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MALE BREAST CARCINOMA

I. A study of the total material reported to the Swedish Cancer Registry 1958–1967 with respect to clinical and histopathologic parameters

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Abstract

During the time period 1958–1967 190 cases of male breast cancer were reported to the Swedish Cancer Registry. The reported cases were thoroughly re-evaluated from the evidence of the clinical records and histopathologic specimens. The material contained 166 cases of histologically verified invasive breast carcinoma which were analyzed with respect to different clinical and histopathologic parameters. In contrast to the rate in females, the breast cancer incidence rate in males did not increase significantly during the period under review, and the age-specific incidence rate did not show a Clemmesen's hook but increased relatively more rapidly at high ages than for female breast carcinoma. The mean age at diagnosis was 4 to 5 years higher in male breast cancer patients than in females. Larger tumours were more frequent among older patients and there was a 5-year shift between the age-distribution curves for small (<2 cm) and larger (2–5 cm) tumours. A similar difference was found between pN0 and pN1 tumours. This difference might reflect the progression rate of male breast cancer. The histopathology pattern and distribution of histologic malignancy grades were similar to those in female breast carcinoma with the exception that lobular carcinoma and medullary carcinoma with lymphoid infiltration were lacking in the male material.

Key words: Breast neoplasms; male carcinoma, epidemiology, symptomatology, stage, grade, histology.

The purpose of this work is to present a total geographic (i.e. completely unselected) material, collected during a limited period of time (1958–1967), of a relatively uncommon tumour disease. In view of the retrospective nature of the study, this report will be limited to the relatively well defined variables incidence and age distribution, tumour stage and histopathology. In a following article methods of treatment and long-term survival as related to the prognostic factors will be presented.

The original data have been thoroughly analyzed. Case records and histopathologic preparations were obtained in all cases. The primary clinical data, methods of treatment, and pathoanatomic data have thus been re-evaluated.

Most studies of male breast carcinoma have concerned relatively small and often selected materials from individual departments, but larger total geographic materials have been described in publications from Denmark, Norway, Sweden, Finland and Israel. Comprehensive reviews have been published by EVERSON & LIPPMAN (27) and SCHEIKE (72). A selection of published investigations on male breast carcinoma, including number of cases and period covered, is given in Table 1.

The material

Only histologically verified invasive carcinoma originating in the parenchyma of the mammary gland in men was included.

Of the 190 cases in the Cancer Registry of Sweden (12), those erroneously registered under the period 1958–1967, those without histopathologic verification, those with non-invasive carcinomas, and cases with malignant tumours other than adenocarcinoma originating in the mammary gland parenchyma were excluded. After this procedure 166 cases from the Cancer Registry material remained. The study thus comprises 166 cases of histologically verified invasive breast carcinoma (Table 2). Excluded cases are listed in Table 3.

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Table 1

Published investigations on male breast cancer (x indicates studies based on a total geographic material). The studies are listed in order of size

	Author		No. of cases	Period of time
x	ADAMI et coll. (1)	Sweden	406	1960–1978
	RIBEIRO (66)	Manchester, England	301	1941–1983
	SCHEIKE (70)	Denmark	257	1943–1972
	HOLLEB et coll. (36)	Memorial Hospital, New York, USA	198	1924–1964
x	STEINITZ et coll. (81)	Israel	187	1960–1976
x	Present material	Sweden	166	1958–1967
	RAMANTANIS et coll. (65)	Athens, Greece	138	1937–1974
x	CARLSSON et coll. (13)	Sweden	135	1968–1973
	FALSAFI (28)	Iran	114	1956–1971
x	The Cancer Registry of Norway (11)	Norway	105	1953–1967
	HELLER et coll. (35)	Memorial Hospital, New York, USA	97	1949–1976
	YAP et coll. (90)	M. D. Anderson Hospital, Houston, USA	84	1945–1975
	MAUSNER et coll. (51)	Philadelphia, USA	72	1951–1964
	HUGGINS & TAYLOR (37)	Boston, USA	60	1914–1955
x	MODAN et coll. (53)	Israel	56	1960–1966
	FOSSÅ (29)	Norway	54	1935–1968
	VANDERBILT & WARREN (87)	Veterans Hospital, Hines, USA	52	1930–1970
	OURIEL et coll. (62)	Rochester, USA	50	1961–1981
x	PELTOKALLIO & KALIMA (64)	Finland	42	1952–1963
	ROBISON & MONTAGUE (67)	M. D. Anderson Hospital, Houston, USA	39	1948–1978
x	AXELSSON & ANDERSSON (4)	Sweden	39*	1962–1963
	CRICHLOW et coll. (18)	Philadelphia, USA	32	1940–1964
	CORTESE & CORNELL (15)	The New York Hospital, Cornell Medical Center, USA	31	1932–1967
	ROSWIT & EDLIS (68)	Veterans Hospital, Bronx, USA	30	1947–1977
	NAGPAL et coll. (57)	India	30	1955–1974
	SINNER (78)	Zurich, Switzerland	27	1919–1960
	GUPTA et coll. (31)	India	27	1966–1978

* These 39 cases are included in this material for the period 1958–1967.

The surgical assessment and treatment took place at 73 hospitals and radiation therapy was given at 43 hospitals. The *initial* pathoanatomic examination was performed at 22 pathology laboratories.

In a patient material of high average age, as is the case for male breast carcinoma, other malignancies, synchronous or asynchronous, occur relatively often, making it difficult to determine whether the tumour in the breast is a metastasis from the other tumour or vice versa, or whether more than one primary tumour is present. This problem has been discussed by, among others, TREVES & HOLLEB (85), HUGGINS & TAYLOR (37), VANDERBILT & WARREN (87) and PANETTIERE (63).

The material includes 16 cases (9.6%) judged to have had other synchronous or asynchronous primary tumours. The 16 cases judged as having multiple malignancy naturally constitute a minimum number, as no systematic anamnestic study or follow-up in this respect has been performed. The cases are presented in Table 4. When cancer of the prostate is present it may be difficult to decide whether a cancer in the breast is primary or secondary (6, 20, 23, 44). In a large postmortem study, BERGE (6) found 22 cases of metastasis to the breast among 2 195 cases of metastatic carcinoma in men. In 20 of these 22 cases the primary tumour was an estrogen-treated prostatic carcinoma. BERGE (6) considered that most of these tumours were caused by metastasis from the prostatic tumour as the duration of exposure to estrogen was so short that hormonal carcinogenesis could not have occurred and the patients had multiple other metastases.

In the present original material 9 cases had been reported to the Cancer Registry as having both prostate and breast cancer. At re-evaluation, 4 of these cases were classified as metastases to the breast from a prostatic carcinoma (Table 3), while in 5 cases there were probably 2 primary tumours (Table 4).

Some of the problems connected with the diagnostics of multiple primaries and of metastasis in the breast from other tumours are illustrated in Figs 1 to 5.

The material includes only one case of bilateral asynchronous mammary carcinomas (0.6%). This is considerably less than would be expected in a material of female

Table 2

The total material of malignant tumours in the male breast reported during the period 1958–1967 and the number of cases of primary invasive carcinoma after re-evaluation

	Total number	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967
Total number of cases of malignant tumour in the male breast	190	20	15	11	29	21	21	18	17	18	20
Excluded cases	24	5	0	1	3	2	3	3	4	3	0
Primary invasive carcinoma of the male breast, confirmed by histopathology and, in a few cases, by cytology	166	15	15	10	26	19	18	15	13	15	20

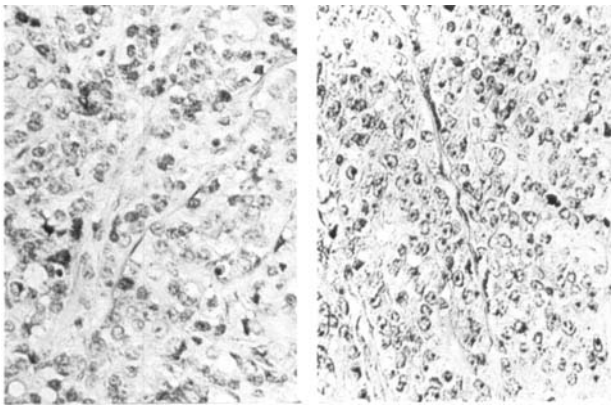

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Fig. 1. a) Inguinal lymph node metastasis from prostate carcinoma 1962 and b) section from a lump in the left breast 1965. The histology is similar to the prostatic lymph node metastasis. Death from generalized prostate carcinoma.

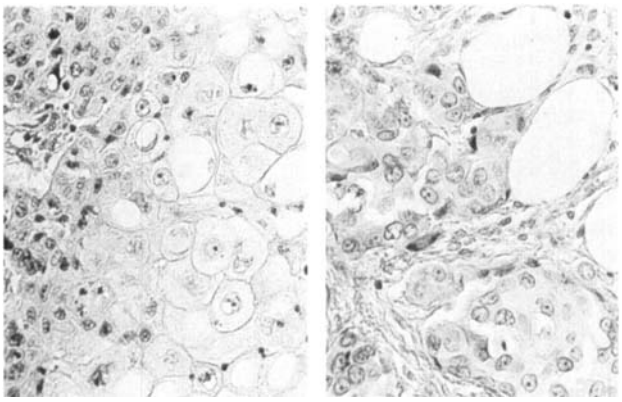

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Fig. 2. a) Section from squamous bronchial carcinoma subjected to pulmectomy in 1960 and b) mastectomy specimen from 1961. Different histology and a 17-year survival confirm two different primary malignancies (bronchial carcinoma and breast carcinoma).

Table 3

Cases not accepted as invasive primary carcinoma of the male breast reported to the Cancer Registry during the period 1958–1967

Exclusion criteria	No of cases
Primary tumour diagnosed prior to the period	2
Histopathologic verification lacking	2
Non-invasive carcinoma	4
Neurofibromatosis Recklinghausen	1
Fibrosarcoma	1
Unspecified sarcomatous tumour	1
Malignant melanoma	2
Malignant lymphoma	1
Basal cell carcinoma	1
Adenoid cystic basal cell carcinoma	1
Skin carcinoma of apocrine type	1
Skin carcinoma, poorly differentiated squamous	1
Malignant tumour not compatible with breast carcinoma	1
Metastases from gastric carcinoma	1
Metastases from prostatic carcinoma (Fig. 1)	4

breast carcinoma. In the literature, bilateral primary cancer has been reported to occur in 0.4 to 2.7 per cent of patients with male breast cancer (16, 56, 70, 85, 89). The relatively good agreement between the reports suggests an increased risk of bilaterality. The risk can be considerably higher than the average, in special subgroups, above all in Klinefelter's syndrome.

Etiology

In view of the retrospective nature of the present work, etiologic background factors could not be analyzed. In the literature, interest has been mainly focused on an abnormal blood-steroid level (10, 19, 59, 73, 74, 80). This may

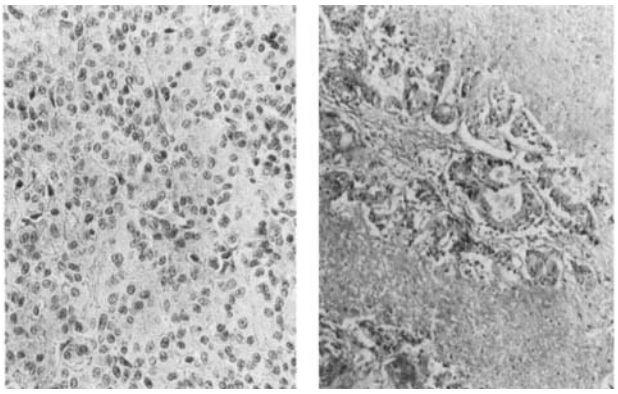

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Fig. 3. a) Mastectomy specimen from 1963 showing breast carcinoma and b) section from liver metastasis obtained at laparotomy for an obstructing colonic carcinoma in 1963. The histology of the metastasis is typical of colonic carcinoma and different from the mammary tumour. Death classified as due to colonic carcinoma.

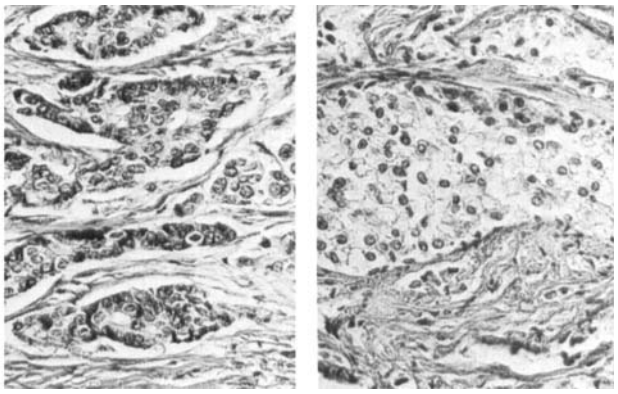

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Fig. 4. a) Mastectomy specimen of an advanced tumour with a history of 5 years and b) post-mortem specimen of the prostate with extensive loco-regional growth. The case is equivocal but was considered to represent multiple malignancies with death from generalized breast carcinoma.

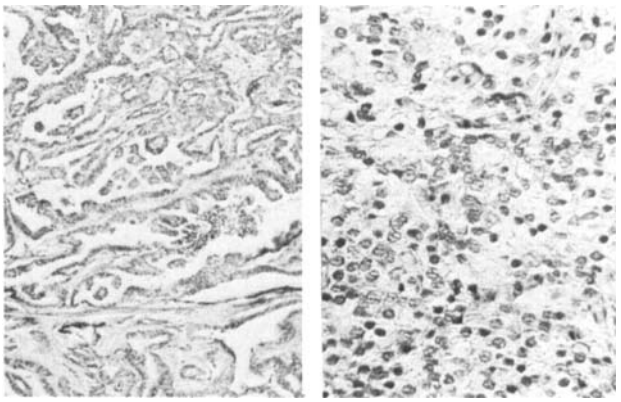

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Fig. 5. a) Endourethral biopsy in 1969 of a prostate carcinoma clinically diagnosed in 1965 and b) mastectomy specimen from 1967. The histology is quite different from the prostate carcinoma and probably represents primary breast carcinoma. Death from uremia was classified as intercurrent with regard to the breast carcinoma.

Table 4

Multiple malignancies

First malignancy	Year	Second malignancy	Year
Bronchial ca.	1960	Breast ca.	1961 (Fig. 2)
Renal ca.	1938	Breast ca.	1965
Seminoma	1944	Breast ca.	1967
Breast ca.	1962	Cystadenoma lymph. salivary gland	1963
Breast ca.	1965	Cholangiocell. ca.	1967
Breast ca.	1959	Hepatoma	1964
Breast ca.	1961	Basal cell ca.	1969
Breast ca.	1964	Basal cell ca.	1965
Breast ca.	1959	Colonic ca.	1968
Breast ca.	1963	Colonic ca.	1963 (Fig. 3)
Basal cell ca.	1961	Breast ca.	1962 Colonic ca. 1968
Breast ca.	1958	Prostatic ca.	1970
Breast ca.	1964	Prostatic ca.	1968
Breast ca.	1966	Prostatic ca.	1967 (Fig. 4)
Prostatic ca.	1955	Breast ca.	1959
Prostatic ca.	1965	Breast ca.	1967 (Fig. 5)

Table 5
Age distribution of female and male breast carcinoma

Age	Histologically verified female breast carcinoma during the period 1959–1965 according to the Swedish Cancer Registry (12) (n=18035)		Histologically verified male breast carcinoma during the period 1959–1965 (n=116)		Histologically verified male breast carcinoma during the period 1958–1967 (n=166)	
	No.	Per cent	No.	Per cent	No.	Per cent
20–29	58	0.3	1	0.9	1	0.6
30–39	764	4.2	3	2.6	4	2.4
40–49	3 449	19.1	8	6.9	9	5.4
50–59	4 240	23.5	29	25.0	39	23.5
60–69	4 595	25.5	33	28.4	50	30.1
70–79	3 629	20.1	29	25.0	39	23.5
80–89	1 300	7.2	13	11.2	24	14.5
	18 035	99.9	116	100.0	166	100.0

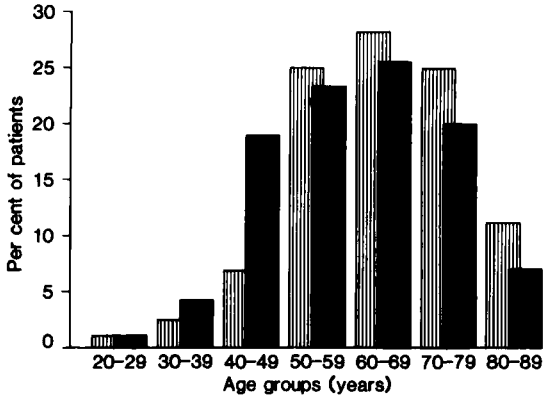

Fig. 6. Age distribution of male and female breast carcinoma. The histogram for male breast carcinoma (▥) is based on the 116 cases of primary adenocarcinoma of the breast registered during the period 1959–1965 and accepted at the present re-evaluation. The histogram for female breast carcinoma (■) is based on the 18035 cases of adenocarcinoma of the breast registered in the Swedish Cancer Registry (12) during the period 1959–1965.

be caused by genetic factors, as in Klinefelter's syndrome (5, 9, 25, 34, 39, 41, 46, 55, 76, 82), but familial accumulation without this syndrome has also been reported (26, 30, 50, 77). Furthermore, DECKER et coll. (21) have reported 3 cases of male breast carcinoma in true hermaphrodites. Changes in steroid levels caused by disturbed liver function and associated with gynecomastia or male breast cancer have been reported in patients with alcoholic liver cirrhosis (91) and bilharzia (7, 24).

Administration of estrogen, above all in cancer of the prostate (6, 36, 43), has been reported to be a risk factor for male breast cancer but the risk appears to be very small. A frequently quoted example of the risk of exogenous administration of estrogen in males is SYMMERS' (83) description of two transsexual young men who after feminizing surgery received considerable amounts of estrogen. Both died of mammary carcinoma. The controversial association between gynecomastia and male breast cancer is also relevant in this context (3, 47, 75).

Other factors discussed are orchitis (58) and ionizing radiation (22, 42, 45, 84).

A recent report (61) indicates that increased levels of prolactin occur in males with breast carcinoma. Our own observations include one man who, owing to gynecomastia in his teens, received radiation therapy to one breast and was then given high-dose neuroleptic treatment for 20 years, because of psychiatric disease, with prolactin elevation as a result. He developed breast carcinoma on the irradiated side at the age of 39 years.

A detailed review of different etiologic factors has been published by MEYSKENS et coll. (52).

Age distribution and incidence

The patients' ages ranged from 29 to 88 years, with a mean of 65 and a median of 66 years. The age distribution is illustrated in Figs 6 and 7, and the age distribution for female breast cancer during the period 1959–1965 is included for comparison (Table 5). The mean age for men was higher than for women with a difference of 4 to 5 years.

The incidence rate according to the Swedish Cancer Registry (12) (defined as malignant tumours of the breast) during the period 1958–1967 and up till 1979, when about 5 cases per million men occurred, is shown in Fig. 8. There was a tendency towards an increasing incidence rate, whereas female breast carcinoma showed a definite increase. The proportion of males among all cases of breast cancer varied between 0.5 and 1 per cent.

Table 6

Mean and median age in male breast cancer (summary of the literature). (x indicates that the figures derive from a total geographic material)

	Author	No. of cases	Mean age	Median age	Range
	Wainwright (88)	325	52.6		
x	Scheike (70)	257	65.2		34–90
	Holleb et coll. (36)	198	56.0		24–85
x	Steinitz et coll. (81)	187	63.4		23–85+
x	Present material	166	65.4	66.0	29–88
	Ramantanis et coll. (65)	138	60.8		35–83
x	Carlsson et coll. (13)	135	69.0		34–92
	Norris & Taylor (60)	113		59.0	21–80
	MacKay & Sellers (48)	91		62.0	
	Yap et coll. (90)	84		61.0	
	Huggins & Taylor (37)	60		63.0	
x	Modan et coll. (53)	56	61.9		25–84
	Fossa (29)	54	64.0		
	Vanderbilt & Warren (87)	52		58.0	33–79
	Ouriel et coll. (62)	50		66.0	29–87
x	Peltokallio & Kalima (64)	42	66.0	66.0	41–91
	Crichlow et coll. (18)	32	60.0		36–82
	Nagpal et coll. (57)	30	51.6		18–83
	Roswit & Edlis (68)	30		65.0	39–87
	Gupta et coll. (31)	27	52.0		28–65
	Smith & Painter (79)	19	67.1		
	Panettiere (63)	16		48.0	26–62
	Ajayi et coll. (2)	12	56.3		

The age-specific incidence rate of male and female breast cancer during the periods 1958–1967 and 1968–1979 according to the Swedish Cancer Registry (12) is shown in Fig. 9. The curve for female breast carcinoma shows the characteristic Clemmesen's hook at the time of the climacterium and a generally increased rate during the later period. The curve for male breast cancer shows no Clemmesen's hook. The age-specific incidence rate increased faster with increasing age than for female breast carcinoma, and male breast cancer accounted for about 1.5 per cent of all cases of breast cancer in the senium.

The age distribution in this material showed good agreement with other Nordic materials (Table 6). In most non-Nordic series the mean age is lower, probably because they represent selected hospital materials. For example, Panettiere (63) reported as low a median age as 48 years in a material from Air Force Hospitals in the USA. That male breast carcinoma is diagnosed and treated about 5 years later than female breast carcinoma may be due to a characteristic biologic feature of the disease but many authors report a considerable delay in the diagnosis, which may give a false picture of the age-related incidence.

As already stated, male breast cancer accounts for between 0.5 and 1 per cent of all cases of breast cancer in Sweden. The figures for Norway, Denmark and Finland are 0.7, 0.8 and 0.5 per cent, i.e. very similar.

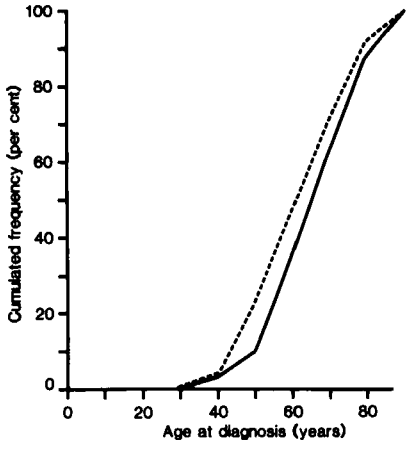

Fig. 7. Cumulative frequency of male (—) and female (---) breast carcinoma in relation to age. The curve for male breast carcinoma is based on all cases of primary adenocarcinoma of the breast registered during the period 1958–1967 and accepted at the present re-evaluation (n=166). The curve for female breast carcinoma is based on the cases of adenocarcinoma of the breast registered in the Swedish Cancer Registry (12) during the period 1959–1965 (n=18035). Five-year strata have been used.

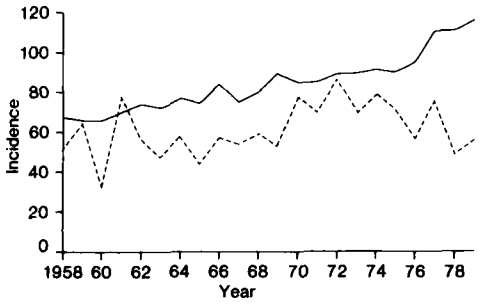

Fig. 8. Incidence rate of male (---) and female (—) malignant neoplasms of the breast per 10^7 males and 10^5 females respectively, during the period 1958–1979 as recorded in the Swedish Cancer Registry (12).

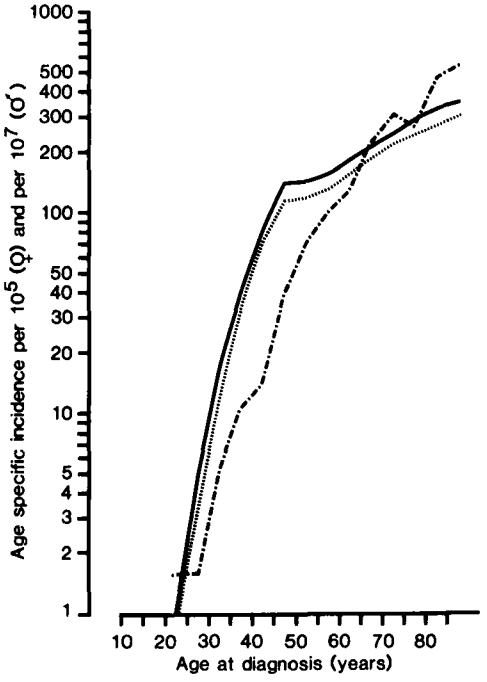

Fig. 9. Age-specific incidence rate of malignant tumours of the female (per 10^5 women) and male (—·—) (per 10^7 men) breast during the period 1958–1979. The incidence rate for women is shown for the periods 1958–1967 (····) and 1968–1979 (——) separately. The incidence axis is logarithmic.

Table 7
Initial symptoms

Symptoms	No. of cases*	Percentage
Lump in the breast	121	72.4
Nipple retraction	7	4.2
Ulceration of the nipple	7	4.2
Painful sensations in the breast	7	4.2
Ulceration of the skin surrounding the nipple	5	3.0
Bloody secretion from the nipple	4	2.4
Nipple eczema	2	1.2
Non-bloody secretion from the nipple	1	0.6
Pain owing to bone metastases	1	0.6
Incidental finding by physician	10	6.0
Not known	2	1.2
	167	100.0

* One patient had asynchronous bilateral cancer.

Table 8
Duration of symptoms (summary of the literature)

Author	Mean duration (months)	Median duration (months)
Present material	14	6
Fosså (29)	13	–
Haagensen (32)	19	–
Huggins & Taylor (37)	–	4.5
Mohardt (54)	27	–
Nagpal et coll. (57)	28.6	–
Roswit & Edlis (68)	–	12
Scheike (71)	20.8	6
Treves & Holleb (85)	–	9
Wainwright (88)	28	–
Yap et coll. (90)	–	12

The proportion of male breast cancer in total breast cancer materials is usually reported to be about 1 per cent (8, 17, 18, 37, 52, 90). Norris & Taylor (60), however reported a material of 4810 cases of breast carcinoma in which 2.4 per cent were men. Gupta et coll. (31) reported 3.2 per cent and Nagpal et coll. (57) 4.6 per cent males in materials from India, and Habibi (33) gave a figure of 6 per cent from Iran. Steinitz et coll. (81) stated that males account for 1.6 per cent of all breast carcinomas among Israeli Jews compared with 4.2 per cent among non-Jews. From Egypt, El-Gazayerli & Abdel-Aziz (24) reported that men accounted for 6.4 per cent of all cases of breast carcinoma and ascribed this finding to liver bilharzia. From Zambia, Bhagwandeen (7) reported an even higher proportion of men (15%) but gave an unusually low figure for the incidence of female breast cancer. Incomplete reporting may of course have influenced these figures.

The incidence rate of female breast cancer in Swedish women increased markedly during the period 1958–1979 but a similar increase was not found in males. One explanation of this difference could be the efforts during recent years to achieve early diagnosis of female breast cancer.

Table 9
Clinical staging according to UICC 1959 and 1978

Stage	Cases staged from clinical data				Cases staged from clinical data or pathology reports			
	UICC 1959		UICC 1978		UICC 1959		UICC 1978	
	No.	Per cent*	No.	Per cent*	No.	Per cent**	No.	Per cent**
I	45	37	12	10	56	39	22	15
II	20	16	53	43	30	21	64	45
III	44	36	44	36	44	31	44	31
IV	13	11	13	11	13	9	13	9
Not known	44		44		23		23	
	166		166		166		166	

* Per cent of 122 cases.
** Per cent of 143 cases.

Symptoms and signs

The initial symptom was noted from the records but the validity of these data is uncertain owing to the patients' high age and the retrospective nature of the material. The initial symptom in the 166 patients (one of whom had asynchronous bilateral cancer, making 167 male breasts with mammary carcinoma) is shown in Table 7. The findings show fairly good agreement with most other publications (28, 36, 70, 90).

Concerning signs at the time of diagnosis, a palpable tumour was reported to be present in 138 breasts (83%). As the male breast is small, a breast tumour is usually partly subareolar. Seventeen patients (10%) had nipple retraction, 19 had ulceration of the nipple (11%) and 14 ulceration of the skin surrounding the nipple (8%). Four patients had skin metastases in the mammary region (2%). Discolouration of the skin was present in 3 cases (2%). Secretion from the nipple occurred in 8 cases (5%), with bloody secretion in 5 cases. Distant metastases were diagnosed in 13 cases (8%).

In 149 of the 166 cases the duration of the symptoms before diagnosis was established. In 23 per cent it was less than 1 month, in 28 per cent 1 to 6 months, in 19 per cent 6 to 12 months, in 13 per cent 12 to 24 months, and in 17 per cent more than 24 months. The literature is summarized in Table 8.

Fifty-one per cent of the tumours in the material were located in the right breast. Many materials of male breast cancer show a left dominance (60, 81, 88), a finding which has frequently been reported for female breast carcinoma (14). Other studies agree with our findings, however (87, 89).

Clinical staging

Clinical classification was performed according to both the UICC 1959 and the current classification, UICC 1978 (86; Table 9). Only in a few cases was the clinical stage stated in the records but it was possible to establish the clinical stage retrospectively from the clinically assessed tumour size and spread in the breast and the axillary lymph node status in 122 cases. In a further 21 cases, in which information on tumour size and/or axillary status was lacking, we established the stage from the pathologist's report on tumour size and the presence of axillary lymph node metastases although we are well aware that assessment of the 'clinical' stage in this way involves an error. In 23 cases. sufficient information for retrospective staging was lacking.

Table 10
Mean and median ages for the different clinical stages

Stage	No.	Age (years)			
		Mean		Median	
I	56	66	64	67	65
II	30	60		62	
III	44	69	69	72	72
IV	13	70		74	
Not known	23	62		64	

In Table 9, the number of cases which could be classified clinically and with the use of the pathologist's reports are presented. Unless otherwise stated, the data on clinical staging in this report refer to the sum of the clinically assessed and from pathology reports constructed stages, classified according to UICC 1959.

The most important difference between the 1959 and 1978 classifications concerns the division between stages I and II. The very marked influence of this difference can be seen in Table 9, which illustrates the importance of correct comparisons.

Scheike (71), using the UICC 1959 classification, found that 'a significant change had occurred in clinical stage

Table 11
Clinical stage in relation to duration of symptoms

Duration of symptoms (months)	Cases with known clinical stage (No.)	Clinical stages			
		I+II		III+IV	
		No.	Per cent	No.	Per cent
≤6	66	46	70	20	30
6–24	43	25	58	18	42
>24	23	9	39	14	61

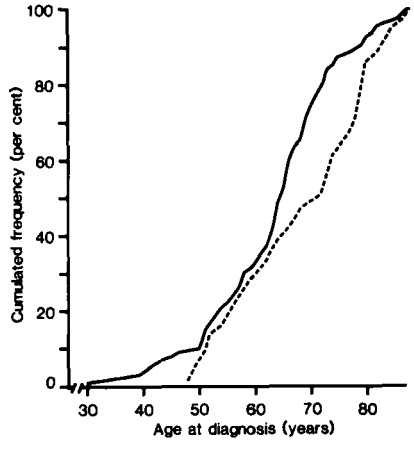

Fig. 10. Cumulative frequency diagram for stages I + II (——) and III + IV (---). The curve for the early stages lies to the left of that for advanced stages at all ages, suggesting that the high mean and median age in advanced stages is not solely due to longer patient's delay among the elderly.

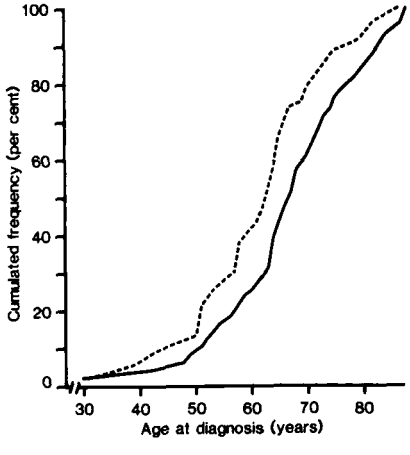

Fig. 11. Cumulative age frequency diagram for histopathologically assessed tumour size. The curves for small and medium-sized tumours show a parallel shift of 4–7 years. Tumour ≤2 cm --- and tumour 2–5 cm ——.

Table 12
Tumour size distribution (n=114)

Size (cm)	No. of cases	Per cent
≤2	53	46
2–5	51	45
>5	10	9

between the period 1943–1957 and 1958–1971, the latter being almost the same period as in our material (1958–1967). He reported from the later period in stage I 44 per cent, stage II 9 per cent, stage III 42 per cent and stage IV 5 per cent, thus a shift from stage II to stage III compared with the present material.

Table 10 shows the mean and median ages for the different stages. Clinical stages III and IV were more common in the older age groups. This may be due to longer patient's delay among elderly persons. However, it might also reflect the fact that progression from stages I and II to stages III and IV takes 5 to 7 years, due to the natural course of the disease. The cumulative age frequency diagram in Fig. 10 suggests a combination of both factors.

A short history and an early stage, and a long history and a late stage, were positively correlated (Table 11).

Pathology

In 114 of the 149 cases operated upon with curative intent, the pathologist's report included information enabling the tumour to be classified by size (Table 12).

As seen from Fig. 11, large tumours were more common in older individuals. This might reflect longer patient's delay among older individuals, but the parallel shift of the curves in all age groups may reflect the time it takes for the tumour to grow.

Histopathologic diagnosis of ipsilateral axillary lymph nodes was possible to obtain only when the axilla was explored in connection with radical or modified radical

Table 13
Axillary lymph node status (summary of the literature)

Author	No. of cases	Period	Incidence of histopathologically verified axillary lymph node metastasis (Per cent)
CRICHLOW (16)	170	1900–1972	55
Present material	91	1958–1967	47
HELLER et coll. (35)	81		45*
NORRIS & TAYLOR (60)	75		61
YAP et coll. (90)	46	1945–1975	65
HAAGENSEN (32)	21	1933–1961	43
CORTESE & CORNELL (15)	20	1932–1967	50

* This figure refers to verified axillary metastasis in relation to all cases, including those in which axillary exploration was not performed. If the latter are excluded, the incidence is 49%.

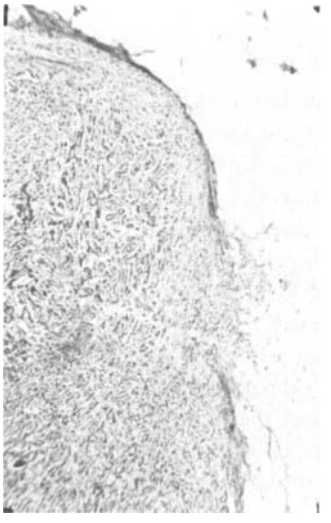

Fig. 12. Early invasion of tumour growth through the lymph node capsule, defined as perinodal growth.

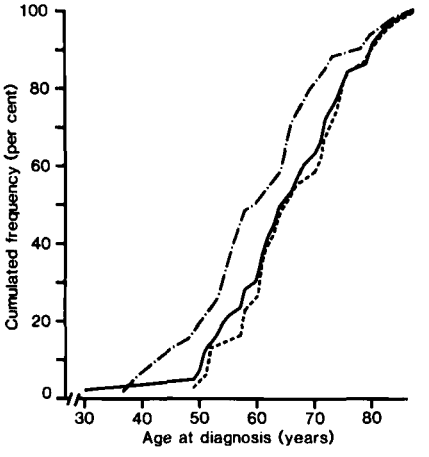

Fig. 13. Cumulative frequency diagram for histopathologically verified ipsilateral axillary node status. There is a parallel shift of 4–6 years between the curves for patients with and without axillary metastases with higher relative frequency of node-positive cases in the higher ages. Nodes negative —·—·, nodes positive ——, nodes positive with perinodal growth – – –.

mastectomy (49 and 43 cases respectively). One specimen was lost, so that altogether 91 axillae could be assessed. In 47 per cent of these, metastases were present, and in 72 per cent of these the tumour had penetrated the lymph node capsule (perinodal growth; Fig. 12) (47, 49). Some other materials with information on histopathologic lymph node status are listed in Table 13.

The age distribution of node-positive and negative patients is illustrated in the cumulative age frequency diagram in Fig. 13. Patients with lymph node metastasis were somewhat older than the others. The parallel shift in all age groups probably reflects the time it takes for the disease to progress from node-negative to node-positive. Conclusions are, however, hampered by the fact a smaller proportion of the elderly were subjected to axillary clearance. The incidence of axillary metastasis and perinodal growth in this material and in a material of female breast carcinoma is compared in Table 14. Axillary metastasis and perinodal growth were somewhat more frequent in men than in women, but there were no remarkable differences.

The clinical and histopathologic axillary findings were compared, when possible, and showed metastasis in 40 per cent, in spite of negative clinical findings, and no

Table 14

Axillary lymph node status. Comparison between male and female breast carcinoma

Histopathologic findings	Male breast carcinoma in Sweden 1958–1967 (n=91)				Female breast carcinoma in Göteborg 1968–1970 (40) (n=197)			
	No.		Per cent		No.		Per cent	
Without axillary metastasis	48		53		116		59	
Axillary metastasis without perinodal growth	12	43	13	47	28	81	14	41
Axillary metastasis with perinodal growth	31		34		53		27	

Table 15

Histopathologic stage distribution

Histopathologic stage	UICC 1959		UICC 1978	
	No.	Per cent*	No.	Per cent*
I	27	28	19	20
II	22	23	30	31
III	34	35	34	35
IV	13	14	13	14
Not known	70		70	
Total	166	100	166	100

* Per cent of 96 cases with known stage.

metastasis in 36 per cent, in spite of clinical suggestion. These findings agree with the observations of JOHNSÉN et coll. (40), who noted 33 per cent false negative and 36 per cent false positive findings in a material of female breast carcinoma subjected to thorough clinical examination of the axilla. These findings underline the uncertainty of clinical staging.

The histopathologic stages based on axillary findings and tumour size are shown in Table 15. The UICC classification of 1959 did not include histopathologic stage but has nevertheless been included in the table with the use of a similar analogy between clinical and histopathologic staging as defined in the UICC 1978 classification.

The tumours in the present material were all invasive ductal carcinomas, sometimes with intraductal papillary formation. In 12 cases there were cyst formations with papillary excrescences on the walls and carcinoma cells infiltrating out into the surrounding breast stroma. In some carcinomas there was cirrhous conversion, especially in central parts. Three tumours were partially colloid carcinomas; there was no case of pure colloid carcinoma. Four tumours might be classified as comedocarcinomas. Three tumours were of medullary carcinoma type but no case of medullary carcinoma with lymphoid infiltration was found. In 5 cases Paget's disease of the nipple together with invasive ductal carcinoma in the breast tissue was present. A further 2 cases were clinically regarded as Paget's disease of the nipple but histopathologically typical Paget's cells were lacking and therefore they were not, in the present survey, classified as Paget's disease.

It is stated in the literature that the histopathology of breast carcinoma is almost identical in men and women (47, 88). One important exception is, however, that lobular carcinoma does not exist in males.

Malignancy grading in the present material was done retrospectively according to the system of HULTBORN & TÖRNBERG (38). This grading should be performed on fairly large sections, and biopsy material alone is not suitable. Cases in which the primary tumour has been preoperatively irradiated should also be excluded from the malignancy grading. Nor should postmortem material or metastases be used for malignancy grading.

The grading is based on the following factors:

a) The ability to form adenomatous or tubular struc-

Table 16

Percentage distribution of the three malignancy grades in the present material of male breast carcinoma and in two materials of female breast carcinoma surgically treated with curative intention

	Male breast carcinoma Period 1958–1967 (n=143)		Female breast carcinoma Period 1968–1970 (n=131)		Hultborn & Törnberg's (38) material of female breast carcinoma. Period 1948–1953 (n=180)	
Malignancy grade	No. of cases	Percentage distribution	No. of cases	Percentage distribution	No. of cases	Percentage distribution
I	27	19	15	12	20	11
II	70	49	70	53	103	57
III	46	32	46	35	57	32
Total	143	100	131	100	180	100

Table 17

Tumour size and axillary lymph node status

Size of tumour	Number of cases with histopathologically known tumour size and axillary status	No lymph node metastasis		Lymph node metastasis		Lymph node metastasis without perinodal growth		Lymph node metastasis with perinodal growth	
		No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
≤2 cm	31	21	68	10	32	5	16	5	16
2–5 cm	32	11	34	21	66	5	16	16	50
>5 cm	6	3	50	3	50	0	0	3	50
Total	69	35		34		10		24	

tures in duct carcinoma or to imitate acini. (Degree of differentiation in a limited sense.)

b) The tendency of the carcinoma to show diffuse 'unrestrained' growth.

c) The delimitation of the carcinoma.

d) The degree of peripheral round-cell (mainly lymphocytes and plasma cells) infiltration.

e) The degree of cellular and nuclear polymorphism, and

f) The frequency of mitosis.

The first two characteristics constitute the main criteria.

Of 149 cases operated upon with curative intent, 143 could be malignancy graded. In Table 16 the distribution of malignancy grades is compared with a female breast carcinoma material from 1968–1970 (40) and with the later part (1948–1953, 180 cases) of HULTBORN & TÖRNBERG's material (38) from the period 1930–1953. Medullary carcinoma with lymphoid infiltration was excluded from the two female materials as this type does not occur in men. The differences between the three materials are negligible. The period 1930–1947 in HULTBORN & TÖRNBERG's (38) material was excluded in the comparison with the modern materials as efficient methods of demonstrating distant metastases were lacking during this period and as cases with severe symptoms, e.g. cancer of the inflammatory type, were not excluded from surgery. The percentage of cases with malignancy grade III was therefore higher.

The mean age was about the same in malignancy grades I, II and III, i.e. 64.5, 65.0 and 65.1 years respectively. Neither was there any significant difference in age distribution in a material of female breast carcinoma (38).

The correlation between some histopathologic variables was studied. The findings concerning tumour size and axillary lymph node status are presented in Table 17. There was a significant positive correlation between these variables if the axillary status was classified as negative or

Table 18
Malignancy grade and tumour size

Malignancy grade	Cases with histopathologically known tumour size and known malignancy grade No.	Tumour size					
		≤2 cm		2–5 cm		>5 cm	
		No.	Per cent	No.	Per cent	No.	Per cent
I	20	13	65	4	20	3	15
II	52	22	42	27	52	3	6
III	38	17	45	18	47	3	8
Total	110	52		49		9	

Table 19
Malignancy grade and axillary lymph node status

Malignancy grade	Cases with known malignancy grade and axillary status	No lymph node metastasis		Lymph node metastasis		Lymph node metastasis without perinodal growth		Lymph node metastais with perinodal growth	
	No.	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
I	12	10	83	2	17	0	0	2	17
II	43	27	63	16	37	6	14	10	23
III	33	10	30	23	70	5	15	18	55
Total	88	47		41		11		30	

Table 20
Malignancy grade and clinical stage

Malignancy grade	Cases with known malignancy grade and clinical stage No.	Clinical stages UICC 1959					
		I		II		III	
		No.	Per cent	No.	Per cent	No.	Per cent
I	20	14	70	5	25	1	5
II	60	28	46	13	22	19	32
III	40	12	30	9	23	19	47
Total	120	54		27		39	

positive only. If the positive group was divided into metastases with and without perinodal growth, no correlation to tumour size could be demonstrated.

The relation between malignancy grade and tumour size is presented in Table 18. There was no significant correlation in the material as a whole. The percentage of tumours ≤2 cm was higher among grade I than among other tumours, however.

The relation between malignancy grade and axillary lymph node status is illustrated in Table 19. A high malignancy grade was significantly more often associated with advanced dissemination to the axilla than a low malignancy grade.

Concerning malignancy grade and clinical stage, there was a significant correlation between high malignancy grade and advanced stage (Table 20).

General discussion

This material of 166 men with primary invasive carcinoma of the mammary gland constituted a total geographic material from Sweden collected during the 10-year period 1958–1967. The material was heterogeneous with respect to documentation, treatment and follow-up. However, a total geographic material collected during a defined period of time contains no selection bias and can therefore be used for description and analysis of the biology of the disease concerned. A material of the size of this one—166 cases— in which many subgroups are subjected to analysis rarely yields significant and conclusive answers but can serve as a basis for hypotheses.

The study also demonstrated the importance of a careful retrospective analysis of records and histopathologic material. Of the 190 cases registered as primary malignant breast tumours only 166 could be accepted as primary invasive breast carcinoma.

There are definite epidemiologic differences between male and female breast carcinoma. Our findings are in agreement with those in other reports from the industrialized countries, that the incidence of male breast cancer is only 0.5 to 1.0 per cent of that of female breast cancer. In contrast to female breast cancer, no definite increase in incidence rate during recent years could be demonstrated. This difference may be related to an artificial increase in the incidence of female breast carcinoma due to increased diagnostic activity, but a biologic difference cannot be excluded. The age-specific incidence was clearly different from that for female breast carcinoma, with no Clemmesen's hook and a steeper rise with age. Male breast carcinoma was diagnosed about 5 years later than female breast carcinoma.

The importance of defining which of the UICC classification systems is used was clearly demonstrated. The inadequacy of clinical examination alone for diagnosis of axillary lymph node involvement was also quite clear.

Analysis of the histopathologic stage distribution showed a difference of about 5 years between patients with tumours <2 cm and those with 2 to 5 cm tumours, and this difference was the same in all age groups. The difference may reflect the time it takes for a tumour to progress from T1 to T2. Theoretically, this provides an epidemiologic opportunity to study doubling times. A corresponding 5-year difference could also be demonstrated between node-negative and node-positive patients, regardless of age, possibly reflecting the time it takes for the disease to progress from pN0 to pN1.

The malignancy grades showed the same distribution as in materials of female breast carcinoma. Histologically, male breast carcinoma did not differ from female breast carcinoma except that lobular carcinoma and medullary carcinoma with lymphoid infiltration were lacking. As in some series of female breast carcinoma, a clear correlation was found between some histopathologic variables of prognostic importance.

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