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Original Paper

Male Breast Cancer: Results of the Treatments and Prognostic Factors in 397 Cases

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From 1960 to 1986, 397 cases of non-metastatic male breast cancer (MBC) treated in 14 French regional cancer centres were reviewed. The median age was 64 years (range 25–93). TNM classification (UICC, 1978) showed seven T0, 79 T1, 162 T2, 31 T3, 74 T4 and 44 unclassified tumours (Tx). Clinical positive lymph nodes were found in 31% of the patients. 24 patients received radiotherapy only, and 373 underwent surgery, 247 of these with postoperative irradiation. Adjuvant chemotherapy and hormonal therapy were used in 71 and 68 patients, respectively. There were 382 infiltrating carcinomas and 15 pure ductal carcinoma *in situ*. Lymph node involvement was found in 56% of infiltrating carcinoma. The oestregen (ER) and progesterone (PgR) receptors were positive in 79% and 77%, respectively, of examined cases. Isolated local and regional recurrence were observed in 8.8% and 4.5% of cases, respectively and 40% of patients developed metastases. The crude survival rates by Kaplan–Meier method were 65% and 38% at 5 and 10 years, respectively, and the disease-specific survival rates (without death due to intercurrent disease or second cancer) was 74% at 5 years and 51% at 10 years. The disease-specific survival rate for pN− and pN+ groups were 77% and 39% at 10 years. The prognostic factors were clinical size (T) and histological axillary status (pN−/pN+). The relative risk of death for pN− was 1.0, 2.0 and 3.2 in the T0–T1, T2 and T3–T4 groups, respectively. For pN+, these relative risks increased 1.9, 3.9 and 6.0 in the same groups. The optimal treatment include modified radical mastectomy and irradiation for cases with risk factors of local relapse (nodal invasion, large tumour with cutaneous or muscular involvement). Locoregional failure had unfavourable prognosis. First-line adjuvant treatment seems to be tamoxifen, due to the very high rate of positive hormonal receptors and the old age of the patients, which contraindicate chemotherapy in many cases. The prognosis of patients with breast cancer is the same in male and female patients when disease-specific survival rate, tumour size and axillary involvement are compared.

Key words: male breast cancer, axillary involvement, treatment, prognostic factors, crude and disease-specific survival

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INTRODUCTION

MALE BREAST CANCER (MBC) is a rare disease, representing in Western countries only 1% of all breast cancer, and less than 1% of all cancers in men. Most reported series number less than 100 cases and cover a long period of time, so treatment modalities may have changed. This large co-operative study allowed us to estimate the histological features, especially nodal involvement, the results of local treatments, the clinical and histological prognostic factors, and the importance of the differences in overall and specific survival in men. The guidelines of local and

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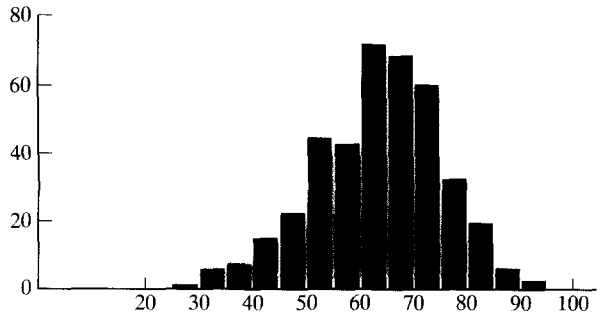

Figure 1. Age distribution (397 patients).

adjuvant treatment are also developed, although applicable only to a small proportion of patients.

PATIENTS AND METHODS

Clinical characteristics

From 1960 to 1986, 397 patients with MBC treated in 14 French regional cancer centres were analysed in a retrospective study based on a standardised registration form. All data were collected in the Paul Strauss Centre, Strasbourg, France. Previously, 40 patients with metastases at time of diagnosis and 7 treated only palliatively, were excluded from further analysis. The median follow-up of the entire study cohort was 74 months. Figure 1 shows the age distribution of the patients, and the median age was 64 years (range: 25–93). A family history of breast cancer was noted in 22 men (5.5%). A previous or synchronous neoplasm was noted in 14 patients (3.5%); 3 had prostatic cancer treated by oestrogens and one had exclusive radiotherapy for a chrondrosarcoma of the seventh left rib.

TNM (UICC 1978) classification of the 397 patients showed: T0, 7; T1, 79; T2, 162; T3, 31; T4, 74 and unclassified tumours (Tx) 44. Clinical positive lymph nodes were found in 31% of the patients. The first symptom was the tumour in 79% of cases, nipple retraction in 10%, nipple discharge in 5.5%, Pagets's disease in 2.7% and mastitis in 1.8%. Other symptoms were noted in 1%. The median clinical size of the tumour was 3 cm. The median delay before diagnosis was 6 months.

Treatment

Figure 2 shows details of the different locoregional treatments. Surgery was performed on 373 patients, the other 24 only receiving radiotherapy. This latter group was older (median age: 71 years) and very often had other associated diseases. Adjuvant chemotherapy was used in 71 patients, 23 receiving CMF, 20 a regimen with anthracycline and 28 various drug combinations.

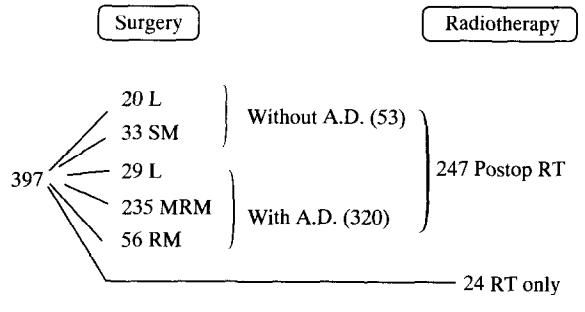

Figure 2. Locoregional treatments. L, lumpectomy; SM, simple mastectomy; MRM, modified radical mastectomy; RM, radical mastectomy; A.D., axillary dissection.

Adjuvant hormonal therapy was prescribed in 68 patients, 8 undergoing orchiectomy, 52 receiving tamoxifen (TAM), and 8 various drugs.

Pathology

Table 1 shows the histological subtype distribution. We noted 15 pure ductal carcinoma *in situ* (DCIS) (3.8%), especially papillary (pure or intracystic). The median histological size of the tumour was 2.5 cm. Skin, nipple or muscle involvement were noted in 100 cases (25%).

Of the 308 patients with infiltrating carcinoma who underwent axillary dissection, 174 (56%) were node positive (pN+). 55 had only one involved lymph node, 35 two or three, and 84 four or more. The risks of axillary involvement were respectively 38%, 55% and 62% for the T0–T1, T2 and T3–T4 groups ($P = 0.006$).

Hormone receptors (HR) were detected in 105 invasive tumours (after 1978); oestrogen receptors (ER) were present in 79% of cases and progesterone receptors (PgR) in 77% at very often high levels.

Statistical methods

The analysis was performed using the Kaplan–Meier method for crude and disease-specific survival. Mantel-Cox's (log-rank) test was used to compare survival curves. Statistical significance was considered to be achieved when $P < 0.05$. To account simultaneously for different potentially prognostic factors, a multivariate analysis by Cox-model was performed. BMDP statistical software was used for all calculations.

RESULTS

Table 2 shows locoregional failure (such as first event) according to treatment. Twenty-one other local recurrences (LR) occurred with associated (11) or previous (10) metastases, three in the radiotherapy only group and 18 in the surgery group. Fourteen other regional recurrences (RR) occurred with (11) or after (3) metastases in the surgery group.

In a second-step analysis, we found LR (±RR) rates of 16.3% (8/49), 6.3% (17/268) and 8.9% (5/56) in patients treated by lumpectomy, simple or modified, and radical mastectomy, respectively ($P = 0.06$). The LR risk was not significantly different between the T1–T2 group (6.4%) and T3–T4 group (4.8%), but in the Tx group, we found a 20.4% rate of LR (9/44).

Among the 14 surgical patients with isolated RR (with or without LR), only 4 had previously axillary dissection. Consequently, regional nodal recurrence occurred only in 1.2% of the patients with axillary dissection (4/320) and in 13% of the patients (10/77) without axillary dissection ($P < 0.0001$).

Table 1. Histological subtypes

Ductal infiltrating carcinomas	349 (87.9%)
SBR I:	44
SBR II:	129
SBR III:	50
NS:	126
Ductal carcinoma *in situ*	15
Papillar carcinoma	9
Colloid carcinoma	2
Other types	22

SBR, Scarff–Bloom–Richardson classification; NS, not specified.

Table 2. Results of locoregional control (LR and RR that occurred with or after metastases were excluded)

		No. of patients with: LR	LR + RR	RR	Total % of LR	Total % of RR
RT group (n = 24)		2	3	1	20.8	16.7
Surgery group (n = 373)	With CWRT* (n = 190)	8	1	3	4.7	2.1
	Without CWRT* (n = 183)	16	5	5	11.5	5.5
Total (n = 397)		26	9	9	8.8	4.5

*CWRT, RT on the chest wall at least 40 Gy.
LR, local recurrence (chest wall); RR, regional recurrence (axilla and/or supraclavicular fossa); RT, radiotherapy.

RR (associated or not with LR) rate was 1.7% if the surgical patients received nodal irradiation (4/232) and 4.3% if not (6/141), and 16.7% (4/24) in exclusively irradiated patients (P = 0.002). 160 patients of the 397 (40%) developed metastases, including 54 after local and or regional relapse (13.6%). 8 patients developed subsequent contralateral breast cancer and 43 (10.8%) developed a second metachronous cancer.

The crude survival rates are 65% and 38% at 5 and 10 years, respectively (Figure 3). The disease-specific survival rates (excluding death by intercurrent disease and second cancer) are 74% and 51% at 5 and 10 years, respectively. Of the 187 patients who died, 113 (60.5%) died of breast cancer, 43 (23%) from intercurrent disease, 19 (10%) from a second cancer, 6 (3%) from complications and 6 (3%) from unknown causes. According to T status, the 5 year crude survival rates of T0–T1, T2 and T3–T4 groups are, respectively 85%, 63% and 51%, and 10 years, respectively 65%, 37% and 18%. The disease-specific survival rates for T0–T1, T2 and T3–T4 groups are, respectively, 88%, 73%, 65% at 5 years and 74%, 48%, 34% at 10 years (Figure 4).

Among the 308 patients with infiltrating carcinoma who underwent axillary dissection, histological involvement remained the best prognostic factor, with a 10 year crude survival rate of 58% and 28% for pN− and pN+ groups, respectively (P < 0.0001). For the same two groups, the disease-specific survival rates were 77% for pN−, and 39% for pN+ (Figure 5). Table 3 shows survival according to the number of involved nodes. The relative risk (RR) of death was analysed by a Cox model including the two previous prognostic factors, T and pN,

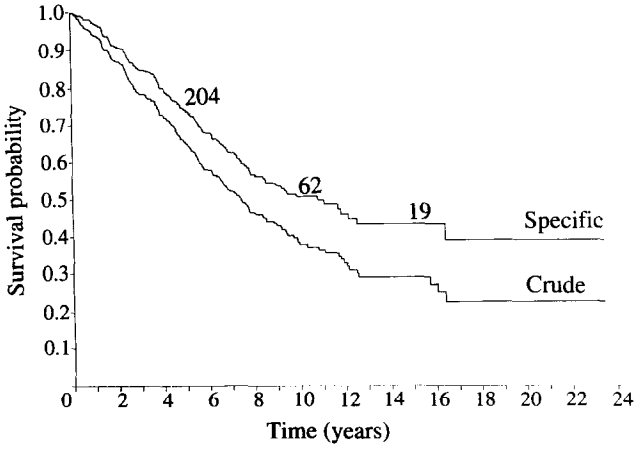

Figure 3. Crude and specific survival (397 patients).

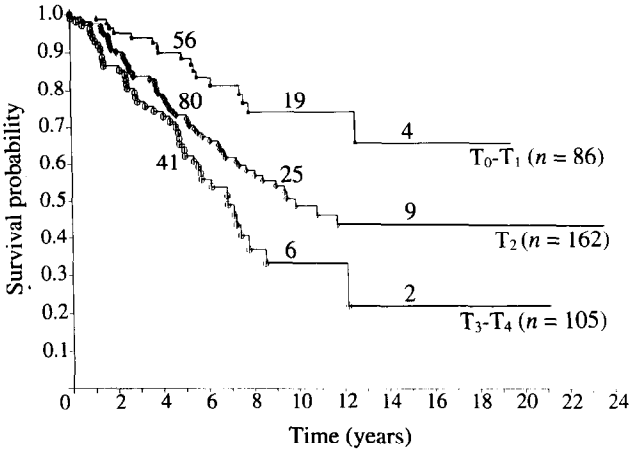

Figure 4. Specific survival according to T stage (353 patients).

Table 3. Crude survival (CS) and disease-specific survival (DSS) according to histological axillary involvement (pN)

	CS		DSS	
	5 years	10 years	5 years	10 years
pN−	82.4%	58%	93%	77%
pN+ 1–3	62%	37%	70%	50%
pN+ >3	60%	19%	64%	24%
All pN+	61%	28%	67%	39%

allowing for interaction. Table 4 shows the different RR for each category. After controlling for T and pN, age was not a significant prognostic factor.

DISCUSSION

Epidemiological and clinical characteristics of MBC have been described previously [1–7]. The aetiology remains as poorly understood as that of female breast cancer, but imbalance (by various mechanisms) in the oestrogen–testosterone ratio is probably implicated [5, 6].

Our report confirms the high median age at onset of disease (64 years), such patients comprising a significant proportion of advanced tumours (T4 = 18.6%) according to several reports [8–15].

In our series, we confirmed the large prevalence of ductal infiltrating carcinoma but 15 men (3.7%) had pure DCIS: a

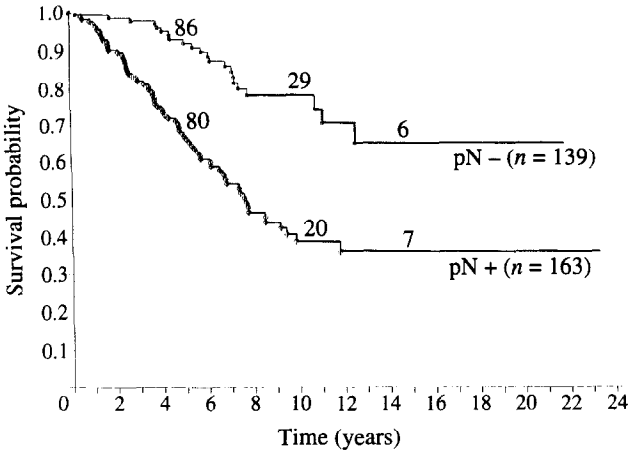

Figure 5. Specific survival according to pN (302 patients).

Table 4. Relative risk of death according to T and pN status

	T0–T1	T2	T3–T4
pN–	1.0	2.0	3.2
pN+	1.9	3.9	6.0

detailed report of these cases has been published previously [15]. In the literature, the DCIS rate varies from 0 to 16% [7, 16], similar to women's series without mammographic screening. In our experience, like others [16, 17], no lobular carcinoma was found, unlike a recent report in which 6 cases were observed [9]. Our axillary involvement rate for infiltrating carcinoma was 56%. The risk is significantly correlated to clinical tumour size, according to other reports [7–9]. This frequency according to stage is higher than in women. Among the patients with axillary dissection, the number of involved nodes were one, 17.8%; two or three, 11.4%; and four or more, 27.3% and very similar results were found in another large multicentric study [8].

Concerning Scarff–Bloom–Richardson grading distribution and the frequency of HR, our series confirmed results of previous reports [18–20]. The presence and level of ER can explain the efficacy of hormonal procedures in advanced MBC [16, 17].

According to other reports [7–9], modified radical mastectomy is the first surgical approach to the treatment of MBC whenever possible. Lumpectomy had an inferior (2-fold) local control rate (borderline significance, $P = 0.06$), but was, nevertheless, applied especially in elderly patients or those with unfavourable medical conditions. Radical mastectomy did not seem superior to modified radical mastectomy. Chest wall irradiation reduced the LR rate, but its impact on survival could not be clearly evaluated. Similarly, supraclavicular and internal mammary node irradiation reduced nodal relapse rate 3-fold ($P = 0.002$).

The interest in locoregional irradiation can be explained by the central topography of the tumour, the frequency of dermis or muscle involvement, and especially by the high rate of axillary involvement. All these factors are known to increase greatly the risk of locoregional relapse in women [21, 22]. We tried to evaluate the impact of chemotherapy and hormonal therapy, but no conclusion was possible since the patient groups were not comparable, in this retrospective analysis, for age, tumour size, nodal involvement and HR status. The same problem was reported by the Milan group in a large series [9] and in other recent reports [16, 17]. Experience with adjuvant therapy for males is very limited, but two studies report the benefits of adjuvant chemotherapy in men [23, 24]. Nevertheless, these data should be considered with caution since the number of patients treated was small (35 cases) and the follow-up short. Moreover, HR are very often positive (over 75%) in men [9, 16, 17] and the median age of patients presenting with MBC is quite high (approximately 65 years), with frequent chronic associated diseases. These facts seem to indicate that, if necessary (for T3–T4 tumours and/or axillary involvement), first-line adjuvant treatment should be tamoxifen [25], which is considered to be as effective as in women. Adjuvant chemotherapy is still applicable for young men with extensive axillary nodal involvement and/or negative HR.

In our study, the crude survival rates were 65% and 38% at 5 and 10 years, respectively. In the literature, 5 year survival rates vary from 14.5 to 64% [2] with, in most cases, a reported value of approximately 40% [14, 30, 31]. However, we note important differences when disease-specific survival rates were analysed (Table 5).

As reported recently by Guinee and associates [8], in a 335 patient multicentric series, 83 (47%) of the 178 deaths were due to causes other than breast cancer. In our series, we found 39.5% of deaths unrelated to breast cancer. The difference between observed survival and specific survival increases clearly with the patient's age at diagnosis [32]. This fact explains the smaller rate of "non-specific deaths" in women and also partly the diffuse concept of unfavourable prognosis in MBC.

The prognostic factors considered in the literature are the same for men and women: tumour size (clinical or histological), SBR grade and especially axillary involvement, usually histologi-

Table 5. Survival rates reported in the literature

Reference	Number of patients n	Crude survival 5 years	Crude survival 10 years	Disease-specific survival 5 years	Disease-specific survival 10 years
Ribeiro [14]	301	39%	18%	43%	26%
Spence *et al.* [26]	81	38%	17%	52%	29%
Appelqvist and Salmo [27]	29	44%	32%	65%	47%
Adami *et al.* [28]	1429	44%	—	60%	—
Lartigau *et al.* [17]	68	—	23%	—	42%
Scheike [29]	249	36%	17%	46%	29%
Current study	397	65%	38%	74%	51%

Table 6. Survival rates reported in the literature according to histological (pN) or clinical (N) nodal status

Reference	n	Analysis	5 year survival		10 year survival	
Lartigau *et al.* [17]	65	Crude			N_0 = 55%	N_{1-2} = 22%
Erlichmann *et al.* [12]	89	Crude	N_0 = 77%	$N_{(1-2)}$ = 37%		
Borgen *et al.* [16]	99	Crude	pN− = 100%	pN+ = 60%		
Guinee *et al.* [8]	224	Disease specific	pN− = 90%	$pN+_{(1-3)}$ = 73%	pN− = 84%	$pN+_{(1-3)}$ = 44%
				$pN+_{(>3)}$ = 65%		$pN+_{(>3)}$ = 14%
Current study	308	Crude	pN− = 82.4%	pN+ = 63%	pN− = 58%	pN+ = 28%
		Disease specific	pN− = 93%	pN+ = 67%	pN− = 77%	pN+ = 39%

cal. Sheike, in a series of 150 cases, found significant differences in the 5 year survival rate between SBR grades I and II ($P < 0.05$) and between grades II and III ($P < 0.01$) [29]. We did not evaluate this parameter due to insufficient data. Axillary involvement clearly remains the best prognostic factor. Table 6 summarises recent data from the literature confirming this fact. The results for disease-specific survival at 5 and 10 yeras are very similar to those of females. The combination (Cox-model) of T and pN status permitted us to decline a clear predictive relative risk of death varying from 1 for T0–T1 pN− (reference group) to 6.0 for the unfavourable T3–T4pN+ group. Only one other study [8] has simultaneously analysed multiple variables of prognosis, where the relative risk was equally correlated especially with pN status, and subsequently with pathological tumour diameter.

Finally, according to recent reports [8, 16], the prognosis of MBC appears similar to that of female, especially if disease-specific survival is analysed and when the clinical or pathological stages are strictly matched. Optimal locoregional control is very important. Modified radical mastectomy is the basic treatment with extensive use of postoperative irradiation. Currently, no clear data concerning the benefits of adjuvant treatment are available, but anti-oestrogens seem to be the first-line approach in the majority of cases. Only a multicentric and prospective study based on common registration criteria and a planned treatment protocol can assess more accurately the prognosis of this rare disease in the future.

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