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BENIGN BREAST DISEASES IN BREAST CANCER SCREENING PROGRAMS IN ITALY (2000-2001)

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***Aims and background*: Screening mammography has been shown to be effective in reducing breast cancer mortality in several randomized clinical trials. One major side effect of screening is the diagnosis of benign breast disease (BBD), which is considered as a nonprogressive lesion, except for a small percentage of lesions considered at high risk. We present data referring to service screening programs active in Italy in 2000 and 2001 and participating in the national survey carried out by the Italian Group for Mammography Screening (GISMa).**

***Methods*: To all centers participating in the GISMa National Survey, we submitted a questionnaire regarding the service screening protocol and main indicators of performance of the local program in the years 2000 and 2001.**

***Results:* A total of 657 detected BBD cases, registered by 23 Italian breast cancer screening centers in women 50 to 69 years of age, are included in this study. The BBD detection rate was 2.5 per 1000 at the first screening test and 1.05 per 1000 at repeated tests. The benign/malignant ratio was 0.34 at the first and 0.22 at the repeated test.**

***Conclusions:* Detection of BBD occurred frequently in breast screening programs, and prognostic implications should be further investigated. Women should be individually informed at screening, and with greater detail at the moment of the recall for assessment, of the implications of BBD detection and receive the necessary, also psychological, counseling to avoid the possible harm related to breast cancer screening.**

Key words: benign breast disease, breast cancer screening.

Introduction

Screening mammography has been shown effective in reducing breast cancer mortality in several randomized clinical trials. Service screening is today active at national and regional levels in many countries in Europe, and there is wide consent that the new challenge is evaluation of the impact of screening mammography on the target population[1,2]. However, breast cancer screening has side effects and possibly harm for the population accepting the invitation to periodically perform the mammographic test.

In scientific literature, the greater attention about screening impact and performance has been addressed to the false-positive results, ie women who were recalled to be assessed after the screening mammogram. High rates of recall are certainly a cause of distress and anxiety for women, and the reasons and predictive values should be monitored[3,4]. Reports from ongoing programs in Italy have shown that the standards suggested by the European Guidelines[5] are achievable in most screening programs[6-8]. However, one of the relevant side effects of screening is the diagnosis of benign breast disease (BBD), which is considered as a nonprogressive lesion, except for a small percentage of lesions considered at high risk.

Protocols in use in service screening state women with a diagnosis of BBD should be counseled to return for repeated screening test at the subsequent screening round. BBDs at high risk of developing breast cancer are pathologically defined[9], but there is still little knowledge about the best follow-up regimen or effective chemoprevention treatment to be implemented in

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this subgroup of lesions. In most cases, BBD is a non-progressive lesion and should not determine changes in the individual follow-up or in the degree of anxiety of the woman.

We present herein data referring to service screening programs active in Italy in 2000 and 2001 and participating in the national survey carried on by the Italian Group for Mammography Screening (GISMa).

Materials and methods

We submitted to all centers participating to the GISMa national survey a questionnaire about the service screening protocol and main indicators of performance of the local program in the years 2000 and 2001. Detailed clinical and histopathologic information was collected on each BBD and its characteristics (histologic type, size, type of intervention). For each case of BBD, data about the mammographic test, examinations performed at recall and intervention procedures were collected. A review of pathologic slides was not performed, and the actual classification of each pathologist was used. Many of the pathologists who participated with their BBD case series are also involved in the GISMa group and cooperate in common research projects. The questionnaire sent for the survey asked the pathologist to classify the lesion according to a list including the common definitions of BBD. According to Fitzgibbons *et al.*[9], we define atypical ductal and lobular hyperplasia as at moderately increased risk (4.0-5.0 times).

BBD detection rates were calculated separately for the prevalent and incident screening tests.

Results

A total of 657 screen-detected BBD cases, registered by 23 Italian breast cancer screening centers in women aged 50 to 69 years, is included in the present study. In the same female population (n = 395,887), 2325 malignant tumors were detected.

The BBD detection rate was 2.5 per 1000 at the first screening test and 1.05 per 1000 at repeated tests. The benign/malignant ratio was 0.34 at the first and 0.22 at the repeated test (Table 1).

The diagnostic work-up followed the usual protocol in most of the cases, with a further mammographic examination performed in 70% of the cases, ultrasonography in 76%, and clinical examination in 80%. Clinical examination was reported as negative in 75%. Cytopathology was performed in 64% of the women, and 33.3% it was inadequate.

Table 1 - Number of screened women and benign breast disease detection rates at prevalent and repeated screening in the GISMa 200-2001 survey

	Prevalence test	Incidence test
Screened women	165282	230605
BBD lesions	414	243
Malignant cases	1221	1104
Detection rate for BBD	2,50	1,05
Detection rate for malignant lesions	7,39	7,79
Benign/Malignant ratio	0,34	0,22

Table 2 - Percentage of benign breast diseases by pathologic report of the lesion. Results from the 2000-2001 GISMa survey

Pathologic report	Prevalence screening	Incidence screening
Fibroadenomas (FA)	21.3	13.6
Cysts	2.4	1.2
Fibrocystic changes	14.3	25.1
Complex fibrocystic changes	16,4	18,9
Mild/Florid hyperplasia (without atypia)	2.4	2.9
Sclerosing adenosis	13.5	11.5
Apocrine atypical metaplasia§	1.9	2.5
Papillomas and papillomatosis	6.5	6.6
Radial Scar§	3.1	1.2
Other complex sclerosing lesions	8.2	7.9
Phylloid tumor	1.0	0.8
Atypical lobular hyperplasia (ALH)	1,9	3.3
Atypical ductal hyperplasia (ADH)	6.3	4,5
ALH + ADH	0.7	0.0

§These lesions are histological findings reported to increase the relative risk of breast cancer, but sufficient data are not yet available.

BBD detected was larger than 2 cm in diameter in 40.3% of the cases at the first screening and in 25.3% at the repeated test.

The type of intervention performed was usually a lumpectomy (60.4%) or a wide exeresis (15.4%); 12.5% underwent a quadrantectomy and 8.8% only a biopsy. There was no information on the intervention for 2.9%.

Table 2 shows BBD lesions according to histopathologic type. The pathologic report was undefined in 6.2% (n = 41).

In the year 2001, data were separately collected, investigating also BBD cases detected by core biopsy, a technique still rarely used in that year (n = 58). Of them, 8 cases were considered "high-risk BBD". All are included in the tables.

Discussion

The results of this BBD survey are part of the annual national survey of the Italian Mammographic Screening programs, and main indicators of performance of the breast cancer screening programs participating in the study were all, including the benign/malignant ratio, within the standards suggested by the European Guidelines[5] for breast cancer screening. That means that service screening is working as expected. This outcome is certainly reassuring and, in this context, the values of the benign/malignant ratio achieved are in good agreement with the expected values, even considering values reported in some international comparisons[6].

The rates of screen-detected BBD detected at open biopsy will not be the correct indicator of screening quality in the future, as recently suggested by Maxwell *et al.*[10] The number of core biopsies with a histologic

benign report was small in our series, but it is growing and should be considered separately in future evaluations. The widespread use of the technique, still practiced in few Italian centers in the year 2001, will change and perhaps increase the BBD rate while reducing the number of open biopsies.

The recent biopsy rate estimate reported in the study of Maxwell *et al*.[10] was 1.63 per 1000 women screened, comparable to the rate at the repeated test observed in the present study. Maxwell *et al*.[10] suggested a quality policy for screening aimed to reduce the rates of low-risk (B2, in their classification) lesions and increase the detection of high-risk BBD. However, the association between radiologic images and high-risk lesions is difficult. A policy addressed to increase the rates of high-risk lesions needs further investigation.

There are several major implications in these results and issues still not perceived by professionals involved in screening programs. First of all, the radiologic pattern and pathologic classification of moderately increased risk *versus* the no or slightly increased risk lesions should be better defined in the European Guidelines[5] and, on the basis of cooperative research, be used to suggest indicators of performance for screening programs more specific than those available today. Little work has been done in a screening setting to compare the pathologic findings between centers and to define the mammographic patterns of interest and prognostic implications.

Service screening should take the responsibility of the BBD diagnosis, treatment and follow-up, offering adequate guarantee of effective follow-up to the attending woman.

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