Original Articles

Carcinoma *in situ* and early breast carcinoma. Survey of the Portuguese Senology Society on the diagnostic tools used in Portugal and their evolution between 1985 and 2000

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Summary

By means of a questionnaire, sent to the Portuguese hospitals which diagnose and treat most female patients with breast cancer, it was intended to assess the situation regarding the diagnosis of carcinoma *in situ* and early breast cancer (T1 or T2, N0 or N1), as well as their evolution between 1985 and 2000.

The hospital participation rate was 65% and a sample of 865 patients was collected, distributed in the years 1985, 1990, 1995 and 2000.

It was found that the presentation form of breast cancer in 1985 was of palpable tumour in 87% of the cases, whereas in 2000 this situation only corresponded to 54% of the patients, being most of the remaining patients diagnosed by imaging without palpable tumour.

In 94% of the patients, the first diagnostic investigation was mammography, associated or not to echography, and the second most frequent investigation was fine-needle aspiration biopsy.

The time evolution of the tumour size showed an increasingly earlier diagnosis. Invasive tumours not more than 1 cm represented 13.2% in 1985 and 20.3% in 2000. On the other hand, breast cancers more than 2 cm and not more than 5 cm decreased from 67.2% in 1985 to 40% in 2000.

When oncology centres and some large university hospitals (Group A) were compared to the other hospitals (Group B), there were no significant differences between the diagnostic methods, although the sequence of diagnostic methods was different in the hospitals in Group A versus those in Group B. It was observed that in more differentiated hospitals the diagnosis was achieved increasingly earlier along the studied periods, and this situation did not occur in the other hospitals.

Key words: Breast cancer; Early breast cancer; Diagnosis; Carcinoma "in situ"; Survey; Portugal.

Introduction

The age-standardised incidence rate in Portugal in 1995 was 70.4 new cases per 100,000 women [1], which provided an annual diagnosis of more than 3,500 new cases of breast cancer per year. In the same period in the European Union the incidence was 89 new cases per 100,000 women [1].

Participating institutions:
Hospital de Santa Maria (Lisbon), Centro Regional de Oncologia de Lisboa (Lisbon), Centro Regional de Oncologia de Coimbra (Coimbra), Hospitais da Universidade de Coimbra (Coimbra), Hospital Distrital de Évora (Évora), Hospital do Desterro (Lisbon), Maternidade Dr. Alfredo da Costa (Lisbon), Maternidade Bissaia Barreto (Coimbra), Centro Hospitalar de Cascais (Cascais), Hospital Garcia de Orta (Almada), Hospital S. José (Lisbon), Hospital Sto. António (Oporto), Hospital Distrital de Faro (Faro), Hospital de S. Francisco Xavier (Lisbon), Hospital Distrital de Santarém (Santarém), Hospital de S. Marcos (Braga), Hospital de Ponta Delgada (Azores).

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On the other hand, the mortality caused by breast cancer in 1995 was 24.9 in Portugal and 30.5 per 100,000 women in the European Union [1]. It is estimated that between the years 2000 and 2050 in Europe there will be an increase in mortality caused by breast cancer of approximately 8.5% [2].

Until the early 90s in Portugal both diagnosis and treatment of breast cancer were concentrated in the three centres of the Portuguese Cancer Institute and in another additional five or six large university hospitals in Lisbon, Oporto or Coimbra. With the appearance of new medical teams interested in senology, the current number of institutions diagnosing and treating this pathology has significantly increased.

The Portuguese Senology Society was created in 1989. Since then it has become responsible for disseminating guidelines on the diagnosis and treatment of breast cancer. Initially, this was achieved through scientific meetings, and later by organizing national consensus meetings on breast cancer. The first consensus meeting

took place in September 1993, followed by three other meetings every three years. The last meeting occurred in May 2002. The conclusions of the consensus meetings may be found in the Internet page of the Society (www.spsenologia.pt).

In order to assess the situation in Portugal, as was done in other countries [3], a commission appointed by the Portuguese Senology Society developed a questionnaire on the diagnosis and treatment of breast cancer from 1985 to 2000 which was sent to the majority of the Portuguese hospitals with breast units. The results of the diagnosis are presented here.

Aims

To assess in Portuguese hospitals with an important number of cases in diagnosing and treating breast cancer, which diagnostic means were used and what their evolution was in the period comprised between 1985 and 2000. The assessment was conducted by means of a questionnaire, under the auspices of the Portuguese Senology Society. This questionnaire was designed by an expert commission and sent to the doctors in charge of the diagnosis and treatment of breast cancer in 26 Portuguese hospitals and cancer centres.

Material and Methods

An extensive questionnaire on the diagnostic methods used in patients with breast cancer treated in 23 Portuguese hospitals (5 university hospitals and 18 non-university hospitals) and in the three regional cancer centres was developed.

In each institution it was requested that a doctor be appointed to be in charge of collecting and filling in the questionnaire.

The following inclusion criteria were defined for each institution:

(a) Female patients with carcinoma *in situ* of the breast or with invasive carcinoma clinically classified as T1N0M0, T1N1M0, T2N0M0 and T2N1M0.

(b) Patients must have been subject to surgical treatment in that institution (modified radical mastectomy or conservative surgery).

(c) Sequential inclusion of the patients treated as of January 1 of the years 1985, 1990, 1995 and 2000.

(d) Inclusion of 20 patients per each of the periods mentioned in the previous section (maximum of 80 patients per institution).

(e) The institution must choose at least two periods (minimum of 40 patients), with the exception of hospitals in the Autonomous Regions of Azores and Madeira.

(f) Assessment of patient conditions on December 31, 2000 or at the time of death or loss of follow-up.

Data were filled in during the last three months of 2001, and in 2002 a computer database was developed. The data were validated and statistically analysed through the SPSS programme.

Of the 26 institutions invited to participate in the assessment, 17 answered (65%), including four of the five university hospitals (80%), two of the three cancer centres (67%) and 11 of the remaining 18 hospitals (61%).

Eight hundred and sixty-five patients were included, of which 61 were from the year 1985 (7.1%), 134 from 1990 (15.5%), 335 from 1995 (38.7%) and 335 from 2000 (38.7%).

The distribution of patients in the institutions showed that three institutions provided data on all four studied periods (1985, 1990, 1995 and 2000), four other institutions provided data on three periods (1990, 1995 and 2000) and the remaining ten institutions provided data on two periods (1995 and 2000). It should be noted that the institutions which provided data on three or four periods (1985, 1990, 1995 and 2000) were those with a larger tradition and more experience in diagnosing and treating breast cancer, and which we named "Group A", whereas the institutions which only provided data on two periods (1995 and 2000) were referred to as "Group B".

Table 1 shows that the average patient age was 57.8 ± 12.9 years, varying between 22 and 91 years. Regarding the hormonal status, 259 patients (31%) were in premenopause and 576 (69%) were in postmenopause. Variations across the studied periods were not significant.

Table 1. — *Average age and hormonal status.*

	1985 n (%)	1990 n (%)	1995 n (%)	2000 n (%)	1985-2000 n (%)
Average age	55.9±11.7	57.7±13.4	57.1±12.9	60.5±12.5	57.8±12.9
Pré-menopause	17 (29)	44 (34)	110 (34)	88 (27)	259 (31)
Post-menopause	42 (71)	86 (66)	217 (66)	231 (73)	576 (69)

Results

Presentation form

When questioned about the reason why the patients had been referred to or had consulted the institution, the results show the detection of a mammary tumour in 570 patients (66%), mammographic and/or echographic changes without palpable tumour in 235 patients (27%), suspicious nipple discharge in 19 patients (2%) and other reasons in 38 patients (4%).

Table 2 shows the time evolution of the presentation form. A significant decrease of "palpable tumour" is clear, having declined from 87% in 1985 to 54% in 2000, along with a significant increase of early diagnosis by mammography associated or not to echography (10% in 1985 vs 37% in 2000).

Table 2. — *Patient presentation.*

	1985 n (%)	1990 n (%)	1995 n (%)	2000 n (%)	1985-2000 n (%)
Palpable tumour	53 (87)	117 (87)	218 (65)	182 (54)	570 (66)
Abnormal mammography/ echography	6 (10)	12 (9)	92 (28)	125 (37)	235 (27)
Suspicious discharge	2 (3)	2 (2)	11 (3)	4 (1)	19 (2)
Other reason	–	3 (2)	13 (4)	22 (7)	38 (4)

Sequence of diagnostic investigations

The assessment of the sequence of diagnostic investigations performed after clinical examination involved mammography associated or not to echography, fine-needle aspiration biopsy (FNAB) with or without image guidance, core needle biopsy (CNB) with or without

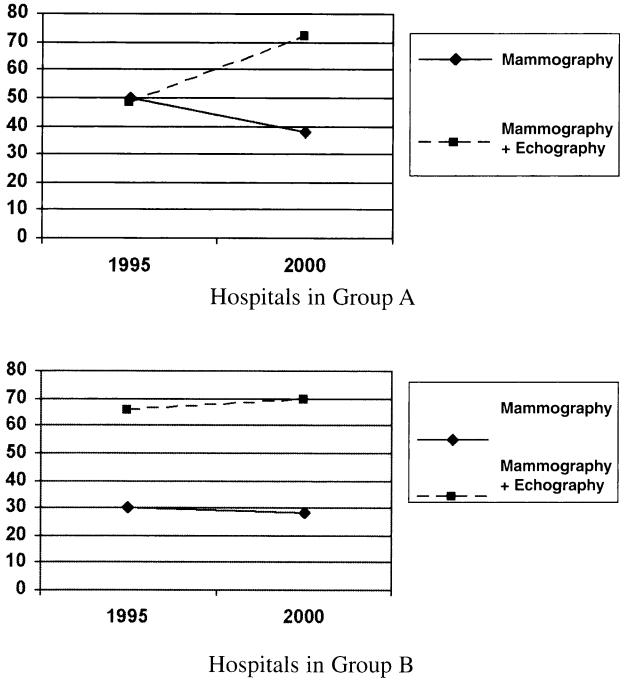


Figure 1. — Percentage of evolution between 1995 and 2000 of mammography with or without echography as the first diagnostic investigation in both hospital groups.

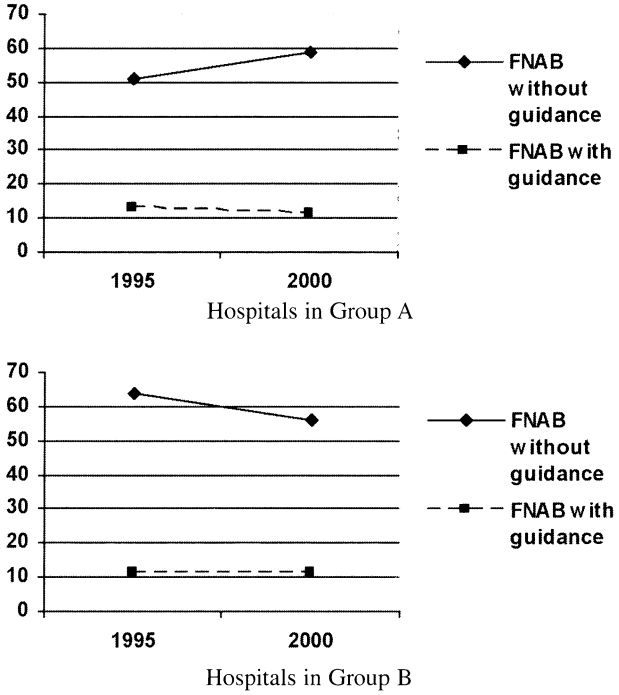


Figure 2. — Percentage of evolution between 1995 and 2000 of fine-neddle aspiration biopsy, with or without image guidance, as a second diagnostic investigation in both hospital groups.

image guidance, incisional or excisional biopsy, frozen section biopsy, and others.

As to the first diagnostic procedure, it was observed that imaging investigations (mammography and/or echography) were performed in 94% of the patients, FNAB without image guidance in 2% and frozen section biopsy in 3%.

The second action in the diagnostic sequence was palpable tumour by FNAB in 53% of the cases or FNAB with image guidance in 8%, whereas frozen section biopsy was performed in 9% of the patients, harpoon- or dye-guided biopsy in 5%, CNB with or without guidance in 5%, incisional or excisional biopsy in 4% and additional imaging investigations in 6% of the cases.

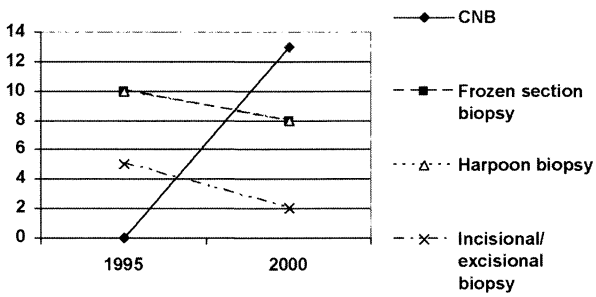
In situations where a third diagnostic procedure was carried out, frozen section biopsy occupied the first position in 6% of the patients, incisional and excisional biopsies were also performed in 6% of the patients; CNB was executed in 5% of the patients, FNAB also in 5% and harpoon- or dye-guided biopsy in 2%.

Figure 1 shows the percentage of evolution between 1995 and 2000 of the first imaging investigation: mammography or mammography and echography. From this figure, it can be seen that the hospitals in Group A, when compared with those in Group B, show different behaviours. The hospitals with a larger experience (Group A) only integrated echography associated with mammography later, whereas hospitals more recently involved in this field (Group B) have given priority to mammography with ecography versus single mammography since 1995.

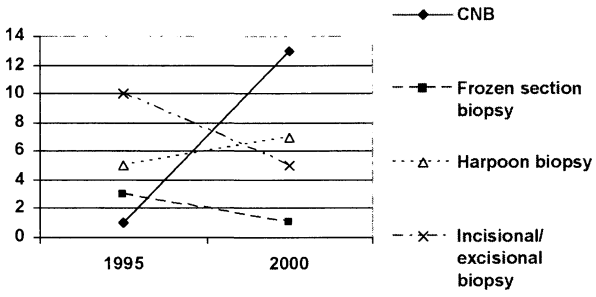
In the hospitals of both Groups A and B, the second most frequent investigation was FNAB with or without image guidance. The most common imaging investigation was ecography. Figure 2 shows the percentage of evolution between 1995 and 2000 of FNAB with or without image guidance. It can be seen that the behaviour does not differ between Group A and B, with a predominance of FNC without image guidance in palpable tumours (51% to 64%). FNAB with image guidance was used in between 11% and 13% of the patients.

In alternative to FNAB, a biopsy of the lesion was the second most used diagnostic procedure. Figure 3 shows the percentage evolution between 1995 and 2000 of the various forms of biopsy used in hospitals in Groups A and B. In 2000 CNB was ranked in first place, with 13%, followed by frozen section biopsy, which varied between 1% (Group B) and 8% (Group A), harpoon-guided biopsy, which ranged between 7% (Group B) and 8% (Group A) and incisional or excisional biopsy, which was used in 2% of the cases in hospitals of Group A and in 5% in hospitals of Group B.

In the situations where biopsy was the third diagnostic procedure, Figure 4 shows the percentage of evolution between 1995 and 2000 of the various forms of biopsy used in the hospitals in Group A and B. According to this figure, in 2000 CNB was performed in 48% of the female patients in the hospitals in Group A versus 12% in those in Group B; frozen section biopsy performed in Group A hospitals diminished from 32% in 1995 to 12% in 2000, and incisional or excisional biopsy ranged between 8% in the hospitals of Group B and 24% in those of Group A.

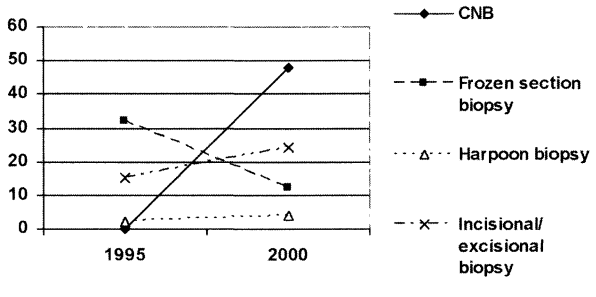


Hospitals in Group A

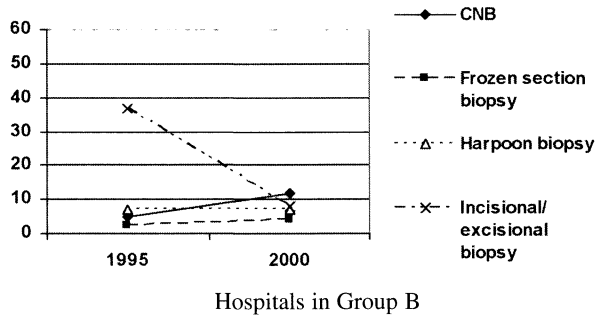


Hospitals in Group B

Figure 3. — Percentage of evolution between 1995 and 2000 of the various biopsy forms, as a second diagnostic investigation in both hospital groups.



Hospitals in Group A



Hospitals in Group B

Figure 4. — Percentage of evolution between 1995 and 2000 of the various biopsy forms as a third diagnostic procedure in both hospital groups.

Fine-needle aspiration biopsy

The results regarding FNAB are presented in Table 3. It should be highlighted that in the period between 1985 and 2000, 8% of the results were false negative and that FNAB was inconclusive in 6% of the female patients. In 69% FNAB was positive and in 16% it was doubtful or suspicious.

Table 3. — *Results of fine-needle aspiration biopsy.*

	1985 n (%)	1990 n (%)	1995 n (%)	2000 n (%)	1985-2000 n (%)
Negative	1 (4)	11 (12)	24 (10)	13 (5)	49 (8)
Doubtful	0	3 (3)	12 (5)	10 (4)	25 (4)
Suspicious	2 (7)	13 (14)	29 (12)	31 (13)	75 (12)
Positive	21 (78)	63 (68)	157 (66)	173 (71)	414 (69)
Inconclusive	3 (11)	2 (2)	17 (7)	16 (7)	38 (6)

Biopsy

In the cases where biopsy was performed, regardless of the method, 3% of the results were found to be false negative, 3% were doubtful biopsies, 16% were carcinomas in situ (15% DCIS and 1% LCIS) and 78% were invasive carcinomas (64% ductal carcinoma, 5% lobular carcinoma and 9% others).

When frozen section biopsy was performed, false negatives were found to be 0.5%, doubtful investigations 4%, carcinomas *in situ* 10% and invasive carcinomas 85.5%.

Clinical stage (TNM classification)

Table 4 presents the distribution of patients according to the tumour (T) and in agreement with the TNM classification, comparing the hospitals in Group A with those of Group B. Carcinomas *in situ* ranged between 5% and 9%, tumours not more than 1 cm (T1a and T1b) between 18% and 20%, tumours more than 1 but not more than 2 cm between 22% and 23% and tumours more than 2 cm but not more than 5 cm 46%.

Table 4. — *Clinical classification of the tumour (T) according to the TNM classification in both hospital groups.*

TNM	Group A = 477 n (%)	Group B = 388 n (%)	Total = 865 n (%)
Without information	12 (2.5)	8 (2.1)	20 (2.3)
Tis	25 (5.2)	34 (8.8)	59 (6.8)
T1a	24 (5.0)	32 (8.2)	56 (6.5)
T1b	63 (13.2)	45 (11.6)	108 (12.5)
T1c	110 (23.1)	85 (21.9)	195 (22.5)
T2	217 (45.5)	177 (45.6)	394 (45.5)
Tx	26 (5.5)	7 (1.8)	28 (3.2)

Table 5 illustrates the distribution of patients according to the axillary clinical evaluation (N) and according to the TNM classification, comparing the hospitals in Group A with those in Group B. It was found that tumours with N0 ranged between 70% and 75% and tumours with N1 between 22% and 26%.

Table 5. — *Clinical classification of the axilla (N) according to the TNM classification in both hospital groups.*

TNM	Group A = 477 n (%)	Group B = 388 n (%)	Total = 865 n (%)
Without information	14 (2.9)	15 (3.9)	29 (3.4)
N0	358 (75.0)	273 (70.4)	631 (72.9)
N1	105 (22.1)	100 (25.7)	205 (23.7)

Figure 5 shows the percentage of evolution in the period comprised between 1985 and 2000 of the diagnosed tumour size (T). There is an increase in the number of carcinomas *in situ* (less than 1% in 1985 and 9% in 2000), invasive carcinomas not more than 1 cm (13.2%

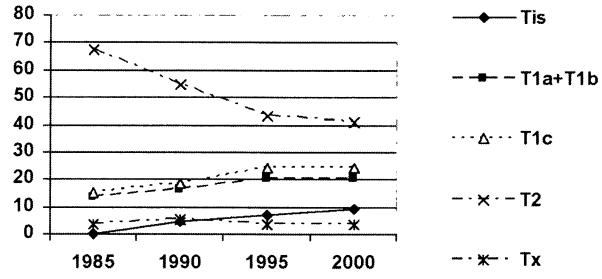
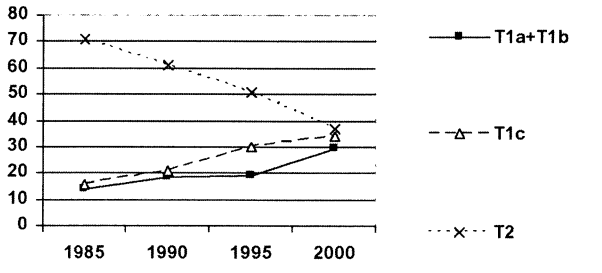
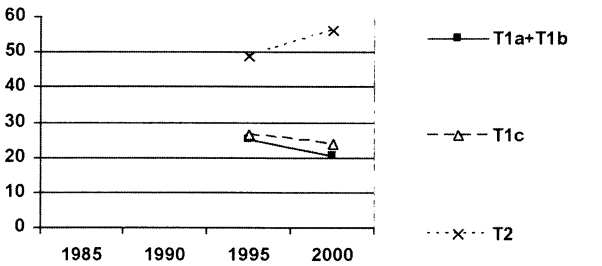


Figure 5. — Percentage of evolution of tumour size in the period between 1985 and 2000.



Hospitals in Group A



Hospitals in Group B

Figure 6. — Percentage of evolution of tumour size in the period between 1985 and 2000 according to the type of hospital.

in 1985 and 20.3% in 2000) and invasive carcinomas more than 1 cm but not more than 2 cm (14.8% in 1985 and 23.9% in 2000). In contrast, tumours more than 2 cm but not more than 5 cm decreased from 67.2% in 1985 to 40.6% in 2000. Figure 6 shows that in the period between 1995 and 2000 this behaviour was different in the hospitals in Group A and in those belonging to Group B. In the first group, there is a clear growth of increasingly earlier diagnosis, whereas in Group B this evolution does not exist, and the percentage of tumours more than 2 cm is still very high. In 2000 in Group A, T2 tumours represented 36.7% while in Group B they represented 56.1%.

Discussion and Conclusions

This assessment by means of a questionnaire was only intended to collect data on tumours not more than 5 cm in diameter (T0, T1 and T2) diagnosed and treated in the surveyed hospitals. It should be highlighted that in 1985 most breast cancers were treated in the three regional cancer centres and in six or seven large hospitals in Lisbon, Oporto and Coimbra. In 2000 the number of hospitals that started diagnosing and treating breast cancer tripled. The Portuguese Senology Society identified 26 hospitals that reported having breast units.

A questionnaire was conducted to assess diagnostic and treatment methods of *in situ* and early breast carcinoma (not more than 5 cm) with the aim of evaluating the conditions in 26 breast units identified in Portugal by comparing these units and assessing the evolution of the period comprised between 1985 and 2000.

The assessment was conducted by sampling with previously defined inclusion criteria and by means of an extensive questionnaire. Seventeen hospitals answered the questionnaire (65%). The group of non-participants only comprised one of the three Oncology Centres and one of the five university hospitals. The remaining seven hospitals with no answer are smaller institutions, some of them with a limited number of cases in the scope of breast pathology.

In terms of diagnosis, 865 female patients were diagnosed. The results regarding the treatment will be published elsewhere.

In 1985, 87% of the patients presented at the institution with a palpable tumour, while in 2000 this percentage decreased to 54%. In the same period, presentation due to assymptomatic tumour (diagnosed by imaging only) rose from 10% to 37%, which implies a significant growth in early diagnosis. Despite this favourable evolution, screening must be encouraged. Comparatively, in the USA in 1983, approximately 30% of the initial presentations were abnormal mammography, while in 1990 this percentage rose to 56%. Furthermore, palpable tumours identified by the patient decreased from 62% (1985) to 42% (1990) [3].

In 94% of the cases the first diagnostic procedure was mammography, associated or not to echography; the second procedure was FNAB in 53%. Frozen section biopsy as the first procedure only took place in 3% of the patients.

Regarding imaging investigations, the more differentiated hospitals (Group A), in 1995, performed mammography in approximately 50% of the patients, and mammography associated to echography in the remaining 50%. In the same period, the less differentiated hospitals (Group B), performed mammography in approximately 30% of the patients, and mammography associated to echography in the remaining 70%. In 2000 both hospital groups revealed similar behaviours, performing mammography associated to echography in approximately 70% of the patients. Although the role of breast echography in screening and staging breast cancer is still controversial [4], the discrepancy between both hospital groups in 1995 can be justified by the fact that the more differentiated hospitals (Group A) have a longer experience in the use of mammography as a diagnostic method and resort to echography in situations defined beforehand. On the other hand, when the hospitals with less experience (Group B) started to apply imaging diagnostic techniques to senology, echography already occupied an important position. In 2000 the situation is similar in both groups and the behaviour change in the more differentiated hospitals (Group A)

is due to an increase in the frequency of performance of echography-guided core biopsy.

As to the various forms of biopsies used, as second or third procedures, it was found in the periods of 1995 and 2000 that frozen section biopsy in the hospitals in Group A ranged between 10% and 8% as a second procedure, and between 30% and 10% as a third procedure; in the hospitals comprised in Group B, frozen section biopsy was never performed in more than 4% of the situations. This difference is justified by tradition being more deeply rooted in hospitals with more experience (Group A), and because some hospitals in Group B have logistic difficulties in performing this investigation.

In both groups CNB as a second procedure only had some relevance in 2000, with 13%. However, as a third procedure it was performed in Group A hospitals in 48% of the patients, whereas in those in Group B it did not go further than 12%.

Regarding harpoon-guided biopsy, mainly used in microcalcifications without ecographic representation, it was performed as a second diagnostic investigation in Group A hospitals in the periods of 1995 and 2000 in 10% and 8% of the patients, respectively, and in Group B hospitals in 5% and 7%, respectively. The differences are not significant.

In conclusion, and regarding the sequence of diagnostic tools, a different behaviour between both hospital groups was observed, particularly in 2000. In most patients after mammography was associated to echography, the hospitals with more experience (Group A) sequentially performed FNAB and CNB in the situations where the lesion was palpable or detectable by image. The other hospitals (Group B) conducted preoperative biopsies much less frequently, independently of the form. On the other hand, in 2000 frozen section biopsy decreased significantly, mainly in the hospitals in Group A, being just 10%.

FNAB, which is the most used second diagnostic investigation, presented 8% false negatives in the periods between 1985 and 2000 (5% in 2000), and it was inconclusive in 6% (7% in 2000). In this questionnaire, data reported in patient files were considered, with no review of the analysis slides, but the percentage of false negatives is considered high.

Biopsy results (excluding the frozen section investigation) showed 3% of false negatives, 78% of invasive carcinomas and 16% of carcinomas *in situ*.

The assessment of the tumour size and the axillary situation, in accordance with the TNM system, and in the period comprised between 1985 and 2000 revealed 19% of tumours not more than 1 cm, 23% of tumours more than 1 but not more than 2 cm and 46% of tumours more than 2 but not more than 5 cm. Situations without information represented only 2%. The axillas were considered negative (N0) in 73% of the patients, with no information in approximately 3%. Considering all of the 477 patients diagnosed and treated in the more differentiated hospitals (Group A) and the 388 in the other hospitals (Group B), no significant difference regarding the tumour size (T), or axillary situation (N) was found, although there is a larger trend for negative axillas in Group A hospitals (75%) than in Group B hospitals (70%).

When the time evolution of the tumour size (T) in the period from 1985 until 2000 is analysed, a significant decrease of tumours more than 2 cm but not more than 5 cm is evident, from 70% in 1985 to about 40% in 2000. On the other hand, there was an increase of all tumours not more than 2 cm. However, when this evolution was analysed in the period between 1995 and 2000, and both hospital groups were compared, it was found that their behaviour was totally opposite. In the more differentiated hospitals (Group A) the diagnosis of tumours not more than 2 cm is increasingly more frequent (approximately 65% in 2000), whereas the other hospitals (Group B) show lower percentages in the two considered periods (around 43% in 2000). This fact also contributes to an explanation of the different behaviours in the sequence of diagnostic methods.

The 1991 a national survey conducted in the USA, and which considered only carcinomas *in situ* and Stage I and II tumours, reported that the percentage of *in situ* and Stage I carcinomas diagnosed in 1983 was 4.8% and 36.3%, respectively; in 1990, these percentages rose to 9.6% for carcinoma *in situ* and 45.5% for Stage I carcinoma [3]. In Portugal in 1985, carcinomas *in situ* represented less than 1% and tumours not more than 2 cm 28%; in 2000, carcinomas *in situ* represented 9% and tumours not more than 2 cm 42.2%.

It can be concluded that despite the favourable evolution of early diagnosis of breast cancer in Portugal, it must significantly improve through the extension of screening to the entire country, and not only to certain regions or privileged areas of influence of the more differentiated hospitals (Group A), which are located in the developed urban areas.

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