4]. These older breast cancer survivors are likely to be quite a heterogeneous group especially with respect to multiple co-morbid conditions [5, 6]. At present, treatment for elderly women is largely extrapolated from data derived from trials in younger patients. [7–11]. Decisions about optimal treatment patterns will ultimately depend on trial data about efficacy and women's treatment preferences [12]. There is currently scant data on the long-term sequelae of different breast cancer treatments to guide older women facing these important decisions [13]. Improvements in life expectancy increase the incentive to allow older women to be treated without major barriers related to age, functional status and social support, even though recent studies showed that less diagnostic activity and less aggressive treatment are associated with poorer survival [14–16].

This review is an attempt to summarize important issues such as screening, risk factors, tumor characteristics and

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considerations for cancer management of early and advanced breast cancer in the geriatric population.

Definition of elderly

The definition of “elderly” is controversial with traditional demographic definition as those exceeding 65 years of age. Census statistics show that this group represents about 12.5% of the population, although this proportion is expected to rise to nearly 40% by the year 2035 [17]. This issue is somewhat complex since there is an increase in the incidence of non-fatal cancers in the oldest-old (90 years and above) accompanied by a lower than expected incidence of metastatic disease, suggesting a form of protective effect in selected elderly subgroups [18]. Any assessment of cancer-specific outcomes where age alone functions as an independent variable needs to factor in age-adjusted life expectancy implying benefit in dividing the elderly cohort into young old, (65–74 years), older old (75–84 years), and oldest old (85 years and above) for the purposes of more accurate analysis. For our purposes, elderly is taken as 70 years and over, representing the accepted age utilized for these analyses in most studies. In this regard, age itself is not the most useful parameter but rather the concept of senescence (the passage of biologic time) as opposed to ageing (the passage of chronological time) is considered to be of more value. In fact, aging is a physiologic process characterized by loss of independence, co-morbidity and geriatric syndromes. Age 70 represents a milestone beyond which older people are found.

Hormone replacement therapy

Hormone replacement therapy (HRT) is widely used for controlling menopausal symptoms. It has also been used for the management and prevention of cardiovascular disease [19], osteoporosis [20] and dementia [21] in older women, but the evidence supporting its use for these indications is largely observational. Results of earlier studies had suggested that long term use of estrogen was likely to be associated with an increased risk of breast cancer [22]. A recent Cochrane Review concluded that HRT is not indicated for the routine management of chronic disease, since in relatively healthy women, a combined continuous therapy significantly increased the risk of breast cancer (after 5 years), thromboembolism or coronary event (after one year), stroke (after 3 years), and gallbladder disease. Moreover among elderly women taking continuous combined HRT, there was a statistically significant increase in the incidence of dementia [23]. The Women’s Health Initiative, a recent randomized controlled

trial, was stopped prematurely in 2002 due to unfavourable risk-benefit ratio [24]. After a mean of 5.2 years of follow-up, the data and safety monitoring board recommended stopping the trial of estrogen plus progestin vs. placebo because the test statistic for invasive breast cancer exceeded the stopping boundary for this adverse effect and the global index statistic supported risks exceeding benefits.

Moreover the decrease in breast-cancer incidence, observed in a recent analysis of data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) registries, seems to be temporally related to the first report of the Women’s Health Initiative and the ensuing drop in the use of HRT among postmenopausal women in the United States [25].

In conclusion, we believe that HRT in women over 70 years is not indicated for therapy and prophylaxis of postmenopausal complaints, but should be individualized for symptomatic women tailoring the regimen and dose to individual needs.

Chemoprevention

In recent years, a number of randomized prospective trials have investigated the use of antiestrogens as a means to reduce the incidence of breast cancer. Cumulative data from multiple adjuvant studies documented the efficacy of tamoxifen in reducing second primary breast cancers in the contralateral breast, supporting its potential as a chemopreventive agent for breast cancer. The safety and second primary data on tamoxifen, together with extensive information on its pharmacokinetics, metabolism, and anti-tumour effects, as well as its potentially beneficial effects on lipid metabolism and osteoporosis, led the National Surgical Adjuvant Breast and Bowel Project (NSABP) to select tamoxifen for testing in the first prospective randomized phase III trial of the efficacy of a chemopreventive agent for preventing breast cancer in women at increased risk of the disease. 13,388 women 35 years of age who were at increased risk of breast cancer according to Gail model risk factors [family history, age, and personal history (i.e., age at first birth, age at menarche, previous breast biopsies)] were randomized to tamoxifen 20 mg/day or placebo for 5 years. The Breast Cancer Prevention Trial and the International Breast Cancer Intervention Study-I [26], demonstrated that tamoxifen can reduce the incidence of both invasive and non-invasive breast cancer as well as of bone fractures in women at increased risk, among older participants. These benefits accrue at the expense of increased risk of endometrial cancer, thromboses, cataracts, and possibly diminished quality of life in postmenopausal women. Recent up-date of the study showed that despite the potential bias caused

by the unblinding of the P-1 trial, the magnitudes of all beneficial and undesirable treatment effects of tamoxifen were similar to those initially reported, with notable reductions in breast cancer and increased risks of thromboembolic events and endometrial cancer [27]. Nevertheless the risk-reducing effect of tamoxifen appears to persist for at least 10 years, but most side effects of tamoxifen do not continue after the 5-year treatment period [28]. In a subset analyses of older postmenopausal women taking raloxifene for the treatment of osteoporosis indicate reduction of breast cancer incidence by more than 70%. These findings led the NSABP to design and launch the STAR trial (P-2, the Study of Tamoxifen and Raloxifene) [29]. The study demonstrated that Raloxifene is as effective as tamoxifen in reducing the risk of invasive breast cancer and has a lower risk of thromboembolic events and cataracts but a non-statistically significant higher risk of non-invasive breast cancer. The risk of other cancers, fractures, ischemic heart disease, and stroke is similar for both drugs. Based on promising data involving reduction of contralateral breast cancer risk in adjuvant studies, several aromatase inhibitors, including letrozole, anastrozole, and exemestane, are being incorporated into trials evaluating their efficacy as preventive agents in women at increased risk [30].

A very important issue for women over 70 years relates to the estimation of the net benefit resulting from the use of chemopreventive agents. There will be women for whom the net effect of chemoprevention will be highly positive such as women with an increase in the level of predicted risk, with a history of LCIS or atypical hyperplasia. An individualized risk assessment remains a key feature of effective chemopreventive use.

Risk factors and biologic aspects

A recent study on risk factors for breast cancer in patients over 75 years showed similarity to younger women [31]. The authors described the age-specific influence of risk factors for postmenopausal breast cancer, with emphasis on women aged 75 or more years. Women with a body mass index in the highest versus the lowest quartile were at increased risk of breast cancer at age 75 or more years. Family history of breast cancer for a first-degree relative and an older age at menopause conferred increased risk for women aged 75 or more years, and a high number of live births were protective. Obesity, a modifiable risk factor, remained positively associated with breast cancer for all age groups of postmenopausal women.

Many studies reviewed the tumor characteristics of breast cancer according to age at diagnosis [2, 17, 32–34] and although breast cancer presentation in elderly patients

may occur at a more advanced stage, both clinical and pathologic data are consistent with less aggressive disease in older woman. Studies from a large number of patients show that elderly breast cancer patients are more likely to have Estrogen (ER)-positive tumors that result in an endocrine responsive disease [32, 33, 35–37].

Other data confirmed that elderly women had more favorable biologic characteristics as demonstrated by lower rates of tumor cell proliferation, a lower expression of human epidermal growth factor receptor 2 (HER-2), a higher expression of ER and progesterone (PR) receptors, a higher frequency of diploidy, a lower frequency of p53 accumulation and a more favorable outcome [38, 39].

Similar results were reported in a recent investigation that showed how elderly patients present with larger tumors and higher nodal involvement than younger patients [33], although more favorable biological characteristics have been noticed. Endocrine responsiveness seems similar in both age groups and similar trends have also been observed for other biological characteristics, while the percentage of HER2/neu negative tumors increases and peritumoral vascular invasion decreases with age. However, neither tumor Grade nor Ki-67 seems to associate with age.

Screening

Women aged 70 and older have the highest incidence and mortality from breast cancer of any age group. Despite this increased burden of disease, studies showed that older women are the less likely to be screened for breast cancer even if recent data support the utility of screening of asymptomatic women aged 70 years and older. A retrospective study in the Netherlands showed a decline of breast cancer-related mortality among women who underwent regular screening mammography up to age 75 years [40]. A number of reviews of the Medicare-linked Surveillance, Epidemiology, and End Results data-base demonstrated the benefits of mammography after age 70 years. Women who underwent at least two mammographic examinations between ages 70 and 79 years experienced a two and one-half fold reduction in breast cancer mortality compared to women who had no examinations [41]. Breast cancer was diagnosed at an earlier stage in women who had undergone screening [42]. Most interesting, mammography up to age 85 years was associated with reduction mortality, and this benefit was experienced also by women with moderate co-morbidity [43].

Because of the results of these studies, reasonable recommendation would be to offer yearly mammography to women up to age 75 years and should be continued after

age 75 years in women without severe co-morbid conditions. In women with multiple co-morbidities, the benefit of screening mammography should be weighed against the estimated life expectancy. This would allow for the collection of data that would further define the cost effectiveness of screening in this older population and lead to more evidence-based health care policy decision.

Diagnosis and staging

Diagnosis and staging is in principle identical to non elderly breast cancer patients [44]. The diagnosis is based on clinical palpation, bilateral mammography and ultrasound. Less value in elderly breast cancer patients has the MRI (magnetic resonance imaging), due to the age related reduction in breast density. Pathologic diagnosis with fine needle aspiration or core needle biopsy should be obtained prior to any surgical procedure. Final pathological diagnosis should be made according to the World Health Organisation classification and the TNM (2003) staging system analyzing all tissue removed.

Treatment

Surgery Until the 80's standard local treatment of early breast cancer consisted of local cancer removal plus axillary surgery either to achieve nodal disease control or to stage the tumor accurately therefore to decide on adjuvant treatment. A surgical team from Scotland first popularized the concept of non-surgical management of breast cancer management in the elderly [45] and several breast surgeons have denied cancer removal for more than 20 years. Such a low-profile attitude is a reason of concern considering the fact that operative mortality for breast cancer in elderly women ranges between 0 and 0.5% [46]. Moreover, geriatric assessment tools are being developed to predict short-term complication for elderly cancer patients [47].

There is evidence that definitive surgery is often not offered to older patients and that management of the axilla is frequently omitted. The National Cancer Database reviewed the records of approximately 550,000 breast cancer patients and found that the >70-year age group was twice as likely not to have axillary node dissection when compared to younger patients [48]. There is no good rationale for denying surgical therapy for breast cancer beyond the age of 70 years [49, 50].

There appears to be no good reason why surgery, when feasible, should differ from what is being offered to younger patients and the very same procedures (i.e. quadrantectomy, lumpectomy or mastectomy) should be taken into consideration [15, 33]. A Cochrane Review conclusively demonstrates how "tamoxifen only" is not the best

option as local progression is higher (tamoxifen 81% vs. surgery 38%), the response rate only lasts 18–24 months, hence patients are due to receive at a later time and more advanced stage [51]. This study also showed that surgery and hormonal therapy were the best option in term of overall survival, breast cancer-specific survival, disease-free survival, with a good quality of life.

Two recent clinical trials in patients with small operable tumors and clinically negative axillary lymph nodes suggested that elderly patients can be treated by conservative surgery and no axillary dissection, which should be reserved for patients who later develop overt axillary disease [52, 53]. Fortunately, the sentinel node biopsy (SNB) procedure has largely solved this problem, allowing an insight of nodal involvement without inducing major side effects [54]. A recent study from the Milano group [55] suggested that elderly patients with tumors smaller than 3.0 cm and no clinical evidence of axillary involvement should be offered a SNB. Patients with positive SN will receive complete axillary dissection; patients with negative SNB will have just follow-up. A patient with tumor larger than 3.0 cm, with no significant comorbidities, complete axillary dissection is suggested.

There is no data contra-indicating breast reconstruction following a mastectomy, with the aim of providing better cosmetic results, and improving the quality of life [50, 56, 57].

In conclusion, we believe that surgery remains the standard of care for the treatment of early breast cancer and that alternative therapies should be reserved for those patients too ill or frail for surgery, or for those who refuse it.

Radiotherapy

In case of breast-conserving surgery standard treatment would entail adjuvant radiation therapy to the remaining mammary gland, or even chest wall irradiation for patients at a high risk of local recurrence.

There is controversy regarding the role of adjuvant radiation therapy following curative breast-sparing surgery. A recent study [58] debated its need in early stages, but its omission was also proven to lead to a reduced breast cancer-specific survival and higher risk of a second ipsilateral breast cancer requiring subsequent mastectomy [59]; it is important to realise how, in the lack of guidelines, the evidence suggests how elderly breast cancer women are commonly denied post-operative radiotherapy [33, 60] or receive it with some delay [61]. The ongoing "Prime II" trial was specifically designed to answer this question for this age group [62].

In a recent Italian study on women receiving breast-conserving surgery, adjuvant radiation therapy was not

offered to 46.3% patients over age 75 vs. 15.5% in the 65–75 years old group and 14.4% in the ages 50–64 years [33]. Patients aged 70–79 years with minimal co-morbidity are the most likely to benefit adjuvant radiation therapy while patients with substantial co-morbidity are least likely to achieve a survival advantage [59]. Another study showed that radiation therapy after breast conserving surgery and 5 years of tamoxifen use were beneficial in reducing recurrences and second primary breast cancers in older women, regardless of their age or comorbidity burden [63]. A population-based cohort study showed that after mastectomy, chest wall irradiation improved survival in women 70 years or older with locally advanced breast cancer [64].

The decision to offer radiotherapy needs to be tailored for each single individual according her fitness, competing risks of mortality from associated morbidities (particularly cardiac/vascular) and the risks of local recurrence.

It is important to evaluate alternative “easier” schedules for these patients such partial breast irradiation [65, 66] or intraoperative radiotherapy to the site of excision for whom the risk of recurrence outside the index quadrant is very low [67, 68].

Adjuvant setting

Endocrine treatment

With their good tolerability and ease of use, endocrine treatments have been evaluated in elderly patients more than any other adjuvant treatment, with data supporting a 5-year course rather than shorter period [69]. In older-women with hormone receptor-positive tumours, tamoxifen is still the most widely used therapy because of its favourable toxicity profile compared to chemotherapy. The value of adjuvant tamoxifen is well established and confirmed in the Oxford overview data [70] and a Cochrane review [51]. Data from the Early Breast Cancer Trialists Collaborative Group demonstrated the benefit of tamoxifen after 15 years of follow-up in patients with ER-positive receptors [70]. A recent study showed that even only one year of tamoxifen resulted in a significant and prolonged disease-free and overall survival [71]. Large phase III trials show no differential effect of tamoxifen versus aromatase inhibitors related to age [72]. More recently the ATAC (Arimidex Tamoxifen Alone or in Combination) study showed a significant advantage in disease free survival and a longer time to recurrence but not in overall survival when using aromatase inhibitor. Treatment with aromatase inhibitor compared with tamoxifen is associated with a decreased risk of endometrial cancer and thromboembolic events, vaginal bleeding, hot flushes; bone loss and arthralgia were more common with anastrozole [73, 74].

Another recent study comparing tamoxifen with letrozole showed a significant benefit for local failure, distant recurrence and contralateral breast cancer when using aromatase inhibitor but with increased cardiovascular events as well as bone fractures, muscular and osteoarticular pain [75].

Careful evaluation of concomitant comorbidities and the different spectrum of toxicity of tamoxifen versus aromatase inhibitors have also to be taken into account when recommending adjuvant endocrine therapy in the elderly population. In our opinion, elderly breast cancer patients with ER and/or PR positive tumours should receive tamoxifen for 5 years. In fact, the long term cardiovascular and skeletal adverse effect associated with aromatase inhibitors should be an issue of concern in these patients. The use of aromatase inhibitors in stead of or in sequence with tamoxifen did not demonstrated survival benefit so far, even if significantly reduces the risk of recurrence compared to tamoxifen. Furthermore, the absolute difference in recurrence-free survival is <5%. Certain subgroup of patients (ER-positive/PR negative, HER2-positive) seems to have a more marked benefit by the use of aromatase inhibitors.

Adjuvant chemotherapy

Even if there is substantial evidence that elderly patients have a relative survival similar to younger patients when given comparable treatments, chemotherapy has been least used and studied in this population [76–81]. Recent investigations show how chemotherapy is associated with a significant mortality reduction among older ER-negative and lymph nodes-positive breast cancer women [81, 82]. In agreement with these studies, the Leukaemia Group B (CALGB) and US Breast Cancer Intergroup showed that the main benefit from chemotherapy was in the hormone receptor-negative patients [83]. Muss et al [84] analyzed the efficacy and tolerability of different and progressively more intense adjuvant chemotherapy in node-positive breast cancer patients. The study concluded that older and younger patients derive similar reduction in breast cancer mortality and recurrence from chemotherapy, but he noticed that the data must be taken with caution, because they were derived from a small and highly selected number, probably, not representative of the elderly population. The Oxford Overview suggested that poly-chemotherapy may induce a significant benefit in terms of relapse and survival rates up to 70 years of age [85]. The International Breast Cancer Study Group Trial VII [86] observed that both CMF (Cyclophosphamide, Methotrexate, 5-Fluorouracil) efficacy and tolerability were reduced in elderly breast cancer patients older than 65 years, with significantly grade III hematological and mucosal toxicities compared to lower incidence in the younger group. For this

reason the amount of drug effectively delivered had to be reduced. In addition the study did not show significant advantage when CMF was added to tamoxifen. Gelman and Taylor [87], proposed a Methotrexate and 5-FU dose adjustment, to better tolerate the treatment. An ICGG (International Collaborative Cancer Group) study showed that the recurrence rate was reduced by 27% when Epirubicin was associated to Tamoxifen in post-menopausal node-positive women, even if toxicity was increased [88]. Ibrahim et al. [89] studied 1,011 breast cancer patients treated with anthracyclines. They compared two age groups (50–63 vs. ≥ 64 years) and identified a higher response rate for the younger group, similar toxicity, as well as overall and disease-free survival. Taxanes have also been given on a 3-weeks schedule in association to G-CSF. Weekly based schedules have shown promising results in the elderly, with regards to tolerability and efficacy [90]. A recent paper observed that 4 cycles of AC (Doxorubicin, Cyclophosphamide) or 6 cycles of CMF are considered adequate treatment for endocrine responsive patients. For patients with endocrine non responsive or endocrine response uncertain disease, anthracycline-containing regimens with or without taxanes were favoured [12].

Moreover, new drugs and new treatment with low toxicity (e.g. capecitabine, vinorelbine, liposomal doxorubicin and weekly taxanes) need to be explored.

New targeted therapies with monoclonal antibody such as Trastuzumab, an humanized monoclonal antibody, have been used in only a few and highly selected elderly patients, but results from recent study showed impressive results [91, 92]. There was a concern since this drug also carries a significant risk of cardio toxicity and requires careful cardiac monitoring, even if no specific data regarding this effect are yet available in the elderly [92].

In conclusion, chemotherapy is feasible and advisable in elderly breast cancer patient. Adjuvant chemotherapy should be an individualized decision, taking into account the estimated absolute benefit, life expectancy, treatment tolerance, and patient preference. New targeted therapies such as with monoclonal antibodies need to be evaluated. Validated tools for predicting clinical benefits are available and widely utilised [93]. Patient's frailty should carefully be assessed with the use of CGA (Comprehensive Geriatric Assessment) tools [94].

Metastatic breast cancer

Surgery

It is also worth mentioning that an increasing number of reports highlight the feasibility and efficacy of surgical resection of liver metastases. This is certainly an infrequent

indication for liver resection, but surgical outcomes from selected series are certainly superior to for any other non-surgical series [95, 96]. Moreover, a recent study showed that in selected metastatic patients with low tumour load (e.g. bone metastases) primary tumour excision can improve survival [97].

Endocrine treatment

The use of endocrine therapy is well established and is the mainstay of systemic management for patients with hormone receptor positive disease without life threatening disease. As first line therapy an aromatase inhibitor should be favoured for their better disease-free survival when compared to tamoxifen [98, 99]. Patients who initially responded to endocrine therapy or who had prolonged stable disease should receive further endocrine therapy until disease becomes endocrine resistant [99]. Fulvestran appears particularly interesting because of its low toxicity profile [100].

Biphosphonates are recommended for all patients with lytic bone metastasis and should be part of the treatment irrespective of age. Early intervention with biphosphonates appears to provide the greatest potential for bone-sparing benefit and palliation of bone related symptoms. This is true especially in women with poor general health and can not receive other agent. Changes in renal function are important to consider when biphosphonates therapy is contemplated, because of the possibility of renal failure. The choice between the various forms is still debated [101].

Chemotherapy

The use of chemotherapy should be considered in endocrine refractory patients, in patients with hormone receptor negative and for women with symptomatic disease who have progression of metastases on endocrine therapy. The debate over combination chemotherapy vs. sequential single agents is ongoing [102]. Combination therapy is associated with higher response rates, time to progression and also toxicity. Preference should be given to chemotherapeutic agents with more "safe" profile. To this aim a number of drugs with minimal toxicity have been developed. These include low dose/weekly docetaxel [103], weekly paclitaxel [104], weekly epirubicin [105] oral capecitabine [106], idarubicin [107] and, capecitabine/vinorelbine [108]. Since in this situation the therapy is only palliative strict follow-up for efficacy/tolerance is needed in elderly breast cancer patients to avoid over-treatment and debilitating side effects.

Trastuzumab (Herceptin) should be considered in elderly patients with metastatic breast cancer whose tumours express HER-2/neu (c-erb).

In conclusion, we believe that the management of advanced breast cancer is palliative, with the aim being to improve the quality of life for patients and ideally prolong survival with the minimum of associated toxicity.

Final summary

Clinicians will have to deal with increasing cancers in the elderly. Current treatment practices in elderly breast cancer patients are extrapolated from the experience gained from randomized clinical trials focusing on a completely different age-group, as well as retrospective series and reviews. An attempt to transfer the results of younger patients to this heterogeneous population should be questioned and discouraged. Treatment optimization for this unique age group can only be achieved by encouraging active participation in clinical trials. Although available age-specific clinical data demonstrate that treatment efficacy is not modified by age, elderly patients are underrepresented in cancer clinical trials [76, 77].

Tailored treatment should be prioritized [109] in the elderly and should be based on biological features (i.e. hormonal receptors, c-erbB2 overexpression, multicentricity); this leads to an increasing need for an accurate biological characterization of breast cancer also for elderly women [33, 110, 111].

The different approaches to local and systemic treatments in elderly patients with breast cancer have been well documented [112–116]. Several reports are showing a poorer prognosis for older women [117] but this difference seems to be related to the substandard treatment offered. Other recent investigations show how older and younger patients with loco-regional breast cancer fare equally [118] and age *per se* should not be the only factor in the decision making process in cancer patients [33, 58–64, 81, 82, 85, 119, 120]. This is crucial where the quality of life should be taken into the greatest account. Acute and chronic medical conditions, nutritional status, poly-pharmacy, level of activity, and disease-specific symptoms, all need to be taken into consideration. Only these concomitant factors, together with the patient's opinion, should lead to the final decision on the type and extent of treatment. It is essential, however, that physicians provide accurate estimates of the risk of relapse, treatment-related side effects and life expectancy when counseling elderly patients with breast malignancy.

Similarly to younger age-groups the surgical approach to elderly should aim for offering the best available option, which is not necessarily the very same treatment modality

[33, 55, 121]. Elderly patients, suitable for breast conservation, should be offered this type of treatment [56, 58] and investigational approaches are developed to decrease distress from 5/6 weeks of daily radiation therapy by innovative, intraoperative, one-shot radiation [67, 68]. This timesaving approach can have a significant impact on patients and physicians decision to use radiation therapy.

In conclusion, the data from this review suggested that the age of the patient should not be ignored when treatment is chosen, but in the optimal management of elderly patients, the general condition and stage of the disease, rather than chronological age alone, should be the determinant factors. When curative treatment is planned, careful assessment of the overall fitness to undergo general anesthesia, surgery and postoperative treatments is crucial. Morbidity and mortality from the procedure need to be weighed against possible survival benefit and potential gains in quality of life [122]. Given the current uncertainty about optimal treatment, clinicians can best serve older patients with early stage breast cancer by involving them in decision-making, taking into account available efficacy data, and individualizing care on the basis of such factors as co morbidity, social support, functional status, and patient preferences for outcomes.

Future directions

The new era of molecular biology is likely to shortly challenge the old era of using clinical variable alone for treatment. Currently, stage of disease, tumour grade, hormone-receptor status, and HER2 status remain the key prognostic factors for determining prognosis and treatment.

The use of microarray technology, which is able to identify a limited number of specific genes that can predict disease free survival, is likely to become a better way to define prognosis and select treatment than are currently used clinical and biological variables, and is of particular interest and importance for elderly patients. Gene array technology seems to be capable of identifying accurate estimates of the risk of metastases and identify low-risk patients, who would derive little to no benefit from chemotherapy.

The explosion in knowledge of molecular biology and the development of targeted therapies is a new era for improving breast cancer treatment. It is very important that elderly patient will be included in these new clinical trials. This will enable individualised treatment recommendations to be developed for these patients.

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