

Breast Cancer in the Elderly

Sonja E. Singletary, M.D.,* Rick Shallenberger, M.P.H.,† and Vincent F. Guinee, M.D., M.P.H.†

From the Departments of General Surgery and Patient Studies,† The University of Texas M. D. Anderson Cancer Center, Houston, Texas*

Objective/Methods

To determine the clinical behavior and outcome of breast cancer in the elderly, a series of 184 women older than age 69 years who received treatment for locoregional breast cancer at The University of Texas M. D. Anderson Cancer Center between 1976 and 1985 were studied for a median of 80 months.

Results

The results indicate that elderly women can tolerate standard surgical therapy and survive disease-free for many years; the breast cancer-specific survival rate of patients in this study was 79% at 7 years. Although 33% of patients had stage I disease, only 10% underwent breast conservation surgery. Despite 46% of patients having stage II and 21% having stage III breast cancer, fewer than 13% received systemic adjuvant therapy. Noncompliance with breast screening guidelines was evident in that only 3% of patients had tumors detected by routine screening mammograms and only 12% by routine physical examinations.

Conclusions

Women with breast cancer should be informed of treatment options and the advantages and disadvantages of each choice based on physiologic rather than chronologic age.

One of eight women in the United States is at risk of having breast cancer in her lifetime. The probability of breast cancer developing is highest in the older woman. Data from the Surveillance Epidemiology and End Results¹ study revealed that for women 80 to 84 years of age, the breast cancer incidence is as high as 435 per 100,000; in contrast, the incidence is 212 per 100,000 in women 50 to 54 years of age. The surgeon's dilemma in choosing the optimal management of breast cancer in the elderly arises from the following long-held beliefs of the natural history of the disease in this patient population: (1) elderly patients have more locally advanced dis-

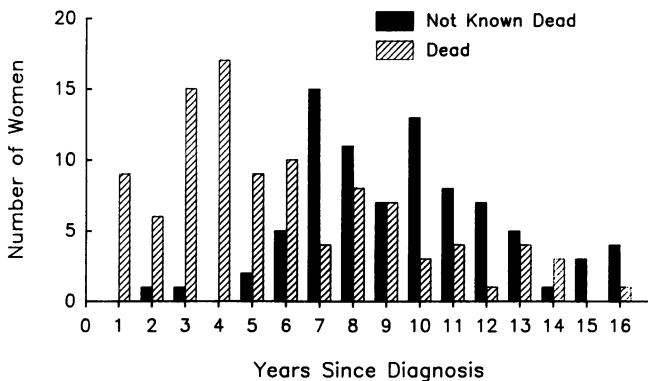
ease at initial presentation; (2) elderly patients have more indolent breast cancer; (3) elderly patients have a limited life expectancy from comorbid conditions other than breast cancer; and (4) elderly patients do not tolerate standard treatment.

To determine whether these beliefs were indeed reflective of the clinical behavior of breast cancer in the elderly, we reviewed the medical records of 184 women older than age 69 years who initially registered with a diagnosis of breast cancer without distant metastasis and received treatment between 1976 and 1985 at The University of Texas M. D. Anderson Cancer Center.

METHODS

We analyzed the medical records of women older than age 69 years who were referred from 1976 to 1985 to the

Address reprint requests to Sonja E. Singletary, M.D., Department of General Surgery, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Box 106, Houston, TX 77030. Accepted for publication January 14, 1993.



Source: Dept. of Patient Studies

Figure 1. Distribution of follow-up time intervals for 184 women seen between 1976 and 1985, with follow-up continued through 1992. Time to death of 101 deceased women is represented by the hatched bars.

M. D. Anderson Cancer Center for definitive treatment of locoregional breast cancer without prior malignancy. The median time interval between diagnosis and last contact or death was 80 months (Fig. 1). Actuarial survival was calculated on the basis of this interval (SPSS Version 9 Statistical Package SPSS Inc., Chicago, IL).²

RESULTS

Clinical and Histologic Presentation

The most frequent method of initial detection of breast cancer (85%) was self-discovery of the tumor by the patient. Only 12% of tumors were found by physicians during routine physical examinations. A screening mammogram with a positive result was obtained in only 5 of the women (3%). The majority of patients (78%) sought medical attention within 2 months of the onset of symptoms.

The most frequent comorbid conditions under active treatment at the time of diagnosis were hypertension (48%), cardiovascular disease (23%), and arthritis (26%). Although 27% of patients had no major health problems requiring treatment and 91% were totally mobile, 2 or more comorbid conditions were present in 29%.

On clinical examination, 36% had primary tumors of 2 cm or smaller (T1), 44% had tumors larger than 2 cm but no larger than 5 cm (T2), and 8% had tumors larger than 5 cm (T3). Only 12% had skin ulceration or dermal lymphatic involvement (peau d'orange) of the breast (T4). The axilla was described as clinically negative (N0) in 71%, as palpable, movable lymph nodes (N1) in 19%, and as fixed or matted lymph nodes (N2) in 10%. Using the current American Joint Commission Cancer Staging System,³ 33% of patients had stage I disease (T1, N0),

46% had stage II (T1, N1; T2, N0-1; T3, N0-1), and 21% had stage III (T3, N2; T4, N0-2).

Primary tumor size, as determined by histologic examination, correlated with the clinical staging in 83% (48 of 58) of T1, 67% (51 of 76) of T2, and 52% (11 of 21) of T3 patients who underwent surgical therapy as the first treatment modality (155 of 184). One hundred sixty patients had an axillary node dissection; histologically positive axillary nodes were found in 66% of these patients described as having a clinically positive axilla and in 31% of those described as having a clinically negative axilla. Of the 65 patients with histologically positive nodes, 42 (65%) had metastases confirmed in 1 to 3 nodes.

Invasive ductal carcinoma was the predominant histologic type (84%). Pure noninvasive disease was detected in five patients, and other histologic types in 24 (colloid or mucinous, 13; invasive lobular, 5; Paget's disease, 3; papillary, 2; and tubular, 1). Of 104 women with known estrogen receptor status, 79% were receptor positive (≥ 10 fmol/mg).

Treatment

Total mastectomy with axillary node dissection (including three radical mastectomies) was performed in 82% of patients. Only 18 patients had breast conservation surgery. Seven patients had total mastectomy without node dissection for debulking, and nine patients received no surgical intervention because of advanced disease and poor performance status. Only three postoperative deaths occurred (at 5 days, 7 days, and 23 days). Each of these deaths was related to myocardial infarction. Only 24% of the remaining patients who had surgery experienced complications. The most common postsurgical problems were related to the wound: infection in 14 patients, hematoma in 5, and minor flap necrosis in 8. Radiation therapy was given to 30% of patients: 10 preoperatively and 44 postoperatively. Complications from the radiation were recorded in fewer than 5%.

Tamoxifen, an antiestrogen, was used as an adjuvant to surgery in only 15 patients with estrogen receptor-positive tumors. Tamoxifen was given as a palliative measure in seven patients with unresectable disease; five had only a minor response and two had a complete remission. However, both of these two patients eventually experienced a relapse in the breast, one at 10 months and the other after 10 years.

Combination chemotherapy was used as an adjuvant in only eight patients on an individual basis. Eleven patients received preoperative chemotherapy for initially unresectable disease. Seven of these 11 patients have remained disease-free.

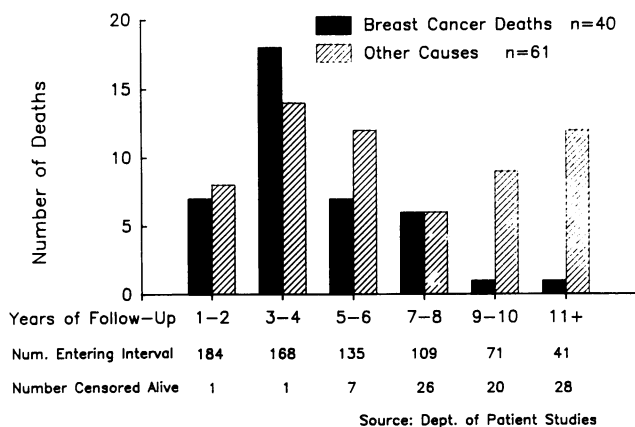


Figure 2. Cause of 101 deaths by years of follow-up in 184 women age 70 years and older with locoregional breast cancer. Death from breast cancer is represented by solid bars. Death from other causes is represented by hatched bars.

Clinical Outcome

Forty-seven patients had recurrent breast cancer; 10 experienced locoregional relapse (in the chest wall or intact breast) only, 24 had distant metastases only, and 13 had both. The median time interval between diagnosis and distant relapse was 33 months. The most common presentations of distant metastases were simultaneous multiple sites in 40%, bone in 27%, and visceral organs in 24%. After distant recurrence, the median survival time was 11 months.

Over a 16-year follow-up period in which living patients have been observed for a median of 106 months, there have been 101 deaths. Forty per cent of these deaths were from breast cancer and 60% from other causes (Fig. 2). The breast cancer-specific survival rate was 79% at 7 years. The most common known cause of death was cardiovascular disease.

DISCUSSION

Our data indicate that elderly patients do not necessarily always present with more locally advanced disease. Most patients in other series³⁻⁵ were classified as having stage III disease because of the large size of the primary tumor rather than the existence of advanced regional disease. Mueller et al.,⁶ in a review of 3,558 patients, reported that early stage breast cancer is equally common in all age groups.

The finding that only 15% of breast cancers in our study were detected by routine physical examination or screening mammograms is disappointing but consistent with other series. In a review of 1,680 women with breast cancer treated in 17 community hospitals, Chu et al.⁷

found that elderly patients were less likely to receive a mammogram or biopsy or be referred for consultation. Makuc et al.⁸ found that older women were also less likely than younger women to have had a recent clinical examination of their breasts by their physicians or to have been instructed in breast self-examination.

In our study, invasive ductal carcinoma was the most common histologic type (84%); only 9% of the patients had tumors of low-grade histologic type (colloid, tubular, or mucinous). Our finding that 79% of breast cancers in this series of elderly patients were estrogen receptor-positive is similar to the finding of Von Rosen et al.⁹ However, no prognostic significance for estrogen receptor status has been observed in patients with axillary nodal metastases or locally advanced disease.^{10,11} Available data suggest that estrogen receptor content in node-negative breast cancer may reflect growth rate rather than metastatic potential and, therefore, serves as a predictor only of the patterns of recurrence (predominantly bone) and a longer disease-free interval.^{10,11}

The assumption that elderly patients have concurrent health problems that override the life-threatening risks from breast cancer has often resulted in less aggressive treatment of breast cancer. Satariano et al.¹² reported that the comorbid conditions described by women with breast cancer are similar to those reported by women in the general population. Arthritis, cardiovascular disease, and hypertension were the predominant health problems for women of this age both with and without breast cancer. Similarly, Koch et al.¹³ found the life expectancy of patients with breast cancers dying of other causes to be similar to that of the sex/age-matched population without breast cancer.

Surgeons' reluctance to perform standard surgical procedures in these patients is based on the assumption that the elderly cannot tolerate surgery. Turnbull et al.¹⁴ demonstrated, in an analysis of 4,050 operations, that the operative mortality rate of patients older than 70 years (4.8%) was similar to that of all ages (3.4%). For breast cancer surgery, most series report an operative mortality rate of 1% or less and that the primary morbidity related to short-term wound complications that respond to conservative management. In those patients with significant comorbid conditions and limited life expectancy, the magnitude of the surgical procedure must be adjusted. A randomized trial conducted by the National Surgical Adjuvant Breast Project (NSABP B-04) has shown that axillary node dissection in patients with clinically negative axilla does not affect survival.¹⁵ Only 20% of patients require a subsequent therapeutic node dissection for clinical evidence of axillary disease. In operable patients at high risk for general anesthesia, a partial or total mas-

tectomy with local anesthesia without an axillary dissection is appropriate.

Recently, tamoxifen has been proposed as an alternative to surgery. Overall response rates have ranged from 49% to 68%; complete responses were noted in 27% to 40% of patients.¹⁶⁻¹⁸ Clinical trials that compared tamoxifen to surgery have not shown a survival difference.¹⁹⁻²¹ However, the median follow-up time of these studies was 3 years or less. Horobin et al.¹⁸ have demonstrated that with a minimum follow-up time of 5 years, the tumors of 62% of 113 patients age 70 years or older with locoregional breast cancer were not controlled by tamoxifen alone. The rate of local relapse continued to increase progressively over time.

Our limited experience with chemotherapy in this age group for locally advanced cancer suggests that there is a reluctance to use aggressive chemotherapy in the elderly. A recent study by the Eastern Cooperative Oncology Group²² of 92 patients age 65 to 90 years with advanced breast cancer who were treated with combination cyclophosphamide, methotrexate, and 5-fluorouracil revealed no significant age trends in toxicity, response, or cycle-by-cycle reduction of chemotherapy dose, based on creatinine clearance.

Because life expectancy may be as long as 10 years or more in patients who have achieved an age of 70 years or older, treatment should be guided by an acceptable benefit/risk ratio to provide optimal quality and quantity of life.

Elderly women have the same right as their younger counterparts to be a part of the decision-making process of their health care. Because randomized clinical trials^{23,24} have not shown a survival difference between conservative breast surgery plus radiation therapy and standard mastectomy, the option to preserve the breast should be discussed with the patient. Radiation has been shown to decrease the likelihood of local recurrence after breast preservation and is well tolerated in the elderly. Clinical judgment should be used in patients with poor performance status regarding the extent of surgery that is necessary to achieve adequate local control. A wide excision of the primary tumor with observation of the clinically negative axilla may be appropriate in selected individuals, especially if staging of the axilla will not alter their therapeutic management. Reliance on tamoxifen alone without surgery may not be sufficient.

Acknowledgments

The authors thank Ms. Darlene Womack for preparing this manuscript.

References

1. Ries LAB, Hankey BR, Edwards BK, eds. Cancer Statistics Review, 1983-1987. Bethesda: National Cancer Institute Division of Cancer Prevention and Control Surveillance Program, 1989 (NIH publication no. 90-2789).
2. Nie NH, Hull CH, Jenkins JG, et al. SPSS Statistical Package for the Social Sciences, Version 9. New York: McGraw Hill, 1986.
3. Davis SJ, Karrer FW, Moor BJ, et al. Characteristics of breast cancer in women over 80 years of age. *Am J Surg* 1985; 150:655-658.
4. Herbsman H, Feldman J, Selders J, et al. Survival following breast cancer surgery in the elderly. *Cancer* 1981; 47:2358-2363.
5. Hunt KE, Fry DE, Bland KI. Breast carcinoma in the elderly patient. *Am J Surg* 1980; 140:339-342.
6. Mueller CB, Ames F, Anderson GD. Breast cancer in 3,558 women: age as significant determinant in the rate of dying and causes of death. *Surgery* 1978; 83:123-131.
7. Chu J, Diehr P, Feigl P, et al. The effect of age on the care of women with breast cancer in community hospitals. *J Gerontol* 1987; 42:185-190.
8. Makuc DM, Freid VM, Kleinman JC. National trends in the use of preventive health care by women. *Am J Public Health* 1989; 79:21-26.
9. Von Rosen A, Gardelin A, Auer G. Assessment of malignancy potential in mammary carcinomas in elderly patients. *Am J Clin Oncol* 1987; 10:61-64.
10. Adami H-O, Graffman S, Lindgren A, Sallstrom J. Prognostic implication of estrogen receptor content in breast cancer. *Breast Cancer Res Treat* 1985; 5:293-300.
11. Qazi R, Chuang J-LC, Drobyski W. Estrogen receptors and the pattern of relapse in breast cancer. *Arch Intern Med* 1984; 144:2365-2367.
12. Satariano WA, Ragheb NE, Dupuis MH. Co-morbidity in older women with breast cancer: an epidemiologic approach. *In* Yancik R, Yates JW, eds. *Cancer in the Elderly: Approaches to Early Detection and Treatment*. New York: Springer, 1989; pp 71-103.
13. Koch M, Hanson J, Gaedke H, Wilson D. Competing causes of death in breast cancer patients. *In* Paterson AHG, Lees AW, eds. *Proceedings of the Second International Symposium on Fundamental Problems in Breast Cancer*, Alberta, Canada. Banff, Alberta: Nijhoff, 1986; pp 265-272.
14. Turnbull AD, Gundy E, Howland WS, Beattie EJ Jr. Surgical mortality among the elderly: an analysis of 4,050 operations (1970-1974). *Clin Bull* 1978; 8:139-142.
15. Fisher B, Redmond C, Fisher ER. Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation in the treatment of breast cancer. *N Engl J Med* 1985; 312:665-673.
16. Akhtar SS, Allan SG, Rodger A, et al. A 10-year experience of tamoxifen as primary treatment of breast cancer in 100 elderly and frail patients. *Eur J Surg Oncol* 1991; 17:30-35.
17. Bradbeer JW, Kyngdon J. Primary treatment of breast cancer in elderly women with tamoxifen. *Clin Oncol* 1983; 9:31-34.
18. Horobin JM, Preece PE, Dewar JA, et al. Long-term follow-up of elderly patients with locoregional breast cancer treated with tamoxifen only. *Br J Surg* 1991; 78:213-217.
19. Bates T, Riley DL, Houghton J, et al. Breast cancer in elderly women: a cancer research campaign trial comparing treatment with tamoxifen and optimal surgery with tamoxifen alone. *Br J Surg* 1991; 78:591-594.
20. Gazet J-C, Ford HT, Bland JM, et al. Prospective randomized trial of tamoxifen versus surgery in elderly patients with breast cancer. *Lancet* 1988; 2:679-681.

21. Robertson JFR, Todd JH, Ellis IO, et al. Comparison of mastectomy with tamoxifen for treating elderly patients with operable breast cancer. *Br Med J* 1988; 297:511–514.
22. Gelman RS, Taylor SG IV. Cyclophosphamide, methotrexate and 5-fluorouracil chemotherapy in women more than 65 years old with advanced breast cancer: the elimination of age trends in toxicity by using doses based on creatinine clearance. *J Clin Oncol* 1984; 2:1404–1413.
23. Fisher B, Redmond C, Poisson R, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1989; 320:822–828.
24. Veronesi U, Salvadori B, Luini A, et al. Conservative treatment of early breast cancer: long-term results of 1,232 cases treated with quadrantectomy, axillary dissection and radiotherapy. *Ann Surg* 1990; 211:250–259.