PROGNOSIS OF BREAST CANCER ON THE BASIS OF TUMOR SIZE AND AXILLARY NODAL STATUS IN PATIENTS WITH EARLY DISEASE

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Os autores estudam e avaliam 124 pacientes com câncer de mama primário, não metastático, estádios clínicos I e II, classificação TNM da UICC, admitidas no Departamento de Mastologia do Hospital do Câncer (A. C. Camargo), Fundação Antonio Prudente, São Paulo, Brasil. O prognóstico do câncer de mama foi avaliado em função do tamanho do tumor e do estado linfonodal axilar em pacientes submetidas a tratamento cirúrgico com mastectomia radical, operação de Halsted, e a mastectomia radical modificada, operação de Patey. Todas as 124 pacientes foram submetidas a tratamento cirúrgico, e em casos selecionados a radioterapia, quimioterapia e/ou endocrinoterapia adjuvantes. O estado linfonodal axilar foi o fator preditivo mais significativo para sobrevida livre de doença e a morte da paciente pela doença. Modelos para o prognóstico do câncer de mama foram selecionados baseados em dados demográficos, clínicos, macroscópicos e patológicos.

Keywords: *Breast cancer - Prognosis - Axillary nodal status - Tumor size - Early disease.*
Unitermos: *Câncer de mama - Prognóstico - Tamanho do tumor - Linfonódulos axilares - Doença precoce.*

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Introduction

Breast cancer is currently one of the most intensely studied malignant neoplasias and, despite the various concepts proposed, so far there is no universally accepted hypothesis to explain the behavior of the disease. The magnitude of the problem emphasizes the need to find possible prognostic factors that may permit better case selection and lead to an informed decision about the correct and appropriate therapeutic conduct to be followed. In Brazil, cancer is the second cause of death in the Southeast and South regions, and cancer the breast is the first cause of death among women. By applying the rates of incidence, age, sex and specific site to the São Paulo population for the year 1990, *Franco* et al. (11) estimated the incidence of cancer for the Capital city for the State of São Paulo and obtained values of 93.000 new cases of cases of cancer in the State and 31.000 in the Capital city, and breast cancer, with 9.261 cases (7,47%) was the most frequent after skin cancer. The survival of women with primary

Table 1 - Relation of tumor size and patient situation on the occasion of the latest visit

	Tumor size			
Category	*0-2 cm*	*2-5 cm*	*>5 cm*	*p*
Alive and disease-free	*14 (20%)*	*56 (80%)*	---	
Alive with disease	---	*5 (100%)*	---	
Death from cancer	*2 (13.3%)*	*24 (80%)*	*2 (6.75%)*	
Death from unspecified causes	*1 (25%)*	*3 (75%)*	---	
Lost to follow-up	*10 (66.7%)*	*4 (26.7%)*	*1 (6.7%)*	*0.1544*

breast cancer is directly related to tumor size and to axillary nodal status as demonstrated by *Wilking* (29). Axillary nodal status, has a great impact on survival and patients with axillary nodal metastases are at a significantly higher risk to develop recurrent systemic disease. The identification of these patients permits a prognosis and the selection of a correct appropriate therapeutic conduct (*Fisher*, 9), (*Nemoto*, 21). The clinical-pathological staging of cancer determines the anatomical extension of current disease and tendency of the tumor to progress and is related to tumor size, regional nodal status and distant metastases. The evolution of this neoplasia continues to be unpredictable since patients with clinically early tumors may develop systemic manifestations from the time of diagnosis, as proved by the fact that more than 30% of small tumors, some of them not palpable, detected by mammography, may have lymph node metastases at the time of diagnosis and that cancer of the breast may recur at a distance up to 20 years or more after the initial treatment (*Tabar*, 26). The objective of the present study was to determine and analyze the prognostic value of tumor size and axillary nodal status and their relationship with recurrence, disease-free survival and overall survival with breast cancer in the early clinical stage.

Patients and methods

The study was conducted on 124 women with primary breast cancer treated in the Breast Department of the Cancer (A. C. Camargo) Hospital, Antonio Prudente Foundation, São Paulo, Brazil. The patients had received no previous treatment, had no other associated neoplasias and were treated from february 1983 december 1986. They presented unilateral breast carcinoma in clinical stages I and II according to the TNM classification of the International Union Against Cancer (4th edition i.e, T_1NoMo (CS I), T_2NoMo (CS II-A), T_1N_1Mo and T_2NoMo (CS-A), T_2N_1Mo and T_3NoMo (CS II-B). Mean age at diagnosis was 5 year and median age was 54 years

Table 2 - Relation of axillary node status and characteristics of the patient on the occasion of the latest visit

Axillary lymph nodes x Tumor size					
			Tumor size		
		0-2 cm	*2.1-5 cm*	*>5*	*p*
Axillary lymph nodes					
Negative		*15 (20.8%)*	*57 (79.2%)*	---	
1-3		*7 (21.9%)*	*25 (78.1%)*	---	
>3		*3 (15%)*	*25 (75%)*	*2 (10%)*	*0.0294*
Disease-free	*With recurrence*	*13 (18.06%)*	*12 (37.5%)*	*13 (65%)*	
	Without recurrence	*59 (81.94%)*	*20 (62.5%)*	*7 (35%)*	*0.0001*
Overall	*Dead*	*11 (15.28%)*	*10 (31.25%)*	*13 (65%)*	
	Alive	*61 (84.72%)*	*22 (68.75%)*	*7 (35%)*	*0.0000*

Table 3 - Relation of axillary node status and survival

Category	Lymph node involvement			
	None	1-3	>3	p
Alive and disease-free	48 (68.6%)	16 (22.9%)	6 (8.6%)	
Alive with disease	3 (60%)	2 (40%)	---------	
Death from cancer	9 (30%)	10 (33.3%)	11 (36.7%)	
Death from unspecified causes	2 (50%)	---------	2 (50%)	
Lost to follow-up	10 (66.7%)	4 (26.7%)	1 (6.7%)	0.0037

(range: 29-84): 48 patients (38.7%) were 30 to 50 years old and 76 patients (61.3%) were older than 50 years. Racial distribution was as follows: 91 patients (73.4%) white and 33 patients (26.6%) non-white, i.e., black or oriental. The site of the primary tumor was right breast in 70 patients (56.5%) and the left breast in 54 patients (43.5%). Fourteen patients (11.3%) were assigned to clinical stage 1 (CS I) and 110 (88.7%) to clinical stage II (CS II). There was a higher frequency of axillary nodal involvement in clinical stage II, with 48 patients (43.7%) having a positive axilla. Seventy-two patients (58.1%) had a free axilla and the remaining 52 (41.9%) had axillary nodal involvement. Among the 14 patients assigned to clinical stage I, 10 had a negative axilla (8.1% of the total and 71.4% of the CS I patients), and 4 (3.25% of the total and 28% of the CS I patients) had a positive axilla, with 1 to 3 involved lymph nodes. Sixty-two of the 110 CS II patients (56.3% of CS II patients and 50% of the total group) had a free axilla and 48 (43.3% of CS II patients and 38.7% of the total group) had a positive axilla as follows: 28 (25.4% of CS II patients and 22.6% of the total) with 1 to 3 involved lymph nodes and 20 (18.2% of CS II patients and 16.1% of the total) with more than 3 involved lymph nodes. The number of dissected lymph nodes ranged from 7 to 54, with a mean number of 24.9 and a median number of 24 (table 4). Of the 72 patients with and axilla free of tumoral involvement, 48 were older than 50, with a higher frequency (63.2%) than for the 24 patients aged 20 to 50 years (50%), and of the 52 patients with axillary involvement 28 were older than 50, although highest frequency occurred among patients aged 20 to 50 years (50.1%) (table 4). All patients were submitted to surgical treatment after an intraoperative frozen biopsy, as follows: 58 (46.8%) were submitted to radical mastectomy, Halsted operation, and 66 (53.2%) to modified radical mastectomy, Patey operation. All operations were perfomed by the same surgical team. Patient follow-up consisted of trimestral visits during the first five years and semestral visits thereafter. The examinations performed for annual reevaluation were: mammography of the remaining breast, chest X-ray, bone scintigraphy, ultrasound of the upper abdomen, and routine laboratory tests. During follow-up of the treated patients, 70 (56.4%) were asymptomatic at latest examination, 5 (4%) were alive with active disease, 4 (3.7%) had died of unspecified causes, 15 (12.5%) were lost to follow-up, and 30 (27.5%) had died of breast cancer. The latest follow-up date was January 1993. Survival data were compared by the *Mantel* (6) - *Cox* (17) test using the KMSURV computer software (*Campos-Filho,* 3). Tumor size ranged from 0.8 to 5,5 cm, with a mean of 3.1 and a median of 3.0 cm. Tumor size was determined during clinical examination and was less than than 2 cm in 26 patients (21.0%) and 2.1 to 5 cm (77.4%). Fifty-six older than 50 had tumors larger than 2.1 cm and larger than 5.0 cm, while 41 patients aged 20 to 50 years had tumors ranging in size from 2.1 to 5.0 cm. The highest frequency of tumors from 2.1 to 5.0 cm ocurred among women

Table 4 - Relation of axillary nodal status and tumor size

			Lymph node involvement			
Survival		Category	None	1-3	<3	p
Disease-free	With recurrence	13 (18,06%)	12 (37.5%)	13 (65%)		
	Whithout recurrence	59 (81.94%)	20 (62.5%)	7 (35%)	0.0001	
Overal	Dead	1 (12.285%)	10 (31.25%)	13 (65%)		
	Alive	1 (84.72%)	22 (68.75%)	7 (35%)	0.0000	

Table 5 - Relation of tumor size with demographic, clinical and therapeutic characteristics of the patients, tumor location and metastasis location

		Tumor size			
Variable	*Category*	*0-2 cm*	*2.1-5 cm*	*>5 cm*	*p*
Age	*20-50 years*	*7 (14.6%)*	*41 (85.4%)*	*-*	*-*
	>50 years	*18 (23.7%)*	*56 (73.7%)*	*2 (2.2%)*	*0,2243*
Race	*White*	*18 (23.7%)*	*71 (78%)*	*2 (2.2%)*	
	non-white	*7 (21.2%)*	*26 (78.8%)*	*-*	*0,6867*
Laterality	*Righ breast*	*10 (14.3%)*	*59 (84.3%)*	*1 (1.4%)*	
	Left breast	*15 (27.8%)*	*38 (70.4%)*	*1 (1.9%)*	*0,1703*
Stage	*CS I*	*14 (100%)*	*-*	*-*	
	CS II	*12 (10.9%)*	*96 (87.3%)*	*2 (1.8%)*	*0,0000*
Surgery	*Halsted*	*12 (20.7%)*	*44 (75.9%)*	*2 (1.8%)*	*0,0000*
	Patey	*13 (19.7%)*	*53 (80.3%)*	*-*	*0.3959*
Chemoterapy	*Done*	*8 (17%)*	*36 (78.3%)*	*2 (4.3%)*	
	Not Done	*17 (21.8%)*	*61 (78.2%)*	*-*	*0,0160*
Hormone therapy	*Done*	*-*	*3 (100%)*	*-*	
	Not Done	*25 (20.7%)*	*94 (77.7%)*	*2 (1.2%)*	*0,6519*
Radiotherapy	*Done*	*14 (20%)*	*74 (82.2%)*		
	Not Done	*11 (32.4%)*	*23 (67.6%)*	*2 (2.2%)*	*0,0872*
Tumor location	*SEQ*	*13 (32.8%)*	*43 (75.4%)*		
	ISQ	*5 (16.7%)*	*24 (80%)*	*1 (1.8%)*	
	ESQ	*3 (33.3%)*	*6 (66.7%)*		
	IIQ	*1 (20%)*	*4 (80%)*	*1 (3.3%)*	
	Central	*-*	*1 (100%)*	*-*	
	QQ Junction	*3 (13.6%)*	*19 (86.4%)*	*-*	*0,0985*
Metastasis	*Absent*	*20 (21.5%)*	*73 (78.5%)*	*-*	
	Bones	*2 (25%)*	*5 (62.5%)*	*-*	
	Lung	*1 (12.5%)*	*7 (87.5%)*	*1 (12.5%)*	
	Liver	*-*	*3 (75%)*	*-*	
	CS	*1 (50%)*	*1 (50%)*	*1 (25%)*	
	other	*1 (11.1%)*	*8 (88.8%)*	*-*	*0,1199*

aged 20 to 50 years. Two patients (1.6%) with a tumor diameter of 5.5 cm were older than 50 years (table 3). The most frequent location of the tumor was in the superoexternal quadrant (SEQ) (57 patients, 46%), followed by the superointernal quadrant (SIQ) (30 patients, 24.2%). The histological type determined by pathology of the intraoperative frozen biopsy was invasive ductal carcinoma not otherwise specified (NOS), in all patients.

Results

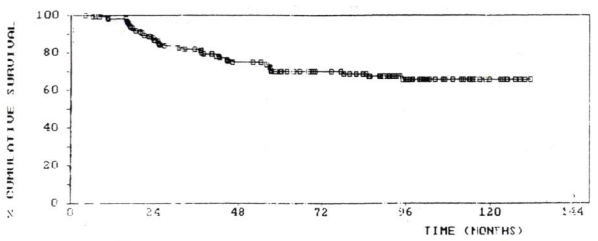
At the time of the diagnosis, some of the 124 patients studied presented disease clinically localized in the breast, whereas others presented disease in the breast and axillary nodes. There was no evidence of locally advanced disease since all patients belonged to clinical stages I and II, and therefore did not present distant metastases. Thirty-five patients (28.2%) had recurrence of the disease and 30 (24.2% of the total and 85.7% of the patients with recurrence) died of cancer of the breast. Age: there was no positive correlation between age and axillary nodal status or between age and tumor size (table 5) . Race: there was no positive correlation between race and axillary nodal status or tumor size (table 5 and 6). Laterality: there was no positive correlation between involved breast and axillary nodal status or tumor size. Involvement of the right breast was more frequent, ocurring in 70 patients (56.6%), also with a higher frequency of tumors measuring 2.1 to 5 cm (69 patients, 84.3%). The frequency of axillary node involvement was slightly higher in the left breast, with 23 affected patients (42.6%) (table 5 and 6). Clinical-pathological staging: as expected, there was a positive correlation between tumor size and clinical stage (table 5).

Table 6 - Relation of axillary nodal status according to the demographic, clinical and therapeutic characteristics of the patients, tumor location and metastasis location

		Axillary lymph node involvement			
Variable	*Category*	*None*	*1-3*	*>3*	*p*
Age	*20-50 years*	*24 (50%)*	*15 (31.3%)*	*9 (18.7%)*	*0,3448*
	>50 years	*48 (63.2%)*	*17 (22.2%)*	*11 (14.5%)*	*Race*
White	*57 (62.6%)*	*19 (20.9%)*	*15 (16.5%)*		
	non-white	*15 (45.5%)*	*13 (39.4%)*	*5 (15.2%)*	*0,1067*
Laterality right breast	*41 (58.6%)*	*19 (27.1%)*	*10 (14.3%)*		
Left breast	*31 (57.4%)*	*13 (24.1%)*	*10 (18.5%)*	*0,7957*	
Stage	*CS I*	*10 (71.4%)*	*4 (28.6%)*	-	
	CS II	*62 (56.4%)*	*28 (25.5%)*	*20 (18.2%)*	*0,2146*
Surgery	*Halsted*	*32 (55.2%)*	*12 (20.7%)*	*14 (24.1%)*	
	Patey	*40 (60.6%)*	*20 (30.3%)*	*6 (9.1%)*	*0,0609*
Chemotherapy	*Done*	*5 (10.9%)*	*25 (54.3%)*	*16 (34.8%)*	
	Not done	*67 (85.9%)*	*7 (9%)*	-	*0,0000*
Hormone therapy	*Done*	---	*2 (66.7%)*	*1 (33.3%)*	
	Not done	*72 (58.8%)*	*30 (24.8%)*	*19 (15.7%)*	*0,1143*
Radiotherapy	*Done*	*39 (43.3%)*	*31 (34.4%)*	*20 (22.2%)*	
	Not done	*33 (97.1%)*	*1 (2.9%)*	---	*0,0000*
Tumor location	*SEQ*	*31 (54.4%)*	*17 (29.8%)*	*9 (15.8%)*	
	ISQ	*18 (60%)*	*5 (16.7%)*	*5 (23.3%)*	
	ESQ	*6 (66.7%)*	*3 (33.3%)*	---	
	Central	---	*1(100%)*	---	
	QQ junction	*16 (72.8%)*	*3 (13.6%)*	*3 (13.6%)*	*0,6693*
Metastasis	*Absent*	*59 (63.4%)*	*23 (24.7%)*	*11 (11.8%)*	
	Bones	*2 (25%)*	*4 (50%)*	*2 (25%)*	
	Lung	*4 (50%)*	*2 (25%)*	*2 (25%)*	
	Liver	---	*2 (50%)*	*2 (50%)*	
	CNS	*1 (50%)*	---	*1 (50%)*	
	Other	*6 (8.4%)*	*1 (3.1%)*	*2 (10%)*	*0,0880*

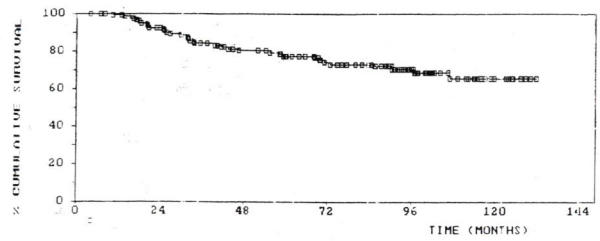
Surgery: there was no positive correlation between surgical treatment and tumor size or axillary nodal status (table 5 and 6). Chemotherapy: among the 46 patients (37,1%) submitted to chemotherapy there was a significant correlation between tumor size and chemotherapy, with a higher frequency for tumors measuring 2.1 a 5 cm (table 5). There was a positive correlation between axillary nodal status and chemotherapy, with a higher frequency of treatment of the axillae with tumor involvement (89.2%) (table 6). Radiotherapy: it was carried out on 90 patients (72.6%). There was no positive correlation between radiotherapy and tumor size. There was a higher frequency of treatment in the presence of tumors larger than 2.1 cm (84.4%) (table 5).There was a significant correlation between axillary nodal status and radiotherapy, with a higher frequency of treatment of axillae with tumor involvement (56.6%) (table 6). Hormone therapy: Adjuvant hormone therapy was carried out on 3 patients (2.4%). There was no positive correlation between hormone therapy and tumor size or axillary nodal status. All of the 3 patients submitted to treatment had tumors ranging in size from 2.1 to 5 cm and axillary node involvement (table 5 and 6). Tumor location: the quadrant most often involved by the tumor and also presenting the largest tumors was superoexternal one (SEQ, 84.2%). However, no significant correlation was observed (table 5 and 6). Site of metastasis: there was no positive correlation between the site of distant metastases and tumor size or axillary nodal status. The absence of metastases was more frequent for 2.1 to 5 cm tumors (78.5%) and for axillae with no tumor involvement (63.4%). There was a higher frequency of distant metastases for 2.1 to 5 cm tumors, with a higher frequency of metastases in axillae with tumor involvement was equivalent (tables 5 and 6). Patient situation

Figure 1A - Disease-free survival



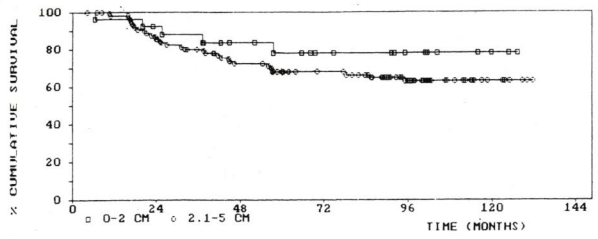
Disease-free survival of patients with cancer of the breast. Actuarial curves obtained by the method of Kaplan-Meyer.

Figure 1 B - Overall survival



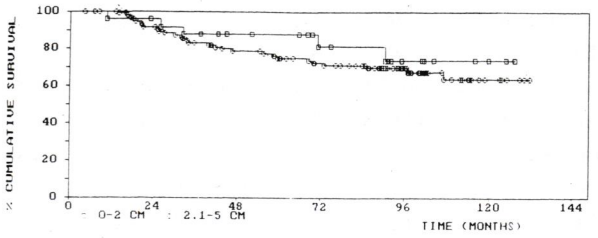
Overall survival of patients with cancer of the breast. Actuarial curves obtained by the method of Kaplan-Meyer.

Figure 2A - Tumor size/DFS



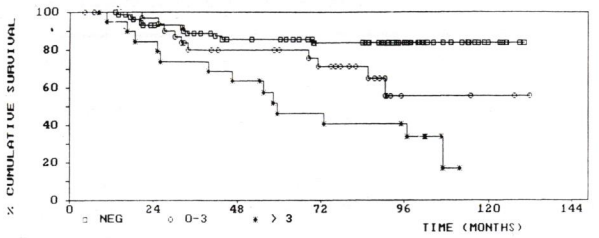
Disease-free survival of patients with cancer of the breast according to tumor size. Actuarial curves obtained by the method of Kaplan-Meyer.

Figure 2B - Tumor size/OS



Overall survival of patients with cancer of the breast according to tumor size. Actuarial curves obtained by the method of Kaplan-Meyer.

Figure 3B - Lymph node/OS



Overall survival of patients with cancer of the breast according to axillary lymph node status. Actuarial curves obtained by the method of Kaplan-Meyer.

on the occasion of the latest visit: there was no positive correlation between tumor size and patient situation on the occasion of the latest visit. There was a higher frequency of patients with 2.1 to 5 cm tumors and 56 were alive, and also a higher frequency of deaths from cancer in 24 patients with 2.1 to 5 cm tumors (table 1). The only two patients with tumors larger than 5 cm died of the disease (table 1). There was a positive correlation between patient situation on the occasion of the latest visit and axillary nodal status. Of the 70 patients who were alive and disease free, 40 (68.6%) had no axillary involvement and 22 had axillary tumor involvement. Of the 30 patients who died of the disease, 9 (30%) had no axillary involvement and 22 (70%) had axillary tumor involvement. Of these, 10 (33,3%) had 1 to 3 positive lymph nodes and 11 have more 3 positive lymph nodes (table 2). There was a positive correlation between axillary nodal and both disease-free (p=0.0000) survival (table 2). There was a high frequency of death from the disease in patients with axillary tumor involvement, even though a few patients without axillary tumor involvement also died of the disease (table 3). Of the 34 patients who died, 30 of them due to breast cancer, 11 had a negative axilla and 23 had axillary involvement, 13 had a negative axilla and 25 a positive axilla. Five-years and 10-years disease-free survival for the 72 patients without axillary involvement was 82.8% and 81%, respectively. Overall 5-years survival of the 72 patients without axillary involvement was 83.3% and 10-years survival was 83.5%. Five-years and 10-years disease-free survival for the 32 patients with 1 to 3 involved axillary nodes was 60.4% and 53.7%, respectively. The patients with more than 3 axillary nodes involved had a 35.2% 5-years survival ad a 29.3% 10-years survival. The 32 patients with tumor involvement of 1 to 3 axillary had a 79.8% 5-year survival and a 55.3% 10-year survival. The 20 patients with tumor involvement of more than 3 axillary nodes had a 45.9% overall 5-year survival and a 16.7% 10-year survival (table 2 and 3 and figures 2 A and B). There was no positive correlation between tumor size and axillary nodal status (table 4 and figures 1 A and B). Among the patients without axillary

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involvement there was a higher frequency of 2.1 to 5 cm tumors (79.2%). Among the 32 patients with tumoral involvement of 1 to 3 axillary nodes, there was a higher frequency of 2.1 to 5 cm tumors. Among the 22 patients with tumor involvement of more than 3 axillary nodes, the highest frequency was also of 2.1 to 5 cm tumors. The 2 patients with tumors larger than 5 cm presented more than 3 nodes with tumor involvement per tumor. The patients with tumors up to 2 cm in size presented a disease-free 5-year and 10-year survival of 78%. Twenty-five patients (20.2%) presented tumors ranging in size from 0.1 to 2.0 cm, distributed as follows: 3 patients with 0.1 to 1.0 cm tumors without axillary involvement were all alive and disease-free; 11 patients with 1.1 to 1.5 cm tumors, 6 of them without axillary involvement and 5 a positive axilla, were all alive and disease-free; of 11 patients with 1.6 to 2.0 cm tumors, 6 of them without axillary involvement and 5 with a positive axilla, 5 were alive and disease-free, 1 was alive with active disease, 4 died of the disease, and 1 died of an unspecified cause (tables 2 and 3). Patients with a tumor size of 2.1 to 5 cm presented an overall 5-year survival of 87.6% and an overall 10-year survival of 73.5%. The patients with 2.1 to 5 cm tumors presented an overall 5-year survival of 74.85% a an overall 10-year survival of 63.5%. Mean disease-free survival was 69.5% and the median value was 77.7% (figures 1 A and B). The patients without axillary involvement presented an overall 5-year survival of 82.8% and an overall 10-year survival of 81%. The remaining cases, with axillary node involvement, presented a lower survival, especially those with more than three lymph nodes involved, distributed as follows: a) 60.4% disease-free and 53.7% overall 5-year survival and 79.8% disease-free and 55.3% overall 10-year survival among patients with involvement of one to three nodes; b) 35.2% disease-free and 29.3 % overall 5-year survival and 45.9% disease-free and 16.7% overall 10-years survival among patients with involvement of more than three nodes (table 3 and figures 3 A and B).

Discussion

Approximately three quarters of all infiltrating carcinomas of the breast are inaccurately defined as ductal infiltrating carcinomas or as adenocarcinomas with no other specification, forming a heterogeneous group. Tumors that exhibit extreme histopathological deviation from normal tissue are often associated with aggressive clinical behavior. (*Fisher* et al., 10), in a statistical study of invasive cancer of the breast, detected a 50% frequency of invasive ductal carcinoma, a 25% frequency of carcinoma combined with other characteristic types, and a 5% of invasive ductal carcinoma and a 10% frequency of invasive lobular carcinoma. The histology of this group of tumors is extremely variable. (*McDivitt* et al., 18), showed that 60% all invasive ductal carcinomas were accompanied by axillary node involvement, with an overall 5-year survival of 59%. It is known that the larger the tumor, the higher the frequency of axillary metastases, with a consequent decreased rate of disease-free and overall survival (*Fisher*, 9), (*Nemoto*, 21), (*Valagussa*, 27). In the present study, tumor size did not have the expected prognostic importance but served as a determinant in terms of recurrence, specially when associated with axillary node involvement. The patients with larger tumors presented a higher frequency of axillary node involvement (32.2%) and a higher frequency of death from cancer of the breast (19.3%) and of recurrence (23.4%). Disease-free survival and overall survival were similar for women with tumors smaller than 2 cm and were reduced in women tumors larger than 2.1 cm. *Fisher* (8), in 1969, showed an inverse relationship between tumor size and survival rate and conclude that if all tumors measuring 2 cm or more (70% in their series) had been removed when they measured 1 to 1.9 cm the recurrence rate at the end of 5 years may have been reduced by 10% to 18% and overall survival would have increased from 11 to 20%. *Eggers* (7), reported a 75% 5-year survival rate for patients with tumors smaller than 2 cm, 24% for patients with tumors measuring 3 to 6 cm, and 16% in patients with tumors larger than 7 cm. Tumor size was consistently associated with clinical stage and was positively correlated with the frequency of axillary nodes with tumor involvement in the 124 patients studied in the present series. *Johnstone* (14) reported that approximately three quarters of patients with tumors larger than 5 cm presented axillary lymph nodes metastases at the time of the initial diagnosis. The larger the tumor, the higher the risk of axillary lymph node metastases, as stated by *Berg* (2). Tumors larger than 6 cm showed a ten-fold higher incidence of axillary lymph node metastases compared to tumors smaller than 2 cm. According to *Koscielny* (16), axillary lymph node metastases are directly proportional to tumor size and do not occur in tumors smaller than 3.6 cm. *Nemoto* (21) detected a close relationship between tumor size and axillary metastases, with tumors of 0.1 to 0.5 cm having a 71.4% frequency of negative axillary lymph nodes, those of 0.6 to 1.0 cm having a 75.3% frequency, those of 1.1 to 2.0 having a 66% frequency, those of 2.1 to 3.0 having a 57.3% frequency, and those of 3.1 to 4.0 cm having a 50% frequency. *Kamby* et al. (15), confirmed these findings and it should be emphasized that clinical stage is, by definition, a variable depending both on the primary tumor and on axillary lymph node involvement. Age is a controversial factor in

survival of breast cancer. The prognosis is more favorable for younger women especially with continuous follow-up for 20-years, as shown by *Hibberd* (12) in a study of more than 2.000 patients with cancer of the breast, in which women aged 20 years had 10-, 20- and 30-year survival rates of 37% 35% respectively, whereas women aged 55 to 64 years had lower 10-, 20- and 30-year survival rates of 35%, 22% and 19%. *Vilcoq* (28), however, considered premenopausal patients to a have a worse prognosis. *Adami* (1), observed a correlation between age and clinical stage, with older patients presenting more advanced disease. In a study of the incidence of prognostic factors among older patients, *Clark* (5), reported tumors with a low rate of proliferation. *Fisher* (10), detected a higher frequency of patients younger than 44 years with tumors larger than 4 cm who presented frequent associations with multicenter focal points of cancer, more than 4 axillary lymph nodes with metastases, and a short disease-free interval. The patients older than 50 years studied here presented larger tumors than younger patients and a higher incidence of axillary lymph node involvement, with more than 3 involved nodes per tumor. Race may a negative effect on the prognosis of cancer of the breast. *Natarajan* (20), noted that black women in more advanced stages than white women and emphasized the sociocultural aspects of American black women. In the present study, white and non-white women presented similar frequencies of tumor size and non-white patients had a higher frequency of axillary node involvement. In the 124 patients studied here, age and race were not determinant factors in terms of prognosis and had no effect on disease-free or overall survival. In the present series there was no significant difference in axillary node involvement between the two surgical techniques used. There was a higher frequency of metastases to the bones and lungs, with a higher incidence in patients with larger tumors. In the present series there was no significant difference between patient situation at latest visit when prognostic factors, tumor size and a axillary node involvement were correlated. *Fisher* (9), demonstrated that the single factor with the highest predictive value for 10- and 20-year survival is the absolute number of axillary nodes with tumor involvement. In a study of 196 patients with early cancer of the breast in which he evaluated tumor size and other prognostic factors, *Hoe* (13) concluded that axillary nodal status was the determinant prognostic factor in terms of survival. Lymph node involvement is related to tumor size. Physical examination often fails to detect positive lymph nodes ranges from 25% to 31% and the frequency of false-negative results ranges from 27% to 33%, *Fisher* (9), *Tabar* (26). These data are important for prognostic reasons and for the indication of adjuvant systemic therapy. Since clinical examination of the axilla fails in one third of all patients, accurate axillary dissection is important for staging purposes. *Fisher* et al. (10), observed that overall and disease-free survival was directly correlated with number of positive lymph node and established a correlation between axillary nodal status and unsuccessful treatment at 5 and 10 years. The number and level of the axillary lymph nodes removed indicate the prognostic. Complete dissection of the three levels of axillary lymph nodes provides maximum prognostic information, removes macroscopic disease from the axilla and avoids the need for axillary radiotherapy. Complete axillary emptying at all three levels would be the only acceptable method for the evatuation of axillary nodal status and more than ten lymph nodes should be removed for a quantitative determination of the real axillary involvement (*Cascinelli*, 4). *Rosen* (24) studied 767 patients treated at the Memorial Sloan Kettering Cancer Center from 1964 to 1970 after a mean follow-up of 18 years and estimated that patients with tumors less than 1.0 cm in size and without axillary involvement, without metastases (T_1NoMo) presented a survival rate of 89%. *McGuire* (19), in a study of prognostic factors for guiding the treatment of patients with no axillary tumor involvement, suggested that all prognostic factors should be taken into consideration. In the present series, axillary lymph node status was the predictive factor for recurrence and death from the disease. Of the 54 patients with involved axillary lymph nodes, 25 (46.3%) died from the disease, although 11 of the 72 patients without tumoral involvement of the axillary nodes (15.3%) also died from the disease. Disease-free survival and overall survival were similar in patients with a negative axilla, exceeding 80% after 10 years. In contrast, disease-free survival and overal survival were significantly decreased in patients with axillary lymph node involvement, and this reduction was directly correlated with greater axillary lymph node involvement. The number of dissected lymph nodes per parameters to determine the aggressiveness of the disease the higher the number of axillary lymph nodes with tumor involvement, the worse the prognosis. In the present study, the 72 patients with a negative axilla had a longer overall survival compared to the 32 patients with a positive axilla, with disease-free an overall survival rates decreasing with increasing involvement of axillary lymph nodes. The present results permit us to confirm the validity and efficacy of conservative treatment of cancer breast in the early clinical stages, with the definition of parameters such as maximum tumor size, tumor multicentricity and multifocality. Clinical evaluation of the axilla is of low accuracy. In T1a tumors have a 10% to 15% possibility of presenting axillary involvement (*Silverstein*, 25). Thus, axillary emptying is of help for diagnosis, prognosis and therapeutic conduct (*Robinson*, 22).

Summary

The objective of this work was the study of 124 patients with primary non-metastatic breast cancer, stage I and II, TNM classification of UICC - International Union Against Cancer, admitted to the Breast Department of the Cancer Hospital, (A. C. Camargo), Antonio Prudente Foundation, São Paulo, Brazil. The prognosis of breast cancer on the basis of tumor size and axillary nodal status was evaluated in the patients submitted to treatment with radical mastectomy, Halsted's operation, radical modified mastectomy or Patey's operation. All 124 patients were submitted to surgical treatment, and in selected cases to radiotherapy and to adjuvant systemic treatment with chemotherapy and/or endocrinotherapy. Axillary nodal status was the most significant factor in the prediction of disease-free interval and overall survival. Tumor size and axillary nodal status were positively associated with tumor recurrence and patient death. Models for the prognosis of breast cancer were selected on the basis of demographic, clinical, macroscopic and pathological data.

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