

Book Review

Breast Cancer in Younger Women—*Journal of the National Cancer Institute Monographs* Number 16, 1994

THIS ISSUE of the *Journal of the National Cancer Institute* (JNCI) Monographs reports on a conference held at the National Institutes of Health dealing with breast cancer in younger women.

In 1993, 12 000 women under 40 years of age were diagnosed with breast cancer in the U.S.A. and the proportion of younger women affected by this disease is increasing by 1% per year, reflecting the general increase in incidence of the disease.

Many aspects of breast cancer in younger women have been addressed, however, many issues were discussed during this meeting including: "Is the incidence of breast cancer in younger women rising? How should we screen younger women? Do younger women respond differently to treatment than older ones? Is childbearing safe after treatment for breast cancer? Is hormone replacement therapy safe? What are the psychological implications for breast cancer in younger women?"

Data from the SEER programme show that summary statistics on breast cancer incidence and mortality are heavily weighted by the higher rates in older age groups. It is, therefore, important to review data by age group to discern a pattern in younger women that may be hidden by the summary data. During the 1980s, and up to 1987, there was little change in the incidence of breast cancer in the group aged 20–39 years after a small increase at the beginning of the decade. Since 1987, the trend has either not changed or is decreasing. However, owing to a dramatic increase in the number of women in the 20–39 year age range, the total number of breast cancers diagnosed in this age group was 5170 in 1970, 7800 in 1980, and more than 10 000 in 1990. Interestingly, patients aged 20–39 years with a breast cancer diagnosis were at a significantly higher risk of developing a second invasive cancer than patients older than 40 years, and their risk decreased with time, whereas for older patients the risk remains lower but constant (observed/expected (O/E) second cancers in women 20–39 years of age: 79.6 during the first year after diagnosis, 45.9 during years 1–4.9, 18.1 during years 5–9.9, 15.4 after more than 10 years; in women 40–49 years of age: O/E 2.2–4.3; in women > 50 years of age: O/E 1.6 constant).

Risk factors for breast cancer in younger women are different to those for older ones. Race, parity and large body size may show opposite effects in pre- than in postmenopausal patients, whereas late age at first birth, never having lactated, oral contraceptive use at early age or of long duration, and especially a positive family history of breast cancer are particularly important for younger patients.

From the pathological perspective early onset breast cancers show a relative increase in the incidence of medullary carcinoma and ductal carcinoma *in situ* (DCIS), and a relative decrease in lobular and tubular cancers. Invasive ductal cancers are generally of higher grade and more proliferating in younger women than in older, which may explain the higher fraction of DCIS, the increased local recurrence rates after breast conserving surgery and the more aggressive natural history of the disease in this

population. Outcome in younger patients is worse than in older patients, but this fact may be explained by a greater frequency of adverse prognostic factors in these patients, especially when considering, in addition to the number of axillary nodes, tumour size and receptor status, the other prognostic indicators such as S-phase fraction and abnormal expression of p53.

Screening in younger women has not shown the same benefits observed in women older than 50 years (decreased mortality from breast cancer, increased use of conservative surgery in case of breast cancer diagnosis). Thus, its use remains controversial and may be restricted to women at high risk of breast cancer. However, in younger women, no more than 20% between the ages of 20 and 39 years show risk factors which would lead to a substantial number of missed breast cancers in this population if this strategy were applied. No published study has shown mortality reduction from selective screening in women at high risk.

Breast cancer growth may be explained for the purposes of prevention as a step-by-step progressive development involving multiple factors acting and evolving over many years, yet reversible for a long period of time. Preventive interventions must have a solid and biological rationale, no serious toxic effects, and long-term acceptability by women.

In Section IV of the JNCI monograph reporting on treatment in younger women, the first paper showed the survival pattern of this patient subgroup as compared to older women. Data were again taken from the SEER programme and they clearly demonstrated that breast cancer takes its greatest toll on younger women, and among these, especially on the black population. The cumulative probability of breast cancer death 5 years after diagnosis is 26.4% (33.7% for black women) for women 20–29 years of age and falls to 15.1% (27.8% for black) for those 40–49 years of age. What could be the explanation for the poor survival of younger women? Many hypotheses can be taken into account: higher oestrogen levels promoting tumour growth in younger patients, worse prognostic factors, lack of competing causes of death, different biology of breast cancer among younger and older women.

The preferred surgical treatment in younger women is a breast conserving procedure. Some studies however, show an increased risk of local recurrence in this patient population. Also conflicting are the data from studies assessing the effect of hormonal milieu at the time of surgery on prognosis.

Adjuvant systemic therapy has been shown to reduce recurrence and mortality in patients below 50 years of age, but specific data for younger women are scarce. Of special interest in these patients is the role of ovarian ablation, which has been used in breast cancer for more than 100 years. Its value is well established in metastatic breast cancer (especially in the receptor-positive population), and data on its effect in the adjuvant setting suggest that the recurrence rate may be reduced by approximately 25% (similar to adjuvant chemotherapy). Metastatic breast cancer is still incurable and patients with locally advanced disease are also likely to die of the disease within a decade. The use of high dose chemotherapy programmes seems essential for the design of possible curative regimens. Interestingly, in the report of the Dana Farber Cancer Institute (DFCI), Boston, those women under 40 years of age with metastatic breast cancer, responding to conventional dose chemotherapy, who underwent high dose treatment had a significantly shorter survival than older women, but the number of patients was too small to draw definitive conclusions.

Two additional themes are of great importance for younger breast cancer patients: the possible late effects of adjuvant systemic therapies and reproductive factors, such as pregnancies

at breast cancer diagnosis and after breast cancer, early menopause and hormone replacement therapy.

Late effects of chemotherapy need special attention. Of relevance, as well as second cancers or leukaemias that have been studied in some series, are other health adverse events such as cardiac toxicity and early menopause after adjuvant systemic therapy. The benefits of adjuvant treatments are well demonstrated but further parallel research efforts are urgently needed to identify therapy-related events that may severely affect the quality of life of long-term survivors, especially among younger women.

Breast cancer diagnosed during pregnancy needs to be treated by a multidisciplinary approach, since the effect of treatment on the fetus must be considered. Pregnant patients show generally a poor prognosis, which may be related more to an initial delay of diagnostic procedures than to worse biological factors.

Amenorrhea after adjuvant systemic therapy is common and related to age. Women under 35 years of age, with pregnancies after breast cancer treatment have been reported, but the data are very limited. However, presently, no danger has been detected for those patients becoming pregnant after breast cancer. A registry of pregnancies detailing potential birth defects of offspring of breast cancer patients seems a very important issue, especially considering the increasing number of young women affected by this disease.

Oestrogen replacement therapy is now widely used to prevent osteoporosis, reduce fracture risks, and possibly reduce cardiovascular morbidity and mortality in postmenopausal women. It is still unknown how these benefits compare with the potential

risk of increased breast cancer recurrence in patients treated for this disease. The MD Anderson Cancer Center in Houston U.S.A. initiated, in 1992, an extremely important randomised trial that addresses the issue of risk versus benefit for hormonal replacement therapy after breast cancer.

The last section of the monograph reports on psychosocial issues. Of great topical interest is the problem of risk perception for women at high risk of developing breast cancer. As many as one-third of these women are reported to have worries that impair their daily functioning. No study has examined the impact of breast cancer on sexual issues across age. It is of interest, however, that patients treated by breast conserving surgery do not experience less psychological distress or differences in sexual behaviour as compared with patients treated by breast amputation.

The monograph is very stimulating, as it reviews most of the problems specific to the younger patient population affected by breast cancer. Despite the many questions asked at the beginning of the conference reported in the issue, very few answers are available for most of the particular problems of this constantly increasing subset of patients, for whom the impact of breast cancer is immense from the human, as well as from the public health, point of view.

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