E2. Controversial issues in the surgical management of the elderly breast cancer patient

E. Bastiaannet[a,b], W. van de Water[a,b], G.J. Liefers[a], C.J.H. van de Velde[a,*]

[a] Department of Surgery, [b] Department of Gerontology & Geriatrics, Leiden University Medical Centre, Leiden, the Netherlands

Introduction

Breast cancer is the most common type of cancer in Western societies and will increasingly affect the lives of elderly women. The population of elderly breast cancer patients is characterised by large individual variation in physical and mental conditions. The development of guidelines is complicated by lack of evidence from randomized controlled trials (RCTs) and the influence of personal preferences in the decision-making process.

Treatment

The possible explanation for age-related administration and outcome of treatment is complex; it reflects decisions based on the view of physicians, patients, relatives and care-givers, and on psychosocial issues and costs, but also on proximity to an oncology and radiotherapy centre [1]. Because comorbidities and functional status significantly affect prognosis and treatment choices, thorough consideration must be given to the overall health of the elderly patient.However, elderly women are still less likely to have surgery for operable breast cancer, even after accounting for comorbidity, functional status, pretreatment stage, social deprivation and type of hospital [2]. National data from the Netherlands show that the percentage of patients who underwent surgery decreased with age; moreover, the proportion of the elderly who received surgery decreased over time [3]. An international comparison showed similar results for other countries [4], even in the lower stages of disease. It is often thought that elderly patients are at a higher risk of morbidity and mortality; moreover, personal preferences of elderly patients may also play a role. Hormonal treatment without surgery has been considered as an alternative treatment option [5], mainly in the very old. However, some data show that an increase in the use of hormonal-only treatment starts already at the age of 65 [3]. For fit elderly patients it has been confirmed (Cochrane meta-analysis [5]) that primary hormonal treatment with tamoxifen is inferior to surgery (with or without hormonal treatment) regarding local control and progression-free survival. However, no difference in overall survival was shown, and data for the frail elderly are not available [1,5]. Most elderly women with early-stage breast cancer are candidates for breast-conserving treatment; however, available data suggest that older patients are less likely to receive such treatment [1]. Besides, if elderly patients did receive breast-conserving surgery (BCS) their chances of receiving radiotherapy were significantly decreased. Several studies have specifically assessed the benefits of radiotherapy in elderly patients and have shown a decrease in the relative rate of breast cancer recurrence. However, the absolute incidence of relapses tended to be low, and data on overall survival were generally absent. Due to the presence of comorbidity and a higher competing risk of mortality with increasing age, the risks and benefits balance and numbers needed to treat will probably be different from those in younger patients. Besides, in surgical treatment decision-making, women's preferences are highly relevant; however, little is known about older breast cancer patients' preferences and the factors they consider important in their treatment choice.

Survival

Data from the TEAM (Tamoxifen Exemestane Adjuvant Multinational) trial have been used to assess the influence of age on disease-specific mortality, all-cause mortality and breast cancer relapse in postmenopausal women with hormone-receptor-positive breast cancer [6]. Disease-specific mortality as a proportion of all-cause mortality decreased with age (78%, 56%, 36% respectively; $P < 0.001$). Disease-specific mortality increased with age; patients aged $\geqslant$75 had a 1.6-fold higher risk of disease-specific mortality than patients <65 years (univariate $P < 0.001$). A fully adjusted model, including treatment and tumour characteristics, showed similar results ($P = 0.002$). Risk of breast cancer relapse increased with increasing age (HR 1.29, multivariable $P = 0.06$). So in this trial, regardless of a higher risk of other-cause mortality and independent of treatment and tumour characteristics, disease-specific mortality increases with age.

In the Western world breast cancer survival has increased considerably over the last decades. The improved outcome of breast cancer has generally been

0959-8049/$ – see front matter

attributed to better treatment options; however, several publications have shown that improved survival does not apply to elderly patients [7–9] On a similar note, a recent European study showed significant improvement of survival from 1988 to 1999 for a variety of cancers, but at a slower rate for elderly patients [10].

Alternative study designs

A critical reappraisal of treatment strategies and better selection of patients who can benefit from available therapies depends on future studies that facilitate the inclusion of a valid representation of older women, and specifically address the heterogeneity of this age group with careful registration of comorbidities and geriatric parameters in order to correlate outcome. The great heterogeneity in the elderly population stretches the possibilities of constructing randomized controlled clinical trials. Therefore we stress the importance of exploring different study designs in this ever-growing population [11,12]. Large, quality-assured prospective cohort studies generate a large amount of reliable data. Moreover, these data are a representative selection of the general population, including the substantial heterogeneity within the elderly. International prospective registration studies (*EURECCA*, European Registration of Cancer Care [13]) and cancer registry collaborations (*EUROCARE*, European cancer registry-based study on survival and care of cancer patients) may fulfil an important role in generating data and obtaining evidence.

Conclusions

Data from several studies confirm that elderly breast cancer patients receive less aggressive treatment, are less often treated according to guidelines, and have a decreased survival compared to their younger counterparts. Although the proportion of women who die of breast cancer is lower, the actual disease-specific mortality of the elderly is higher. In order to improve future outcome of elderly patients with breast cancer, it is important not only to prevent over-treatment of frail elderly patients but also to identify fit elderly patients who can profit from tailored treatments with chemotherapy or biologicals.

Conflict of interest statement

All authors have no conflict of interest to disclosure.

Acknowledgements

Dutch Cancer Society (KWF 2007-3968), Netherlands Cancer Registry (NCR), and Geriatric Oncology in the Netherlands (GeriOnNe).

References

[1] Wildiers H, Kunkler I, Biganzoli L, et al. Management of breast cancer in elderly individuals: recommendations of the International Society of Geriatric Oncology. *Lancet Oncol* 2007 Dec,**8**(12), 1101–1115.

[2] Lavelle K, Moran A, Howell A, Bundred N, Campbell M, Todd C. Older women with operable breast cancer are less likely to have surgery. *Br J Surg* 2007 Oct,**94**(10), 1209–1215.

[3] Bastiaannet E, Liefers GJ, de Craen AJ, et al. Breast cancer in elderly compared to younger patients in The Netherlands: stage at diagnosis, treatment and survival in 127,805 unselected patients. *Breast Cancer Res Treat* 2010 Dec,**124**(3), 801–807.

[4] Kiderlen M, Bastiaannet E, Walsh PM, et al. Surgical treatment of early stage breast cancer in elderly: An international comparison. Accepted Breast Cancer Res Treat 2011.

[5] Hind D, Wyld L, Reed MW. Surgery, with or without tamoxifen, vs tamoxifen alone for older women with operable breast cancer: cochrane review. *Br J Cancer* 2007 Apr 10,**96**(7), 1025–1029.

[6] van de Water W, Markopoulos C, Van de Velde CJH, et al. Disease specific mortality increases with age in postmenopausal patients diagnosed with hormone receptor positive breast cancer – a TEAM study analysis. *JAMA* 2012; accepted.

[7] Tejler G, Norberg B, Dufmats M, Nordenskjold B. Survival after treatment for breast cancer in a geographically defined population. *Br J Surg* 2004 Oct,**91**(10), 1307–1312.

[8] Hughes S, Barbachano Y, Ashley S, et al. Time trends in the outcome of elderly patients with breast cancer. *Breast J* 2008 Mar,**14**(2), 158–163.

[9] Bastiaannet E, Portielje JE, van de Velde CJH, et al. Lack of survival gain for elderly women with breast cancer. *Oncologist* 2011,**16**(4), 415–423.

[10] Quaglia A, Tavilla A, Shack L, et al. The cancer survival gap between elderly and middle-aged patients in Europe is widening. *Eur J Cancer* 2009 Apr,**45**(6), 1006–1016.

[11] van de Water W, Bastiaannet E, Liefers GJ. [Treatment of breast cancer in the elderly is not evidence-based]. *Ned Tijdschr Geneeskd* 2011,**155**(42), A3359.

[12] van de Water W, Bastiaannet E, van de Velde CJH, Liefers GJ. Inclusion and analysis of older adults in RCTs. *J Gen Intern Med* 2011 Aug,**26**(8), 831.

[13] van Gijn W, van de Velde CJH. Improving quality of cancer care through surgical audit. *Eur J Surg Oncol* 2010 Sep,**36 Suppl 1**, S23-S26.