ELSEVIER

Comparison of Male and Female Breast Cancer Incidence Trends, Tumor Characteristics, and Survival

TERESA D. HILL, PHD, HARRY J. KHAMIS, PHD, JERZY E. TYCZYNSKI, PHD, AND HANS (J.) BERKEL, MD, PHD

PURPOSE: To compare male and female breast cancer and to determine the predictors of tumor characteristics and survival in both genders.
METHODS: Male ($n = 2923$) and female breast cancer cases ($n = 442{,}500$) from the Surveillance, Epidemiology and End Results (SEER) registry were analyzed. Joinpoint regression was performed to detect changes in incidence trends from 1973 to 2001. Multiple logistic regression was used to regress each of four outcome variables (STAGE, LATERALITY, ESTROGEN, and PROGESTERONE RECEPTOR STATUS) on four demographic variables. Cox proportional hazards regression modeling was used to determine significant predictors of death of breast cancer after adjusting for demographic factors.
RESULTS: Both men and women aged less than 50 years were at higher risk for advanced breast cancers. Males were at higher risk than females for advanced tumors among non-whites. The risk of breast cancer death among all cases was lower for each 10-year increase in age by 2%, higher for those who are unmarried than for those who are married by 12% and 13% higher for non-whites than for whites.
CONCLUSIONS: Some important gender differences were detected with respect to factors associated with tumor characteristics, but gender was not a significant predictor of survival after adjusting for the other demographic variables.
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KEY WORDS: Breast Neoplasms Male, Breast Neoplasms Female, SEER Program, Survival, Epidemiology, Hormone Receptor.

INTRODUCTION

The epidemiology of female breast cancer is the topic of numerous research projects and manuscripts each year. Since there are over 215,000 new cases of breast cancer in women annually in the United States alone, case ascertainment is not a barrier to the conduct of epidemiologic studies—both descriptive and analytical. In men, however, there will only be an estimated 1450 annual incident cases of breast cancer in the U.S. in 2004 (1). Due to the rarity of breast carcinoma in men, much of the research—based on case series with relatively small samples—has focused on prognosis and genetic factors (2–7).

International population-based descriptive analyses, such as reports from Israel ($n = 187$) (8), Scandinavia ($n = 1529$) (9), central Italy ($n = 32$) (10), and Iceland ($n = 31$) (11) have reported comparable findings with respect to male breast cancer incidence (it is rare—less than 1 per 100,000 per year) and the mean age (male cases are, on average, half a decade older than female cases). However, most of our knowledge on the etiology of male breast cancer has been extrapolated from these small studies, underscoring the importance of determining similarities and differences between male and female breast cancer (12, 13). More recently, a study of gender- and age-specific incidence rate curves by Anderson et al. (14) reported stable incidence rates among men, compared with increasing trends among women. A comparison of prognostic factors led to the conclusion that male breast cancer is more similar to postmenopausal female breast cancer than premenopausal breast cancer (14).

Two recent studies have reported findings related to male breast cancer survival (15, 16). Atalay et al. (15) reported an overall 73% 5-year survival and 45% disease-free survival among men diagnosed with breast cancer. A study by El-Tamer et al. (16) compared male breast cancer survival with that of women and found that men had better disease-specific survival. However, it should be noted that small sample sizes were a limitation of both studies: the Atalay study included 55 male breast cancer patients from a single hospital; the El-Temar study was based on 53 male patients and 53 matched female controls.

The purpose of this study was to use data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute to describe the

From the Cancer Prevention Institute, Dayton, OH (T.D.H., J.E.T., H.J.B.); Statistical Consulting Center, Wright State University, Dayton, OH (H.J.K.); Division of Cancer Control & Prevention, Wright State University, Dayton, OH (T.D.H., J.E.T., H.J.B.).
Address correspondence to: Teresa D. Hill, Ph.D., Cancer Prevention Institute, 4100 South Kettering Blvd., Dayton, OH 45439-2092. Tel.: (937) 293-8508 Ext. 3030; Fax: (937) 293-7652. E-mail: hill@cancerpreventioninstitute.org
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Selected Abbreviations and Acronyms

CI = confidence interval
EAPC = estimated average percent changes
ER = estrogen receptor
JR = joinpoint regression
NOS = not otherwise specified
OR = odds ratio
PR = progesterone receptor
RR = risk ratio
SD = standard deviation
SEER = Surveillance, Epidemiology and End Results
SMSA = Standard Metropolitan Statistical Areas

epidemiology of male breast cancer, to compare gender- and race-specific incidence trends, and to determine if demographic factors and/or tumor characteristics are associated with disease-specific survival of breast cancer in men or women.

METHODS

Study Population

Cases included 2923 male breast cancer cases submitted to the 11 population-based cancer registries participating in the SEER Program from 1973 to 1999 (17). Gender comparisons use the 442,500 female breast cancer cases submitted to these registries during the same time interval. Additional cases (2000–2001) became available during the review of this manuscript and were included in the time trend analyses using joinpoint regression (JR) (18). Covering approximately 26% of the US population, the SEER Program routinely collects data on patient demographics, primary tumor site, morphology, stage at diagnosis, and follow-up for vital status. For those patients having more than one primary breast cancer diagnosis, the first instance of breast cancer was selected.

Statistical Methods

Breast cancer incidence trends. Joinpoint regression was performed to provide the estimated annual percentage change (EAPC) and to detect points in time where significant changes in trends occurred (19–21). The corresponding 95% confidence interval (CI) for each EAPC was also calculated. The JR model describes continuous changes in incidence rates and uses the grid-search method to fit the regression function with unknown joinpoints. The annual age-adjusted rates from 1973 to 2000 are examined and the points in time when the direction of the trends changes significantly are detected.

Univariate analysis. Unadjusted frequencies by gender were estimated for demographic variables and tumor characteristics using SPSS version 10.0 software (22). Inferential statistics are not presented for univariate comparisons, since the large number of comparison cases leads to consistent significant findings (even for extremely small observed differences).

Multivariate analysis. Multivariate analyses were performed using SAS version 9.0 software (23). All inferences were made at the 0.05 level of significance. Multiple logistic regression modeling was used to regress each of four outcome variables—STAGE, LATERALITY, ER (Estrogen Receptor) STATUS, and PR (Progesterone Receptor) STATUS—on four demographic variables (AGE, MARITAL STATUS, GENDER, and RACE). Each demographic variable was dichotomized: AGE (< 50, $\geqslant 50$), MARITAL STATUS (Married, Not married) and RACE (White, Non-white). Four logistic regressions were performed, one for each outcome. In each case, a backward selection procedure was used to identify those demographic variables that had a significant effect on the outcome variable.

Survival time was analyzed for each of four predictors (STAGE, LATERALITY, ER STATUS, and PR STATUS) after adjusting for demographic variables (AGE, MARITAL STATUS, GENDER, and RACE). AGE was treated as a continuous variable, MARITAL STATUS was dichotomized (Married, Not married), and RACE was dichotomized (White, Non-white). The Cox proportional hazards regression model was used to compare the survival rate between the two levels of each predictor variable after adjusting for the demographic factors. The proportional hazards assumption was tested using Cox's test, including interaction terms involving the covariates and $\log(t)$, where t = time variable; the interaction terms were tested for statistical significance (significance implying violation of the proportional hazards assumption).

RESULTS

Incidence

The incidence rate of male breast cancer (1992–1999) is 1.2 per 100,000 compared with 150.1 per 100,000 among women, indicating that approximately 1 out of every 150 breast cancers occurs in a male. JR analysis resulted in the trends displayed in Fig. 1. Among men of all ages, a significant 4.8% decrease in incident rates was noted from 1973 to 1977 (95% CI, − 9.8 to 0.5). Since then—beginning in 1978—men have experienced a 1.2% increase (95% CI, 0.7 to 1.8) in breast cancer incidence. There were too few cases in the subcategories "non-white" and "< 50" to determine if significant race and/or age differences exist in males. By contrast, the large number of female cases allowed for age- and race-specific trends to be determined. White women aged less than 50 years experienced a 1.3% decline from 1973 to 1979 (95% CI, − 2.5 to − 0.1) followed by a 2.8% increase from 1980 to