Cancer Causes and Control **15**: 321–328, 2004.

Population-based statistics for women diagnosed with inflammatory breast cancer (United States)

Phyllis A. Wingo[1,*], Patricia M. Jamison[1], John L. Young[2] & Paul Gargiullo[3]
[1]*Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA, USA;* [2]*Rollins School of Public Health, Emory University, Atlanta, GA, USA;* [3]*Division of Epidemiology and Surveillance, National Immunization Program, Atlanta, GA, USA*

Received 28 July 2003; accepted in revised form 29 December 2003

Key words: breast cancer, incidence, inflammatory.

Abstract

Objective: The purpose of this study was to use population-based information to describe the demographic and tumor characteristics of inflammatory breast cancer (IBC) – the most aggressive form of this disease.
Methods: IBC cases diagnosed during 1994 through 1998 were reported to 26 population-based cancer registries covering approximately 40% of the US population. Rates were expressed per 100,000 female population and age-adjusted to the 2000 US population. Ninety-five percent gamma confidence limits were estimated for the rates.
Results: Among the 3626 women diagnosed with IBC during 1994–1998, the majority were 40–59 years old. Most tumors were diagnosed at a regional (68.9%) or distant (25.3%) stage and were poorly differentiated (49.4%). The rate of IBC was 1.3 per 100,000 for all races combined. Black women had the highest risk (1.6) and Asian and Pacific Islander women the lowest (0.7).
Conclusions: IBC is an extremely rare form of breast cancer. More precise diagnostic criteria are needed to distinguish it from less aggressive forms of the disease. Future studies should use a population-based design and collect detailed clinical information, including the presence of erythema, edema or peau d'orange appearance of the skin, and other clinical signs of disease.

Introduction

Inflammatory breast cancer (IBC) is the most aggressive form of this cancer [1–3]. The prognosis for patients with IBC is poor, with only 32–42% surviving three years [4]. IBC is rare, estimated to makeup about 1–6% of breast cancer cases in the United States [1, 5, 6], and the criteria for establishing the diagnosis are controversial [7, 8].

Singletary *et al.* [7] noted that a clinical diagnosis of IBC depended on three factors: erythema, which is probably related to increased heat; skin edema or peau d'orange, which appears as exaggerated hair follicle pits secondary to tumor blockage of the lymphatics; and wheals or ridging of the skin, which suggests that the lymphatics have filled with tumor cells. The onset of symptoms is usually rapid – frequently within three months. The rapid onset may result in an initial misdiagnosis of IBC as acute mastitis or breast abscess [9, 10].

Several investigators have attempted to clarify the clinical and pathologic definition of the disease [1, 8]. Bonnier *et al.* [8] described true IBC, occult IBC, and pseudo-IBC and argued for pathologic confirmation of dermal lymphatic emboli or extensive lymph node involvement as indicative of true IBC. Levine *et al.* used data from the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) program and also used three diagnostic definitions – clinical presentation only, pathologic presentation only (ICD-O-2 M-8530/3), and both clinical presentation and pathologic features [8, 11].

Although very few studies have examined risk factors for IBC, it appears to occur more frequently among

* Address correspondence to: Phyllis A. Wingo, Centers for Disease Control and Prevention, 4770 Buford Highway NE, MS K53, Chamblee, GA 30341-3717, USA. Ph.: +1-770-488-4783; Fax: +1-770-488-4759; E-mail: pwingo@cdc.gov

younger than older women [1]. Obese women may also have a greater risk of developing the disease [12]. In addition, one study has suggested that incidence rates may be higher among black women than white women, although the rate estimates were variable and based on small numbers [4]. Rates for both black and white women nearly doubled from the mid-1970s to the early 1990s, and the pattern of better survival for white women compared with black women for all histologic types of breast cancer combined was also observed for IBC [4].

Population-based studies of this very rare form of breast cancer are quite limited [1, 4]. This study provides the opportunity to describe selected tumor characteristics and demographic patterns of IBC in the United States in a large, population-based data set from the North American Association of Central Cancer Registries (NAACCR), which represents state and metropolitan area cancer registries supported by the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention (CDC) and the SEER Program of NCI.

Materials and methods

Cancer cases

The NAACCR data set contained cancer cases from registries meeting NAACCR standards for high data quality. These criteria were as follows: (1) data were available for all five years 1994–1998, (2) registries' assessment of the number of duplicate reports on the file was less than 0.1%, (3) all records passed a set of standardized edits, and (4) after adjustment for duplicates, all registries had 90% or higher case ascertainment for all five years. States that agreed to participate in the analysis were Arizona, Colorado, Connecticut, Delaware, Hawaii, Idaho, Illinois, Iowa, Kentucky, Louisiana, Montana, Nebraska, New Hampshire, New Jersey, North Carolina, Pennsylvania, Rhode Island, Utah, Washington, West Virginia, Wisconsin, and Wyoming. Metropolitan area registries included in the analysis were Atlanta, Detroit, Los Angeles, and the Greater San Francisco Bay Area. The cases used in our analysis were reported from registries covering 40% of the US population. From the NAACCR data set of 3233 cases of breast cancer in men and 363,801 cases of breast cancer in women, this analysis included 19 men and 3626 women with a new diagnosis of IBC during 1994–1998. The IBC case definition was based on a pathologic diagnosis – the ICD-O-2 morphology code M-8530/3 inflammatory adenocarcinoma [11].

Population counts

Population counts were based on projections using the 1990 census from the Population Estimates Program of the US Bureau of the Census with support from NCI through an interagency agreement. The population estimates are race- and sex-specific county population estimates aggregated to the state or metropolitan-area level that were incorporated into NCI's SEER*Stat software [13]. The SEER*Stat population estimates are a modification of the annual time series of July 1 county population estimates (by five-year-age groups, sex, race, and Hispanic origin). In addition, estimates used in this analysis for Asian/Pacific Islander and white populations in Hawaii were modified according to sample survey data collected by the Hawaii Department of Health and provided by the Epidemiology Program of the Cancer Research Center of Hawaii.

Statistical analyses

Cumulative rates for 1994–1998 were expressed per 100,000 female population and were age-adjusted to the 2000 US standard population by five-year-age groups. Ninety-five percent gamma confidence limits (CL) were estimated from SEER*Stat using the methods of Fay and Feuer [13, 14]. For all analyses, rates were suppressed when the category of interest contained fewer than 20 cases. Rate ratios (RR) were estimated as the ratio of the rate in one subgroup of women to the rate in another subgroup. z-Tests were used to detect departures of the RR from unity. z-Statistics were based on the sum of the Poisson variances of the two rates being compared [15]. Because the difference in log rates has an approximately normal distribution, the RR were transformed to natural logarithms, and variances applicable to log rates were used for the z-test and 95% confidence intervals [16].

Analyses by race and ethnicity

Race and Hispanic origin are abstracted from medical records. The use of surname lists and/or birthplace to classify race and ethnicity varies from registry to registry [17]. NAACCR studies are currently underway to assess the feasibility of applying standard methods for producing incidence rates for specific populations other than black or white [17]. However, these efforts had not yet been completed by the time this analysis was initiated. For this reason, specific criteria were established for the inclusion of registries for the analyses of racial and ethnic populations. First, the standard census classifications for race and ethnicity with available denominator data were used – white, black, American

Indian/Alaskan Native, and Asian/Pacific Islander. Hispanic origin was also included, although the classification is not mutually exclusive from the other racial populations studied. We assumed that state-wide registries with sufficiently large specific racial and Hispanic populations would be likely to have more experience and motivation to consistently apply coding rules for race and ethnicity, resulting in less misclassification and overall better quality data than registries with small such populations. Second, states were eligible for inclusion in the analysis of a specific racial or ethnic population only if the population size was at least 100,000 and the count of IBC cases was at least 20. States were included in the analyses of Hispanic populations only if no more than 3% of cases were reported with unknown Hispanic origin. This approach was a delicate balance between the need to include as many states in the analyses as possible and the need for high quality race and ethnicity data. (The limitations of this approach and the consequent statistical implications are described in more detail in the Discussion).

This approach necessarily resulted in different numbers of registries for the analysis of each racial and ethnic population (26 registries for white women, 21 registries for black women, 18 for Asian and Pacific Islander women, 5 for American Indian/Alaska Native women, and 13 for women of Hispanic origin). The five states excluded from the analyses of black women were Idaho, Montana, New Hampshire, Utah, and Wyoming; the number of black women available for analysis was 429. Eight states were excluded from the analyses of Asian/Pacific Islander populations – Delaware, Idaho, Montana, Nebraska, New Hampshire, Rhode Island, West Virginia, and Wyoming; the number of Asian/Pacific Islander women available for analysis was 82. In contrast, rates for American Indians were based on data from five states – Arizona, Montana, North Carolina, Washington, and Wisconsin; the number of American Indian women available for analysis was 19. The designation 'American Indian' is used throughout because few, if any, Alaska Natives were included, even though the standard US Bureau of the Census category 'American Indian/Alaska Native' was the source for the population counts. Finally, rates for Hispanics were based on data from 14 registries – the metropolitan areas of Detroit, Los Angeles, and the Greater Bay Area in California, plus the states of Arizona, Colorado, Connecticut, Idaho, Iowa, Kentucky, Nebraska, Rhode Island, Utah, Washington, and Wyoming. However, the number of Hispanic women available for analysis was 159, and the number of women who were classified as non-Hispanic was 1582 after exclusions for unknown Hispanic origin.

Results

In the 22 states and the four metropolitan areas included in the analysis, 1% of new diagnoses of breast cancer among women during 1994–1998 were IBC (Table 1). Percentages varied by age and race/ethnicity and generally were highest among black and Hispanic women and women diagnosed before age 50 years. Among men, the percentage was small (0.59%).

Of the 19 men with a new diagnosis of IBC during 1994–1998, 18 were white and one was Asian/Pacific

Table 1. Percent of females with breast cancer who have a diagnosis of inflammatory breast cancer by age, race, and ethnicity, United States, 1994–1998

	All Races combined[a] (%)	White (%)	Black (%)	Asian/Pacific Islander (%)	Hispanic origin[b] (%)
Total	1.00	0.96	1.40	0.85	2.04
<40	1.75	1.80	1.74	[c]	3.92
40–49	1.40	1.37	1.89	0.77[d]	2.66
50–59	1.20	1.19	1.28	1.39	1.29
60–69	0.91	0.87	1.35	0.57[e]	2.02
70–79	0.62	0.61	0.96	[c]	[c]
80+	0.64	0.62	1.03	[c]	[c]

[a] 'All races combined' total does not equal 'white + black + Asian/Pacific Islander' because of 20 cases with American Indian/Alaska Native race, 20 cases with unknown race and six cases with other race.

[b] Hispanic origin is not mutually exclusive from white, black, and Asian/Pacific Islander, and American Indian/Alaskan Native. 1885 IBC cases were excluded because there were fewer than 20 cases of Hispanic origin in the state or because more then 3% of cases in the state were missing information on Hispanic origin.

[c] Calculations are suppressed for fewer than 20 cases.

[d] Ages <50.

[e] Ages 60+.

Islander. They ranged in age at diagnosis from 41 to 90 years and had an average age of 69.2 years. Tumors for all 19 cases were microscopically confirmed. Only one was diagnosed at a localized stage, whereas 14 were diagnosed at a regional stage, three had metastasized to distant sites, and one was unstaged. No tumors were well differentiated, four were moderately differentiated, ten were poorly differentiated, one was undifferentiated, and four had unknown grade. The remainder of the Results is focused on women diagnosed with IBC.

During 1994–1998, 19 American Indian women who resided in the five states included in the analyses of this population were diagnosed with IBC. All of these tumors were microscopically confirmed. The ages of these women ranged from 33 to 80 years, and their average age was 55.5 years. All but one case received a late stage diagnosis; nine were diagnosed at the regional stage, and nine had disease that had metastasized to a distant site. Similarly, nine tumors were poorly differentiated or grade III, and seven were unstaged. For the remainder of the Results, findings for these 19 women are not presented separately but are included in the 'all races' category.

Of the new diagnoses of IBC that occurred among 3626 women during 1994–1998, 97.8% were microscopically confirmed. Seventeen diagnoses were confirmed by direct visualization without microscopic confirmation, and 24 were clinical diagnoses only. The percentage that was microscopically confirmed did not vary appreciably by race, ranging from 96.7% among black women to 99.4% among Hispanic women.

Regardless of race or ethnicity, the percentage of cases diagnosed at a local stage was small, 2.0% or lower (Tables 2 and 3). For most women, IBC was diagnosed at a regional stage – nearly 70% (regional by direct extension only for 21.7%, regional lymph node involvement only for 5.1%, both for 35.1%, and regional, not otherwise specified (NOS) for 7.0%). Tumors in white women had a similar stage distribution (Table 2). Although most tumors in black women were diagnosed at a regional stage (59.7%), the percentage diagnosed at a distant stage (34.3%) was larger than for other racial and ethnic populations studied. The stage distribution of IBC tumors in Asian/Pacific Islander women was similar to that in white women, except for the larger percentage of tumors classified as regional by direct extension only (28.1%). However, these findings are based on small numbers. Among all races combined, 3.7% of IBC cases were unstaged.

IBC tumors tended to be grade III, poorly differentiated. White women had the lowest percentage of poorly differentiated tumors (48.9%), and Hispanic women had the highest (61.6%) (Tables 2 and 3). These data should be interpreted with caution since tumor grade was unknown for about 30% of white, black, and Asian/Pacific Islander women and for about 20% of Hispanic women.

The average age of women diagnosed with IBC during 1994–1998 was 57.6 years with a range of 50.5 years for Hispanic women to 58.1 years for white women (Tables 2 and 3). Among white women, most cases of IBC were diagnosed between ages 40 and 69 years; 22.2% were diagnosed at ages 40–49 years, 24.2% at ages 50–59 years, and 20.0% at ages 60–69 years. Among black women, 29.1% of IBC cases were diagnosed at ages 40–49 years, 20.0% at ages 50–59 years, and 19.8% at ages 60–69 years. Among Asian/Pacific Islander women, 41.5% of women were diagnosed at ages 60–69 years. Finally, among women of Hispanic origin, the majority of women receiving new diagnoses of IBC were aged 40–49 years (32.1%).

Regardless of race, rates increased from about 0.2 per 100,000 among women younger than age 40 and peaked at ages 50–69 years before declining (Tables 2 and 3). The peak age-specific rates ranged from 3.4 per 100,000 among white women ages 60–69 years to 4.2 per 100,000 among black women of the same ages (Table 2). IBC rates among Hispanic women also peaked at ages 60–69 years at 4.7 per 100,000 (Table 3). The peak age-specific rate for Asian/Pacific Islander women, however, appeared to occur among women aged 50–59 years at diagnosis although detailed analyses by age were constrained by small numbers (Table 2). IBC rates among older black women (those who were at least 70 years old) were also high, 3.6–3.7 per 100,000.

Among the 3626 women who received new diagnoses of IBC during 1994–1998, the age-adjusted rate of IBC was 1.3 per 100,000 (95% CL: 1.3–1.4) for all races combined (Table 2). Among the racial and ethnic populations included in this study, the rate of IBC was highest among black women (1.6 per 100,000) and lowest among Asian/Pacific Islander women (0.7 per 100,000) (Table 2). The IBC rate for Hispanic women was the same as the rate for non-Hispanic women ($p = 0.38$) (Table 4). Black women had a 20% higher risk of receiving a new IBC diagnosis than white women (RR: 1.2; 95% CL: 1.1–1.3) (Table 4). In contrast, Asian/Pacific Islander women had half the risk of being diagnosed with IBC as white women (RR: 0.5; 95% CL: 0.4–0.7).

Discussion

The demographic and tumor characteristics of IBC in our study differed considerably from the well-estab-

Table 2. Characteristics and age-adjusted rates of inflammatory breast cancer by race, United States, females, 1994–1998[a]

	All races combined[b] (n = 3626)			White (n = 3066)			Black (n = 429)			Asian/Pacific Islander (n = 82)		
	%	Rate	95% CL	%	Rate	95% CL	%	Rate	95% CL	%	Rate	95% CL
Total	100	1.3	1.3–1.4	100	1.3	1.3–1.4	100	1.6	1.4–1.7	100	0.7	0.5–0.9
Stage												
Localized	2.0	0.0	0.0–0.0	2.0	0.0	0.0–0.0	2.1	[c]		2.4	[c]	
Regional, direct extension only	21.7	0.3	0.3–0.3	21.8	0.3	0.3–0.3	21.2	0.3	0.3–0.4	28.1	0.2	0.1–0.3
Regional, regional lymph nodes only	5.1	0.1	0.1–0.1	5.3	0.1	0.1–0.1	4.7	0.1	0.0–0.1	0.0	[c]	
Regional, direct extension and regional lymph nodes	35.1	0.5	0.4–0.5	35.7	0.5	0.4–0.5	30.8	0.5	0.4–0.6	37.8	0.3	0.2–0.4
Regional, NOS	7.0	0.1	0.1–0.1	7.7	0.1	0.1–0.1	3.0	[c]		4.9	[c]	
Distant	25.3	0.3	0.3–0.4	23.9	0.3	0.3–0.3	34.3	0.5	0.5–0.6	24.4	0.2	0.1–0.3
Unstaged	3.7	0.0	0.0–0.1	3.7	0.0	0.0–0.1	4.0	[c]		2.4	[c]	
Grade												
Well differentiated, I	1.6	0.0	0.0–0.0	1.6	0.0	0.0–0.0	1.9	[c]		0.0	[c]	
Moderately differentiated, II	14.3	0.2	0.2–0.2	14.6	0.2	0.2–0.2	12.4	0.2	0.1–0.3	11.0	[c]	
Poorly differentiated, III	49.4	0.7	0.6–0.7	48.9	0.6	0.6–0.7	52.5	0.8	0.7–0.9	54.9	0.4	0.3–0.5
Undifferentiated, IV	5.5	0.1	0.1–0.1	5.7	0.1	0.1–0.1	4.2	[c]		6.1	[c]	
Unknown	29.2	0.4	0.4–0.4	29.1	0.4	0.4–0.4	29.1	0.5	0.4–0.6	28.1	0.2	0.1–0.3
Mean Age	57.6			58.1			55.2			53.4		
Age												
<40	10.1	0.2	0.2–0.2	9.7	0.2	0.2–0.3	12.8	0.3	0.2–0.4			
40–49	23.2	2.1	2.0–2.3	22.2	2.1	1.9–2.2	29.1	2.8	2.3–3.4	31.7[d]	0.3	0.2–0.4
50–59	24.0	3.3	3.0–3.5	24.2	3.3	3.0–3.5	20.0	3.2	2.6–3.9	41.5	2.8	1.9–3.9
60–69	19.9	3.4	3.2–3.7	20.0	3.4	3.1–3.7	19.8	4.2	3.3–5.2	26.8[e]	1.2	0.7–1.8
70–79	14.3	2.9	2.6–3.1	15.0	2.9	2.6–3.1	11.7	3.6	2.7–4.8		[c]	
80+	8.4	2.7	2.4–3.0	8.9	2.7	2.4–3.0	6.5	3.7	2.5–5.4		[c]	

[a] Rates are per 100,000 female population. 'Total' rates are age-adjusted to the 2000 US standard population by 5-year-age groups.
[b] All races combined' total does not equal 'white + black + Asian/Pacific Islander' because of 20 cases with American Indian/Alaska Native race, 20 cases with unknown race and six cases with other race.
[c] Rates and confidence intervals are suppressed for fewer than 20 cases.
[d] Ages <50.
[e] Ages 60+.

lished characteristics of more common forms of breast cancer. Reflecting the aggressive nature of IBC, only 2% of IBC cases in our study were diagnosed at a localized stage; by comparison, 64% of all malignant breast cancer histologies combined were diagnosed at this stage in SEER during 1994–1998 [18]. Similarly, IBC tumors were more likely to be grade III in our study, while the largest percentage of tumors for all breast cancers combined in SEER were grade II [unpublished data from 13]. On average, IBC occurred at a younger age than female breast cancer for all histologic types combined; the average age at diagnosis was 62.1 years for women diagnosed with all forms of malignant breast cancer in SEER and 57.6 years for women diagnosed with IBC in our study. Age-specific rates of IBC in our study peaked at ages 60–69 years before declining for older ages, whereas age-specific rates of malignant breast cancer in SEER increased with age until ages 80–84 years. For all ages combined, black women had higher rates of IBC than did white women, but this relationship was reversed for all histologic types of breast cancer combined.

The findings of higher rates of IBC among black women than white women and the younger age at diagnosis for IBC than for other histologic types of breast cancer are consistent with findings in the literature [1, 4]. To our knowledge, the lower rate of IBC among Asian/Pacific Islander women than among white women has not been previously reported, although this finding is consistent with findings for overall rates of breast cancer in the same populations [15].

Considerable debate persists about what combination of clinical and/or histologic features are needed for a diagnosis of IBC [1, 4, 7, 8]. The recent publication of the

Table 3. Characteristics and age-adjusted rates of inflammatory breast cancer by Hispanic origin, United States, females, 1994–1998[a]

	Hispanic[b] (n = 159)			Non-Hispanic (n = 1582)		
	%	Rate	95% CL	%	Rate	95% CL
Total	100	1.4	1.2–1.7	100	1.6	1.5–1.6
Stage						
Localized	0.0	[c]		0.7	[c]	
Regional, direct extension only	29.6	0.4	0.3–0.6	25.2	0.4	0.4–0.4
Regional, regional lymph nodes only	1.3	[c]		2.3	0.0	0.0–0.0
Regional, direct extension and regional lymph nodes	41.5	0.6	0.5–0.8	35.9	0.6	0.5–0.6
Regional, NOS	0.6	[c]		9.6	0.2	0.1–0.2
Distant	26.4	0.4	0.3–0.5	23.5	0.4	0.3–0.4
Unstaged	0.6	[c]		2.7	0.0	0.0–0.1
Grade						
Well differentiated, I	1.9	[c]		1.7	0.0	0.0–0.0
Moderately differentiated, II	13.2	0.2	0.1–0.3	16.8	0.3	0.2–0.3
Poorly differentiated, III	61.6	0.9	0.7–1.1	51.1	0.8	0.7–0.9
Undifferentiated, IV	3.8	[c]		6.5	0.1	0.1–0.1
Unknown	19.5	0.3	0.2–0.4	24.0	0.4	0.3–0.4
Mean Age	50.5			58. 5		
Age						
<40	22.6	0.3	0.2–0.5	8.9	0.2	0.2–0.3
40–49	32.1	2.8	2.1–3.7	21.9	2.3	2.1–2.6
50–59	14.5	2.3	1.4–3.4	24.9	4.0	3.6–4.4
60–69	20.1	4.7	3.2–6.6	19.8	4.1	3.7–4.6
70–79	6.3	[c]		15.2	3.6	3.2–4.1
80+	4.4	[c]		9.2	3.4	2.9–4.0

[a] Rates are per 100,000 female population. 'Total' rates are age-adjusted to the 2000 US standard population by 5-year-age groups.
[b] Hispanic origin is not mutually exclusive from white, black, Asian/Pacific Islander, and American Indian/Alaskan Native. 1885 IBC cases were excluded because there were fewer than 20 cases of Hispanic origin in the state or because more then 3% of cases in the state were missing information on Hispanic origin.
[c] Rates and confidence intervals are suppressed for fewer than 20 cases.

Table 4. Rate ratios of inflammatory breast cancer by age, race, and ethnicity, United States, females, 1994–1998[a]

Age	Black to white			Asian/Pacific Islander to white			Hispanic[b] to non-Hispanic		
	RR	95% CL	*p*-Value	RR	95% CL	*p*-Value	RR	95% CL	*p*-Value
Total	1.2	1.1–1.3	<0.01	0.5	0.4–0.7	<0.01	0.9	0.8–1.1	0.38
<40	1.2	0.9–1.6	0.21	[c]			1.4	0.9–2.0	0.11
40–49	1.4	1.1–1.7	<0.01	0.4[d]	0.3–0.6	<0.01	1.2	0.9–1.6	0.22
50–59	1.0	0.8–1.2	0.82	0.9	0.6–1.2	0.33	0.6	0.4–0.9	0.01
60–69	1.2	1.0–1.5	0.07	0.4[e]	0.3–0.6	<0.01	1.1	0.8–1.7	0.46
70–79	1.3	0.9–1.7	0.13	[c]			0.6	0.3–1.2	0.17
80+	1.4	0.9–2.0	0.10	[c]			0.9	0.4–2.0	0.82

[a] Rates are per 100,000 female population. 'Total' rates are age-adjusted to the 2000 US standard population by 5-year-age groups.
[b] Hispanic origin is not mutually exclusive from white, black, Asian/Pacific Islander, and American Indians/Alaskan Native. 1885 IBC cases were excluded because there were fewer than 20 cases of Hispanic origin in the state or because more than 3% of cases in the state were missing information on Hispanic origin.
[c] Rates and confidence intervals are suppressed for fewer than 20 cases.
[d] Ages <50.
[e] Ages 60+.

American Joint Committee on Cancer's *Cancer Staging Manual*, 6th edition, defines IBC as primarily a clinical diagnosis:

> … a clinicopathologic entity characterized by diffuse erythema and edema (peau d'orange) of the breast, often without an underlying palpable mass. These clinical findings should involve the majority of the skin of the breast. Classically, the skin changes arise quickly in the affected breast. Thus the term inflammatory carcinoma should not be applied to a patient with neglected locally advanced cancer of the breast presenting late in the course of her disease. This clinical presentation is due to tumor emboli within the dermal lymphatics, which may or may not be apparent on skin biopsy. Involvement of the dermal lymphatics alone does not indicate inflammatory carcinoma in the absence of clinical findings. In addition to the clinical picture, however, a biopsy is still necessary to demonstrate cancer either within the dermal lymphatics or in the breast parenchyma itself. [19, pp. 225–226].

Bonnier *et al*. [8] distinguished between primary and secondary IBC; they used the latter characterization when the tumor was identified before the appearance of inflammatory symptoms. In a case series, they described three types of IBC: (1) typical IBC in 76% of cases – that is, IBC with enlargement of the breast, redness, and edema covering more than one-third of the skin over the breast, emboli often present in the subdermal lymphatics, lymph node involvement, and frequently no palpable tumor; (2) occult IBC in 13% of cases – that is, IBC with no inflammatory signs but with dermal lymphatic tumor emboli; and (3) pseudo-IBC in 11% of cases – that is, IBC with symptoms like those of patients in the first group but with better circumscribed tumors, no carcinoma cells in subdermal lymphatics, and generally no lymph node involvement. Three- and five-year survival rates were not different for groups 1 and 2; however, group 3 had better survival than the other two groups. Bonnier and colleagues concluded that although a diagnosis of true IBC might be suspected from the clinical findings, pathology with dermal lymphatic emboli or extensive lymph node involvement was needed to confirm the diagnosis. When sections and tissue block samples were examined for the presence of dermal lymphatic emboli, however, these features were generally observed in about three-fourths of cases. Levine and colleagues classified IBC cases according to the presence of clinical and/or pathologic signs of disease and found that three year survival was highest among women with only clinical signs of disease (62%) and lowest among those with clinical and pathologic signs of disease (34%) [1].

Like the most recent population-based study of IBC based on data from SEER, our study used a conservative definition of IBC, the ICD-O-2 code M-8530/3, which is a pathologic diagnosis [4, 11]. Some cases of true IBC may have been excluded if the pathologist did not use this specific terminology. Some clinicians and pathologists believe that 'inflammatory carcinoma' is strictly a clinical rather than a pathologic diagnosis. Patients with a clinical diagnosis of IBC based on the appearance of the breast, a pathologic indication of dermal lymphatic involvement, and a histologic type other than M-8530/3 may have been missed. Therefore, the estimates of IBC incidence rates in our study should be considered conservative.

The magnitude of the underestimation may be greater than 35% [1, 13, unpublished data from SEER]. Among 795 histologically confirmed diagnoses of IBC (based on ICD-O-2 code M-8530/3) in women residing in nine SEER areas during 1994–1998, 590 (74%) also had IBC classified according to the extent of disease code 70 [personal communication from Lynn Ries, May 2003]. However, another 450 cases with other histologic types of breast cancer, not M-8530/3, had only the SEER extent of disease code for IBC.

Other limitations include the quality of race and Hispanic origin data in registries [17], use of population projections from the 1990 census [20], and the small numbers of cases among Asian/Pacific Islanders and American Indian/Alaska Natives. Cancer incidence rates for some racial and ethnic populations may be limited by problems in ascertaining race and by misreporting of race and ethnicity on the basic records (medical records, death certificates, and census reports) from which information is collected on cancer incidence, deaths, and populations at risk [21–24]. Recent studies suggest that reporting of race for the white and black populations is generally reliable, but biases are more serious for some smaller populations, particularly American Indians [23, 24]. Moreover, analyses of the new census data suggest that there are sizable differences between the enumerated 2000 census and the population projections for the late 1990s from the enumerated 1990 census for some populations [20]. Recalculation of these rates using new intercensal race-specific population estimates may produce different rates and different relationships between rates for different populations. An underestimate of black women in the population projections may explain the higher rates of IBC in black compared to white women in this study.

Statistically, since different states were included in the calculation of rates for specific populations, differences

could be attributable to geographic factors. To address this concern, we repeated the analyses including all 26 registries in the calculations of rates and CL for each population. The resulting rates did not differ appreciably, and the CL were more narrow. Based on the inclusion criteria previously mentioned, this study included cases from 40% of the US White population, 37% of the US Black population, 26% of the US American Indian population, and 52% of the US Asian Pacific Islander population. Independent of race categorization, 27% of the US Hispanic population was included. Although the results from these additional analyses did not produce different conclusions, the results may be biased if race or Hispanic origin was substantially underreported in the states with race-specific populations currently described as small. As the quality of coding for race and ethnicity improves over time, these issues should dissipate.

IBC is an extremely rare form of breast cancer. Because this form of breast cancer is rapidly fatal, more precise diagnostic criteria are needed to distinguish it from less aggressive forms of disease. Future clinical studies of IBC should be based on a population-based set of cases and should involve the detailed collection of clinical data, such as the presence of erythema, edema or peau d'orange appearance of the skin, and other clinical signs of disease. These studies should also include surgical assessment, such as full axillary dissection, pathologic examination by an expert panel to assess the presence of dermal lymphatic involvement, and testing for known biologic markers.

Acknowledgements

Supported in part by the Centers for Disease Control and Prevention under cooperative agreement U75/CCU51598 to the North American Association of Central Cancer Registries.

References

1. Levine PH, Steinhorn SC, Ries LG, Aron JL (1985) Inflammatory breast cancer: the experience of the surveillance, epidemiology, and end results (SEER) program. *J Natl Cancer Inst* **74**: 291–297.
2. Margoles RG, Fisher B, Hortobagyi H, Bloomer WG (2000) Neoplasms of the breast. In: Bast RC, Kufe DW, Pollock RE, Weichselbaum RR, Holland JF, Frei E, eds. *Cancer Medicine*, 5th edn. Hamilton, Ontario: B.C. Decker Inc.
3. Jaiyesimi IA, Buzdar AU, Hortobagyi G (1992) Inflammatory breast cancer: a review. *J Clin Oncol* **10**: 1014–1024.
4. Chang S, Parker SL, Pham T, Buzdar AU, Hursting SD (1998) Inflammatory breast carcinoma incidence and survival, the surveillance, epidemiology, and end results program of the National Cancer Institute, 1975–1992. *Cancer* **82**(12): 2366–2372.
5. Taylor G, Meltzer A (1938) Inflammatory carcinoma of the breast. *Am J Cancer* **33**: 33–49.
6. Haagensen C (1971) *Diseases of the Breast*, 2nd edn. Philadelphia, PA: Saunders, pp. 576–584.
7. Singletary SE, Ames FC, Buzdar AU (1994) Management of inflammatory breast cancer. *World J Surg* **18**: 87–92.
8. Bonnier P, Charpin C, Lejeune C, *et al*. (1995) Inflammatory carcinomas of the breast: a clinical pathological, or a clinical and pathological definition? *Int J Cancer* **62**: 382–385.
9. Dahlbeck SW, Donnelly JF, Theriault RL (1995) Differentiating inflammatory breast cancer from acute mastitis. *Am Fam Physician* **52**: 929–934.
10. Brooks HL, Mandava N, Pizzi W, Shah S (1998) Inflammatory breast carcinoma: a community hospital experience. *Am College Surgeons* **186**: 622–629.
11. Percy C, Van Holten V, Muir C, eds. (1990) *International Classification of Diseases for Oncology*, 2nd edn. Geneva, Switzerland: World Health Organization.
12. Chang S, Buzdar AU, Hursting SD (1998) Inflammatory breast cancer and body mass index. *J Clin Oncol* **16**: 3731–3735.
13. *SEER*Stat 2001* (2003) Bethesda, MD: National Cancer Institute. Also available from: URL: http://seer.cancer.gov/seerstat [accessed 2003, January 13].
14. Fay MP, Feuer EJ (1997) Confidence intervals for directly standardized rates: a method based on the gamma distribution. *Statist Med* **16**: 791–801.
15. Ries LAG, Eisner MP, Kosary CL, *et al*. eds. (2002) *SEER Cancer Statistics Review, 1973–1999*. Bethesda, MD: National Cancer Institute. Also available from: URL: http://www.seer.cancer.gov/csr/1973_1999 [accessed 2002, June 14].
16. Katz D, Baptista J, Azen SP, Pike MC (1978) Obtaining confidence intervals for the risk ratio in cohort studies. *Biometrics* **34**: 469–474.
17. O'Malley C, Hu KU, West DW (2002) North American association of central cancer registries: race and ethnicity identifier assessment project. Also available from: URL http://www.naaccr.org, http://www.naaccr.org/Training/files [accessed August 2002].
18. Ries LAG, Eisner MP, Kosary CL, *et al*. eds. (2001) *SEER Cancer Statistics Review, 1973–1998*. Bethesda, MD: National Cancer Institute.
19. Greene FL, Page DL, Fleming ID, *et al*. eds. (2002) *AJCC Cancer Staging Manual*, 6th edn. New York: Springer-Verlag, pp. 221–240.
20. US Cancer Statistics Working Group (2002) *United States Cancer Statistics: 1999 Incidence*. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute.
21. Rosenberg HM, Maurer JD, Sorlie PD, *et al*. (1999) Quality of death rates by race and Hispanic origin: a summary of current research. *Vital Health Stat* **2**(128).
22. Poe GS, Powell-Griner E, McLaughlin JK, Placek PJ, Thompson GB, Robinson K (1993) *Comparability of the Death Certificate and the 1986 National Mortality Followback Survey*. Hyattsville, MD: National Center for Health Statistics.
23. Kolonel LH, Goodman MT (1992) Racial variation in cancer: fact or artifact? *J Natl Cancer Inst* **84**: 916–917.
24. Hogan H (1993) The 1990 post-enumeration survey: operations and results. *J Am Stat Assoc* **88**: 1047–1060.