Chapter 13
Cancer of the Female Breast

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INTRODUCTION

This study presents survival analyses for female breast cancer based on 302,763 adult cases from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). This chapter focuses on the influence of extent of disease (extension of tumor, size, nodal involvement, number of nodes involved), histology, histologic grade, receptor status, and demographic factors on female breast cancer survival.

MATERIALS AND METHODS

The NCI contracts with medically oriented nonprofit institutions -- such as universities and state health departments -- to obtain data on all cancers diagnosed in residents of the SEER geographic areas except basal cell and squamous cell carcinomas of the skin and in situ cervical cancer.

SEER selects areas on the basis of their ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. The analysis in this article is from 12 geographic areas representing approximately 14% of the United States population. The geographic areas include the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, San Jose, Los Angeles, and Seattle; Alaska Natives; and ten counties in rural Georgia. All registries contributed data for diagnosis years 1988-2001 except Los Angeles, which contributed data for 1992-2001.

Each registry is responsible for abstracting the records of all cancer patients who reside in the given area. To ensure maximal ascertainment of cancer cases, registries seek records from hospitals, laboratories, and all other health service units that provide diagnostic services. Data collected on each patient include patient demographics, primary tumor site, morphology, diagnostic methods, extent of disease, and first course of cancer-directed therapy. A separate record is coded for each primary cancer. With the exception of cases of in situ carcinoma of the uterine cervix, all patients are followed from diagnosis to death, allowing for detailed survival analysis.

SEER has collected extent-of-disease (EOD) information on all cancers since the inception of the program. The detail and amount of information collected, however, have varied over time. In 1988, there were some minor revi-

Table 13.1: Cancer of the Female Breast: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
365,042	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
309,467	55,575	Select first primary only
307,746	1,721	Exclude death certificate only or at autopsy
305,757	1,989	Exclude unknown race
305,483	274	Active follow-up and exclude alive with no survival time
305,455	28	Exclude children (Ages 0-19)
303,045	2,410	Exclude no or unknown microscopic confirmation
302,763	282	Exclude sarcomas

sions to the breast cancer EOD scheme so that SEER EOD information could be easily converted into the TNM staging classifications based on the third edition of the American Joint Committee on Cancer (AJCC) Manual for Staging of Cancer (1). (The AJCC TNM schemes are the same as those published by the International Union Against Cancer.)

The term localized refers to tumors that are confined to breast tissue only. Regional refers to tumors that have metastasized to the regional lymph nodes or have extended directly from the breast to the pectoral fascia, subcutaneous tissue, chest wall, ribs, or skin (peau d'orange, satellite nodules, etc.). Distant refers to distant metastases or further direct extension.

Analysis

The survival analysis was based on 5-year relative survival rates calculated by the life-table method. The relative survival rate was used to estimate the effect of cancer on the survival of the cohort. Relative survival is observed survival divided by survival that would be expected in the absence of cancer; thus, relative survival adjusts for the normal mortality that the cohort would experience from other causes of death. When relative survival is 100%, a patient cohort has the same chance to live 5 more years as a cancer-free cohort based on the same age, race, and sex.

Exclusions

The following were excluded from the analysis: male breast cancers, cases in which the breast cancer was not the first primary, cases identified through autopsy and death certificate only, cases with unknown race, cases with unknown survival time, cases where the age at diagnosis was less than 20, cases with no microscopic confirmation, and sarcomas. After exclusions, 302,763 adult female breast cancers diagnosed from 1988 to 2001 were available for analysis (Table 13.1). Of these 44,875 (14.8%) were in situ and 257,888 (85.2%) were malignant. Note that 45,033 cases were Stage 0 which includes in situ plus Paget disease of the nipple with no underlying tumor.

RESULTS

This analysis is based on prognostic factors for breast cancer, with an emphasis on extent of disease at diagnosis especially the role of tumor size, extension of the primary tumor, and lymph node status. Survival rates were also calculated by demographic characteristics such as age and race (white, black). In most tables, each prognostic factor is presented both individually and in relation to a second factor.

Stage

As expected, survival rates varied by stage (Table 13.2). For patients of all ages, patients diagnosed in stages 0 and I had a 100% 5-year relative survival rate. The five-year relative survival rate for stage II was 86%; for stage III,

Table 13.2: Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Age (20+) and AJCC Stage (3rd edition), 12 SEER Areas, 1988-2001

Age (Years)	AJCC Stage													
	Total		0		I		II		III		IV		Unknown	
	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	302,763	89.3	45,033	100.0	108,346	100.0	91,989	86.2	16,928	57.2	11,222	19.9	29,245	83.4
20-34	6,802	77.8	563	98.7	1,565	94.5	3,042	77.6	649	50.5	291	17.5	692	74.4
35-39	12,827	83.5	1,665	99.7	3,343	95.1	5,231	82.1	1,021	55.8	384	19.4	1,183	79.4
40-44	24,914	88.0	4,615	99.9	7,127	97.0	8,790	86.3	1,667	59.4	683	25.8	2,032	83.0
45-49	33,784	89.5	6,382	100.0	10,400	97.6	11,427	87.8	2,132	62.6	968	25.4	2,475	85.2
50-54	34,868	89.5	6,462	100.0	12,023	98.3	10,857	86.7	1,943	59.2	1,147	20.5	2,436	85.4
55-59	32,701	89.6	5,496	100.0	12,029	99.0	9,920	87.5	1,636	57.5	1,234	19.5	2,386	84.6
60-64	32,680	90.1	4,930	100.0	12,949	100.0	9,306	86.7	1,587	57.3	1,308	18.9	2,600	86.3
65-69	34,435	91.0	4,986	100.0	14,194	100.0	9,404	87.8	1,542	57.6	1,374	20.3	2,935	84.6
70-74	32,686	91.8	4,363	100.0	13,731	100.0	8,697	87.2	1,408	57.8	1,299	17.7	3,188	86.9
75-79	27,134	91.4	3,141	100.0	11,101	100.0	7,295	86.2	1,335	54.8	1,147	15.6	3,115	82.4
80-84	17,475	90.7	1,683	100.0	6,461	100.0	4,684	87.0	999	52.5	792	20.7	2,856	77.6
85+	12,457	86.6	747	100.0	3,423	100.0	3,336	83.9	1,009	41.5	595	14.8	3,347	78.9

Table 13.3: Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Race and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage													
	Total		0		I		II		III		IV		Unknown	
Race	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
All Races	302,763	89.3	45,033	100.0	108,346	100.0	91,989	86.2	16,928	57.2	11,222	19.9	29,245	83.4
White	254,919	90.4	37,397	100.0	94,023	100.0	76,296	87.1	13,467	60.0	8,970	21.2	24,766	84.8
Black	25,467	78.4	3,782	100.0	6,448	97.5	8,564	78.5	2,270	40.1	1,532	12.6	2,871	71.7

"Total" category includes 22,377 cases that are neither white nor black.

57%. For stage IV, the relative survival rate was poor: 20%. The 5-year relative survival rate for unknown stage was just below that for stage II.

Stage at diagnosis and age at diagnosis

For all stages combined, the survival rates increased by age group from 78% for 20-34 to 92% for 70-74 and then decreased to 87% for 85 years and over. For stage I, relative survival increased with age, approaching 100% for those aged 60 and older. For Stage III, survival rates ranged from 41 to 63% with the youngest and oldest age groups experiencing the worst survival rates. Stage IV cases had the worst survival for each age group (Table 13.2).

Stage and race

The overall 5-year relative survival rates were 90% for whites and 78% for blacks (Table 13.3). The fact that black women had a less favorable stage distribution than white women does not fully explain the survival differential, since even within each stage grouping except Stage 0, blacks had poorer survival. "All Races" category includes 22,397 cases that are races other than white or black.

Stage and Grade (Adenocarcinoma)

For adenocarcinomas, 5-year relative survival rates decreased by stage at diagnosis as expected (Table 13.4). Patients diagnosed with stage I cancer had a 5-year relative survival rate of 100%; those diagnosed with stage IV had a rate of 21%. Histologic grade was also a predictor of outcome except for grades 3 and 4; survival was highest for grade 1 and lowest for grade 3 or 4 and intermediary for grade 2. Survival ranged from 100% for grade 1 stage I down to 14% for grade 4 stage IV. In stages II-IV, histologic grade played an important prognostic role.

Stage and Histology

Table 13.5 contains a similar breakdown by stage and histology. The highest relative survival rates were for tubular and adenoid cystic adenocarcinomas (100%) and the lowest was for inflammatory carcinoma (34%). Even within stage IV disease, there were wide variations in survival by histology from 11% for inflammatory to 34% mucinous adenocarcinoma or papillary adenocarcinoma.

Size and Stage

The effect of tumor diameter (size) on survival is shown for all stages in Table 13.6. Size is categorized by 5-mm groups. The size groupings were chosen so that the middle size in each group was 0.5, 1.0, 1.5, 2.0, 2.5,…, 9.5 cm, respectively; the sizes most frequently cited in the hospital medical record. Five-year relative survival rates ranged from 100% for <8 mm tumors to 34% for diffuse tumors.

Due to the interrelationship of tumor size and extent of disease, results are given by size category for different extension groups: tumors localized to the breast, those regional by nodes, those regional by extension (peau d'orange, pectoral fascia, chest wall, extensive skin involvement, etc.), those with distant metastasis, and those with unknown extension.

Within each extension category, tumor size played an important prognostic role (Table 13.6). Patients with small tumors and either regional nodal involvement or direct extension of the tumor survived as well or better than those with large tumors confined to the breast. It should be noted, however, that there was a relationship between size and extension of the tumor. Tumors confined to the breast were smaller in general than tumors with distant metastases. For example, 59.5% of the localized tumors measured 17 mm or less compared to less than 7% for those with distant metastases. For those with distant disease 39% had tumors that measured over 57 mm or were diffuse (Table 13.7).

Table 13.4: Adenocarcinoma of the Female Breast (Non Stage 0): Number of Cases and 5-Year Relative Survival Rates (%) by Histologic Grade and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown	
Grade	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	251,828	87.6	107,595	100.0	90,994	86.3	16,576	57.5	10,270	20.5	26,393	84.9
1	32,620	100.0	21,588	100.0	7,173	98.7	599	79.4	325	31.1	2,935	97.6
2	80,761	93.2	38,784	100.0	29,435	91.4	3,956	69.3	2,110	26.9	6,476	89.3
3	74,165	77.6	22,096	96.8	34,322	79.6	8,028	50.9	3,947	17.1	5,772	71.7
4	5,946	78.6	1,888	98.2	2,545	80.2	667	53.8	329	13.8	517	72.3
Unknown	58,336	87.1	23,239	100.0	17,519	87.5	3,326	57.2	3,559	20.2	10,693	86.6

Excludes 45,033 stage 0 cases and 5,902 non-adenocarcinomas not in stage 0.

Adenocarcinoma defined as histologies 8050,8140-8147,8160-8162,8180,8190-8191,8200-8202,8204,8210-8215,8220-8221,8250-8255,8260-8264,8270-8272,8280-8281,8290,8300,8310-8325,8330-8337,8340-8347,8350,8360-8361,8370-8375,8380-8384,8390-8392,8400-8410,8413,8420,8430,8440-8444,8450-8454,8460-8463,8470-8473,8480-8482,8490,8500-8506,8510,8520-8525,8530,8540-8543,8550,8560,8570-8574,8576,8940-8941.

Extension of tumor and nodal involvement

The SEER data allow for the extension categories presented in Tables 13.6 and 13.7 to be evaluated in greater detail. The localized extension category is limited to those tumors confined to breast tissue. Regional by direct extension cases can be further divided into those involving subcutaneous tissue, those involving the pectoral fascia, those involving the chest wall, ribs, and muscles versus those with extensive skin involvement (skin edema, peau d'orange, ulceration of the skin of breast, satellite nodules in skin, etc.). The AJCC (5th edition) T-categories of T1-T3a include tumors confined to breast tissue, those involving subcutaneous tissue and those involving the pectoral fascia and the specific T-category is assigned based on the size of tumor. Table

Table 13.5: Cancer of the Female Breast (Non Stage 0): Number of Cases and 5-Year Relative Survival Rates (%) by Histology and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown	
Histology	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	257,730	87.1	108,346	100.0	91,989	86.2	16,928	57.2	11,222	19.9	29,245	83.4
Adeno, NOS	5,559	62.2	1,137	99.0	1,341	81.4	453	49.4	1,460	15.3	1,168	64.9
Tubular adeno	3,771	100.0	2,939	100.0	286	95.8	13	~	8	~	525	99.7
Infiltrating duct	183,122	87.5	79,900	100.0	68,437	85.1	10,597	57.5	6,493	20.3	17,695	83.6
Scirrhous adeno	456	81.7	172	94.3	188	83.9	16	~	30	13.5	50	71.7
Mucinous adeno	6,476	98.3	3,643	100.0	1,665	94.8	176	75.0	120	33.8	872	95.7
Comedo	5,020	89.9	2,218	99.3	1,653	82.7	223	51.3	82	19.4	844	96.0
Lobular	20,140	91.6	7,640	100.0	7,594	93.0	1,600	72.6	921	30.5	2,385	87.9
Infiltrating duct & lobular	16,060	92.9	6,801	100.0	6,564	91.4	1,013	69.8	375	29.0	1,307	89.5
Inflammatory carcinoma	2,668	34.1	<5	~	25	49.5	2,003	40.9	570	11.2	67	21.6
Paget	1,937	82.6	498	95.8	524	77.7	193	46.3	66	14.3	656	93.0
Papillary adeno	1,646	94.5	741	100.0	463	92.3	67	85.7	43	34.2	332	92.6
Adenoid cystic/ cribriform	712	100.0	409	100.0	177	95.3	14	~	6	~	106	96.3
Other adeno	4,261	89.1	1,494	98.7	2,077	88.8	208	57.7	96	21.2	386	84.6
Medullary	3,122	89.5	1,037	98.2	1,703	88.8	131	63.2	33	29.6	218	75.1
Other Non-adeno	5,785	64.8	699	99.2	945	80.1	348	42.4	952	13.8	2,841	70.1

Excludes 45,033 stage 0 cases.

~ Statistic not displayed due to less than 25 cases.
NOS: Not Otherwise Specified; adeno: adenocarcinoma

Table 13.6: Malignant Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (%) by Tumor Size (mm) and Extension, Ages 20+, 12 SEER Areas, 1988-2001

	Extension											
	Total		Localized		Regional by Nodes		Regional by Extension		Distant		Unknown	
Tumor Size (mm)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
All sizes	257,888	87.1	160,105	97.4	64,224	82.3	14,075	64.7	14,359	24.4	5,125	62.9
Micro focus	4,439	98.9	4,016	100.0	332	88.2	59	74.9	20	~	12	~
Mammography only	944	97.9	842	99.9	77	81.1	13	~	<5	~	8	~
3-7	21,231	100.0	19,261	100.0	1,635	94.8	166	88.9	102	30.3	67	93.8
8-12	47,548	99.8	39,561	100.0	6,879	94.3	624	87.3	349	34.7	135	84.3
13-17	43,576	95.8	31,659	98.9	10,202	91.0	1,046	86.9	509	29.2	160	80.2
18-22	37,530	90.3	23,347	95.2	11,728	86.4	1,497	78.2	766	32.6	192	60.2
23-27	22,163	85.9	11,985	92.1	8,177	83.1	1,284	75.1	622	29.6	95	65.5
28-32	17,160	78.9	8,220	89.4	6,605	75.8	1,355	67.3	822	23.5	158	52.2
33-37	7,791	76.0	3,318	87.2	3,321	73.0	763	64.4	353	26.5	36	49.3
38-42	8,346	71.5	3,212	83.3	3,394	72.7	973	61.2	664	24.7	103	47.4
43-47	3,397	69.7	1,168	84.0	1,492	69.5	493	54.4	223	27.5	21	~
48-52	5,303	65.9	1,615	83.4	2,160	68.1	829	55.9	621	24.1	78	57.9
53-57	1,638	67.6	481	87.2	701	67.5	320	54.6	131	25.2	5	~
58-62	3,221	60.7	788	82.8	1,249	64.9	656	54.8	468	20.2	60	55.5
63-67	875	60.9	214	86.2	373	58.4	187	50.3	96	32.4	5	~
68-72	1,953	57.5	431	86.0	703	64.5	432	47.3	349	19.6	38	48.6
73-77	484	61.4	108	88.9	197	65.8	113	46.0	63	23.2	<5	~
78-82	1,675	51.8	308	83.4	519	63.5	429	49.7	385	13.7	34	32.2
83-87	272	62.6	56	82.4	90	71.9	72	60.1	53	25.9	<5	~
88-92	760	55.5	141	81.9	237	71.2	205	48.5	167	20.6	10	~
93-97	164	51.1	33	90.3	43	51.2	55	51.6	33	3.9	0	~
>97	2,510	45.2	378	79.1	516	64.8	760	48.4	806	15.1	50	26.4
Diffuse	3,686	34.1	67	79.3	109	63.4	311	45.7	3,174	30.7	25	37.5
Unknown	21,222	72.7	8,896	96.9	3,485	79.2	1,433	55.6	3,579	18.2	3,829	63.0

Excludes 44,875 in situ cases.
Unknown size category includes Paget disease of the nipple with no demonstrable tumor.
~ Statistic not displayed due to less than 25 cases.

13.8 shows that patients with tumors confined to the breast survived better at 5 years than patients whose tumor had invaded the subcutaneous tissue or the pectoral fascia (93% vs. 72% to 69%). Invasion of the subcutaneous tissue and involvement of the pectoral fascia had similar 5-year survival rates. Within stage IIIB (AJCC/UICC staging classification, 5th edition) and with regional by direct extension (LRD staging classification), extensive skin involvement had a less favorable outcome than involvement of the chest wall, ribs, etc. For each extension category, involvement of the lymph nodes still remained a predictor of survival. Even for cases with distant metastases, 5-year survival ranged from 32% when regional lymph nodes are negative to only 12% when distant lymph nodes were involved.

Size of tumor and nodal involvement

In data from 1988-2001, the size of the tumor has first been taken from the pathology report and then from radiology reports if there was no path or no size information on path. If there was no size given on either report, the clinical size was used. Figure 13.1 shows the relationship of tumor size to the percentage of women who have lymph node involvement. The curve shown on the graph shows the logistic regression fit. The size of the primary tumor

Table 13.7: Malignant Cancer of the Female Breast: Tumor Size (mm) Distribution by Extension, Ages 20+, 12 SEER Areas, 1988-2001

	Extension											
	Total		Localized		Regional by Nodes		Regional by Extension		Distant		Unknown	
Tumor Size (mm)	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
All sizes	257,888	100.0	160,105	100.0	64,224	100.0	14,075	100.0	14,359	100.0	5,125	100.0
Micro focus	4,439	1.7	4,016	2.5	332	0.5	59	0.4	20	0.1	12	0.2
Mammography only	944	0.4	842	0.5	77	0.1	13	0.1	<5	0.0	8	0.2
3-7	21,231	8.2	19,261	12.0	1,635	2.5	166	1.2	102	0.7	67	1.3
8-12	47,548	18.4	39,561	24.7	6,879	10.7	624	4.4	349	2.4	135	2.6
13-17	43,576	16.9	31,659	19.8	10,202	15.9	1,046	7.4	509	3.5	160	3.1
18-22	37,530	14.6	23,347	14.6	11,728	18.3	1,497	10.6	766	5.3	192	3.7
23-27	22,163	8.6	11,985	7.5	8,177	12.7	1,284	9.1	622	4.3	95	1.9
28-32	17,160	6.7	8,220	5.1	6,605	10.3	1,355	9.6	822	5.7	158	3.1
33-37	7,791	3.0	3,318	2.1	3,321	5.2	763	5.4	353	2.5	36	0.7
38-42	8,346	3.2	3,212	2.0	3,394	5.3	973	6.9	664	4.6	103	2.0
43-47	3,397	1.3	1,168	0.7	1,492	2.3	493	3.5	223	1.6	21	0.4
48-52	5,303	2.1	1,615	1.0	2,160	3.4	829	5.9	621	4.3	78	1.5
53-57	1,638	0.6	481	0.3	701	1.1	320	2.3	131	0.9	5	0.1
58-62	3,221	1.2	788	0.5	1,249	1.9	656	4.7	468	3.3	60	1.2
63-67	875	0.3	214	0.1	373	0.6	187	1.3	96	0.7	5	0.1
68-72	1,953	0.8	431	0.3	703	1.1	432	3.1	349	2.4	38	0.7
73-77	484	0.2	108	0.1	197	0.3	113	0.8	63	0.4	<5	0.1
78-82	1,675	0.6	308	0.2	519	0.8	429	3.0	385	2.7	34	0.7
83-87	272	0.1	56	0.0	90	0.1	72	0.5	53	0.4	<5	0.0
88-92	760	0.3	141	0.1	237	0.4	205	1.5	167	1.2	10	0.2
93-97	164	0.1	33	0.0	43	0.1	55	0.4	33	0.2	0	0.0
>97	2,510	1.0	378	0.2	516	0.8	760	5.4	806	5.6	50	1.0
Diffuse	3,686	1.4	67	0.0	109	0.2	311	2.2	3,174	22.1	25	0.5
Unknown	21,222	8.2	8,896	5.6	3,485	5.4	1,433	10.2	3,579	24.9	3,829	74.7

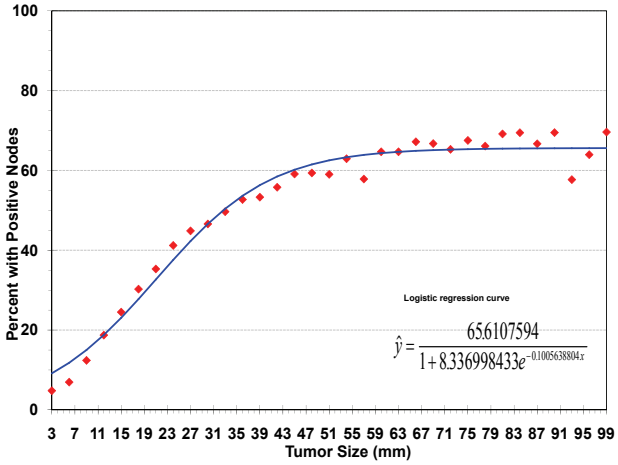
Excludes 44,875 in situ cases.
Unknown size category includes Paget disease of the nipple with no demonstrable tumor.

correlated with the percentage of women who had lymph node involvement in that the larger the tumor the higher the percentage of cases with lymph node involvement. While few women with very small tumors had lymph node involvement, over 60% of women with tumors over 54 mm had regional lymph nodes involved at the time of diagnosis. Five-year relative survival rates were high for women with small tumors and positive lymph nodes; they were lower for women with large tumors and positive lymph nodes. Survival rates decreased as size of tumor increased even when nodal involvement is divided into no positive lymph nodes, 1-3 lymph nodes positive, and 4 or more lymph nodes positive (Figure 13.2, Table 13.9). There were few cases with 4 or more nodes involved that had small tumors; therefore, the survival rate is not shown for the smallest size categories. This is consistent with the data from Table 13.7, which show that only a small proportion of women with regional lymph nodes involved had tumors less than 8 mm in diameter.

Receptor Status

Information on estrogen receptor (ER) and progesterone receptor (PR) status has been collected since 1990. Table 13.10 shows the 3-year relative survival rates by estrogen receptor status (ER) and progesterone receptor status (PR). ER positive tumors had better relative survival rates than

Figure 13.1: Cancer of the Female Breast: Existence of Positive Nodes by Tumor Size, 12 SEER Areas, 1988-2001



ER negative for each PR group. Women with ER+ and PR+ had a 97% 3-year relative survival rate compared with only 83% for women with PR- and ER-.

Table 13.11 shows the 3-year relative survival rates by ER status, historic stage, and age. Within each stage, ER status is an important prognostic variable. Even within distant stage, the 5 year relative survival rate was 28% for ER negative but much higher, 50% for ER positive women. Younger women have a higher percentage of cases that are ER negative than older women. This contributes towards the younger women having poorer survival than older women.

Laterality and Tumor Location

Table 13.12 shows the relationship between relative survival rates with respect to left or right breast and location within the breast. Laterality, left or right side, did not have any noticeable effect on survival. It should be noted that left or right designates the side where the tumor originated. The location of the tumor within the breast did not seem to be of prognostic value except when it was not specified.

DISCUSSION

While breast cancer survival rates overall are generally good, they vary by patient and tumor characteristics. Although stage has a large impact on survival, other factors such as tumor size, histology, ER status, PR status, grade, age, race, and number of positive nodes also played a role in prognosis. Some of these results expand on an earlier analysis performed on earlier SEER data (2).

Breast cancer is the number one cancer among U.S. women and it is expected that 212,920 women will be diagnosed with breast cancer in 2006 (3). Although breast cancer is a major disease in the US for women, its survival rates are better overall than those for many other types of cancer (4). The 5-year relative survival rate for localized invasive disease (all tumor sizes combined) was 97%. For patients diagnosed in stage I (tumor size < 20 mm), the 5-year relative survival rate was 100%. Some groups, however, especially young women, had a less favorable outcome. For women diagnosed in stage I, those 20-34 years of age had a 94% 5-year relative survival rate, compared to 100% for those over age 60. Differences by age are even greater for stage II patients.

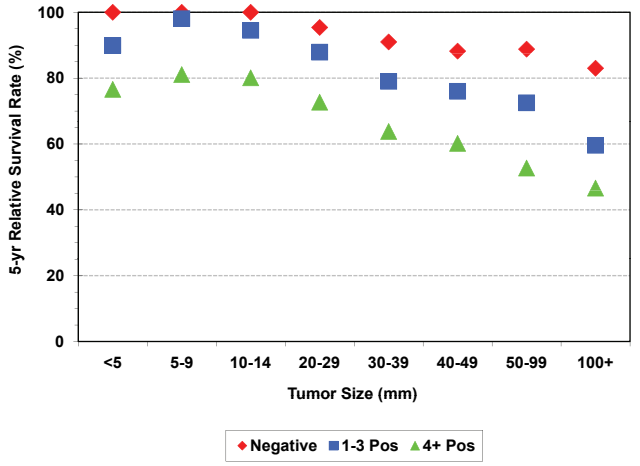
Table 13.8: Malignant Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (%) by Tumor Extension and Lymph Node Status, Ages 20+, 12 SEER Areas, or 13 1988-2001

	Nodes Involved											
	Total		Negative Regional		Positive Regional		Fixed Regional		Distant		Unknown	
Extension	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	257,888	87.1	154,918	97.2	73,153	77.5	5,009	55.2	1,719	22.9	23,089	61.4
Confined to breast	223,777	93.0	149,125	98.2	60,249	83.3	3,088	68.2	335	48.0	10,980	86.7
Subcutaneous tissue	7,481	71.7	2,320	87.7	4,036	68.5	317	51.5	47	26.5	761	51.2
Pectoral fascia	1,916	69.2	724	84.7	899	62.0	95	49.4	16	~	182	61.5
Chest wall, ribs, muscles	897	62.2	289	79.8	371	56.6	63	30.7	12	~	162	56.6
Extensive skin involvement	3,994	47.3	777	66.7	1,946	48.8	411	35.1	138	14.8	722	37.0
Inflammatory	3,173	39.9	343	60.5	1,603	41.6	269	34.7	131	19.3	827	34.0
Distant metastasis	10,500	18.7	1,038	32.3	3,247	21.2	681	17.0	902	12.3	4,632	15.5
Unknown	6,150	62.7	302	77.4	802	67.4	85	49.9	138	35.2	4,823	62.0

Excludes 44,875 in situ cases.

~Statistic not displayed due to less than 25 cases.

Figure 13.2: Cancer of the Female Breast: 5-Year Relative Survival Rate (%) by Tumor Size & Number of Nodes, Ages 20+, 12 SEER Areas, 1988-2001



Relative survival, like the name implies, is relative to the general population. When relative survival is 100%, the correct interpretation is that the cohort of patients has the same chance to live 5 more years as cancer-free persons of the same age and sex. This does not mean that no woman will die of breast cancer but rather that they may be under better medical surveillance than the general population and that their excess risk of breast cancer deaths is offset by their lower excess risk of dying from other non-cancer causes.

Even though relative survival rates increased with age at diagnosis until age 70, then decreased for the oldest age groups (Table 13.2), the survival differences by age were not due to differences in the stage distribution. Except for older patients having a higher proportion of unstaged disease, the stage distribution was similar for all age groups. Also, understaging of disease probably occurred with greater frequency among older patients, since many older patients did not have axillary node dissections. Since the relative survival rate adjusts for other causes of death, the differences in survival rates by age should not be attributed to the older patients dying from causes other than cancer at a higher rate than the younger cohorts. While for most other cancer sites, relative survival rates decreased with increasing age, this was not true of breast cancer except for the oldest age group.

There was a correlation between tumor size and percentage of women with positive lymph nodes (Figure 13.1). The survival rates generally decreased as the tumor size and the number of lymph nodes involved increased (Figure 13.2).

These data show that the evaluation of regional and distant lymph nodes should not be ignored when a patient has distant metastases. For patients with distant metastases, involvement of lymph nodes still plays an important prognostic role (Table 13.8). Those with no lymph node involvement have a 5-year relative survival rate of 32%; in contrast, the corresponding rate was 12% for those with distant lymph nodes involved.

While this analysis shows the value of the TNM system of staging, both tumor size and extent of disease influence the survival rates. Figure 13.3 shows the survival curves by the T, N, and M components of AJCC stage, 5th edition. Even though T1 (< 20 mm) N0 M0 has a distinct survival curve from T2 (20-50 mm) N0 M0, which in turn has a distinct survival curve from T3 (> 50 mm) N0 M0, other size groupings would also have produced distinct survival curves. The size groupings in any staging scheme are artificial and a matter of convenience. As shown (Table 13.6), survival rates vary by small changes in the tumor size. This points out that there was significant variation in survival within each TNM size category. Similarly, this chapter also points out that within extension (of tumor) groupings in TNM or within N1, there are survival variations when these groups are further subdivided by how far the tumor has extended (Table 13.8) or by the number of lymph nodes involved (Table 13.9), respectively.

Based on a large cohort, the probability of lymph node involvement directly correlates with the size of the primary tumor. Further, there is a survival relationship among tumor size, extension of tumor, and number of lymph nodes involved.

Figure 13.3: Cancer of the Female Breast: Relative Survival Rates (%) of Breast Cancer by Combinations of T, N, and M, Ages 20+, 12 SEER Areas, 1988-2001

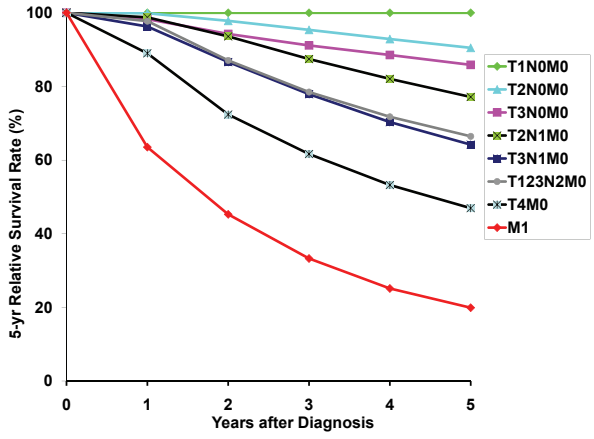


Table 13.9: Cancer of the Female Breast : Number of Cases and 5-Year Relative Survival Rates (%) by Tumor Size (mm) and Regional Lymph Nodes Involved, Ages 20+, 12 SEER Areas, 1988-2001

	Nodes Involved									
	Total		0 Nodes		1-3 Nodes		4+ Nodes		Unknown Number	
Tumor Size (mm)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total	302,763	89.3	148,192	98.8	43,418	86.8	26,923	65.5	84,230	81.2
1-4	21,530	100.0	9,721	100.0	563	89.9	197	76.6	11,049	100.0
5-9	37,075	100.0	23,816	100.0	2,261	98.1	541	81.1	10,457	100.0
10-19	93,875	97.2	58,654	100.0	14,035	94.5	4,475	80.1	16,711	91.8
20-29	54,610	88.0	27,139	95.4	12,194	87.9	6,440	72.7	8,837	75.7
30-39	23,880	78.1	9,497	91.0	5,704	79.0	4,412	63.8	4,267	61.3
40-49	11,786	72.1	3,866	88.2	2,692	76.0	2,753	60.2	2,475	54.2
50-99	17,015	63.2	4,120	88.8	3,135	72.5	5,054	52.7	4,706	45.7
100+	2,580	46.8	382	83.0	290	59.6	670	46.6	1,238	32.6
Diffuse	3,734	35.1	218	84.0	350	51.1	907	39.6	2,259	27.0
Unknown	36,678	84.9	10,779	100.0	2,194	81.8	1,474	63.1	22,231	78.4

Unknown size category includes Paget disease of the nipple with no demonstrable tumor.

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Table 13.10: Malignant Cancer of the Female Breast: Number of Cases and 3-Year Relative Survival Rates (%) by Progesterone Receptor (PR) and Estrogen Receptor (ER) Status, Ages 20+, 12 SEER Areas, 1990-2001

	ER Status							
	Total		Positive		Negative		Other/Unknown	
PR Status	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)
Total (1990+)	230,922	92.1	140,857	96.4	43,030	83.6	47,035	87.2
Positive	118,718	96.6	112,352	97.1	5,618	88.5	748	90.7
Negative	59,375	86.5	22,623	92.7	36,204	82.9	548	83.1
Other/Unknown	52,829	88.2	5,882	96.8	1,208	83.2	45,739	87.2

Table 13.11: Female Malignant Breast Cancer: 3-Year Relative Survival Rates (%) by Age (20+), SEER Historic Stage and ER Status, 12 SEER Areas, 1990-2001

Age/Historic Stage	ER Status									
	Total		Positive		Negative		Borderline		Other/Unknown	
	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)
All Ages (1990+)	230,922	92.1	140,857	96.4	43,030	83.6	1,502	86.5	45,533	87.2
Localized	144,309	99.2	91,097	100.0	24,698	95.2	877	94.5	27,637	98.2
Regional	69,408	88.3	43,208	93.7	14,978	76.3	540	79.8	10,682	84.4
Distant	12,814	38.6	5,700	50.0	3,001	27.6	72	40.1	4,041	30.8
Unstaged	4,391	73.0	852	81.2	353	57.4	13	~	3,173	72.6
Ages 20-49 (1990+)	58,630	90.5	31,200	95.4	16,020	83.8	574	88.2	10,836	86.6
Localized	32,123	97.2	17,271	98.9	8,624	94.5	318	94.0	5,910	96.4
Regional	22,424	87.7	12,624	93.9	6,274	77.4	225	85.4	3,301	84.3
Distant	3,068	44.0	1,157	59.7	1,001	33.6	27	42.6	883	35.5
Unstaged	1,015	77.9	148	87.6	121	59.6	<5	~	742	79.0
Ages 50-64 (1990+)	75,173	92.3	46,305	96.2	14,540	84.5	479	87.7	13,849	88.2
Localized	46,733	98.8	29,446	100.0	8,471	95.3	279	95.5	8,537	98.2
Regional	23,080	89.7	14,724	94.4	4,952	78.0	173	81.0	3,231	87.1
Distant	4,275	39.7	1,913	51.6	1,013	26.9	21	~	1,328	32.4
Unstaged	1,085	76.4	222	76.8	104	62.5	6	~	753	78.0
Ages 65+ (1990+)	97,119	93.0	63,352	97.2	12,470	82.4	449	82.8	20,848	87.0
Localized	65,453	100.0	44,380	100.0	7,603	95.9	280	94.0	13,190	99.1
Regional	23,904	87.5	15,860	92.8	3,752	71.7	142	68.0	4,150	82.3
Distant	5,471	34.2	2,630	43.9	987	21.5	24	~	1,830	26.9
Unstaged	2,291	68.5	482	81.2	128	50.2	<5	~	1,678	66.4

~Statistic not displayed due to less than 25 cases.

Table 13.12: Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (%) by Subsite and Laterality, Ages 20+, 12 SEER Areas, 1988-2001

Subsite	Laterality					
	Total		Right		Left	
	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total (With Distinct Laterality)	301,375	89.5	147,546	89.6	153,829	89.4
Nipple	3,089	90.1	1,507	90.1	1,582	90.2
Central	18,567	88.9	8,996	88.6	9,571	89.1
Upper Inner	26,847	93.0	12,875	93.3	13,972	92.7
Lower Inner	15,494	92.3	7,242	92.5	8,252	92.0
Upper Outer	106,575	91.9	53,103	91.8	53,472	91.9
Lower Outer	18,788	91.2	8,909	91.6	9,879	90.8
Axillary Tail	2,159	86.9	1,076	86.3	1,083	87.4
Overlapping	58,813	88.9	29,039	89.1	29,774	88.6
Other/unknown	51,043	82.4	24,799	82.6	26,244	82.2

Excludes 1,388 cases classified as only one (unknown) side, bilateral, or paired site/no information.