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Breast Cancer in the Southeastern Netherlands, 1960–1989: Trends in Incidence and Mortality

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Temporal trends in incidence and mortality in breast cancer were examined in the southeastern Netherlands using data from the population-based Eindhoven Cancer Registry. In the period 1960–1989 the incidence rate of first primary breast cancer approximately doubled in all age groups. The increase mainly occurred before 1975 and after 1985, when no screening activities were performed. This trend appeared to be a result of an average yearly increase in incidence of localised and distant tumours with both 4.6%, whereas the incidence of regional tumours did not change. Simultaneously, breast cancer mortality remained unchanged in women aged under 60, and only increased by a yearly average of 0.7% in women aged 60–74 and of 0.9% in women aged 75 and over. These differing trends in incidence and mortality, which can only partially be explained by earlier detection, suggest an improved survival of breast cancer.
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INTRODUCTION

THE INCIDENCE of breast cancer in females shows a large variation between countries, with the highest rates in North America, Australia and northwest Europe, and the lowest rates in Africa, Asia and the Middle East [1]. In northern European countries age-adjusted incidence rates are almost twice those of southern and eastern Europe [1]. It is well documented that the incidence of female breast cancer has increased in many countries over the past decades [2,3]. In Europe, the geographical variation in breast cancer mortality has become smaller since the 1950s, because rates have increased, especially in countries with initial low rates [4].

We investigated temporal trends in incidence and mortality in breast cancer in an unscreened population in the southeastern Netherlands between 1960 and 1989 using the population-based Eindhoven Cancer Registry. We differentiated between first and second primary breast cancers, and between invasive tumours and ductal carcinomas *in situ* (DCIS), as a precursor of invasive breast cancer [5].

PATIENTS AND METHODS

Data used for this study came from the Eindhoven Cancer Registry, which was founded in 1955 and became part of the Comprehensive Cancer Centre South in 1983. The registry covers a growing area; between 1960 and 1969 it consisted of 15 municipalities with approximately 300 000 inhabitants. In 1989 it had increased to 51 municipalities with about 1 million inhabitants in an area of 2500 km^2. The data were derived from copies of the pathologist's reports, from the patient records in the community hospitals and from the regional Radiotherapy Institute. Since 1975, data on patients with *in situ* tumours were also registered. Registration methods remained unchanged during the study period, although coding became more refined. Both in old and new municipalities covered by the registry, completeness could be assumed from analyses of referral patterns and registration procedures as well as various comparisons of incidence, for instance with cancer mortality. The composition of the population, subdivided into age, sex and municipality was derived yearly from the Department of Population Statistics of the Dutch Central Bureau of Statistics (CBS). Regional mortality rates were obtained from the cause of death register at the CBS. Data on all new patients with primary breast cancer were analysed since 1960, when all patients with cancer were reported by local pathologists to the registry.

Stage at diagnosis was recorded on the basis of clinical examination, supplemented by the pathologist report. Stage was classified into three categories: localised, if the cancer was confined to the breast regardless of size; regional, if it passed the bounds of the breast, remaining in its immediate neighbourhood, or to the regional lymph nodes; distant, if it involved tissues beyond those immediately draining or neighbouring the breast.

Contralateral breast cancer and ipsilateral breast cancer differing in histology from the previous breast cancer and diagnosed more than 2 months after the first, were considered as a second primary.

Annual crude rates were computed per 100 000 person-years with the regional female population as a denominator, and age-specific rates for the age groups 30–44, 45–59, 60–74 and 75 years and over. Stage-specific trends in incidence were calculated, assuming that patients with unknown stage had a similar stage distribution as patients with a known stage in the same year. Age-adjustment was performed by direct standardisation according to the World Standard Population (WSR: World Standardised Rate) [1]. For the display of time-trends, 3-year running averages were used. For comparison reasons, incidence rates of second primaries were also calculated per 100 000 person-years. To reduce the chance that previous (first) breast tumours would be unknown at the registry these rates are given only since 1965. The trend in incidence of second primary

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DCIS was displayed as a 5-year running average because of small numbers. To summarise a trend in incidence or mortality rates, a linear regression line was fitted to the data and the slope of the line expressed in terms of the average yearly percentage change. A P value for the significance of the slope of the line was calculated.

RESULTS

Incidence and stage distribution of first primary breast cancer

Between 1960 and 1989, 7169 patients developed a first primary invasive breast cancer. The mean age at diagnosis increased from 57 years in the 1960s to 60 years between 1985 and 1989. The crude incidence rate of first primary breast cancer increased from 35 per 100 000 in 1960–1961 to 93 in 1988–1989, age-adjusted from 37 in 1960–1961 to 70 in 1988–1989. Three periods can be recognised: a fairly constant increase between 1960 and 1973, a plateau between 1974 and 1983 and a sharp increase after 1983. The average yearly increase in incidence was 2.0% for both age groups 30–44 and 45–59, 1.7% for age group 60–74 and 2.4% for age group 75 years and over (P values < 0.001) (Fig. 1).

Stage at diagnosis was unknown for 4% of the patients in 1960–1969, for 11% in 1970–1979 and for 4% in 1980–1989. The incidence rates of both localised and distant tumours increased with an yearly average of 3.6% (P values < 0.001), whereas the incidence rate of regional tumours did not significantly change ($P = 0.5$). This resulted in a marked increase in the percentage of localised tumours from 37% in the 1960s to 54% in the 1980s and of distant tumours from 4 to 7%, whereas the percentage of regional tumours decreased from 59 to 39%. There was a significant trend towards a more favourable stage with time (χ^2 for trend: $P < 0.001$), which continued in the 1980s.

Incidence of second primary breast cancer and DCIS

Between 1965 and 1989, 414 second primary invasive breast cancers were detected. The age-adjusted incidence rate increased gradually from 1.7 per 100 000 in 1965–1966 to 5.8 in 1988–1989. Between 1975 and 1989, 91 DCIS were detected as a first primary, and 11 as a second primary. The age-adjusted incidence of first primary DCIS increased from 0.2 per 100 000 in 1975–1976 to 2.1 in 1988–1989 ($P < 0.001$), and of second primary DCIS from 0.05 in 1975–1979 to 0.3 in 1985–1989.

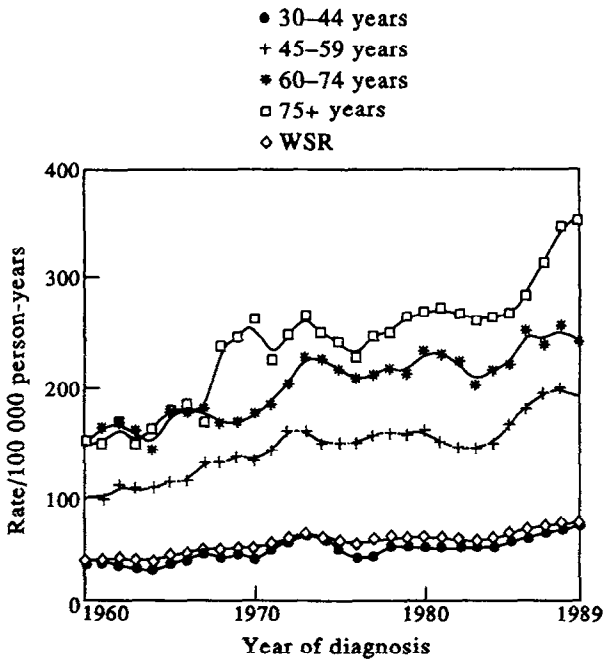

Fig. 1. Age-specific incidence rates per 100 000 person-years in southeastern Netherlands. WSR: age-adjusted rates according to the World Standard Population.

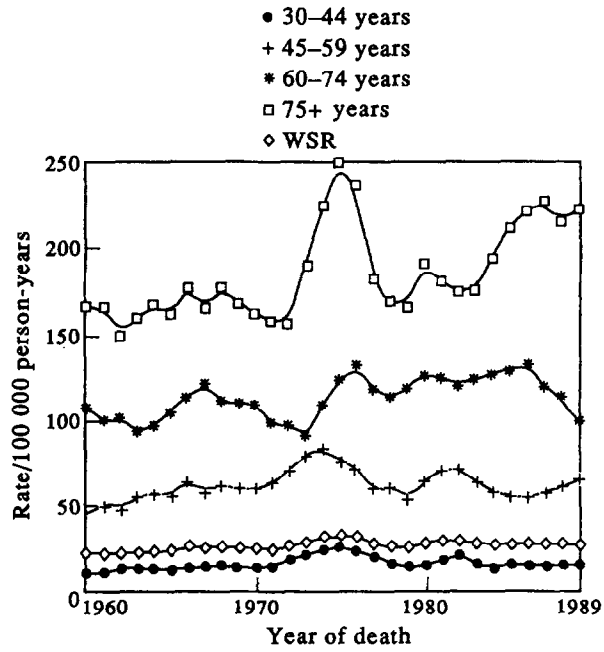

Fig. 2. Breast cancer mortality in southeastern Netherlands per 100 000 person-years in four age groups.

Mortality

Since 1960 there was no significant trend in breast cancer mortality in women aged under 60 years, whereas for age group 60–74 an average yearly increase of 0.7% occurred ($P = 0.047$), and of 0.9% for age group 75 years and over ($P = 0.03$) (Fig. 2). Breast cancer mortality showed a peak in all age groups in the mid-1970s, and a sharp increase in the oldest age group in the last 5 years of the study period (1985–1989). Age-adjusted breast cancer mortality increased from 21.8 per 100 000 in 1960–1961 to 25.4 in 1988–1989 ($P = 0.046$). Simultaneously, total female mortality decreased considerably with 20 to 40% in the various age groups (P values < 0.001); age-adjusted from 588 to 367 per 100 000. Breast cancer as a cause of death increased in all age groups, mainly in women aged 75 years and over, although in this group only 2–3% of total mortality was due to breast cancer.

DISCUSSION

As in many other countries in Europe, the incidence rate of breast cancer in the southeastern Netherlands has increased, at least since 1960, and approximately doubled in every age group. It can be accounted for by an increase in localised and distant tumours, whereas incidence rates of regional tumours levelled. Simultaneously, breast cancer mortality remained almost unchanged (except for women of 75 years and over). The marked decrease in deaths due to other causes, however, made breast cancer proportionally a more important cause of death.

Some under-registration may partly explain the increase in incidence in the oldest age group in the 1960s, although the markedly increased breast cancer mortality rate affirms this trend. A more accurate registry can probably not be the reason

for the overall increase in incidence, because cooperation with surgeons, pathologists and radiotherapists has always been very good. Furthermore, the period 1955–1959, in which underreporting was probably highest, was excluded from the study.

Among the risk factors the higher age of women at first birth, lower fertility rate, earlier menarche, delayed menopause and use of exogenous oestrogens and contraceptives may be involved [6–9]. However, the changes of these risk factors would rather explain the increase in women under 60 years and not the increase in the elderly. The increase in incidence of second primary breast cancer can largely be explained by the increasing number of women alive with a first primary.

In the study region mammography was gradually introduced between 1974 and 1978 and cytology between 1979 and 1987, making earlier detection possible. Although stage at diagnosis gradually became more favourable it is unlikely that earlier detection can explain the fairly continuous increase in incidence, because a large part of the increase would then be temporary [10]. Furthermore, the increase in incidence of localised tumours did not lead to a decrease of tumours in higher stages, and mortality did not decrease.

Due to better detection modalities and the increasing number of patients with axillary lymph node dissection, gradually more lymph nodes were detected, leading to higher registered stages in actually unchanged tumours [11,12]. This affirms the trend towards earlier diagnosis, which may be attributed to better diagnostic techniques and to the growing awareness in women of the significance of breast lumps.

The differing trends in incidence and mortality can partly be explained by earlier detection and suggest an improved survival, which is possibly due to better treatment results [13]. Furthermore, current diagnostic aids may also enable detection of slower growing tumours which previously would remain undetected [14,15].

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