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Original Research

Why have breast cancer mortality rates declined?

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ABSTRACT

The recent decline in breast cancer mortality in the USA might be due to prevention or to screening mammography or to improved treatment protocols. We sought to determine which factors are likely to be responsible for the observed decline in breast cancer mortality.

We used the Surveillance, Epidemiology and End Results (SEER) database to estimate incidence rates, mortality rates, and survival from breast cancer for white women who were diagnosed with invasive breast cancer from 1975 to 2011.

From 1975 to 2010, the mortality of breast cancer declined from 32 per 100,000 per year to 21 per 100,000 per year (34%). At the same time, the incidence increased by 30%, in particular for localized breast cancers (62%) without a commensurate decline in the number of regional breast cancers. From 1975 to 2002, 10-year survival increased by 28% (from 64.9% to 82.8%). The increase in survival was greater for regional cancers (23%), than for localized (10%) or for distant cancers (3%).

The decline in breast cancer mortality in the USA from 1975 to 2010 is unlikely to be the result of advances in prevention or screening. The large increase in the incidence of localized cancers without a corresponding decrease in advanced breast cancers suggests a prominent stage shift, due to overdiagnosis. The drop in the mortality rate could be accounted for by an improvement in cancer survival, likely due to increased use of adjuvant chemotherapy over the period.

Introduction

It is widely acknowledged that deaths from breast cancer in the United States have been decreasing over the past few decades but the determinants of change are in want of explanation [1]. There are many possible factors, but two schools of thought predominate. Advocates of mammography claim that early detection is bearing fruit [2–4]. This could be through formal mammographic screening or because better awareness leads to smaller cancers, palpable or not [5]. The other school of thought attributes the decline to adjuvant systemic therapies, including cytotoxic drugs, adjuvant hormonal therapies and biologics such as Herceptin [6–8]. There may also be a small contribution from regional radiotherapy [9,10]. One might consider the possibility that the breast cancers are changing, perhaps as a consequence of evolving changing patterns of risk factors. Moreover, the current patient population may not be identical to that of the past, due to the impacts of fertility and immigration on the ethnic distribution of American women [11,12]. To provide compelling evidence in favor of one or another position would require detailed information on demographics, risk factors, screening behaviors, clinical presentation, treatments received and outcomes for a large and representative sample of American women. Given limited information, such as cancer incidence, stage, mortality and case-fatality at several points in time in a fixed population, one can venture an educated guess. In the United States, this information has been compiled through the Surveillance, Epidemiology, and End Results (SEER) registry system and is available to researchers without cost.

In the following pages, we analyze incidence, mortality and case-fatality rates for the last several decades and seek to measure and explain the decline in mortality. Cancer incidence refers to the number of new cancers diagnosed in a given calendar year, relative to the size of the population at risk and is described in terms of cases per 100,000 women per year. Age-adjusted mortality describes the number of women who die from breast cancer in a given calendar year, relative to the size of the population. It is described in terms of deaths per 100,000 women per year. The reference year is the year of death and the deaths are from breast cancer for patients who were treated *at any time in the past* (in this sense they reflect *prior* treatment protocols). Case-fatality describes the probability

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of death from breast cancer for a patient diagnosed in a given year and reflects *current* treatment protocols; i.e., a woman who is diagnosed at age 38 and dies at age 42 is included in the under 40 group for case fatality but in the 40–50 group for mortality. In theory, case-fatality considers the remaining life of the patient (who ultimately dies of breast cancer or another cause) but for practical reasons it is often used to describe deaths which occur in a specific follow-up time period (e.g. five years or ten years following diagnosis). In the event that a new, effective treatment is introduced, the impact on case-fatality should be immediate, but there should be a lag of several years before an impact on mortality is noticed. In order to simplify the interpretation of these data (i.e., to remove the potential effect of demographic and ethnic change over the past 40 years) we restrict our analyses to white women.

Materials and methods

Data source and software

The Surveillance, Epidemiology and End Results (SEER) research database contains information on 2,899,726 women with invasive breast cancer. Since its inception in 1973, SEER has been a comprehensive source of cancer incidence and survival in the United States [13]. It encompasses approximately 26% of new breast cancer diagnoses in the country. For statistical purposes, various combinations of the SEER registries are available, depending on the time period and the specific registries included. For this study, we used the SEER 9 registry database (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah) [14] and the SEER18 registry database (SEER13 [SEER9 plus Los Angeles, San Jose-Monterey, Rural Georgia, and the Alaska Native Tumor Registry] plus the Greater California, Kentucky, Louisiana, New Jersey, and Greater Georgia [15]. We used SEER*Stat version 8.1.5 to estimate incidence and survival rates from SEER databases [16].

Mortality

We used SEER mortality database to estimate age-adjusted breast cancer mortality rates (deaths from breast cancer per 100,000 women) for each year from 1975 to 2010 [17]. These analyses included all cases and subgroups defined by age of diagnosis.

Incidence

We used the SEER9 registry database to estimate the age-standardized incidence rates (adjusted to the 2000 US Standard Population) of breast cancer in women diagnosed with breast cancer for each year from 1975 to 2011. Given that Seattle-Puget Sound and Atlanta registries joined the SEER program in 1974 and 1975, respectively, we did not include the years 1973 and 1974 in our analyses. We included women who were classified as 'white' in the SEER 9 and had microscopically confirmed invasive breast cancer at diagnosis.

We used the Collaborative Staging Schema version 0204 to select 'breast' as primary site of cancer. For the cancer incidence analyses, we used the SEER historic stage A to define three categories of breast cancer stage at diagnosis: localized, regional and distant breast cancer. From the SEER*Stat software, we generated age-standardized incidence rates (cases per 100,000 per year) for localized, regional and distant breast cancers, and for all breast cancers combined. We performed subgroup analyses to estimate incidence rates of localized, regional and distant breast cancer (cases per 100,000) for women <50 years and women 50 years and above.

Survival

We used SEER18 registries database to estimate breast cancer-specific survival [15]. We selected women whose cancers were histologically confirmed, who had a known age at diagnosis and for whom follow-up data was available. We excluded women with missing survival time in the database and women with an unknown cause of death. From 1973 we used SEER historic stage A and estimated 10-year breast cancer-specific survival for localized, regional and distant breast cancers, and all cancers combined.

In order to estimate survival according to stage using a more granular staging system, we used Adjusted American Joint Committee on Cancer (AJCC) 6th Stage (1988+) and classified all invasive breast cancers into AJCC stages I–IV [18]. These data were available only for women diagnosed from 1988 on and it is premature to estimate ten years survival, hence we estimated 5-year breast cancer-specific survival for each stage. We performed subgroup analyses for women <50 years and women 50 years and above, and for women with estrogen receptor-positive and estrogen receptor-negative tumors. We used Kaplan–Meier method of survival estimation and calculated 95% confidence intervals.

Based on the 5-year breast cancer-specific survival estimates for the two years 1990 and 2006, we calculated the absolute increase in five-year survival over the 16-year period (percentage change in survival from 1990 to 2006 as well as the relative improvement in survival (%), the absolute reduction in mortality and the proportionate reduction in mortality. To estimate the number of deaths from breast cancer that were avoided in 2006, attributable to the improvement in survival, we first calculated the estimated number of deaths assuming 1990 five-year survival rates and compared these to the actual number of deaths reported in the 2006 cohort. Using the same approach we conducted subgroup analyses to estimate number of deaths avoided for women <50 years (ER-positive and ER-negative) and women 50 years and above (ER-positive and ER-negative).

Results

From 1990 to 2010, the age-adjusted breast cancer mortality rate from all breast cancers fell from 33.0 per 100,000 per year to 21.3 per 100,000 per year, a decline of 36% (Fig. 1). Prior to 1990, rates were stable. The decline was 41% for women under age 40, was 51% for women aged 40–49 and was 34% for women age 50 and older (Fig. 2).

Fig. 3 shows that during the period of rapid decline in mortality (1989–2009) there was no commensurate decline in cancer incidence. This effectively eliminates from consideration the possibility that there were fewer deaths from cancer because there were fewer cases of cancer.

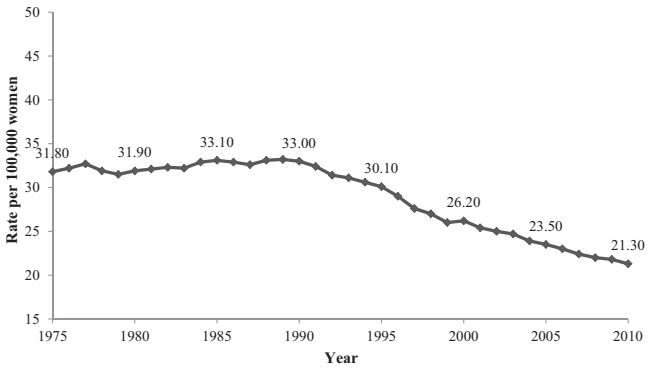

Fig. 1. Breast Cancer Mortality Rates in US White: SEER 1975–2010. *Abbreviations*: SEER, Surveillance, Epidemiology and End Results.